NICE National Institute for Health and Care Excellence

Developing NICE guidelines: the manual

Process and methods

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Contents

1 Introduction and overview

The National Institute for Health and Care Excellence (NICE) is a non-departmental public body that provides national guidance and advice to improve health and social care in England. 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 their own 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 other engagement work)
- 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 developers of other guidance, stakeholders and users of NICE guidelines.

The processes and methods described in this manual are based on internationally recognised standards, and the experience and expertise of the teams at NICE, the contractors that work with NICE, NICE committee members and stakeholders. They 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.

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 manual covers methods and processes for clinical, public health and social care topics, and service guidance (see appendix A). 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 methods for the guideline or the individual evidence review, together with the reasons for the choice. 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.

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 and Social Care).

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
- the health and care burden, and the potential to improve outcomes and quality of life.

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 Social Care, 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 following core principles:

- 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, including carers, 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 the light of new evidence or intelligence 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.

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 used 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, a range of other non-randomised evidence, such as observational evidence (including that derived from the analysis of primary data sources such as patient registries), experimental and qualitative evidence, may also be used to inform assessments of effectiveness, or aspects of effectiveness. This evidence 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 agrees or differs ('triangulation'). When there is little or no evidence, the committee may also use expert testimony, make consensus recommendations using their knowledge and experience, or make recommendations for further research.

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 (Developing NICE guidelines: how to get involved).

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 likely to be insufficient (for example, when the topic covers a population group that is not part of the committee, such as children, or adults 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).

NICE's equality objectives and equality programme 2016–2020 summarises NICE's legal and other equality obligations and describes NICE's approach to meeting them, particularly the process of equality impact assessment. 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). Identifying 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 informed of progress by email. NICE also adds information on progress to the guideline page on the NICE website. The schedule for the guideline, the scope and details of the committee are also available on the NICE website.

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, and they may be invited to provide evidence during guideline development. NICE

formally responds to comments from registered stakeholders, and these responses are published on the NICE website. Stakeholders support implementation of the guideline once it is published.

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 (for example, GP practices)
- 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 write responses 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.

Although NICE is established as an England-only body, our 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 and those who speak for them or are funded by them (collectively referred to as 'tobacco organisations') cannot register as stakeholders. This is in line with NICE's obligation under Article 5.3 of the WHO Framework Convention on Tobacco Control (FCTC) to protect public health policies from the commercial and other vested interests of the tobacco industry. Tobacco organisations are simply referred to as 'respondents'. Any comments received during consultation from respondents are reviewed for factual inaccuracy claims and are made public along with any responses.

NICE staff and contractors who work with the committee

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

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 processes have 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. Staff with responsibility for quality assurance must declare any interests, which are managed in line with NICE's policy on declaring and managing interests for board members and employees. Quality assurance takes place throughout development and during checks of the guideline after publication (surveillance). The responsibilities of NICE staff involved in guideline quality assurance are summarised below:

- The NICE **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 NICE **guideline lead** 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 guideline lead also advises the committee chair and the developer on matters of method and process. Guideline commissioning managers help them with this.

- The NICE clinical, public health or social care **adviser** is responsible for providing advice during all stages of guideline development.
- The NICE **technical lead** is responsible for ensuring the technical quality of the non-economic evidence reviews.
- The NICE **economic lead** is responsible for ensuring the technical quality of the economic evidence and any economic analysis.

Quality assurance of guideline surveillance reflects quality assurance of guideline development. The NICE associate director – surveillance is responsible for ensuring that processes are followed and that decisions to update or not update guidelines are robust and fit for approval by NICE's Guidance Executive. The NICE technical adviser – surveillance ensures the technical quality of the surveillance review, and the NICE clinical, public health or social care adviser provides advice at all stages.

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 documenting the recommendations, committee discussions and decisions, evidence reviews and methods.

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.

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. Sometimes developers may commission other organisations to review the evidence.

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 evidence tables and writes brief summaries (including GRADE tables, GRADE-CERQual or evidence statements, if used) 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 media relations team

The media relations team supports committee members, the developer, and NICE staff with responsibility for quality assurance, on all aspects of communications, including contacts with the media and managing any issues, throughout guideline development and after publication.

