



*National Institute for
Health and Clinical Excellence*

The guidelines manual

April 2006

The guidelines manual

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 1.3.

The document replaces 'Guideline development methods: information for national collaborating centres and guideline developers' (last updated March 2005) and 'The guideline development process – an overview for stakeholders, the public and the NHS' (published February 2004; N0472).

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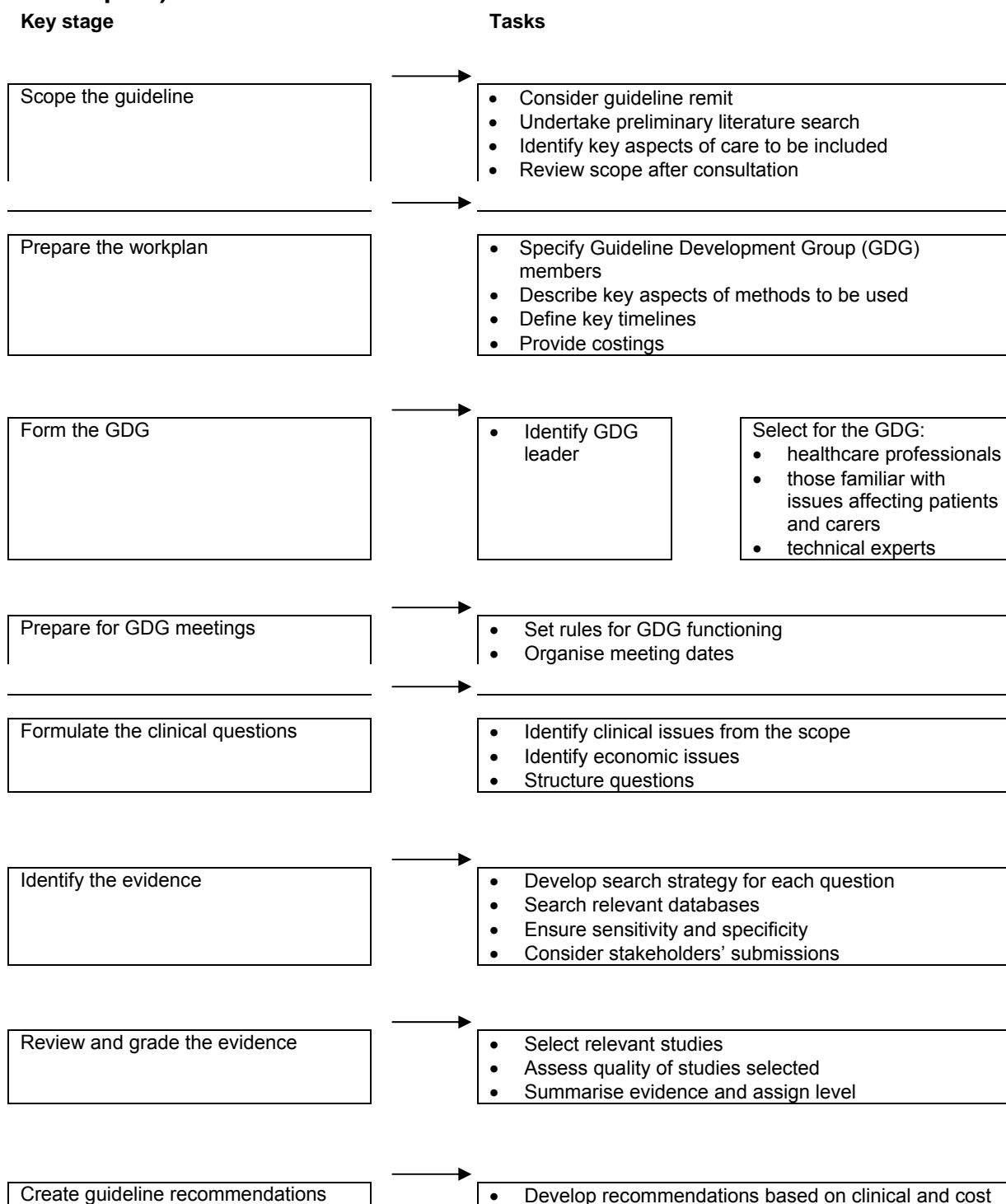
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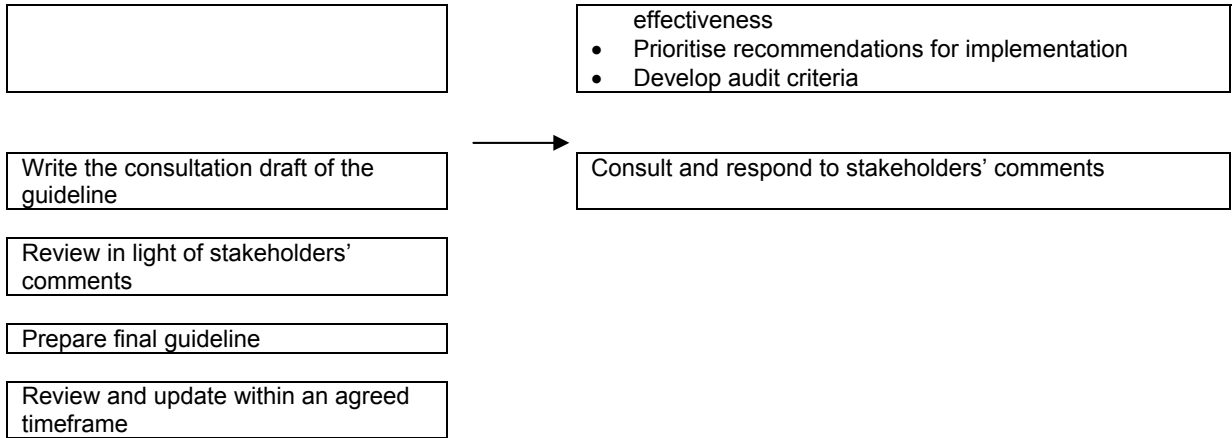
Overview of the guideline development process

The information in this document has been prepared primarily for those involved in the development of guidelines for NICE. Appendix L contains a summary of the guideline development process for stakeholders, the public and the NHS. This will be printed and published separately during 2006.

Figure 1 A summary of key stages of NICE guideline development (for developers)



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Changes from the March 2005 manual

Chapter	Change	Page numbers affected
1	1.1 Sentence on public health guidance. Sentence on social value judgements report.	
	1.1.1 Sentence about purpose of guidelines.	
	1.1.2 Section on service guidance.	
2	2.1 Change to details of where notes on completing templates are available	
3	3.1.1. sentence about confidentiality in second para	
	3.1.3 Section on economic considerations.	
	3.1.8 12-18 months as development period.	
	3.1.10 Section on development period	
	3.2 The economic plan.	
6	6.1 NCCs not expected to search grey literature.	
	Box 6.1 Search for economic papers – including details of databases to be searched	
	6.2 Whole section changed – new process for stakeholder submission of evidence	
7	7.2 Sentence about class of recommendations deleted	
	7.2.1 Sentence about classification of recommendations deleted	
	7.2.2 new section on information from stakeholders replaces section on unpublished data	
	7.2.3.1 Sentence about grading recommendations deleted.	
	7.2.3.2 Sentence about grading recommendations deleted.	
	7.3.1 Info about data synthesis and sensitivity analysis deleted from end of 1st para.	
	7.3.2 New section on conducting a meta-analysis	
	Further reading New ref added 'Analysing and presenting results.'	
8	Title: incorporating health economics and assessing resource impact	
	8.1 Sentence about health economist as core member of GDG. Bullet points about role of health economist.	

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	8.1.1 Advising on economic issues – 1st para re HE's role in GDG understanding economics consequences. 3rd para on other economic concepts.	
	8.1.2 Section on reviewing information.	
	8.1.3 Bullet: the most important topics are selected for economic analysis	
	8.1.3.1 Section: prioritising topics for further economic analysis.	
	8.2 1st para on economic evaluation as part of modelling approach. End of 2nd para, alternatives to QALYs. 3rd para, trade offs.	
	8.2.1 1st bullet specification of question for economic analysis	
	8.3 3rd para value for money end of 4th para, social value judgements and economic assessment of questions not prioritised for it.	
	Further reading 'Economics notes series', 'Economic Evaluation in Health Care: merging theory with practice', 'How to develop cost-conscious guidelines'	
11	intro – deletion of info on classifying recommendations	
	11.1 Addition of info in economic evidence and making research recommendations.	
	table 11.1 Specifying 'clinical' evidence in rows 1b, 2 & 3. Row 4 re cost effectiveness.	
	11.2 2nd sentence re importance of recommendation wording. 4th bullet re recommendation classes deleted. 7th bullet info on enforceable legislation added. 8th bullet added re patient involvement 9th bullet added re 'negative' recs	
	11.2.1 2nd para re cross referencing to other recs	
	11.2.4 Section on classifying recs deleted.	
	11.2.4 (new number) 1st bullet re use of generic drug name/not naming manufacturer.	
	11.2.5 2nd para re use of tables for recs.	
	Box 11.2 added – examples of published recs	
	11.3 3rd sentence – deciding on key priorities	
	Table 11.5 deletion of GRP from intro.	

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12	Title addition of 'clinical'.	
	2nd para addition of the Clinical Accountability, Service Planning and Evaluation.	
13	3rd sentence addition of GDG.	
	13.1.1.4 alternatives to algorithms added.	
	13.3 last bullet addition of info re explanations. 2nd para info on use background material added. 3rd para addition of info about standard text on patient centred care. 4th para change to how editors comment	
	13.5 (and elsewhere) 'Information for the public' changed to 'information for patients and carers'. 2nd para summary is 'primarily for patients'. 4th para addition of info about adding links to non-NHS organisations.	
14	14.1.1 2nd para change to treatment of comments from individuals.	
	14.2 the consultation process: change to process.	
	14.2.2 new section: expert review.	
	14.2.3.1 change to sign off process for full version.	
	14.2.3.3 Info for patients and carers.	
	14.2.3.4 QRG.	
	14.3 2nd & 3rd paras.	
	14.3.1 GDG reviewer – 1st para and last para.	
	14.3.2 sign-off and typesetting.	
15	Intro changes to info about updating.	
	15.2.2 Addition of para after bullet list re one member of GDG being responsible for keeping track of changes in evidence.	
	15.3 new section triggers for updating.	
	15.4 new section process for updates.	
	'Further reading' addition of 'Validity of the Agency for Healthcare Research and Quality clinical practice guidelines: how quickly do guidelines become outdated?'. 'Further reading' addition of 'Validity of the Agency for Healthcare Research and Quality clinical practice guidelines: how quickly do guidelines become outdated?'.	

1 Introduction

The National Institute for Clinical Excellence (NICE) was established on 1 April 1999. On 1 April 2005 it joined with the Health Development Agency to become the National Institute for Health and Clinical Excellence (also known as NICE). NICE is part of the NHS and its role is to provide independent, authoritative and reliable guidance on promoting good health and preventing and treating ill health for patients and carers, healthcare professionals and the wider public.

1.1 NICE guidance

NICE issues guidance developed through its clinical guidelines, technology appraisals, interventional procedures and public health work programmes. NICE's clinical guidelines cover broad aspects of clinical care and the clinical management of specific conditions. In contrast, its technology appraisals cover the use of individual medicines, medical devices, diagnostic techniques, surgical procedures and other clinical interventions. The interventional procedures programme produces guidance on the safety and efficacy of surgical, endoscopic and endovascular procedures and allied techniques, identifying those safe and efficacious enough for routine use. The public health programme develops guidance on promoting good health and preventing ill health for those working in the NHS, local authorities and the wider public and voluntary sector.

Although the methods for developing the various forms of guidance differ, all guidance follows the principles set out in the report 'Social value judgements: principles for the development of NICE guidance' (2005) available from www.nice.org.uk/svjguidance. The development processes are underpinned by NICE's key principles of basing recommendations on the best available evidence and involving all stakeholders in a transparent and collaborative manner. Stakeholders include national organisations that represent patients and carers, healthcare professionals and companies that have an interest in the guidance under development.

1.1.1 Clinical guidelines

NICE's clinical guidelines are recommendations, based on the best available evidence, for the care of people by healthcare professionals. In general, clinical guidelines have been defined as: 'systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances', although they are also relevant to health service managers.¹

NICE guidelines are expected to promote both clinically effective and cost-effective care. Good clinical guidelines change the process of healthcare,

¹ The definition is from: Committee to Advise the Public Health Service on Clinical Practice Guidelines. Institute of Medicine. Field MJ, Lohr KN, editors (1990) *Clinical practice guidelines: directions for a new program*. Washington, DC: National Academy Press.

ensure more efficient use of healthcare resources and improve outcomes for patients. For example, well-constructed and up-to-date clinical guidelines:

- provide recommendations for the care of patients by healthcare professionals
- can be used to develop standards to assess the clinical practice of healthcare professionals (for example, by the professionals themselves, NHS trusts, health authorities or primary care groups)
- can be used in the education and training of healthcare professionals
- can help patients to make informed decisions, and improve communication between the patient and healthcare professionals.

1.1.2 Service guidance

The NICE guidelines programme sometimes extends beyond clinical practice to cover aspects of service delivery. This service guidance is developed primarily for service commissioners rather than health professionals. It has a focus on the broad configuration and provision of clinical services rather than on details of clinical practice.

Service guidance may be a separate piece of guidance that addresses only interventions that are likely to have implications for the configuration of services (for example, the 'Guidance on cancer services' series). It is developed according to the same methods as clinical guidelines, with minor changes to reflect the focus on service delivery.

In some cases, a clinical guideline may also make recommendations on aspects of service delivery but only if these are included in the remit.

1.2 The aim of this document

This document provides advice on the processes that the guideline developers need to use when producing guidelines. It has been prepared primarily to support organisations developing guidelines commissioned by NICE, but it is likely to be useful and of interest to all guideline developers and therefore to a broader audience. The general aspects of NICE's guideline development process are described in appendix L.

The advice in this document draws on international guideline development methodology, the expertise of NICE's guidelines advisors and the experience of the organisations commissioned to develop NICE guidelines: the national collaborating centres (NCCs). It is based on internationally acceptable criteria of quality, as articulated by the AGREE instrument (www.agreetrust.org).

The structure of this document follows the development of the guideline from its inception through to publication. The guideline topics are commissioned by the Department of Health. This document does not cover in detail how the guideline subject areas are selected. This information can be accessed at www.nice.org.uk/ts.home and is described, in brief, in appendix L.

We welcome comments on the content of this document and suggested topics for inclusion. These should be addressed to: Francoise.Cluzeau@nice.org.uk

1.3 Updating the document

The formal process for updating this manual will begin 3 years after publication. In exceptional circumstances, and only when it is anticipated that there will be significant changes to the process, the interval will be reduced to 2 years.

1.3.1 Interim updates

In some situations, it may be necessary to make small changes to the process before a formal update. 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 the following criteria:

- a fundamental stage in the process is neither added nor removed
- a fundamental methods technique or step is neither added nor removed
- one or more stakeholders will not obviously be disadvantaged
- the efficiency, clarity or fairness of the process or methodology will be improved.

Changes that meet these criteria will be published on the NICE website. The web version of the manual will be updated and a note to this effect will be placed on the opening page. Stakeholders in guidance under development at the time of change will be notified if they are affected by the change. Stakeholders in newly commissioned guidance will be advised to consult the website to familiarise themselves with the updated development process at the start of the project.

2 Scoping the guideline

Guideline topics are selected by the Department of Health, which identifies the main areas to be covered by the guideline in a specific remit (see appendix L). This remit is then translated into the scope document for the guideline (usually known simply as the 'scope'). Preparing the scope is the first stage in developing a guideline, and it determines the shape of future work. The scope is drafted by the NCCs, consulted upon, and signed off by NICE. This chapter describes what the scope is, and how it is drafted and then finalised following consultation with stakeholders.

2.1 Purpose of the scope

The purpose of the scope is to:

- provide an overview of what the guideline will include and exclude
- identify the key aspects of care that must be included
- set the boundaries of the development work and provide a clear framework to enable work to stay within the priorities agreed by NICE and the NCC and the remit from the Department of Health
- inform the development of the clinical questions and search strategy
- inform professionals and the public about the expected content of the guideline
- keep the guideline to a reasonable size to ensure that its development can be carried out within an 18-month period.

The scope provides a framework within which to conduct the development work. Its content briefly describes the background epidemiology relevant to the disease or condition and defines the aspects of care that the guideline will cover in terms of:

- population 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
- interventions and treatments to be included and excluded – for example, diagnostic tests, surgical, medical and psychological treatments and rehabilitation, lifestyle advice.

To assist in preparing the scope, NICE has developed a template that sets out the format and identifies what should be included, and guidance notes for completing the template (these are available from NICE's webboard for NCCs, and the guidelines team). It is not necessary to include clinical questions within the scope, although the scope will later inform the development of the clinical questions by the Guideline Development Group (GDG) (see chapter 5). References are not included in the scope. However, NCCs should keep a detailed record of references used to underpin all sections of the scope, and these should be available on request.

2.2 Drafting the scope

The steps in producing a first draft of the scope for consultation include considering the remit, searching the literature and consulting with experts.

2.2.1 Considering the remit

The remit received by NICE from the Department of Health forms the basis of the scope, and all areas specified by the remit are normally addressed in the scope. There may be circumstances in which NICE requests clarification from the Department of Health on the remit and the allocated topic before initial scoping can begin. This may involve redefining the topic in order to specify the boundaries and the magnitude of the work.

In general, service configuration and delivery issues should not be included in a guideline unless specifically requested in the remit. When service-delivery guidance is required, the development process is fundamentally the same as for clinical guidelines. Key differences in the process relate to the evidence base and the composition of the GDG (see chapters 6 and 4, respectively).

