NICE National Institute for Health and Care Excellence

Process and methods guides

Developing NICE guidelines: the manual

http://www.nice.org.uk/article/pmg20

Published: 31 October 2014 last updated: 22 July 2015

Contents

1 Introduction and overview

The National Institute for Health and Care Excellence (NICE) is an independent public body that provides national guidance and advice to improve health and social care in England. NICE guidance offers evidence-based recommendations made by independent Committees on a broad range of topics. This manual explains the processes and methods used to develop and update NICE guidelines. For more information on the other types of NICE guidance and advice (including technology appraisal guidance), see About NICE on the NICE website.

1.1 NICE guidelines

NICE guidelines make evidence-based recommendations on a wide range of topics, from preventing and managing specific conditions, improving health, and managing medicines in different settings, to providing social care and support to adults and children, and planning broader services and interventions to improve the health of communities. They aim to promote individualised care and integrated care (for example, by covering transitions between children's and adult services and between health and social care).

Guideline recommendations set out:

- the care and services that are suitable for most people with a specific condition or need
- the care and services suitable for particular populations, groups or people in particular circumstances or settings (for example, when being discharged from hospital)
- ways to promote and protect good health or prevent ill health
- the configuration and provision of health and social care services, and/or
- how national and local public sector organisations and partnerships can improve the quality of care and services (for example, how the NHS and social care services work together).

Many guideline recommendations are for individual health and social care practitioners, who should use them in their work in conjunction with judgement and discussion with people using services. Some recommendations are for local authorities, commissioners and managers, and cover planning, commissioning and improving services; others are for providers (organisations providing services), schools, and local and national organisations and partnerships in the public, private and voluntary sectors. Guideline recommendations are also useful for people who use

health and social care services (including people who purchase their own social care), their families and carers, and organisations representing their interests.

In addition to the recommendations, guidelines also summarise the evidence behind the recommendations and explain how the recommendations were derived from the evidence.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive.

1.2 Information about this manual

This manual explains the processes and methods NICE uses for developing, maintaining and updating NICE guidelines. It is primarily for:

- NICE staff involved in developing guidelines
- NICE contractors (such as those doing evidence reviews, economic analysis and fieldwork)
- members of the Committees that develop the guidelines (see section 1.5).

It is also likely to be of interest to a broader audience, including other developers of guidance, stakeholders and users of NICE guidelines.

The processes and methods described in this manual are based on internationally recognised guideline development methodology, and the experience and expertise of the teams at NICE, the contractors that work with NICE, NICE Committee members and stakeholders. The processes and methods are based on internationally accepted criteria of quality, as detailed in the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument, and primary methodological research and evaluation undertaken by the NICE teams. They draw on the Guideline Implementability Appraisal tool to ensure that recommendations are clear and unambiguous, making them easier to implement. They are also designed to fulfil the requirements of theNICE accreditation scheme.

This manual describes the development of NICE guidelines from referral through to publication, implementation, checking the need for an update and updating. The guideline development

process is summarised in section 1.6. There is also information in chapter 12 on the support NICE provides to help organisations use each guideline.

This is the first edition of the manual that covers all NICE guidelines. Previously, guidelines were developed using 4 sets of processes and methods:

- The guidelines manual for clinical guidelines, including a slightly modified process for 'short' guidelines, Interim methods guide for developing service guidance and Interim clinical guideline surveillance process and methods guide and Interim process and methods guide for the clinical guideline updates using standing Committees pilot programme
- Methods for the development of NICE public health guidance and The NICE public health guidance development process for public health topics
- Interim methods guide for developing medicines practice guidelines, and Medicines practice guideline – Integrated process statement for medicines practice topics
- The social care guidelines manual for social care topics.

These manuals were based on the same over-arching core principles common to all NICE guidance. However, they had evolved to include some procedural and/or methodological differences, depending on the areas and the evidence base that they covered. This manual brings together methods and processes for developing guidelines on the whole range of topics, with the aim of achieving consistency of approach, and rationalising differences where appropriate. In some cases the best approach may vary depending on the topic; this manual gives alternatives and examples to help choose which approach to follow. Options should be considered from the outset, and the approach discussed and agreed with NICE staff with responsibility for quality assurance. The chosen approach should be documented in the evidence review or guideline, together with the rationale for the choice. The use of, and rationale for, the approach agreed for each guideline will also be documented by NICE staff with responsibility for quality assurance. Decisions will be reviewed for consistency. In exceptional circumstances, significant deviations from the methods and process described in this manual may be needed; in these cases, NICE's Senior Management Team must approve the approach before guideline development begins.

All guidelines produced using this manual are known as NICE guidelines. In the short-term the Interim methods guide for developing service guidance will stand. These interim methods will be incorporated in this manual at its next revision.

1.3 Choice of guideline topics

NICE guidelines are a key source for the development of NICE quality standards and therefore new guidelines developed by NICE are usually chosen from a library of topics for quality standards and then agreed with the relevant commissioning body (NHS England or the Department of Health).

Decisions on which library topics to develop guidelines on, and in what order, are based on factors such as:

- whether there is existing NICE-accredited guidance on which to base a quality standard that encompasses the whole of the topic
- the priority given to the topic by commissioners and professional organisations, and organisations for people using services, their families and carers.

A topic selection oversight group at NICE considers topics for guideline development, taking these factors into account. NICE then discusses topics identified in this way with NHS England, the Department of Health and Public Health England, and a prioritised list is agreed by these 3 bodies.

Topics are then formally referred to NICE and scheduled into NICE's guideline development plans.

1.4 Key principles for developing guidelines

NICE develops guidelines according to the same core principles we use for all our guidance:

- Guidance is based on the best available evidence of what works, and what it costs.
- Guidance is developed by independent and unbiased Committees of experts.
- All our Committees include at least 2 lay members (people with personal experience of using health or care services, or from a community affected by the guideline).
- Regular consultation allows organisations and individuals to comment on our recommendations.

- Once published, all NICE guidance is regularly checked, and updated in light of new evidence if necessary.
- We are committed to advancing equality of opportunity and ensuring that the social value judgements we make reflect the values of society.
- We ensure that our processes, methods and policies remain up-to-date.

NICE also considers dissemination and implementation when developing guidelines.

Using the best available evidence to develop recommendations

NICE guideline recommendations are based on the best available evidence. We use a wide range of different types of evidence and other information – from scientific research using a variety of methods, to testimony from practitioners and people using services.

Review questions guide the search for evidence, and the type of evidence that gives the best 'fit' depends on the type of question (see chapter 4). For example, a randomised controlled trial is often the most appropriate type of study to assess the efficacy or effectiveness (including cost effectiveness) of an intervention. However, other study designs (including observational, experimental or qualitative) may also be used to assess effectiveness, or aspects of effectiveness. These may include ways of delivering services, or the experience of people using services and how this contributes to outcomes. For some topics, there is little evidence from scientific studies, or the evidence is weak or contradictory. In these cases, we look for evidence from other sources to see if it concurs or differs ('triangulation').

Whatever evidence is used, it is selected and quality assessed using clear and appropriate methods (see chapters 5, 6 and 7).

Involving people affected by the guideline

When developing guidelines, NICE involves people who might be affected by the guideline recommendations in a collaborative and transparent way. This includes commissioners, practitioners and others involved in providing services. People using health and care services, carers and the public also contribute to ensure that guidelines address issues relevant to them, reflect their views, and meet their health and social care needs.

There are 2 main ways to get involved: organisations can register as a stakeholder and individuals can join (or advise) a Committee that works on guidelines. There is more information about stakeholders and Committee members in section 1.5 and in our guide for stakeholders and the public.

The Public Involvement Programme at NICE provides advice and support to Committees, Developers and NICE staff, about involving the public in developing NICE guidelines. A public involvement adviser is allocated to each topic.

Practitioners and people who use health and care services, family members, carers and the public may also be involved as:

- expert witnesses invited to give testimony to the Committee (see section 3.5)
- members of a reference group, focus group or other advisory group set up when standard involvement and consultation processes are insufficient (for example, when the topic covers a population group that is not part of the Committee, such as children or people with a learning disability; see section 10.1).

Advancing equality and making social value judgements

NICE is committed to ensuring that its guideline development process:

- fully meets duties under the Equality Act (2010) to have due regard to the need to eliminate discrimination, foster good relations and advance equality of opportunity in relation to people who share the protected characteristics of age, disability, gender reassignment, marriage and civil partnership, pregnancy and maternity, race, religion or belief, sex, and sexual orientation, including the public sector equality duty to tackle discrimination and provide equality of opportunity for all
- enables it to meet requirements under the Human Rights Act (1998).

A statement from NICE's Board summarises NICE's legal and other obligations and describes NICE's approach to meeting them, particularly the process of equality analysis. NICE uses this approach to consider not just equality in relation to groups sharing the characteristics protected by the Equality Act (2010) but also health inequalities arising from socioeconomic factors or associated with the shared circumstances, behaviours or conditions of particular groups (for example, looked-after children, people who are homeless, people who misuse drugs and people

in prison). Identification of such groups is an aspect of NICE's compliance with both general public law requirements to act fairly and reasonably, and human rights obligations.

NICE guidelines, and the procedures NICE uses to develop them, also take account of NICE's principles on social value judgements.

1.5 Who is involved

The Committee

The Committee is the independent advisory group that considers the evidence and develops the recommendations, taking into account the views of stakeholders. It may be a standing Committee working on many guideline topics, or a topic-specific Committee put together to work on a specific guideline (see chapter 3). Committee members include practitioners (both specialists in the topic and generalists), service or care providers or commissioners, and others working in the area covered by the guideline (see chapter 3). In addition, at least 2 members of every Committee are people using services, their family members or carers, or members of the public and community or voluntary sector with relevant experience (lay members).

If needed for a topic, the Committee can co-opt members with specific expertise to contribute to developing some of the recommendations (see sections 3.3 and 3.4).

Registered stakeholders

Registered stakeholders are organisations that have registered with NICE because they have an interest in the guideline topic, or they represent people whose practice or care may be directly affected by the guideline. They play an important role in developing and advocating for, or implementing, NICE guidelines. During guideline development NICE keeps registered stakeholders and the public informed of progress by email and by adding information to the guideline page on the NICE website. The schedule for the guideline, the scope and details of the Committee and teams involved are also available on the guideline page.

Stakeholder organisations are encouraged to get involved in guideline development in a range of ways. The NICE website explains how to register as a stakeholder and how to contribute to the development of a guideline. Registered stakeholders comment on the draft scope and draft guideline, may provide evidence, and support implementation of the guideline. NICE formally

responds to all comments from registered stakeholders, and these responses are published on the NICE website.

Stakeholders include:

- national organisations for people who use health and social care services, their families and carers, and the public
- local Healthwatch organisations and local organisations that have no national group to participate on their behalf
- national organisations that represent health and social care practitioners and other relevant professionals whose practice may be affected by the guideline, or who can influence uptake of the guideline recommendations
- public sector providers and commissioners of care or services
- private, voluntary sector and other independent providers of care or services
- companies that manufacture medicines, devices, equipment or adaptations, and commercial industries relevant to public health (excluding the tobacco industry)
- organisations that fund or carry out research
- Government departments and national statutory agencies
- overseas agencies with a remit covering England.

Individuals cannot register as stakeholders but NICE encourages anyone with an interest in the topic to express their views to a registered stakeholder listed on the guideline page on the NICE website. Although NICE will consider comments on the draft scope and guideline from individuals, we do not have the resources to respond to these comments.

Local or regional professional or practitioner groups, and local or regional groups for people who use health and social care services cannot register as stakeholders unless there is no national organisation that represents the group's specific interests.

NICE is established as an England-only body, and acknowledges that its guidelines are used in other countries in the UK. We want our guidelines to be useful in these countries, so encourage stakeholders from anywhere in the UK to take part in developing them.

Tobacco companies with an interest in a particular guideline topic can register to comment on the draft scope and the draft guideline. Their comments are carefully considered and are made public with those of registered stakeholders. However, the term 'respondent' rather than 'stakeholder' is used for a tobacco company to acknowledge NICE's commitment to Article 5.3 of the WHO Framework Convention on Tobacco Control. This sets out an obligation to protect the development of public health policy from any vested interests of the tobacco industry.

NICE staff and contractors who work with the Committee

The Committees are assisted by teams whose work covers quality assurance, guideline development, evidence review and support.

These teams are represented at Committee meetings and contribute to discussions. They are not Committee members, do not contribute to the quorum of the Committee or the development of recommendations during meetings, and do not hold voting rights.

Quality assurance by NICE

NICE staff carry out quality assurance of the guideline to ensure that the process has been followed appropriately, and that the methods are clear and transparent. This includes ensuring that the reviews of the evidence and any economic analysis are up-to-date, credible, robust and relevant. They also check that there is a valid link between the evidence and the recommendations. These staff may also be responsible for commissioning the Developer. Quality assurance takes place throughout guideline development; key tasks are referred to in relevant sections of this manual.

The **Centre Director** is responsible for ensuring that the guideline is produced in accordance with this manual. The Centre Director is also responsible for appointing the Committee Chair and Committee members.

The **Associate Director** is responsible for the development and quality assurance of the guideline (including the scope), and has delegated responsibility for approving the consultation draft and the final guideline, before approval by NICE's Guidance Executive. The Associate

Director also advises the Committee Chair and the Developer on matters of method and process. For some guidelines, guideline commissioners help them with this.

The **technical lead** is responsible for ensuring the technical quality of the non-economic evidence reviews. They also commission, coordinate and quality assure any fieldwork and quality assure any additional consultation with people affected by the guideline.

The **economic lead** is responsible for ensuring the technical quality of the economic evidence and any economic analysis.

Development

The **Developer** may be a team within NICE, or in an organisation contracted by NICE to develop guidelines. The Developer is responsible for scoping the guideline, supporting the Committee and writing the guideline in accordance with the Committee's discussions and decisions.

Administrators, **coordinators** and **project managers** provide administrative and management support to the Committee, planning and scheduling the work, arranging meetings, liaising with stakeholders and all individuals and organisations contributing to the development of guidelines.

Evidence review

The **evidence review team** (comprising an information specialist, systematic reviewer and for most guidelines an economist) identifies, reviews and summarises the evidence, and undertakes economic analyses. This team may be within NICE, or an organisation contracted by NICE.

The **information specialist** identifies relevant literature to answer the review questions (see chapter 5), creates databases to manage the search results and keeps a log of search results and strategies.

The **systematic reviewer** critically appraises the evidence, distils it into tables and writes brief summaries (evidence statements) for presentation to the Committee (see chapter 6). The reviewer also summarises the main issues with the evidence for the Committee and contributes to their discussions.

For most guidelines, an **economist** identifies potential economic issues in discussion with the Committee, summarises the published economic evidence and performs additional economic analyses as needed (see chapter 7).

Support

Staff from other NICE teams work on the guidelines at different stages. They may attend Committee meetings and comment on the guideline during consultation and at other times.

NICE communications team

The press team and communications lead support Committee members, the Developer, and NICE staff with responsibility for guideline quality assurance, on all aspects of communications, including contacts with the media and managing any issues, throughout guideline development and after publication.

Implementation team

The implementation team works with the Committee, and NICE staff carrying out quality assurance to produce information on implementation in the guideline. This identifies the most significant implementation challenges, and signposts support that can help organisations put guideline recommendations into practice.

In addition, implementation consultants and associates work with local organisations to promote the guideline.

NICE Public Involvement Programme

The Public Involvement Programme (PIP) advises on ways to effectively involve people who use health and care services, family members, carers and the public, and supports their participation in guideline development. PIP encourages organisations representing service user, carer and community interests to register as stakeholders. It also advertises for people using services, carers and the public to apply to join Committees and supports them in their roles as Committee members.

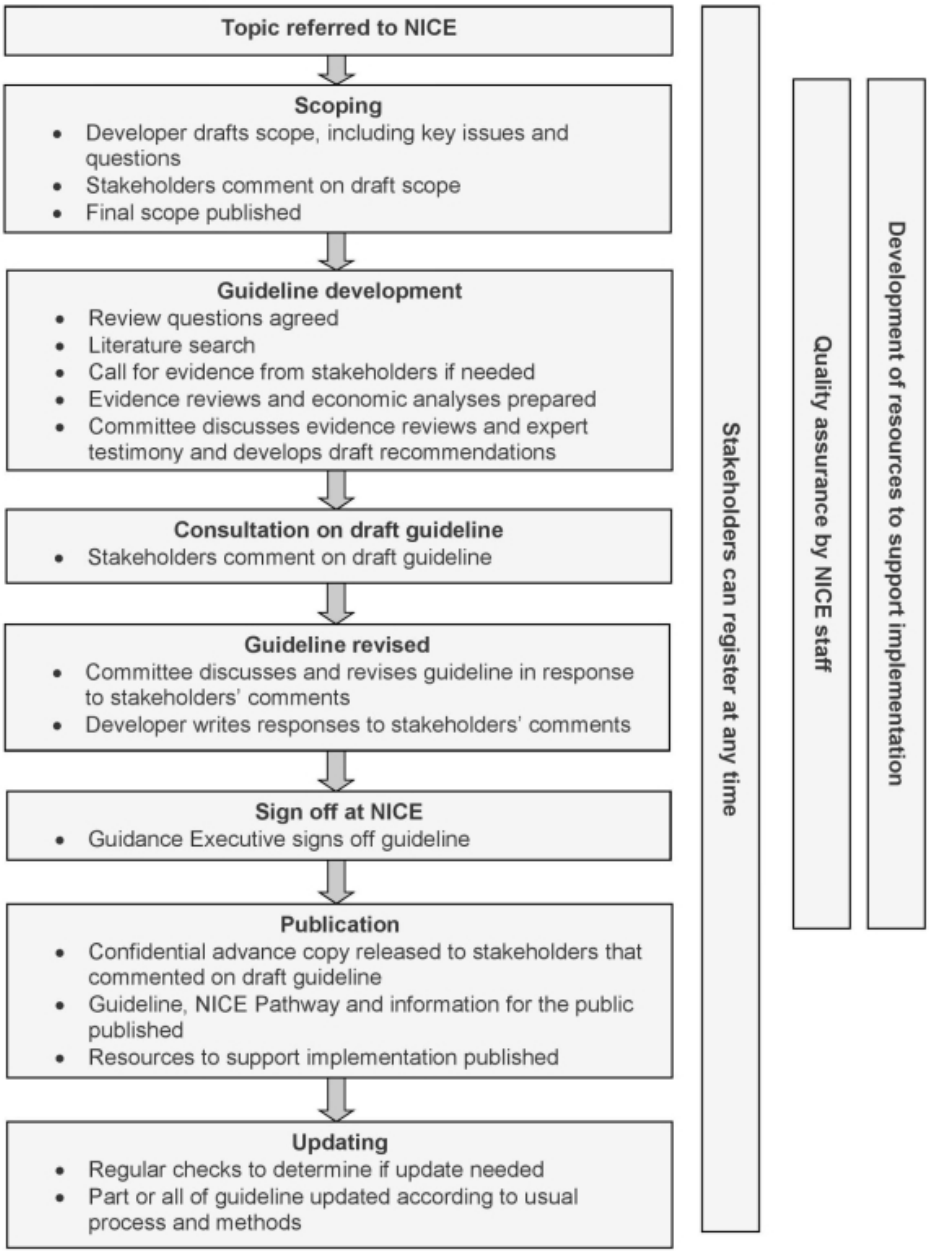
NICE publishing team

Editors from the publishing team work with the Committee, the Developer and NICE staff with responsibility for guideline quality assurance. They ensure that the guideline and related products (including the NICE pathway and information for the public) are written and presented in a way that is clear and accessible to a range of different audiences.

1.6 Main stages of guideline development

The development time for guidelines is usually between 12 and 27 months (from the start of scoping to publication), depending on the size and scope of the topic. Figure 1.1 summarises the main stages.

Figure 1.1 Stages of guideline development



1.7 Publication and implementation of the guideline

Guidelines are published on the NICE website in a range of formats (including information for the public) alongside the summarised evidence and resources to help users implement the guideline. In addition, the guideline is included in NICE Pathways – a practical, online resource bringing

together all NICE guidance and support resources on a topic, with links to implementation, related NICE guidance and other pathways.

Resources to help people put the guideline into practice include tools that help users assess what needs to change. These resources inform action planning or audit, estimate costs and savings to help build a business case, or meet the education and learning needs of practitioners (see chapter 12 for information about the support available to help implement guideline recommendations).

1.8 Updating this manual

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

When significant changes are made, there will be a stakeholder consultation. The updated manual will then be published, along with a list of changes from the previous version of the manual. Stakeholders involved in guidelines under development at the time of the change will be notified if they are affected by the change. Stakeholders of newly commissioned guidelines will be advised to consult the website at the start of the project to familiarise themselves with the updated manual.

We welcome comments on the content of this manual and suggested subjects for inclusion in the next update. These should be addressed to nice@nice.org.uk.

Interim updates

In some situations, it may be necessary to make small changes to the manual before a formal update is due. These may be either minor, insubstantial changes or more significant changes for which formal consultation with stakeholders is necessary. New methods may be piloted before formal consultation, to fully assess the implications before recommending changes. For small changes to be put in place without stakeholder consultation, they must fulfil all of the following criteria:

- no fundamental stage in the process is added or removed
- no fundamental method, technique or step is either added or removed

- no stakeholders will obviously be disadvantaged
- the efficiency, clarity or fairness of the process or methodology will be improved.

Changes that meet all of these criteria will be published on the NICE website. The manual will be updated, and changes from the previous version of the manual will be listed.

1.9 References and further reading

Craig P, Dieppe P, McIntyre S et al. on behalf of the MRC (2008) Developing and evaluating complex interventions: new guidance. London: Medical Research Council

Craig P, Cooper C, Gunnell D et al. on behalf of the MRC (2011) Using natural experiments to evaluate population health interventions: guidance for producers and users of evidence. London: Medical Research Council

Davidson K, Goldstein M, Kaplan RM et al. (2003) Evidence-based behavioral medicine: what it is and how do we achieve it? Annals of Behavioral Medicine 26: 161–71

Dixon-Woods M, Agarwal S, Young B et al. (2004) Integrative approaches to qualitative and quantitative evidence. London: Health Development Agency

Flay BR (1986) Efficacy and effectiveness trials (and other phases of research) in the development of health promotion programs. Preventive Medicine 15: 451–74

Graham H, Kelly MP (2004) Health inequalities: concepts, frameworks and policy. London: Health Development Agency

Kelly MP, Morgan A, Bonnefoy J et al. (2007) The social determinants of health: developing an evidence base for political action. Final report to the World Health Organization Commission on the Social Determinants of Health, from the Measurement and Evidence Knowledge Network. London: National Institute of Health and Clinical Excellence

Kelly MP, Stewart E, Morgan A et al. (2009) A conceptual framework for public health: NICE's emerging approach. Public Health 123: e14–20

Kelly MP, Morgan A, Ellis S et al. (2010) Evidence-based public health: A review of the experience of the National Institute of Health and Clinical Excellence (NICE) of developing public health guidance in England. Social Science and Medicine 71:1056–62

Lomas J, Culyer T, McCutcheon C et al. (2005) Conceptualizing and combining evidence for health system guidance: final report. Ottawa: Canadian Health Services Research Foundation

Michie S, Berentson-Shaw J, Pilling S et al. (2007) Turning evidence into recommendations: protocol for a study of guideline development group. Implementation Science 2: 29

Nutbeam D (1998) Evaluating health promotion – progress, problems and solutions. Health Promotion International 13: 27–44

Ogilvie D, Hamilton V, Egan M et al. (2005) Systematic reviews of health effects of social interventions: 1. Finding the evidence: how far should you go? Journal of Epidemiology and Community Health 59: 804–8

Ogilvie D, Egan M, Hamilton V et al. (2005) Systematic reviews of health effects of social interventions: 2. Best available evidence: how low should you go? Journal of Epidemiology and Community Health 59: 886–92

Pawson R (2006) Evidence-based policy: a realist perspective. London: Sage

Popay J, editor (2005) Moving beyond effectiveness in evidence synthesis: methodological issues in the synthesis of diverse sources of evidence. London: National Institute for Health and Clinical Excellence

Victora C, Habicht J, Bryce J (2004) Evidence-based public health: moving beyond randomized trials. American Journal of Public Health 94: 400–5

Weightman A, Ellis S, Cullum A et al. (2005) Grading evidence and recommendations for public health interventions: developing and piloting a framework. London: Health Development Agency

Weiss CH (1995) Nothing as practical as good theory: exploring theory-based evaluation for comprehensive community initiatives for children and families. In: Connell JP, Kubisch A, Schorr

LB et al., editors New approaches to evaluating community initiatives: concepts, methods and context. Washington DC: Aspen Institute

2 The scope

The scope sets out what a NICE guideline will and will not cover. Preparing the scope is the first step in developing a guideline. The scope is used to create a framework for the development work (see chapters 4 to 7).

This chapter describes the purpose of the scope, who is involved in developing the scope, the stages of scope development and amending the final scope after publication on the NICE website (in exceptional circumstances only).

2.1 Purpose of the scope

The scope sets boundaries that ensure the work stays within the referral and informs any relevant quality standard (see section 1.3). The scope:

- defines the population(s) and setting(s) that will and will not be covered
- describes what the guideline will consider
- identifies the key issues and lists the key questions that will be considered
- describes the economic perspective(s) to be used.

The draft scope will usually be based on:

- a brief description of the guideline topic (for example, a description of the condition or disease, health or social care services, organisation of services, or areas of public health practice)
- a brief overview of the context (current policy and practice) in which the guideline will be developed
- a summary of why the guideline is needed and where it will add value, including how the relationship between commissioners and providers may affect outcomes and costs
- how the guideline will link to other NICE recommendations and quality standards (published or in development)

- potential equality issues among groups sharing protected characteristics and how these will be considered
- health inequalities associated with socioeconomic factors and with inequities in access for certain groups to healthcare and social care, and opportunities to improve health.

The title of the guideline (as given in the scope) should accurately reflect the content of the scope and needs to be considered very carefully. Occasionally, it may be necessary when preparing the scope to seek clarification from the commissioning body (see section 1.3) on the referral (for example, to clarify how the NICE guideline will add value in relation to existing non-NICE guidance or to specify the boundaries and the extent of the work).

When recommendations in an existing guideline are being updated the scope of the existing guideline may be used. For more information, see chapter 13.

2.2 Who is involved in developing the scope

The draft scope is prepared by the Developer, with other input depending on the guideline topic. Topic-specific expertise may be provided by the Committee Chair and 1 or 2 other members of the Committee (if early appointment is appropriate) and the topic adviser if there is one (see section 3.4). Lay expertise may be provided by a lay person recruited specifically to support scope development, or a lay member of the Committee if early recruitment is appropriate.

A lead from NICE's Pathways team, NICE's Public Involvement Programme and implementation team should usually be involved, as well as the lead from NICE's quality standards team when there is a linked quality standard (see section 1.3). The evidence review team's information specialist, systematic reviewer and economist may also be involved. NICE staff with responsibility for quality assurance are also involved. The draft scope is signed off by a senior NICE staff member with responsibility for quality assurance.

2.3 Stages of scope development

The scope is developed in 7 stages:

- stage 1: the scoping search
- stage 2: understanding the context

- stage 3: identifying the population and key issues
- stage 4: planning the NICE Pathway
- stage 5: checking the population and selected key issues with stakeholders
- stage 6: consulting on the draft scope
- stage 7: finalising the scope after consultation.

Stage 1: the scoping search

To support scope development a scoping search is undertaken. The first step is to identify related NICE guidance. This is done by an information specialist at NICE and is updated if new issues are identified at a scoping workshop.

The search for other types of evidence to support scope development is undertaken by the Developer. This search may identify:

- guidance from other developers
- policy and legislation
- key systematic reviews and epidemiological reviews
- economic evaluations
- information on current practice, including costs and resource use and any safety concerns
- types of interventions that may be appropriate and their safety
- statistics (for example, on epidemiology), national prevalence data and data on the natural history of the condition
- information on the views and experiences of people using services, their family members or carers, or the public.

The search should not aim to be exhaustive. It should be based on the need to inform the development of the draft scope and the issues to be discussed at a scoping workshop (if this is held). The search should focus on identifying high-level information, such as reviews of the

evidence. If there is insufficient high-level information, the scoping search should be extended to a key database to identify relevant primary studies.

The sources searched should be informed by the topic, the type of questions the guideline will seek to address and the type(s) of evidence sought.

In some cases, a scoping search for economic evidence may be conducted (see section 7.4).

Appendix F provides a list of suggested sources for the scoping search.

For a guideline that is an update of existing NICE guidance, and for which the scope is being modified, the Developer can use any background information (including briefing papers and searches undertaken as part of the process for reaching an update decision) to inform the searches at the scoping stage. (See chapters 13 and 14 for information on updating guidelines).

More information on identifying evidence to support guideline development is provided in chapter 5.

Stage 2: understanding the context

In order to develop guidelines that identify and promote effective practice, it is important to understand current context. Context can include the reason for referral of the topic, burden of disease, the differential impact of disease or services and outcomes (in relation to socioeconomic factors or equity issues), how care is currently delivered and who is responsible for commissioning and providing it, the cost of care, workforce issues and variance in service organisation, use of interventions, legislative or regulatory frameworks, or user experience and safety concerns. Understanding the current context and how the guideline topic fits within this context will help to ensure that:

- the guideline focuses on achieving improvement in areas where it is most needed
- potential implementation issues are identified early and used to inform the guideline and relevant implementation activity/resources.

NICE's implementation team works with the Developer to support scoping, and prepare relevant contextual information. This information becomes an integral part of guideline development: it is developed iteratively alongside the guideline and is published as part of the final guideline.

Using a conceptual framework to construct a logic model

For some guidelines, it may be helpful to construct a topic-specific conceptual framework (see appendix A for an example).

The framework can be used to:

- help define the key issues involved in a broad topic area
- specify where more focused and clearly defined topics fit into the library of guideline topics developed so far by NICE.

Topics are mapped onto the vectors of causation outlined in the framework (population, environment, society and organisations) and cross-classified according to the potential level of intervention (population, community, organisation, family, domestic or individual).

The framework may also be used to construct a logic model (see appendix A for an example). This model should incorporate the assumed relationships between action and outcomes described in the conceptual framework.

Stage 3: identifying the population and key issues

Stage 3 includes identifying the population and considering the key issues for inclusion in the scope. These may have emerged during preliminary work, or may be identified by the scoping search, considering any health inequalities and impacts on equality, and consulting experts.

Identifying the population to be covered and the most important aspects of the topic to be covered by the guideline is critical because it determines the breadth and depth of the work. It ensures that the guideline focuses on areas in which providers and commissioners of care or services most need advice (for example, areas in which there is unacceptable variation in practice or uncertainty about best practice, areas of unsafe practice, uncertainty around the optimal service configuration, or where new evidence suggests current practice may not be optimal). The process should ensure that a range of care or services is considered, including key areas for quality improvement, and that the resulting guideline can be used to inform the development of a NICE quality standard.

Equality issues at the scoping stage

During development of the scope, it is important to consider and assess any equality issues to establish:

- whether there is any risk of unlawful discrimination arising from the guideline and any opportunities for advancing equality
- whether there might need to be reasonable adjustments to a recommendation to avoid putting any group of disabled people covered by the scope at a substantial disadvantage
- whether, and to what extent, particular equality issues should be included in the scope.

Considerations should be reflected in the equality impact assessment. The draft scope should set out the groups or issues that have been identified for specific consideration – including, when relevant, a statement to indicate that no groups or issues have been identified.

Identifying and prioritising key issues

Box 2.1 lists the criteria (including relevant equality issues) that should be considered when identifying and prioritising key issues, health inequalities and impacts on equality. At this stage, the Developer (in discussion with other teams) should also consider the composition of the Committee, and the approach to be taken when key population groups are excluded from Committee membership (for example, for topics covering children or people with a learning disability – see appendix B).

Box 2.1 Factors to consider when identifying and prioritising key issues for inclusion in the draft scope

Uncertainty or disagreement on best practice

Is there variation in current care provision and practice?

Is there variation in the level of integration of care and support for people using services or accessing care?

Is there evidence suggesting that common practice may not be best practice?

Is there debate in the literature?

Potential to improve outcomes or make better use of resources

How many people are affected and in which age groups or sectors of the population?

What is the potential for improved outcomes at acceptable cost?

What is the potential for reducing ineffective care?

What is the potential to provide care in a more efficient way (for example, through organisation of services to integrate care and support, or telecare)?

Are there safety concerns that need addressing?

What is the potential for achieving cost savings with acceptable outcomes?

Potential for avoiding unlawful discrimination, advancing equality and reducing health inequalities

Are there any health inequalities or impacts on equality?

Are there any specific access issues (for example, by population, geographical location or group sharing a protected characteristic)?

Are exclusions (for example, populations, interventions or settings, or groups sharing a protected characteristic) justified?

Have all relevant mental health issues been considered, including where topics focus on physical health problems?

Are there any specific issues for people with a learning disability?

Do inequalities in prevalence, access, outcomes or quality of care for any groups (particularly those sharing protected characteristics) need to be addressed by the scope?

In the cases of any group of disabled people, might there be a need to consider reasonable adjustments when making recommendations?

Likelihood that the guideline could contribute to change

Is a new review of the evidence or an economic evaluation likely to reduce existing uncertainties?

How does the guideline fit with existing legal frameworks, statutory and professional guidance or government policies, and what is its anticipated impact?

What is the potential for achieving consensus within the Committee and in the wider stakeholder community?

Other important factors

Will the guideline update or incorporate any recommendations in other published NICE guidance?

Will the guideline take into account other NICE guidance (for example, technology appraisal guidance)?

How does the topic relate to existing NICE Pathways?

Where is it proposed that the topic will fit into NICE Pathways?

Are there any particular issues about how the topic will be incorporated into NICE Pathways, or about how it should be presented in NICE Pathways?

Key issues and questions addressing these issues should be included in the scope. Depending on the type of guideline, whether it is an update (see chapter 14) and the type of question, these could be very high level or could more precisely describe the populations, interventions, or particular approaches and aspects of service delivery to be compared and the outcomes of interest (see chapter 4 and Interim methods guide for developing service guidance). These questions will be used as the basis for structured review questions (see chapter 4).

Examples of key issues and questions are shown in box 2.2.

Box 2.2 Examples of key issues and questions that could be included in draft scopes for consultation

Issues relating to services

Rehabilitation programmes to support people back to work

Integration of services to support people after a stroke

Key questions relating to services

What types of rehabilitation programmes should be provided to support people back to work?

What types of nurses and how many are needed to provide safe care in adult intensive care units?

How can services be organised to provide integrated and coordinated support to people after a stroke?

Issues relating to interventions

Training to assist foster carers in managing difficult behaviour

Pharmacological interventions to treat pneumonia

Identifying pregnant women who smoke

Key questions relating to interventions

What training should be provided to assist foster carers in managing difficult behaviour?

What antibiotics should be used and for how long when treating pneumonia?

What interventions (or types of interventions) are effective at identifying pregnant women who smoke?

Issue relating to experience of people using services

Information and support for people with epilepsy

Coordination and integration of support for people with learning disabilities

Key question relating to experience of people using services

What are the information and support needs of people with epilepsy, and how should these be met?

How does coordinated/integrated support (or the lack of it) affect the experience of people with learning disabilities?

Key question relating to health inequalities and equality

Are there population groups, including those sharing a protected characteristic, who may be affected by poor access to service or treatment?

The scope should include a section listing the main outcomes of interest to be used when considering the evidence. This need not be an exhaustive list, but should always include quality of life and some important condition- or service-specific outcomes that are important to people receiving care or using services or those providing care or services. Core outcome sets may be used where appropriate; one source is the COMET database. It is also likely to include capability, functioning, effectiveness, cost effectiveness, resource use and safety. It is also desirable to specify any negative effects of different approaches such as adverse effects of treatment, or aspects of service delivery considered in the guideline (see also Interim methods guide for developing service guidance).

Stage 4: planning the NICE Pathway

Identifying related NICE guidance (both published and in development) is a key element of scoping. This helps to see where and how the guideline recommendations are likely to relate to existing recommendations in other guidance and where they may fit into NICE Pathways.

This process should aim to identify any areas of potential overlap and gaps where new recommendations would be of value, and to inform stakeholders of the range of published NICE guidance relevant to the topic.

While the draft scope is being developed, the publishing team at NICE begins to consider how the new NICE guideline will be incorporated into NICE Pathways and the likely links between the areas covered by the new guideline and other parts of NICE Pathways. A pathway outline is developed in collaboration with the Developer and should support the development of the scope. It is based on the information available from the scoping search and comments from registered stakeholders on the draft scope and the final scope. The pathway outline is reviewed and amended as necessary throughout guideline development to take account of the recommendations developed.

Stage 5: checking the population and selected key issues with stakeholders

It is important to seek the views of stakeholders to confirm that the population group(s) and key issues identified by the Developer are relevant and appropriate. This includes organisations led by people using services, and organisations that represent the interests of people with the condition or people using services and their family members or carers, or the public.