NICE resource impact assessment team

The resource impact assessment team works with the committee, and NICE staff carrying out quality assurance, to provide information on the resource impact (costs and savings) of recommendations. Final cost estimates are available to support the implementation of the guideline.

NICE adoption and impact team

The adoption and impact team produces tools and signposts to other support that can help organisations put guideline recommendations into practice. The implementation support team works with external organisations on selected priority areas, which depend on the interests of our partner organisations and resources.

NICE system engagement team

The system engagement team includes the field team who work with regional and local organisations to promote the guideline and help to put it into practice. The NICE endorsement and shared learning programmes also support implementation with external resources and implementation case study examples.

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.

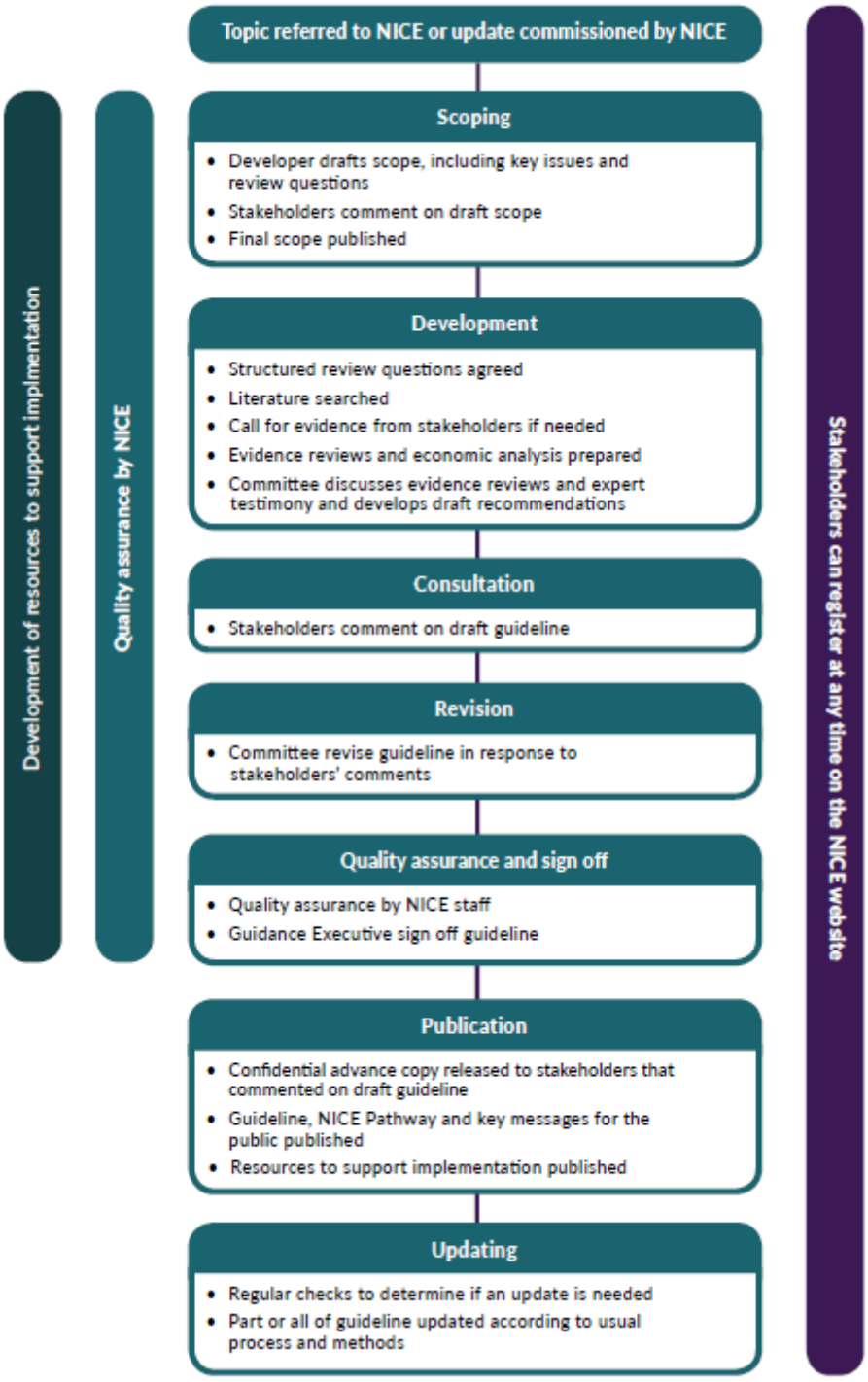
NICE publishing team

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 are written and presented in a way that is clear and accessible to a range of different audiences. They develop the NICE Pathway (which brings together everything NICE says on a topic in an interactive flowchart) and for some topics may produce a visual summary of the recommendations.