2.2.2 Preliminary search of literature (stage-one search)

A broad preliminary search of the literature is important to obtain an overview of the issues likely to be covered by the guideline – the clinical need and the clinical management of the condition – and to help define key areas. It also informs the NCC of the volume of literature likely to be available in the topic area, and therefore the amount of work required. The focus of this stage-one search is to identify systematic reviews and guidelines relevant to the topic. The main sources to use during this preliminary search are listed in box 2.1, but other sources may be used depending on the guideline topic. More information on searching is given in chapter 6.

Box 2.1 Main sources to use for the stage-one search to identify systematic reviews and guidelines

- Medline
- Cochrane Library
- US Guidelines Clearinghouse
- National Electronic Library of Health (NeLH)
- NICE and health technology assessment (HTA) websites for current and planned guidelines and HTAs
- For service-delivery guidance, Health Management Information Service (HMIS) and Health Management Information Consortium (HMIC)

2.2.3 Consulting with experts and potential GDG members

It is invariably helpful, and therefore should be considered an essential step, to consult with clinical experts in the field and patients when preparing the draft scope. This consultation ensures that all relevant areas have been considered and enables the NCC to define the expertise and experience required within the GDG. Some NCCs consider GDG membership at this stage and involve potential members in drafting the scope and starting to formulate the clinical questions that the guideline has to address (GDG membership is covered in chapter 4).

2.3 The consultation process

The draft scope is checked by one of NICE's editors prior to consultation and may be modified by NICE in consultation with the NCC. It is then subject to consultation with stakeholders over a 4-week period. During the consultation period, the scope is posted on the NICE website (www.nice.org.uk).

Comments are invited from stakeholder organisations and guideline review panels (GRPs).

2.3.1 Stakeholder organisations

Stakeholder organisations representing healthcare professionals, the NHS, patients and carers, and companies with an interest in a particular topic can register interest in a particular guideline. During the consultation period a meeting is organised for registered stakeholders, including patient and carer organisations, to provide details about the scope and the guideline development timetable. The NCC, together with staff from NICE, outlines the guideline development process, the nature of stakeholder input into the guideline, and the processes of recruitment to the GDG and evidence submission. This is followed by a discussion around the content of the scope. This meeting does not replace the formal process for submitting comments in writing.

2.3.2 Guideline review panels

There are four GRPs, and each guideline will be allocated to an individual panel. The relevant information is presented on the NICE website (www.nice.org.uk). The GRPs play an important role in providing NICE with external validation of its guideline development process. For each guideline, the focus of the panel's work is to review the scope and drafts of the guideline to ensure, in particular, that stakeholders' comments have been addressed appropriately.

During consultation, all GRP members and the GRP Chair receive the draft scope. GRP members submit their individual comments via the Chair to NICE. The GRP Chair collates and summarises these comments into a formal report to NICE. The GRP comments are then circulated to the guideline developers along with the comments from the stakeholders.

The Chair is expected to comment on the following.

- Overall size of the scope, and whether it is reasonable within the timescale for development.
- Potential specific methodological issues that may arise.
- Whether the scope falls within the remit from the Department of Health.
- Clarity of areas detailed in the scope.
- Whether the scope is limited to the NHS.
- Any other concerns or queries about the proposed limits to the scope.

2.4 Finalising the scope after consultation

2.4.1 Dealing with stakeholders' comments

The NCC and NICE review the scope in the light of comments received, in consultation with each other. Stakeholders may ask that additional aspects of care be included in the guideline, which could make the development of the guideline unmanageable within the time permitted. 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. Suggestions clearly outside the original remit should not be included. If the NCC 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 stakeholders' comments and the action taken by the NCC and NICE in response to each comment must be clearly documented in a table, which will be published on the NICE website when the scope is finalised. The process for responding to stakeholders' comments should follow the principles described in section 14.1.

2.4.2 Signing off the scope

After consultation, GRP members and the Chair review the revised scope and consider whether stakeholders' comments have been appropriately and adequately addressed by the developers. The GRP Chair then prepares a report. Subject to any amendments requested in the Chair's report, NICE signs off the scope.

Once the scope has been signed off, the GDG should not make changes without prior consultation with NICE, and this should be done only in exceptional circumstances. The finalised scope is posted on NICE's website.

3 Preparing the workplan

A workplan is prepared by the NCC to set out the guideline development process for each guideline. Its purpose is to specify methods, timelines and costings. It is an internal document that becomes a formal agreement between the NCC and NICE and is the reference from which the progress of the work can be assessed. It is expected that the methods described in the workplan will reflect those stated in this document unless there are specific reasons for them to differ. This chapter describes the structure of the workplan and the stages in its development.

3.1 *Structure of the workplan*

Key components of the workplan include information on membership of the GDG, identification of evidence, approach to assessing clinical and cost effectiveness, stakeholder involvement, writing of the guideline, review processes, project management, costing and timelines. To assist in preparing the workplan, NICE has developed a template and a set of instructions for using it, setting out the format and components that should be included (the template and notes are available from NICE's Guidelines webboard for NCCs). Clinical questions should not be in the workplan as it is important not to pre-empt the clinical questions that the GDG will agree. It is reasonable, however, to include a summary of areas that the clinical questions might address.

3.1.1 Membership of the guideline development group

The workplan should include the range of roles needed in the GDG. Names of proposed members are not required at this stage. Recruiting members can take 3–4 months, so work on this needs to begin early and should be discussed with NICE before formal submission of the workplan (see chapter 4). Details should be provided about how the proposed constituency of the GDG relates to the subject area of the guideline and to stakeholders.

There should be some explanation of how the members will be selected, a description of the size of the group and comment on the implications for group functioning, and descriptions on how members' interests will be declared, how conflicts of interest will be identified and recorded, and how confidentiality of draft documents will be ensured (see appendix A). There should also be a description of how the educational needs of group members will be met and how the meetings will be run to achieve effective group functioning, as well as practical considerations about the venue and timetable of these meetings. It is important to specify the decision-making methods that will be used, and this should include a detailed description of any formal consensus methods that are likely to be used in the development process. Box 3.1 presents an example of membership of a GDG.

Box 3.1 The membership proposed for the GDG for the development of the guideline 'Antenatal care: routine care for the healthy pregnant woman' (NCC for Women and Children's Health [NCC WCH], August 2002).

- Two midwives
- Two obstetricians
- Two general practitioners
- One paediatrician
- One radiographer
- One representative of the confidential enquiries into maternal deaths
- Two consumer representatives
- Four methodologists (information scientist, systematic reviewer, health economist, Director NCC-WCH)

3.1.2 Identification of evidence

The workplan should describe any existing guidelines, health technology assessment (HTA) reviews from organisations other than NICE, and other NICE guidance that will inform the guideline, how evidence will be identified and synthesised, and how areas without evidence will be handled.

A preliminary search of the literature will be required to inform some of these areas.

3.1.2.1 Existing guidelines, HTA reviews and other NICE guidance

Information identified during the stage-one search conducted during scoping should be listed in the workplan (see chapter 2). Existing guidelines from NICE and other organisations, HTA reviews, and NICE technology appraisals, interventional procedures and public health guidance should be listed, with details of publication dates. (Chapter 10 gives information on linking NICE guidelines to the other NICE guidance programmes.)

3.1.2.2 Evidence identification and synthesis

The workplan should include a description of the databases that will be searched, and the time period from which evidence will be sourced and the reasoning for this selection. It should list the likely search strategies to be used and note whether foreign language journals will be included. However, in many clinical areas the evidence base is not influenced by the inclusion of foreign language journals. Therefore, in most cases, foreign papers need not be translated.

Ideally, the volume of papers that will be identified in the search should be estimated. How the final set of papers will be decided on and how long the evidence-synthesis process will take should also be determined. To do this, the NCC should conduct a preliminary stage-two search (see chapter 6). It is also necessary to indicate whether searches will be repeated during the development of the guideline recommendations.

The workplan should also describe:

- how the evidence will be synthesised to produce a summary

- if meta-analysis is to be used, the areas of the guideline to which it will be applied
- how the evidence will be displayed (narrative summary, evidence tables, meta-analysis and trial tables)
- the levels of evidence (as described in chapter 7).

3.1.2.3 Areas lacking evidence

The workplan should describe how areas without any evidence will be dealt with (see chapter 9). This section should also describe the steps that will be taken to address the availability of evidence at subsequent review (for example, by highlighting the need for further research in a particular area in the research recommendations section of the guideline; see section 11.4).

3.1.3 Economic considerations

The workplan should outline how economic assessments of alternative patterns of care that will be evaluated by the guideline will be integrated within the guideline. A more detailed economic plan should be prepared alongside the workplan (see section 3.2).

3.1.4 Key priorities for implementation

From the recommendations the GDG will identify between five and ten key priorities for implementation; these are the recommendations that are most likely to have a high impact on patients' outcomes and on reducing variations in clinical management (see section 11.3). The workplan should describe how these key priorities will be selected.

3.1.5 Stakeholder involvement

The workplan should include a brief description of any additional steps that will be taken to gather stakeholders' views (patient/carers and professionals); for example, seeking comments from expert peer reviewers. Stakeholders must also be contacted for evidence submission (see section 6.2).

3.1.6 Writing the guideline

The details of the person or people who will be responsible for writing the versions of the guideline should be included. For example, this may be a systematic reviewer or other members of the GDG if this has been explicitly agreed, or a professional writer.

3.1.7 Review processes

This section should indicate any peer-review stages (in addition to the stakeholder consultations) that will form part of the process – for example, comments or advice from experts, researchers or patient/carers (see section 14.2.2).

3.1.8 Project management

Any steering groups or project-management groups that will be used to support the guideline development process should be described. The document should include a Gantt chart of the project that includes staff

working on the project, with details of the time period and estimated proportion of time that they will work on the project, and a timetable of work.

The timetable of the guideline process should contain a detailed estimate of key dates, including a development period running usually between 12 and 18 months. This timetable should give GDG meeting dates, deadlines for submission of evidence, and estimates of time for literature searches and reviews.

3.1.9 Costs

The maximum variable costs for the project (broken down by financial year) should be estimated in the workplan. These should be costs over and above those allocated in the infrastructure costs for the NCC. The variable costs primarily include: travel expenses for GDG members, costs of meetings and costs of paper retrieval. Advice on appropriate levels of funding is available from NICE.

3.1.10 Development time

The key dates for delivery of the guideline should be estimated after careful consideration in the light of the anticipated workload, because the date of the delivery of the draft will determine the timing of the consultation. These dates are published on the NICE website, and should not be changed without consultation with NICE. The time from first GDG meeting to submission of the draft of the guideline is usually between 12 and 18 months. The workplan template gives a standard table identifying the key dates.

3.2 *The economic plan*

Alongside the general workplan, the NCC prepares an economic plan. This document identifies the initial priorities for further economic analysis and the proposed methods for addressing these questions (see section 8.1.3.1). This document is prepared by the guideline economist in consultation with the rest of the NCC technical team and GDG, and signed off by NICE usually by 3 months after the first GDG. Over the course of guideline development, this economic plan is likely to change. For example, as the clinical evidence is reviewed it may become apparent that further evaluation is not necessary for some topics that were initially prioritised for economic analysis. Any such changes in the economic plan should be agreed between the NCC and NICE.

4 Forming and running a guideline development group

Convening an effective guideline development group (GDG) is one of the most important stages in producing a guideline. The GDG agrees the clinical questions, considers the evidence and develops the recommendations. Membership of the GDG therefore needs to be multidisciplinary, comprising clinicians (both content-area specialists and generalists), patients and/or carers and technical experts. The GDG's exact composition needs to be tailored to the topic covered by the guideline. It should reflect the range of stakeholders or groups whose professional activities or care will be covered by the guidelines and should include at least two members with experience or knowledge of patient/carer issues.

In addition to the GDG members, individuals with relevant expertise may be co-opted for discussions. Manufacturers of pharmaceutical products or medical devices have input into the guideline development process through the GRPs and as stakeholders.

This chapter covers the core elements of forming and running a GDG, including the identification of members and the Chair, and aspects of running the group. Further information on nominating GDG members is given in appendix L.

4.1 Forming the GDG

It is essential to form the GDG as early in the process as possible, so that members are potentially able to comment on the draft scope before it is sent to stakeholders for consultation (see chapter 2). Selecting the correct constituency for the GDG is described in section 3.1.1. This section details the roles of the different types of GDG members and how they should be identified and selected.

A workable size for the GDG is 10 to 12 people, plus the technical team. This balances the opportunity for individuals to contribute effectively with the need for a broad range of experience and knowledge. The GDG should reflect an appropriate balance of ethnicity, depending on the guideline topic. Ideally, GDG members should be drawn from different parts of England and Wales (because the guideline applies to the NHS in England and Wales), but this will be influenced by the available expertise. Professional members may come from other parts of the UK if they cannot be recruited from England and Wales. All GDG members are expected to attend all meetings and to have a commitment to guideline development. New members should not usually be added to the group once development meetings are under way, because this disturbs the group process. In exceptional circumstances, if additional expertise is needed or if a member needs to be replaced, the NCC should discuss and agree this with NICE (see section 4.1.2.1).

There are four key constituents of the GDG:

- the Chair

4 Forming and running a guideline development group

The guidelines manual

- professional members
- patient/carer members
- technical experts.

The following sections outline the roles of the members and describe how they should be selected.

4.1.1 The GDG Chair

To work well, a GDG needs an effective Chair and it is essential to identify this person as soon as the NCC starts work on the scope. The Chair guides the group in terms of task (developing the guideline) and process (how the group works). The Chair also facilitates the interpersonal aspects of the group processes, so that the group works in a spirit of collaboration, with a balanced contribution from all members (see box 4.1).

Box 4.1 Key roles and functions of the GDG Chair

The Chair needs relevant background knowledge, including:

- in-depth knowledge or appreciation of the scope of the guideline and the topics to be covered during GDG meetings
- good knowledge of the skills mix within the group.

To facilitate the **group process**, the Chair:

- sets up the rules for GDG functioning, based on rules developed by the NCC if appropriate
- assists with the planning of the GDG meetings
- ensures that the group has relevant information and required resources
- establishes a climate of trust and mutual respect between 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:

- has a directive role in steering the discussions according to the agenda
- keeps the group discussion unified and avoids disruption by sub-conversations and dominance by some members
- encourages constructive debate, without forcing agreement
- winds up repetitive debate
- summarises the main points and key decisions from the debate.

4.1.1.1 *Selecting the Chair*

The Chair may be suggested by informal networks, be nominated, or selected through open advertisement. It is important that potential Chairs are briefed carefully beforehand on the importance of the role, the time commitment and the need for confidentiality. NCCs should consider the Chair's conflicts of interests before making a decision on their appointment, and ensure that any changes in their interests during their time as Chair are reported.

The Chair should be selected as someone who is neutral and who has enough expertise in coordinating groups of healthcare professionals and patients/carers so that the appointment is acceptable to all. The Chair is usually expected to have a good understanding of the guideline topic and is therefore likely to be a clinician. On occasion, however, he or she may be someone with facilitative skills who is not an expert in the topic area. Although clinical knowledge is not essential, it is usually advantageous.

4.1.2 Professional members

Professional members should represent the perspective(s) of the healthcare workers involved in the care of patients affected by the guideline topic. They are on the group as clinicians, and detailed research expertise is not essential, although an understanding of evidence-based medicine is desirable.

The roles and responsibilities of the professional members of the GDG are shown in box 4.2.

Box 4.2 Key roles of professional GDG members

GDG members from the healthcare professions are expected to:

- contribute constructively to meetings and have good communication and team-working skills; this should include commitment to the needs of patients/carers
- use background knowledge and experience of the management of, and services for, the topic to provide guidance to the technical members carrying out systematic reviews and economic analyses
- read all relevant documentation and make constructive comments and proposals at (and between) GDG meetings
- use their own informal networks to inform their contribution
- with other members of the group, formulate recommendations based on the evidence reviews
- advise on how to identify best practice in areas where research evidence is absent, weak or equivocal.

They are not expected to:

- review the evidence
- search for literature
- write the guideline
- represent the views of their nominating organisation.

4.1.2.1 Selecting professional members

There are two broad approaches to identifying healthcare professionals for the GDG.

- Writing to key stakeholder organisations for nominations. It is important to be specific about the expertise that is required – for example, clinical experience, guidelines knowledge, ability to work as part of a team, ability to deliver to deadlines – and how much time will be required. Ideally, two

or three nominations should be requested so the most appropriate person for the group can be selected.

- Following up an individual expression of interest. If a healthcare professional has shown interest in joining the GDG or has been suggested through an informal network, his or her professional organisation or College should be approached for approval, or asked whether it would like to nominate the person formally. However, approval of the relevant organisation or college is not a prerequisite for membership of a GDG.

It is generally wise to interview potential members before making a final selection, to be explicit about the reasons a choice has been made, and to provide effective feedback, especially if nominations for one position have come from more than one organisation. Potential members should be asked to declare interests **before** a firm offer is made (see section 4.2). GDG members should ensure that they make sufficient time to be involved in the development and should make a formal commitment to attend every GDG meeting. If a member persistently fails to attend meetings, the NCC should consider replacing him or her.

4.1.3 Patient/carer members

There should be at least two members with experience and/or knowledge of patient/carer issues on each GDG (the 'patient/carer members'). This is to ensure that patient and carer issues, as well as healthcare professionals' views, inform the guideline development process. In general, the patient/carer members will have direct experience of the condition as a patient or a carer/family member and/or as officers or members of a patient or carer organisation or support group. Healthcare professionals are well represented on GDGs, so patient/carer members usually do not have a healthcare professional background. The patient/carer members have equal status on the GDG. Their specific roles are shown in box 4.3. Patient/carer members should **not** be excluded from specific activities carried out by other members of the group (for example, consensus methods). If there are too many nominations for patient/carer members, nominees who are not included in the GDG may be asked to comment on the draft guideline as expert peer reviewers (see section 14.2.2).