For some guidelines, registered stakeholders (see section 1.5) may be invited to a scoping workshop to talk about the key issues in the scope, and discuss any other aspects as needed. A workshop may be held if the referral is in a new area, there is a new audience for NICE guidelines or a guideline topic or an area of practice has unique complexities. Following discussions with the Developer, NICE staff with responsibility for quality assurance decide whether, and when, to hold a scoping workshop, and document the rationale for the decision. They also arrange the workshop.

The workshop is usually held before the consultation on the draft scope, but may be held during or after the consultation period. Attendance is usually limited to 1 person from each registered stakeholder organisation. In some circumstances, an organisation can nominate more than 1 person (for example, if it represents the views of both practitioners and people using services) if space permits.

If there are large numbers of stakeholders, it may not be practical for all registered stakeholders to attend. NICE may specify groups or roles of stakeholders who are needed to attend. The aim of the workshop is to include as wide a range of views as possible.

People attending the workshop should bring as wide a perspective of relevant views as possible. Attendees, including representatives of relevant service user, carer and community organisations, should have specific knowledge of, or experience in, the topic area.

The scoping workshop, if held, is in addition to the formal consultation on the draft scope. Stakeholder organisations with representatives attending the scoping workshop are also encouraged to submit comments in writing as part of the scope consultation. Depending on the needs of stakeholder groups, virtual workshops, such as webinars, may be held in place of face-to-face workshops.

The scoping workshop is chaired by a senior member of NICE staff with responsibility for guideline quality assurance.

The objectives of the scoping workshop may include:

- obtaining feedback on the selected key issues, including any important considerations for implementation

- identifying contextual issues, such as national policy or areas of care in which there is known variation in service provision
- obtaining views on what should be included and what should be excluded (for example, populations, settings, interventions)
- identifying which people using services or population subgroups should be specified for particular consideration (if any)
- considering existing NICE recommendations and how the planned guideline relates to them
- seeking views on the composition of the Committee (see section 3.1)
- encouraging applications for Committee membership.

People attending the scoping workshop are sent the initial draft of the scope, which is intended as a starting point for discussion.

At the workshop, NICE staff with responsibility for quality assurance, the Developer and other teams provide details about:

- the scope
- the timetable and process for guideline development
- the nature of stakeholder input into the guideline (including the involvement of people using services, family members and carers).

For some guidelines they will also provide details about the processes for recruiting Committee members (see chapter 3).

This is followed by a structured discussion of the key issues. The discussions and key themes that emerge from the scoping workshop are summarised by the Developer. The summary includes a list of organisations represented at the scoping workshop. When the scoping workshop is held before consultation, this summary is posted on the NICE website during consultation on the scope, along with the initial draft of the scope that was discussed during the meeting. When the scoping workshop is held during consultation, the summary is posted on the NICE website with the final scope.

For some topics, additional meetings or specific discussions with key stakeholders may be needed. However, this is exceptional and the reasons will be documented in the guideline.

If a scoping workshop has been held, the Developer (with input from other teams) considers the issues raised and refines the scope after the workshop.

Equality impact assessment

Before the draft scope is signed off for consultation, an equality impact assessment is completed by the Developer and the Committee Chair to show which equality issues have been identified and considered during scoping, and to provide assurance that risks of adverse impacts on equality of any exclusions from the scope have been assessed and can be justified. The equality impact assessment is signed off by a member of NICE staff with responsibly for quality assurance, and published on the NICE website with the draft scope. The assessment is updated by the Developer and the Committee Chair after the scope consultation.

Stage 6: consulting on the draft scope

The draft scope is signed off for consultation by a senior member of NICE staff with responsibility for quality assurance. It is posted on the NICE website for a 4-week consultation, and registered stakeholders and respondents are notified. Information and prompts to support stakeholder and respondent input are posted with the draft scope. The purpose of these prompts is to seek their views on key issues (such as whether the identified outcome measures are complementary to locally defined measures) and to ask what should be included or excluded.

Comments are invited from registered stakeholders and respondents. In particular circumstances, comments will also be solicited from the relevant regulatory organisation; for example, the Medicines and Healthcare products Regulatory Agency (MHRA), when the off-label use of medicines is likely to be considered within the guideline, or when advice is required on regulations related to medicines.

Registered stakeholders and respondents comment on the draft scope (and later on the draft guideline and evidence; see section 10.1). When registering, and when commenting on the draft scope and draft guideline, stakeholders are asked to disclose whether their organisation has any direct or indirect links to, or receives or has ever received funding from, the tobacco industry. Disclosures will be included with the published consultation responses.

The Developer, NICE's Public Involvement Programme and implementation team (see section 1.5) routinely review the list of registered stakeholders to check whether any key organisations are missing. Registered stakeholders are also encouraged to identify potential stakeholders who are not registered.

Stage 7: finalising the scope after consultation

Dealing with stakeholder comments

After consultation, the Developer finalises the scope in line with the comments received and the referral for the guideline.

Sometimes registered stakeholders ask for the scope of a guideline to be broadened (for example, to include additional aspects of care, an additional population, a wider age range or an additional setting). The extra work could make the development of the guideline unmanageable within the time permitted. Therefore, the overall workload needs to be considered before the scope is expanded, but suggestions that might improve care or services should not be ignored. This may mean removing other 'lower-priority' areas, in consultation with the lead for any related quality standards.

If the Developer considers that a request to expand the scope would mean the guideline could not be completed on schedule, this should be discussed with the NICE Centre Director. Suggestions that are clearly outside the original referral should not be included.

All comments from registered stakeholders, and the actions taken by the Developer and NICE in response to each comment, are clearly documented by the Developer in a 'scope consultation table'. This is published on the NICE website with the final scope. The process for responding to comments from registered stakeholders should follow the principles described in section 10.2.

Signing off the final scope

The final scope is signed off by a senior member of NICE staff with responsibility for quality assurance. Once the final scope has been published no changes should be made to it except in exceptional circumstances.

The final scope, the scope consultation table with comments from registered stakeholders and responses to these comments, and the equality impact assessment are posted on the NICE website.

2.4 Amending the final scope after publication on the NICE website

In exceptional circumstances, the final scope may need amending after it has been signed off and posted on the NICE website. For example, amendments may be needed in the light of policy changes, the withdrawal of a medicine, or inclusion of a NICE technology appraisal in development (see section 8.1). The decision on whether to amend the scope is made by a senior member of NICE staff with responsibility for quality assurance, based on advice from the Committee or Developer as appropriate.

If a final scope is amended after publication, registered stakeholders are informed and the revised scope is published on the NICE website. No further consultation on the scope would usually be expected.

2.5 References and further reading

Kelly MP, Stewart E, Morgan A et al. (2009) A conceptual framework for public health: NICE's emerging approach. Public Health 123: e14–20

Kelly MP, Morgan A, Ellis S et al. (2010) Evidence-based public health: A review of the experience of the National Institute of Health and Clinical Excellence (NICE) of developing public health guidance in England. Social Science and Medicine 71: 1056–62

Pawson R (2006) Evidence-based policy: a realist perspective. London: Sage

US Centers for Disease Control and Prevention (2005) The guide to community preventive services: what works to promote health? Atlanta: US Centers for Disease Control and Prevention

Weiss CH (1995) Nothing as practical as good theory: exploring theory-based evaluation for comprehensive community initiatives for children and families. In: Connell JP, Kubisch A, Schorr LB et al., editors New approaches to evaluating community initiatives: concepts, methods and context. Washington DC: Aspen Institute

3 Decision-making Committees

3.1 Introduction

This chapter describes the different types of decision-making Committees, the training of Committee members, the general principles of Committee meetings and how Committees make group decisions.

A decision-making Committee (either a standing Committee or a topic-specific Committee) draws on its expertise to develop recommendations in the areas defined by the guideline scope. Convening an effective Committee is therefore one of the most important stages in producing a NICE guideline. The Committee:

- may refine and agree the review questions to be addressed by the evidence reviews (for example, when topic-specific input is needed to further define outcomes or specify appropriate comparators) as defined in the scope
- may advise on developing the review protocol and alternative analyses
- considers the evidence
- develops the recommendations
- considers factors that may help or hinder implementation ('levers and barriers')
- advises on implementation support that may be needed.

Therefore the Committee needs to be multidisciplinary and include:

- practitioners (specialists and generalists, and/or academics)
- lay members (people using services, family members and carers, and members of the public and community or voluntary sector with relevant experience).

Committee members are selected for their knowledge and experience, and do not represent their organisation(s). Lay members should be willing to reflect the experiences of a wide range of people affected by the guideline rather than basing their views solely on personal experience. All Committee members are independent of NICE.

In most cases, organisations with a direct commercial interest in interventions or services are not represented on the Committee because of potential conflicts of interest, but they contribute to guideline development as registered stakeholders. However, there may be situations in which members of such organisations are included to ensure that this perspective is represented. For example, when guidelines are likely to cover systems and processes relevant to the pharmaceutical or medical devices industries, the Committee may include members of the Association of the British Pharmaceutical Association (ABPI).

The exact composition of the Committee is tailored to the guideline topic and is agreed by the Developer and NICE staff with a role in guideline quality assurance. Developers should ensure that all Committees can comprehensively consider mental health aspects of guideline topics (Royal College of Psychiatrists 2013). Members with expertise in service transformation, change management or implementation science are actively recruited to support the Committee in considering implementation issues throughout guideline development.

For some guideline topics, it may be important for the Committee to include other types of expert (for example, an epidemiologist, researcher, statistician or economist with specialist knowledge). Members with experience of integrating delivery of services across service areas may also be recruited, particularly where the development of a guideline requires more flexibility than conventional organisational boundaries permit. If the guideline contains recommendations about services, Committee members are needed with a commissioning or provider background, in addition to members from relevant professional or practitioner networks or local authorities.

As far as possible, the Committee should aim for diversity in membership, an objective of NICE's equality policy. Equality and anti-discrimination considerations are reflected at every stage of recruitment.

Ideally, Committee members are drawn from different parts of England, but this depends on the expertise available and does not exclude anyone from any other country in the UK.

All Committee members, including practitioner, provider, commissioner and lay members, have equal status, acknowledging the importance of the expertise and experience that each member brings to the Committee.

The Committee may also be supported by expert witnesses who are invited for discussion of specific areas only (see section 3.5). Expert witnesses do not have voting rights.

3.2 Forming the Committee

The Committee can be formed in 2 ways:

- from members of a NICE standing Committee, with additional recruitment of topic expert members
- from multidisciplinary recruitment of all Committee members (topic-specific Committee).

The resulting Committee should, as far as practically possible, reflect the range of stakeholders and groups whose activities, services or care will be covered by the guideline. The type of Committee chosen is likely to reflect the nature of the work.

When it is not possible to recruit people affected by the guideline as lay Committee members (for example, when the guideline covers children), other approaches are needed to ensure that their views and experiences are incorporated. Depending on the review questions, the evidence base, and the age of people affected by the guideline, these might include working with an external agency to obtain expert testimony or user views on specific questions, or consulting with a reference group of people using services, at key stages of guideline development. It could involve testing selected draft recommendations with people affected by the guideline (see section 10.1). For all guidelines covering children and young people and those focusing on people with a learning disability or cognitive impairment, the Developer should consider how to involve people affected by the guideline when they begin work on the topic, and should reflect this in its plans. (See appendix B and the section on involving children and young people in NICE's patient and public involvement policy.) If other approaches to engaging people affected by the guideline are needed, the Developer should document the rationale, together with a proposal for the work, including possible methods to be used, and the anticipated costs. The proposal should be discussed and agreed with members of NICE staff with a quality assurance role, and approved by the Centre Director. Where the work is approved, the rationale and methods should be documented in the guideline.

All Committee members are recruited in accordance with NICE's policy and procedure for recruitment and selection to advisory bodies and topic expert groups. Positions are advertised on the NICE website and other appropriate places (for example, NICE Twitter, social media and websites of stakeholders, Medical Royal Colleges and professional organisations), and relevant stakeholders are notified. Candidates are required to submit a declaration of interests, curriculum vitae (CV) and covering letter, or application form in the case of lay members.

The Committee Chair

The Chair guides the Committee in terms of task (developing the guideline, focusing on any referral, the scope and timescale) and process (how the group works). The Chair helps the Committee to work collaboratively, ensures a balanced contribution from all Committee members, and is mindful that some members may need support to ensure full participation.

The Chair is appointed for their expertise and skill in chairing groups, and although they may have some knowledge of the topic, this is not their primary role in the group. Specialist knowledge is provided by other Committee members, including in some cases a topic adviser (see section 3.4).

The Chair ensures adherence to NICE's equality policy and that the Committee takes account of NICE's principles on social value judgements. The Chair and a senior member of the Developer's team consider any potential conflicts of interest of Committee members. The Chair also ensures that the guideline recommendations reflect the evidence and the Committee's considerations. The Chair may be appointed before guideline scoping and may contribute to early development of the scope. NICE has some standing Chairs who may be appointed to chair more than 1 topic-specific Committee (see section 3.4). More details on the role of the Chair can be found in the Terms of Reference and Standing Orders (see appendix D).

3.3 Standing Committees

NICE has multiple standing Committees in operation at any one time. Some guideline topics are allocated to a standing Committee before scoping.

Standing Committees usually include between 12 and 18 members (both practitioner and lay members). The size of the Committee depends on the complexity and breadth of the guideline. Some members are generalists (core members) and some have specialist expertise (topic expert members). Each standing Committee consists of:

- a Chair
- core members
- topic expert members.

Additional members with specialist knowledge may also be co-opted to the Committee for 1 or more meetings to provide expert input. Unlike expert witnesses, co-opted Committee members contribute to the development of recommendations. However, they do not have voting rights and do not count towards the quorum.

More details on the role of Committee members can be found in the Terms of Reference and Standing Orders (see appendix D).

Core members of standing Committees

The number of core members of a standing Committee depends on the complexity and breadth of the guideline programme, but is usually between 6 and 12. This number allows members to contribute effectively to discussions while including a broad range of experience and knowledge. Core members should include at least 1 practitioner member.

Some core members will have experience of commissioning or implementing interventions, services or care at regional and local levels. Others will have specific expertise in assessing the quality of the evidence presented to the Committee, and in its interpretation.

Core members should include at least 1 lay member. Lay members help ensure that the Committee's recommendations are relevant to specific groups or to the general public. They also help to identify where the recommendations should acknowledge general or specific preferences and choice by people using services, family members and carers, or members of the wider public.

Core members of a standing Committee are appointed to a single Committee for a 3-year term in the first instance.

Topic expert members of standing Committees

When a new guideline is allocated to a standing Committee, the core members of the Committee are complemented by topic expert members. They have specialist knowledge of the topic and may include providers, commissioners and practitioners, and should include at least 1 lay member. The lay member either has direct experience of the topic or is a member of a relevant organisation or support group. The number of topic expert members varies but should be no more than half of the total number of Committee members.

Topic expert members are usually recruited for a specific guideline, but may be appointed for up to 3 years, at the discretion of NICE, so that they can work on subsequent related guidelines. This might mean they move between standing Committees during their term, depending on the guidelines being produced. All members are eligible for reappointment after 3 years.

The process of appointing topic expert members is completed at least 6 weeks before the first Committee meeting for the guideline. Topic expert members are full members of the Committee, with voting rights. They join in discussions, contribute to the formulation of recommendations and count towards the quorum.

3.4 Topic-specific Committees

Usually the Chair and members of a topic-specific Committee are appointed for the development of a particular guideline. But NICE does have some standing Chairs who may be appointed to chair more than 1 topic-specific Committee. The Chair, the topic adviser (if there is one) and possibly 1 or 2 other Committee members are likely to be appointed before guideline scoping and contribute to the development of the scope (see chapter 2).

The final composition of a topic-specific Committee is agreed during scoping by the Developer and NICE staff with a role in guideline quality assurance. The Committee usually comprises between 13 and 15 members. This number allows members to contribute effectively to discussions while including a broad range of experience and knowledge. Occasionally when the topic is very broad, a larger Committee may be convened. A topic-specific Committee is made up of:

- a Chair
- a topic adviser (not all topic-specific Committees have topic advisers)
- practitioner and professional members, providers and commissioners
- at least 2 lay members (people using services, family members and carers, and members of the public, community or voluntary sector with relevant experience).

Additional members may also be co-opted to the Committee for 1 or more meetings to provide expert input to support the development of recommendations. Co-opted members do not have voting rights and do not count towards the quorum.

The topic adviser of a topic-specific Committee

A topic adviser with specialist knowledge may be appointed to a topic-specific Committee (for example, when the Committee Chair does not have topic expertise). The topic adviser is a member of the Committee but also supports the Developer. The topic adviser contributes to the development of the scope (see chapter 2) and is therefore appointed before scoping work starts.

The topic adviser's exact responsibilities depend on the guideline and the expert input needed. Responsibilities may include working with the systematic reviewer on the evidence reviews (if topic-specific knowledge is needed), or checking the guideline to ensure that the terminology and language are correct. If no topic adviser is appointed for a guideline, the Committee Chair undertakes these responsibilities.

Practitioner and professional members of topic-specific Committees

Practitioner and professional members of a topic-specific Committee may be recruited before the scope is finalised (see section 2.2). They should reflect the views and experiences of practitioners, professionals, providers and commissioners working in the area covered by the guideline.

Practitioner and professional Committee members have appropriate knowledge and skills; detailed research expertise is not necessary, although an understanding of evidence-based practice is essential and some experience of service transformation or delivering integrated services across boundaries is desirable. Practitioner and professional members contribute their own views to the Committee and do not represent the views of their professional organisations.

A topic-specific Committee usually includes between 9 and 11 practitioner or professional members (occasionally when the topic is very broad, more members may be recruited). The spread of interest and experience of practitioner and professional members is agreed between the Developer and members of NICE staff with responsibility for guideline quality assurance.

Lay members of topic-specific Committees

All Committees have at least 2 lay members with experience or knowledge of issues that are important to people using services, family members and carers, and the community affected by the guideline. This helps to ensure that the guideline is relevant to people affected by the recommendations and acknowledges general or specific preferences and choice.

Lay members usually have direct experience of the condition, services or topic being covered by the guideline – as a patient, service user, carer or family member, or as a member or an officer of a lay stakeholder organisation or support group. However, they do not represent the views of any particular organisation.

3.5 Other attendees at Committee meetings

Expert witnesses

If the Committee does not have sufficient evidence to make recommendations in a particular area (for example, if there are gaps in the evidence base or subgroups are under-represented), it may call on external experts (expert witnesses) who can provide additional evidence from their experience and specific expertise, and help the Committee to consider and interpret the evidence.

Once the Committee has established that it needs evidence in a particular area from an expert witness, Committee members and NICE's Public Involvement Programme are asked by the Developer to nominate experts who might fulfil this role. Expert witnesses may also be identified by the Developer or NICE staff with a quality assurance role, or if required, by active recruitment through stakeholder organisations and the NICE website. Experts may be drawn from a wide range of areas as appropriate, including government and policy, research, practice, people using services and carers, or the community and voluntary sector.

Expert witnesses attending a Committee meeting are invited to answer questions from members of the Committee. They may be invited to present their evidence at a Committee meeting in the form of expert testimony based on a written paper. The written expert testimony paper may be shared with the Committee before the meeting or the paper may be submitted by the expert after the meeting. Sometimes the Developer writes up the expert testimony and agrees this with the witness after the meeting. Expert testimony papers are posted on the NICE website with other sources of evidence when the guideline is published.

Expert witnesses are not members of the Committee; they do not have voting rights, and they should not be involved in the final decisions or influence the wording of recommendations.

Committee support roles

The Committee is assisted by a range of people, who have a role in:

- quality assurance
- development
- evidence review
- support.

These are technical and project management staff from the evidence review team, Developer and/or NICE staff with a quality assurance role. Other NICE staff (such as editors and members of the implementation team) also attend some meetings. They are not Committee members and do not have voting rights at Committee meetings.

Public access to meetings

Enabling public access to advisory body meetings is part of NICE's commitment to openness and transparency. It enables stakeholders and the public to better understand how evidence is assessed and interpreted, how consultation comments are taken into account and how recommendations are formulated. Logistic and resulting financial pressures prevent NICE from enabling public access to all guideline Committee meetings. Standing Committee meetings are usually held in public; topic-specific Committee meetings are held in private. Public access to standing Committee meetings is arranged according to the NICE policy (see appendix D).

To promote public access to standing Committee meetings, NICE publishes a notice with a draft agenda, alongside details of how the meeting can be accessed, on its website in advance of the meeting.

Standing Committee meetings may be held entirely in public or split into 2 parts: part 1 with the public having access and part 2 (a closed session) with no public access. A closed session may be needed if, for example, expert evidence involves the disclosure of a person's health problems, or the consideration of national policy that has not been agreed by ministers, or if the drafting of recommendations might affect commercial interests. On rare occasions a standing Committee meeting may be entirely closed. The decision to hold a closed session is made by the Committee Chair and the NICE Centre Director responsible for the guideline.

3.6 Code of conduct and declaration of interests

Declaring interests

All Committee members and anyone who has direct input into the guideline (including the Developer, the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. For Committee members, this happens on application for Committee membership. Any relevant interests, or changes to interests, should also be declared publicly at the start of each Committee meeting. Before each meeting, any potential conflicts of interest are considered by the Committee Chair and a senior member of the Developer's team. Any decisions to exclude a person from all or part of a meeting should be documented. Any changes to a member's declaration of interests should be recorded in the minutes of the meeting. Declarations of interests are published with the final guideline.

Code of conduct and confidentiality

NICE has developed a code of conduct (appendix E) for Committee members, which sets out the responsibilities of NICE and the Committee, and the principles of transparency and confidentiality.

Everyone who sees documents containing confidential information or who is party to part 2 (closed session) discussions about a guideline before public consultation must sign a confidentiality agreement before becoming involved.

If Committee members are asked by external parties – including stakeholders, their professional organisation or the media – to provide information about the work of the Committee, they should contact the Developer for advice.

Terms of Reference for Committees

Details of the role of Committee members, and the procedural rules for managing the work of Committees, can be found in the Terms of Reference and Standing Orders for Committees (see appendix D).

All Committee members should be committed to developing NICE guidelines according to NICE's methods and processes, and to working within NICE's equality policy.

New members, with the exception of co-opted members, should not usually be added to the Committee after the first meeting, because this may disturb the group dynamic. However, when a resignation leaves a gap in experience and expertise, recruitment of new members is considered.

3.7 Identifying and meeting training needs of Committee members

Induction

All Committee members, including topic expert members and co-opted members, receive an induction from NICE and/or the Developer covering:

- key principles for developing NICE guidelines
- the process of developing NICE guidelines, including the importance of being familiar with relevant chapters of this manual
- how the elements of the guideline development process fit together, and the relationship to quality standards and products supporting implementation
- the role of the Committee, including Terms of Reference and Standing Orders (see appendix D), and how lay members contribute
- the role of the Developer and NICE teams
- formulating review questions
- reviewing evidence
- the basics of how economics are used in decision-making
- developing and wording recommendations
- how guidelines are presented on the NICE website (including NICE Pathways)
- information about implementation
- NICE's social value judgements and equality policy

- declaration of interests.

All Committee members are encouraged to provide information to NICE staff about any needs they have for additional support to enable them to participate fully in the work of the Committee.

All Committee members are informed of NICE's most recent principles on social value judgements and most recent statement of its equality policy.

The induction may be scheduled on appointment of the member, or during an early Committee meeting. To work effectively, Committee members may need training and support in some technical areas of guideline development, such as systematic reviewing and economics. Such sessions are arranged by NICE or the Developer, as required. Before beginning their work in a Committee, members may also be invited to observe a meeting of another Committee.

The person selected to perform the role of Committee Chair may need support and training so that they can carry out their role effectively. The Chair needs in-depth knowledge of the NICE guideline development process and an understanding of group processes. Anyone appointed as a Committee Chair is required to attend a specific induction session, which in addition to the above covers the key tasks that the Chair is expected to perform, including:

- facilitating meetings so that all Committee members are involved
- ensuring that lay members of the Committee can contribute to discussions
- ensuring that disabled people who are members (including topic expert, co-opted or lay members) can contribute to discussions
- declaring interests and dealing with conflicts of interest
- planning and organising the work of the Committee, including how the evidence is considered, consensus approaches and developing recommendations.

In addition to the specific induction session, the Developer should identify and meet any additional training needs of a Committee Chair. The Developer may consider a 'buddying' approach in which a new Committee Chair learns from someone with previous experience.

Training for lay members

Lay members of the Committee are offered training by NICE's Public Involvement Programme. This is in addition to the induction and any training they receive alongside other members of the Committee, and allows specific questions and needs to be addressed on topics such as:

- the role of economics in guideline development
- critical appraisal of evidence
- developing recommendations from evidence
- support for getting the guideline into practice.

The training also advises lay members about effective participation in guideline development and gives them the opportunity to learn from people who have had a lay role on previous Committees.

3.8 Committee meetings

General principles

The Committee is multidisciplinary and its members bring with them different beliefs, values and experience. All these perspectives are valued by NICE and should be considered. Each member should have an equal opportunity to contribute to the development of the guideline, and should receive any additional support they need to do this. For this reason, it is important for the Chair to check that the terminology used is understood by all Committee members and is clarified if needed. The Chair should ensure that there is sufficient discussion to allow a range of possible approaches to be considered, while keeping the group focused on the guideline scope, the evidence being reviewed, and the timescale of the project.

Meeting documentation

Meeting documentation is usually sent to Committee members to arrive at least 5 working days before a Committee meeting.

Committee meetings are formally minuted by the Developer and the minutes are approved at the next meeting. The approved minutes of each meeting are posted on the NICE website during guideline development. The information includes:

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

Meeting schedule

The number of Committee meetings depends on the size and scope of the topic. There may be between 2 and 15 meetings for each topic; most are 1-day meetings, but some may take place over 2 days.

Initial meetings

During the initial meeting(s), it may be helpful to establish a framework that clarifies the objectives of the Committee, the specific tasks that need to be carried out and the timetable. This allows the group to focus on the task and to develop a working relationship that is structured and well defined.

Initial meetings may be used to consider the background to the guideline, the scope, and plans for the evidence reviews and any economic analysis that is needed. Drafts or completed evidence reviews may be included in initial meetings if they are available. At initial meetings of standing Committees, topic expert members may be invited to give presentations on their area of work, practice or experience, to familiarise core Committee members with key topic issues.

If review questions and protocols are still in development, the evidence review team presents draft review questions and their plans for the evidence reviews (the protocol) to the Committee for comment (chapter 4 describes the process of developing review questions). The Committee

is asked whether the planned evidence reviews and economic analysis are likely to answer the review questions. Committee members are asked to suggest any amendments or improvements (for example, to further define outcomes or specify appropriate comparators).

During initial meetings, the Committee may also be asked to discuss the development plans and to suggest areas that might benefit from expert testimony. The Committee may be asked to suggest people who can provide that testimony and discuss and consider evidence.

For some topics, the Committee may also be asked to discuss options or plans for involving groups who may not be part of the decision-making process (for example, children and young people or people with a learning disability or cognitive impairment; see section 3.2).

The pathway outline (see section 2.3) will be updated throughout development in collaboration with the Committee.

Development meetings

Evidence reviews and economic analyses are presented to the Committee over the course of a defined number of meetings. The Committee considers the evidence review for each review question, any economic analysis and any additional evidence (for example, expert testimony, views of service users from a reference group, information from focus groups or other exceptional consultation activity). It discusses how these answer the review questions and summarises each area of evidence. To facilitate guideline development, the Committee may work in smaller subgroups whose proposals are then agreed by the whole Committee.

The Committee also discusses the wording of any draft recommendations (see chapter 9). The discussion and rationale for the recommendations is recorded.

NICE staff (for example, the lead editor, implementation leads, public involvement lead and communications lead for the guideline) may give presentations and/or provide information to explain their roles to the Committee. Committee members may be asked to volunteer to work with NICE on the following:

- the NICE Pathway and information for the public (see section 1.7)
- activities and tools that support implementation of the guideline (see chapter 12)

- promoting the guideline (see chapter 11).

Their roles are described in more detail in the sections indicated above.

Final meetings

Towards the end of guideline development, the Committee discusses and agrees the final wording of the draft guideline for consultation, including the draft recommendations (see chapter 9).

After consultation the Committee discusses the comments received during consultation, any changes needed to the guideline, and agrees the final wording of the recommendations (see chapter 11).

Record-keeping

The Developer should maintain records throughout guideline development and ensure that record-keeping standards are appropriate for audit. The following information should be readily available if requested by NICE staff with a quality assurance role:

- details of the Committee members, including declarations of interest
- details of the search strategies, including when the most recent searches were conducted
- details of the included and excluded studies and associated review protocols
- data-extraction forms
- evidence tables
- details of the economic analysis, including any working models
- minutes of Committee meetings
- any additional information presented to the Committee (for example, expert testimony papers, presentations, examples of practice).

3.9 Making group decisions and reaching consensus

Reaching agreement

Committee members need to make collective decisions throughout guideline development. This can include agreeing the review questions (see chapter 4) and protocols (see section 4.5), interpreting the evidence to answer these questions (see chapters 6 and 7) and developing recommendations (see chapter 9).

There are many different approaches to making group decisions, and there are no rules that set out which approach should be used in which circumstances. Also, because Committees work in different ways to reflect their individual membership, it is difficult to be prescriptive about the approach that should be used. In most cases, the Committee reaches decisions through a process of informal consensus. In all cases the approach used should be documented.

The role of the Committee Chair in reaching consensus is to ensure that:

- everyone on the Committee, including members with disabilities, can present their views
- assumptions can be debated
- discussions are open and constructive.

The Chair needs to allow sufficient time for all Committee members to express their views without feeling intimidated or threatened, and should check that all of them agree to endorse any recommendations. If the Committee cannot come to consensus in a particular area, the reasons for this should be documented, and the wording of the recommendation reflect any underlying uncertainty (see chapter 9).

Formal consensus within the group

In exceptional circumstances, some Committees may choose to use formal voting procedures or formal consensus methods for certain decisions (for example, when members disagree or when there is no evidence; see appendix D). NICE does not offer advice on which of the many methods might be used. However, the methods for achieving consensus should be recorded in the minutes of the meeting and a clear statement made about the factors that have been considered. This should also be documented in the guideline, ensuring the process is as transparent as possible.

The views of all Committee members should be considered, irrespective of the method used to reach consensus.

Formal consensus outside the group

Exceptionally, the Committee may wish to identify wider views on best practice (for example, if the literature search has found no evidence that addresses the review question) by using formal consensus methods (for example, the Delphi technique or the nominal-group technique) outside of the group. The use of these methods and the constituency of the wider group should be discussed on a case-by-case basis with members of NICE staff with responsibility for guideline quality assurance, and the NICE Public Involvement Programme lead. The final decision on whether these methods are warranted is made by NICE staff with responsibility for quality assurance. If it is decided that such methods may be used, the planning and methods will be clearly documented and the methods described in the guideline.

3.10 References and further reading

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

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

Elwyn G, Greenhalgh T, Macfarlane F (2001) Groups: a guide to small groups. In: Healthcare, management, education and research. Abingdon: Radcliffe Medical Press

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

Kelly MP, Moore TA (2012) The judgement process in evidence-based medicine and health technology assessment. Social Theory and Health 10: 1–19

4 Developing review questions and planning the evidence review

At the start of guideline development, the key issues and questions listed in the scope may need to be translated into review questions.

Review questions define the boundaries of the review and therefore must be clear and focused. They are the framework for the design of the literature searches, inform the planning and process of the evidence review, and act as a guide for the development of recommendations by the Committee.

This chapter describes how review questions are developed and agreed. It describes the different types of review question and provides examples. It also provides information on the different types of evidence and how to plan the evidence review. The best approach may vary depending on the topic. Options should be considered by the Developer, and the chosen approach discussed and agreed with NICE staff with responsibility for quality assurance. The approach should be documented in the review protocol (see table 4.1) and the guideline, together with the rationale for the choice.

4.1 Number of review questions

The number of review questions for each guideline depends on the topic and the breadth of the scope. However, it is important that the total number of questions:

- is manageable
- can be covered in the time and with the resources available
- provides sufficient focus for the guideline, and covers all areas outlined in the scope.

Review questions can vary considerably in terms of both the number of included studies and the complexity of the question and analyses. For example, a single review question might involve a complex comparison of several interventions with many primary studies included. At the other extreme, a review question might address the effects of a single intervention and there may be few primary studies meeting the inclusion criteria. The number of review questions for each guideline will therefore vary depending on the topic and its complexity.

4.2 Developing review questions from the scope

The review questions should cover all areas specified in the scope but should not introduce new areas. They will often build on the key questions in the scope and usually contain more detail.

Review questions are usually drafted by the Developer. They may then be refined and agreed with people with specialist knowledge and experience (for example, the Committee members). This enables the literature search to be planned efficiently. Sometimes the questions need refining once the evidence has been searched; such changes to review questions should be agreed with a member of NICE staff with a quality assurance role, and documented in the evidence review.

4.3 Formulating and structuring different review questions

When developing review questions, it is important to consider what information is needed for any planned economic modelling. This might include information about quality-of-life, rates of, and inequalities in, adverse effects and use of health and social care services. In addition, review questions often cover acceptability and accessibility of interventions, and experiences of practitioners or people using services and the public. The nature and type of review questions determines the type of evidence reviews and the type of evidence that is most suitable (for example, intervention studies or qualitative data); both the type of evidence review and type of evidence need careful consideration (Petticrew and Roberts 2003). The process for developing a review question is the same whatever the nature and type of the question.

Review questions should be clear and focused. The exact structure of each question depends on what is being asked. The aims of questions will differ, but are likely to cover at least one of the following:

- extent and nature of the issue as described in the scope
- factors, causal mechanisms and the role of the various vectors
- interventions that work in ideal circumstances and might work in specific circumstances or settings (the extent to which something works, how and why)
- a relevant programme theory, theory of change, or mechanisms of action likely to explain behaviour or effects

- views and experiences of people using services or people who may be affected by the recommendation, including how acceptable and accessible they find the intervention
- practitioners' or providers' views, experiences and working practices (including any factors hindering the implementation of the intervention and factors supporting implementation)
- costs and resource use
- potential for an intervention to do harm or have unintended consequences.

If a conceptual map or logic models are developed, they can be useful when developing review questions (see appendix A).

When review questions are about the effectiveness of interventions, additional types of evidence review may be needed to answer other aspects or aims of the question. For example, additional evidence reviews might address the views of people using services or the communities where services are based, or barriers to use as reported by practitioners or providers. Sometimes, a review may use different sources of evidence or types of data (for example, a review may combine current practice or map quantitative information with qualitative data).

There are examples of different types of review questions and the type of evidence that might best address them throughout this chapter.

Review questions about the effectiveness of an intervention

A helpful structured approach for developing questions about interventions is the PICO (population, intervention, comparator and outcome) framework (see box 4.1).

However, other frameworks exist (such as SPICE; setting, perspective, intervention, comparison, evaluation) and can be used as appropriate.

Box 4.1 Formulating a review question on the effectiveness of an intervention using the PICO framework

Population: Which population are we interested in? How best can it be described? Are there subgroups that need to be considered?

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

Comparators: Are there alternative(s) to the intervention being considered? If so, what are these (for example, other interventions, standard active comparators, usual care or placebo)?

Outcome: Which outcomes should be considered to assess how well the intervention is working? What is really important for people using services? Core outcome sets may be used where appropriate; one source is the COMET database.

For each review question, factors that may affect the outcomes and effectiveness of an intervention, including any wider social factors that may affect health and any health inequalities, should be considered. The setting for the question should also be specified if necessary. To help with this, outcomes and other factors that are important should be listed in the review protocol. In general, a maximum of 7–10 outcomes should be defined.

Box 4.2 Examples of review questions on the effectiveness of interventions

- What types of mass-media intervention help prevent children and young people from taking up smoking? Are the interventions delaying rather than preventing the onset of smoking?
- Which of the harm-reduction services offered by needle and syringe programmes (including advice and information on safer injecting, onsite vaccination services, and testing for hepatitis B and C and HIV) are effective in reducing blood-borne viruses and other infections among people who inject drugs?
- What types of intervention and programme are effective in increasing physical activity levels among children under 8 – particularly those who are not active enough to meet the national recommendations for their age – or help to improve their core physical skills?
- Does brief advice from GPs increase adult patients' physical activity levels?
- What are the most effective school-based interventions for changing young people's attitudes to alcohol use?
- For people with IBS (irritable bowel syndrome), are antimuscarinics or smooth muscle relaxants effective compared with placebo or no treatment for the long-term control of IBS symptoms? Which is the most effective antispasmodic?
- Which first-line opioid maintenance treatments are effective and cost effective in relieving pain in patients with advanced and progressive disease who require strong opioids?
- What reporting and learning systems are effective and cost effective in reducing medicines-related patient safety incidents, compared with usual care?

Review questions about pharmacological management will usually only include medicines with a UK marketing authorisation for some indication, based on regulatory assessment of safety and efficacy. Use of a medicine outside its licensed indication (off-label use) may be considered in some circumstances; for example, if this use is common practice in the UK, if there is good evidence for this use, or there is no other medicine licensed for the indication (see also the section on recommendations on medicines, including off-label use of licensed medicines). Medicines with no UK marketing authorisation for any indication will not usually be considered in a guideline because there is no UK assessment of safety and efficacy to support their use.