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

Guideline recommendations are published on the NICE website alongside the rationales for the recommendations, evidence reviews, including summaries of the committee discussions, and methods. Any resources to help users implement the guideline are also published. The guideline recommendations are also included in NICE Pathways – an online tool that brings together

everything NICE says on a topic in an interactive flowchart. Pathways are structured and signposted so users can find relevant recommendations quickly and easily. They are not care 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

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

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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).

2.1 Purpose of the scope

The scope sets boundaries that ensure the work stays within the referral and the resulting guideline can support 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 and will not consider
- identifies the key issues that will be considered and lists the draft questions
- describes the economic perspective(s) to be used.

The scope also includes:

- 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 build on, rather than simply reproduce, the actions required by legislation and statutory guidance
- how the guideline will link to other NICE recommendations and quality standards that are published or in development (chapter 8).
- a draft outline of the NICE Pathway (everything NICE says on a topic in an interactive flowchart)
- 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. 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 a guideline is being updated or replaced, the scope of the existing guideline may be used unchanged, the scope of the existing guideline may be modified or a new scope developed. The scope lists which sections will be updated, and any that will be removed, for example, because they are now covered by other NICE guidance or by legislation or other sources of advice, or are no longer current practice.

2.2 Who is involved in developing the scope

The draft scope is prepared by the developer or by a team at NICE, with other input depending on the guideline topic. Topic-specific expertise may be provided by 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 1 or more lay people recruited specifically to support scope development, or 1 or more lay members of the committee if early recruitment is appropriate.

When several related guidelines are being developed simultaneously, cross-representation of expertise on each scoping group may also be considered.

The following are usually involved:

- a lead from NICE's Pathways team
- a lead from NICE's public involvement programme
- a lead from NICE's resource impact assessment team
- the developer's information specialist, systematic reviewer and economist
- NICE staff with responsibility for quality assurance.

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: identifying and making decisions on overlaps with other NICE guidance
- 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 sources searched will depend on the topic, the type of questions the guideline will seek to address and the type(s) of evidence sought. Unpublished sources of data that might provide relevant high-quality evidence, such as audits and registries, should also be identified at this stage. Topic advisers or committee members may also identify relevant sources and evidence.

The search for evidence to support scope development should identify any appropriate:

- NICE guidance and 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
- audits, surveys and registries
- types of interventions that may be appropriate and their safety
- statistics (for example, on epidemiology or service configuration), 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 can also reveal the evidence base, start to identify gaps in the evidence and indicate whether there is sufficient evidence to answer the draft questions. At this stage, tools that cluster search results into topics can be helpful. The search should focus on identifying secondary sources, such as reviews of the evidence. If there is insufficient review-level information, the scoping search should be extended to identify relevant primary studies and data sources (including those sources that might not be identified using traditional search strategies). When searching for systematic reviews, it may be efficient to limit any searches of databases that are sources for DARE (Database of Abstracts of Reviews of Effects) to studies indexed after December 2014, when the searches to identify studies for DARE ceased.

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

The search should be fully documented (see section 5.9) and if new issues are identified at a scoping workshop, the search may be updated. 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 of the existing guideline 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.

When gaps in the evidence are identified, NICE staff with responsibility for quality assurance, the developer or committee members (if recruited early) may believe that there is relevant evidence not identified by the searches. In these cases, the developer should start to compile a list of the gaps during scoping, along with details of stakeholders who might be able to provide information, as part of a call for evidence (see section 5.5) or as expert witnesses (see section 3.5).