Box 4.3 Key roles of patient/carer members

The key contributions of patient/carer members are to:

- ensure that clinical questions embrace patient as well as professional issues
- identify grey literature (for example, patient surveys) highlighting patient issues that may inform the work of the GDG
- consider the extent to which published evidence has measured and taken into account outcome measures that patients consider important
- identify areas where patient preferences and patient choice may need to be acknowledged in the guideline
- ensure that recommendations address patient issues and concerns
- ensure that the guideline as a whole, and the recommendations specifically, are sensitively worded (for example, treating patients as people not as objects of tests, investigations or treatments).

4.1.3.1 Selecting patient/carer members

NICE's Patient and Public Involvement Programme (PIIP) administers the nomination process for the patient/carer members of the GDG. Patient/carer members may be nominated by a patient or carer organisation or can apply by responding to advertisements posted on the NICE website.

- The PIIP runs a session during the stakeholder meeting (held during the consultation on the scope) to explain the patient/carer nomination process (see chapter 2); patient and carer organisations may wish to attend the stakeholder meeting before they decide to nominate potential members (this meeting is held during the scope consultation phase) and potential nominees should be invited to attend where possible. Appendix L has further details.
- The PIIP contacts all registered patient and carer stakeholder organisations with details about how to nominate potential GDG members. Written information includes a mini 'job description' and a person specification to help people decide whether they have the experience and skills to make an effective contribution to the group.
- The PIIP also offers advice and support on the application process, both to nominating organisations (for example, organisations unable to attend the stakeholder meeting) and to individual applicants.
- All potential patient/carer members are asked to complete an application form, with details of their nominating organisation (if applicable), showing how their skills and experience meet the specified requirements.
- The PIIP sends all completed applications to the NCC, and the NCC selects the patient/carer GDG members from the applications received according to the job description and person specification. The NCC makes the final selection by speaking to potential applicants either by telephone or in person.
- If there are too many nominations for patient/carer members, nominees who are not included in the GDG may be asked to comment on the draft as expert reviewers (see section 14.2.2).

4.1.4 Technical experts

In addition to stakeholder representatives, members with technical experience and expertise are vital in the GDG. They usually include a lead systematic reviewer, an information specialist, a health economist and a project manager, and form the core team working on the guideline within the NCC. For some guideline topics, it may be important to include in the GDG an epidemiologist with knowledge in the area.

NCC staff acting as members of a GDG should be allowed to vote. To avoid the NCC having too much influence in a vote, no more than three NCC members should be allowed to vote on any one issue. For each vote, the NCC should decide which of its staff are most appropriate to vote; these would normally be NCC staff with particular knowledge of the issue under discussion.

4.1.4.1 Systematic reviewer

The role of the systematic reviewer is to provide summarised tables of the evidence to inform other GDG members. The role may include: setting evidence-based questions; abstracting; critical/quality appraisal of evidence using a validated system; distillation of evidence into tables; synthesis of evidence into statements; and maintenance of comprehensive audit trails. The systematic reviewer is a core member of the technical team and, as such, is crucial to the dissemination, presentation and debate of the evidence within the GDG.

4.1.4.2 Information specialist

The information specialist identifies relevant literature to answer the clinical questions developed by the GDG (see chapter 5). The role may include: setting evidence-based questions; designing and testing population and study filters; leading the discussion of the questions and their parameters within the GDG; identifying relevant databases to search; maintaining audit trails including search strategies and rationales and search results; and keeping track of papers in the document-delivery process.

4.1.4.3 Health economist

The role of the health economist is to inform the GDG about potential economic issues and to perform additional economic analyses. This is defined in more detail in chapter 8.

4.1.4.4 Project manager

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

4.1.5 GDG membership for service guidance

When service guidance is being developed, we recommend that additional members of the GDG are appointed 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 interest in the topic.

4.2 Identifying interests and conflict of interest

4.2.1 Declaring interests

Potential members of the GDG, and any individuals having direct input into the guideline (including expert peer reviewers), should provide a formal written declaration of personal interests. Appendix A1 contains NICE's standard policy for declaring interests, and a form to use for this. Potential members of the GDG should complete this form before any decision is made about their involvement.

Any changes to a group member's conflicts of interests should also be recorded at the start of each GDG meeting. The Chair, in discussion with the NCC Director, should determine whether these interests are significant.

If a member of the GDG has a possible conflict of interest with only a limited part of the guideline development or recommendations, that member may continue to be involved in the overall process but should withdraw from involvement in the area of possible conflict. This action should be documented and be open to external review. If it is considered that an interest could impair the person's objectivity throughout the development of a guideline, he or she should not be invited to join the group.

4.2.2 Code of conduct and confidentiality

NICE has developed a code of conduct for GDG members and external members, which sets out the responsibilities of NICE and the GDG, and the principles of transparency and confidentiality (see appendix A2). This includes a confidentiality agreement form. The NCC should require all those who have sight of documents, or are party to discussions, relating to a guideline before public consultation to sign the form before becoming involved. NCCs should also ensure that all GDG members have a copy of NICE's report on social value judgements before they are recruited on the GDG. 'Social value judgements: principles for the development of NICE guidance' (December 2005; available from www.nice.org.uk/svjguidance).

4.2.3 Dealing with enquiries on GDG work

If GDG members are asked to provide information about the work of the GDG by external parties other than their stakeholder or professional organisation (for example, if they have been contacted by a journalist) they should contact NICE first (see appendix A3). They should declare this at the next GDG meeting and inform the NCC director.

4.3 Identifying and meeting training needs

4.3.1 Chair

The person selected to perform this crucial role may need support and training to ensure he or she has in-depth knowledge of the NICE guideline development process and an understanding of the group processes involved in carrying out the role effectively. The NCC should identify and meet any training needs soon after the Chair has been appointed.

Training should focus on two key roles.

- The task. The Chair must be clear about the status of the scope, the need to formulate clinical questions, and the schedule of topics for each meeting. The Chair must keep the group to task, and ensure recommendations are developed on time.
- The process. Unless the Chair is an experienced facilitator, he or she may need training in this. Particular attention may need to be given to ensuring the patient/carers' views are given appropriate weight by the group. The NCC may wish to consider a 'buddying' approach in which a new GDG Chair may learn from someone more experienced.

4.3.2 Professional members

To work effectively, GDG members may need technical training and support in areas of guideline development. The Chair and the NCC should be aware of the type of training individual GDG members may need at the beginning of the guideline development process so that they can provide the necessary support. Provision of training for GDG members and the Chair should be provided by the NCC in consultation with NICE.

4.3.3 Patient/carers members

The PPIP offers dedicated training to patient and carer members on all NICE GDGs and also gives a short presentation to all GDG members, at the first meeting, on the role of patient/carers members.

4.4 *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.

4.4.1 General principles

Because the GDG is multidisciplinary, its members will bring with them different beliefs, values and experience. All these perspectives should be listened to and each member should have an equal voice in the process. It is important to check that the terminology members use is understood by all and clarified when needed. The Chair should ensure 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. The GDG leader needs to allow sufficient time for all members to express their views without feeling intimidated or threatened and should check that **all** the members in 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.

4.4.2 Specific tasks

There are specific aspects of the process that need to be covered in the first or second GDG meeting.

The first meeting should focus on induction of the group into the process of guideline development, how systematic reviews are performed, the role of health economics in decision-making, how patient/carers members contribute and the role of the GDG. GDG members should also be made aware of the principles contained in the report 'Social value judgements: principles for the development of NICE guidance' (www.nice.org.uk/svjguidance).

NICE and the PPIP staff will give presentations to explain how all elements of the guideline development programme fit together.

The second meeting should focus on developing clinical questions. The group should examine the scope and build questions based on it. It may be helpful to establish an explicit framework that clarifies the objectives of the work, the specific tasks needed and the timetable. This enables the group to focus and to develop a working relationship that is structured and well defined.

4.4.3 Role of external members

Occasionally, people external to the group may attend a meeting, either as observers or as experts. They may be healthcare professionals, patients or carers, or other experts. They are expected to follow the code of conduct of the GDG and to sign the confidentiality form.

4.4.3.1 Observers

Observers need the permission of the group before they can attend a GDG meeting. An observer attending a GDG meeting should sit apart from the group and not enter into the discussions unless invited to do so by the GDG. Observers may also include members of NICE.

4.4.3.2 Experts

Experts attending a GDG are present because of their knowledge in a particular area. Therefore, it is important that they sit within the group and enter fully into any discussion. However, they are not full members of the group; they do not have voting rights and should not be involved in the final wording of recommendations.

4.5 Further reading

Royal College of General Practitioners (1995) *The development and implementation of clinical guidelines: report of the clinical guidelines working group*. London: Royal College of General Practitioners.

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

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

Choudhry NK, Stelfox HT, Desky AS (2002) Relationships between authors of clinical practice guidelines and the pharmaceutical industry. *Journal of the American Medical Association* 287:612–17.

5 Developing clinical questions

Once the final scope of the guideline is agreed, the next stage is to refine it into structured clinical questions. These questions vary depending on the scope, but must be clear, focused and closely define the boundaries of the topic. They are important both as the starting point for the subsequent systematic literature review, and as a guide to facilitate the development of recommendations by the GDG. The clinical questions should be developed as soon as the GDG is convened.

This chapter describes how clinical questions are selected, how they are formulated and how they are agreed. It describes the different types of question that may be required, and gives examples.

5.1 Number of questions

The exact number of clinical questions required for each guideline depends on the topic and the breadth of the scope. However, it is important that the number of questions is of a manageable size for the GDG to handle, especially in relation to the agreed timescale. For guidelines taking 18 months to develop, about 30 questions would be a reasonable number. If a guideline topic requires a larger number of questions it may be necessary to divide it into subtopics.

5.2 Selecting questions from the scope

Clinical questions should address all the areas covered in the scope, and should avoid introducing new aspects not specified in the scope. They will, however, contain more detail than the scope, and should be seen as building on the fundamental framework of the guideline as laid out in the scope.

The questions are usually drafted by the technical experts. They should then be refined and agreed by all GDG members through discussions. The different perspectives of GDG members ensure that the right questions are identified, thus enabling the literature search to be planned efficiently. Often, however, the main questions need refining once the evidence has been searched, and this may generate subquestions (see chapter 6). Questions may also be submitted by stakeholders for the GDG to consider. The GDG should be explicit about the rationale it uses for selecting questions and should keep a detailed record of the proceedings leading to the decisions made.

5.3 Formulating and structuring clinical questions

A good clinical question is clear and focused. It should be formatted in terms of a specific patient problem because this helps identify the clinically relevant evidence. Its exact structure will depend on the question being asked, but it is likely to fall into one of three main areas: intervention, prognosis and diagnosis.

5.3.1 Questions about interventions

Questions about interventions usually represent the majority of questions for a particular guideline. Each intervention listed in the scope is likely to require at least one clinical question, and possibly more depending on the populations and outcomes of interest.

A helpful structured approach to formatting questions about interventions is the patient intervention comparison and outcome (PICO) framework (see box 5.1). This divides each question into four components: the **patients** (the population under study); the **interventions** (what is being done); the **comparisons** (other main treatment options); and the **outcomes** (the measures of how effective the interventions have been).

Box 5.1 Features of a well-formulated question on effectiveness intervention – the PICO guide

Patients/population: which patients or population 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?

Outcome: what is really important for the patient? Which outcomes should be considered: intermediate or short-term measures; mortality; morbidity and treatment complications; rates of relapse; late morbidity and readmission; return to work, physical and social functioning and other measures such as quality of life; general health status; costs?

For each question, the GDG should take into account the various confounding factors that may influence the outcomes and effectiveness of treatment. To facilitate this process, it may be helpful to construct a diagram listing outcomes and other key criteria the group has considered important. Once the question has been framed, key words can be identified as potential search terms. Examples of questions on the effectiveness of an intervention are presented in box 5.2.

The most appropriate study design to answer a question relating to an intervention is likely to be a randomised controlled trial (RCT). Further information on the side effects of a drug may be obtained from a cohort study.

There are, however, circumstances when an RCT is unnecessary (for example, giving insulin for a diabetic coma). In such situations all the following criteria should be fulfilled.

- An adverse outcome is likely if untreated (high/very high control-event rate).
- Treatment gives a dramatic benefit (high relative-risk reduction).
- The side effects of treatment are acceptable (high/very high number needed to harm).
- There is no alternative treatment.
- There is a convincing physiopathological basis to treatment.

Box 5.2 Examples of clinical questions on the effectiveness of interventions. Questions used during the development of guidelines by the NCC for Women's and Children's Health.

- Does clomifene citrate increase pregnancy rates in women with unexplained infertility compared with no treatment?
Fertility: assessment and treatment for people with fertility problems. *NICE clinical guideline no. 11* (2004). Available from www.nice.org.uk/CG011
- Do antibiotics reduce wound infection in women who have had an elective Caesarean section compared with no treatment?
Caesarean section. *NICE clinical guideline no. 13* (2004). Available from www.nice.org.uk/CG013
- Do insulin pumps improve blood sugar control in adolescents with type 1 diabetes mellitus compared with multiple insulin injections?
Type 1 diabetes: diagnosis and management of type 1 diabetes in children, young people and adults. *NICE clinical guideline no. 15* (2004). Available from www.nice.org.uk/CG015
- In women of reproductive age, are intrauterine devices effective contraception compared with oral contraceptives?
Long-acting reversible contraception. *NICE clinical guideline no. 30* (2005). Available from www.nice.org.uk/CG030

5.3.2 Questions about diagnosis

Questions relating to diagnosis do not involve an intervention designed to treat a particular condition, therefore the PICO framework is not a helpful structure. Questions should still be clear and focused, but they have to pick up key issues specifically relevant to diagnostic tests, for example their accuracy, reliability, safety and acceptability to the patient. Examples of questions relating to diagnosis are given in box 5.3.

Box 5.3 Examples of clinical questions on diagnosis. Questions used in the development of the guideline on lung cancer by the NCC for Acute Care. MRI, magnetic resonance imaging; CT, computed tomography; PET, positron emission tomography.

What is the diagnostic accuracy of:

- MRI compared with CT in assessing invasion of mediastinal structures and chest wall invasion in patients with potentially curable lung cancer?
- MRI compared with CT in assessing the presence of cerebral metastases in patients with stage III disease?
- PET compared with the histological results or follow up of more than 6 months in the detection of distant metastases (in brain/bone/adrenals/liver) in patients with lung cancer?
- abdominal ultrasound compared with the reference standard (histological results or follow up of more than 6 months) in the detection of distant metastases (in adrenals/liver) in patients with lung cancer?

Lung cancer: the diagnosis and treatment of lung cancer *NICE clinical guideline no. 24* (2005). Available from www.nice.org.uk/CG024

The most appropriate study designs to answer a question relating to diagnosis are likely to be cross-sectional cohort studies or blind prospective comparisons of the investigation with a gold standard.

5 Developing clinical questions

5.3.3 Questions about prognosis

In some situations the prognosis of a particular condition is of fundamental importance, over and above its general significance in relation to specific interventions. Areas where this is particularly likely to occur relate to assessment of risk, for example in terms of behaviour modification or screening and early intervention. Examples of questions relating to prognosis are given in box 5.4.

Box 5.4 Examples of clinical questions on prognosis. Questions used in the development of the guideline on familial breast cancer by the NCC for Primary Care.

- Does family history discriminate patients who should be referred?
 - Which are the symptoms, signs and other features that raise a suspicion of cancer in women, and those that make cancer less likely as a diagnosis?
 - Which are the symptoms, signs and other features that raise a suspicion of cancer in a man presenting with a breast abnormality, and those that make cancer less likely as a diagnosis?
 - Does trauma have a role in initiating breast cancer?
- Familial breast cancer: classification and care of women at risk of familial breast cancer in primary, secondary and tertiary care *NICE clinical guideline no. 14* (2004). Available from www.nice.nhs.uk/CG014

The most appropriate study designs to answer a question relating to prognosis are likely to be cross-sectional cohort studies or blind prospective comparisons of the finding with a gold standard.

5.3.4 Questions about service-delivery guidance

In general, clinical guidelines do not cover issues of service delivery, but sometimes NICE receives a remit from the Department of Health specifically asking for service-delivery guidance. Examples of questions on service-delivery guidance are given in box 5.5.

Box 5.5 Examples of clinical questions on service-delivery guidance

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- Is nurse telephone consultation in out-of-hours primary care effective and safe?
- What is the impact of home-based support in early labour on the rate of Caesarean and instrumental birth?
- Which types of in-patient care produce better clinical and social outcomes for young people with mental health problems?

Ideally the most appropriate study design to answer these questions is an RCT. However, a wide variety of methodological approaches and study designs have been used.

5.4 Further reading

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

New Zealand Guidelines Group (2001) *Handbook for the Preparation of Explicit Evidence-based Clinical Practice Guidelines*. Wellington: New Zealand Guidelines Group. Available from www.nzgg.org.nz

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:A12–13.

6 Identifying the evidence

The identification and selection of evidence is an essential step towards answering the clinical questions developed by the GDG. It is important to ensure that this process is as thorough and unbiased as possible. Searching should focus on locating the best evidence from all relevant sources – potentially, this involves extensive work. Ongoing research should also be identified as this may be important when formulating recommendations and planning updates to the guideline. The aim is to generate a comprehensive body of evidence that will:

- allow the clinical questions to be answered
- highlight any significant gaps in the evidence base where formal consensus methods may be needed.

The evidence used by the GDG will come from two main sources:

- searches of electronic databases by the technical staff at the NCC
- via stakeholder organisations that are invited to submit relevant information.

Information on linking guidelines with other NICE guidance (published and in progress) is given in chapter 10.

6.1 Database searching

Developing a search strategy is an iterative process. The strategy will go through several stages of refinement following discussions of the search results with the GDG. The literature search undertaken for the scope (the stage-one search) may have to be revisited to ensure that specific aspects of the clinical questions have been adequately covered. It is not possible to define a search strategy that will be appropriate for all scenarios. The stages in box 6.1 may need to be modified for some clinical questions. NCCs are not routinely expected to search the grey literature.