A review question about the effectiveness of an intervention is usually best answered by a randomised controlled trial (RCT), because a well-conducted RCT is most likely to give an unbiased estimate of effects. More information (for example, information about long-term effects) may be obtained from other sources. Advice on finding data on the adverse effects of an intervention is available in the Cochrane handbook for systematic reviews for interventions.

RCTs provide the most valid evidence of the effects of interventions. However, such evidence may not always be available. In addition, for many health and social care interventions it can be difficult or unethical to assign populations to control and intervention groups (for example, for interventions which aim to change policy). In such cases, a non-randomised controlled trial might be a more appropriate way of establishing cause and effect. The Medical Research Council (MRC) has produced guidance on evaluating complex interventions (Craig et al. 2008) and using natural experiments to evaluate population health interventions (Craig et al. 2011).

There are also circumstances in which an RCT is not needed to confirm the effectiveness of an intervention (for example, giving insulin to a person in a diabetic coma compared with not giving insulin or reducing speed limits to 20 mph to reduce the severity of injuries from road traffic accidents). In these circumstances, there is sufficient certainty from non-RCT evidence that an important effect exists. In these circumstances due consideration needs to be given to the following:

- whether an adverse outcome is likely if the person is not treated (evidence from, for example, studies of the natural history of a condition)
- if the intervention gives a large benefit or shows a clear dose–response gradient that is unlikely to be a result of bias (evidence from, for example, historically controlled studies)
- whether the side effects of the intervention are acceptable (evidence from, for example, case series)
- if there is no alternative intervention
- if there is a convincing pathophysiological basis for the intervention.

Review questions about cost effectiveness

For more information on review questions about cost effectiveness, see chapter 7.

Review questions about the accuracy of diagnostic tests

Review questions about diagnosis are concerned with the performance of a diagnostic test or test strategy. Diagnostic tests can include identification tools, physical examination, history-taking, laboratory or pathological examination and imaging tests.

Broadly, review questions that can be asked about a diagnostic test are of 3 types:

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

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

The PICO framework can be useful when formulating review questions about diagnostic test accuracy (see box 4.3). However other frameworks (such as PPIRT; population, prior tests, index test, reference standard, target condition) can be used if helpful.

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

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

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

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

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

Outcome: The diagnostic accuracy of the test or test strategy for detecting the target condition. This is usually reported as test parameters, such as sensitivity, specificity, predictive values, likelihood ratios, or – when multiple thresholds are used – a receiver operating characteristic (ROC) curve. This should also include issues of importance to people having the test, such as acceptability.

A review question about diagnostic test accuracy is usually best answered by a cross-sectional survey in which both the index test(s) and the reference standard are performed on the same sample of people. Case–control studies are also used to assess the accuracy of diagnostic tests, but this type of study design is more prone to bias (and often results in inflated estimates of diagnostic test accuracy). Further advice on the types of study to include in reviews of diagnostic test accuracy can be found in the Cochrane handbook for diagnostic test accuracy reviews.

Box 4.4 Examples of review questions on diagnostic test accuracy

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

What are the most appropriate methods/instruments for case identification of conduct disorders in children and young people?

Although assessing test accuracy is important for establishing the usefulness of a diagnostic test, the value of a test lies in how useful it is in guiding treatment decisions or the provision of services, and ultimately in improving outcomes. 'Test and treat' studies compare outcomes for people who have a new diagnostic test (in combination with a management strategy) with outcomes of people who have the usual diagnostic test and management strategy. These types

of study are not very common. If there is a trade-off between costs, benefits and harms of the tests, a decision-analytic model may be useful (see Lord et al. 2006).

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

Review questions about prognosis

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

Information about prognosis can be used within guidelines to:

- classify people into risk categories (for example, cardiovascular risk or level of need) so that different interventions can be applied
- define subgroups of populations that may respond differently to interventions
- identify factors that can be used to adjust for case mix (for example, in investigations of heterogeneity)
- help determine longer-term outcomes not captured within the timeframe of a trial (for example, for use in an economic model).

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

Review questions about prognosis may be closely related to questions about aetiology (cause of a disease or need) if the outcome is viewed as the development of the disease or need based on

a number of risk factors. They may also be closely related to questions about interventions if one of the prognostic factors is treatment. However, questions about interventions are usually better addressed by controlling for prognostic factors.

Box 4.5 Examples of review questions on prognosis

Are there factors related to the individual (characteristics either of the individual or of the act of self-harm) that predict outcome (including suicide, non-fatal repetition, other psychosocial outcomes)? For people who are opioid dependent, are there particular groups that are more likely to benefit from detoxification?

A review question about prognosis is best answered using a prospective cohort study with multi-variate analysis. Case–control studies are not usually suitable for answering questions about prognosis because they do not estimate baseline risk, but give only an estimate of the likelihood of the outcome for people with and without the prognostic factor.

Review questions about views and experiences of people using or providing services, family members or carers and the public

Most review questions should ensure that views and experience of people using or providing services, family members or carers and the public are considered when deciding on the type of evidence review, the type of evidence, and how these views will be sought.

In some circumstances, specific questions should be formulated about the views and experience of people using services, family members or carers and the public to ensure that the question is person-centred. The views and experiences of those providing services may also be relevant. These views and experiences, which may vary for different populations, can cover a range of dimensions, including:

- views and experiences of people using or providing services, family members or carers or the public on the effectiveness and acceptability of given interventions
- preferences of people using services, family members or carers or the public for different treatment or service options, including the option of foregoing treatment or care

- views and experiences of people using or providing services, family members or carers or the public on what constitutes a desired, appropriate or acceptable outcome.

Such questions should be clear and focused, directly relevant to the topic, and should address experiences of an intervention or approach that are considered important by people using or providing services, family members or carers or the public. Such questions can address a range of issues, including:

- information and support needs specific to the topic
- elements of care or a service that are of particular importance to people using or providing services
- factors that encourage or discourage people from using interventions or services
- the specific needs of certain groups of people using services, including those sharing the characteristics protected by the Equality Act (2010)
- which outcomes reported in studies of interventions are most important to people using services, family members or carers or the public.

As for other types of review question, questions that are broad and lack focus (for example, 'What is the experience of living with condition X'?) should be avoided.

NICE guidelines should not reiterate or re-phrase recommendations from the NICE guideline on patient experience in adult NHS services, the NICE guideline on service user experience in adult mental health or other NICE guidelines on the experience of people using services. However, whether there are specific aspects of views or experiences that need addressing for a topic should be considered during the scoping of every guideline. Specific aspects identified during scoping should be included in the scope if they are not covered by existing guidelines and are supported as a priority area. These are likely to be topic specific and should be well defined and focused.

Box 4.6 Examples of review questions on the views or experiences of people using or providing services, family members or carers or the public

What information and support should be offered to children with atopic eczema and their families and carers?
What elements of care on the general ward are viewed as important by patients following their discharge from critical care areas?
How does culture affect the need for and content of information and support for bottle or breastfeeding?
What are the perceived risks and benefits of immunisation among parents, carers or young people? Is there a difference in perceived benefits and risks between groups whose children are partially immunised and those who have not been immunised?

A review question about the views or experiences of people using or providing services, family members or carers or the public is likely to be best answered using qualitative studies and cross-sectional surveys, although information on views and experiences is also becoming increasingly available as part of wider intervention studies.

When there is a lack of evidence on issues important to people affected by the guideline (including families and carers, where appropriate), the Developer should consider seeking information via a targeted call for evidence (see section 5.5), or approaching key stakeholders who may have access to additional data sources, such as surveys of user views and experiences, to present as expert testimony (see section 3.5).

Exceptionally, when the information gap cannot be addressed in other ways, the Developer may commission a consultation exercise with people affected by the guideline to obtain their views on specific aspects of the scope or issues raised by the Committee, or to validate early draft recommendations before consultation with registered stakeholders. (For more information, see the section on fieldwork with practitioners and targeted consultation with people using services and appendix B.) The Developer should document the rationale, together with a proposal for the work, including possible methods and the anticipated costs. The proposal should be discussed and agreed with members of NICE staff with a quality assurance role, and approved by the Centre Director. Where the work is approved, the rationale and methods should be documented in the guideline.

Review questions about service delivery

Guidelines often cover areas of service delivery. These might include how delivery of services could improve.

Box 4.7 Examples of review questions on service delivery

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

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

What types of needle and syringe programmes (including their location and opening times) are effective and cost effective?

How can access to immunisations be increased?

What regional or city level commissioning models, service models, systems and service structures are effective in:

- reducing diagnostic delay for TB?
- improving TB contact tracing?
- improving TB treatment completion?

A review question about the effectiveness of service delivery models is usually best answered by an RCT. However, a wide variety of methodological approaches and study designs have been used. Other types of questions on service delivery are also likely to be answered using evidence from study types other than RCTs.

Depending on the type of review questions, the PICO framework may be appropriate but other frameworks can be used.

When a topic includes review questions on service delivery, approaches described in NICE's Interim methods guide for developing service guidance may be used. Such methods should be agreed with NICE and should be clearly documented in the final guideline.

Review questions about epidemiology

Epidemiological reviews describe the problem under investigation and can be used to inform other review questions. For example, an epidemiological review of accidents would provide

information on the most common accidents, as well as morbidity and mortality statistics, and data on inequalities in the impact of accidents.

Examples of review questions that might benefit from an epidemiological review include:

- What are the patterns of physical activity among children from different populations and of different ages in England?
- Which populations of children are least physically active and at which developmental stage are all children least physically active?
- What effect does physical activity have on children's health and other outcomes in the short- and long-term?

The structure of the question and the type of evidence will depend on the aim of the review.

Another use of epidemiological reviews is to describe relationships between epidemiological factors and outcomes – a correlates review. If an epidemiological review has been carried out, information will have been gathered from observational studies on the nature of the problem. However, further analysis of this information – in the form of a correlates review – may be needed to establish the epidemiological factors associated with any positive or negative behaviours or outcomes.

Examples of review questions that might benefit from a correlates review include:

- What factors are associated with children's or young people's physical activity and how strong are the associations?
- What are the factors that encourage or discourage people from taking part in physical activity?
- How do the factors that encourage or discourage people from taking part differ for the least active subpopulations and age groups?

Review questions about the implementation of recommendations

Review questions on how best to implement recommendations may be considered appropriate for some topics.

The type of review question depends on the issue but is likely to fit into 1 of the types described above (for example, 'What is the effectiveness of an intervention to increase a practitioner's awareness of a specific condition?' is an example of an intervention question and would be addressed using the same methods as any other intervention question). The question 'What are the views of practitioners who provide this service?' would be addressed using the same methods as those used to address questions about views and experiences of people using services.

When deciding if review questions about implementation are appropriate for a guideline, current practice should be considered to identify areas of inappropriate variation in which recommendations about implementation would be of value.

4.4 Evidence used to inform recommendations

In order to formulate recommendations, the guideline Committee needs to consider a range of evidence about what works generally, why it works, and what might work (and how) in specific circumstances. The Committee needs evidence from multiple sources, extracted for different purposes and by different methods.

Scientific evidence

Scientific evidence is explicit, transparent and replicable. It can be context free or context sensitive. Context-free scientific evidence assumes that evidence can be independent of the observer and context. It can be derived from evidence reviews or meta-analyses of quantitative studies, individual studies or theoretical models. Context-sensitive scientific evidence looks at what works and how well in real-life situations. It includes information on attitudes, implementation, organisational capacity, forecasting, economics and ethics. It is mainly derived using social science and behavioural research methods, including quantitative and qualitative research studies, surveys, theories, cost-effectiveness analyses and mapping reviews. Sometimes, it is derived using the same techniques as context-free scientific evidence. Context-sensitive evidence can be used to complement context-free evidence, and can so provide the basis for more specific and practical recommendations. It can be used to:

- supplement evidence on effectiveness (for example, to look at how factors such as occupation, educational attainment and income influence effectiveness)

- inform the development of logic models (see section 2.3 and appendix A) and causal pathways (for example, to explain what factors predict teenage parenthood)
- provide information about the characteristics of the population (including social circumstances and the physical environment) and about the process of implementation
- describe psychological processes and behaviour change.

Quantitative studies may be the primary source of evidence to address review questions on:

- the effectiveness of interventions or services (including information on what works, for whom and under which circumstances)
- measures of association between factors and outcomes
- variations in delivery and implementation for different groups, populations or settings
- resources and costs of interventions or services.

Examples of the types of review questions that are addressed using quantitative evidence include:

- How well do different interventions work (for example, does this vary according to age, severity of disease)?
- What other factors affect how well an intervention works?
- How much resource does an intervention need to be delivered effectively and does this differ depending on location?

Scientific evidence need not be quantitative information alone.

Qualitative studies may be the primary source of evidence to address review questions on:

- the experiences of people using services, family members or carers or practitioners (including information on what works, for whom and under which circumstances)
- the views of people using services, family members or carers, the public or practitioners

- opportunities for and factors hindering improvement (including issues of access or acceptability for people using services or providers)
- variations in delivery and implementation for different groups, populations or settings
- factors that may help or hinder implementation
- social context and the social construction and representation of health and illness
- background on context, from the point of view of an observer (and not necessarily that of a person using services or a practitioner)
- theories of, or reasons for, associations between interventions and outcomes.

Examples of the types of review questions that are addressed using qualitative evidence include:

- How do different groups of practitioners, people using services or stakeholders perceive the issue (for example, does this vary according to profession, age, gender or family origin)?
- What social and cultural beliefs, attitudes or practices might affect this issue?
- How do different groups perceive the intervention or available options? What are their preferences?
- What approaches are used in practice? How effective are they in the views of different groups of practitioners, people using services or stakeholders?
- What is a desired, appropriate or acceptable outcome for people using services? What outcomes are important to them? What do practitioner, service user or stakeholder groups perceive to be the factors that may help or hinder change in this area?
- What do people affected by the guideline think about current or proposed practice?
- Why do people make the choices they do or behave in the way that they do?
- How is a public health issue represented in the media and popular culture?

Quantitative and qualitative information can also be used to supplement logic models (see section 2.3 and appendix A). They can also be combined in a single review (mixed methods) when appropriate (for example, to address review questions about factors that help or hinder implementation or to assess why an intervention does or does not work).

Examples of questions for which qualitative evidence might supplement quantitative evidence include:

- How acceptable is the intervention to people using services or practitioners?
- How accessible is the intervention or service to different groups of people using services? What factors affect its accessibility?
- Does the mode or organisation of delivery (including the type of relevant practitioner, the setting and language) affect user perceptions?

Often reviews of quantitative or qualitative studies (secondary evidence) already exist. Existing reviews may include systematic reviews (with or without a meta-analysis or individual patient data analysis) and non-systematic literature reviews and meta-analyses). Well-conducted systematic reviews (such as Cochrane intervention and diagnostic test accuracy reviews) may be of particular value as sources of evidence. Some reviews may more useful as background information or as additional sources of potentially relevant primary studies. This is because they may:

- not cover inclusion and exclusion criteria relevant to the guideline topic's referral and parameters (for example, comparable research questions, relevant outcomes, settings, population groups or time periods)
- group together different outcome or study types
- include data that are difficult or impossible to separate appropriately
- not provide enough data to develop recommendations (for example, some reviews do not provide sufficient detail on specific interventions making it necessary to refer to the primary studies).

Conversely, some high-quality systematic reviews, such as Cochrane reviews, may provide enhanced data not available in the primary studies. For example, authors of the review may have contacted the authors of the primary studies or other related bodies in order to include additional relevant data in their review, or an individual patient data analysis may have been conducted. In addition, if high-quality reviews are in progress (protocol published) at the time of development of the guideline, the Developer may choose to contact the authors for permission to access pre-publication data for inclusion in the guideline (see section 5.5).

Reviews can also be useful when developing the scope and when defining review questions, outcomes and outcome measures for the guideline evidence reviews. The discussion section of a review can also help to identify some of the limitations or difficulties associated with a topic, for example, through a critical appraisal of the state of the evidence base. The information specialists may also wish to consider the search strategies of high-quality systematic reviews. These can provide useful search approaches for capturing different key concepts. They can also provide potentially useful search terms and combinations of terms, which have been carefully tailored for a range of databases.

Occasionally high-quality reviews that are directly applicable to the guideline review question may be used as a source of effectiveness data, particularly for complex organisational, behavioural and population level questions.

When considering using results from an existing high-quality review, due account should be taken of the following:

- The parameters (for example, research question, inclusion and exclusion criteria) of the review (see screening questions in the systematic review checklist in appendix H) are sufficiently similar to those of the guideline topic to be able to answer 1 or more specific review questions. In such cases, a search should be undertaken for primary studies published after the search date covered by the existing review.
- Whether the use of existing high-quality reviews will be sufficient to address the guideline review question if the evidence base for the guideline topic is very large.

Colloquial evidence

'Colloquial evidence' can complement scientific evidence or provide missing information on context. It can come from expert testimony (see section 3.5), from members of the Committee, from a reference group of people using services (see section 3.2 and appendix B) or from comments from registered stakeholders (see section 10.1). Colloquial evidence includes evidence about values (including political judgement), practical considerations (such as resources, professional experience or expertise and habits or traditions, the experience of people using services) and the interests of specific groups (views of lobbyists and pressure groups).

An example of colloquial evidence is expert testimony. Sometimes oral or written evidence from outside the Committee is needed for developing recommendations, if limited primary research is

available or more information on current practice is needed to inform the Committee's decision-making. Inclusion criteria for oral or written evidence specify the population and interventions for each review question, to allow filtering and selection of oral and written evidence submitted to the Committee.

Other evidence

Depending on the nature of the guideline and the topic, other sources of relevant evidence such as reports, audits, and standard operating procedures may be included. The reasonableness and rigour of the process used to develop the evidence is assessed as well as the relevance of the evidence to the topic under consideration.

See also chapter 8 on linking and using other guidance.

4.5 Planning the evidence review

For each guideline evidence review, a review protocol is prepared that outlines the background, the objectives and the planned methods. This protocol will explain how the review is to be carried out and will help the reviewer to plan and think through the different stages. In addition, the review protocol should make it possible for the review to be repeated by others at a later date. A protocol should also make it clear how equality issues have been considered in planning the review work, if appropriate.

Structure of the review protocol

The protocol should describe any differences from the methods described in this manual (chapters 5–7), rather than duplicating the methodology stated here. It should include the components outlined in table 4.1.

When a guideline is updating a published guideline, the protocol from the published guideline, if available, should be used as the basis for outlining how the review question would be addressed. Information gathered during the formal check of the need to update the guideline should also be added. This might include new interventions and comparators, and extension of the population.

Table 4.1 Components of the review protocol

Component	Description
Review question(s)	The review question(s)
Context and objectives	Short description; for example, 'To estimate the effectiveness and cost effectiveness of…' or 'To estimate the acceptability of…'
Searches	To include: • sources to be searched (see chapter 5) • plans to use any supplementary search techniques, when known at the protocol development stage, and the rationale for their use (see section 5.4) • limits to be applied to the search (see section 5.4)
Types of study to be included	Inclusion and exclusion criteria, based on the 'ideal' study designs to be included, and the study designs to be included if the 'ideal' study designs are not available. In some circumstances, a decision to include only 'ideal' study designs may be made. This should also be documented here
Participants/ population	Inclusion and exclusion criteria, using the structured framework (for example, PICO, SPICE) such as setting, or age
Intervention(s), exposure(s)	Inclusion and exclusion criteria, based on the intervention, treatment, exposure or approach that will be included
Comparator(s)/control	Inclusion and exclusion criteria, based on the alternative(s) to the intervention being considered
Outcome(s)	Inclusion and exclusion criteria, based on the outcomes that will be considered

Data extraction and quality assessment	Brief details of: • data extraction • how the quality assessment and applicability will be presented (by whole study, or by outcome – GRADE) • any deviations from the methods and processes described in this manual
Strategy for data synthesis	Brief details of the proposed approach to data synthesis and analysis, and details of any alternative analysis to be undertaken if the planned analysis is not possible
Analysis of subgroups or subsets	Brief details of any subgroups that will be considered (for example, population or intervention types)
Any other information or criteria for inclusion/exclusion	For example, the equality issues that will be considered when reviewing the evidence, based on the equality impact assessment conducted during scoping of the guideline

Process for developing the review protocol

The review protocol should be produced by the evidence review team after the review question has been agreed and before starting the evidence review. It should then be reviewed and approved by NICE staff with responsibility for quality assurance.

The review protocol, principal search strategy (see section 5.4) and a version of the economic plan (see section 7.5) are published on the NICE website at least 6 weeks before the release of the draft guideline. Any changes made to a protocol in the course of guideline development should be agreed with NICE staff with responsibility for quality assurance and should be described. Consideration should be given to registering review protocols on the PROSPERO or SRDR databases.

4.6 References and further reading

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

Cochrane Diagnostic Test Accuracy Working Group (2008) Cochrane handbook for diagnostic test accuracy reviews (updated December 2013). The Cochrane Collaboration

Craig P, Dieppe P, McIntyre S et al. on behalf of the MRC (2008) Developing and evaluating complex interventions: new guidance. London: Medical Research Council

Craig P, Cooper C, Gunnell D et al. on behalf of the MRC (2011) Using natural experiments to evaluate population health interventions: guidance for producers and users of evidence. London: Medical Research Council

Harden A, Garcia J, Oliver S et al. (2004) Applying systematic review methods to studies of people's views: an example from public health research. Journal of Epidemiology and Community Health 58: 794–800

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

Kelly MP, Swann C, Morgan A et al. (2002) Methodological problems in constructing the evidence base in public health. London: Health Development Agency

Kelly MP, Moore TA (2012) The judgement process in evidence-based medicine and health technology assessment. Social Theory and Health 10:1–19

Lomas J, Culyer T, McCutcheon C et al. (2005) Conceptualizing and combining evidence for health system guidance: final report. Ottawa: Canadian Health Services Research Foundation

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

Muir Gray JM (1996) Evidence-based healthcare. London: Churchill Livingstone

Ogilvie D, Hamilton V, Egan M et al. (2005) Systematic reviews of health effects of social interventions: 1. Finding the evidence: how far should you go? Journal of Epidemiology and Community Health 59: 804–8

Ogilvie D, Egan M, Hamilton V et al. (2005) Systematic reviews of health effects of social interventions: 2. Best available evidence: how low should you go? Journal of Epidemiology and Community Health 59: 886–92

Petticrew M (2003) Why certain systematic reviews reach uncertain conclusions. British Medical Journal 326: 756–8

Petticrew M, Roberts H (2003) Evidence, hierarchies, and typologies: horses for courses. Journal of Epidemiology and Community Health 57: 527–9

Popay J, Rogers A, Williams G (1998) Rationale and standards for the systematic review of qualitative literature in health services research. Qualitative Health Research 8: 341–51

Popay J, editor (2006) Moving beyond effectiveness in evidence synthesis: methodological issues in the synthesis of diverse sources of evidence. London: National Institute for Health and Clinical Excellence

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

Rychetnik L, Frommer M, Hawe P et al. (2002) Criteria for evaluating evidence on public health interventions. Journal of Epidemiology and Community Health 56: 119

Tannahill A (2008) Beyond evidence – to ethics: a decision making framework for health promotion, public health and health improvement. Health Promotion International 23: 380–90

Victora C, Habicht J, Bryce J (2004) Evidence-based public health: moving beyond randomized trials. American Journal of Public Health 94: 400–5

Woolgar S (1988) Science: the very idea. London: Routledge

5 Identifying the evidence: literature searching and evidence submission

5.1 Introduction

The systematic identification of evidence is an essential step in developing NICE guidelines. Systematic literature searches should be thorough, transparent and reproducible to minimise 'dissemination biases' (Song et al. 2000). These may affect the results of reviews and include publication bias and database bias.

This chapter provides advice on the sources to search and on how to develop strategies for systematic literature searches to identify the best available evidence. It also provides advice on other areas of information management that form an important part of guideline development. These include quality assurance, re-running searches, documenting the search process, and the use of reference management software. The methods for undertaking scoping searches are described in chapter 2.

NICE encourages the use of search methods that balance precision and sensitivity. The aim is to identify the best available evidence to address a particular question without producing an unmanageable volume of results.

A flexible approach to the search for evidence should be adopted, guided by the subject of the question and type of evidence sought. This includes:

- selecting appropriate sources according to the eligibility/inclusion criteria of the review question, as specified in the review protocol
- using supplementary search techniques, such as citation searching, as appropriate
- continuous review of how best to find evidence and where.

A flexible approach will allow evidence to be identified both systematically and in the most efficient manner. For example, for a review question on the effectiveness of a pharmacological intervention it may be possible to search a relatively small number of sources (see section 5.3) and to develop a systematic search strategy using the PICO framework (see section 5.4). For questions about complex interventions, the evidence may be more widely scattered across

sources and less consistently described. In these cases it may be necessary to search a much wider range of sources and to consider using supplementary searching approaches.

For information on searching for economic evidence see chapter 7.

5.2 Search protocols

Search protocols should be developed by the information specialist and agreed with the other members of the evidence review team and Developer before undertaking a systematic search. Search protocols are part of the review protocol (see table 4.1), which is signed off by NICE staff with responsibility for quality assurance. When developing search protocols, the information specialist may ask the Committee to provide expertise (for example, when a condition is described in many different ways in the literature).

Search protocols pre-define how the evidence is identified and provide a basis for developing the search strategies. Search protocols should include the following elements:

- sources to be searched (see section 5.3)
- plans to use any supplementary search techniques, when known at the protocol development stage, and the rationale for their use
- limits to be applied to the search.

5.3 Sources

Searches should include a mix of databases, websites and other sources depending on the subject of the review question and the type of evidence sought.

For most searches there will be key sources that should be prioritised for searching, and other potentially relevant sources that could be considered for searching. It is important to ensure adequate coverage of the relevant literature and to search a range of sources, but there should be a clear rationale for including sources, with only those likely to yield relevant results included. (See also section 7.4 for information on searching for economic literature.)

The selection of sources will vary according to the requirements of the review question. For reviews of the effectiveness of pharmacological interventions, the Cochrane Central Register of

Controlled Trials (CENTRAL), EMBASE and MEDLINE should be prioritised for searching. For other questions, it might be as or more important to search other sources. Examples of other sources include, but are not limited to, PsycINFO (psychology and psychiatry), ASSIA (Applied Social Sciences Index and Abstracts), Social Policy and Practice, Social Care Online, Sociological Abstracts, HMIC (Health Management Information Consortium) and HealthTalkOnline. Sources of grey literature (for example, reports, statistics, ongoing research) and conference abstracts may also be important for some review questions.

A list of sources is provided in appendix G as a starting point for identifying potential relevant sources. The chapter on searching for studies in the Cochrane handbook for systematic reviews of interventions also offers a good overview and examples of sources to search (Lefebvre et al. 2011).

5.4 Developing search strategies

Devising a search strategy

Review questions can be broken down into different concepts, which can be combined to devise a search strategy. For example, the PICO (population, intervention, comparator and outcome) or the SPICE (setting, perspective, intervention, comparison, evaluation; Booth 2004) framework can be used to structure a search strategy. It is important to consider which concepts to include in the strategy because some concepts may not be mentioned in the titles, abstracts or subject headings of a database record. This is a particular challenge when the literature is less well defined and/or indexed. It is important to ensure that relevant studies are not missed as a result of an overly complex search structure.

When the relevant literature for a question is less well defined or indexed, a multi-stranded approach to searching may be more efficient. This involves developing several shorter search strategies (strands) with an emphasis on precision. Each strand should reflect 1 way in which the relevant literature may be described. The strands are then combined.

Review questions that overlap and can be grouped together should be identified for searching purposes. For example, questions with the same population may involve comparing several interventions. This should make it possible to carry out 1 search that covers all the interventions.

Identifying search terms

Search strategies should usually consist of a combination of subject headings and 'free-text' terms from the titles and abstracts of relevant studies. When identifying subject headings, variations in thesaurus and indexing terms for each database should be taken into account: for example, MeSH (Medical Subject Headings) in MEDLINE, Emtree in Embase. Not all search concepts will have a subject heading, so free-text terms should also be used. Free-text terms may include synonyms, acronyms and abbreviations, spelling variants, old and new terminology, brand and generic medicine names, and lay and medical terminology.

Comprehensively identifying search terms may present challenges. For example, for public health or social care reviews many databases do not use a controlled vocabulary for indexing records. Sometimes controlled vocabularies are used but do not include terms that adequately cover the search concept(s), which often cross a number of disciplines. In addition, the use of natural language varies between studies, and concepts may not be described in a consistent way. In light of these challenges, the development of a search strategy should always be an iterative process between the information specialist(s), the Developer and, when necessary, the Committee and NICE staff with a quality assurance role.

For a guideline that is being updated, previous search strategies should be reviewed and used to inform search strategy design.

Limits and filters

Searches should be limited to studies reported in English except in exceptional circumstances (for example, when there is a lack of evidence reported in English but awareness of high-quality evidence published in other languages; Morrison et al. 2012).

When there are likely to be animal studies in the evidence base, these can be excluded from the search results in some databases. For example, in Ovid MEDLINE one method is:

1. Final search set

2. Exp Animals/ not Humans/

3. 1 not 2

Limiting searches by date will depend on the topic and the nature of the evidence base (for example, when most of the research was published). If there are relevant good-quality published systematic reviews (see chapter 4), it may be possible to limit additional searching to the time since the searches for the published reviews were conducted. The date range for the search, and the use of existing reviews, should be agreed before searching and documented in the search protocol (see section 5.2).

Depending on the review question, it may be appropriate to limit searches to particular study designs. For example, for review questions on the effectiveness of interventions, it may be more efficient to search for systematic reviews, followed by controlled trials followed by observational studies. This prevents unnecessary searching and review work. The best way to limit searches by study design is to use an appropriate search filter (strings of search terms), rather than using database publication type field limits.

Other search filters relating to age, setting, geography, health inequalities and equality can also be applied as relevant. The most comprehensive list of available search filters is the search filter resource of the InterTASC Information Specialists' Sub-Group. Search filters should, however, be used with caution because concepts such as study design, age, setting and geography may not be adequately described in the title or abstract of a database record, and may not be captured by the indexing.

NICE is not prescriptive about which search filters should be used because there is often limited evidence on the performance of individual filters. There are known areas where search filters have been shown to perform poorly and use should be avoided (for example, for identifying diagnostic studies; Beynon et al. 2013). Alternative methods for refining a search to achieve an adequate balance of sensitivity and precision should be used when filters are not appropriate. These include multi-stranded searching or supplementary search techniques.

Supplementary search techniques

Supplementary search techniques should be used in addition to database searching when it is known, or reasonably likely, that relevant evidence is either not indexed in bibliographic databases and/or that it is difficult to retrieve from databases in a way that adequately balances sensitivity and precision. Supplementary search techniques might include forward and backward citation searching, journal hand-searches or contacting experts and stakeholders.

Reviews (for example, systematic reviews, literature reviews and meta-analyses) may provide an additional source of primary studies. The reference lists in the reviews can be used to identify potentially relevant primary studies.

Supplementary search techniques should follow the same principles of transparency and reproducibility as other search methods.

Supplementary search techniques should be considered at the outset and documented in the search protocol (see section 5.2), if possible. They should also be documented in the evidence review.

5.5 Calls for evidence from stakeholders

Stakeholders' role in providing evidence

In some topic areas or for some review questions, NICE staff with responsibility for quality assurance, the evidence review team, Developer or Committee may believe that there is relevant evidence in addition to that identified by the searches. Examples include ongoing research when an intervention or service is relatively new, studies that have been published only as abstracts, data about the off-label use of medicines, data on harms, economic models, and studies of the experiences of people using services, their family members or carers, or practitioners. In these situations, the Developer may invite stakeholders, and possibly also other relevant organisations or individuals with a significant role or interest, to submit evidence. A call for evidence is issued directly to registered stakeholders and via the NICE website.

A call for evidence specifies the type of evidence being sought and, if appropriate, the review question being addressed. A call for evidence can be made at any point during the development of a guideline, but usually happens in the earlier stages. The time allocated for submission of evidence depends on the type of evidence and level of detail needed. A typical call lasts for 2–4 weeks, but it may be longer.

If it is likely that regulatory authorities hold relevant data, the appropriate regulatory authority may be approached to release those data as part of the call for evidence.

To simplify copyright considerations, only references or links should be submitted, or details of contacts for unpublished research. The Developer will then obtain full copies of all relevant

papers or reports, paying a copyright fee if necessary. Copies of full papers, in electronic or hard copy form, should not be submitted in response to a call for evidence.

NICE will not consider the following material as part of a call for evidence:

- promotional material
- unsubstantiated or non-evidence-based assertions of effectiveness
- opinion pieces or editorial reviews
- potentially unlawful or other inappropriate information.

Registered stakeholders, relevant organisations or individuals approached are only able to submit evidence during a call for evidence, or during consultation on the draft guideline. Evidence submitted at other stages of guideline development is not considered, and the sender is informed.

Confidential information

Information or data that may be considered confidential include data that may influence share price values ('commercial in confidence') and data that are deemed intellectual property ('academic in confidence', that is, awaiting publication).

Confidential information should be kept to an absolute minimum. For example, information submitted should be limited to the relevant part of a sentence, a particular result from a table or a section of code. NICE does not allow a whole study to be designated confidential. As a minimum, a structured abstract of the study or economic model must be made available for public disclosure during consultation on the guideline. Results derived from calculations using confidential data are not considered confidential unless back-calculation to the original confidential data is possible.

When the Developer sends out a call for evidence, respondents are asked to complete a checklist that identifies the location of all confidential information contained in their submission, and for how long the information is likely to remain confidential. In addition to completing the checklist, respondents should indicate the part of their submission that contains the confidential information. All confidential information should be underlined. Information that is submitted under 'commercial in confidence' should also be highlighted in turquoise; information submitted under

'academic in confidence' should be highlighted in yellow. The underlining and highlighting should be maintained so that the Committee knows which parts are confidential.

When documents are prepared for consultation and publication, NICE and the evidence review team work with the data owners to agree a compromise between confidentiality and transparency, and strive to release as much information as possible. Any information that is still confidential is removed by the evidence review team, and a note added to explain what has been done. NICE needs to be able to justify the recommendations in its guidelines on the basis of the evidence considered by the Committee.

Documenting evidence received in response to a call for evidence

Information received from registered stakeholders, relevant organisations or individuals in response to a call for evidence should be recorded systematically and the details cross-checked against evidence identified through database searching (for example, to check if it has already been assessed). Information should be assessed in the same way as published studies identified through the searches (see chapter 6).

Disclosing links with the tobacco industry

When submitting evidence in response to a call for evidence, stakeholders are asked to disclose whether their organisation has any direct or indirect links to, or receives or has ever received funding from, the tobacco industry. Disclosures will be included with the evidence presented to the Committee.

5.6 Health inequalities and equality and diversity

All searches should be inclusive, capturing evidence related to health inequalities or impacts on equality relevant to the guideline topic. For example, if the population group is 'older people' a search for 'older people' should pick up subpopulations such as 'disabled older people' or 'black and minority ethnic older people'. Similarly, if the setting is 'communities and religious places', the search terms should cover all relevant faith settings (such as 'church', 'temple' and 'mosque').

5.7 Quality assurance

For each search, the principal database search strategy should be quality assured by a second information specialist to maintain a high, consistent standard for identifying the evidence. A checklist should be used to ensure clarity and consistency when peer reviewing search strategies. An example is the PRESS checklist (Sampson et al. 2008) or the CADTH checklist (Canadian Agency for Drugs and Technology in Health care 2008), which is adapted from PRESS.

5.8 Reference management

Electronic records of the references retrieved by searches should be stored using reference management software such as Endnote. Records can be exported from bibliographic databases and imported automatically into the software using import filters. Records of references from non-database sources can be added to reference management software manually, or stored as Word files by the Developer.

5.9 Documenting the search

Details of the search are published on the NICE website with the consultation on the draft guideline, and the final guideline.

Records should be kept of the searches undertaken during guideline development for all review questions to ensure that the process for identifying the evidence base is transparent and reproducible.

For each question, or group of questions, the following information should be documented:

- date(s) on which the searches were carried out, including the date(s) of any re-run searches (see section 5.10)
- names of the databases, database host systems and database coverage dates
- names of any other sources searched
- search strategies for all sources, annotated to explain any decisions on included and excluded terms which are not self-explanatory

- details of any supplementary searching undertaken, including the rationale
- any limits or search filters applied to the search (for example, language, date, study design).

5.10 Re-running searches

Searches undertaken to identify evidence for each review question may be re-run to identify any further evidence that has been published since the search was last run. For example, searches should be re-run if the evidence base changes quickly, or if there is reason to believe that substantial new evidence exists, or if the development time is longer than usual.

A decision to re-run searches will be taken by the Developer, in discussion with the review team and members of NICE staff with a quality assurance role.

If evidence is identified after the last cut-off date for searching but before publication, a judgment on its impact should be made by the Developer and NICE staff with a quality assurance role. In exceptional circumstances, this evidence can be considered if its impact is judged as substantial.

5.11 References and further reading

Beynon R, Leeflang MM, McDonald S et al. (2013) Search strategies to identify diagnostic accuracy studies in MEDLINE and EMBASE. Cochrane Database of Systematic Reviews 2013, Issue 9.