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
- the burden of disease
- the differential impact of disease or services and outcomes (in relation to socioeconomic factors or equity issues)
- how care and support is currently delivered and who is responsible for commissioning and providing it
- the cost of care and support
- workforce issues and variance in service organisation
- use of interventions
- legislative or regulatory frameworks
- 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 and resource impact are identified early and used to inform the guideline and relevant resources.

The developer continues to collect contextual information during development so that the guideline can adapt to changes in context.

Using a conceptual framework to construct a logic model

For some guidelines, it may be helpful to construct a topic- or question-specific conceptual framework. Two different, but interlinked, models can be used: problem-oriented and design-oriented.

A problem-oriented conceptual model can aid understanding of existing or planned interventions or services and identify areas for improvement. It provides information on how factors interact and ensures that key areas are approached in the most logical and efficient way. It helps to focus questions, as well as identifying how the discrete questions are linked and how much of the intervention or service will be covered. A problem-oriented conceptual model can be developed as part of the scoping process (for example, at the stakeholder scoping workshop) and should not be limited by what is feasible.

The problem-oriented model links to a design-oriented conceptual model (or logic model), which is used to inform the structure, assumptions and data needed for simulation models (implementation models) to assess effectiveness (including cost effectiveness). The design-oriented model can also be used to help structure the review questions and to specify the data and evidence needed to develop an economic model to inform recommendations.

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, by considering any health inequalities and impacts on equality, and consulting experts.

Identifying the population is critical because it helps determine the breadth and depth of the work. It also means that feasible measures can be included in any related NICE quality standard.

Identifying the key issues ensures that the guideline focuses on areas in which providers and commissioners of care and support, 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. It may also be important to identify populations in which there is evidence to suggest different effects from an intervention due to the intervention's mechanism of action; for example, subgroups with different responses to pharmacological interventions resulting from underlying genetic variation.

Consideration should be given as to whether there are specific aspects of the views or experiences of people using services that need addressing. When these are identified, they should be included in the scope if they are not covered by existing guidelines and are supported as a priority area (see chapter 4).

Guidelines do not usually include key issues that are covered by other arms-length or government

bodies such as the Department of Health and Social Care, NHS England or Public Health England. They do not usually cover training requirements, because these are the responsibility of the Royal Colleges and professional associations, but they may make recommendations on the need for specific knowledge and skills for a particular aspect of care.

The process should ensure that a range of care and support, or services is considered, including key areas for quality improvement, and that the resulting guideline can be used to inform the development or update 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
- whether the guideline offers any opportunities for advancing equality
- whether there might need to be reasonable adjustments to a recommendation to avoid putting any group of 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 factors (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 NICE staff with responsibility for quality assurance) 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 – see section 3.2 and 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 and support 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?

What is the potential for improving employment outcomes among people out of work because of ill health?

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 and support for any groups (particularly those sharing protected characteristics) need to be addressed by the scope?

Might there be a need to consider reasonable adjustments for a particular group 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 draft 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). These draft questions will be used as the basis for the final review questions (see chapter 4) in the guideline.

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

Box 2.2 Examples of key issues and draft 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

Draft 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 behaviour that challenges

Pharmacological interventions to treat pneumonia

Digital interventions to support behaviour change

Identifying pregnant women who smoke

Draft questions relating to interventions

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

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?

What interventions (including art therapy) are effective in treating mild to moderate depression?

Issues relating to experience of people using services

Information and support for people with epilepsy

Coordination and integration of support for people with a learning disability

Making structural changes to homes to support independent living

Draft questions 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 a learning disability?

Issues relating to health inequalities and equality

Differential access to services or treatment for different population groups, including those

sharing a protected characteristic

Draft key questions relating to health inequalities and equality

How can structural interventions and aids to support independent living be delivered for people who live in rented accommodation?

Identifying the main outcomes

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 and support or using services, or those providing care and support or services. Core outcome sets should be used if these are suitable based on quality and validity; one source is the COMET database. The Core Outcome Set Standards for Development (COS-STAD) and Core Outcome Set Standards for Reporting (COS-STAR) should be used to assess suitability. The outcome list is 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 appendix A).

Stage 4: identifying and making decisions on overlaps with other guidance

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. Because NICE Pathways bring together everything NICE says on a topic, they should be used to identify potential overlap between guidelines and to inform stakeholders of the range of relevant published NICE guidance.