Box 6.1 Stages of database searching (this is a guide only)

Stage-one search

Identification of systematic reviews and guidelines (see chapter 2).

Stage-two search

Identification of RCTs, primarily, although there may be some clinical questions where other primary research is more relevant. Agreed clinical questions should be mapped against the available primary evidence.

Search standard databases only – Embase, Medline, the Cochrane Library and Cumulative Index to Nursing and Allied Health Literature (CINAHL).

Relevant economic papers should be identified by addition of an economic search filter to the clinical searches and by searches of an economic database (see section 8.1.2):

- NHS EED (NHS Economic Evaluation Database) (www.york.ac.uk/inst/crd/crddatabases.htm).

For more advanced searches use:

- the Cochrane Library (www.nelh.nhs.uk/cochrane.asp), using the filter developed for identifying clinical studies, and/or
- HEED (Health Economic Evaluation Database) (www.ohe-heed.com).

Stage-three search

Supplementation of the primary research evidence identified in stage two, if needed. In some cases, enough high-quality RCTs will have been identified to answer the clinical questions. In other cases, a full literature search will be needed to map against the questions. The following sources should be searched.

- Standard databases – Embase, Medline, Cochrane Library, CINAHL.
- Subject-specific databases – for example, Allied and Complementary Medicine (AMED), or PsychINFO – when relevant to the questions.
- Wider sources if these are considered important by the GDG. This evidence may include conference proceedings or other grey literature, though hand searching is not expected. Examples of wider sources include:
 - HTA database (www.york.ac.uk/inst/crd/htahp.htm)
 - ERIC (Education Resources Information Center) (www.eric.ed.gov)
 - Conference Papers Index (www.datastarweb.com)
 - NRR (National Research Register) (www.doh.gov.uk/research/nrr.htm)
 - PEDro (Physiotherapy Evidence Database) (www.pedro.fhs.usyd.edu.au)
 - SIGLE (System for Information on Grey Literature in Europe) (for further information, visit the SIGLE home page www.kb.nl/eagle)
 - the Kings Fund Library (www.kingsfund.org.uk)
 - Association of the British Pharmaceutical Industry (ABPI) clinical trials database (www.cmrinteract.com/clintrial)
 - hospital episode statistics (HES) (www.doh.gov.uk/hes)
 - patient episode data Wales (PEDW)
 - national or regional registers (for example, cancer registers)
 - national or regional audits
 - surveys of patients' experiences.

6.1.1 Sensitivity and specificity

The key attributes of a search strategy are sensitivity (ability to identify relevant information) and specificity (ability to exclude irrelevant documents). Sensitivity and specificity will be influenced by the time period covered (see below) and by the search terms used. There needs to be a trade-off between conducting an exhaustive search that will need additional resources and undertaking a more modest search that may miss some small studies that would not alter the overall findings. Exhaustive searching on every topic may not be practical or even necessary.

6.1.2 Time period for searching

Date parameters should be set to take into account sensitivity and specificity; the timings should reflect the number of hits and the topic. The period that the search should cover depends on the guideline topic and when the bulk of the research was published. The time limits for the search should be agreed by the GDG, in consultation with experts in the area.

Where adequate published systematic reviews exist, additional searching may be limited to updating, covering the time period since the review was conducted. Existing reviews may not address all the relevant outcomes, however, and in this case new searching may be required. Contacting review authors for updates should be considered, particularly for reviews found in the Cochrane Library.

6.1.3 Documenting the search

The process for identifying the evidence should be repeatable and transparent. The search strategy, including search terms, should be documented. This is important because it provides an audit trail describing modes of searching and reasons for changes and amendments. A full description of an appropriate documentation process is provided in 'Undertaking systematic reviews of research on effectiveness: CRD's guidance for those carrying out or commissioning reviews' (CRD Report Number 4, see 'Further reading' below). Electronic records of the references retrieved should be stored in a bibliographic database such as Reference Manager, ProCite or Endnote, as should details of ongoing research. This type of database allows the use of 'cite-as-you-write' and can be linked into word processors to facilitate the production of reference lists for the preparation of the guideline.

6.1.4 Timetabling

Searches should be prioritised by topic according to the material required for GDG meetings. Additional time may be needed for areas with a lot of pharmacological topics, where there are likely to be large numbers of published papers. This should be taken into consideration early on in the process and should be included in the planning. Specific searches will need to be carried out for each of the topics that will be discussed at the planned GDG

meetings. The example in box 6.2 shows the scheduled GDG meetings for each of the topics covered in the osteoporosis guideline.

Box 6.2 Adapted GDG meeting plan and schedule for the development of the guideline 'Osteoporosis: prevention, treatment and assessment of osteoporosis' (NCC for Nursing and Supportive Care).

HRT, hormone-replacement therapy; SERMs, selective oestrogen-receptor modulators.

Month 1:	Introduction
Month 3:	Clinical questions and submission of evidence
Month 5:	Assessment of factors predicting fracture risk (bone measures, biochemical markers, other independent risk factors)
Month 7:	Identification of individuals at risk for intervention. Assessment of risk assessment tools
Month 10:	Pharmacological interventions for osteoporosis in primary and secondary care settings (to consider half of the interventions – for example, anabolic steroids, bisphosphonates, HRT, SERMs and testosterone)
Month 12:	Pharmacological interventions for osteoporosis in primary and secondary care settings (to consider the remaining interventions – for example, calcitonin, calcitriol, calcium, calcium and vitamin D, vitamin D alone, parathyroid hormone, fluoride and strontium)
Month 14:	Non-pharmacological interventions for osteoporosis in primary and secondary care settings (cessation of smoking, dietary factors, reduced alcohol consumption, physical activity, self-management)

6.1.5 Updating searches

Searches should be updated between 6 and 8 weeks before the consultation. In addition, efforts should be made to identify major relevant publications after this date. In exceptional circumstances, these should be appraised and considered by the GDG.

6.2 Stakeholders' submissions of evidence

For some clinical questions, the GDG and NCC may have good reason to believe that information relevant to addressing clinical questions or sub-questions exists that they have not found through their standard searches. Examples may include where the NCC are aware of ongoing research in a field, where a technology is relatively new, studies that have only been published as abstracts, data on adverse effects, economic models, studies of patients', carers or healthcare professionals' experiences.

In these situations, the NCC may call for evidence. This call should be to all stakeholders. It should specify the question being addressed and the type of evidence being sought in detail, for example, in terms of participants, intervention, comparisons, outcome and study design for questions of effectiveness. These calls for evidence may be made at any point during development of the guideline, and stakeholders should usually be given 4 weeks to respond. The GDG may choose not to issue any calls for evidence for a guideline.

6.2.1 Confidential information

In addition to published studies, stakeholders may submit relevant unpublished data or studies in response to a call for evidence.

Box 6.3 summarises what may, and may not, be considered confidential by NICE.

Box 6.3 Definitions of what may be considered confidential

- Data that can be included as confidential include those that may influence share price values (CIC) or are intellectual property (that is, data awaiting publication).
- Confidential information should be kept to an absolute minimum, for example just the relevant section of the sentence, the particular result from a table or the section of code
- NICE will not agree that a whole study can be designated confidential. At a minimum a structured abstract of the study or economic model will have to be made available for public disclosure at the time of the guideline's consultation.
- 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.

When stakeholders submit confidential data, they should mark the relevant parts, for example by using a highlighter pen on a hard copy or the highlighter function in a word processor. These markings should then be maintained on those sections so that the GDG know which parts are confidential. When drafts and final documents are prepared for publication, the NCC should ensure those sections are replaced by a note stating that confidential information has been removed, so that the public are aware of exactly where confidential data have been used.

Following the principles in box 6.3 the amount of confidential information should be kept to a minimum, and as a minimum some summary should be publicly available by the time of the consultation on the guideline. Because NICE needs to be able to justify the recommendations in guidelines on the basis of the evidence considered by the GDG, NICE and the NCC will work with the data owners to find an agreed solution to the balance between confidentiality and transparency (www.nice.org.uk/page.aspx?o=229411).

6.2.2 Information not eligible for submission

Stakeholders are asked **not** to submit the types of evidence listed in box 6.4.

Box 6.4 Stakeholder material *not* eligible for consideration by the GDG

- Studies with weak designs when 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 a survey)

6.2.3 Documenting evidence from stakeholder submissions

Information received from stakeholders should be entered into a bibliographic database as described above and the details cross-checked with evidence identified through database searching. It should be assessed in the same way as published studies identified through the searches (see section 7.2.2).

6.3 Additional requirements for service guidance

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

- identify the gaps between current clinical practice, service provision and patient experience and what it 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 clinical outcomes.

A detailed baseline assessment of service activity is therefore needed and should be conducted before the GDG starts work. This should be available for consideration early in the development process, and ideally early enough to inform the scope. The following data sources might be used to provide 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 of Population Census and Survey (OPCS).

6.4 Further reading

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

New Zealand Guidelines Group (2001) *Handbook for the Preparation of Explicit Evidence-based Clinical Practice Guidelines*. Wellington: New Zealand Guidelines Group. Available from www.nzgg.org.nz

7 Reviewing and grading the evidence

Studies identified following the literature search need to be reviewed to identify the most appropriate data to help answer the clinical questions and to ensure that the recommendations are based on the best available evidence. This process should be explicit and transparent and should be carried out through a systematic review process. This involves four major steps: selecting relevant studies; assessing their quality; synthesising the results; and grading the evidence.

7.1 Selecting studies of relevance

Before acquiring papers for assessment, the information scientist or the reviewer who carried out the search needs to 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 eliminated. A quick check of the remaining abstracts should identify those that are clearly not relevant to the clinical questions and should be excluded at this stage.

Next, the remaining abstracts should be scrutinised against the inclusion criteria agreed by the GDG. Abstracts that do not meet the criteria should be eliminated. If there is any doubt about inclusion, this should be resolved by discussion with the GDG. Once the sifting is complete, hard copies of the selected studies can be acquired for assessment. Studies that fail to meet the inclusion criteria should be excluded. Those that meet the criteria can be assessed. Because there is always an element of bias in selecting the evidence, double sifting of a random selection of abstracts should be performed periodically.

The study-selection process should be clearly documented and should detail the inclusion criteria that were applied.

7.2 Assessing the quality of studies

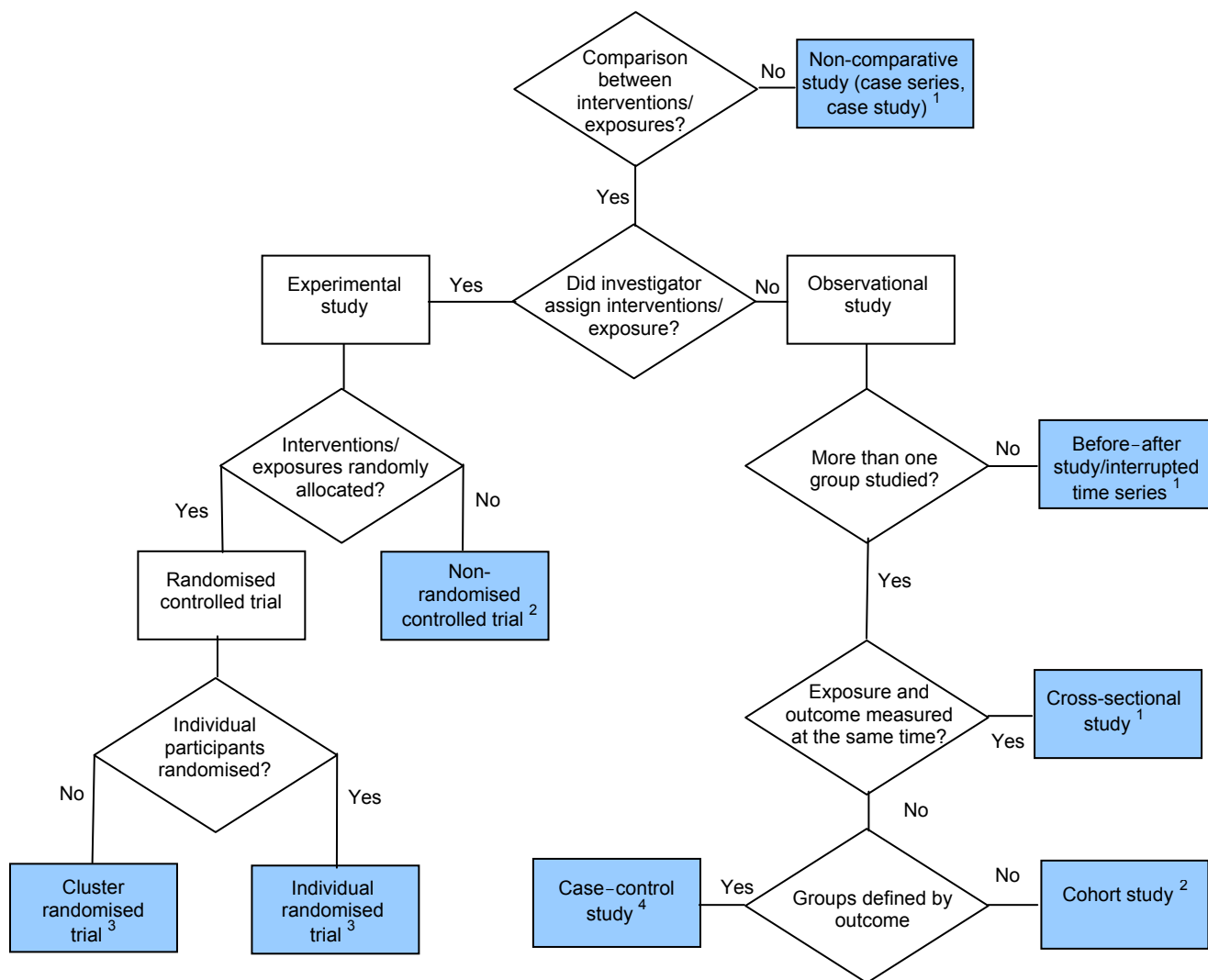
The quality of studies should be evaluated from an assessment of the methods and methodology used. This is a key stage in the guideline development process because the result will affect the level of evidence ascribed to the study.

The first stage is to determine the study design so that the appropriate criteria can be applied in their assessment (see section 7.2.1). Because it is sometimes difficult to establish the exact design used in studies, NICE has developed an algorithm to help systematic reviewers classify study design for answering questions of effectiveness (See figure 7.1). Algorithms for questions of diagnosis and prognosis are in preparation.

Figure 7.1. Algorithm for classifying study design for questions of effectiveness

Key

- 1 = currently no checklist
- 2 = cohort study checklist, see appendix D
- 3 = RCT checklist, see appendix C
- 4 = case-control study checklist, see appendix E



7.2.1 Published studies

In the second stage, the published studies selected from the search should be assessed for their methodological rigour against a number of criteria. Because these criteria will differ according to the study type, a range of checklists have been designed to provide a consistent approach to the assessment and its reporting. NICE recommends the checklists developed originally by the MERGE (Method for Evaluating Research and Guideline Evidence) Group in Australia and modified by the Scottish Intercollegiate Guidelines Network (SIGN) (see section 7.5). These checklists may be used to assess the selected studies. Health-economics studies should be assessed with the Drummond checklist (see appendix G). All these checklists are presented in Appendices B to H, together with explanatory notes on their use. The overall assessment of each study is graded using a code '++', '+' or '-', based on the extent to which the potential biases have been minimised.

To minimise any potential bias in the assessment, independent assessment by two reviewers on a random selection of papers is desirable. Any differences arising from this should be discussed fully at the GDG meeting.

7.2.2 Information from stakeholders

Published or unpublished data received from stakeholders or other sources should be assessed in the same way as other evidence captured in the search (see chapter 6 for details of handling confidential information). Authors should be contacted and requested to provide the necessary information so that the reviewers can complete the relevant quality checklist, or to provide details on individual patient data.

If the GDG decides not to use a piece of evidence, the reason should be made explicit.

7.2.3 Published guidelines

Relevant published guidelines may be identified in the search. These are either NICE guidelines or other guidelines.

7.2.3.1 NICE guidelines

These should be fully referenced and the evidence underpinning the recommendations should be left unchanged, provided it is not out of date. The wording of the recommendation may be changed to reflect the topic of the guidelines, but the guidance should not go beyond the evidence base.

If there is new published evidence that would significantly alter the existing recommendations, the NCC should follow the methodology for early update that is described in section 15.3.

7.2.3.2 Other guidelines

Other relevant published guidelines identified in the search should be assessed for quality using the AGREE instrument² to ensure they have

sufficient documentation to be considered. There is no cut-off point for accepting or rejecting a guideline and each group 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 in the full guideline.

Reviews of evidence from other guidelines that cover clinical questions formulated by the GDG can be considered as evidence provided:

- the review of evidence is assessed using the appropriate checklist from the technical manual and is judged to be of high quality
- they are accompanied by the evidence statement and evidence table(s)
- the evidence is updated according to the methodology for early update that is described in section 15.3.

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 address or a full reference to 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. The exceptions are recommendations from NHS policy (for example, National Service Frameworks).

7.3 Summarising the evidence

7.3.1 Data extraction and evidence tables

Data should be extracted to a standard template, for inclusion in an evidence table. Evidence tables help identify the similarities and differences between studies, including key characteristics of the study population and interventions or outcome measures; this provides a basis for comparison. They also help determine if it is possible to calculate a mean estimate of effect. In some circumstances and if the necessary data are available, it may be appropriate to carry out a meta-analysis.

The information to be extracted may vary depending on the clinical question, the level of detail and the analysis needed. Appendix I provides a template for information that should be included in evidence tables related to intervention studies. Information from studies of the accuracy of diagnostic tests should be reported using the template provided in appendix J.

² 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.