Booth A (2004) Formulating answerable questions. In Booth A, Brice A, editors. Evidence-based practice for information professionals. London: Facet Publishing, pp 61–70

Canadian Agency for Drugs and Technology in Health care (2008) CADTH Peer Review Checklist for Search Strategies. Adapted from: Sampson M, McGowan J, Lefebvre C, Moher D, Grimshaw J. PRESS: Peer Review of Electronic Search Strategies [Internet]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2008. [cited 2014 Jul 14]. Available from: http://www.cadth.ca/en/publication/781

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

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

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

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

Morrison A, Polisena J, Husereau D et al. (2012) The effect of English-language restriction on systematic review-based meta-analyses: a systematic review of empirical studies. International Journal of Technology Assessment in Health Care 28: 138–44

Sampson M, McGowan J, Lefebvre C, et al. (2008) An evidence-based checklist for the peer review of electronic search strategies PRESS: Peer Review of Electronic Search Strategies. Ottawa: Canadian Agency for Drugs EBC.

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

6 Reviewing research evidence

Reviewing evidence is an explicit, systematic and transparent process that can be applied to both quantitative (experimental, observational and correlational) and qualitative evidence (see chapter 4). The key aim of any review is to provide a summary of the relevant evidence to ensure that the Committee can make fully informed decisions about its recommendations. This chapter describes how evidence is reviewed in the development of guidelines.

Evidence reviews for NICE guidelines need to summarise the evidence, notwithstanding its limitations so that the Committee can interpret evidence and make recommendations, even where there is uncertainty.

Studies identified during literature searches (see chapter 5) need to be reviewed to identify the most appropriate information to answer the review questions, and to ensure that the guideline recommendations are based on the best available evidence. The evidence review process used must be explicit and transparent. The process used to inform guidelines involves 6 main steps:

- writing the review protocol (see section 4.5)
- identifying and selecting relevant evidence
- extracting and synthesising the results
- assessing quality
- interpreting the results
- deriving evidence statements.

Any substantial deviations from these steps need to be agreed, in advance, with NICE staff with a quality assurance role.

6.1 Selecting relevant evidence

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

Published studies

Titles and abstracts of the retrieved citations should be screened against the inclusion criteria defined in the protocol, and those that do not meet these should be excluded. Unless agreed beforehand with NICE staff with a quality assurance role, title and abstract screening should be undertaken independently by 2 reviewers (that is, titles and abstracts should be double-screened) using the parameters set out in the review protocol. If reviewers disagree about a study's relevance, this should be resolved by discussion or by recourse to a third reviewer. If, after discussion, there is still doubt about whether or not the study meets the inclusion criteria, it should be retained. If double-screening is only done on a sample of the retrieved citations (for example, 10% of references), inter-rater reliability should be assessed and reported in the guideline. If it is low, the reason for this should be explored and a course of action agreed to ensure a rigorous selection process.

However, this process is resource intensive. When deciding on the most appropriate strategy, a balance should be struck between the complexity of the topic and the potential risk of excluding studies inappropriately. Strategies could include checking with other members of the evidence review team, the topic adviser (if there is one), the Developer, and the Committee Chair or the Committee, checking of random samples, or using IT solutions such as text mining.

Once the screening of titles and abstracts is complete, full versions of the selected studies should be acquired for assessment. As with title and abstract screening, full studies should usually be checked independently by 2 reviewers, with any differences being resolved. As above, alternative strategies to ensure that studies are not excluded inappropriately can be used (such as checking with the Committee or checking of random samples). Studies that fail to meet the inclusion criteria once the full version has been checked should be excluded at this stage.

The study selection process should be clearly documented and include full details of the inclusion and exclusion criteria. A flow chart should be used to summarise the number of papers included and excluded at each stage of the process and this should be presented in the evidence review (see the PRISMA statement). Each study excluded after checking the full version should be listed, along with the reason for its exclusion. Ideally, if additional information is needed to complete the quality assessment, the investigators should be contacted.

Conference abstracts

Conference abstracts seldom contain enough information to allow confident judgements about the quality and results of a study, but they can be important in interpreting evidence reviews. Conference abstracts should therefore not be excluded from the search strategy. But it can be very time consuming to trace the original studies or additional data, and the information found may not always be useful. If enough evidence has been identified from full published studies, it may be reasonable not to trace the original studies or additional data related to conference abstracts. But if limited evidence is identified from full published studies, tracing the original studies or additional data may be considered, to allow full critical appraisal of the data and to make judgements on their inclusion or exclusion from the evidence review. Ideally, if additional information is needed to complete the quality assessment, the investigators should be contacted.

Sometimes conference abstracts can be a good source of other information. For example, they can point to published studies that may be missed, they can help to estimate how much evidence has not been fully published (and so guide calls for evidence and judgements about publication bias), or they can identify ongoing studies that are due to be published.

Legislation and policy

Relevant legislation or policies may be identified in the literature search and used to inform guidelines. Legislation and policy does not need quality assessment in the same way as other evidence, given the nature of the source. Recommendations from national policy or legislation can be quoted verbatim in the guideline [for example, Health and Social Care Act (2012)], where needed.

Unpublished data and studies in progress

Any unpublished data should be quality assessed in the same way as published studies (see section 6.2). Ideally, if additional information is needed to complete the quality assessment, the investigators should be contacted. Similarly, if data from studies in progress are included, they should be quality assessed in the same way as published studies. The same principles for the use of confidential data should be applied (see section 5.5) and, as a minimum, a structured abstract of the study must be made available for public disclosure during consultation on the guideline.

Grey literature

Grey literature may be quality assessed in the same way as published literature, although because of its nature, such an assessment may be more difficult. Consideration should therefore be given to the elements of quality that are likely to be most important.

6.2 Assessing the quality of the evidence

Introduction

Quality assessment is a critical stage in reviewing the evidence. It requires a systematic process of assessing bias through considering the appropriateness of the study design and the methods of the study. Every study should be assessed using an appropriate checklist. The quality is then summarised by individual study and, if using the GRADE approach, by outcome across all relevant studies. Details of methodology checklists for studies addressing different types of review question and the methods used for assessing quality are given below. Whatever the type of review question or the method used for assessing quality, critical thinking should be used to ensure that relevant biases are considered fully. The Cochrane handbook for systematic reviews of interventions gives a full description of potential biases for intervention studies and how they may be assessed. Quality assessment applies to qualitative and quantitative studies, including economic studies.

Making judgements about the overall quality of studies can be difficult. Before starting the review, an assessment should be made to determine which quality appraisal criteria from the appropriate checklist are likely to be the most important indicators of quality for the review question being addressed. These criteria will be useful in guiding decisions about the overall quality of individual studies and whether to exclude certain studies. They will also be useful when summarising and presenting the body of evidence as a whole (see section 6.4). Topic-specific input (for example, from Committee members) may be needed to identify the most appropriate quality criteria.

Characteristics of data should be extracted to a standard template for inclusion in an evidence table (see appendix H for examples of evidence tables).

Options for quality assessment should be considered by the Developer, and the chosen approach discussed and agreed with NICE staff with responsibility for quality assurance. The approach should be documented in the review protocol (see table 4.1) together with the rationale for the choice. Each study included in an evidence review should usually be quality assessed by

1 reviewer and checked by another. Any differences in quality grading should be resolved by discussion or recourse to a third reviewer. Alternate strategies for quality assessment may be used depending on the topic and the review question. Strategies for different types of review questions are given below.

Quality assessment of systematic reviews (secondary evidence)

Reviews should be assessed using the methodology checklist for systematic reviews and meta-analyses (see appendix H). If needed, high-quality systematic reviews can be updated or their primary studies used as evidence for informing a new review. However, the original systematic review should be cited and its use acknowledged as evidence.

Quality assessment of studies of interventions

The Cochrane handbook for systematic reviews of interventions (Higgins and Green 2011) lists design features in tables 13.2a and 13.2b for quantitative studies with allocations to interventions at the individual and group levels respectively. Once the study design has been classified, the study should be assessed using the methodology checklist appropriate for that type of study (see appendix H). Box 13.4a of the Cochrane handbook for systematic reviews of interventions provides useful notes for completing the appropriate checklist.

The quality of a study can vary depending on which of its measured outcomes is being considered. For example, short-term outcomes may be less susceptible to bias than long-term outcomes because of greater loss to follow-up with the latter. It is therefore important when summarising evidence that quality is considered according to outcome.

Quality assessment of studies of cost effectiveness

For more information about the quality assessment of studies of cost effectiveness, see chapter 7.

Quality assessment of studies of diagnostic test accuracy

Studies of diagnostic test accuracy should be assessed using the methodology checklist for QUADAS-2 (Quality Assessment of Studies of Diagnostic Accuracy included in Systematic Reviews; see appendix H).

Quality assessment of studies of prognosis or prediction models

Studies of prognosis or prediction models should be assessed using the methodology checklist for prognostic or prediction model studies (see appendix H).

Quality assessment of studies on the views and experiences of people using services, their families and carers, the public or practitioners

Studies about the views and experiences of people are likely to be qualitative studies or cross-sectional surveys. Qualitative studies should be assessed using the methodology checklist in appendix H.

There is no well-validated methodology checklist for the quality appraisal of cross-sectional surveys. Such surveys should be assessed for the rigour of the process used to develop the survey questions and their relevance to the population under consideration, and for the existence of significant bias (for example, non-response bias).

Quality assessment of the evidence

There are two approaches to presenting the quality assessment of the evidence – either at the whole study level or by outcome across multiple studies. Either approach can be used, but this should be documented in the review protocol.

Quality assessment by individual study

Studies are rated ('++', '+' or '−') individually to indicate their quality, based on assessment using a checklist, appropriate to the study design. Quality ratings are shown in box 6.1.

Box 6.1 Quality ratings

++ All or most of the checklist criteria have been fulfilled, and where they have not been fulfilled the conclusions are very unlikely to alter.
+ Some of the checklist criteria have been fulfilled, and where they have not been fulfilled, or are not adequately described, the conclusions are unlikely to alter.
– Few or no checklist criteria have been fulfilled and the conclusions are likely or very likely to alter.

If a study is not assigned a '++' quality rating, key reasons why this is the case should be recorded, alongside the overall quality rating, and highlighted in the guideline.

Quality assessment by outcome – the GRADE approach to assessing and rating quality

The GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach for review questions about interventions has been used in the development of NICE clinical guidelines since 2009. For more details about GRADE, see the Journal of Clinical Epidemiology series, appendix H and the GRADE working group website.

GRADE is a system developed by an international working group for rating the quality of evidence in systematic reviews and guidelines; it can also be used to grade the strength of recommendations in guidelines. The GRADE system is designed for use for reviews and guidelines that examine alternative management strategies or interventions, which may include no intervention or current best management. The key difference from other assessment systems is that GRADE rates the quality of evidence for a particular outcome across studies and does not rate the quality of individual studies.

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

Before starting an evidence review, an initial rating should be applied to the importance of outcomes, in order to identify which outcomes of interest are both 'critical' to decision-making and 'important' to people using services and the public. This rating should be confirmed or, if absolutely necessary, revised after completing the evidence review and documented in the guideline, noting any changes. This should be clearly separated from discussion of the evidence, because there is potential to introduce bias if outcomes are selected on the basis of the results. An example of this would be choosing only outcomes for which there were statistically significant results. It may be important to note outcomes that were not considered important for decision-making, and why (such as surrogate outcomes if longer-term, more relevant outcomes are available).

The GRADE system assesses the quality of the evidence for intervention studies by looking at features of the evidence found for each 'critical' and 'important' outcome. This is summarised in box 6.2.

Box 6.2 The GRADE approach to assessing the quality of evidence for intervention studies

The GRADE system assesses the following features for the evidence found for each 'critical' and each 'important' outcome:

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

For observational studies the effect size, effect of all plausible confounding and evidence of a dose–response relationship are also considered.

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

High – further research is very unlikely to change our confidence in the estimate of effect.

Moderate – further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low – further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low – any estimate of effect is very uncertain.

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

- it also integrates a review of the quality of cost-effectiveness studies

- it does not use 'overall summary' labels for the quality of the evidence across all outcomes or for the strength of a recommendation, but uses the wording of recommendations to reflect the strength of the evidence (see chapter 9).

In addition, although GRADE does not yet cover all types of review questions, GRADE principles can be applied and adapted to other types of questions. Any substantial changes to GRADE should be agreed with the NICE staff with responsibility for quality assurance before use.

GRADEpro software can be used to prepare the GRADE profiles. These are evidence profiles that contain a 'quality assessment' section that summarises the quality of the evidence and a 'summary of findings' table that presents the outcome data for each critical and each important outcome. The 'summary of findings' table includes a limited description of the quality of the evidence and may be presented in the evidence review to help readers quickly understand the quality of the evidence base. Full GRADE profiles should also be available (for example, in an appendix).

6.3 Equality and diversity considerations

NICE's equality and diversity duties are expressed in a single public sector equality duty ('the equality duty' see section 1.4). The equality duty supports good decision-making by encouraging public bodies to understand how different people will be affected by their activities. For NICE, much of whose work involves developing advice for others on what to do, this includes thinking about how people will be affected by its recommendations when these are implemented (for example, by health and social care practitioners). In addition to meeting its legal obligations, NICE is committed to going beyond compliance, particularly in terms of tackling health inequalities. Specifically, NICE considers that it should also take account of socioeconomic status in its equality considerations.

Ensuring inclusivity of the evidence review criteria

Any equalities data specified in the review protocol should be included in the evidence reviews. At the data extraction stage, reviewers should refer to the PROGRESS-Plus criteria (including age, sex, sexual orientation, disability, ethnicity, religion, place of residence, occupation, education, socioeconomic position and social capital; Gough et al. 2012) and any other relevant protected characteristics. Review inclusion and exclusion criteria should also take the relevant groups into account.

Ensuring that the relevant data are appropriately extracted and presented in the evidence statements

Equalities evidence should be considered during the drafting of the reviews. It should be included in the data extraction process and should appear in the summary evidence statements.

6.4 Presenting and summarising evidence

Presenting evidence

The following sections should be included in the evidence review:

- summary of the evidence, including the 'summary of findings' table from the GRADE profile (if this improves readability and the GRADE system has been used)
- evidence statements
- full GRADE profiles or links to the profiles in an appendix (if GRADE has been used)
- evidence tables.

The evidence should usually be presented for each review question; however, alternative methods of presentation may be needed for some evidence reviews (for example, where review questions are closely linked and need to be interpreted together). In these cases, the principles of quality assessment, data extraction and presentation, and evidence statements should still apply.

Any substantial deviations in presentation need to be agreed, in advance, with a member of NICE staff with responsibility for quality assurance.

Evidence tables

Evidence tables help to identify the similarities and differences between studies, including the key characteristics of the study population and interventions or outcome measures. This provides a basis for comparison.

Data from identified studies are extracted to standard templates for inclusion in evidence tables. The type of data and study information that should be included depends on the type of study and

review question, and should be concise and consistently reported. Appendix H contains examples of evidence tables for quantitative studies (both experimental and observational).

The types of information that could be included are:

- bibliography (authors, date)
- study aim, type (for example, randomised controlled trial, case–control study) and setting (for example, country)
- funding details (if known)
- population (for example, source, eligible and selected)
- intervention, if applicable (for example, content, who delivers the intervention, duration, method, mode or timing of delivery)
- comparator, if applicable (for example, content, intervener, duration, method, mode or timing of delivery)
- method of allocation to study groups (if applicable)
- outcomes (for example, primary and secondary and whether measures were objective, subjective or otherwise validated)
- key findings (for example, effect sizes, confidence intervals, for all relevant outcomes, and where appropriate, other information such as numbers needed to treat and considerations of heterogeneity)
- inadequately reported or missing data
- comments on quality, based on the quality assessment.

If not being used in any further statistical analysis or reported in GRADE tables, effect sizes with confidence intervals should be reported, as should exact p values (whether or not significant) with the test from which they were obtained, if this is a quality concern. Where p values are inadequately reported or not given, this should be stated. Any descriptive statistics (including any mean values) indicating the direction of the difference between intervention and comparator should be presented. If no further statistical information is available, this should be clearly stated.

The quality ratings of the study should also be given. When study details are inadequately reported, absent or not applicable, this should be clearly stated.

The type of data that should be included in evidence tables for qualitative studies is shown in the example in appendix H. This could include:

- bibliography (authors, date)
- location (for example, UK)
- funding details (if known)
- population or participants
- study design
- theoretical perspective adopted (such as grounded theory)
- key aims, objectives and research questions; methods (including analytical and data collection technique)
- key themes/findings (including quotes from participants that illustrate these themes/findings, if appropriate)
- gaps and limitations
- the study's quality rating.

Summarising evidence

A summary of the evidence should be produced. The content of this summary will depend on the type of question, the type of evidence included and whether GRADE is used. It should also identify and describe any gaps in the evidence.

Narrative summaries

The narrative summary places a study and its findings in context. It should highlight key factors influencing the results observed, interpret the results and give more detail than presented in the evidence tables. Each narrative summary should include:

- a brief description of the study design, methodology, population, setting and research questions or outcomes (if appropriate) for all relevant studies
- a summary of the key findings
- a summary of the quality ratings (expanding, as appropriate, on study strengths and weaknesses), applicability issues and any other relevant contextual points.

Commentary on the scale and nature of the evidence base may also be useful.

The narrative summary should conclude with a short discussion, followed by 1 or more evidence statements. These should reflect the key findings, the quantity, quality and consistency of the evidence, and its applicability to the review question (including its applicability to people affected by the guideline).

Narrative summaries of all studies and interventions should be incorporated in the main findings of the evidence review. They should be organised by review question and could be divided into smaller subcategories, such as outcome measure, setting or subpopulation.

If GRADE is used, the narrative summary needs only to be very brief and describe key features of the included studies and any other important information that is not included in the GRADE tables. For example, applicability is included in the GRADE tables so does not need to be included in the narrative summary.

Summary tables

If appropriate (for example, when GRADE is used), short summary tables (based on the 'summary of findings' table from the GRADE profile or the narrative summaries) should be included with the main findings (usually before an evidence statement) or in the appendices. For example, these might:

- summarise the information gleaned for different review questions
- summarise the study types, populations, interventions, settings or outcomes for each study related to a particular review question
- organise and summarise studies related to different outcomes.

Summarising and presenting results for studies of interventions

Meta-analysis may be appropriate if treatment estimates from more than 1 study are available. Recognised approaches to meta-analysis should be used, as described in the manual from Centre for Reviews and Dissemination (2009), in Higgins and Green (2011) and technical support documents developed by the NICE Decision Support Unit.

NICE prefers data from head-to-head RCTs to compare the effectiveness of interventions. However, there may be situations when data from head-to-head studies of the options (and/or comparators) of interest are not available. In these circumstances, indirect treatment comparison analyses should be considered.

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

The same principles of good practice for evidence reviews and meta-analyses should be applied when conducting indirect treatment comparisons or network meta-analyses. The rationale for identifying and selecting the RCTs should be explained, including the rationale for selecting the treatment comparisons included. A clear description of the methods of synthesis is required. The methods and results of the individual trials should also be documented. If there is doubt about the relevance of particular trials, a sensitivity analysis in which these trials are excluded should also be presented. The heterogeneity between the results of pairwise comparisons and inconsistencies between the direct and indirect evidence on the interventions should be reported, using coherence statistics such as the deviance information criterion (DIC).

When multiple options are being appraised, a network meta-analysis should be considered. Consideration should also be given to presenting pair-wise meta-analyses to help validate the network meta-analysis.

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

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

If sufficient relevant and valid data are not available to include in meta-analyses of head-to-head trials, or mixed or indirect treatment comparisons (network meta-analysis), the analysis may have to be restricted to a qualitative overview that critically appraises individual studies and presents their results.

Further information on complex methods for evidence synthesis is provided by the technical support documents developed by the NICE Decision Support Unit.

Evidence from a network meta-analysis can be presented in a variety of ways. The network of evidence can be presented as tables. It should also be presented diagrammatically with the direct and indirect treatment comparisons clearly identified and the number of trials in each comparison stated. Further information on how to present the results of network meta-analyses is provided by the technical support documents developed by the NICE Decision Support Unit.

There are several ways to summarise and illustrate the strength and direction of quantitative evidence about the effectiveness of an intervention if a meta-analysis is not done. Forest plots can be used to show effect estimates and confidence intervals for each study (when available, or when it is possible to calculate them). They can also be used to provide a graphical representation when it is not appropriate to do a meta-analysis and present a pooled estimate. However, the homogeneity of the outcomes and measures in the studies needs to be carefully considered: the forest plot needs data derived from the same (or justifiably similar) outcomes and measures.

If a forest plot is not appropriate, other graphical forms may be used (for example, a harvest plot [Ogilvie et al. 2008]).

If additional statistical analysis, such as meta-analysis, is not possible or appropriate, a narrative summary of the evidence and its quality should be presented.

Summarising and presenting results for studies of cost effectiveness

For more information on summarising and presenting results for studies of cost effectiveness, see chapter 7.

Summarising and presenting results of studies of diagnostic test accuracy

Information on methods of presenting and synthesising diagnostic test accuracy is being developed (http://srdta.cochrane.org and www.gradeworkinggroup.org). If meta-analysis is not possible or appropriate, a narrative summary of the quality of the evidence should be based on the quality appraisal criteria from QUADAS-2 (see appendix H) that were considered most important for the review question being addressed.

Numerical summaries of evidence on diagnostic test accuracy may be presented as tables. Meta-analysis of numerical summaries from different studies can be complex and relevant published technical advice (such as that from the NICE Technical Support Unit or Decision Support Unit) should be used to guide reviewers.

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

Summarising and presenting results of studies of prognosis

There is currently no well-designed and validated approach for summarising evidence from studies on prognosis or prediction models. A narrative summary of the quality of the evidence should therefore be given, based on the quality appraisal criteria from appendix H that were considered most important for the review question being addressed. Characteristics of data should be extracted to a standard template for inclusion in an evidence table (see appendix H). Methods for presenting and synthesising evidence on prognosis and predication models are being developed (www.gradeworkinggroup.org).

Results from the studies included may be presented as tables to help summarise the available evidence. Reviewers should be wary of using meta-analysis to summarise large observational studies, because the results obtained may give unfounded confidence in the study results. However, results should be presented consistently across studies (for example, the median and ranges of predictive values across all the studies).

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

Summarising and presenting results of studies of the views and experiences of people using services, their families and carers, the public or practitioners

The quality of the evidence should be described in a narrative summary, based on the quality appraisal criteria from appendix H that were considered the most important for the review question being addressed. If appropriate, the quality of the cross-sectional surveys included should also be summarised.

The quality assessment of included studies could be presented in tables. Methods for synthesising evidence from qualitative studies (for example, meta-ethnography) are evolving, but the routine use of such methods in guidelines is not currently recommended.

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

Other presentations of qualitative evidence

Qualitative evidence occurs in many forms and formats and so different methods may be used to synthesise and present it. As with all data synthesis, the key is transparency. It is important that the method used can be easily followed. It should be written up in clear English and any analytical decisions should be clearly justified.

In some cases, the evidence is synthesised and then summarised. In other cases, a narrative summary may be adequate. The approach used depends on the volume and consistency of the evidence. If the qualitative evidence is extensive, then a recognised method of synthesis is preferable. If the evidence is more disparate and sparse, a narrative summary approach may be more appropriate.

Reporting sparse, disparate qualitative evidence

Qualitative reviews may comprise relatively few papers or have an inconsistent focus (for example, they may involve different settings, populations or interventions). If the papers have little in common, it is not appropriate to synthesise them. Instead, a narrative summary of the key

themes (including illustrative quotes) of each paper should be provided, as well as a full evidence table for each study (for example, the methods, the participants and the underlying rationale).

Both the narrative summary and the evidence table should identify all the main themes reported: only themes that are not relevant to the review should be left out and these omissions should be clearly documented. As in all qualitative research, particular attention should be paid to 'outliers' (other themes) and views that disagree with or contradict the main body of research.

The narrative summary should be divided up under headings derived from the review question (for example, the settings of interest) unless good reasons are documented for not doing so. The narrative should be summarised into evidence statements that note areas of agreement and contradiction.

Synthesising qualitative evidence

The simplest and most rigorous approach to presenting qualitative data in a meaningful way is to analyse the themes (or 'meta' themes) in the evidence tables and write a narrative based on them. This 'second level' thematic analysis can be carried out if enough data are found, and the papers and research reports cover the same (or similar) factors or use similar methods. (These should be relevant to the review questions and could, for example, include intervention, age, population or setting.)

Synthesis can be carried out in 1 of 2 ways. More simply, papers reporting on the same factors can be grouped together to compare and contrast themes, focusing not just on consistency but also on any differences. The narrative should be based on these themes.

A more complex but useful approach is 'conceptual mapping' (see Johnson et al. 2000). This involves identifying the key themes and concepts across all the evidence tables and grouping them into first level (major), second level (associated) and third level (subthemes) themes. Results are presented in schematic form as a conceptual diagram and the narrative is based on the structure of the diagram.

Alternatively, themes can be identified and extracted directly from the data, using a grounded approach (see Glaser and Strauss 1967). Other potential techniques include meta-ethnography (see Noblit and Hare 1988) and meta-synthesis (see Barroso and Powell-Cope 2000), but expertise in their use is needed.

Reporting 'bias' or variation

Any review or, particularly, any synthesis of qualitative data, must by its nature mask some of the variations considered important by qualitative researchers (for example, the way the researcher interacts with research participants when gathering data). Reviewers should, as far as possible, highlight any significant causes of variation noted during data extraction.

Evidence statements

Evidence reviews for both qualitative and quantitative studies should include a narrative summary and GRADE tables where used, and should conclude with 1 or more supporting evidence statements.

The evidence statements should provide an aggregated summary of all of the relevant studies or analyses (such as economic models or network meta-analyses), regardless of their findings. They should reflect the balance of the evidence, its strength (quality, quantity and consistency) and applicability. The evidence statements should summarise key aspects of the evidence but can also highlight where there is a lack of evidence (note that this is different to evidence for a lack of effect). In the case of intervention studies, evidence statements should reflect what is plausible, given the evidence available about what has worked in similar circumstances. This may also be supported by additional information about aspects of the evidence such as setting, applicability or methodological issues.

Evidence statements are structured and written to help Committees formulate and prioritise recommendations. They help Committees decide:

- whether or not there is sufficient evidence (in terms of strength and applicability) to form a judgement
- whether (on balance) the evidence demonstrates that an intervention, approach or programme can be effective or is inconclusive
- the typical size of effect (where there is one) and associated measure of uncertainty
- whether the evidence is applicable to people affected by the guideline and contexts covered by the guideline.

Evidence statements should be included in the final guideline.

Structure and content of evidence statements

One or more evidence statements are prepared for each review question or subsidiary question. (Subsidiary questions may cover a type of intervention, specific population groups, a setting or an outcome.)

Each evidence statement should stand alone as an accessible, clear summary of key information used to support the recommendations (see section 9.1). The guideline should ensure that the relationship between the recommendations and the supporting evidence statements is clear.

Evidence statements if GRADE is not used

Evidence statements should refer to the sources of evidence and their quality in brief descriptive terms and not just by acronyms. Each statement should also include summary information about the:

- content of the intervention, if applicable (for example, what, how, where?)
- population(s) and setting(s) (for example, country), if applicable
- outcome(s), the direction of effect (or correlation) and the size of effect (or correlation) if applicable
- strength of evidence (reflecting the appropriateness of the study design to answer the question and the quality, quantity and consistency of evidence)
- applicability to the question, people affected by the guideline and setting (see section 6.3).

Note that the strength of the evidence is reported separately to the direction and size of the effects or correlations observed (if applicable).

Where important, the evidence statement should also summarise information about:

- whether the intervention has been delivered as it should be (fidelity of the intervention)
- what affects the intervention achieving the outcome (mechanism of action).

Terminology of evidence statements

Terms that describe the strength of the evidence should be used consistently and their definitions should be reported in the methodology section. A set of standardised terms is given in box 6.3. However, the evidence base for each review may vary, so the review team should define how these terms have been used.

Box 6.3 Examples of standardised terms for describing the strength of the evidence

No evidence[1] 'No evidence was found from English-language trials published since 1990…". (Be clear about the sources and inclusion criteria.)

Weak evidence 'There was weak evidence from 1 (−) RCT'.

Moderate evidence 'There was moderate evidence from 2 (+) controlled before and after studies'.

Strong evidence 'There was strong evidence from 2 (++) controlled before and after studies and 1 (+) RCT'.

Inconsistent evidence. Further commentary may be needed on the variability of findings in different studies. For example, when the results of (++) or (+) quality studies do not agree. In such cases, the review team may qualify an evidence statement with an explanatory sentence or section that gives more detail.

[1] Note that no evidence is not the same as evidence of no effect.
RCT, randomised controlled trial.

The terms should not be used to describe other aspects of the evidence, such as applicability or size of effect (see below for suitable terminology).

'Vote counting' (merely reporting on the number of studies) is not an acceptable summary of the evidence.

If appropriate, the direction of effect (impact) or correlation should be summarised using 1 of the following terms:

- positive
- negative

- mixed
- none.

However, appropriate context/topic-specific terms (for example, 'an increase in HIV incidence', 'a reduction in injecting drug use' and 'smoking cessation') may be used.

If appropriate, the size of effect (impact) or correlation and the degree of uncertainty involved, should be reported using the scale applied in the relevant study. For example, an odds ratio (OR) or relative risk (RR) with confidence interval (CI), or a standardised effect size and its standard error, may be quoted. Where an estimate cannot be explained, every effort should be made to relate it to interpretable criteria or conventional public health measures. If it is not possible to provide figures for each study, or if there are too many studies to make this feasible, the size of effect or correlation can be summarised using the following standardised terms:

- small
- medium
- large.

These terms should be used consistently in each review and their definitions should be reported in the methodology section.

Quantitative evidence statements

An example of an evidence statement about the effectiveness of an intervention is given in box 6.4 and an example of an evidence statement from a correlates review is given in box 6.5. These examples have been adapted from the originals and are for illustrative purposes only:

Box 6.4 Example of an evidence statement about the effectiveness of an intervention

There is strong evidence from 4 studies (2 UK[1,2] and 2 US[3,4]) to suggest that educational interventions delivered by youth workers may reduce the incidence of hazardous drinking by young people. Two (++) RCTs[1,2] and 1 (+) NRCT[3] showed reduced risk (95% confidence interval) in the intervention group: 0.75 (0.58–0.94)[1]; 0.66 (0.57–0.78)[2]; 0.42 (0.18–0.84)[3]. Another (+) RCT[4] showed reduced risk but was not statistically significant: 0.96 (0.84–1.09). However, 1 (−) NRCT[5] found increased risk of binge drinking in the intervention group: 1.40 (1.21–1.74).

1 Huntley et al. 2009 (++)

2 Axe et al. 2008 (++)

3 Carmona et al. 2010 (+)

4 White et al. 2007 (+)

5 Kelly et al. 2006 (−).

RCT, randomised controlled trial; NRCT, non-randomised controlled trial.

Box 6.5 Example of an evidence statement from a correlates review

There is moderate evidence from 3 UK cross-sectional studies (2 [+][1,2] and 1 [−][3]) about the correlation between young people's communication skills around safer sex and a reduction in the number of teenage pregnancies. The evidence about the strength of this correlation is mixed. One (+) study[1] found that discussing condom use with new partners was associated with actual condom use at first sex (OR 2.67 [95% CI 1.55–4.57]). Another (−) study[3] found that not talking to a partner about protection before first sexual intercourse was associated with teenage pregnancy (OR 1.67 [1.03–2.72]). However, another (+) study[2] found small correlations between condom use, discussions about safer sex ($r=0.072$, $p<0.01$) and communication skills ($r=0.204$, $p<0.01$).

1 Kettle et al. 2007 (+)

2 Jarrett et al. 2007 (+)

3 Morgan et al. 2000 (−)

OR, odds ratio; CI, confidence interval.

Assessing the applicability of the evidence

The Committee also needs to judge the extent to which the evidence reported in the reviews is applicable to the areas for which it is developing recommendations. A body of evidence should

be assessed to determine how similar the population(s), setting(s), intervention(s) and outcome(s) of the selected studies are to those outlined in the review question(s).

The following characteristics should be considered:

- population – age, sex/gender, race/ethnicity, disability, sexual orientation, gender re-assignment, religion/beliefs, pregnancy and maternity, socioeconomic status, health status (for example, severity of illness/disease), other characteristics specific to the topic area/review question(s)
- setting – country, geographical context (for example, urban/rural), delivery system, legislative, policy, cultural, socioeconomic and fiscal context, other characteristics specific to the topic area/review question(s)
- intervention – feasibility (for example, in terms of health and social care services/costs), practicalities (for example, experience/training needed), acceptability (for example, number of visits/adherence needed), accessibility (for example, transport/outreach needed), other characteristics specific to the topic area/review question(s)
- outcomes – appropriate/relevant, follow-up periods, important health effects.

After this assessment, the body of evidence in each evidence statement should be categorised as:

- directly applicable
- partially applicable
- not applicable.

A statement detailing the category it falls into and the reasons why should appear at the end of the evidence statement. It should state: 'This evidence is (directly, partially or not) applicable because ...'. An example of an applicability statement is shown in box 6.6.

Box 6.6 Example of an applicability statement

This evidence is only partially applicable to people in the UK who inject drugs. That is because all these studies were conducted in countries in which needles are mainly sold by pharmacies (USA, Russia and France), rather than freely distributed, as is the norm in the UK[1].

[1] This has been adapted from the original and is for illustrative purposes only.

If the Committee is not able to judge the extent to which the evidence reported in the reviews is applicable to the areas/topics for which it is developing recommendations, it may ask for additional information on the applicability of the evidence.

Although similar issues are considered when assessing the applicability of economic data, there are some important differences (see chapter 7).

A summary of the assessment should be included when describing the link between the evidence and the recommendations (see section 9.1).

Evidence statements if GRADE is used

If GRADE is used, short evidence statements for outcomes should be presented after the GRADE profiles, summarising the key features of the evidence on clinical effectiveness (including adverse events as appropriate) and cost effectiveness. The evidence statements should include the number of studies and participants, the quality of the evidence and the direction of estimate of the effect (see box 6.7 for examples of evidence statements), and the importance of the effect (that is, whether the size of the effect is meaningful). An evidence statement may be needed even if no evidence is identified for a critical or important outcome.

Box 6.7 Examples of evidence statements if GRADE is used

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

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

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

Evidence statements for qualitative data

Evidence statements developed from qualitative data do not usually report the impact of an intervention on behaviour or outcomes, and do not report statistical effects or aggregate measures of strength and effect size. They should summarise the evidence, its context and quality, and the consistency of key findings and themes across studies. Areas where there is little (or no) concurrence should also be summarised. An example of an evidence statement developed from qualitative data is given in box 6.8.

Box 6.8 Example of evidence statements developed from qualitative data

Two UK studies (1 [+][1] and 1 [++][2]) and 1 (+) Dutch study[3] reported on the views of teenage mothers. In 1 (+) study[1] of teenage mothers interviewed in a family planning clinic and 1 (++) study[2] of teenage mothers who responded to a questionnaire at their GP surgery, the participants agreed that access to education was the thing that helped them most after they had their child. However, this was not reported as a key theme in the Dutch study[3] of health visitor perceptions of teenage mothers' needs.

[1] Ellis 1999 (+)

[2] Swann 2000 (++)

[3] Nolan 2004 (+).

Six studies comprising 94 participants showed that information on the diagnosis was highly desired, and should be provided as soon as possible to reduce anxiety. Information that does more than merely convey facts, but that also directs the patients and carers to practical sources of support, was a common wish.

6.5 References and further reading

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

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

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

Barroso J, Powell-Cope GM (2000) Meta-synthesis of qualitative research on living with HIV infection. Qualitative Health Research 10: 340–53

Bowling A (2002) Research methods in health: investigating health and health services. Buckingham: Open University Press

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

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

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

Dixon-Woods M, Agarwal S, Young B et al. (2004) Integrative approaches to qualitative and quantitative evidence. London: Health Development Agency

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

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

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

Egger M, Davey Smith G, Altman DG (2000) Systematic reviews in health care: meta-analysis in context. London: British Medical Journal Books

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

Glaser BG, Strauss AL (1967) The discovery of grounded theory: strategies for qualitative research. New York: Aldine de Gruyter

Gough D, Oliver S, Thomas J, editors (2012) An introduction to systematic reviews. London: Sage

GRADE Working Group (2004) Grading quality of evidence and strength of recommendations. British Medical Journal 328: 1490–4

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

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

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

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

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

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

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

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

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

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

Harden A, Garcia J, Oliver S et al. (2004) Applying systematic review methods to studies of people's views: an example from public health research. Journal of Epidemiology and Community Health 58: 794–800

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

Jackson N, Waters E for the Guidelines for Systematic Reviews of Health Promotion and Public Health Interventions Taskforce (2005) Guidelines for systematic reviews of health promotion and public health interventions. Australia: Deakin University

Johnson JA, Biegel DE, Shafran R (2000) Concept mapping in mental health: uses and adaptations. Evaluation and Programme Planning 23: 67–75

Kelly MP, Swann C, Morgan A et al. (2002) Methodological problems in constructing the evidence base in public health. London: Health Development Agency

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

National Collaborating Centre for Methods and Tools (2011) AMSTAR: assessing methodological quality of systematic reviews. Hamilton, Ontario: McMaster University

Noblit G, Hare RD (1988) Meta-ethnography: synthesising qualitative studies. London: Sage

Ogilvie D, Hamilton V, Egan M et al. (2005) Systematic reviews of health effects of social interventions: 1. Finding the evidence: how far should you go? Journal of Epidemiology and Community Health 59: 804–8

Ogilvie D, Egan M, Hamilton V et al. (2005) Systematic reviews of health effects of social interventions: 2. Best available evidence: how low should you go? Journal of Epidemiology and Community Health 59: 886–92

Ogilvie D, Fayter D, Petticrew M et al. (2008) The harvest plot: a method for synthesising evidence about the differential effects of interventions. BMC Medical Research Methodology 8: 8

Oxford Centre for Evidence-Based Medicine (2009) Levels of evidence and grades of recommendation.