This process should aim to identify any gaps where new recommendations would be of value, and areas where recommendations already exist (see chapter 8).

The publishing team at NICE develops an outline of the NICE Pathway in collaboration with the developer to support the development of the scope.

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 reasons 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. The aim of the workshop is to include as wide a range of 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 whether there are specific aspects of the views or experiences of people using services that need addressing and are not covered by existing guidelines
- 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, main outcomes)
- 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 a 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 also explain the processes for recruiting committee members (see chapter 3).

This introduction is followed by a structured discussion of the key issues.

After the scoping workshop, the developer writes a summary of the discussions and key themes that emerged. The summary includes a list of organisations represented at the workshop. When the workshop is held before consultation on the scope, this summary is posted on the NICE website during consultation, along with the draft of the scope that was refined after the scoping workshop. 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 are notified. Information and prompts to support stakeholder 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 in line with what matters to people with the condition or people using services) and to ask what should be included or excluded. NICE asks stakeholders to suggest areas where cost savings could be achieved.

Comments are invited from registered stakeholders. 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 comment on the draft scope (and later on the draft guideline and evidence; see section 10.1). Comments should be constructed as reasoned argument and be submitted for the purpose of improving the draft scope. NICE reserves the right not to respond to comments that are hostile or inappropriate.

Tobacco companies and those who speak for them or are funded by them (collectively referred to as 'tobacco organisations') cannot register as stakeholders. Tobacco organisations are simply referred to as 'respondents'. Any comments received during consultation from respondents are reviewed for factual inaccuracy claims and are made public along with any responses.

The developer, NICE staff responsible for quality assurance and NICE's public involvement

programme (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. When the guideline covers social care, the NICE team with responsibility for social care should be asked about appropriate stakeholders.

Stage 7: finalising the scope after consultation

Dealing with stakeholder comments

After consultation, the developer finalises the scope in line with the comments received ensuring that the scope stays in line with 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 and support, an additional population, a wider age range or an additional setting).

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 NICE staff with responsibility for quality assurance. Sometimes lower-priority areas are removed from the scope to keep the development work manageable. This is done in collaboration with the lead for any related quality standards. 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. Comments received from non-registered stakeholders and individuals are reviewed by the developer and NICE. A formal response is not given and these comments are not made available on the NICE website.

NICE reserves the right to summarise and edit comments received during consultations, or not to publish them at all, if we consider the comments are too long, or publication would be unlawful or otherwise inappropriate.

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

Kirkham JJ, Gorst S, Altman DG et al. (2016) Core Outcome Set–STAndards for Reporting: The COS-STAR Statement. PLoS Medicine 13: e1002148

Kirkham JJ, Davis K, Altman DG et al. (2017) Core Outcome Set-STAndards for Development: The COS-STAD Recommendations. PLoS Medicine 14: e1002447

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
- advises on developing the review protocol and alternative analyses
- considers the evidence
- develops the recommendations for practice and research
- considers the likely costs and savings associated with implementing 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, professionals, providers, commissioners and researchers (specialists and generalists – from the public, private or voluntary sectors, or other independent providers of care and support, or services)
- 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 champion the perspectives of people who use services, carers or the public. They do not have a healthcare, public health or social care professional or practitioner

background in the topic. 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 Industry (ABPI). Any conflicts of interests should be managed in accordance with NICE's policy on declaring and managing interests for NICE advisory committees.

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 recruited if needed 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 with a commissioning or provider background are needed, in addition to members from relevant professional or practitioner networks or local authorities.

When several related guidelines are being developed at the same time, some committee members may sit on more than one committee, depending on expertise.

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 and anonymised data from recruitment is submitted to NICE's corporate office who use this to report to the NICE Board.

Ideally, committee members have experience of the UK healthcare setting and are drawn from different parts of England. But this depends on the expertise available and does not exclude people

from other countries 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 co-opted members who are invited to contribute to formulating recommendations in a specific part of the guideline only. They take part fully in discussions, but do not have voting rights or count towards quorum.

Expert witnesses may also be invited to some committee meetings to provide additional evidence (see section 3.5).

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.