7.3.2 Conducting a meta-analysis

A full description of data synthesis, including meta-analysis and extraction methods, is available from the report produced by the Centre for Review and Dissemination ('Undertaking systematic reviews of research on effectiveness: CRD's guidance for those carrying out or commissioning reviews', see 'Further reading' below). The Cochrane Collaboration provides some detailed advice on meta-analysis in its handbook (section 8 of the 'Cochrane handbook for systematic reviews of interventions', see 'Further reading' below).

Meta-analysis is appropriate if there are enough relevant and valid data from studies that use comparable measures of outcome. Before any statistical pooling is carried out, an assessment should be made of the degree of, and reasons for, heterogeneity in the studies and their results, as excessive heterogeneity might suggest meta-analysis is not appropriate. Detailed advice is given in the sources quoted above.

Where meta-analysis is not appropriate, the analysis may have to be restricted to a qualitative overview that critically appraises individual studies and presents their results. The characteristics and limitations of the data (that is, population, intervention, setting, sample size and validity of the evidence) need to be fully reported. Forest plots are a useful tool to illustrate the effects estimated from individual studies and pooled analyses.

Eligible studies with no outcome data should be noted in the text. An estimate of the proportion of eligible data that are missing (because some studies will not include all relevant outcomes) is useful for each analysis.

7.3.3 Levels of evidence

7.3.3.1 *Intervention studies*

Studies that meet the minimum quality criteria should be ascribed a level of evidence to help the guideline developers and the eventual users of the guideline understand the type of evidence on which the recommendations have been based.

There are many different methods of assigning levels to the evidence and there has been considerable debate about what system is best. A number of initiatives are currently under way to find an international consensus on the subject. NICE has previously published guidelines using different systems and is now examining a number of systems in collaboration with the NCCs and academic groups throughout the world to identify the most appropriate system for future use.

Until a decision is reached on the most appropriate system for the NICE guidelines, we advise the NCCs to use the system for evidence shown in table 7.1.

Table 7.1 Levels of evidence for intervention studies. Reproduced with permission from the Scottish Intercollegiate Guidelines Network; for further information, see 'Further reading'.

Level of evidence	Type of evidence
1 ⁺⁺	High-quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1 ⁺	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1 ⁻	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias*
2 ⁺⁺	High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal
2 ⁺	Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal
2 ⁻	Case-control or cohort studies with a high risk of confounding, bias, or chance and a significant risk that the relationship is not causal ^a
3	Non-analytic studies (for example, case reports, case series)
4	Expert opinion, formal consensus
^a Studies with a level of evidence '–' should not be used as a basis for making a recommendation (see section 7.4)	

It is the responsibility of the GDG to endorse the final levels given to the evidence, although it may delegate this process to the systematic reviewers.

7.3.3.2 Diagnostic studies

The system described above covers studies of treatment effectiveness. However, it is less appropriate for studies reporting diagnostic tests of accuracy. In the absence of a validated ranking system for this type of test, NICE has developed a hierarchy for evidence of accuracy of diagnostic tests that takes into account the various factors likely to affect the validity of these studies (table 7.2). Because this hierarchy has not been systematically tested, NICE recommends that the NCCs use the system when appropriate, on a pilot basis, and report their experience to us.

Table 7.2 Levels of evidence for studies of the accuracy of diagnostic tests. Adapted from ‘The Oxford Centre for Evidence-based Medicine Levels of Evidence’ (2001) and the Centre for Reviews and Dissemination ‘Report Number 4’ (2001).

Levels of evidence	Type of evidence
Ia	Systematic review (with homogeneity) ^a of level-1 studies ^b
Ib	Level-1 studies ^b
II	Level-2 studies ^c Systematic reviews of level-2 studies
III	Level-3 studies ^d Systematic reviews of level-3 studies
IV	Consensus, expert committee reports or opinions and/or clinical experience without explicit critical appraisal; or based on physiology, bench research or ‘first principles’

^a Homogeneity means there are no or minor variations in the directions and degrees of results between individual studies that are included in the systematic review.

^b Level-1 studies are studies:

- that use a blind comparison of the test with a validated reference standard (gold standard)
- in a sample of patients that reflects the population to whom the test would apply.

^c Level-2 studies are studies that have **only one** of the following:

- narrow population (the sample does not reflect the population to whom the test would apply)
- use a poor reference standard (defined as that where the ‘test’ is included in the ‘reference’, or where the ‘testing’ affects the ‘reference’)
- the comparison between the test and reference standard is not blind
- case–control studies.

^d Level-3 studies are studies that have **at least two or three** of the features listed for level-2 studies.

7.4 Using the quality checklists to grade the evidence

In the quality assessment, each paper receives a quality rating coded as ‘++’, ‘+’ or ‘–’. Usually, studies rated as ‘–’ should not be used as a basis for making a recommendation. If good-quality studies are available to help answer the clinical question, and their outcomes are consistent, the ‘–’ rated studies should be rejected. If there is a body of reasonable, but fairly weak, evidence showing a consistent effect and there are ‘–’ studies that show the same effect, the ‘–’ studies should be included in the evidence table to demonstrate the extent of consistent evidence. If the ‘–’ studies suggest a different outcome they should be left in the evidence table for further discussion with the GDG; they should not be used to support the recommendation as their inclusion as supporting evidence would weaken the recommendation.

7.5 Further reading

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

Deeks JJ, Higgins, JPT, Altman DG, editors. Analysing and presenting results. In: Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Interventions 4.2.5* [updated May 2005] Oxford: the Cochrane Collaboration, section 8. www.cochrane.org/resources/handbook (accessed 13 March 2006).

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

Eccles M and Mason J (2001). How to develop cost-conscious guidelines. *Health Technology Assessment* 5(16).

Khan KS, Kunz R, Kleijnen J et al. (2003) *Systematic Reviews to Support Evidence-based Medicine. How to Review and Apply Findings of Healthcare Research*. London: Royal Society of Medicine Press.

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

Scottish Intercollegiate Guidelines Network (2002) *SIGN 50. A Guideline Developer's Handbook*. Edinburgh: Scottish Intercollegiate Guidelines Network.

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

8 Incorporating health economics in guidelines and assessing resource impact

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 in clinical decisions, and the incorporation of good-quality health-economic evidence into clinical guidelines can help make this less arbitrary and more consistent.

The GDG should take decisions based on the best available evidence of both clinical and cost effectiveness. This chapter describes the most appropriate role for the health economist in the development of NICE clinical guidelines, and suggests possible approaches to considering economic evidence in the guideline process.

8.1 The role of health economists in guideline development

The health economist is a core member of the GDG alongside the rest of the NCC technical team and should be involved at the earliest opportunity – from the beginning of scoping if possible. The economist should attend all GDG meetings.

The health economist may have skills that are specific to economic analysis, and the expertise of all 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 economist may be able to input usefully into interpretation of clinical data.

The role of the health economist in guideline development is:

- to advise on economic aspects of the clinical issues or questions
- to review economic literature
- to prioritise topics for further economic analysis through discussion with the GDG, NCC and NICE
- to carry out additional cost-effectiveness analyses.

The relative weight given to each role will vary from guideline to guideline. There may be large differences between guidelines in the size of the relevant economics literature, its relevance, its quality, its timeliness, and its generalisability. In some areas there may be high-quality data that can be used in economic models, whereas in other areas there is little data.

8.1.1 Advising on economic issues

The health economist should encourage the group to consider the economic consequences of the guideline recommendations as well as the clinical implications. A formal presentation to the group of the basic underlying principles of health economics should be given at the first GDG meeting. Further presentations later in the guideline development may be useful. It is particularly important that the group understands that economic analysis is not simply a matter of estimating the consequences of a recommendation in terms

of use of resources, but is concerned with the evaluation of both costs **and** health benefits. They should also 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 in clinical guidelines.

Assessment of cost-effectiveness is carried out for the purpose of maximising health gain. If resources are employed in interventions that are not cost effective then less health gain is achievable (that is, there is a greater 'opportunity cost'). The GDG should be encouraged to consider recommendations that:

- are slightly less effective than current practice but that free up a substantial amount of resources that can be reinvested, as well as those that
- increase clinical effectiveness at an acceptable level of increased cost.

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, measurement of quality of life and quality-adjusted life-years (QALYs). The 'British medical journal' has published a series of 'economics notes' that gives other concepts that the health economist may wish to explore with the GDG (see 'Further reading').

8.1.2 Reviewing information

Examining relevant published economic information is an important component of guideline development. Literature searching is the domain of the information scientist, but the health economist should be consulted about the economic search strategy. This should include a search of HEED and/or NEED. Addition of economic terms to searches of clinical databases such as MEDLINE is also helpful. Economic search filters have been developed by the Centre for Reviews and Dissemination and used extensively (see 'Further reading'). A health economist should review the abstracts and select the economic papers for inclusion, and appraise and summarise these as appropriate.

A thorough systematic review should be attempted. However, in some cases, it may be necessary to limit the search. For example, it may be appropriate to limit the search to UK-based studies, to a specific date range, to full economic evaluations, or to studies that base the estimate of clinical effect on a particular source (for example, an RCT or systematic review) if the amount of economic information is unmanageable. Any inclusion or exclusion criteria should be clearly defined and reported in the guideline methods.

Papers that are identified for inclusion should be critically appraised using a validated checklist (for example, see appendix G of Philips et al 2004, or Drummond and Jefferson 1996). These economic checklists reflect the conventional criteria for economic evaluation (see Drummond et al 2005).

The key criteria for assessing the relevance and quality of published economic evaluations are:

- **Relevance to the guideline question**
For example, did the study assess both the costs and effects, from an appropriate perspective, of all relevant alternatives, for the appropriate patient population, in a relevant setting?
- **Are there likely to be any important biases in the data used?**
This includes an assessment of both the internal validity and appropriateness for the relevant population of estimates of:
 - epidemiology (disease incidence, prevalence and progression)
 - risk assessment or test accuracy (sensitivity and specificity)
 - treatment effects
 - quality of life (utility) weights
 - resource use
 - and unit costs.
- **Are there any other important potential sources of bias?**
 - For modelling studies, this could include assumptions such as the choice of health states, the possible transitions between them, or the time horizon. It could also include omission of some costs or consequences (such as side effects).
 - For trial-based evaluations, biases may arise from assumptions about the extrapolation (or non-extrapolation) of observations.
- **Was cost-effectiveness estimated using the correct methods?**
This includes appropriate use of discounting, incremental analysis and uncertainty analysis.

In addition, a commentary on the quality of each paper should be presented.

8.1.3 Economic analysis

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

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

- the most important topics are selected for economic analysis
- the overall modelling approach is appropriate
- all 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.

8.1.3.1 *Prioritising topics for further economic analysis*

Economic analysis is potentially useful for any question where one intervention or programme is compared with another. This includes comparisons of methods of prevention, screening, risk assessment, diagnosis,

monitoring, rehabilitation and follow-up, as well as treatment. It may also include comparisons of different combinations or sequences of interventions, as well as individual components on the patient management algorithm. However, given the broad scope of many guidelines, it will not be possible to conduct original analyses for every component. Selecting topics for further economic analysis, including modelling, should be a **joint** decision between the health economist and the other GDG members. The selection should be based on systematic consideration of the potential value of economic analysis across all guideline questions.

An economic analysis will be more useful if it is likely to influence the recommendation and if the health and financial consequences of the recommendation are high. The value of an 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 analysis will reduce this uncertainty.

For a particular topic, economic modelling may not be warranted if, for example, the clinical evidence is so uncertain that even a ball-park figure for cost effectiveness cannot be estimated or, alternatively, if the published evidence on cost effectiveness is so reliable that further 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.

The rationale for the initial prioritisation of topics should be explained in the economic plan, to be agreed early in guideline development (see section 3.2). The health economist should take the lead in preparing this document, but the contents should be agreed with the GDG, and formally 'signed off' between the NCC and NICE. It may become clear during development, as the effectiveness and cost-effectiveness evidence is appraised, that the initial selection of topics for economic analysis needs revision. If so, changes to the economic plan should be agreed between the economist, other GDG members, the NCC and NICE.

8.2 Modelling approaches

Economic evaluation will usually be conducted in the form of a cost-effectiveness analysis (CEA), with the health effects measured in some appropriate non-monetary outcome indicator. In circumstances where CEA is not appropriate, other validated methods may be used.

CEA 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 quality-of-life score (measured on a 0–1 scale). There are well-documented methodological problems with QALYs; however, this is also true of other approaches. The NICE technology appraisal programme

continues to follow the QALY approach. Where suitable data are available, this approach should also be followed in guideline development. However, where there are not sufficient data to estimate QALYs gained, an alternative measure of effectiveness might be considered for the CEA (such as the life-years gained or cases averted, or some more disease-specific outcome).

A CEA could be modelled around a single well-conducted RCT or it might be modelled using decision-analytic techniques, with probability, cost and health-outcome data coming from a variety of published sources. In clinical guidelines there is often a trade-off between the range of new analyses that the economist can conduct, and the complexity of each piece of analysis. Simple methods may be used when 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 sometimes provide a sufficiently reliable estimate of cost-effectiveness. In other situations, a more complicated approach, such as Markov modelling or discrete event simulation, may be warranted.

Specific guidance on methods can be found in NICE's 'Guide to the methods of technology appraisal' (available from www.nice.org.uk). In particular, the manual recommends that a 'reference-case' analysis is conducted using the following assumptions.

- All health effects on individuals are included.
- Costs are measured from the perspective of the NHS and personal social services.
- Equity weightings are not applied to QALYs.
- Costs and health outcomes are discounted at 3.5%.
- Health-related quality of life is valued using choice-based elicitation methods, a representative sample of the general population, and validated generic health-state instruments. (It is unlikely that there will be time to collect original quality-of-life valuations, therefore data collected by alternative methods may be used but should be suitably qualified.)
- The time horizon should be chosen so as to incorporate sufficiently all important costs and effects.

Departures from the reference case can be adopted, but these would have to be highlighted and reasons given.

8.2.1 General principles

Regardless of the 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.
- 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.

- Uncertainty (around both internal and external validity) should be discussed fully and explored by sensitivity analysis (and, where data allow, statistical analysis).
- Limitations of the approach and methods taken should be fully discussed.
- Conventions on reporting economic evaluations should be followed (see Drummond and Jefferson, 1996).
- Analysis should be carried out in collaboration between the health economist and the rest of the GDG.

8.3 Economic evidence and guideline recommendations

For an economic analysis to be useful, it must be incorporated into 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, of one strategy compared with the next most effective alternative strategy.

Where one intervention appears to be more effective than another, the GDG will have to determine whether the increase in cost associated with the increase in effectiveness represents reasonable 'value for money'. There is no empirical basis for assigning a particular value (or values) to the cut-off between cost effectiveness and cost ineffectiveness. The consensus among NICE's economic advisors is that NICE should, generally, accept as cost effective those interventions with an incremental cost-effectiveness ratio of less than £20,000 per QALY and that there should be increasingly strong reasons for accepting as cost effective interventions with an incremental cost-effectiveness ratio of over £30,000 per QALY.

GDGs have discretion to take into account those factors they consider most appropriate when determining cost effectiveness. In doing so, they should make reference, as appropriate, to the principles outlined in the NICE's report 'Social value judgements: principles for the development of NICE guidance' (available from www.nice.org.uk/svjguidance). When a question 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 where necessary.

8.4 Estimating the resource and cost impact of the recommendations

Before commissioners and trusts can implement a NICE guideline they need to assess the resource and cost implications that this may have on their services. Therefore, there should be an estimate of the cost implications for

the NHS in England and Wales of adopting the recommendations. Performing this assessment is not, however, within the remit of the NCC, and NICE undertakes a separate, but parallel, resource-impact analysis. This is done during the validation period of the guideline in consultation with the NCC and the GDG. During the course of guideline development, the GDG is asked to identify the key resource and cost issues. This will inform the assessment of resource impact once the recommendations have been agreed. There are more details on the process for developing cost-impact assessments on the NICE website (www.nice.org.uk/costreportprocess).

8.5 Further reading

Raftery J, editor (1999–2001) Economics notes series. *British Medical Journal* (bmj.bmjournals.com)

Briggs AH, Goeree R, Blackhouse G et al. (2002) Probabilistic analysis of cost effectiveness models: choosing between treatment strategies for gastroesophageal reflux disease. *Medical Decision Making* 22:290–308.

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, Sculpher MJ, Torrance GW et al. (2005) *Methods for the Economic Evaluation of Health Care Programmes* 3rd edition. Oxford: Oxford University Press.

Drummond MF and McGuire A (2001) *Economic Evaluation in Health Care: merging theory with practice* Oxford: Oxford University Press.

Eccles M and Mason J (2001). How to develop cost-conscious guidelines. *Health Technology Assessment* 5(16).

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. Available from: www.york.ac.uk/inst/crd/report6.htm

Palmer S, Raftery J (1999) Economics notes. Opportunity cost. *British Medical Journal* 318:1551–2.

Philips Z, Ginely L, Sculpher M et al. (2004) Review of good practice in decision-analytic modelling in health technology assessment. *Health Technology Assessment* 8(36).

9 Making group decisions and reaching consensus

Throughout the development of a guideline, GDG members need to make collective decisions. These include generating clinical questions, agreeing the best evidence to answer these questions, and formulating recommendations. There are many different approaches to making group decisions and reaching consensus – there is no blueprint about which approach should be used in which circumstances as research is still lacking in this area. Also, because GDGs will function in different ways to reflect their individual membership, it is difficult to be prescriptive about the approach that should be used. This chapter describes the use of focus groups and formal consensus methods, and examines how they may be used by the GDG at key decision points during guideline development.

9.1 Focus groups

In most cases, a process of informal consensus within the GDG is sufficient to formulate recommendations based on the best available evidence. In areas where information is lacking, however, it may be useful to run specific focus groups to inform this decision-making process. This may occur in areas where it is important to gain wider understanding of particular perspectives, for example from patients or ethnic groups.