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

Petticrew M (2003) Why certain systematic reviews reach uncertain conclusions. British Medical Journal 326: 756–8

Petticrew M, Roberts H (2003) Evidence, hierarchies, and typologies: horses for courses. Journal of Epidemiology and Community Health 57: 527–9

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

Popay J, editor (2005) Moving beyond effectiveness in evidence synthesis: methodological issues in the synthesis of diverse sources of evidence. London: National Institute for Health and Clinical Excellence

Popay J, Rogers A, Williams G (1998) Rationale and standards for the systematic review of qualitative literature in health services research. Qualitative Health Research 8: 341–51

Ring N, Jepson R and Ritchie K (2011) Methods of synthesizing qualitative research studies for health technology assessment. International Journal of Technology Assessment in Health Care 27: 384–390

Rychetnik L, Frommer M, Hawe P et al. (2002) Criteria for evaluating evidence on public health interventions. Journal of Epidemiology and Community Health 56: 119

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

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

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

Sutton AJ, Jones DR, Abrams KR et al. (2000) Methods for meta-analysis in medical research. London: John Wiley

Swann C, Falce C, Morgan A et al. (2005) HDA evidence base: process and quality standards for evidence briefings. London: Health Development Agency

Tooth L, Ware R, Bain C et al. (2005) Quality of reporting of observational longitudinal research. American Journal of Epidemiology 161: 280–8

Tugwell P, Pettigrew M, Kristjansson E et al. (2010) Assessing equity in systematic reviews: realising the recommendations of the Commission on the Social Determinants of Health. British Medical Journal 341: 4739

Turner RM, Spiegelhalter DJ, Smith GC et al. (2009) Bias modelling in evidence synthesis. Journal of the Royal Statistical Society, Series A (Statistics in Society) 172: 21–47

Victora C, Habicht J, Bryce J (2004) Evidence-based public health: moving beyond randomized trials. American Journal of Public Health 94: 400–5

Weightman A, Ellis S, Cullum A et al. (2005) Grading evidence and recommendations for public health interventions: developing and piloting a framework. London: Health Development Agency

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

7 Incorporating economic evaluation

7.1 Introduction

This chapter describes the role of economics in developing NICE guidelines, and suggests possible approaches to use when considering economic evidence in guideline development. It also sets out the principles for conducting new economic modelling if there is insufficient published evidence that can be used to assess the cost effectiveness of key interventions, services or programmes.

It should be noted that significant methodological developments in this area are anticipated, and this manual will be updated in response to these developments. Developments in methodology for considering the economic aspects of delivering services will also be taken into account.

7.2 The role of economics in guideline development

Economic evaluation compares the costs and consequences of alternative courses of action. Formally assessing the cost effectiveness of an intervention, service or programme can help decision-makers ensure that maximum gain is achieved from limited resources. If resources are used for interventions or services that are not cost effective, the population as a whole gains fewer benefits.

It is particularly important for Committee members to understand that economic analysis is not only about estimating the resource consequences of a guideline recommendation, but is concerned with evaluating costs in relation to benefits (including benefits to quality of life) and harm of alternative courses of action. NICE social value judgements usually take precedence over economics.

Guideline recommendations should be based on the balance between the estimated costs of the interventions or services and their expected benefits compared with an alternative (that is, their 'cost effectiveness'), rather than solely on the total cost or resource impact of implementing them. So, if the evidence suggests that an intervention, service or programme provides significant benefits at an acceptable cost per person, it is likely to be recommended even if it would be expensive to implement across the whole population. However, when implementing guideline recommendations, commissioners and decision-makers need to know the resource and cost implications for their organisations. Where appropriate, NICE carries out a separate cost–impact

analysis and publishes this alongside the guideline, as part of its support for putting guidelines into practice.

Defining the priorities for economic evaluation should start during scoping of the guideline, and should continue when the review questions are being developed. Questions on economic issues mirror the review questions on effectiveness, but with a focus on cost effectiveness. Economic evaluation typically involves 2 stages. The first is a literature review of published evidence to determine whether the review questions set out in the scope have already been assessed by economic evaluations. Reviews of economic evidence identify, present and appraise data from studies of cost effectiveness. They may be considered as part of each review question undertaken for a guideline. If existing economic evidence is inadequate or inconclusive for 1 or more review questions, then the second stage may involve a variety of economic modelling techniques such as adapting existing economic models or building new bespoke models from existing data.

Reviews of economic evidence and any economic modelling are quality assured by the Developer and a member of NICE staff with responsibility for quality assurance. The nature of the quality assurance will depend on the type of economic evaluation, but will consider the evaluation in terms of the appropriate reference case and be based on a methodology checklist (for example, those in appendix H).

7.3 The reference case

A guideline may consider a range of interventions, commissioned by various organisations and resulting in different types of benefits (outcomes). It is crucial that reviews of economic evidence and economic evaluations undertaken to inform guideline development adopt a consistent approach depending on the type of interventions assessed. The 'reference case' specifies the methods considered consistent with the objective of maximising benefits from limited resources. NICE is interested in benefits to patients (for interventions with health outcomes in NHS settings), to individuals and community groups (for interventions with health and non-health outcomes in public sector settings) and to people using services and their carers (for interventions with a social care focus).

Choosing the most appropriate reference case depends on whether or not the interventions undergoing evaluation:

- are commissioned by the NHS alone or by any other public sector body
- focus on social care outcomes.

The reference case chosen should be agreed for each decision problem (relevant to a review question), should be set out briefly in the scope and detailed in the economic plan. A guideline may use a different reference case for different decision problems if appropriate (for example, if a guideline reviews interventions with non-health- and/or social care-related outcomes). For guidelines covering service delivery, it is not currently clear what reference cases are most appropriate and this manual will be updated in the future in response to methodological developments.

Table 7.1 summarises the reference case according to the interventions being evaluated.

Table 7.1 Summary of the reference case

Element of assessment	**Interventions with health outcomes in NHS settings**	**Interventions with health and non-health outcomes in public sector and other settings**	**Interventions with a social care focus**
Defining the decision problem	The scope developed by NICE		
Comparator	Interventions routinely used in the NHS, including those regarded as current best practice.	Interventions routinely used in the public sector, including those regarded as best practice.	Interventions routinely delivered by the public and non-public social care sector[1].
Perspective on costs	NHS and PSS.	Public sector – often reducing to local government. Societal perspective (where appropriate). Other (where appropriate); for example, employer.	

Perspective on outcomes	All direct health effects, whether for people using services or, when relevant, other people (principally family members or informal carers).	All health effects on individuals. For local government and other settings, non-health benefits may also be included.	Effects on people for whom services are delivered (people using services and/or carers).
Type of economic evaluation	Cost–utility analysis.	Cost–utility analysis. Cost-effectiveness analysis. Cost–consequences analysis. Cost–benefit analysis. Cost-minimisation analysis.	
Synthesis of evidence on outcomes	Based on a systematic review.		
Time horizon	Long enough to reflect all important differences in costs or outcomes between the interventions being compared.		
Measuring and valuing health effects	QALYs[2]: the EQ-5D is the preferred measure of health-related quality of life in adults.		
Measure of non-health benefits	Not applicable.	Where appropriate, to be decided on a case-by-case basis.	Capability measures where an intervention results in both capability and health or social care outcomes.
Source of data for measurement of quality of life	Reported directly by people using service and/or carers.		

Source of preference data for valuation of changes in health-related quality of life	Representative sample of the UK population.
Discounting	The same annual rate for both costs and health effects (currently 3.5%). Sensitivity analyses using rates of 1.5% for both costs and health effects may be presented alongside the reference-case analysis. In certain cases, cost-effectiveness analyses are very sensitive to the discount rate used. In this circumstance, analyses that use a non-reference-case discount rate for costs and outcomes may be considered.
Equity considerations: QALYs	A QALY has the same weight regardless of the other characteristics of the people receiving the health benefit.
Equity considerations: other	Equity considerations relevant to specific topics, and how these were addressed in economic evaluation, must be reported.
Evidence on resource use and costs	Costs should relate to the perspective used and should be valued using the prices relevant to that perspective. Costs borne by people using services and the value of unpaid care may also be included if they contribute to outcomes.
[1] Social care costs are the costs of interventions which have been commissioned or paid for in full, or in part by non-NHS organisations [2] Quality-adjusted life years	

Interventions with health outcomes in NHS settings

For decision problems where the intervention evaluated is solely commissioned by the NHS and does not have a clear focus on social care or public health outcomes, the reference case for 'health outcomes in NHS settings' should be chosen.

More details on methods of economic evaluation for interventions with health outcomes in NHS settings can be found in NICE's Guide to the methods of technology appraisal 2013. This includes a reference case, which specifies the methods considered by NICE to be the most appropriate for analysis when developing technology appraisal guidance. The reference case is consistent with the NHS objective of maximising health gain from limited resources.

Productivity costs and costs borne by people using services and carers that are not reimbursed by the NHS or social services should not usually be included in any analyses (see the Guide to the methods of technology appraisal 2013). That is, a societal perspective will not normally be used.

Interventions with health and non-health outcomes in public sector and other settings

For decision problems where the interventions evaluated are commissioned in full or in part by non-NHS public sector and other bodies, the reference case for 'interventions with health and non-health outcomes in public sector and other settings' should be chosen. This reference case may be most appropriate for some public health interventions.

Most public health interventions are paid for by an arm of government, and so a public sector perspective on costs is usually used. This considers all the costs of implementing the intervention, and changes to downstream costs as a result of implementing the intervention. In some cases, the downstream costs are negative, and refer to cost savings. For example, an intervention such as increasing physical activity, whose outcomes may include the prevention of type 2 diabetes, may be paid for by local government, but may result in cost savings to the NHS in the form of fewer or delayed cases of diabetes. A public sector cost perspective would aggregate all these costs and cost savings. A narrower local government cost perspective would consider only the cost of implementation, whereas an NHS cost perspective would consider only the cost savings. When examining interventions that are not paid for by an arm of government (such as work place interventions), the perspective on costs should be discussed and agreed with the NICE staff with responsibility for quality assurance.

Productivity costs are not included in either the reference-case or non-reference-case analyses; exceptions (for example, when evaluating interventions in the workplace) can only be made with the agreement of NICE staff with a quality assurance role.

For public health interventions, all direct health effects for people using services or, when relevant, other people such as family members or informal carers will be included. Non-health benefits may also be included. When required, the perspective will be widened to include those sectors that do not bear the cost of an intervention but receive some kind of benefit from it.

Interventions with a social care focus

For decision problems where the interventions evaluated have a clear focus on social care outcomes, then the reference case on 'interventions with a social care focus' should be chosen.

Public sector funding of social care for individual service users is subject to eligibility criteria based on a needs assessment and a financial assessment (means test). Therefore users of social care may have to fund, or partly fund, their own care. A public sector perspective on costs should still be adopted, but should consider different scenarios of funding.

A public sector perspective is likely to be a local authority perspective for many social care interventions, but downstream costs that affect other public sector bodies may be taken into account where relevant, especially if they are a direct consequence of the primary aim of the intervention. When individuals may pay a contribution towards their social care, 2 further perspectives may also be pertinent: a societal perspective (which takes account of changes to the amount that individuals and private firms pay towards the cost of care, on top of the public sector contributions) and an individual perspective (which accounts for changes in individual payments only). Productivity costs are not included in either the reference-case or non-reference-case analyses; exceptions can only be made with the agreement of NICE staff with responsibility for quality assurance.

For social care interventions, the usual perspective on outcomes will be all effects on people for whom services are delivered including, when relevant, family members or informal carers. When required, the perspective may be widened to include those sectors that do not bear the cost of an intervention but receive some kind of benefit from it.

Other perspectives

Other perspectives (for example, employers) may also be used to capture significant costs and benefits that are material to the interventions. If other perspectives are used, this should be agreed with NICE staff with responsibility for quality assurance before use.

7.4 Reviewing economic evaluations

Identifying and examining published economic evidence that is relevant to the review questions is an important component of guideline development. The general approach to reviewing economic evaluations should be systematic, focused and pragmatic. The review protocol (see section 4.5) and the principal search strategy (see section 5.4) should be posted on the NICE website 6 weeks before consultation on the draft guideline.

Searching for economic evidence

The approach to searching for economic evidence should be systematic. The strategies and criteria used should be stated explicitly in the guideline and applied consistently.

The advice in section 5.4 about how to develop search strategies may be relevant to the systematic search for economic evaluations. The types of searches that might be needed are described below.

Initial scoping search to identify economic evaluations

A scoping search may be performed to look for economic evaluations relevant to current practice in the UK and therefore likely to be relevant to decision-making by the Committee (see chapter 3). This should cover areas likely to be included in the scope (see chapter 2).

Economic databases (see appendix G) should be searched using the population terms used in the evidence review. Other databases relevant to the topic and likely to include relevant economic evaluations should also be searched using the population terms with a published economics search filter (see section 5.4), and limited by publication date to the most recent complete year; it may be appropriate to extend these searches beyond economic databases if there is reason to believe that relevant economic evaluations may not yet be indexed in the economic databases.

Further systematic search to identify economic evaluations

For some review questions a full systematic search, covering all appropriate sources and all years, should be performed to identify all relevant economic evaluations. This should include all review questions for which economic considerations are relevant. Mostly, the search will be conducted using the strategies derived with/from the review question(s) combined with a search

filter(s) to identify economic evaluations and outcome data. However, an alternative is for economic evaluations and quality-of-life data to be identified alongside evidence for effectiveness.

Selecting relevant economic evaluations

The process for sifting and selecting economic evaluations for assessment is essentially the same as for effectiveness studies (see section 6.1). The review should be targeted to identify the papers that are most relevant to current UK practice and therefore likely to inform the Committee's decision-making.

Inclusion criteria for sifting and selecting papers for review should specify populations and interventions relevant to the review question. They should also specify:

- An appropriate date range, because older studies may reflect outdated practices.
- The country or setting, because studies conducted in other countries might not be relevant to the UK. In some cases it may be appropriate to limit consideration to the UK or countries with similar healthcare systems.

The review should also usually focus on economic evaluations that compare both the costs and consequences of the alternative interventions under consideration. Cost–utility, cost–benefit, cost-effectiveness, cost-minimisation or cost–consequences analyses can be considered depending on what the Committee deems to be the most relevant perspective and likely outcomes for the question. Non-comparative costing studies, 'burden of disease' studies and 'cost of illness' studies should usually be excluded. On occasion, the published economic evidence is extremely sparse. In such cases, the inclusion criteria for studies may be broadened. The decision to do this is taken by the guideline Developer in consultation with NICE staff with responsibility for guideline quality assurance and, when appropriate, with the Committee or its Chair.

Assessing the quality of economic evaluations

All economic evaluations relevant to the guideline should be appraised using the methodology checklists (see appendix H). These checklists should be used to appraise unpublished economic evaluations, such as studies submitted by registered stakeholders and academic papers that are not yet published, as well as published papers. The same criteria should be applied to any new economic evaluations conducted for the guideline (see section 7.6).

Exclusion of economic evaluations will depend on the amount of higher-quality evidence and the degree of certainty about the cost effectiveness of an intervention (when all the evidence is considered as a whole). Weaker studies are more likely to be excluded when cost effectiveness (or lack of it) can be reliably established without them.

Sometimes reported sensitivity analyses indicate whether the results of an evaluation or study are robust despite methodological limitations. If there is no sensitivity analysis, judgement is needed to assess whether a limitation would be likely to change the results and conclusions. If necessary, the health technology assessment checklist for decision-analytic models (Philips et al. 2004) may also be used to give a more detailed assessment of the methodological quality of economic evaluations and modelling studies. Judgements made, and reasons for these judgements, should be recorded and presented in the guideline.

Summarising and presenting results for economic evaluations

Cost-effectiveness or net benefit estimates from published or unpublished studies, or from bespoke economic evaluations conducted for the guideline, should be presented in the guideline, for example, using an 'economic evidence profile' (see appendix H). This should include relevant economic information (applicability, limitations, resource use, costs, cost-effectiveness and/or net benefit estimates as appropriate). It should be explicitly stated if economic information is not available or if it is not thought to be relevant to the review question.

A short evidence statement that summarises the key features of the evidence on cost effectiveness should be included in the evidence review.

7.5 Prioritising questions for further economic analysis

If a high-quality economic analysis that addresses a key issue and is relevant to current practice has already been published, then further modelling may not be needed. However, often the economic literature is not sufficiently robust or applicable. Bespoke economic analyses should be developed selectively, unless an existing analysis can easily be adapted to answer the question.

Economic plans

The full economic plan initially identifies key areas of the scope as priorities for further economic analysis and outlines proposed methods for addressing review questions about cost effectiveness. The full economic plan may be modified during development of the guideline; for

example, as evidence is reviewed, it may become apparent that further economic evaluation is not necessary for some areas that were initially prioritised. A version of the economic plan setting out the questions prioritised for further economic analysis, the population, the interventions and the type of economic analysis is published on the NICE website before the guideline goes out for consultation (see section 4.5). The rationale for the final choice of priorities for economic analysis should be explained in the guideline.

Discussion of the economic plan with the Committee early in guideline development is essential to ensure that:

- the most important questions are selected for economic analysis
- the methodological approach is appropriate (including the reference case)
- all important effects and resource costs are included
- effects and outcomes relating to a broader societal perspective are included if relevant
- additional effects and outcomes not related to health or social care are included if they are relevant.

The number and complexity of new analyses depends on the priority areas and the information needed for decision-making by the Committee. Selection of questions for further economic analysis, including modelling, should be based on systematic consideration of the potential value of economic analysis across all key issues.

Economic analysis is potentially useful for any question in which an intervention, service or programme is compared with another. It may also be appropriate in comparing different combinations or sequences of interventions, as well as individual components of the service or intervention. However, the broad scope of some guidelines means that it may not be practical to conduct de novo economic analysis for every component.

The decision about whether to carry out an economic analysis therefore depends on:

- the potential overall expected benefit and resource implications of an intervention both for individual people and the population as a whole

- the degree of uncertainty in the economic evidence review and the likelihood that economic analysis will clarify matters.

Economic modelling may not be warranted if:

- It is not possible to estimate cost effectiveness. However, in this case, a 'scenario'' or 'threshold' analysis may be useful.
- The intervention has no likelihood of being cost saving and its harms outweigh its benefits.
- The published evidence of cost effectiveness is so reliable that further economic analysis is not needed.
- The benefits sufficiently outweigh the costs (that is, it is obvious that the intervention is cost effective) or the costs sufficiently outweigh the benefits (that is, it is obvious that the intervention is not cost effective).
- An intervention has very small costs, very small benefits and very small budget impact.

7.6 Approaches to bespoke economic evaluation

General principles

Regardless of the methodological approach taken, the general principles described below should be observed. Any variation from these principles should be described and justified in the guideline. The decision problem should be clearly stated. This should include a definition and justification of the interventions or programmes being assessed and the relevant groups using services (including carers).

Economic analyses should be explicitly based on the guideline's review questions. When a logic model has been used to develop the review questions, linking the structure of the economic model to the logic model should be considered. The logic model illustrates causal pathways linking determining factors, interventions and outcomes (see chapter 2 and appendix A for details). For guidelines covering public health topics, a topic-specific conceptual framework is used, and the framework may also be used to construct a logic model involving human behaviour, the social, environmental and biological determining factors of health.

The economic analysis should include comparison of all relevant alternatives for specified groups of people affected by the intervention or using services. Any differences between the review question(s) and the economic analysis should be clearly acknowledged, justified, approved by the Committee and explained in the guideline. The interventions or services included in the analysis should be described in enough detail to allow stakeholders to understand exactly what is being assessed. This is particularly important when calculating the cost effectiveness of services.

An economic analysis should be underpinned by the best-quality evidence. The evidence should be based on and be consistent with that identified for the relevant review question. If expert opinion is used to derive information used in the economic analysis, this should be clearly stated and justified in the guideline.

If existing economic models are used to inform new economic analyses, how these studies are being adapted or used in new analyses should be outlined clearly.

The structure of any economic model should be discussed and agreed with the Committee early in guideline development. The rationale for the structure of the model should be clearly outlined. Potential alternatives should be identified and considered for use in sensitivity analysis. All relevant costs that change as a result of an intervention should be taken into account. These may include costs to the NHS, other central government departments, local government, private employers and individuals (for example, changes in salaries). In addition, costs associated with changes in employment status of carers, and the value of unpaid care, should be considered for inclusion.

All economic analyses should be validated, with details of the validation process outlined in the guideline. Useful and practical validation methods include:

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

Results should be reported of any analyses conducted to demonstrate external validity. However, relevant data should not be omitted just to facilitate external validation (for example, not including trials so that they can be used for subsequent validation).

Conventions on reporting economic evaluations should be followed (see Drummond and Jefferson 1996) to ensure that reporting of methods and results is transparent. For time horizons that extend beyond 10 years, it may be useful to report costs and effects for the short (1–3 years) and medium (5–10 years) term. The following results should be presented where available and relevant:

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

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

Economic model(s) developed for the guideline are available to registered stakeholders during consultation on the guideline. These models should be fully executable and clearly presented.

Different approaches to economic analysis

There are different approaches to economic analysis. If economic analysis is needed, the most appropriate approach should be considered early during the development of a guideline, and reflect the content of the guideline scope.

Cost–utility analysis is a form of cost-effectiveness analysis that uses utility as a common outcome. It considers people's quality of life and the length of life they will gain as a result of an intervention or a programme. The health benefits are expressed as quality-adjusted life years (QALYs), an outcome that can be compared between different populations and disease areas. Costs of resources, and their valuation, should be related to the prices relevant to the sector.

If a cost–utility analysis is not possible (for example, when outcomes cannot be expressed using a utility measure such as the QALY), a cost–consequences analysis may be considered. Cost–consequences analysis considers all the health and non-health benefits of an intervention

across different sectors and reports them without aggregating them. It is useful when different outcomes cannot be incorporated into an index measure. When conducting cost–consequences analysis, it is helpful to produce a table that summarises all the costs and outcomes and enables the options to be considered in a concise and consistent manner. Outcomes that can be monetised are quantified and presented in monetary terms. Some benefits may be quantified but cannot readily be put into monetary form (for more details see the Department for Transport's Transport Analysis Guidance (TAG) unit 2.11). Some benefits cannot readily be quantified (such as reductions in the degree of bullying or discrimination) and should be considered by decision-making Committees as part of a cost–consequences analysis alongside benefits that can be quantified.

All benefits (even if they cannot be quantified) and costs of an intervention are considered when deciding which interventions represent the best value. Effectively, cost–consequences analysis provides a 'balance sheet' of outcomes that decision-makers can weigh up against the costs of an intervention (including related future costs).

If, for example, a commissioner wants to ensure the maximum health gain for the whole population, they might prioritise the incremental cost per QALY gained. But if reducing health inequalities is the priority, they might focus on interventions that work best for the most disadvantaged groups, even if they are more costly and could reduce the health gain achieved in the population as a whole.

Cost-effectiveness analysis uses a measure of outcome (a life year saved, a death averted, a patient-year free of symptoms) and assesses the cost per unit of achieving this outcome by different means. The outcome is not separately valued, only quantified; so the study takes no view on whether the cost is worth incurring, only focusing on the cost of different methods of achieving units of outcome. Cost-minimisation analysis is the simplest form of economic analysis, which can be used when the health benefits of an intervention are the same as those of the status quo, and when there are no other criteria for whether the intervention should be recommended. For example, cost-minimisation analysis could be used to decide whether a doctor or nurse should give routine injections when it is found that both are equally effective at giving injections (on average). In cost-minimisation analysis, an intervention is cost effective only if its net cost is lower than that of the status quo. The disadvantage of cost-minimisation analysis is that the health benefits of an intervention cannot often be considered equal to those of the status quo.

Cost–benefit analysis considers health and non-health benefits but converts them into monetary values, which can then be aggregated. Once this has been done, 'decision rules' are used to decide which interventions to undertake. Several metrics are available for reporting the results of cost–benefit analysis. Two commonly used metrics are the 'benefit-cost-ratio' (BCR) and the 'net present value' (NPV) – see the Department for Transport's Transport Analysis Guidance (TAG) Unit A1.1 for more information.

Cost–utility analysis is required routinely by NICE for the economic evaluation of health-related interventions, programmes and services, for several reasons:

- When used in conjunction with an NHS/personal social services (PSS) perspective, it provides a single yardstick or 'currency' for measuring the impact of interventions. It also allows interventions to be compared so that resources may be allocated more efficiently.
- Where possible, NICE programmes use a common method of cost-effectiveness analysis that allows comparisons between programmes.

However, because local government is largely responsible for implementing public health and wellbeing programmes and for commissioning social care, NICE has broadened its approach for the appraisal of interventions in these areas. Local government is responsible not only for the health of individuals and communities, but also for their overall welfare. The tools used for economic evaluation must reflect a wider remit than health and allow greater local variation. The nature of the evidence and that of the outcomes being measured may place more emphasis on cost–consequences analysis and cost–benefit analysis for interventions in these areas.

The type of economic analysis that should be considered is informed by the setting specified in the scope of the guideline, and the extent to which the benefits resulting from the intervention extend beyond health.

There is often a trade-off between the range of new analyses that can be conducted and the complexity of each piece of analysis. Simple methods may be used if these can provide the Committee with enough information on which to base a decision. For example, if an intervention is associated with better outcomes and fewer adverse effects than its comparator, then an estimate of cost may be all that is needed. Or a simple decision tree may provide a sufficiently reliable estimate of cost effectiveness. In other situations a more complex approach, such as Markov modelling or discrete event simulation, may be warranted.

Measuring and valuing effects for health interventions

The QALY is the measure of health effects preferred by NICE, based on patient-reported changes in health-related quality of life. The EQ-5D is the preferred measure of health-related quality of life in adults, and combines both quantity and health-related quality of life into a single measure of health gain. The value placed on health-related quality of life of people using services (or their carers) should be based on a valuation of public preferences elicited from a representative sample of the UK population.

For some economic analyses, a flexible approach may be needed, reflecting the nature of effects delivered by different interventions or programmes. If health effects are relevant, the EQ-5D-based QALY should be used. When EQ-5D data are not available from relevant clinical studies, EQ-5D data can be sourced from the literature. When obtained from the literature, the methods used for identifying the data should be systematic and transparent. The justification for choosing a particular data set should be clearly explained. When more than 1 plausible set of EQ-5D data is available, sensitivity analyses should be carried out to show the impact of the alternative utility values. When EQ-5D data are not available, they may be estimated by mapping other health-related quality-of-life measures or health-related benefits observed in the relevant studies to the EQ-5D. The mapping function chosen should be based on data sets containing both health-related quality-of-life measures. The statistical properties of the mapping function should be fully described, its choice justified, and it should be adequately demonstrated how well the function fits the data. Sensitivity analyses exploring variation in the use of the mapping algorithms on the outputs should be presented. When necessary, consideration should be given to alternative standardised and validated preference-based measures of health-related quality of life that have been designed specifically for use in children. The standard version of the EQ-5D has not been designed for use in children. An alternative version for children aged 7–12 years is available, but a validated UK valuation set is not yet available.

If mapping to the EQ-5D is not possible (for example, if no data are available) other approaches may be used (for more details see NICE's Guide to the methods of technology appraisal 2013).

Measuring and valuing effects for non-health interventions

For some decision problems (such as for interventions with a social care focus) the intended outcomes of interventions are broader than improvements in health status. Here broader, preference-weighted measures of outcomes, based on specific instruments, may be more appropriate. For example, social care quality-of-life measures are being developed and NICE will

consider using 'social care QALYs' if validated, such as the ASCOT (Adult Social Care Outcome Toolkit) set of instruments used by the Department of Health in the Adult Social Care Outcomes Framework indicator on social care-related quality of life.

Similarly, depending on the topic, and on the intended effects of the interventions and programmes, the economic analysis may also consider effects in terms of capability and wellbeing. For capability effects, use of the ICECAP-O (Investigating Choice Experiments for the Preferences of Older People – CAPability) instruments may be considered by NICE when developing methodology in the future. If an intervention is associated with both health- and non-health-related outcomes, it may be helpful to present these elements separately.

Economic analysis for interventions with health outcomes in NHS settings

Economic analyses conducted for decisions about interventions with health outcomes in NHS settings should usually follow the reference case in table 7.1 described in NICE's Guide to the methods of technology appraisal 2013. Advice on how to follow approaches described in NICE's Guide to the methods of technology appraisal 2013 is provided by the technical support documents developed by NICE's Decision Support Unit. Departures from the reference case may sometimes be appropriate; for example, when there are not enough data to estimate QALYs gained. Any such departures must be agreed with members of NICE staff with a quality assurance role and highlighted in the guideline with reasons given.

Economic analysis for interventions with health and non-health outcomes in public sector settings

The usual perspective for the economic analysis of public health interventions is that of the public sector. This may be simplified to a local government perspective if few costs and benefits apply to other government agencies.

Whenever there are multiple outcomes, a cost–consequences analysis is usually needed, and the Committee weighs up the changes to the various outcomes against the changes in costs in an open and transparent manner.

A societal perspective may be used, and will usually be carried out using cost–benefit analysis. When a societal perspective is used, it must be agreed with NICE staff with responsibility for quality assurance and highlighted in the guideline with reasons given.

Economic analysis for interventions with a social care focus

For social care interventions, the perspective on outcomes should be all effects on people for whom services are delivered (people using services and/or carers). Effects on people using services and carers (whether expressed in terms of health effects, social care quality of life, capability or wellbeing) are the intended outcomes of social care interventions and programmes. Although holistic effects on people using services, their families and carers may represent the ideal perspective on outcomes, a pragmatic and flexible approach is needed to address different perspectives, recognising that improved outcomes for people using services and carers may not always coincide.

Whenever there are multiple outcomes, a cost–consequences analysis is usually needed, and the Committee weighs up the changes to the various outcomes against the changes in costs in an open and transparent manner.

Any economic model should take account of the proportion of care that is publicly funded or self-funded. Scenario analysis may also be useful to take account of any known differences between local authorities in terms of how they apply eligibility criteria. Scenario analysis should also be considered if the cost of social care varies depending on whether it is paid for by local authorities or by individual service users; the value of unpaid care should also be taken into account where appropriate.

It is envisaged that the analytical difficulties involved in creating clear, transparent decision rules around the costs that should be considered, and for which interventions and outcomes, will be particularly problematic for social care. These should be discussed with the Committee before any economic analysis is undertaken and an approach agreed.

Identification and selection of model inputs

An economic analysis uses decision-analytic techniques with probability, cost and outcome data from the best available published sources.

The reference case across all 3 perspectives (table 7.1) states that evidence on effects should be obtained from a systematic review. Although it is desirable to conduct systematic literature reviews for other inputs to be used in economic modelling, this is time-consuming and other pragmatic options for identifying inputs may be used. This could include using data from the studies identified in the review of evidence on effects. Alternatives could include asking

Committee members and other experts for suitable papers or eliciting their opinions. When a systematic review is not possible, transparent processes for identifying other possible model inputs should be used; their quality should be assessed and their inclusion or exclusion justified. If existing economic models are being used, or are informing a new analysis, the way these models are adapted or used should be outlined clearly.

Additional searches may be needed; for example, if searches for evidence on effects do not provide the information needed for economic modelling. Additional information may be needed on:

- disease prognosis
- the relationship between short- and long-term outcomes
- quality of life
- adverse events
- resource use or costs.

For some questions, there may be good reason to believe that relevant and useful information exists outside of literature databases or validated national data sources. Examples include ongoing research, a relatively new intervention and studies that have been published only as abstracts. Typically, the method for requesting information from stakeholders is through a call for evidence (see section 5.5).

For some guidelines, econometric studies provide a supplementary source of evidence and data for bespoke economic models. For these studies, the database 'Econlit' should be searched as a minimum.

If expert opinion is used to derive information used in the economic analysis, this should be clearly stated and justified in the guideline.

Information on costs may be found in the Personal Social Services Research Unit report on unit costs of health and social care or the Department of Health reference costs. Information on costing can be found in the NICE's Assessing cost impact: methods guide 2011 or obtained from a costing analyst in NICE's implementation team. Some information about public services may

be better obtained from national statistics or databases, rather than from published studies. Philips et al. (2004) provide a useful guide to searching for data for use in economic models.

As outlined in NICE's Guide to the methods of technology appraisal 2013, the public list prices for technologies (for example, medicines or medical devices) should be used in the reference-case analysis. When there are nationally available price reductions (for example, for medicines procured for use in secondary care through contracts negotiated by the NHS Commercial Medicines Unit), the reduced price should be used in the reference-case analysis to best reflect the price relevant to the NHS. The Commercial Medicines Unit publishes information on the prices paid for some generic medicines by NHS trusts through its Electronic Market Information Tool (eMIT), focusing on medicines in the 'National Generics Programme Framework' for England. Analyses based on price reductions for the NHS will be considered only when the reduced prices are transparent and can be consistently available across the NHS, and when the period for which the specified price is available is guaranteed. When a reduced price is available through a patient access scheme that has been agreed with the Department of Health, the analyses should include the costs associated with the scheme. For medicines that are predominantly prescribed in primary care, prices should be based on the Drug Tariff. In the absence of a published list price and a price agreed by a national institution (as may be the case for some devices), an alternative price may be considered, provided that it is nationally and publicly available. If no other information is available on costs, local costs obtained from the Committee may be used.

Quality-of-life data are often needed for economic models. Many of the search filters available are highly sensitive and so, although they identify relevant studies, they also detect a large amount of irrelevant data. An initial broad literature search for quality-of-life data may be a good option, but the amount of information identified may be unmanageable (depending on the key issue being addressed). It may be more appropriate and manageable to incorporate a quality of life search filter when performing additional searches for key issues of high economic priority. The provision of quality-of-life data should be guided by the economist at an early stage during guideline development so that the information specialist can adopt an appropriate strategy. Two resources for identifying useful utility data for economic modelling are the database of preference weights on the CEA (Cost-Effectiveness Analysis) Registry website and the technical support document developed by NICE's Decision Support Unit.

Exploring uncertainty

The Committee should discuss any potential bias and limitations of economic models. Sensitivity analysis should be used to explore the impact that potential sources of bias and uncertainty could have on model results.

Deterministic sensitivity analysis should be used to explore key assumptions used in the modelling. This should test whether and how the model results change under alternative, plausible scenarios. Common examples of when deterministic sensitivity analysis could be conducted are:

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

Deterministic sensitivity analysis should also be used to test any bias resulting from the data sources selected for key model inputs.

Probabilistic sensitivity analysis can be used to account for uncertainty arising from imprecision in model inputs. The use of probabilistic sensitivity analysis will often be specified in the economic plan. Any uncertainty associated with all inputs can be simultaneously reflected in the results. In non-linear decision models where outputs are a result of a multiplicative function (for example, in Markov models), probabilistic methods also provide the best estimates of mean costs and outcomes. The choice of distributions used should be justified; for example, in relation to the available evidence or published literature. Presentation of the results of probabilistic sensitivity analysis could include scatter plots or confidence ellipses, with an option for including cost-effectiveness acceptability curves and frontiers.

When a probabilistic sensitivity analysis is carried out, a value of information analysis may be considered to indicate whether more research is necessary, either before recommending an intervention or in conjunction with a recommendation. The circumstances in which a value of

information analysis should be considered will depend on whether more information is likely to be available soon and whether this information is likely to influence the decision to recommend the intervention.

When probabilistic methods are inappropriate, the impact of parameter uncertainty should be thoroughly explored using deterministic sensitivity analysis, and the decision not to use probabilistic methods should be justified in the guideline.

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

Discounting

Cost-effectiveness results should reflect the present value of the stream of costs and benefits accruing over the time horizon of the analysis. For the reference case, the same annual discount rate should be used for both costs and benefits (currently 3.5%).

The specific discount rate varies across NICE programmes and over time. NICE considers that it is usually appropriate to discount costs and health effects at the same annual rate of 3.5%, based on the recommendations of the UK Treasury for the discounting of costs.

Sensitivity analyses using 1.5% as an alternative rate for both costs and health effects may be presented alongside the reference-case analysis. When treatment restores people who would otherwise die or have a very severely impaired life to full or near full health, and when this is sustained over a very long period (normally at least 30 years), cost-effectiveness analyses are very sensitive to the discount rate used. In this circumstance, analyses that use a non-reference-case discount rate for costs and outcomes may be considered. A discount rate of 1.5% for costs and benefits may be considered by the Committee if it is highly likely that, on the basis of the evidence presented, long-term health benefits are likely to be achieved. However, the Committee will need to be satisfied that the recommendation does not commit the funder to significant irrecoverable costs.