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. NICE's public involvement programme can advise on options and methods for involving people affected by the guideline. They can target adverts for committee members to specific groups and signpost to sources of specialist advice. (See appendix B and the section on involving children and young people in NICE's patient and public involvement policy.) They will work with the developer on tailored support where this is needed.

For some topics it may be possible to recruit young people aged 16 to 18 years or people with a learning disability as members of the committee, or as co-opted members or topic experts. With specialist support and reasonable adjustments, a developer has successfully included people with a learning disability as committee members for NICE guidelines on improving care for this

population. This was achieved through specialist support and adjustments to the process to enable their full and equal involvement.

When there are particular reasons why people affected by the guideline cannot be recruited as lay committee members (for example, when the guideline covers children), other approaches are needed to ensure that their views and experiences are incorporated in the recommendations. These might include working with an external agency to obtain user views or consulting with a reference group of people using services, at key stages of guideline development. For example, for the guideline on child abuse and neglect, the developer commissioned the independent charity Against Violence and Abuse (AVA) to recruit and facilitate an expert reference group of young people as a subgroup of the committee (see the summary report). Another approach could involve a targeted consultation with people affected by the guideline to fine-tune selected draft recommendations (see section 10.1 and appendix B).

If other approaches to engaging people affected by the guideline are needed, the developer should document the reasons, together with a proposal for the work, including possible methods to be used, and the anticipated costs and time. The proposal should be discussed and agreed with members of NICE staff with a quality assurance role, and approved by the centre director. When the work is approved, the reasons for the approach 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, 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. They are encouraged to complete an equality monitoring form.

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 many 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 should ideally 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 contribute to formulating recommendations in a specific part of the guideline.

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. All members are eligible for re-appointment after 3 years.

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 and takes into account the final scope of the guideline. Topic expert members are full members of the committee, with voting rights. They join in discussions, contribute to formulating 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 by the developer and NICE staff with a role in guideline quality assurance and takes into account the final scope for the guideline. 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); examples of topics where there may be more than 2 lay members include topics where personalisation and choice are particularly important, where a scope is large and covers different areas, and topics covering all age groups.

Additional members with specialist knowledge may also be co-opted to the committee for 1 or more meetings to contribute to formulating recommendations in a specific part of the guideline.

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.

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 2.3). 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, to 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.

Before seeking expert testimony from children or other vulnerable groups, expert advice should be sought about the ethics and implications of the involvement. Adjustments and additional support may be needed, such as giving testimony via video recording, or in private session. There is no minimum age for young people providing expert testimony. If a child or young person attends a committee meeting, they must be accompanied by their parent, carer or other appropriate adult with responsibility for their welfare (see appendix on safeguarding in NICE's patient and public involvement policy).

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
- support.

These are technical and project management staff from the developer and/or NICE staff with a quality assurance role. Other NICE staff (such as editors and members of the NICE resource impact assessment 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. Public access to all guideline committee meetings is not possible because of

financial pressures. In addition, all or part of a meeting may need to be held in closed session because 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 the drafting of recommendations might affect commercial interests.

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. 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, including the chair, and anyone who has direct input into the guideline (including the developer and expert witnesses) must declare any potential conflicts of interest in line with NICE's policy on declaring and managing interests for NICE advisory committees. For committee members, including the chair, 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 recorded in a register for each guideline and are published on NICE's website.

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 resource impact and how this is considered alongside the economic evidence
- information about implementation
- NICE's social value judgements and equality policy
- declaration of interests.

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.

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.

Training for the committee chair

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 the chairs' induction session provided by NICE, 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 people requiring adjustments 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. The training 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.

The developer takes formal minutes during committee meetings and these are reviewed and 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 are usually 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 their plans for the evidence reviews (draft review protocols) 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 cognitive impairment; see section 3.2).

The outline of the NICE Pathway (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 analyses 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, public involvement lead and media relations lead for the guideline and members of the resource impact assessment team) 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, which brings together everything NICE says on a topic in an interactive flowchart
- activities and tools that support implementation of the guideline (see chapter 12)
- promoting the guideline (see chapter 11).
- developing content for the information for the public section on the topic webpage, including the guideline's key messages

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 draft recommendations and the rationales for the recommendations
- details of the included and excluded studies and associated review protocols
- data-extraction forms
- draft evidence reviews with 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 lay members, 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 methods, 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

In certain cases, for example, if the literature search has found no evidence that addresses the review question, the committee may wish to identify wider views on best practice by using formal consensus methods (such as 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. In all cases the approach used should be documented.