Details on how to conduct focus groups have been described elsewhere (see 'Further reading') and the rules for using focus groups are not rigidly defined. In all cases, however, the group facilitator has a key role in conducting the process, which is similar to that of the facilitator's role in the nominal-group technique (see section 9.2.2). Some recommendations for running a focus group to inform guideline development are provided in box 9.1.

Box 9.1 Recommendations for running a focus group

- Introduce the group
- Outline the aims of the session (for example, to understand the issues important to patients in the provision of palliative care)
- Outline the procedures for discussion (for example, explain that while honest views are welcome the process is time-limited and the facilitator may have to curtail a discussion if necessary to achieve the objectives of the meeting)
- Define the boundaries of the discussion, outlining the areas of clinical management that will be covered and those that will be excluded
- Ensure that all members talk about topics that provide insight into the area under discussion
- Check that the terminology members use is understood by all and let the group know that clarifications may be requested
- Summarise the key themes at various points of the discussion to help members crystallise their views or to modify them if needed

9.2 Formal consensus methods

In some guidelines there will be core areas of the scope where the scientific evidence needed to answer the clinical questions is of such poor quality, or is inconsistent or non-existent, that the GDG needs to adopt a more formal method of consensus. Using a formal approach will make it possible to trace back how a group came to a decision, and will be explicit and transparent.

Three formal approaches are used regularly in the field of healthcare:

- the Delphi technique
- the nominal-group technique
- the consensus-development conference.

Each has its own advantages and shortcomings. Their use should be tailored to the needs of the guideline group, the type of questions to be answered, and also the time available in the guideline process, as the techniques can be very detailed and time intensive. Often people use hybrids of the methods to make the work more manageable.

Regardless of the consensus method used, there should be a detailed description of the process that was used and the results. Box 9.2 presents the minimum criteria that should be included when reporting the consensus method.

Box 9.2 Core reporting criteria for use of formal consensus methods in developing guidelines

- What method was used and what were the reasons for choosing it?
- What areas of the guideline were addressed by the consensus methods and what were the exclusion criteria?
- How were the questions or statements for collecting opinion developed?
- How many people participated, what were their denominations and how were they recruited?
- What was the process used for eliciting views (meeting, postal survey) and for voting (for example, electronic, paper)?
- How was agreement defined? (Were the definitions strict or relaxed? Were outliers included or excluded? Were any members' views weighted?)

The composition of a group of individuals selected for formal consensus should reflect the full range of characteristics of those they are trying to represent. A homogeneous group will reach greater consensus, because specialists tend to favour the interventions/views with which they are familiar. However, such a group may not be wholly representative of the healthcare workers whose practice is being addressed in the guideline, and is unlikely to represent the views of patients. An HTA report suggests that a consensus group of 10–12 people is probably sufficient to allow conclusions to be reached – including more people would be unlikely to result in the group reaching different conclusions (see 'Further reading'). In most cases, therefore, the GDG itself will fulfil the requirements for a consensus group. It should also be noted that a good facilitator is crucial to the quality of the

process, and that convergence of views is more likely after continued discussion. However, there may be circumstances when convergence is not possible. The guideline text should highlight where convergence has not been possible and where areas of disagreement remain.

9.2.1 The Delphi method

The Delphi method involves sending participants questionnaires by post and asking them to record their views. The specific issues highlighted by respondents are then circulated in a second questionnaire and participants are asked to respond to these issues. The responses to these issues are collated by the organisers and sent back to participants in a summary form. Participants are usually given the chance to revise their views in light of the group feedback. This process could be repeated several times. The judgements of the participants are statistically aggregated, sometimes after weighting for expertise. The participants never meet or interact directly.

The logic behind the Delphi method is partly statistical; combined participants' views should, in general, lead to more reliable estimates than estimates from an individual. It is also considered to be an effective way of exchanging information between large numbers of people at a relatively low cost. However, this method diminishes the positive aspects of interaction found at face-to-face meetings.

9.2.2 The nominal-group technique

Unlike the Delphi technique, the nominal-group technique is more a method of obtaining a practical result quickly and is effective in obtaining consensus from a range of participants in diverse settings, such as healthcare. It is also recognised as a method for generating a wide range of ideas in situations where the group has to solve problems. Therefore, the method could also be used to generate the clinical questions at the beginning of the guideline development process.

The nominal-group technique uses a variety of postal (or computer) and face-to-face techniques to elicit a consensus view. Individual participants record their ideas independently and privately. The ideas are collected in turn from individuals and are fed back to the group when they are brought together for discussion, followed by a further private vote.

The nominal-group technique uses a facilitator to structure the discussion. The facilitator should be either an expert on the topic or a credible non-expert. Each idea is discussed in turn, so the discussion covers all the ideas rather than only one or two. Controlling the interaction so that all participants have the opportunity to express their views is believed to reduce the dominance of the discussion by one or two vocal members.

The NCC for Acute Care has recently used a modified nominal-group technique to identify areas of agreement when the evidence base from the literature was inadequate. Details of this process are given in the full guideline 'Routine preoperative testing: evidence, methods and guidance', available from the NICE website.

9.2.3 A variation of the nominal-group technique

A variation of the nominal-group technique has been 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: management of chronic heart failure in adults in primary and secondary care', available from the NICE website.

9.2.4 Consensus-development conference

The consensus-development conference consists of a selected group of about ten people who are brought together to reach consensus on an issue. They are presented with evidence by various interest groups or experts who are not part of the decision-making group. They then retire and consider the questions in light of the evidence presented and attempt to reach a consensus. Both the open part of the conference and the private group are chaired.

9.3 Further reading

Murphy MK, Black NA, Lamping DL et al. (1998) Consensus development methods, and their use in clinical guideline development. *Health Technology Assessment 2*.

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

10 Linking guidelines to other NICE guidance

As the number of pieces of NICE guidance increases, there are more topics spanning work programmes. Clinical guidelines cover broad aspects of management of a particular disease or condition. Public health programme guidance and public health intervention guidance deal with the promotion of good health and the prevention of ill health. Technology appraisals focus on the clinical and cost effectiveness of individual or groups of technologies, such as new drugs, surgical procedures or medical devices, and interventional procedures guidance covers the safety and efficacy of interventional procedures used for diagnosis or treatment. Details of the other programmes' development processes and methods can be found at www.nice.org.uk.

The scoping stage of a clinical guideline should involve identifying topics from other programmes that are relevant to the guideline (see chapter 2).

This chapter deals with the approaches to be taken when:

- guidance from another programme relevant to a guideline has already been published and requires incorporation in a guideline
- NICE wishes a GDG to update an existing piece of guidance during the course of its work, or
- a relevant piece of guidance from another programme is being developed concurrently.

10.1 Technology appraisals

10.1.1 A previously published technology appraisal

When a newly commissioned guideline topic covers an area for which there is a previously published multiple technology appraisal (MTA) there are two possible approaches.

- The technology appraisal is incorporated verbatim in the guideline as described in section 10.1.3.3.
- The technology appraisal is updated through the guideline development process.

NICE will make a judgement in conjunction with the NCC about whether the appraisal might usefully be updated through the guideline development process. Planning the update of a technology appraisal is outlined in the 'Guide to the technology appraisal process' (www.nice.org.uk/page.aspx?o=201972). The NCC has formal input into this process as a commentator for the appraisal. The final decision will be taken by NICE's Guidance Executive before the workplan is signed off.

10.1.2 Updating a technology appraisal in a guideline

The objective for a GDG in updating a technology appraisal is to determine whether any new evidence that has become available since the publication of

the appraisal means the original recommendations need to be changed. The original recommendations should be changed only if warranted by new evidence, and if supported by cost-effectiveness analysis. The reasons for any changes should be clearly documented in the full version of the guideline.

The following mechanisms will facilitate this.

- NICE will supply relevant data about the original appraisal topic to the NCC and GDG. The GDG will be able to refer to this information but may not quote commercial-in-confidence data without the permission of the data owner.
- The appropriate link person in the Centre for Health Technology Evaluation (for example, the technical lead or technical advisor for the original appraisal and/or the Associate Director) will advise the GDG and NCC on updating the appraisal recommendations.
- Cost-effectiveness analysis may be done by updating the health economics model used in the original appraisal, either via NICE or by going directly to the academic group commissioned to review the evidence (the Technology Assessment Group). Alternatively the GDG may decide to develop a new model. This should follow the principles for economic evaluation described in section 8.2.

10.1.3 Concurrent development of a guideline and an appraisal

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

- timing
- exchange of information
- publication of recommendations.

10.1.3.1 Timing

The development of related guidelines and appraisals should be coordinated so that the published appraisal recommendations can be incorporated into the guideline before the guideline goes out for consultation. Details of the timelines should be negotiated between the NCC and the NICE guidelines and appraisals teams.

10.1.3.2 Exchange of information

Information exchange is mutually beneficial to the Appraisal Committee 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.

Multiple technology appraisal (MTA)

- At an early GDG meeting a member of the Appraisals Team may be invited to outline the appraisal process, highlighting differences between the appraisal and guideline development process, the opportunities for input from the GDG to the appraisal process and the status of the ongoing relevant appraisals.

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- A representative for 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 development group meetings as appropriate.
- The GDG will act as a commentator for the relevant MTA. Commentators have an opportunity to comment on all documents (scope, assessment report, appraisal consultation document) but they are not required to make a submission and they do not have the right to appeal.
- One person from the GDG should be nominated to act as a link with the appraisal technical lead. This will normally be the Chair. Guidance for GDG members on attendance at NICE Appraisal Committee meetings is available in appendix A5.
- The guideline's health economist and the Technology Assessment Group should work together to ensure that the economic models for the guideline and the appraisal are consistent.

Single technology appraisal (STA)

The methodology for single technology appraisals (STAs) is still undergoing consultation. An addendum will be added to the guidelines manual as soon as the final documents for this section are available. In the meantime, guidelines that incorporate STA guidance will need to be considered on a case-by-case basis.

10.1.3.3 Publication of technology appraisal recommendations

The GDG should not publish recommendations in areas already covered in the scope of any relevant ongoing appraisal. Published technology appraisal recommendations that do not need updating should be reproduced unchanged in the most appropriate section of a guideline. If a technology appraisal is being incorporated into a clinical guideline, any proposed change to the wording must be discussed with the Appraisals Team and agreed by NICE's Guidance Executive. This should only occur on rare occasions when an existing appraisal recommendation extends beyond the simple recommendation of the use of a technology (for example, into the setting or circumstances for its use) and it is being superseded by a systematic review of that aspect within the guideline. This cannot apply to the central recommendation of an appraisal.

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

If a guideline is addressing a question that relates to an appraisal, but covers different population groups or drug indications, the GDG should apply techniques comparable to those used for the appraisal in assessing the clinical and cost-effectiveness evidence. The final recommendations in the guidelines for these groups or indications may be different from the appraisal recommendations if there is evidence of differing safety, effectiveness or cost-effectiveness.

10.2 Interventional procedures (IP)

10.2.1 Published interventional procedure guidance

As for technology appraisals, existing relevant interventional procedure (IP) guidance will be identified during scoping and before the workplan is signed off. There are two possible options.

1. If a GDG decides that a relevant IP has insufficient impact to justify a clinical question, the IP guidance should simply be referred to in a section of the guideline as 'other related NICE guidance'. The IP Associate Director, the lead analyst and the Interventional Procedures Advisory Committee (IPAC) chair will be added as stakeholders to enable them to review the relevant sections of the guideline during the consultation period. For IPs not selected as clinical questions, the NCC would not search for new evidence. However, if the NCC happens to find some new evidence on that IP during their other searches, they should inform the IP Associate Director and the lead analyst.
2. If, in the opinion of the GDG, an IP has become an important part of standard or mainstream practice in the NHS, the GDG may decide to cover the area with a clinical question and thereby update the IP. It is anticipated that IPs will rarely justify a clinical question if IPAC judged that the IP was not safe or efficacious. The final decision to update an IP in a guideline should be agreed between NICE and the NCC.

10.2.2 Updating an interventional procedure in a guideline

When an IP is updated in a guideline this will include consideration of relative effectiveness and/or cost effectiveness, as well as safety and efficacy. The following process and principles should be followed.

- The GDG needs to determine whether new evidence has become available since the publication of the IP to justify a change in the IPAC view on safety and efficacy.
- The GDG should consider the procedure's effectiveness relative to other possible interventions and, if prioritised for health economic assessment, its cost effectiveness.
- The GDG should decide whether the procedure is important enough in the care pathway to justify economic evaluation.
- If a new intervention includes the use of a drug the licensing position should be taken into account and any consideration of off-label use should follow the process outlined in section 11.2.4.
- The IP Associate Director, the lead analyst and the IPAC chair will be added to the list of stakeholders for the guideline (see section 10.2.1).

10.2.3 Concurrent development of a guideline and an IP

The NCCs should check the IP publication list during the guideline development phase and, if the development group considers it appropriate, include any new publications in its final searches before submission of the first draft of the guideline.

If an IP has not been finalised at the time of the guideline consultation, the guideline should cross-refer to the interventional procedure consultation document.

10.3 Public health guidance

10.3.1 What does public health guidance cover?

There are two types of NICE public health guidance.

- Public health intervention guidance makes recommendations on specific types of activity ('interventions') that help to reduce people's risk of developing a disease or condition or promote or maintain a healthy lifestyle. An example is brief interventions for smoking cessation in general practice. NICE's Public Health Interventions Advisory Committee (PHIAC) takes 1 year to develop this type of guidance.
- Public health programme guidance deals with broader action for the promotion of good health and the prevention of ill-health. This guidance focuses on wider topics such as prevention of obesity. NICE establishes programme development groups (PDGs) to develop this type of guidance, which takes 18 months.

10.3.2 Dealing with overlapping referrals

NICE is currently establishing a mechanism for dealing with topics it receives from the Department of Health that may overlap across programmes. The precise details of processes and methods will be developed in the course of 2006 but they are likely to follow the principles set out below.

10.3.2.1 Thematic referrals

These will be topics for which new joint guidance is being developed across NICE guidance programmes (for example prevention and treatment of obesity). Two guidance groups will usually be established: for the example of obesity, this would be a PDG for prevention and a GDG for treatment. There will be a joint Chair for the two groups, and there may be overlapping membership and occasional joint meetings.

The two groups will work to a joint timetable, methodology and process, based on the processes and methods for guidance production and agreed before the work starts.

10.3.2.2 Overlapping referrals

Other overlapping referrals fall into two broad types: the topic is in an area covered by more than one NICE guidance programme; or a public health intervention might in the future become part of a clinical guideline.

An example of the same subject applying to more than one NICE guidance programme is the role of vitamin D supplementation in pregnancy. This would be of equal interest to a GDG working on an antenatal care guideline, and the maternal and child nutrition PDG. One team will review the evidence, taking into account the questions of both GDG and PDG. The team will report the review findings to both sets of guideline developers. NICE will decide on a

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case-by-case basis which team will review the evidence. The review methods will be agreed in advance to suit the requirements of the groups.

An example of a public health intervention that might become part of a future clinical guideline is needle-exchange schemes. The public health intervention guidance may be published, in development, a new referral, or needing updating because of new evidence. For these overlapping referrals, it is proposed that a group is set up in NICE, with input from guidelines commissioning managers and technical leads, to prepare a set of options, taking into account programme timelines and processes. The options will be considered by NICE and the final decisions will be incorporated in the scope of the guideline.

11 Creating guideline recommendations

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

- translating the evidence into recommendations
- wording the recommendations
- possible approaches to prioritising recommendations for implementation
- formulating research recommendations.

11.1 Translating the evidence into recommendations

Once the GDG has examined the clinical and economic evidence and discussed its suitability to answer the clinical questions, it needs to turn the evidence into recommendations. If the evidence is very strong, the process should be straightforward and the evidence should translate directly into a recommendation. Principles for interpreting the economic evidence are set out in section 8.3. However, in many cases direct translation may not be possible; some reasons and possible solutions for this are described in table 11.1. In some circumstances the GDG may decide to make a research recommendation as set out in section 11.4).

Table 11.1 Translating evidence into recommendations: challenges and possible solutions

Challenge	Possible solution
The literature search has found no evidence that answers the clinical question	The GDG should consider using consensus to identify current best practice. This process should be robust and should follow the methods of formal consensus or resolve the issues through discussions in the group (see chapter 9)
The quality of the clinical evidence is poor (levels 1, 2, 3 and 4)	
The available clinical evidence is conflicting and of a similar level	All efforts should be made to identify studies that are most applicable to the population covered by the guideline and the recommendations should be based on those studies
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 the recommendations from the evidence, for example from high-quality evidence in a largely similar but different patient group. The group will need to make its approach very explicit, stating the basis it has used for extrapolating from the data and the assumptions they have made
There is no published estimate of cost-effectiveness that is applicable to the relevant population.	The GDG should consider whether to develop their own estimate of cost-effectiveness through further economic

	analysis (see section 8.1.3). 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. This should be done through GDG consensus.
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It is likely that, when formulating the recommendations, there will be instances where members of the GDG disagree about the content of the final product. Formal consensus methods can be used in agreeing the final recommendations (see section 9.2). Whatever the approach used, there should be a clear record of the proceedings and how areas of disagreement have been handled.

11.2 Wording the guideline recommendations

Wording the final guideline recommendations may be one of the most important aspects of the development process. The recommendations will be the focus of attention for most readers when the guideline is published, so the wording must be unambiguous and easy to translate into clinical practice. The final wording should be agreed by the GDG (see chapter 5), but should take into account the following principles – these are described in more detail in the following sections.