Subgroup analysis

The relevance of subgroup analysis to decision-making should be discussed with the Committee. When appropriate, economic analyses should estimate the cost effectiveness of an intervention in each subgroup.

Equity considerations

NICE's economic evaluation of healthcare and public health interventions does not include equity weighting – a QALY has the same weight for all population groups.

It is important to recognise that care provision, specifically social care, may be means tested, and that this affects the economic perspective in terms of who bears costs – the public sector or the person using services or their family. Economic evaluation should reflect the intentions of the system. Equity considerations relevant to specific topics, and how these were addressed in economic evaluation, must be reported.

7.7 Using economic evidence to formulate guideline recommendations

For an economic analysis to be useful, it must inform the guideline recommendations. The Committee should discuss cost effectiveness in parallel with general effectiveness when formulating recommendations (see chapter 9).

Within the context of NICE's principles on social value judgements, the Committee should be encouraged to consider recommendations that:

- increase effectiveness at an acceptable level of increased cost, or
- are less effective than current practice, but free up sufficient resources that can be re-invested in public sector care or services to increase the welfare of the population receiving care.

The Committee's interpretations and discussions should be clearly presented in the guideline. This should include a discussion of potential sources of bias and uncertainty. It should also include the results of sensitivity analyses in the consideration of uncertainty, as well as any

additional considerations that are thought to be relevant. It should be explicitly stated if economic evidence is not available, or if it is not thought to be relevant to the question.

Recommendations for interventions informed by cost–utility analysis

If there is strong evidence that an intervention dominates the alternatives (that is, it is both more effective and less costly), it should normally be recommended. However, if 1 intervention is more effective but also more costly than another, then the incremental cost-effectiveness ratio (ICER) should be considered.

Health benefits

The cost per QALY gained should be calculated as the difference in mean cost divided by the difference in mean QALYs for 1 intervention compared with the other.

If 1 intervention appears to be more effective than another, the Committee has to decide whether it represents reasonable 'value for money' as indicated by the relevant ICER. In doing so, the Committee should also refer to NICE's principles on social value judgements (also see below).

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

The degree of certainty around the ICER. In particular, advisory bodies will be more cautious about recommending a technology when they are less certain about the ICERs presented in the cost-effectiveness analysis.

The presence of strong reasons indicating that the assessment of the change in the quality of life has been inadequately captured, and may therefore misrepresent, the health gain.

When the intervention is an innovation that adds demonstrable and distinct substantial benefits that may not have been adequately captured in the measurement of health gain.

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

Non-health benefits

Outside the health sector it is more difficult to judge whether the benefits accruing to the non-health sectors are cost effective, but it may be possible to undertake cost–utility analysis based on measures of social care-related quality of life. The Committee should take into account the factors it considers most appropriate when making decisions about recommendations. These could include non-health-related outcomes that are valued by the rest of the public sector, including social care. It is possible that over time, and as the methodology develops (including the establishment of recognised standard measures of utility for social care), there will be more formal methods for assessing cost effectiveness outside the health sector.

Recommendations for interventions informed by cost–benefit analysis

When considering cost–benefit analysis, the Committee should be aware that an aggregate of individual 'willingness to pay' (WTP) is likely to be more than public-sector WTP, sometimes by quite a margin. If a conversion factor has been used to estimate public sector WTP from an aggregate of individual WTP, the Committee should take this into account. In the absence of a conversion factor, the Committee should consider the possible discrepancy in WTP when making recommendations that rely on a cost–benefit analysis.

The Committee should also attempt to determine whether any adjustment should be made to convert 'ability-to-pay' estimates into those that prioritise on the basis of need and the ability of an intervention to meet that need.

The Committee should not recommend interventions with an estimated negative net present value (NPV) unless other factors such as social value judgements are likely to outweigh the costs. Given a choice of interventions with positive NPVs, Committees should prefer the intervention that maximises the NPV, unless other objectives override the economic loss incurred by choosing an intervention that does not maximise NPV.

Care must be taken with published cost–benefit analyses to ensure that the value of the health benefits have been included. Older cost–benefit analyses, in particular, often consist of initial costs (called 'costs') and subsequent cost savings (called 'benefits') and fail to include health benefits.

Recommendations for interventions informed by cost–consequences analysis

The Committee should ensure that, where possible, the different sets of consequences do not double count costs or benefits. The way that the sets of consequences have been implicitly weighted should be recorded as openly, transparently and as accurately as possible. Cost–consequences analysis then requires the decision-maker to decide which interventions represent the best value using a systematic and transparent process. Various tools, such as multi-criteria decision analysis (MCDA), are available to support this part of the process. MCDA is currently in its infancy in healthcare evaluation and if it is to be used, it should only be used experimentally.

Recommendations for interventions informed by cost-effectiveness analysis

If there is strong evidence that an intervention dominates the alternatives (that is, it is both more effective and less costly), it should normally be recommended. However, if 1 intervention is more effective but also more costly than another, then the ICER should be considered. If 1 intervention appears to be more effective than another, the Committee has to decide whether it represents reasonable 'value for money' as indicated by the relevant ICER.

The Committee should use an established ICER threshold. In the absence of an established threshold, the Committee should estimate a threshold it thinks would represent reasonable 'value for money' as indicated by the relevant ICER.

The Committee should take account of NICE's principles on social value judgements when making its decisions.

Recommendations for interventions informed by cost-minimisation analysis

Cost minimisation can be used when the difference in benefits between an intervention and its comparator is known to be small and the cost difference is large (for example, whether doctors or nurses should give routine injections). If it cannot be assumed from prior knowledge that the difference in benefits is sufficiently small, ideally the difference should be determined by an equivalence trial, which usually requires a larger sample than a trial to determine superiority or non-inferiority. For this reason, cost-minimisation analysis is only applicable in a relatively small number of cases.

Recommendations when there is no economic evidence

When no relevant published studies are found, and a new economic analysis is not prioritised, the Committee should make a qualitative judgement about cost effectiveness by considering potential differences in resource use and cost between the options alongside the results of the review of evidence of effectiveness. This may include considering information about unit costs. The Committee's considerations when assessing cost effectiveness in the absence of evidence should be explained in the guideline.

Further considerations

Decisions about whether to recommend interventions should not be based on cost effectiveness alone. The Committee should also take into account other factors, such as the need to prevent discrimination and to promote equity. The Committee should consider trade-offs between efficient and equitable allocations of resources. These factors should be explained in the guideline.

7.8 References and further reading

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

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

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

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

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

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

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

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

Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. (2013) Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement Br Med J, 346: 1

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

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

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.

National Institute for Health and Clinical Excellence (2012) Social care guidance development methodology workshop December 2011: report on group discussions

NICE Decision Support Unit (2011) Technical support document series [accessed 27 January 2014]

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

Raftery J, editor (1999–2001) Economics notes series. British Medical Journal [accessed 27 January 2014]

Wanless D (2004) Securing good health for the whole population. London: HM Treasury

8 Linking to other guidance

This chapter describes how guidelines link to other NICE guidance in the topic area and guidance from other developers.

8.1 Linking to other NICE guidance

Related NICE guidelines, technology appraisal guidance, interventional procedures (IP) guidance and diagnostic and medical technologies guidance should be identified during scoping of a guideline (see chapter 2). This includes identifying any related in development or published guidance and guidelines.

This chapter describes possible approaches to be taken when scoping of a NICE guideline identifies:

- related in development or published NICE technology appraisal guidance
- related in development or published NICE guidelines
- related published or in development IP guidance.

These approaches may differ because of the funding recommendation for NICE technology appraisal guidance and the special arrangements for NICE interventional procedures.

There are also provisions for NICE teams to discuss and agree appropriate action when relevant guidance from other NICE programmes is identified.

Related NICE technology appraisal guidance

Significant new medicines

A first assessment of a new medicine or a significant licence extension for an existing medicine is usually carried out as a technology appraisal. However, it can instead be carried out through the guideline development process but only when this has been agreed by both the Department of Health and the manufacturer.

Related published technology appraisal guidance

When scoping of a NICE guideline identifies related published technology appraisal guidance, there are 5 possible approaches:

- The recommendations from technology appraisal guidance are incorporated verbatim into the guideline that is being developed.
- A cross-reference to the technology appraisal guidance is included in the guideline that is being developed.
- The recommendations from technology appraisal guidance are modified to make them specific to the guideline, if the population or indication is different.
- The technology appraisal guidance is updated through the guideline development process.
- The technology appraisal guidance is updated through the relevant technology appraisal process.

Before a decision to incorporate or update a technology appraisal is made, the NICE appraisals programme prepares a technology appraisal review proposal. There are 2 reasons for this:

- new evidence may indicate that the appraisal should be updated as a technology appraisal rather than through the guideline development process, or
- if technology appraisal guidance is incorporated into new guidelines, the technology appraisal will usually be placed on the static list (see the technology appraisal process guides).

Developing a review proposal involves consulting with the relevant stakeholders for the technology appraisal (see the technology appraisals process guide for details). To ensure there is enough time for this, it is essential that all related technology appraisal guidance is identified as early as possible in guideline development, preferably in the early stages of scoping (see chapter 2).

Incorporating NICE technology appraisal guidance in a guideline

When recommendations from a published technology appraisal are incorporated into a new guideline, they should usually be reproduced unchanged (verbatim). Under exceptional

circumstances, changes to recommendation wording may be proposed (for example, because the appraisal recommendation covers both primary and secondary care, but the new guideline covers secondary care only). Any proposed change to the wording of an appraisal recommendation must be discussed with NICE's appraisals programme and agreed by NICE's Guidance Executive. This should be done on a case-by-case basis.

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

A guideline covers the same medicine as published technology appraisal guidance but for a different population or indication

Sometimes a guideline covers a medicine for which there is technology appraisal guidance, but for a different population or indication (condition). In these cases, the Committee developing the guideline recommendation should assess evidence of effectiveness using methodologies comparable with those used in the technology appraisal. The guideline recommendations may be different from the technology appraisal recommendations if there is evidence of differing safety or effectiveness for the population or indications covered by the guideline.

Updating technology appraisal guidance

In exceptional circumstances technology appraisal guidance is updated in a guideline. A technology appraisal is likely to be suitable for updating in a guideline only if all of the following conditions are met (see the policy on updating technology appraisals in guidelines):

- The technology falls within the scope of the guideline.
- There is no proposed change to an existing patient access scheme or flexible pricing arrangement for the technology, or no new proposal(s) for such a scheme or arrangement.
- There is no new evidence that is likely to lead to significant changes in the estimate of effectiveness of a technology.

- The technology is well established within the NHS. Evidence that a technology is not well established may include the following:
    - spending on the technology for the indication that was appraised continues to rise
    - there is evidence of unjustified variation across the country in access to the technology
    - there is plausible and verifiable information to suggest that the availability of the technology is likely to be reduced if the funding recommendation were removed
    - the technology is excluded from the payment by results (PbR) tariff.
- Stakeholder opinion, expressed in response to consultation on a review proposal for the technology appraisal, is broadly supportive of the proposal.

When scoping of a guideline identifies related published technology appraisal guidance, the NICE technology appraisals team prepares a technology appraisal review proposal. The guideline Developer comments on the review proposal. It also comments on any agreed update, which allows it to have formal input into the process of updating the appraisal. Planning the update of a technology appraisal is described in the technology appraisal process guide.

The final decision on whether to update technology appraisal guidance in a guideline is taken by NICE's Guidance Executive.

When technology appraisal guidance is updated and changed in a guideline, the appraisal is withdrawn when the guideline is published. The funding recommendation associated with the technology appraisal no longer applies. Similarly, any patient access scheme agreed as part of the technology appraisal no longer applies unless the manufacturer commits to continue the scheme.

Early planning is essential to identify how the guideline Developer will update technology appraisal guidance within a guideline. The Developer should consider whether there are any data not in the public domain that are likely to be of use in updating the technology appraisal. If so, the Developer should call for evidence from registered stakeholders, using the procedures described in section 5.5.

If there is significant new evidence or a change in costs since the technology appraisal guidance was published, the Developer conducts an assessment of cost effectiveness (economic evaluation) to determine whether a change in the recommendations is appropriate. In exceptional circumstances, it may not be clear that an economic analysis is needed until the evidence is reviewed and discussed by the Committee. Nevertheless, the Developer should start planning for any economic analysis at an early stage. The intended approach to cost-effectiveness (economic) analysis for technology appraisal updates should be included in the economic plan and discussed with the Committee and a member of NICE staff with responsibility for quality assurance.

The approach should follow the principles described in chapter 7 and should be similar to that used in the technology appraisal. Any differences must be justified by changes in the evidence base or the decision context (for example, a broader range of comparators in the guideline).

The Developer may sometimes consider that cost effectiveness can best be assessed by updating an existing economic analysis (for example, the economic model provided by the Assessment Group for the technology appraisal or a model submitted by a manufacturer or sponsor). If so, this should be discussed with a member of NICE staff with responsibility for quality assurance during development of the economic plan.

For appraisals in development, NICE's technology appraisal team may use the appraisal consultation period as an opportunity to consult on plans for a future update or incorporation within a guideline.

Developing a guideline and technology appraisal guidance concurrently

When a technology appraisal is developed at the same time as a related NICE guideline, 3 important aspects should be considered to ensure that the final recommendations in the guideline and the appraisal are complementary and consistent:

- timing
- exchange of information
- publication of recommendations.

The development of a related guideline and technology appraisal should ideally be coordinated so that the published appraisal recommendations can be incorporated into the consultation draft

of the guideline. If the technology appraisal recommendations have not been finalised at the time of the guideline consultation, the guideline consultation draft should cross-refer to the appraisal consultation document or final appraisal determination. Timelines should be agreed between the Developer, NICE staff with responsibility for quality assurance of guidelines, and the technology appraisals team at NICE.

New technology appraisal referral

When a new technology appraisal has been referred, and a guideline is already being developed in this area, NICE's technology appraisals team informs the Developer and NICE staff with responsibility for guideline quality assurance that the technology appraisal is relevant to the guideline. But the technology appraisal does not form part of the guideline.

Sharing of information between the Committee developing the technology appraisal guidance and the Committee developing the guideline is important for both. The Committee developing the guideline needs to be aware of progress in related technology appraisal topics. The following should therefore be in place.

- A member of NICE's technology appraisals team is invited to an early guideline Committee meeting to outline the technology appraisal process. Differences between processes for developing appraisals and guidelines, the opportunities for the guideline Committee to be involved in the appraisal process and the status of the ongoing relevant appraisals are discussed.
- A member of NICE's technology appraisals team advises the guideline Committee on the integration of the appraisal into the guideline, and is invited to attend guideline Committee meetings as appropriate.
- The guideline Committee comments on the relevant appraisal(s) through the Developer (see technology appraisal process guide).
- The guideline Committee Chair (or a delegate) and the Developer's Director (or a delegate) liaise with the technical lead for the appraisal. They attend relevant Appraisal Committee meetings unless they have a conflict of interest, in which case another guideline Committee member will be selected to attend.

- For multiple technology appraisals (MTAs), the guideline Developer's economists and the appraisal Assessment Group's economists work together to ensure that the economic models for the guideline and the appraisal are consistent.
- For single technology appraisals (STAs), the guideline Developer's economist familiarises themselves with the manufacturer's economic model and the critique of the model by the Evidence Review Group.

The guideline Committee cannot publish its own recommendations on areas already covered by the scope of an ongoing technology appraisal or a published technology appraisal unless NICE has agreed that the technology appraisal guidance will be updated in the guideline.

Related NICE guidelines

Related published or in development NICE guidelines should be identified by the Developer at the scoping stage. The scope should document which NICE guidelines are considered relevant for the guideline that is being developed. Any other related NICE guidelines that are highlighted during guideline development should be discussed and a joint approach agreed with NICE staff with responsibility for quality assurance.

During scoping, identified related guidelines should be reviewed to determine whether the guideline in development will cross-refer to existing published recommendations (that is, the key issue(s) will be excluded from the scope of the guideline in development) or whether the guideline in development will consider similar review questions (that is, the key issues are included in the scope of the guideline in development).

When a guideline in development will cross-refer to recommendations in a published guideline, this will be specified in the scope.

When a similar review question is identified in a published NICE guideline, and the evidence review underpinning any recommendations is considered appropriate, the Committee developing the guideline can choose to cross-refer to the recommendation(s) in the published guideline or to draft a new recommendation(s), based on the evidence review for the published guideline.

When the review question is similar and the evidence review is considered appropriate, the Committee should formally determine and document that:

- the review question in the guideline in development is similar to the question addressed in the published guideline
- the evidence review underpinning any recommendations is not likely to have changed significantly since the publication of the related guideline
- the evidence review for the review question in the published guideline is relevant and appropriate to the question in the guideline in development.

How the recommendations are linked to the evidence should be documented and should note areas of agreement and difference with the Committee for the published guideline (for example, in terms of key considerations – balance of benefits/harms/costs, interpretation of the evidence).

Based on consideration of the evidence and the recommendation, the Committee may decide to cross-refer to the recommendation in the published guideline if it is happy to accept the intent and exact wording, and any future changes to that recommendation (for example, changes made as part of an update).

If the Committee considers that the intent and therefore the wording of the published recommendation are not appropriate for the guideline in development, or future changes are not likely to be acceptable to the Committee, a new recommendation can be made. When a published recommendation is adapted for inclusion in another guideline (that is, not simply cross-referenced but included with changes to wording), the changes need to be clearly justified and based on explicit and objective reasons (that is, changes should not be based on the Committee's views alone – either views on interpretation of the evidence or the wording of the published recommendation). The rationale for this decision should be documented in the appropriate section of the guideline.

The evidence review used to underpin an adapted recommendation or a cross-reference to a recommendation in a published guideline should be clear in the appropriate sections of the guideline (for example, the review protocol, evidence tables).

If the review question is not considered similar enough or the evidence review is not considered appropriate, the Committee may request that a new systematic review is conducted. This should follow NICE's standard processes and methods, as described in this manual. The decision to conduct a new review should be documented in the section that describes how the evidence is linked to the recommendations.

Related interventional procedures guidance

Published interventional procedures guidance

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

Any related published IP guidance should be identified during the scoping phase of a guideline. There are 2 approaches, depending on whether the recommendation in the IP guidance is for 'normal' or 'special' arrangements for clinical governance, consent and audit or research. Because guidelines focus on placing established treatments in the care pathway, they will generally only include IP guidance that recommends 'normal' arrangements.

IP guidance with recommendations for 'normal' arrangements

There are 2 possible scenarios, depending on whether the IP guidance is identified in the scope as an area to be included.

Review question not justified. If the scoping group for a guideline decides that IP guidance for which 'normal' arrangements are recommended is relevant to the guideline but does not justify a review question, the IP guidance is simply referred to in the guideline as related NICE guidance. The Developer does not search for new evidence on procedures that are not incorporated into a review question. However, if in the course of their search for evidence for the guideline the Developer finds new relevant evidence on that procedure, they inform the IP team at NICE.

Review question justified. If the scoping group for a guideline considers that IP guidance with 'normal' arrangements is likely to justify a review question, this is highlighted in the draft scope for the guideline. During consultation on the draft scope, the IP team consults its specialist advisers to find out whether the procedure is becoming standard NHS practice. NICE staff with responsibility for guideline quality assurance and the IP team then draft a joint paper for NICE's Guidance Executive describing the intention to investigate the effectiveness of the procedure in the guideline, the justification for this decision and what is currently known about the availability of new evidence. At this stage any indications within the IP guidance that are outside the scope of the guideline are also highlighted to NICE's Guidance Executive.

If the procedure is included in the final scope of the guideline, the Developer considers its effectiveness using standard methods for guideline development (see chapters 6 and 7).

When the Committee has reviewed the evidence and considered its recommendation(s), NICE staff with responsibility for guideline quality assurance and the IP team inform NICE's Guidance Executive of how the draft guideline recommendations are likely to affect the IP guidance.

Usually the IP guidance remains active, unless there are exceptional circumstances. This is because the IP guidance relates to the efficacy and safety of the procedure, and so the guideline and the IP guidance address different questions. Therefore IP guidance remains current even if recommendations on efficacy and safety are supplemented by a guideline recommendation on the effectiveness of a procedure for 1 or more indications. IP guidance may also contain more detailed information about the procedure that may be of value to practitioners and people considering having the procedure. Importantly, the IP guidance may also specify conditions for use of the procedure; for example, that the surgeon should have training, or that the procedure should be carried out within the context of a multidisciplinary team. The guideline will include a cross-reference to the IP guidance, and the NICE webpage for the IP guidance will include a note referring to the guideline.

When appraisal of the evidence indicates that a procedure is not effective, the guideline will recommend that it should not be used. In such cases the IP guidance for that procedure will be withdrawn. In some cases the guideline and the IP guidance may address different but overlapping indications. This will mean that sometimes IP guidance will remain current even if it is replaced by a guideline for 1 or some indications. A separate decision will be made for each piece of IP guidance affected in this way.

When there is considerable uncertainty about the clinical or cost effectiveness of an interventional procedure, a decision should be made about whether the IP guidance stands, whether it should be updated, or whether it should be withdrawn.

The guideline Committee may decide to make a 'research only' recommendation. The decision to make a 'research only' recommendation for a procedure with published recommendations for 'normal' arrangements will be taken by the guideline Committee in consultation with NICE. In this instance, the relevant IP guidance will be withdrawn.

These decisions are made on a case-by-case basis, and require that NICE staff with responsibility for guideline quality assurance and the IP team agree and present a paper to NICE's Guidance Executive.

IP guidance with recommendations for 'special' arrangements

If the guideline Committee considers that a procedure with recommendations for 'special' arrangements has become part of NHS practice and falls into the subject area of a review question, the Committee formally notifies the procedure to the IP team to allow for potential review of the IP guidance. If on re-assessment the procedure's status is changed to 'normal' arrangements, the Developer considers the procedure's effectiveness and cost effectiveness (see the section on IP guidance with recommendations for 'normal' arrangements). If the procedure retains its 'special' arrangements status (because of concerns about its safety, or because the long-term efficacy is unknown and important), the IP guidance should be listed in the guideline as related NICE guidance.

IP guidance published with recommendations for 'research only' or 'do not use'

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

Developing a guideline and IP guidance concurrently

When a newly notified procedure has been scoped and it has been agreed that it will be assessed by the IP team, and a guideline is already being developed in this area, the IP team informs the Developer and NICE staff with responsibility for guideline quality assurance that the notified procedure is relevant to the guideline, but the procedure does not form part of the guideline.

8.2 Guidance from other developers

Sometimes relevant guidelines published by organisations other than NICE are identified in the search for evidence and considered appropriate for inclusion in the evidence base. Guidelines

produced by organisations accredited by NICE are not subject to further quality appraisal because the process for producing the guideline has already undergone formal appraisal by NICE.

Published guidelines produced by organisations not accredited by NICE are assessed for quality using the AGREE II instrument. There is no cut-off point for accepting or rejecting a guideline, and each Committee needs to set its own parameters. These should be documented in the methods of the guideline, with a summary of the assessment. The full results of the assessment should be presented with the guideline.

Reviews of evidence from other guidelines that cover review questions being addressed by the Committee may be considered as evidence if:

- they are assessed using the appropriate methodology checklist (see appendix H) and are judged to be of high quality
- they are accompanied by an evidence statement and evidence table(s)
- the review is assessed as being sufficiently up-to-date.

If using evidence from published guidelines, the Committee should create its own evidence summaries or statements (see section 6.4). Evidence tables from guidelines published by other organisations should be referenced with a direct link to the source website or a full reference of the published document. The Committee should formulate its own recommendations, taking into consideration the whole body of evidence.

Recommendations from guidelines published by other organisations should not be quoted verbatim.

8.3 References and further reading

Brouwers MC, Kho ME, Browman GP et al. (2010) AGREE II: advancing guideline development, reporting and evaluation in health care. Canadian Medical Association Journal 182: E839–42

9 Developing and wording recommendations and writing the guideline

The guideline contains the Committee's recommendations along with details of the methods used to develop them and the evidence they were based on. The way in which these are presented may vary but the information provided includes:

- background and context for the guideline – such as the need for the guideline, epidemiology (if relevant), current practice and the policy context
- the methods used during guideline development – highlighting the rationale for options taken, any deviations from the methods and processes described in this manual
- the evidence – details of the evidence, any analysis and modelling, and any gaps in the evidence
- considerations – how the Committee developed the recommendations with links between the evidence and the recommendations
- the recommendations
- recommendations for future research
- information about the guideline – including the scope, changes to published recommendations (if the guideline is an update), members of the Committee and the Developer's team, the evidence review team, staff with responsibility for quality assurance, stakeholders, and declarations of interest
- standard information – including a statement about person-centred care (if relevant for the topic), and copyright and disclaimers
- information about the most challenging changes in practice and suggestions that may help users of the guideline address these.

The guideline recommendations are the distillation of the Committee's development work. They should be clear, understandable by the intended audience without reference to the evidence reviews, and based on the best available evidence. This chapter describes the key stages in developing guideline recommendations:

- interpreting the evidence to make recommendations
- wording the recommendations
- prioritising recommendations for future consideration in quality standard development
- highlighting recommendations for implementation support
- formulating research recommendations.

It also summarises how the guideline recommendations are incorporated into NICE Pathways.

9.1 Interpreting the evidence to make recommendations

Recommendations are developed using a range of scientific evidence (see section 4.4) and other evidence – such as expert testimony, views of stakeholders, people using services and practitioners, Committee discussions and debate (see chapter 3).

The Committee must use its judgement to decide what the evidence means in the context of the guideline referral and decide what recommendations can be made to practitioners, commissioners of services and others. The evidence is assessed for validity, reliability and bias, but also requires interpretation, especially an assessment of its implicit and explicit value base. Evidence also needs to be assessed in light of any conceptual framework and theories relating to individual and organisational behaviour change.

The Committee should also take account of a range of issues (including any ethical issues, social value judgements, equity considerations and inequalities in outcomes, particularly impacts on people sharing the characteristics protected by equality legislation) and policy imperatives (see chapter 1). This ensures that its recommendations are ethical, practical, specific and lawful.

Assessment and interpretation of the evidence to inform the guideline recommendations is at the heart of the work of the Committee.

The guideline should explain clearly how the Committee moved from the evidence to each recommendation, and should document how any issues influenced the decision-making. A simple table may be used to show how the evidence was used to develop the recommendations, and should describe the relative value placed on outcomes, benefits and harms, resource use, and the overall quality of the evidence, as well as other considerations of the Committee.

The summary of the Committee's considerations may also be used to integrate the findings from several evidence reviews that are related to the same recommendation or group of recommendations.

Quality of the evidence

The Committee is presented with evidence statements and, if used, GRADE tables that describe the number, type and quality of the studies for each review question and provide an overall rating of confidence (high, moderate, low or very low) in estimates of effect for each outcome. The Committee should agree that the evidence statements, and, if used, GRADE tables, are a fair summary of the evidence and should discuss any uncertainty in the evidence, including the presence, likely magnitude and direction of potential biases.

The evidence statements or, if used, GRADE tables summarise the applicability or indirectness of the evidence to people affected by the guideline and the setting. The Committee discusses the applicability of the evidence before making recommendations.

Trade-off between benefits and harms of an intervention

A key stage in moving from evidence to recommendations is weighing up the magnitude and importance of the benefits and harms of an intervention, and the potential for unintended consequences. This may be done qualitatively (for example, 'the evidence of a reduction in medicines errors in care homes outweighed a small increase in staff workload and resources') or quantitatively using a decision model.

The Committee should assess the extent to which the available evidence is about efficacy (the extent to which an intervention produces a beneficial result under ideal conditions), effectiveness (the extent to which a specific intervention, when used under ordinary circumstances, does what it is intended to do) or both. Often the distinction between the 2 is not made clear; this may be of particular importance in reports of complex interventions, because these are often evaluated only in pragmatic studies.

If several possible interventions are being considered, it is useful to include discussion of the relative position of an intervention within a pathway of care or service model, based on effectiveness.

The Committee should also assess the extent to which the recommendations may impact on health inequalities. This needs to be made clear, regardless of whether the recommendation is aimed at the whole population, specific subgroups or a combination of both.

Trade-off between economic considerations and resource use

As noted in section 7.7, the Committee should discuss cost effectiveness in parallel with general effectiveness when formulating recommendations.

The guideline should include an explanation of how the implications of costs, resource use and economic considerations were taken into account in determining the cost effectiveness of an intervention. Again, this may be informal, or may be more formal and include economic modelling (see chapter 7).

If several possible interventions are being considered, it is useful to include discussion of the relative position of an intervention within a pathway of care or service model, based on cost effectiveness.

Extrapolation of evidence

Sometimes evidence identified for a specific population or setting may include principles that could be extrapolated to other populations and/or settings. For example, a review of systems for managing medicines in care homes for people with dementia may identify good practice that is relevant in other care home settings. The use of extrapolation must be considered carefully by the Committee, with explicit consideration of the features of the condition or interventions that allow extrapolation. This also applies when extrapolating findings from evidence in different care settings. The Committee should consider and document any similarities in case mix, staffing, facilities and processes.

If GRADE is used, this would be accounted for in the overall quality assessment.

Availability of evidence to support implementation (including evidence from practice)

The Committee should also judge to what extent it will be possible to put the recommendations into practice. It can use expert oral or written testimony, the experience of Committee members or results from fieldwork or consultation with people using services, where this has been

conducted. It may also be able to draw on qualitative studies or other forms of evidence relating to organisational and political processes.

The Committee should consider the extent of change in practice that will be needed to implement a recommendation, staff training needs, policy levers and funding streams, and the possible need for carefully controlled implementation with, for example, training programmes. This should be documented in the guideline and in any relevant resources which support implementation.

Size of effect and potential impact on population health

The Committee should consider whether it is possible to anticipate effect sizes at the population level, if this is appropriate for the topic. If this is the case, it is important to consider effect sizes along the whole causal chain, not just at the end points.

Wider basis for making recommendations

The Committee should take into account a range of issues (including any ethical issues, social value judgements, equity considerations and inequalities in outcomes) and policy imperatives, as well as equality legislation (see chapter 1) to ensure that the guideline recommendations are ethical, practical and specific. There are no hard-and-fast rules or mechanisms for doing this: the Committee should make conscious and explicit use of its members' skills and expertise. All evidence needs interpretation: evidence alone cannot determine the content of a recommendation. The development of evidence-based recommendations involves inferential, inductive or deductive reasoning:

- inferential because it involves moving from what is known (the evidence) to uncertainty about what is reasonably expected to happen as a consequence of implementing a recommendation
- inductive when it is derived from evidence
- deductive when it is drawn from theory or methodological principles.

NICE's principles on social value judgements explicitly acknowledge that non-scientific values are brought to bear, and all of NICE's advisory Committees are encouraged to take account of (and to make explicit) the value judgments they make. The Committee may also draw upon the principles outlined in the report on ethical issues in public health by the Nuffield Council on Bioethics when making its judgements.

Conceptual framework or logic model

When the Committee is developing its recommendations, it should consider any conceptual framework or logic model/s that have been developed because they may help to identify any practical issues involved with a recommendation that will change practice (see appendix A).

Equality considerations

The guideline should also document how the Committee's responsibilities under equality legislation and NICE's equality policy have been discharged in reaching the recommendations (see section 1.4). The Committee needs to consider whether:

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

Insufficient evidence

If evidence of effectiveness for an intervention is either lacking or too weak for firm conclusions to be reached, the Committee has several options. It may make recommendations based on the limited evidence, using expert opinion; or it make no recommendation; or it may recommend that the intervention is used only in the context of research (see section 9.5). Factors the Committee should consider before issuing 'only in research' recommendations include:

- The intervention should have a reasonable prospect of providing cost-effective benefits to people using services.
- The necessary research can realistically be set up or is already planned, or people using services are already being recruited for a study.

- There is a real prospect that the research will inform future NICE guidelines.

The same principles for wording recommendations should be used (see section 9.2), reflecting the strength of the evidence, and the considerations should be documented fully.

Strength of recommendations

As soon as the Committee has discussed the evidence, it should start drafting recommendations. The Committee should decide what it wants to recommend and, if possible and appropriate, which sectors (including which practitioners or commissioners within those sectors) should act on the recommendations.

The concept of the 'strength' of a recommendation (Schunemann et al. 2003) is key to translating evidence into recommendations. This takes into account the quality of the evidence but is conceptually different.

Some recommendations are 'strong' in that the Committee believes that the vast majority of practitioners or commissioners and people using services would choose a particular intervention if they considered the evidence in the same way as the Committee. This is generally the case if the benefits clearly outweigh the harms for most people and the intervention is likely to be cost effective.

However, there is often a closer balance between benefits and harms, and some people would not choose an intervention whereas others would. This may happen, for example, if some people are particularly likely to benefit and others are not. In these circumstances, the recommendation is generally weaker, although it may be possible to make stronger recommendations for specific groups of people.

The GRADE system allocates labels or symbols to represent the strength of a recommendation. NICE has chosen not to do this, but to reflect the strength in the wording of the recommendation (see section 9.2). NICE uses 'offer' (or similar wording such as 'measure', 'advise', 'commission' or 'refer') to reflect a strong recommendation, usually where there is clear evidence of benefit. NICE uses 'consider' to reflect a recommendation for which the evidence of benefit is less certain.

For all recommendations, a general principle of NICE guidelines is that people using services and the wider public should be informed of their options and be involved in decisions about their care.

There might be little evidence of differences in cost effectiveness between interventions. However, interventions that are not considered cost effective should not usually be offered to people because the opportunity cost of that course of action has been judged to be too great (see chapter 7).

The Committee's view of the strength of a recommendation should be clear from its discussions, as reported in the guideline.

Some recommendations may be highlighted for possible use in the development of a quality standard (see section 9.3).

In most cases the Committee reaches decisions through a process of informal consensus, but sometimes formal voting procedures are used. The proceedings should be recorded and a clear statement made about the factors considered and the methods used to achieve consensus. This ensures that the process is as transparent as possible.

A summary of the generic and specific issues considered and the key deliberations should be included in the guideline

Principles of person-centred care

All NICE guidelines advocate the principles of person-centred care; there are also 2 NICE guidelines specifically on the experience of people using services: Patient experience in adult NHS services and Service user experience in adult mental health. The recommendations from these guidelines and the general principles of patient-centred care should not be re-stated. However, any specific aspects of views and experiences that need addressing can be considered, and recommendations made. These might relate to communication, information and support needs, or the consequences of particular interventions.

9.2 Wording the recommendations

Writing the recommendations is one of the most important steps in developing a guideline. Many people read only the recommendations, so the wording must be concise, unambiguous and easy to translate into practice by the intended audience. As a general rule, each recommendation, or bullet point within a recommendation, should contain only 1 main action.

The Committee must take account of NICE's integrated approach to presenting recommendations across different areas, which includes using consistent language to avoid misunderstanding and to make the recommendations as accessible as possible to a wide audience.

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

- focus on the action that needs to be taken, and where appropriate, who needs to take this action
- include what readers need to know
- reflect the strength of the recommendation
- emphasise the involvement of people using services, carers where appropriate, and the public in making decisions
- be 'person-centred'
- use plain English and avoid vague language and jargon
- use language and terms that NICE has agreed to ensure consistency across guidelines and other products
- follow NICE's standard advice on recommendations about medicines, waiting times and ineffective interventions.

The recommendations should (when possible and not obvious from the context of the guideline) clearly detail the intended audience for the recommendation (who is responsible for implementing it), the intended population, the setting (if relevant), what specifically should be done, and, where relevant, what the timeframe is for doing it.

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

Focus on the action

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

Recommendations should use direct instructions wherever possible because they are clearer and easier to follow. They should usually start with a verb describing what the reader should do, for example, 'offer', 'consider', 'measure', 'advise', 'discuss', 'ask about', 'commission' (see box 9.1).

Box 9.1 Examples of guideline recommendations that start with a verb

- Record the person's blood pressure every 6 months.
- Discuss the transition to adult services and ensure that the young person feels fully involved. Start planning at least 6 months before the discharge from child and adolescent mental health services (CAMHS).
- Advise pregnant women to limit their intake of oily fish to 2 portions a week.
- Encourage staff who regularly come into contact with people whose health and wellbeing could be at risk to provide them with a brief intervention. (The risk could be due to current behaviours, sociodemographic characteristics or family history).

Sometimes it is clearer to start with details of the population covered by the recommendation or other details, particularly if recommending different actions for slightly different circumstances or to make the sentence structure simpler (see box 9.2).

Box 9.2 Examples of guideline recommendations that don't start with a verb

- If surgery is an option, refer the patient to a specialist surgeon to discuss the risks and benefits.
- Within 4 weeks of initial diagnosis, identify the specific needs of people with dementia and their carers arising from ill health, physical disability, sensory impairment, communication difficulties, problems with nutrition, poor oral health and learning disabilities. Record all specific needs and how they will be addressed in the care plan.
- As part of the local joint strategic needs assessment (JSNA), gather information on where, when and how often smokeless tobacco cessation services are promoted and provided to local South Asian communities – and by whom. Aim to get an overview of the services on offer.
- If operating a local formulary covering a small population, consider sharing resources and establishing joint processes with neighbouring local formulary decision-making groups to avoid duplicating work.

Recommendations about service organisation or if the audience is not the practitioner

- Care should be provided by a multidisciplinary team.

Recommendations that specify that a specific type of practitioner, person or organisation should carry out an intervention or action

- An occupational therapist should assess the patient's needs.
- When acting as a doctor, dentist or pharmacist signatory, establish that the clinical and pharmaceutical content is accurate and supported by the best available evidence.
- Providers of existing interventions should work with researchers to ensure they are rigorously evaluated.
- For each patient group direction, the provider organisation should:
    - identify a senior, responsible person from within the service to authorise named, registered health professionals to practise under the patient group direction
    - ensure that authorised health professionals have signed the appropriate documentation

Recommendations that use 'must' or 'must not' should be worded in the passive voice (see below for more details)

Reflect the strength of the recommendation

Some recommendations can be made with more certainty than others (see the section on strength of recommendations). This concept of the 'strength' of a recommendation should be reflected in the consistent wording of recommendations within and across guidelines. There are 3 levels of certainty:

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

Recommendations for activities or interventions that should (or should not) be used should use directive language such as 'offer' (or 'do not offer'), 'advise', 'ask about' or 'commission'.

Recommendations for which there is a closer balance between benefits and harms (activities or interventions that could be used) should use 'consider'. 'Consider' indicates that the recommendation is made with less certainty. To minimise confusion, 'consider' should only be used to indicate the strength of a recommendation. Other wording rather than 'consider' should be used for 'be aware of', 'explore' or similar. 'Take other factors into account' or similar should be used instead of 'consider other factors'. 'Assess' and 'think about' are other possible alternatives to 'consider'. 'Consider offering' should be avoided because of potential confusion with the wording of strong recommendations. Also, it might be misinterpreted to mean that a health or social care practitioner may consider offering an intervention without discussing it with the patient or person using services.

If there is a legal duty to apply a recommendation, or the consequences of not following a recommendation are extremely serious, the recommendation should use 'must' or 'must not' and be worded in the passive voice. When there is a legal duty to apply a recommendation, the recommendation should contain a reference to the supporting documents.

Examples of recommendations made with the 3 different levels of certainty are given in box 9.3.

Box 9.3 Examples of recommendations made with 3 different levels of certainty

Recommendations for activities or interventions that must or must not be used

- Ultra-rapid detoxification under general anaesthesia or heavy sedation (where the airway needs to be supported) must not be used. This is because of the risk of serious adverse events, including death.
- Patient group directions must be authorised only by an appropriate authorising body in line with legislation.

Recommendations for activities or interventions that should or should not be used

- Do not routinely offer pharmacological or mechanical VTE prophylaxis to patients with cancer having oncological treatment who are ambulant.
- Offer a trial of supervised pelvic floor muscle training of at least 3 months' duration as first-line treatment to women with stress or mixed urinary incontinence.
- If a smoker's attempt to quit is unsuccessful using NRT, varenicline or bupropion, do not offer a repeat prescription within 6 months, unless special circumstances have hampered the person's initial attempt to stop smoking, when it may be reasonable to try again sooner.
- Record the person's blood pressure every 6 months.

Recommendations for activities or interventions that could be used

- Consider combination chemotherapy to treat patients with advanced breast cancer for whom a greater probability of response is important and who understand and are likely to tolerate the additional toxicity.
- Consider collaborating with other organisations and sharing existing educational materials to ensure a comprehensive approach.

Include what readers need to know

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

- Define any specialised terminology that is used in the recommendations. Avoid using abbreviations unless the audience is likely to be more familiar with the abbreviation than with the term in full. If abbreviations are essential, define them at first mention and in a glossary. Do not use abbreviations for groups of people; for example, write 'people from black, Asian and minority ethnic backgrounds' rather than 'BAMEs' or 'BMEs'.
- Define the intended audience for the recommendation (where possible and if it is not obvious from the context). For some guideline topics, it may be necessary to group recommendations for specific practitioner or professional groups (for example, care home staff or social care commissioners).
- Define the population if it is not obvious from the context. Often it is necessary to define the group or population only in the first of a group of recommendations, if it is clear that the subsequent recommendations in that section relate to the same population.
- Define the setting(s) where the intervention is to be delivered where necessary if it is not obvious from the context.
- Include cross-references to other recommendations in the guideline if necessary to avoid the need to repeat information such as treatment regimens or components of the intervention or service.
- Do not include reasons justifying the recommendation unless this will increase the likelihood that it will be followed – for example, if it is required by legislation, involves a change in usual practice or needs particular emphasis.
- Avoid trade names. Give the recommended international non-proprietary name (rINN), as listed in the British national formulary (BNF). Usually, only the generic name is needed. Occasionally (for example, if referring to a specific preparation or device), the proprietary name may be given in parentheses at first mention. Do not give the manufacturer's name. Any reference to products (for example, pedometers or brand names of medicines) and services (for example, slimming clubs) should be made in general terms to avoid giving the impression that NICE endorses a particular brand.
- Include only 1 main action in each recommendation or bullet point.

Emphasise the involvement of people using services

Recommendations should acknowledge the role of people who are directly affected by them, or the role of organisations or other people who are affected (for example, family members, carers or advocates), in any decision-making.

To emphasise the role of people using services or the public in decision-making (and, as appropriate, that of a family member, carer, or advocate of a person using services) and the need for them to consent to treatment or an intervention, generally use verbs such as 'offer' and 'discuss' in recommendations, rather than 'prescribe' or 'give'. As described above, 'consider' is used for recommendations on interventions that could be used, and implies that more discussion with the person will be needed.

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

Use plain English and avoid jargon

Using plain, consistent wording is an important part of NICE's integrated approach to presenting guidelines and other products, and is in line with gov.uk style.

Follow the principles of effective writing as described in Writing for NICE and NICE's approach to consistency in language and terms across guidelines and other products.

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

Examples

- Instead of 'an intervention may be offered', say 'consider the intervention'.
- Instead of 'an intervention is recommended', say 'offer the intervention'.
- Instead of 'an intervention is helpful', say 'offer the intervention' or 'consider the intervention'.

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

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

The Developer should follow NICE's standard procedure when referring to medicines. This includes using standard wording when off-label use of medicines is recommended.

Do not give dosages routinely

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

Off-label use of licensed medicines

Using a UK licensed medicine outside the terms of its marketing authorisation is classed as off-label use. Make it clear in the recommendation if the recommended use of a medicine is outside its licensed indication.

Recommendations are usually about the uses of medicines (often referred to as the licensed indications) for which the regulatory authority has granted a marketing authorisation, either in the UK or under the European centralised authorisation procedure. However, there are clinical situations in which the off-label use of a medicine may be judged by the prescriber to be in the best clinical interests of the patient. Off-label use may be recommended if the clinical need cannot be met by a licensed product and there is sufficient evidence and/or experience of using the medicine to demonstrate its safety and efficacy to support this. Off-label prescribing is particularly common in pregnant women and in children and young people (see below) because these groups have often been excluded from clinical trials during medicine development. When prescribing a medicine off-label, the prescriber should follow relevant professional guidance (for example, the General Medical Council's Good practice in prescribing medicines – guidance for doctors) and make a clinical judgement, taking full responsibility for the decision for the patient under his or her direct care. In addition, the patient (or those with authority to give consent on

their behalf) should be made fully aware of these factors and provide informed consent, which should be documented by the prescriber.

A licensed medicine is accompanied by an SPC, which includes the indications, cautions and contraindications for a medicine based on an assessment of safety, quality and efficacy by the regulatory authority. The guideline Developer and Committee should check recommended uses against the licensed indications listed in the SPC, and include the following standard information with the recommendation if the medicine does not have a UK marketing authorisation for the use being recommended:

At the time of publication ([month year]), [name of drug] did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing medicines – guidance for doctors for further information.

Additional information can be added as needed. In cases where the SPC for a medicine specifically mentions a caution or contraindication for its use but the Committee wishes to recommend the medicine, this should be stated clearly in the recommendation. The evidence that the Committee has considered in reaching the conclusion that use in these circumstances can be justified should be clearly set out in the guideline.

If there is no information on dosage regimens available in a recognised source (such as the BNF), the guideline Developer should include dosage information in the guideline recommendations and alert the NICE implementation team to ensure that this is disseminated to prescribers.

Prescribing medicines outside their licensed indications to children and young people

In certain circumstances medicines are prescribed outside their licensed indications (off-label use) to children and young people because the clinical need cannot be met by licensed medicines; for example, for an indication not specified in the marketing authorisation, or administration of a different dose. The Standing Committee on Medicines (a joint committee of the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists Group) has issued a policy statement on the use of unlicensed medicines and the use of licensed medicines for unlicensed indications in children and young people. This states clearly

that such use is necessary in paediatric practice and that doctors are legally allowed to prescribe medicines outside their licensed indications where there are no suitable alternatives and where use is justified by a responsible body of professional opinion (Joint Royal College of Paediatrics and Child Health/Neonatal and Paediatric Pharmacists Group Standing Committee on Medicines 2013).

Therefore, if there is no alternative treatment and there is a sufficient evidence base and/or experience of using the medicine to demonstrate its safety and efficacy, a guideline may recommend use of a medicine outside its licensed indications for treating a child or young person, in line with this policy. It is expected that prescribers will use the SPC to inform their prescribing decisions for individual patients, and they should be able to justify using a medicine outside its licensed indications. Informed consent should be obtained from the child and/or their parent or guardian as appropriate and should be documented.

Using tables in recommendations

Do not use tables to summarise several actions in 1 recommendation. Such tables make it more difficult to link the recommended actions to the summaries of the evidence.

9.3 Highlighting areas for future consideration in quality standard development

NICE guidelines can cover large areas of care and, as a result, often contain a considerable number of recommendations relevant to the many review questions. Where a linked quality standard is planned, the Committee may choose to discuss which recommendations might be suitable for consideration within the quality standard development process.

Recommendations that may be highlighted should:

- be in areas in which there is evidence or consensus that there is variation in the delivery of care to people using services (in particular, aspects of care or services that are not widely provided and/or not considered to be standard practice, but that are feasible to provide)
- focus on key requirements for high-quality care or service provision that are expected to contribute to improving the effectiveness, safety and experience of care or services
- be measurable and therefore suitable for development as quality measures.

Some members of the guideline Committee may be invited to apply to join the Quality Standards Advisory Committee that is developing a related quality standard, as specialist Committee members.

9.4 Highlighting recommendations for implementation support

The guideline Committee should attempt to identify recommendations that should be highlighted in the information on implementation in the guideline or that might require additional implementation efforts at a local level. Criteria include whether a recommendation:

- relates to an intervention that is not part of routine care or service provision
- will need changes in service delivery
- will need retraining of staff or the development of new skills and competencies
- highlights the need for practice to change
- affects, and needs to be implemented across, a number of agencies or settings (complex interactions)
- may be viewed as potentially contentious, or difficult to implement for other reasons.

There should be a clear record of which criteria were considered particularly important by the Committee for each highlighted recommendation.

9.5 Formulating research recommendations

The Committee is likely to identify areas in which there are uncertainties or in which robust evidence is lacking. NICE has published a Research recommendations process and methods guide, which details the approach to be used to identify key uncertainties and associated research recommendations.

For guidelines where there could be many hundreds of uncertainties, it will not be possible to document every uncertainty in detail. Similarly, although Committees could write research recommendations for dealing with each uncertainty, this is not likely to be feasible. Therefore the Committee should select key research recommendations that are likely to inform future

decision-making (based on a systematic assessment of gaps in the current evidence base) for inclusion in the guideline. Methods such as value of information analyses can be useful in this process. Further information about how research recommendations should be derived can be found in the research recommendation process and methods guide.

9.5 Incorporating the guideline recommendations into NICE Pathways

The Committee and Developer should refer to both the guideline scope and the pathway outline when developing the guideline. This includes taking account of the links to other NICE Pathways and the guidance identified as related to the guideline topic at the scoping stage. The Committee and Developer should aim for the guideline structure to be compatible with NICE Pathways. They should also consider the links with existing pathways to help integrate the new topic into NICE Pathways.

The NICE Pathway is drafted by an editor in the NICE publishing team. Drafting begins when most of the draft recommendations are available for guideline consultation. Work continues during consultation on the draft guideline. The publishing team works with the Developer's lead(s) for the NICE Pathway, who may be members of the guideline Committee.

Further drafts of the NICE Pathway are prepared in the light of comments received.

When the recommendations are finalised, the editor checks the NICE Pathway against the final recommendations and makes changes if necessary.

9.6 References and further reading

Brown P, Brunnhuber K, Chalkidou K et al. (2006) How to formulate research recommendations. British Medical Journal 333: 804–6

Claxton K, Sculpher MJ (2006) Using value of information analysis to prioritise health research: some lessons from recent UK experience. Pharmacoeconomics 24: 1055–68

Glasziou P, Del Mar C, Salisbury J (2003) Evidence-based medicine workbook. London: British Medical Journal Books

Joint Royal College of Paediatrics and Child Health/Neonatal and Paediatric Pharmacists Group Standing Committee on Medicines (2013) The use of unlicensed medicines or licensed medicines for unlicensed applications in paediatric practice

Kelly MP, Moore TA (2012) The judgement process in evidence\u2011\based medicine and health technology assessment. Social Theory and Health 10:1–19

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

Michie S, Johnston M (2004) Changing clinical behaviour by making guidelines specific. British Medical Journal 328: 343–5

Nuffield Council on Bioethics (2007) Public health: ethical issues. London: Nuffield Council on Bioethics

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

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

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

Tannahill A (2008) Beyond evidence – to ethics: a decision making framework for health promotion, public health and health improvement. Health Promotion International 23: 380–90

Weightman A, Ellis S, Cullum A et al. (2005) Grading evidence and recommendations for public health interventions: developing and piloting a framework. London: Health Development Agency

Yale University (2011) Guideline Implementability Appraisal (GLIA)

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

Consultation with stakeholders is an integral part of the guideline development process. Comments received from registered stakeholders are a vital part of the quality-assurance and peer-review processes, and it is important that they are addressed appropriately. Registered stakeholders and respondents are notified of the consultation dates and times in advance via the guideline page on the NICE website, and are reminded by email.

This chapter describes the validation process for draft guidelines. It includes information on what happens during the consultation, the principles of responding to stakeholder comments after the consultation and when a second consultation may be needed.

Before the draft guideline is signed off for consultation, an equality impact assessment is completed by the Developer and the Committee Chair to show which equality issues have been identified and considered during guideline development. The equality impact assessment is signed off by a member of NICE staff with responsibly for quality assurance, and published on the NICE website with the draft guideline. The assessment is updated by the Developer and the Committee Chair after the consultation.

10.1 What happens during consultation

Commenting on the draft guideline

The draft version of the guideline is posted on the NICE website for consultation with registered stakeholders and respondents. Stakeholders can register at any point during guideline development. NICE informs registered stakeholders and respondents that the draft is available and invites them to comment by the deadline. Questions for stakeholders are posted with the draft guideline. The purpose of these questions is to seek stakeholder views on factors such as what will help or hinder local users put the draft recommendations into practice, or the potential equality impact. Consultation usually lasts for 6 weeks. A 4-week consultation may be used for partial guideline updates or small guidelines (for example, guidelines on systems and processes that relate to the use of medicines in different care settings and within provider and commissioning organisations).

NICE is unable to accept:

- more than 1 set of comments from each registered stakeholder organisation
- comments that are not presented correctly on the form provided
- comments with attachments such as research articles, letters or leaflets.

In these cases, NICE will invite a registered stakeholder to resubmit a single set of comments with no attachments before the consultation deadline. NICE is unable to accept any comments received after the consultation deadline.

Stakeholders and respondents should make sure that any confidential information or information that the owner would not wish to be made public is clearly underlined and highlighted (see the section on confidential information in chapter 5 for more details). Confidential information should be kept to a minimum. Stakeholders should explain why the information is confidential and if and when it will become publicly available.

Where views on the guideline are shared by more than 1 stakeholder organisation, NICE encourages these organisations to work together to produce a joint response. This should be submitted by 1 registered stakeholder; other stakeholders supporting the joint response should respond to the consultation noting their endorsement.

When registering, and when commenting on the draft scope and draft guideline, stakeholders are asked to disclose whether their organisation has any direct or indirect links to, or receives or has ever received funding from, the tobacco industry. Disclosures will be included with the published consultation responses.

Fieldwork with practitioners and targeted consultation with people using services

When a draft guideline on novel, complex or sensitive areas is issued for consultation the Developer may, in exceptional cases, decide that the feasibility of the draft recommendations should also be tested. This may be done in fieldwork with people providing services, or a targeted consultation with people using services.

Fieldwork tests how easy it will be for policy makers, commissioners, practitioners and professionals to implement the draft recommendations and how the recommendations might work in practice, including their relevance and acceptability to the people using services or people affected.

Targeted consultations test draft recommendations directly with people using services, and where appropriate their families or carers. The main criteria for considering this are:

- the topic covers novel or sensitive areas, or
- the evidence on users' views is weak or lacking, or
- people affected by the guideline are not participants in the guideline's decision-making and consultation processes (for example, children).

The Developer should document the rationale for undertaking the fieldwork or targeted consultation, with a proposal including consideration of the methods to be used, and the anticipated costs. The proposal should be discussed with members of NICE staff with a quality assurance role, and approved by the Centre Director. If the work is approved, the rationale and methods should be documented in the guideline.

Fieldwork and targeted consultation usually happen at the same time as draft guideline consultation, but can be undertaken earlier in the process (for example, to validate selected draft recommendations with people using services before guideline consultation).

The results of any fieldwork or targeted consultation are considered by the Committee. The Committee uses this information to refine and prioritise the recommendations after consultation. This includes making them more specific to different groups of practitioners, where appropriate.

Further details on fieldwork are given in appendix I. There are more details on consultation with people using services in appendix B.

External expert review

Although NICE does not routinely commission peer review from external experts, members of NICE staff with a quality assurance role, or the Developer, may occasionally consider arranging additional external expert review of part or all of a guideline, or an evidence review, executable model or economic analysis. For example, review by external experts may be valuable if novel methods have been used in developing an evidence review.

External expert reviewers may include practitioners, those commissioning care, academics (for example, with expertise in economic or meta-analysis), or people with a lay perspective. Experts are selected on the basis of their experience in the particular issue under review.

External expert review may take place during guideline development or during consultation on the draft guideline. If it occurs during development the comments are not published, but the reviewer(s) should be named in the guideline. Comments from external expert reviewers during the development of the guideline should be discussed by the Committee. If the reviewers also comment during consultation, their comments are responded to in the same way as comments from registered stakeholders and are published in the guideline consultation table on the NICE website under 'external expert reviewers'. All external expert reviewers are required to complete a declaration of interests form (see section 3.6).

10.2 Principles of responding to stakeholder comments

After consultation the Committee discusses the comments received during consultation, proposes any changes needed to the guideline, and agrees the final wording of the recommendations.

This section describes how Developers should respond to consultation comments. The NICE policy on managing guidance consultation comments should also be taken into account. The same principles apply when responding to comments on the draft scope (see chapter 2).

Developers must take the following key points into account when responding to comments from registered stakeholders:

- Each comment must be acknowledged and answered as directly, fully and with as much information as possible.
- For a draft guideline, the Committee must consider whether changes to the guideline are needed as a result of consultation comments; any changes to the guideline must be agreed by the Committee before publication.
- If changes are made to a guideline as a result of a consultation comment, this must be made clear in the response to the comment. If no changes have been made, it should be clear from the response why not.
- Developers should maintain an audit trail of any changes made to the guideline.

Registered stakeholders who have commented on the draft guideline are sent the final guideline, in confidence 2 weeks before publication (see chapter 11). Comments and responses are made available on the NICE website when the final guideline is released.

Comments received from non-registered stakeholders and individuals are reviewed by the Committee. A formal response is not given and these comments are not made available on the NICE website. However, if they result in changes to the guideline this is recorded in the Committee meeting minutes.

Comments received after the deadline are not considered and are not responded to; in such cases the sender will be informed.

When evidence is highlighted by stakeholders during consultation, this should be considered for inclusion in the guideline. The Developer will take the evidence into account:

- if it meets all of the inclusion criteria for the relevant review (as set out in the review protocol), and should have been identified in the guideline searches/screening
- if it falls within the timeframe for the guideline search parameters.

Any effects on the guideline of including new evidence will be considered, and any further action agreed between the Developer and NICE staff with a quality assurance role.

If the new evidence falls outside of the timeframe for the guideline searches, the impact on the guideline will still need to be considered, and any further action agreed between the Developer and NICE staff with a quality assurance role.

10.3 When a second consultation may be needed

In exceptional circumstances, NICE may consider the need for a further 4-week stakeholder consultation after the first consultation. This additional consultation may be needed if either:

- information or data that would significantly alter the guideline were omitted from the first draft, or
- evidence was misinterpreted in the first draft and the amended interpretation significantly alters the draft recommendations.

NICE staff with responsibility for guideline quality assurance make the final decision on whether to hold a second consultation.

11 Finalising and publishing the guideline

This chapter describes quality assurance and sign-off of the guideline after consultation, publication of the guideline, and launching and promoting the guideline.

11.1 Quality assurance of the guideline

After agreed changes have been made to the guideline in response to consultation comments from registered stakeholders, the guideline is reviewed by NICE staff with responsibility for guideline quality assurance. They check that the changes made to the guideline are appropriate and that the Developer has responded appropriately to the registered stakeholder comments. Further changes to the guideline may be needed; the Developer continues to maintain an audit trail of all the changes. The NICE Pathway, information for the public and any supporting resources are amended in line with any changes to the guideline. These also undergo quality assurance and are signed off within NICE.

Equality impact assessment

Before the guideline is signed off for publication, the equality impact assessment is updated by the Developer and the Committee Chair to show whether any additional equality issues have been identified during consultation, and how these have been addressed. The equality impact assessment is published on the NICE website with the final guideline.

11.2 Signing off the guideline

NICE's Guidance Executive considers and approves guidelines for publication on behalf of the NICE Board. The Guidance Executive is made up of NICE Executive Directors, Centre Directors and the Communications Director.

When considering a guideline for publication, the Guidance Executive reviews a report from NICE staff with responsibility for guideline quality assurance. The report details whether the guideline:

- addresses all the issues identified in the scope
- is consistent with the evidence quoted

- was developed using the agreed process and methods
- was developed with due regard to the need to eliminate discrimination, advance equality and foster good relations
- is clear and coherent
- follows the agreed template.

If any major issue is identified by the Guidance Executive it may be necessary for the Committee to meet again to address the problem.

The Guidance Executive does not comment at other stages during the development of the guideline.

11.3 Releasing an advance copy to stakeholders

Registered stakeholders who have commented on the draft guideline (see chapter 10) and agreed to conditions of confidentiality, are sent the final guideline (and a copy of the responses to stakeholder consultation comments) 2 weeks before publication. This information is confidential until the guideline is published. This allows registered stakeholders to highlight to NICE any substantive errors, and to prepare for publication and implementation. It is not an opportunity to comment further on the guideline. NICE should be notified of any substantive errors at least 1 week before publication of the guideline.

11.4 Publication

The guideline, NICE Pathway, information for the public and most routine support tools (see chapter 12) are published on the NICE website at the same time.

11.5 Launching and promoting the guideline

The Developer and Committee work with NICE's communications and implementation teams to disseminate and promote awareness of the guideline at the time of publication and afterwards. It is useful to consider at an early stage of guideline development how the guideline will be promoted.

Members from the NICE communications and implementation teams discuss with the Developer and the Committee opportunities for promoting the guideline. Committee members may be asked to take part in such activities.

With help from the Committee and the Developer, they identify how to reach relevant audiences for the guideline, including people using services, carers, the public, practitioners and providers.

NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as:

- notifying registered stakeholders of publication
- publicising the guideline through NICE's newsletter and alerts
- issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.

NICE may also use other means of raising awareness of the guideline – for example, newsletters, websites, training programmes, conferences, implementation workshops, NICE field team support and other speaking engagements. Some of these may be suggested by Committee members (particularly members affiliated to organisations for people using services and carer organisations). Each guideline is different and activities for raising awareness will vary depending on the type and content of the guideline.

Press launches

When there is likely to be substantial media interest, NICE may hold a press conference before publication of the guideline. This form of briefing allows for a more structured and considered exchange of information between NICE and the media, during which any potentially controversial aspects of the guideline can be explained and set in context. It also gives journalists an opportunity to interview people involved in developing the guideline and other contributors – including people with experiences related to the guideline or representatives from charities and other stakeholders who are supportive of the work.

In addition to a press launch, the communications team may set up interviews or filming with Committee members ahead of the guideline launch. NICE can make good use of case studies or experts to illustrate or explain the guideline recommendations. They help to give context to the

guideline, explain why the work has been carried out and can illustrate where recommendations have already been put in place or where lessons have been learned.

Information is provided to the media under embargo until the launch date for the guideline. Committee members should ensure that NICE is made aware of any press enquiries they receive before the guideline is launched.

Committee members may also wish to arrange separate events at which practitioners, providers, commissioners and people using services and the public can learn more about the guideline. In such cases, NICE's communications and implementation teams should be involved at the earliest possible opportunity.

12 Resources to support implementation

This chapter describes how NICE develops resources to support implementation of the guideline and other ways that NICE helps users of the guideline to put the recommendations into practice.

12.1 Introduction

To help users put guidelines into practice, NICE:

- ensures that implementation issues are analysed and considered as an integral part of guideline development
- ensures that all guideline topics are routinely considered for the provision of baseline assessment and resource impact assessment tools
- summarises the key challenges for practice and the interventions and/or factors that may help users address these (this will be regularly reviewed and updated, including as part of the guideline updating process – see chapter 13)
- provides additional support for some guideline topics informed by priorities identified in the quality standards library (in collaboration with NHS England, the Department of Health and Public Health England) and the selection of improvement areas within the quality standard development process
- provides information about the uptake of NICE recommendations to inform decisions about whether to update a guideline.

12.2 Routine guideline implementation tools

The information about implementation within each guideline is informed by implementation needs analysis carried out during guideline development and by the guideline consultation. It draws from and contributes to updating the information on context prepared during scoping and guideline development. The purpose of the information on implementation is to provide a concise summary for local action that identifies the most challenging changes in practice that may be faced by guideline users. It also advises on factors or interventions that may help address these, signposting to other advice. NICE routinely provides a baseline assessment tool for each guideline at the time of publication. This is a modifiable Excel spread sheet that organisations

can use to identify whether they are in line with practice recommended by NICE, and to help them plan and record activity to implement the guideline recommendations.

NICE resource impact assessment tools are intended to help organisations assess the potential costs and savings associated with implementing the guideline. A resource impact assessment commentary and an associated resource impact assessment template are produced for guideline publication if they add value. The template enables a local estimate to be made of the potential costs and savings involved in implementing the guideline. Where the resource impact is deemed not to be significant or cannot be estimated with any degree of certainty, a shorter narrative commentary is produced.

In response to needs analysis, NICE may produce or signpost to other resources as well as the routine tools. These may include patient decision aids and online learning.

12.3 Additional tools and activities in conjunction with partners

Organisations and individuals, both lay and practitioner, can play a key role in supporting the implementation of the guideline. The implementation needs analysis may indicate that further support is needed. If this is the case NICE will seek the support of external partners to help with this. Resources to support guideline implementation can be formally endorsed by NICE if they are accurately informed by NICE content. Education and learning tools or activities, commissioning support, including audit, measurement and benchmarking tools, and other support resources could be identified or produced with external partners. Quality standard improvement areas inform the focus of support so, where possible (and subject to planning with relevant partners), the availability of tools and activities is timed to coincide with publication of the related quality standard.

NICE's implementation team needs the input of the Developer and Committee members to develop and deliver the support tools and to ensure effective working with external partners. Details of how Committee members can get involved and what they are expected to do are given during their induction. Members of the implementation team may also attend Committee meetings immediately before and after the guideline consultation to get the Committee's input.

12.4 Other NICE implementation support

The following services and resources help to put all NICE guidance and standards into practice:

- A team of 8 implementation consultants support local organisations to implement NICE guidance and use quality standards.
- Medicines Prescribing Centre Associates deliver specialist support for high-quality, cost-effective prescribing and medicines optimisation through its network and local workshops.
- The NICE website offers the following:
    - a shared learning database of how NICE guidance has been implemented in practice
    - the quality and productivity collection, which illustrates projects resulting in quality improvement or productivity savings
    - the uptake database which contains data on uptake of NICE guidance recommendations.
- An implementation strategy group made up of external academics meets twice a year to inform the NICE implementation strategy with new and ongoing developments in implementation science.

12.5 References and further reading

Auerbach AD, Landefeld CS, Shojania KG (2007) The tension between needing to improve care and knowing how to do it. New England Journal of Medicine 357: 608–13

Baker R, Camosso-Stefinovic J, Gillies C et al. (2010) Tailored interventions to overcome identified barriers to change: effects on professional practice and health care outcomes. Cochrane Database of Systematic Reviews issue 3: CD005470

Cabana MD, Rand CS, Powe NR et al. (1999) Why don't physicians follow clinical practice guidelines? A framework for improvement. JAMA 282: 1458–65

Eccles M, Grimshaw J, Walker A et al. (2005) Changing the behavior of healthcare professionals: the use of theory in promoting the uptake of research findings. Journal of Clinical Epidemiology 58: 107–12

Leng G, Moore V, Abraham S, editors (2014) Achieving high quality care – practical experience from NICE. Chichester: Wiley

Michie S, Johnston M, Hardeman W et al. (2008) From theory to intervention: mapping theoretically derived behavioural determinants to behaviour change. Techniques in Applied Psychology: An International Review 57: 660–80

13 Ensuring that published guidelines are current and accurate

This chapter describes the process and methods for checking that published guidelines are current and deciding whether updates are needed.

13.1 Checking that published guidelines are current

NICE is committed to keeping guidelines current. A formal check of the need to update a guideline is usually undertaken by NICE every 2 years, and is always undertaken at least every 4 years from the date of guideline publication. This seeks to identify recommendations that are no longer current or need to be revised.

The check will be scheduled for 2 years post publication in cases where, for example, new evidence is anticipated, or the evidence base is large and moves quickly.

In exceptional circumstances, for example, when medicines or interventions are withdrawn, new technology is released, or there are significant changes to policy, context, legislation or infrastructure, the check may be brought forward.

When safety concerns are highlighted, the need to update recommendations is assessed on a case-by-case basis without the need for a formal check.

Given the number of published guidelines that make up NICE's guideline topics, the number of checks needed is considerable. To address this, adaptive processes and methods are used for checking that published guidelines are current. These are less resource intensive at the 2-year, 6-year and 10-year time points (where used), with more thorough checks at 4 and 8 years.

The process broadly relies on assessing 2 elements that influence the decision to update a published guideline:

- intelligence gathering on the perceived current relevance of the guideline, which may include responses to questionnaires, information on guideline and quality standard implementation, external enquiries about the guideline recommendations, internal intelligence (such as NICE's guideline issues log), related NICE guidance and quality standards (including

placeholder statements in NICE quality standards), medicines licensing information, relevant national policy, and

- abstracts of primary or secondary evidence that has been published since the end of the search period for the guideline, with critical appraisal of key papers.

At each time point, decisions on the need to update a guideline are based on a cumulative assessment of the relevant research evidence published since guideline publication.

A number of elements are common to all checks, but at some time points specific tasks are undertaken. The key elements of the process are summarised in table 13.1.

The 2-year, 6-year and 10-year checks

Checks at 2, 6 and 10 years are limited to areas covered by the scope of the published guideline and to specific study types. The literature search for new primary or secondary evidence is conducted with specific limits imposed (for example, identifying systematic reviews only).

External queries and comments received since publication of the guideline should also be considered. Intelligence gathered from questionnaires, related NICE guidance and quality standards, information about guideline implementation and other information (changes in medicines licensing and updated national policy) may also be considered.

The 2-year, 6-year and 10-year checks may not be needed for some guidelines (for example, if new evidence is unlikely within a short timeframe). Guidelines will state, at the time of publication, whether a check of the need for an update will be undertaken every 2 years.

The 4-year and 8-year checks

Checks at 4 and 8 years after guideline publication involve a more rigorous exploration of any changes in the evidence base than those undertaken at 2, 6 and 10 years. More extensive searches are undertaken to identify any new primary and secondary studies, including any economic studies. The focus is on the scope of the published guideline, but any additional areas or changes in practice that are identified during the process are also considered if they fall within the referral of the published guideline (see section 1.3).

A literature search is conducted across a range of sources. These may vary from topic to topic. They are selected according to their relevance to the topic and are based on those used in the published guideline.

Committee members and topic experts for the published guideline are surveyed for their opinions on the relevance of the published guideline, recent developments in the topic area and their knowledge of any new important evidence since publication of the guideline. In some circumstances (for example, when a significant period of time has passed since the guideline was published), members of the relevant Quality Standards Advisory Committee, or others with expertise, may be surveyed. The status of any related NICE guidance is also checked.

Presenting the results of checks of whether published guidelines need updating

All new relevant published evidence found from literature searches is summarised and any studies that may have an important impact on any recommendations are highlighted. The main themes of the new relevant evidence across the guideline are also summarised, along with any other identified information (such as changes in licensing indications for a medicine or updated national policy). This information forms the basis of a review proposal for NICE's Guidance Executive: either a public consultation document or a decision paper depending on the time point of the check.

There is no public consultation on the decision at 2-year, 6-year or 10-year checks, because a decision not to update at these points is verified at the subsequent check. There is a 2-week consultation with stakeholders who are registered for the published guideline when information summarised at the 4-year and 8-year checks (and at every 4-year check thereafter) indicates that a 'no update' decision should be considered.

Stakeholders are also consulted when it is proposed that a guideline is either withdrawn or placed on the static list (see section 13.3).

Consultation dates and times are posted in advance on the guideline page on the NICE website, and stakeholders are reminded by email.

Stakeholders who are registered for the published guideline are informed when a decision is made to update it. There is no consultation on this decision because it has been based on the availability of new evidence, and is usually supported by stakeholders.

Table 13.1 Key elements of the process for checking whether a published guideline needs updating

Time since publication	Key elements of the process
2 years	• Limited to scope of published guideline • Limited evidence review and summary of new evidence (with limits imposed, for example, including evidence from systematic reviews only or randomised controlled trials only) • Intelligence gathering from questionnaires, external enquiries, related NICE guidance, updated national policy, medicines licensing information and information on implementation • No consultation
4 years	• Also considers key areas within the referral of the guideline, but outside the scope of the published guideline • Literature search and summary of new evidence • Intelligence gathering from questionnaires, external enquiries, related NICE guidance, updated national policy, medicines licensing information and information on implementation • Consultation only when 'no update' considered
6 years	• Limited to scope of published guideline • Limited evidence review and summary of new evidence (with limits imposed, for example, including evidence from systematic reviews only or randomised controlled trials only) • Intelligence gathering from questionnaires, external enquiries, related NICE guidance, updated national policy, medicines licensing information and information on implementation • No consultation

8 years	• Also considers key areas within the referral of the guideline but outside the scope of the published guideline • Literature search and summary of new evidence • Intelligence gathering from questionnaires, external enquiries, related NICE guidance, updated national policy, medicines licensing information and information on implementation • Consultation only when 'no update' considered
10 years	• Limited to scope of published guideline • Limited evidence review and summary of new evidence (with limits imposed, for example, including evidence from systematic reviews only or randomised controlled trials only) • Intelligence gathering from questionnaires, external enquiries, related NICE guidance, updated national policy, medicines licensing information and information on implementation • No consultation

13.2 Deciding whether an update of a guideline is needed

The process for deciding whether an update of a guideline is needed is the same at 2-, 4-, 6-, 8- and 10-year time points.

Decisions are based on a balanced assessment of new relevant evidence published since guideline publication, the views of the Committee and topic experts, and other sources of information on the continued relevance of the guideline. Updates may also be triggered by placeholder statements within NICE quality standards.

The findings of the check on the need for an update are discussed with the Chair and/or members with topic expertise of the Committee for the published guideline. All proposals go through an internal validation process (including sign-off by the Associate Director and Director) before submission to NICE's Guidance Executive.

Given the number of guidelines that make up NICE's guideline topics, the capacity needed for updating guidelines is considerable. To address this, a number of options are available for updating a guideline depending on the extent of the new evidence and the continued relevance of the guideline recommendations. The review proposal submitted will be one of the options shown in table 13.2.

Table 13.2 Proposed decisions available following a check of the need to update a guideline

Proposed decision	Scenario	Outcome and actions
Full update with scope of published guideline	All sections of the guideline need updating. No new areas have been identified that would require an extension of the scope of the published guideline.	Use scope of published guideline. Do not consult on the scope. Inform stakeholders. Develop guideline using standard guideline development methods and process.
Full update with modified scope	All sections of the guideline need updating. New areas have been identified that require extension of the scope, within the referral of the published guideline. Existing areas may no longer be priorities, within the referral of the published guideline.	Prepare a new scope. Consult on the scope. Develop guideline using standard guideline development methods and process.