- Recommendations should usually stand alone (see section 11.2.1).
- Recommendations should be action-oriented (see section 11.2.2).
- Recommendations should avoid giving directives to the NHS on waiting times (see section 11.2.3).
- Recommendations referring to drug use should use the generic drug name, avoid stating dosages and indicate where the recommendation refers to off-label use (see section 11.3.5).
- Tables can be used to present recommendations but only where this substantially improves clarity (see section 11.3.6).
- Recommendations should take the patient into consideration and should avoid the use of words such as 'subjects' or 'individuals' rather than 'people' or 'patients'.
- Recommendations should be worded with an advisory 'should', not 'must'. When the recommendation links to enforceable legislation, such as Health and Safety regulations, there should be a clear reference to the relevant documents.
- Recommendations should be worded in a way that acknowledges the patient's involvement in discussions about treatment options – for example, that treatments should be 'offered' to the patient, rather than 'prescribed' or 'given'.
- Recommendations can state explicitly if certain treatments or activities should not be undertaken or should be stopped (see box 11.2 for example).

Examples of recommendations from guidelines are shown in box 11.2 at the end of this section.

11.2.1 Stand-alone recommendations

Guideline recommendations should be clear and concise, but should contain enough information that they can be understood without reference to other supporting material. This is particularly important because in the NICE guideline recommendations are published without the background details in the full guideline. Any terminology included in the recommendations therefore needs to be clearly defined and unambiguous.

If appropriate, it is acceptable to include cross-references to other recommendations to avoid the need to repeat information such as treatment regimens or definitions of terms.

11.2.2 Action-oriented recommendations

Guideline recommendations should focus on what needs to be done, and should not contain background information. When writing recommendations, the author should have in mind a reader who is saying 'what does this mean for me?'

11.2.3 Avoiding waiting- and referral-time target directives to the NHS

The guideline should refer, where appropriate, to waiting- or referral-time targets set by the Department of Health or the Welsh Assembly Government. Exceptionally, where no such target exists but the GDG feels it essential to indicate a maximum time for progress to the next intervention, it should seek the agreement of NICE to include such information. In each case, the group should indicate what, in its view, the maximum elapsed time should be. It should follow the star system NICE has developed for its published referral guidelines (box 11.1).

Box 11.1 NICE's star system for referral priorities

****	Is seen immediately*
***	Is seen urgently†
**	Is seen soon†
*	Has a routine appointment†
▲	Is seen within an appropriate time depending on his or her clinical circumstances (discretionary)
*Within a day. †In most cases, trusts and primary care trusts should be advised to work to local definitions of maximum waiting times in each of these categories.	

11.2.4 Referring to drugs

There are three points to consider when referring to a drug: the name, the dose, and whether or not it carries a licence for that particular indication (that is, is the recommendation for off-label use?).

- Drug name: the recommended International Non-proprietary Name (rINN) for medicinal substances as in the 'British national formulary' should be used (see the NICE 'Style guide' for further information). Normally, only the generic name should be used; in some cases (for example when referring to a specific device), it may be appropriate to give the proprietary name in brackets at first mention. The manufacturer should not be named.
- Dosages: in general, recommendations should not include drug dosages. Instead, readers should be referred to the summary of product characteristics, which also includes details on possible side effects. If there is evidence that a particular drug is often prescribed at the wrong dosage, or if there is clear evidence about the effectiveness of different dose levels it may occasionally be appropriate to include information on dose levels. Summaries of product characteristics can be found in the Electronic Medicines Compendium (www.emc.medicines.org.uk).
- Off-label use: guideline recommendations normally fall within licensed indications; exceptionally, and only where clearly supported by evidence, use outside a licensed indication may be recommended. This should be made clear in the wording of the recommendation. The guideline will assume that prescribers will use the summary of product characteristics to inform their decisions for individual patients.

11.2.5 Use of tables

Tables may be used to present recommendations if this will improve clarity. Note, however, that adding tables can cause difficulties in posting the document on the website, so please be sure that a table is necessary to present information most effectively for readers.

If it will improve clarity, a table may be used to present information that should be shared with patients, or information that health professionals need to know.

Box 11.2 Examples of recommendations from NICE guidelines published to date

- Healthcare professionals should wear double gloves when performing or assisting at caesarean sections on women who have tested positive for HIV, to reduce the risk of HIV infection of healthcare professionals during surgery.
From: Caesarean section. *NICE clinical guideline* no. 13 (www.nice.org.uk/CG013)
- For people with eating disorders presenting in primary care, GPs should take responsibility for the initial assessment and the initial coordination of care. This includes the determination of the need for emergency medical or psychiatric assessment.
From: Eating disorders: core interventions in the treatment and management of anorexia nervosa, bulimia nervosa and related eating disorders. *NICE clinical guideline* no. 9 (www.nice.org.uk/CG009)
- Healthcare staff should always consider whether the person with MS has any impairment of attention, memory and executive functions sufficient to be

a problem, or to be a contributing factor to their current clinical status.

From: Multiple sclerosis: management of multiple sclerosis in primary and secondary care. *NICE clinical guideline* no. 8 (www.nice.org.uk/CG008)

- Healthcare professionals should ensure that patients having enteral or parenteral nutrition in the community and their carers:
 - are kept fully informed and have access to appropriate sources of information in formats, languages and ways that are suited to an individual's requirements. Consideration should be given to cognition, gender, physical needs, culture and stage of life of the individual
 - have the opportunity to discuss diagnosis, treatment options and relevant physical, psychological and social issues
 - are given contact details for relevant support groups, charities and voluntary organisations.

From: Nutrition support in adults. Nutrition support in adults: oral nutrition support, enteral tube feeding and parenteral nutrition. *NICE clinical guideline* no. 32 (www.nice.org.uk/CG032)

- For individuals who have experienced a traumatic event, the systematic provision to that individual alone of brief, single-session interventions (often referred to as debriefing) that focus on the traumatic incident, should **not** be routine practice when delivering services.

From: Post-traumatic stress disorder (PTSD): the management of PTSD in adults and children in primary and secondary care. *NICE clinical guideline* no. 26 (www.nice.org.uk/CG026)

11.3 Prioritising recommendations for implementation

Most guidelines cover a large clinical area and, as a result, often contain a considerable number of recommendations needed to answer the many clinical questions. Users of the guidelines will need to decide in what order to implement the recommendations. To help these decisions, developers should identify key priorities for implementation, which are the recommendations likely to have the biggest impact on patients' care and patients' outcomes in the NHS as a whole. The number of recommendations prioritised in this way may vary depending on the guideline, but should normally be between five and ten.

There are many different criteria that could be used to select these key priorities for implementation, but it is important that the GDG takes the final decision. Although there is no blueprint for selecting key priorities for implementation, fundamental criteria include whether a recommendation is likely to:

- have high **impact** on patients' outcomes, including mortality and morbidity
- have a high impact on **reducing variation**
- lead to a **more efficient use of NHS resources**
- mean patients reach critical points in the care pathway more quickly.

The choices may be based on information such as existing audit data at national level, but may also draw on the experience of clinicians and patients or carers involved in the GDG. They will also be informed by a broad range of stakeholders as part of the formal consultation process.

Whatever the method adopted, there should be a clear record of the criteria used for selecting the key priorities for implementation and the process for agreeing them.

11.4 Formulating research recommendations

The GDG is likely to identify areas where good evidence is lacking and future research is needed to inform updates of the guidelines. This section provides a framework for formulating research recommendations and for selecting research recommendations to include in NICE guidelines.

11.4.1 Principles for formulating research recommendations

Research recommendations can cover questions about effectiveness, the accuracy of a test or clinical prediction rules, rates of harms or other events, patients' experience, and patient-defined outcomes, costs, and service delivery and organisation. They may also recommend that a full systematic review be carried out on a specific topic. Each research recommendation should be formulated as one question, or a set of closely related questions. It should consider the importance of issues relating to gender, ethnicity and people with special needs.

A research recommendation should have two components: a well formulated, answerable question (table 11.4); and a statement about the importance of the recommended research, to assist the prioritisation process (table 11.5).

Table 11.4 Checklist for formulating answerable research questions using the PICO model

P I C O is a widely used mnemonic summarising the four major components of every clinical or research question: **p**atient, **i**ntervention, **c**omparison and **o**utcome.

<p>Patient, population or problem</p>	<p>What is the primary problem, disease or condition you are interested in? What are the most important characteristics of the population or patient group to be studied?</p> <p><i>Consider:</i></p> <ul style="list-style-type: none"> • diagnosis, disease stage, co-morbidity • gender, age, ethnic group, specific exclusions • clinical setting (for example, community or secondary care).
<p>Intervention or indicator</p>	<p>Which main intervention, treatment, management strategy, clinical prediction rule or prognostic factor are you considering? What risk factor was the patient/population exposed to?</p> <p><i>Consider:</i></p> <ul style="list-style-type: none"> • type, frequency, dose, duration (for intervention or exposure) • prognostic factor (define) • diagnostic or screening test.
<p>Comparison or control</p>	<p>What is the main alternative(s) or control to compare with the intervention?</p> <p><i>Consider:</i></p> <ul style="list-style-type: none"> • all the parameters mentioned above under population, patient and intervention, where applicable

	<ul style="list-style-type: none"> reference standard for test accuracy (give details).
Outcome	<p>What will the researcher need to measure, improve, influence or accomplish? What are the clinical or patient-related outcomes of the intervention that should be measured?</p> <p><i>Consider:</i></p> <ul style="list-style-type: none"> outcomes to be measured (for example, mortality, morbidity, quality of life, patient perception) method of measurement (type, frequency or timing of measure) test characteristics (for example, how to measure the clinical utility of the test in given setting) the need for blinding of patient, provider or outcome assessor.

Table 11.5 Why is this question important? A checklist for the explanatory paragraph and criteria for selecting important recommendations

Draft a paragraph explaining the need for the research, using the following headings. The GDG can then use these headings to select the five most important research recommendations to appear in the NICE version of the guideline.

1. Relevance to NICE	How would the answer to this question change future NICE guidance ? (that is, generate new knowledge and/or evidence)
2. Importance to patients or the population	What would be the impact of any new or altered guidance on NHS patients ? (for example, patient acceptability, quality of life, morbidity or disease prevalence, severity or mortality)
3. Relevance to the NHS	What would be the impact of any new or altered guidance on the NHS ? (for example, financial advantage, effect on staff, relevance to strategic planning or service delivery)
4. National priorities	Is the question relevant to a national clinical priority area (such as a National Service Framework)? Please specify the relevant document.
5. Lack of current evidence	<p>How much research has been carried out in this area to date? What are the problems, if any, with this previous research?</p> <p>Has there been a previous systematic review? Please give details.</p>
6. Feasibility	Is the proposed research ethically and technically feasible ? Can it be carried out in a realistic timescale and at an acceptable cost ?

7. Other comments	Mention any other important issues such as potential funders or outcome of previous attempts to address this issue or methodology problems. However, please remember that this is not a research protocol.
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NOTE: Continuous feedback by users is essential in order to improve the above questionnaire. How user-friendly, acceptable, reliable and valid is it? How successful is it in generating clear, precise and potentially answerable recommendations?

11.4.2 Selecting research recommendations for the NICE guideline

To help prioritise research recommendations and ensure that they are adequately promoted, the GDG should select a maximum of five recommendations to include in the NICE guideline. These should be the most important research recommendations, as defined by the criteria in table 11.5. These should be in the format of a question, with explanatory text, with an overall length of not more than 150 words (for an example, see box 11.3).

The five selected recommendations will be added to a database on the NICE website, and will go through a process for prioritising research recommendations from published NICE guidance. Any other evidence gaps in the guideline scope identified during the development of the guideline can be listed in the full version of the guideline.

Box 11.3 An example of a research question, from the referral guidelines for suspected cancer, developed by the NCC for Primary Care

Educational interventions

Would an educational intervention (for example, training in consulting skills, workshops on the features of cancer, a computerised decision support system) for primary healthcare professionals reduce the delays in identifying and referring patients with suspected cancer?

Why this is important

Cancer is a relatively uncommon diagnosis in primary care and it can be difficult to identify patients who may have cancer because they often present with non-specific symptoms or signs that also occur in common benign conditions. The early detection of cancer – one of the priorities for implementation of the cancer NSF – is crucial for the treatment to be successful, so early referral from primary care professionals should have an impact on cancer survival rates. Further research in primary care is urgently needed to generate a better evidence-base for the update of this guideline in 4 years' time.

11.4.3 Other research recommendations

Other important research recommendations lying outside the guideline scope should be communicated to research and development funders such as the National Coordinating Centre for Health Technology Assessment, the NHS Service Delivery and Organisation Programme or the Medical Research Council.

11.5 Further reading

Glasziou P, Del Mar C, Salisbury J. (2003). *Evidence-Based Medicine Workbook*. London: BMJ Books.

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.

National Institute for Clinical Excellence (2004). Research and Development Strategy. London: NICE www.nice.org.uk/page.aspx?o=114221 [accessed 3 March 2005]

12 Developing clinical audit criteria

Once guideline recommendations have been formulated, they can be used to develop clinical audit criteria for use in practice. An audit criterion can be defined as 'a systematically developed statement that can be used to assess the appropriateness of specific healthcare decisions, services and outcomes'³. Because audit criteria are essential implementation tools for monitoring the uptake and impact of guidelines they need to be clear and straightforward for organisations and professionals to use.

NICE has commissioned the Clinical Accountability, Service Planning and Evaluation (CASPE) Research Unit and Health Quality Service (HQS) to develop the audit criteria for all its guidance as part of its implementation strategy. CASPE will draft audit criteria for all guidelines for which stakeholder consultation starts on or after 1 April 2006.

A process document describing the key steps, processes and timing of developing the audit criteria is being prepared. This will state the objectives for the clinical audit; and give guidance on carrying out the clinical audit (such as which patients to include), deciding when to repeat it and how to compare results over time.

³ The definition is from: Committee on Clinical Practice Guidelines. Institute of Medicine. Field MJ, Lohr KN (1992) *Guidelines for clinical practice: from development to use*. Washington, DC: National Academy Press.

13 Writing the guideline

Following the process of guideline development, four separate documents are published: the full guideline, the NICE guideline, a quick-reference guide and the information for patients and carers. This chapter describes key principles for writing guidelines, and describes what each version should include. The NCC (with the GDG) writes the full and NICE guidelines; NICE editorial staff write the information for patients and carers and the quick reference guide, working with the NCC and GDG.

13.1 Principles for writing guidelines

13.1.1 Language and style

Key points to consider are highlighted here. NCCs should follow the NICE style guide when preparing the NICE guideline (the guide is available from the NCC guideline webboard).

The full version should be written in a style that can be understood by the non-specialist healthcare practitioner, or by someone who has a good knowledge of the area but is not a trained clinician (for example, a patient living with the condition who would have an in-depth knowledge of the disease and treatment options).

Paragraphs and headings should be used to make it easy for readers to navigate the document.

13.1.1.1 Bulleted lists

When listing items within a paragraph, 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.

13.1.1.2 Tables and figures

Tables need to be readily understood, and have a clear, informative title. Footnotes should be included only if they are essential for readers to understand the table. A table should not be used if it presents an inappropriate or inaccurate comparison. Comparisons 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. Tables or figures may be reproduced from another source only with written permission, usually from the publisher.

13.1.1.3 Abbreviations

Abbreviations should be used sparingly, and following the NICE 'Style guide' (available on the NCC webboard). If a term is used only a few times, it is usually appropriate to use the wording in full. However, if general readers will be more familiar with the abbreviation it may be used throughout the guideline

and defined at first use. The final guideline may be downloaded in sections, so abbreviations should be re-defined at the first use in each section. A list of abbreviations should be included if a lot are used.

13.1.1.4 Algorithm

The full guideline and NICE guideline should contain an algorithm (or algorithms). This is a flow chart of the clinical decision pathway described in the guideline, where decision points are represented with boxes, linked with arrows. The algorithm should be uncluttered; boxes should be limited to those defining the clinical problem and those representing a clear decision point. There should be few arrows and these should flow from top to bottom. A logical sequence should be maintained so that all decisions flow from the questions that precede them. 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 can be summarised in other ways, including tables, boxes and flowcharts showing the care pathway.

Algorithms and other summary charts should summarise recommendations, and not go beyond the key messages of the recommendations.

13.2 Guideline structure

13.2.1 The full guideline

The full guideline contains all the recommendations, plus details of the methods used and the underpinning evidence. The structure and format of the full guideline are at the discretion of the NCC, but core elements should be:

- a section containing all the recommendations and algorithm(s)
- introduction
 - responsibility and support for guideline development
 - funding
 - GDG membership
 - patient and carer involvement
 - epidemiological data
 - experience of those receiving care, or service use
 - outcomes
 - clinical issues
 - aim and scope of the guideline
- methods
 - literature-search strategy
 - sifting and reviewing the literature
 - synthesising the evidence
 - economic analysis
 - assigning levels to the evidence
 - areas without evidence and consensus methodology
 - forming recommendations
 - consultation
 - related guidance: details of related NICE technology appraisals or clinical guidelines that are published or in preparation

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- guideline recommendations
 - evidence statements
 - recommendations
 - scheduled review of the guideline
 - recommendations for research
- references
- clinical questions
- appendices, which may include:
 - evidence tables (preferably on a CD-ROM), see chapter 7
 - details of search strategies.

For examples of published guidelines, refer to the NICE website.

13.3 The NICE guideline

The NICE guideline presents the recommendations from the full version in a format focused on implementation by healthcare workers and by NHS bodies. The length of the NICE guideline will therefore depend on the number of recommendations in the full guideline. NCCs should use NICE's Word template when preparing this version. The most recent version of the NICE template and notes on how to use it are posted on the guidelines webboard for NCCs. The main information that NCCs need to add to the NICE guideline template is:

- a brief introduction explaining why the topic is important, and the key issues the guideline will address
- key priorities for implementation
- the recommendations
- brief details of the scope
- research recommendations, and an explanation of why each recommendation is important.

Background information should not usually be included with the recommendations in the NICE guideline. Occasionally, very brief summaries may be given if essential to understanding or implementing the recommendations.

The template includes a statement on patient-centred care, covering general issues such as informed consent, sharing information tailored to the patient's needs, and involving and supporting carers. Recommendations on these issues should not be included unless there are special reasons to do so.