Partial update with scope of published guideline	Defined sections of the guideline need updating. No new areas have been identified that would require an extension of the scope of the published guideline.	Use the relevant parts of the scope of the published guideline. Do not consult on the scope Inform stakeholders. Develop guideline using standard guideline development methods and process.
Partial update with modified scope	Defined sections of the guideline need updating. New areas have been identified that require extension of the scope, within the referral of the published guideline. Existing areas may no longer be priorities, within the referral of the published guideline.	Prepare a new scope. Consult on the scope. Develop guideline using standard guideline development methods and process.
No update	No new evidence has been identified that would overturn any of the recommendations. There is no evidence from practice to indicate that any of the recommendations need changing. There is no evidence from practice that the scope of the published guideline needs changing.	The guideline is not updated. A check of the need for an update is made again after another 2 or 4 years, or A check of the need for an update is made within 2 years. This would be an exception – for example, if it is clear that new evidence critical to the decision is soon to be published. Registered stakeholders for the published guideline are consulted on 'no update' proposals only at 4-year and 8-year checks .

Refreshing the guideline	Amendments to the wording of recommendations are needed to reflect current practice context and, sometimes, to meet current editorial standards.	If a decision not to update is made, the guideline recommendations may be edited to ensure that they meet current editorial standards, reflect the current policy and practice context. Revisions should not change the meaning of the recommendation unless changes support NICE's duties under equality legislation or reflect the latest wording of any recommendations incorporated from other NICE programmes
Transferring the guideline to the static list	A full literature search identified no new evidence or upcoming trials (in the next 3–5 years) and/or No NICE quality standard is commissioned.	Topics that have undergone a full check of the need for an update and have 'no update' proposed are considered for the 'static list', with consultation on the proposed decision. Guidelines on the static list will remain extant and will be checked for the need for an update at 5-year intervals, or if new evidence emerges.
Withdrawing some recommendations or the whole guideline	The recommendations no longer apply.	This decision is made exceptionally – for example, it may be decided that the recommendations in a guideline no longer apply but that the guideline is not of sufficiently high priority for updating. In this case the guideline is withdrawn. Consult with registered stakeholders on the decision.

The final decision on whether to carry out a full or partial update of a guideline is taken by NICE's Guidance Executive following advice from the NICE Centre Director. The decision will take into account the competing priorities of other guideline topics and the capacity to undertake the work.

13.3 The 'static list'

Occasionally the need for updating a guideline does not need to be considered every 2 or 4 years. The recommendations are still current and should be implemented, but are unlikely to change in the foreseeable future (because the evidence base is unlikely to change). In this case the guideline is transferred to the 'static list', after consultation with registered stakeholders.

Guidelines are placed on the static list when:

- no quality standard has been commissioned, or
- a full check of the need for an update yields a 'no update' decision and no major ongoing research or studies are identified as due to be published within the next 3–5 years.

When a guideline is placed on the static list, this is made clear on the guideline's home page on the NICE website.

Guidelines on the static list are checked every 5 years to determine whether they should remain on the list. Routine 2- or 4-yearly checks of the need for an update are not carried out on guidelines transferred to the static list.

The circumstances in which a guideline may be taken off the static list include:

- The check at 5 years of the need for an update yields new evidence that may have an impact on the recommendations.
- Stakeholders notify NICE of new evidence that may have an impact on the recommendations. This may happen at any time and may include new information on the safety of an intervention.
- A quality standard is commissioned that relates to the topic of the guideline.

When a guideline is transferred from the static list it undergoes a check of the need for an update as at the 2- or 4-year time points, depending on the circumstance.

13.4 Withdrawing the guideline

Sometimes NICE's Guidance Executive decides that the recommendations in a guideline no longer apply, but that the guideline is not of sufficiently high priority for updating. In this case NICE's Guidance Executive will recommend that the whole guideline or specific recommendations are withdrawn. This decision will be consulted on with registered stakeholders.

13.5 Exceptional updates

Exceptionally, significant new evidence may mean an update of a guideline is agreed before the next scheduled check of the need for updating (particularly when safety or safeguarding issues need to be addressed).

The evidence might be a single piece of evidence, an accumulation of evidence or other published NICE guidance. Examples include significant data from published studies, changes in licensing and patents or warnings issued by licensing agencies, major changes in costs or changes in legislation.

Determining the need for an exceptional update

The NICE Centre responsible for the guideline advises NICE's Guidance Executive on the need for an exceptional update and which recommendations are being considered for updating. The Centre also advises on whether there is any other evidence (published, unpublished or from ongoing studies) that is relevant.

If NICE's Guidance Executive decides that an exceptional update is needed, registered stakeholders are informed of the planned approach.

14 Updating guidelines

14.1 Scheduling updates

When scheduling updates of guidelines, NICE prioritises topics according to users' need for both new and updated guidelines.

14.2 Full updates of guidelines

If a full update of a guideline is needed either:

- a new scope is prepared, following the process described in chapter 2, or
- the scope of the published guideline is used and registered stakeholders are informed.

Recruitment of Committee members follows the usual process (see chapter 3). The Developer informs all members of the topic-specific Committee, or topic-expert members of the standing Committee, for the published guideline that a new Committee is being recruited. The composition of the Committee should be tailored to new requirements if a new scope has been developed. The guideline is developed using the same methods and process as for a new guideline and the draft is subject to the normal 4- to 6-week consultation period (see chapter 10). The Developer should maintain records appropriate for audit (see section 3.8). The usual process for finalising and publishing the guideline is followed (see chapter 11).

14.3 Partial updates of guidelines

If only part of a guideline needs to be updated, either:

- a new scope is prepared, following the process described in chapter 2, or
- parts of the scope of the published guideline are used (as determined by the check of the need for an update; see chapter 13), and registered stakeholders are informed.

In both cases, the scope is clear about exactly which sections of the guideline are being updated and which are not, including any sections that may be withdrawn (for example, if they are now covered in another guideline). The scope also makes it clear that all the recommendations in the published guideline, including those that are not being updated, will be checked to ensure that

they comply with NICE's equality duties. These recommendations can also be considered for refreshing (see section 14.4).

The guideline is developed using the same methods and process as for a new guideline. Partial updates using the scope of the published guideline use the review questions and review protocols already defined by the existing guideline. However, if the review questions and/or protocols are unavailable, need refinement, or if there is ambiguity in the published guideline, the Developer may approach the Committee members with topic expertise for advice before starting the evidence review.

Partial updates of guidelines are subject to the same level of scrutiny as full updates and new guidelines. The underlying principles of transparency of process and methodological rigour continue to hold. The draft is subject to a 4-week consultation period (see chapter 10). The Developer should maintain records appropriate for audit (see section 3.8). The usual process for finalising and publishing the guideline is followed (see chapter 11).

14.4 Refreshing the guideline

Sometimes a decision is made not to update the guideline or parts of it but the recommendations may need refreshing to ensure that they remain in line with current editorial standards and current practice context (for example, changing from primary care trusts to clinical commissioning groups). Refreshing recommendations ensures that they are checked for any essential changes.

These might involve:

- changing recommendations in older guidelines from the passive voice to direct instructions
- changes to reflect NICE's current policy on recommendation wording (for example, to reflect the involvement of people using services and the public in decisions)
- changes so that recommendations do not conflict with NICE's duties under legislation and NICE's equality policy
- changes to reflect the current wording of any recommendations incorporated from other NICE guidance

- changes to reflect a change in the availability of medicines or a change in service configuration (for example, a change from primary care trusts to clinical commissioning groups)
- changes to address any feedback received on clarity and interpretation.

Changes should be kept to a minimum and should not change the intent of the recommendation unless the change relates to the availability of a medicine, a change in service configuration, legislation or equality duty.

Refreshing a guideline ensures that recommendations do not promote practice that has a negative impact on equality, do not conflict with other NICE guidance, and reflect current treatment options.

14.5 Presenting updates

A full update replaces an existing guideline and has a new set of recommendations, new evidence reviews and new sections detailing the Committee's discussion of the evidence. When a full update is published the old guideline is withdrawn. The NICE Pathway and information for the public are revised in line with the new recommendations.

When presenting partial updates of guidelines, the aim is to ensure that there is a single set of publications that bring together the updated information and relevant information from all previous versions of the guideline. In this way, readers of the updated guideline will be able to easily identify what has changed. The rest of this section covers general principles to be used when part of a guideline has been updated.

Preparing a partial update for consultation

Before consultation, the Developer should check the following:

- All sections of the guideline have been updated as agreed.
- It is clear in the guideline which sections have been updated, which text has been replaced, and which sections are open for comment during consultation.

- Recommendations from sections in which the evidence has not been re-considered have been checked to determine whether any changes are essential (for example, if a medicine is no longer available).
- Changes to refreshed recommendations in sections that have not been updated are kept to a minimum (for example, changing from the passive voice to direct instructions).
- A summary of changes to recommendations is included.
- The status of any guidance incorporated into the previous version of the guideline has been confirmed with NICE. For example, has the other guidance been updated by the guideline update?
- All recommendations (new, updated and unchanged) have been assessed for the purposes of updating the information on implementation in the guideline.
- All recommendations (new, updated and unchanged) have been assessed with respect to NICE's equality duties.

Preparing the final version of a partial update for publication

The Developer should check the following:

- It is clear in the guideline which sections have been updated, and whether the recommendations have been updated or amended, or are unchanged from the previous published version of the guideline.
- The summary of changes to recommendations has been revised in line with the final recommendations.

The NICE Pathway, information for the public and resources to support implementation are also updated.

14.6 Post-publication changes

Measures are in place throughout the development of a guideline to ensure that errors in the collection, synthesis, interpretation or presentation of the evidence are avoided as far as possible. However, on rare occasions errors may be found after publication of the guideline. There may also be occasions when clarification is requested and, if warranted, changes may be

made in response to enquiries. Errors may not always warrant changes to the guideline, in which case they will be logged for consideration when the guideline is considered for updating. If an error is found, the following criteria and process is used to determine whether changes are necessary.

Criteria and process for changes after publication

Corrections or changes to a published guideline are made if an error:

- puts users of health or care services at risk, or affects their care or provision of services, or
- damages NICE's reputation, or
- significantly affects the meaning of a recommendation.

If it is necessary to correct an error or include a clarification in a published guideline, NICE's process for dealing with post-publication changes is followed. An explanation of the decisions and actions taken is sent to the person or organisation that reported the error or requested clarification.

Sometimes recommendations need to be removed because a medicine has been removed from the market or a few recommendations have been updated or replaced by recommendations in another guideline.

The guideline and the NICE Pathway are amended. The information for the public and resources to support implementation are also amended if necessary. The changes are explained in the guideline and pathway (and the information for the public if needed). Depending on the nature and significance of the change and the time since publication of the guideline, registered stakeholders may also be notified.

Routine maintenance

Routine maintenance changes may also be made after publication of a guideline. These include minor changes such as updating or fixing broken links or updating standard text in line with agreed template changes.

14.7 References and further reading

Clark E, Donovan EF, Schoettker P (2006) From outdated to updated, keeping clinical guidelines valid. International Journal for Quality in Health Care 18: 165–6

Eccles M, Rousseau N, Freemantle N (2002) Updating evidence-based clinical guidelines. Journal of Health Services Research and Policy 7: 98–103

Shekelle P, Eccles MP, Grimshaw JM et al. (2001) When should clinical guidelines be updated? British Medical Journal 323: 155–7

Shekelle PG, Ortiz E, Rhodes S et al. (2001) Validity of the Agency for Healthcare Research and Quality clinical practice guidelines: how quickly do guidelines become outdated? JAMA 286: 1461–7

Shojania KG, Sampson M, Ansari MT et al. (2007) Updating systematic reviews. AHRQ Technical Reviews and Summaries, technical review 16. Rockville, MD: Agency for Healthcare Research and Quality

Turner T, Misso M, Harris C et al. (2008) Development of evidence-based clinical practice guidelines (CPGs): comparing approaches. Implementation Science 3: 45–52

15 Appendices

Appendices A to I can be found on the NICE website.

Glossary

Abstract

Summary of a study, which may be published alone or as an introduction to a full scientific paper.

AGREE (Appraisal of Guidelines for Research and Evaluation)

An international collaboration of researchers and policy makers whose aim is to improve the quality and effectiveness of practice guidelines. The AGREE II instrument, developed by the group, is designed to assess the quality of guidelines.

Allocation

The process by which study participants are allocated to a treatment group.

Applicability

How well an observation or the results of a study or review are likely to hold true in a particular setting.

Association

Statistical relationship between 2 or more events, characteristics or other variables. The relationship may or may not be causal.

Audit trail

Clear record of actions so that the reasons for the actions are apparent to a third party. For example, the reasons for changes to a draft guideline should be clearly recorded.

Baseline

A set of measurements before any intervention starts (after any initial 'run-in' period with no intervention), with which subsequent results are compared.

Bias

Systematic (as opposed to random) deviation of the results of a study from the 'true' results, caused by the way the study is designed or conducted.

Citation searching

Citation searching (also known as 'snowballing') can help to identify additional research. It has 2 dimensions:

- Backward citation searching is reviewing references cited in studies identified for inclusion in the review.
- Forward citation searching involves searching for additional studies that cite articles known to be relevant (such as those identified for inclusion in the review).

Committee

The advisory group that considers the evidence and develops the recommendations, taking into account the views of stakeholders. NICE has standing Committees (which work on multiple guidelines) and topic-specific Committees (which are put together for a single guideline topic). Members include practitioners and professionals (both specialists and generalists, and/or academics), care providers and commissioners, people using health and care services and/or their family members or carers, or people from communities affected by the guideline.

Committee Chair

A member of the Committee who leads Committee meetings, and ensures that the Committee keeps to the scope of the guideline, works collaboratively and adheres to NICE's equality policy and principles on social value judgements. The Chair completes the equality impact assessment with the Developer at scoping and final guideline stages, approves the draft guideline for

consultation, and advises the Developer on responses to comments from registered stakeholders.

Comparator

The standard (for example, another intervention or usual care) against which an intervention is compared in a study. The comparator can be no intervention (for example, best supportive care).

Conceptual framework

A theoretical structure of assumptions, principles and rules, which holds together the ideas comprising a broad concept.

Confidence interval (CI)

The confidence interval is a way of expressing how certain we are about the findings from a study, using statistics. It gives a range of results that is likely to include the 'true' value for the population. A wide confidence interval indicates a lack of certainty about the true effect of the test or treatment – often because a small group of patients has been studied. A narrow confidence interval indicates a more precise estimate (for example, if a large number of patients have been studied).

Consultation table

A table of all the comments received by NICE during consultation on a scope or draft guideline. The Committee considers the comments received, and the Developer then responds to the comments in the table.

Contractors

Organisations contracted to do some aspects of guideline development for NICE. This might include doing evidence reviews or fieldwork, or the Developer role.

Co-opted members

An expert invited to 1 or more meetings to contribute to formulating recommendations in a specific part of the guideline. They take part fully in discussions, but do not have voting rights. Co-opted members can include people with expertise in user, carer or community experience and views, as well as those with professional or practitioner expertise.

Core members (standing Committee)

The core members of a standing Committee include at least 1 practitioner and 1 lay member, and may include an economist. A standing Committee usually has between 6 and 12 core members. They serve for an initial period of up to 3 years and work on all guidelines developed by the Committee during that period.

Correlates review

Correlates reviews describe relationships between epidemiological factors and outcomes.

Cost–benefit analysis

In a cost–benefit analysis, the costs and benefits are measured using the same monetary units (for example, pounds sterling) to see whether the benefits exceed the costs.

Cost–consequences analysis

In a cost–consequence analysis, the costs (such as treatment and hospital care) and the consequences (such as health outcomes) of a test or treatment are compared with those for a suitable alternative. Unlike cost–benefit analysis or cost-effectiveness analysis, it does not attempt to summarise outcomes in a single measure (such as the quality-adjusted life year) or in financial terms. Instead, outcomes are shown in their natural units (some of which may be monetary) and it is left to decision-makers to determine whether, overall, the treatment is worth carrying out.

Cost-effectiveness analysis

In a cost-effectiveness analysis, the benefits are expressed in non-monetary terms related to health, such as symptom-free days, heart attacks avoided, deaths avoided or life years gained (that is, the number of years by which the intervention extends life). Cost-effectiveness analysis assesses the cost of achieving the same benefit by different means.

Cost-minimisation analysis

In a cost-minimisation analysis, the costs of different interventions that provide the same benefits are compared. If they are equally effective, only the costs are compared because the cheapest intervention will provide the best value for money. In practice, there are relatively few cost-minimisation analyses because it is rare for 2 healthcare interventions to provide exactly the same benefits.

Cost–utility analysis

In a cost–utility analysis, the benefits are assessed in terms of both quality and duration of life, and expressed as quality-adjusted life years (QALYs).

Cross-sectional survey

An observational study in which a population is examined to see what proportion has a particular outcome or has been exposed to a specific risk factor, or both. Cross-sectional surveys are usually used to determine the prevalence of outcomes or exposures to risk factors in populations. This type of survey may also be called a cross-sectional study or a prevalence study. Although cross-sectional surveys often provide useful estimates of disease burden for a particular population, they are less reliable for determining the prevalence of very rare conditions or conditions of short duration. Because cross-sectional surveys are descriptive rather than analytical, they cannot be used to estimate the relationship between cause and effect.

Decision-analytic model (and/or technique)

A model of how decisions are or should be made. This could be one of several models or techniques used to help people to make better decisions (for example, when considering the

trade-off between costs, benefits and harms of diagnostic tests or interventions). See also Markov modelling.

Delphi technique

A technique used for reaching agreement on a particular issue, without the participants meeting or interacting directly. It involves sending participants a series of questionnaires asking their views. After completing each questionnaire, participants are asked to give further views in the light of the group feedback until the group reaches a predetermined level of agreement. The judgements of the participants may be analysed statistically.

Developer

The team responsible for scoping the guideline, supporting the Committee and writing the guideline in light of the Committee's discussions and decisions. The team includes administrators, coordinators and project managers who provide administrative and management support to the Committee, plan and schedule the work, arrange meetings, and liaise with stakeholders and all other people and organisations contributing to guideline development.

Discounting

Costs and perhaps benefits incurred today have a higher value than costs and benefits occurring in the future. Discounting health benefits reflects individual preference for benefits to be experienced in the present rather than the future. Discounting costs reflects individual preference for costs to be experienced in the future rather than the present.

Dosage

The amount of a medicine to be taken, including the size and timing of the doses.

Economist

A person with skills in economic analysis whose role is to advise on economic aspects of the key issues or questions, review economic literature, prioritise topics for further analysis and carry out additional cost-effectiveness analyses.

Effect (as in treatment effect, effect size)

The observed association between interventions and outcomes, or a statistic to summarise the strength of the observed association.

Effectiveness

The extent to which an intervention produces an overall benefit under usual or everyday conditions. In this manual effectiveness includes cost effectiveness unless otherwise indicated.

Epidemiological review

Epidemiological reviews describe a problem in terms of its causes, distribution, control and prevention, and can be used to help focus the review questions. For example, an epidemiological review of accidents would provide information on the most common accidents, morbidity and mortality statistics, and data on inequalities in the impact of accidents.

Equity

Fair distribution of resources or benefits.

Evidence

Information on which a decision or recommendation is based. Evidence can be obtained from a wide range of sources, including randomised controlled trials, observational studies and expert opinion (of practitioners, people using services, family members and carers).

Evidence profile

A table summarising, for each important outcome, the quality of the evidence and the outcome data (used as part of the GRADE approach to assessing the quality of the evidence).

Evidence review team

The team that identifies and reviews the evidence, and undertakes economic analyses:

- The information specialist identifies relevant literature to answer the review questions (see chapter 5), creates databases to manage the search results and keeps a log of search results and strategies.
- The systematic reviewer critically appraises the evidence, distils it into tables and writes brief summaries (evidence statements). The reviewer also summarises the main issues for the Committee and contributes to its discussions.
- The economist identifies potential economic issues to be considered in the guideline and performs economic analyses.

Exceptional update

Update of a guideline carried out sooner than originally planned because new data have become available.

Exclusion criteria (literature review)

Explicit criteria used to decide which studies should be excluded from consideration as potential sources of evidence.

Exclusion criteria (study participants)

Criteria that define who is not eligible to participate in a study.

Expert witness

An expert invited to attend a Committee meeting to provide evidence from their experience and specific expertise. Expert witnesses answer questions from Committee members and may be invited to present evidence in the form of expert testimony, which is published on the NICE website when the guideline is published. Expert witnesses are not members of the Committee. They have expert knowledge of 1 or more of the following areas: experience and views of

practitioners; people using services; carers or the community and voluntary sector; government and policy; or research and practice.

External validity

The degree to which the results of a study hold true in non-study situations (for example, in routine NHS practice). It may also be referred to as the generalisability of study results to non-study populations. For example, the external validity of a study that took place in Spain may be questioned if the results are applied to people in Australia.

Extrapolation

In data analysis, predicting the value of a parameter outside the range of observed values.

Fieldwork

Fieldwork tests how easy it will be for policy makers, commissioners and practitioners to implement recommendations and how recommendations might work in practice. Practitioners' experience and views are used to fine-tune the draft recommendations to ensure that the final recommendations are understood and interpreted as the Committee intended, even without supporting information.

Follow-up

Observation over a period of time of a person, group or defined population to observe changes in health status or health- and social care-related variables.

Forest plot

A type of graph used to display the results of a meta-analysis.

Formal consensus methods

Formal consensus methods are techniques that can be used to enable a Committee to reach an agreement on a particular issue. Methods include Delphi and nominal group techniques, and

consensus development conferences. These methods may be used during guideline development when there is a lack of strong research evidence in a particular area.

Free-text terms

Terms used for searching that are not controlled vocabulary as used in the database or information source, but standard terms used in natural language.

Generalisability

The extent to which the results of a study based on measurements in a particular population or a specific context hold true for another population or in a different context.

GRADE (Grading of Recommendations Assessment, Development and Evaluation)

A systematic and explicit approach to grading the quality of evidence and the strength of recommendations. GRADE is an evolving system and is continuously being adapted and extended to cover different areas and types of evidence; for example, CERQUAL for qualitative evidence and GRADE for diagnostic studies. See the GRADE Working Group for the latest news and publications. Moved Appendices chapter.

Grey literature

Literature that is not formally published or that has a limited distribution, such as institutional reports. Grey literature may not be easily identified through standard bibliographic retrieval systems.

Health inequalities

The gap in health status and in access to health services between different groups, for example, those with different socioeconomic status or different ethnicity, or populations in different geographical areas. More information on health inequalities can be found on the Department of Health website.

Health-related quality of life

A combination of a person's overall physical, mental and social wellbeing; not merely the absence of disease.

Health Technology Assessment

Independent research about the effectiveness, costs and broader impact of healthcare (treatments and tests) for those who plan, provide or receive care in the NHS. The Health Technology Assessment (HTA) programme is part of the National Institute for Health Research (NIHR).

Implementation

The process of putting guideline recommendations into practice.

In confidence material

Information (for example, the findings of a research project) defined as 'confidential' because its public disclosure could affect the commercial interests of a particular company ('commercial in confidence') or the academic interests of a research or professional organisation ('academic in confidence').

Inclusion criteria (literature review)

Explicit criteria used to decide which studies should be considered as potential sources of evidence.

Incremental cost-effectiveness ratio (ICER)

The difference in the mean costs in the population of interest divided by the differences in the mean outcomes in the population of interest.

Index test

The test in a study which is being compared with the best available test (the reference standard).

Indication (specific)

The defined use of a medicine as licensed by the Medicines and Healthcare products Regulatory Agency (MHRA).

Indirect treatment comparison

An analysis to compare interventions that have not been compared directly in a head-to-head, randomised trial.

Information for the public

A summary of the key messages of the guideline in everyday language, written for users of health and care services, carers and the public. It follows the principles of the Information Standard.

Internal validity

A measure of how well a research study has been designed and how well it avoids bias. That is, the extent to which the cause-and-effect relationships in a study are true for the people and conditions of the study.

Key issues

Key issues are included in the scope of a guideline and broadly define aspects of care or service provision for which most advice is needed.

Key questions

Key questions are included in the scope of a guideline and are broad questions related to the areas defined by the key issues. Key questions relate to the effectiveness and cost effectiveness of interventions that are being considered for a given population. Key questions are then used to develop more detailed review questions.

Lay member

A member of the Committee who has personal experience of using health or care services, or who is from a community affected by the guideline. A lay member can also be someone with experience as a carer, an advocate, or a member or officer of a voluntary or community organisation.

Literature review

A summary of the evidence from several studies, with conclusions about the findings. It may or may not be systematically researched and developed.

Logic model

A model that incorporates the assumed relationships between action and outcomes as described in the conceptual framework.

Marketing authorisation

This was previously known as a product licence. Marketing authorisation is granted to medicines that meet the standards of safety, quality and efficacy set by the Medicines and Healthcare products Regulatory Agency (MHRA). It is normally necessary before a medicine can be prescribed or sold.

Markov modelling

A decision-analytic technique that characterises the prognosis of a group by assigning group members to a fixed number of health states and then modelling transitions among the health states.

Medical devices

All products, except medicines, used in healthcare for the diagnosis, prevention, monitoring or treatment of illness or disability.

Medicines and Healthcare products Regulatory Agency (MHRA)

The Executive Agency of the Department of Health that is responsible for protecting and promoting public health and patient safety by ensuring that medicines, healthcare products and medical equipment meet appropriate standards of safety, quality, performance and effectiveness, and are used safely.

Meta-analysis

The use of statistical techniques in a systematic review to integrate the results of several studies. (Definition from The Cochrane Collaboration website.)

Meta-ethnography

A process for sorting and combining the findings from qualitative studies.

Model inputs

Information needed for economic modelling. This may include information about prognosis, adverse effects, quality of life, resource use or costs.

Narrative summary

Summary of findings presented as a written description rather than, for example, as a graph or table.

Net benefit estimates

In cost-effectiveness and cost–utility analysis, the net benefit estimate can be expressed in outcomes (for example, using quality-adjusted life years [QALYs]) or monetary terms. The net health (or outcome) benefit is the difference between the total expected QALYs (or outcome) and the health (or outcomes) expected to be forgone elsewhere (the total expected costs divided by the maximum acceptable incremental cost-effectiveness ratio [ICER] value). The net monetary benefit is the difference between the monetary value of total expected QALYs (our outcome) multiplied by the maximum acceptable ICER value [ICER] and total expected costs. In cost–benefit analysis, the net benefit estimate is the estimate of the amount of money remaining after all payments made are subtracted from all payments received. This is used in the economic evidence profile for guidelines.

Network meta-analysis

An analysis that compares 2 or more interventions using a combination of direct evidence (from studies that directly compare the interventions of interest) and indirect evidence (from studies that do not compare the interventions of interest directly).

NICE guidance

Recommendations produced by NICE. There are 5 types of guidance:

- guidelines covering clinical topics, medicines practice, public health and social care
- interventional procedures guidance
- technology appraisals guidance
- medical technologies guidance
- diagnostics guidance.

All guidance is developed by independent Committees and is consulted on.

NICE guidelines

Recommendations (and the evidence they are based on) on broad topics covering health, public health and social care in England. NICE guidelines include clinical, medicines practice, public health and social care guidelines.

NICE Pathways

NICE Pathways are interactive topic-based diagrams that aim to provide users with a way to quickly navigate all NICE guidance recommendations on a particular topic.

Non-randomised controlled trial

These are trials in which participants (or groups) are allocated to receive either the intervention or a control (or comparison intervention) but the allocation is not randomised. This type of study is often called a controlled before-and-after (CBA) study.

Observational study

Retrospective or prospective study in which the investigator observes the natural course of events with or without control groups (for example, cohort studies and case–control studies).

Odds ratio (OR)

An odds ratio compares the probability of something happening in one group with the probability of it happening in another. An odds ratio of 1 shows that the probability of the event happening (for example, a person developing a disease or a treatment working) is the same for both groups. An odds ratio of greater than 1 means that the event is more likely in the first group than the second. An odds ratio of less than 1 means that the event is less likely in the first group than in the second group.

Sometimes probability can be compared across more than 2 groups – in this case, one of the groups is chosen as the 'reference category', and the odds ratio is calculated for each group compared with the reference category.

P value

The p value is a statistical measure that is used to indicate whether or not an effect is statistically significant.

People using services and the public

Anyone who is using health or care services, or a member of the public affected by a guideline.

Personal social services

Care services for vulnerable people, including those with special needs because of old age or physical disability and children in need of care and protection. Examples are residential care homes for older people, home help and home care services, and social workers who provide help and support for a wide range of people (Department of Health definition).

PICO (population, intervention, comparison and outcome) framework

A structured approach for developing review questions about interventions. The PICO framework divides each question into 4 components: the population (the population being studied), the interventions (what is being done), the comparators (other main treatment options) and the outcomes (measures of how effective the interventions are).

Placeholder statements

In NICE quality standards, placeholder statements are used for areas of care in need of quality improvement but for which there is no evidence-based guidance available to formulate quality statements or measures.

Practitioner

A healthcare, social care or public health worker.

Prognosis

A probable course or outcome of a disease. Prognostic factors are characteristics of a patient or disease that influence the disease course. A good prognosis is associated with a low rate of undesirable outcomes; a poor prognosis is associated with a high rate of undesirable outcomes.

Project manager

The staff member who oversees and facilitates the guideline development process.

Proprietary name

The brand name a manufacturer gives to a medicine or device it produces.

QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies-2)

A tool for assessing the quality of studies of the accuracy of diagnostic tests.

Qualitative research

Qualitative research explores people's beliefs, experiences, attitudes, behaviour and interactions. It asks questions about how and why, rather than how much. It generates non-numerical data, such as a person's description of their pain rather than a measure of pain. Qualitative research techniques include focus groups and in-depth interviews.

Quality-adjusted life years (QALY)

A measure of the state of health of a person or group in which the benefits, in terms of length of life, are adjusted to reflect the quality of life. One QALY is equal to 1 year of life in perfect health.

Quality assurance

NICE staff carry out quality assurance of the guideline, including reviews of the evidence and any economic analysis, to ensure that it is up-to-date, credible, robust and relevant. These staff may also be responsible for commissioning the Developer.

- The Centre Director is responsible for ensuring that the guideline is produced in accordance with this manual. The Centre Director is also responsible for appointing the Committee Chair and Committee members.
- The Associate Director is responsible for the development and quality assurance of the guideline, and has delegated responsibility for approving the consultation draft, the final guideline, and other documents, before final approval by NICE's Guidance Executive. The Associate Director also advises the Chair of the Committee and the Developer on matters of method and process.
- The technical lead is responsible for the technical quality assurance of the evidence reviews and other work undertaken by the Developer. The technical lead commissions, coordinates and quality assures any fieldwork.
- The economic lead is responsible for ensuring the technical quality of the economic evidence and any economic analysis.

Quality of life

See Health-related quality of life.

Quorum

The smallest number of group members that must be present for a valid meeting. The quorum of a Committee is 50% of the total potential membership. No business may be conducted unless the quorum is reached.

Randomised controlled trial (RCT)

Trials in which participants (or clusters) are randomly allocated to receive either intervention or control. If well implemented, randomisation should ensure that intervention and control groups differ only in their exposure to treatment.

Recommendations

Specific advice in NICE guidelines on the care and services that are suitable for most people with a specific condition or need, or for particular groups or people in particular circumstances (for example, when being discharged from hospital). Recommendations may also cover ways to promote good health or prevent ill health, or how organisations and partnerships can improve the quality of care and services.

Reference case

The reference case specifies the methods considered by NICE to be the most appropriate for estimating clinical and cost effectiveness when developing guidance. These are also consistent with an NHS objective of maximising health gain from limited resources.

Reference standard (or gold standard)

A method, procedure or measurement that is widely accepted as being the best available to test for or treat a disease.

Research recommendations

Recommendations for future research that cover areas of uncertainty or gaps in the evidence identified during guideline development.

Respondent

Tobacco companies with an interest in a particular guideline topic. They can register to comment on the draft scope and the draft guideline and their comments are made public with those of registered stakeholders. The term 'respondent' acknowledges NICE's commitment to Article 5.3

of the WHO Framework Convention on Tobacco Control. This sets out an obligation to protect the development of public health policy from any vested interests of the tobacco industry.

Review protocol

A document that outlines the background, objectives and planned methods for an evidence review.

Review questions

Review questions guide a systematic review of the literature. They address only the key issues and questions covered in the scope of the guideline, and will usually be structured with a framework (for example, using PICO or SPICE).

Scoping search

A search of key sources at the scoping stage to identify previous guidelines, health technology assessment reports, key systematic reviews, randomised controlled trials and economic evaluations relevant to the guideline topic. The search also includes the NICE website, government, charity, and other community and voluntary sector websites to identify relevant policies and documents.

Scoping workshop

The scoping workshop is attended by registered stakeholders and is held when key issues that need discussion have been identified by the Developer. The workshop may be held before during or after consultation.

Search filter

A collection of search terms designed to retrieve certain types of study (for example, those using a specific study design or on a specific topic).

Sensitivity (of a test)

This refers to how well a test detects what it is testing for. It is the proportion of people with the disease or condition that are correctly identified by the study test.

Sensitivity analysis

A means of exploring uncertainty in the results of economic evaluations. There may be uncertainty because data are missing, estimates are imprecise or there is controversy about methodology. Sensitivity analysis can also be used to see how applicable results are to other settings. The analysis is repeated using different assumptions to examine the effect of these assumptions on the results.

- Deterministic sensitivity analysis investigates how bias in selecting data sources for key model parameters might affect the results.
- One-way sensitivity analysis (univariate analysis) varies each parameter individually to investigate how this affects the results.
- Probabilistic sensitivity analysis assigns probability distributions to uncertain parameters and incorporates these into models using decision-analytic techniques (for example, Monte Carlo simulation).

Social care

Social care generally refers to all forms of personal care and other practical assistance for children, young people and adults who need extra support. This includes:

- vulnerable children and young people (those who are at risk of, or who are already experiencing social and emotional problems)
- children, young people and adults with learning or physical disabilities or mental health problems
- people who misuse drugs or alcohol
- older people.

Specificity (of a test)

This refers to how well a test detects what it is testing for. The proportion of people classified as negative by the reference standard who are correctly identified by the study test.

SPICE framework

A structured approach for developing review questions that divides each question into 5 components: setting, perspective, intervention, comparison and evaluation (SPICE).

Stakeholders

Stakeholders are organisations with an interest in a particular guideline topic; they may represent people whose practice or care is directly affected by the guideline.

They include: national organisations for people who use health and social care services, their families and carers, and the public; local Healthwatch organisations; national organisations that represent health and social care practitioners and other people whose practice may be affected by the guideline, or who can influence uptake of the guideline recommendations; public sector providers and commissioners of care or services; private, voluntary sector and other independent providers of care or services; companies that manufacture drugs, devices, equipment or adaptations, and commercial industries relevant to public health; organisations that fund or carry out research; government departments and national statutory agencies.

As a party to the WHO Framework Convention on Tobacco Control, the United Kingdom has an obligation to protect the development of public health policy from the commercial and vested interests of the tobacco industry. When registering, commenting on the draft scope and draft guideline, and submitting evidence in response to a call for evidence, stakeholders are asked to disclose whether their organisation has any direct or indirect links to, or receives or has ever received funding from, the tobacco industry. We will still carefully consider all consultation responses from the tobacco industry and from those with links to the industry. Disclosures will be included with the published consultation responses and with evidence presented to the Committee.

Stakeholders are encouraged get involved at all stages. Registered stakeholders comment on the draft scope and draft guideline, may provide evidence, and support implementation of the guideline.

Standing Committee

A Committee consisting of core members who work on multiple guidelines. Topic expert members are brought in to work on specific guidelines.

Survey

See cross-sectional study.

Systematic review

A review that summarises the evidence on a clearly formulated review question according to a predefined protocol, using systematic and explicit methods to identify, select and appraise relevant studies, and to extract, analyse, collate and report their findings. It may or may not use statistical meta-analysis.

Time horizon

The time period over which the main differences between interventions in effects and the use of resources in health and social care are expected to be experienced, taking into account the limitations of the supporting evidence.

Topic adviser (topic-specific Committee)

A member of the Committee who also works closely with the Developer to provide topic-specific support.

Topic expert members (of a standing Committee)

Experts on the topic of a guideline who join a standing Committee to work on that guideline. They may include lay members, practitioners, providers and commissioners.

Topic-specific Committee

A Committee consisting of members appointed for the development of a specific guideline.

Treatment options

The choices of intervention available.

Changes after publication

July 2015: Added a link to the COMET database to information on core outcome sets. Updated the glossary entries for committee chair and GRADE. Changed the term 'stakeholder' to 'respondent' in the case of tobacco companies. Changed costing tools to resource impact assessment tools. Made minor changes related to the suspension of the safe staffing programme. Added overseas agencies with a remit covering England to stakeholders list.

February 2015: Definition of quorum updated in the manual and Appendix D. Minor maintenance on other sections.

About this manual

This manual describes the methods used in the development of NICE guidelines. It will be updated as described in section 1.8.

Nothing in this manual shall restrict any disclosure of information by NICE that is required by law (including in particular but without limitation the Freedom of Information Act 2000).

Produced by the National Institute for Health and Care Excellence (October 2014)

Copyright

ISBN: 978-1-4731-0809-7