The NICE guideline should include the algorithm(s) (see above). It may also include tables if these will help the reader.

The NICE editorial team comments on the NICE guideline during the consultation, and provides an edited version for the developers to use when revising the recommendations. The editors and developers may meet to discuss suggested changes during the consultation. The editors also edit the final draft, working closely with designated members of the NCC and GDG

(see section 14.3). The NCC is responsible for ensuring the wording of the recommendations in the full guideline matches the final NICE guideline.

13.4 Quick reference guide

The quick reference guide (QRG) presents recommendations in a format most useful to the end user, and is printed and distributed to clinicians and managers in the NHS. It generally contains all guideline recommendations, but may be tailored to specific audiences, with signposting to the NICE guideline for more details if needed.

The QRG is written by the NICE editorial team, working closely with designated members of the NCC and GDG. It may be based partly on the algorithms the NCC produces. General discussions on content and possible formats may begin early in the guideline development process, and a detailed brief is prepared during the consultation.

The QRG is written once the NCC has submitted the final draft of the guideline. There is a summary for guideline developers of the process for producing the QRG on the Guidelines webboard for NCCs.

13.5 Information for patients and carers

The information for patients and carers ('Understanding NICE guidance') is written during the consultation by a member of the NICE editorial team, working closely with the NCC and designated members of the GDG, and with the Patient and Public Involvement Programme. There is a summary for guideline developers of the process for producing the information for patients and carers on the guidelines webboard for NCCs.

The information for patients and carers summarises the recommendations in the NICE guideline in everyday language primarily for patients. It does not describe the condition or interventions in any more detail than is needed to understand the guidance. It aims to:

- help patients, their carers and families, and the wider public understand the recommendations in the guideline
- inform discussions between clinicians and patients, and help decision-making about the treatment and management of the condition.

It may be used by hospitals and other organisations in the NHS, and by patient and carer organisations, to develop their own information leaflets.

The information for patients and carers gives contact details or website addresses for relevant NHS organisations. Details may also be given for up to five national charities or other organisations that meet specific criteria.

14 Consultation and dealing with stakeholders' comments

Consultation with stakeholders is an integral part of the NICE guideline development process. Comments received from stakeholders are a vital part of the quality-assurance and peer-review processes, and it is important they are addressed appropriately. This chapter advises the NCCs on responding to stakeholder comments following consultation – the principles apply equally to comments received on the scope and draft guidelines. Information on what to expect during the consultation process is also included.

14.1 Principles of responding to stakeholders' comments

14.1.1 Format of comments

All comments received by NICE are entered into a comments table in a Word file, which is sent to the NCC to elicit responses from the GDG. The table contains the following information.

- Organisation – name of organisation that submitted the comments.
- Chapter/section – depending on the document that has been sent for consultation. This column can be sorted by the developers to facilitate the identification of comments by section.
- Comments – comments received from stakeholders, entered unchanged.
- Responses – blank column for developers to complete.

It is expected that most comments will be received from registered stakeholders. These comments, and the responses, are posted on the website once the relevant documents are published. Individuals or non-registered stakeholders may also comment on documents posted on the website. These comments are treated in the same way as comments from registered stakeholders, except that they are not published on the web. Comments from the GRPs and GDG reviewers are entered into similar tables, and should be responded to in a similar way.

14.1.2 How to respond

The following key points should be taken into account when responding to comments.

- 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 noted.
- If changes are made to the document, this must be made clear in the response. If no changes have been made, it should be clear why not.
- For comments made on draft guidelines:
 - responses and changes must be made with the agreement of the whole GDG, preferably through a meeting. This meeting needs to be arranged early in the process to ensure that GDG members will be available

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- any subsequent changes to guideline documents need to be reflected in both the NICE and full guidelines, and an audit trail of changes must be maintained.

Examples of responses to specific comments received in relation to the NICE guideline on schizophrenia are given in table 14.1.

Table 14.1 Examples of responses to stakeholder comments received on the NICE guideline for schizophrenia (NCC for Mental Health)

Type of comment	Example response
Compliments about the guideline	<ul style="list-style-type: none">• Thank you for your comments.
Specific change was recommended and has subsequently been made.	<ul style="list-style-type: none">• 4.4.5.2 sentence added.• 5.1.1 Electronics medicines compendium website added.• All corrections listed have been made.
A specific change was recommended and has subsequently been partially made.	<ul style="list-style-type: none">• Noted - partially amended.• This is a NICE technology appraisal recommendation and cannot be changed. However, we have included occupational assessment in 1.1.1.1 of the short form, 2.8 in the long form.
A specific change was recommended and has subsequently NOT been made.	<ul style="list-style-type: none">• The GDG is satisfied with the revised and prioritised audit criteria as they now stand, following consultation and appended to the long form. There is a balance between that which could be audited and services' capacity to do so.• We are seeking here to clarify terminology, and not to comment on mechanisms, which will not be addressed in the guideline.
Asks for something that is outside the scope of the guideline.	<ul style="list-style-type: none">• Thank you for drawing attention to this. We have noted your comments, but some aspects, e.g. diagnosis, remain outside the scope of the guideline.• This is very interesting and worth pursuing. However, as physical exercise is outside the scope of this guideline we are unable to make such a research recommendation.• Outside the scope of the guideline, and is currently covered by Mental Health Act legislation and guidance.

14.2 The consultation process

The production of different versions of the guideline means the consultation process, and dealing with subsequent comments, can be complex and lengthy. This section describes what to expect during the consultation phase on the draft versions of the guideline. Appendix L gives further information on the timescales for this process.

14.2.1 Consultation on the full and NICE versions

Draft versions of the full and NICE versions of the guideline are available on the website for the consultation and registered stakeholders are informed that the documents are available. The guideline may also be sent to expert peer reviewers identified by the NCC, and non-registered stakeholders may view the guideline versions on the NICE website. NICE encourages people, however, to comment through their registered organisation. Comments are also received from members of the GRP.

The GRP members send comments to NICE via the GRP Chair, aiming to ensure that:

- the guideline is clinically relevant
- any major areas of concern are identified
- the guideline contains realistic expectations for NHS service providers.

The Chair is expected to ensure that:

- all elements of the agreed scope have been addressed
- the guideline produces recommendations for the NHS only, and not for other bodies (for example, education, social care).

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

Once any changes have been agreed by the GDG in response to comments received, modifications need to be made to both the full version and the NICE guideline before returning the documents to NICE for the final sign-off. Any changes in the recommendations also need to be translated into the information for patients and carers. It is essential for developers to keep an audit trail of what changes have been made, where, by whom, and for what purpose.

14.2.2 External expert review

NCCs will be encouraged to consider arranging additional external expert advice for part or all of their guidelines. This may take place during guideline development or at the consultation stage. If during development, the process and comments should remain confidential, but the adviser should be named in the final guideline. If during consultation the comments will be treated as comments from non-registered stakeholders and will not be published. The names of such advisers will be published in the full guideline.

From 2006–07 NICE will commission in-depth expert statistical and health economic review of all guidelines through a third party. This will take place at the consultation stage. Comments will be treated as comments from non-registered stakeholders. Names of commissioned expert reviewers will be published only with their consent.

14.2.3 Signing off the guideline versions

Once the consultation has been completed and the comments have been addressed in the guideline versions (the full guideline, the NICE guideline),

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the documents are returned to NICE to be edited (see section 14.3) and signed off. The quick-reference guide and information for the patients and carers are not subject to consultation, and will be signed off by NICE.

14.2.3.1 The full guideline

The full guideline is signed off by NICE on advice from the GRP after the panel has reviewed the tables of comments and responses to the consultation. If there are any outstanding issues raised by the Chair at this point NICE will inform the NCC, indicating whether the guideline will be signed off in its present state or will need to be changed.

The NCC should respond to any issues raised by the Chair indicating how it will amend the document, or if it is not willing to make changes the NCC should provide a detailed explanation why not. This may lead to further dialogue between the NCC, the Director of the Centre for Clinical Practice and the GRP Chair. Any changes at this point again need to be translated into all the versions. The NCC should maintain an audit trail of changes made.

14.2.3.2 The NICE guideline

The NICE guideline is signed off by NICE's Guidance Executive. The sign off does not occur until the full guideline has been finally signed off by NICE.

14.2.3.3 Information for patients and carers

The information for patients and carers is written by NICE's editors (see section 14.3), working with designated members of the GDG and NCC. It is signed off by a representative from the PPIP and the Clinical Practice Programme Director or Associate Director, taking into account comments received during its development and the developers' responses.

14.2.3.4 Quick reference guide

The editors discuss the content and format of the quick reference guide with the NCC and GDG during the consultation process. They write the first draft of the quick reference guide after final draft of the guideline is delivered to NICE, and work with designated members of the GDG and NCC to ensure clinical accuracy. The final draft of the quick reference guide is signed off by NICE.

14.3 Editing and final checking before publication

The NICE editorial team will work with the NCC throughout the consultation period and sign off, and have a formal responsibility for NICE's publications – that is, the NICE guideline, the quick-reference guide and the information for patients and carers. The team will edit the 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.

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The editors will comment on the wording of recommendations during the consultation. When the final drafts of the full and NICE guideline are returned to NICE, they will:

- edit the NICE guideline
- draft the quick reference guide
- update the draft information for patients and carers in line with changes to the recommendations and advice from the developers.

The editors scan the full guideline, but do not do any detailed work on it.

The members of the NICE editorial team are experienced medical editors/writers, but will need advice from the guideline developers to ensure that the documents are clinically correct, and that the recommendations of the GDG are presented accurately. This will involve the NCC technical team and a clinical expert nominated by the GDG to act on their behalf – the ‘GDG reviewer’.

14.3.1 The GDG reviewer

Before the NICE documents are signed off, the editorial team will send the edited NICE guideline and latest drafts of the quick reference guide and information for patients and carers to the NCC for checking. The NCC should ensure that GDG reviewer sees the documents at this stage. The GDG reviewer has an important role in answering final queries on behalf of the group before publication, and must be prepared to respond rapidly if required. If other members of the GDG are acting as leads for the information for patients and carers, and the quick reference guide, they will also need to see the drafts at this stage. All comments from the NCC and GDG at this stage should be checked and collated before they are returned to the editors, and any conflicting views from the GDG resolved.

When reviewing the documents, the GDG reviewer(s) should read and aim to consider all of the text afresh. However, he or she should pay particular attention to:

- queries and comments from the editorial team (these will be highlighted in the text)
- dosages, units, normal ranges/abnormal cut-offs (for example, for electrolytes or blood constituents)
- consistency of the recommendations between the full guideline, NICE guideline, algorithm(s) and the information for patients and carers
- contact and reference details.

It is also vital that the GDG reviewer checks that the management pathways in the algorithm(s) are correct. The information for patients and carers will have been written in language that can be understood by a lay reader, and the GDG reviewer should check that this has not meant that inaccuracies or inappropriate generalisations have been introduced, and that the definitions and explanations of medical terms are correct.

It is important to check all the documents carefully at this stage as only essential changes can be made after sign-off.

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14.3.2 Sign-off and typesetting

When all changes have been agreed, the NCC is responsible for transferring changes in the recommendations into the full guidelines.

Once the guideline has been signed off, the editors will send the NICE guideline and the proofs of the information for patients and carers and quick reference guide for a final check by the developers. This check will need to be done quickly (usually within 48 hours), so the editors will give as much notice as possible of when to expect the proofs.

15 Updating guidelines and correcting errors

Guidelines developed by NICE are published with the expectation that they will be reviewed and updated. A study of guidelines in the US suggested that the majority are out of date in some important respect within 3 years of publication. The need for updates is a balance between reflecting changing evidence with the need for stability in guidance because frequent changes to guideline recommendations would make implementation difficult. This balance will vary between guidelines and so the process for updating needs to be flexible.

This chapter provides information on updating guidelines – when it is required and the processes involved. It also describes the process for correcting errors that are identified after publication.

15.1 Responsibility for updating

The responsibility for updating a guideline usually rests with the NCC that originally developed it. In exceptional circumstances, an NCC may be asked to update a guideline developed elsewhere, possibly because of capacity issues; this will only occur after consultation between the relevant NCCs and NICE.

15.2 Facilitating the updating process

Regardless of which group has responsibility for updating a guideline, the process will be facilitated if the NCC maintains clear records and obtains relevant post-publication information.

15.2.1 Maintaining clear records

The NCC should maintain careful records throughout the guideline development process to ensure that those responsible for the update will have access to the following information:

- details of the GDG
- search strategy details, including when the most recent search was conducted
- copies of papers used in guideline development
- data-extraction forms
- evidence tables
- minutes of GDG meetings.

15.2.2 Obtaining relevant post-publication information

The NCC should collect information relevant to the guideline. This includes any information that might affect the timing or content of subsequent updates, such as:

- copies of any queries or comments received following publication
- audit data, where a specific audit relating to the guideline has been initiated
- errors identified in the guidelines after publication.

In addition, one member of the GDG is retained with the task of keeping up to date with changes in the evidence, and advising the NCC of significant changes.

15.3 Triggers for updating

There are two main reasons for updating a particular guideline – new evidence emerges, or errors are found in the original guideline. Other changes that might affect all guidelines, such as a decision to change the format of guidelines, are not considered here.

15.3.1 Substantial new evidence emerges

This might be one single piece of evidence, an accumulation of relevant pieces of evidence, or other published NICE guidance sufficient to make it likely that one or more recommendations in the guideline needs changing in an important way. It is difficult to set exact criteria for what might be considered as the types of evidence that might prompt an update are diverse. For example, the important evidence might be a large randomised trial, evidence on important harms from observational studies, evidence on new diagnostic tests, changes in licensing or warnings issued by licensing agencies, or major changes in costs.

15.3.2 The original guideline needs important improvements

While we hope this would be rare, there may be errors in the original guideline, and it is important to have a mechanism to cope with the possibility.

15.4 Process for updates

This document describes a single process to respond to both types of trigger for an update.

15.4.1 Up to 2 years after publication

During this time, NICE and the NCC will not actively seek new evidence beyond collating post-publication comments, unless it was identified in the original guideline that important new information was likely to emerge during this period.

One member of the original GDG will take responsibility for advising the NCC if important new information has become available that might make recommendations out of date.

Evidence may also be submitted by researchers or other stakeholders, explaining why they consider any new information sufficient to require changing guideline recommendation(s). There is a risk that this could be used as a lobbying mechanism, but it would be difficult for a responsive system to avoid this risk.

The new information then needs to be considered for relevance and importance. First, the Director of the Centre for Clinical Practice will decide if the information is indeed new and potentially important.

The guidelines manual

We then propose a two-stage process.

- First, the need for an update will be discussed by the Centre for Clinical Practice and the relevant NCC at their next quarterly review meeting. The NCC will be notified in advance. If the new evidence has not come via the GDG member surveying the literature, the NCC will be expected to consult that GDG member about the need for an update.
- Next, if it is decided that an update is likely to be needed, the Centre for Clinical Practice will convene an expert advisory group consisting of invited external experts, representatives of NICE (Director or Associate Director of the Centre for Clinical Practice, relevant Guidelines Commissioning Manager, Health Economist, representative of NICE's Patient and Public Involvement Programme), and representatives of the NCC (GDG clinician, relevant NCC staff).

The expert advisory group will be asked to provide guidance on the following questions.

- Is the update necessary? (This question might not always be necessary if it is obvious in what respect a guideline is out of date. However, it might be a useful opportunity in most cases to check for other new evidence and to help plan the extent of the update required.)
- Are the group aware of other evidence (published, unpublished, or from ongoing studies) that might either affect the response to evidence, or require important changes in other recommendations?
- Which recommendations need to be reviewed in the light of new evidence?

Using the advice from the expert advisory group, the Director of the Clinical Practice Centre will then decide, with the NICE Guidance Executive, the need for an update, and commission the relevant NCC to do the work. Stakeholders will be informed at this point.

It is anticipated that most updates within 2 years of publication will affect only a small number of recommendations. The update will be undertaken by a 'mini-GDG' set up by the NCC. This will include some representatives from the original GDG, but its composition will be tailored to the requirements of the section(s) to be updated. The time needed to undertake the update and the validation process required will be negotiated with the NCC. The expectation will be that for most small updates, there will be one or two meetings of the mini-GDG to consider the new evidence and formulate new recommendations, a limited consultation period (4 weeks), and one meeting of the mini-GDG to consider stakeholder responses.

The reason for early updates is to be responsive to new evidence, so it is imperative that changes to recommendations are published quickly. NICE will work with NCCs to design a process that can move from availability of new evidence to publication within 6 months.

15.4.2 At 2 years after publication – review and optional update

The NCC will undertake searches for new evidence, using versions of the original search strategies modified to be precise rather than sensitive.

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However, it is difficult to set exact criteria for these searches as the types of evidence that might prompt an update are diverse. For this reason, it is proposed to supplement searches with expert consultation. This will be achieved by contacting the original GDG members where possible to comment on the presence of important new information.

New information would then be fed into the same process as described above to decide on the need for an update.

Changes to the scope would not normally be considered at this stage.

15.4.3 At 2 to 4 years after publication

During this time, the same arrangements apply as in the first 2 years after publication (section 15.4.1).

15.4.4 At 4 years after publication – review

At this stage, the process will be the same as at 2 years (section 15.4.2), except that changes to the scope could be considered. The decision whether to update will depend on the availability of new information, and there will be no commitment to update automatically after 4 years, as there is now. If it was decided not to update at 4 years, a timetable would be set for the guideline for future checks for new evidence.

The NCC and NICE will review the evidence and agree, in consultation with the Guidance Executive, whether the guideline requires:

- a complete update with a new scope
- a complete update using the existing scope
- an update of specific sections
- merging with other existing guidelines and updating of specific sections
- splitting into more than one guideline
- no update.

15.5 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, Morton SC, 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* 286:1509–11.