3.10 Further contributions of committee members

Some committee members may be invited to apply to join the Quality Standards Advisory Committee that is developing a quality standard related to the guideline. Some members may also be invited to contribute to a future review of the guideline and a check of the need for an update.

3.11 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 draft questions listed in the scope should be translated into review questions and review protocols.

Review questions define the scope of the review and therefore must be clear and focused. They provide 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 appendix I) and the guideline, together with the reasons 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 review questions:

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

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 investigate the effects of a single intervention compared with a single comparator and there may be few primary studies or no study 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 key areas specified in the scope but should not introduce new areas. They should build on the draft questions in the scope and usually contain more detail.

Review questions are usually drafted by the developer. They are then refined and agreed with 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 (with reasons) should be agreed with a member of NICE staff with a quality assurance role, and documented in the review protocol and evidence review.

4.3 Formulating and structuring different review questions

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
- causal mechanisms, or associations between factors or variables and the outcome of interest, the epidemiology or aetiology of a disease or condition
- interventions that work best in ideal circumstances and might work in specific circumstances or settings (the extent to which something works, how and why)
- technologies or tests that work best to diagnose certain diseases or conditions
- 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, and whether there might be differences in people's values and preferences that might affect uptake of a recommended 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.

Conceptual or logic models can be useful when developing 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 that is most suitable (Petticrew and Roberts 2003). There are examples of different types of review questions and the type of evidence that might best address them throughout this chapter. Developers should consider whether particular review questions might be addressed through analysis of primary data, based on an understanding of the evidence base and different sources available (see section 2.3).

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 examined?

Comparators: Are there alternative(s) to the intervention being examined? 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 (including outcomes on both benefits and harms)? What is really important for people using services? Core outcome sets should be used if suitable based on quality and validity; one source is the COMET database. The Core Outcome Set Standards for Development (COS-STAD) and Core Outcome Set Standards for Reporting (COS-STAR) should be used to assess the suitability of identified core outcome sets.

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. Outcomes (on both benefits and harms) and other factors that are important should be pre-specified in the review protocol. In general, a maximum of 7 to 10 outcomes should be defined. Guidance on prioritising outcomes is provided by the GRADE working group.

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 are the most effective methods of care planning, focusing on improving outcomes for people with dementia and their carers?
- What is the effectiveness and cost effectiveness of intermediate care and reablement for people living with dementia?

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, and 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 of interventions and SuRe Info (Summarized Research in Information Retrieval for HTA) resource.

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 assessing association or possible 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 health interventions delivered at population level (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 mechanism of action (such as a pathophysiological basis) for the intervention.

When review questions are about the effectiveness of interventions, additional types of evidence

reviews may be needed to answer different aspects 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 [that is, a mixed methods review]). A review on effectiveness may also include evidence of the intervention's mechanism of action, that is, evidence of how the intervention works. Some reviews may also include analysis of large, high-quality primary data sources (such as patient registries).

Review questions that consider implementation

Review questions on effectiveness may also consider implementation, for example, 'What systems and processes should be in place to increase shared decision-making?'

Review questions that consider cost effectiveness

For more information on review questions that consider 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 (or diagnostic yield) of a test or a number of tests individually against a comparator (the reference standard)
- questions about the diagnostic accuracy (or diagnostic yield) 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 PICTO (population, index test, comparator, target condition and outcome) 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 PICTO framework

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

Index test[s]: The test or test strategy being evaluated for accuracy.

Comparator/reference standard: 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 study in which both the index test(s) and the reference standard are performed on the same sample of people. Cohort and case–control studies are also used to assess the accuracy of diagnostic tests, but these types of study design are more prone to bias (and often result 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

What is the accuracy of imaging (MRI, CT scan, PET scan, X-ray, ultrasonography) for diagnosing osteomyelitis compared with invasive bone biopsy?

What is the accuracy of D-dimer assay for diagnosing deep vein thrombosis compared with compression ultrasonography?

In people suspected of having coronary artery disease, can multi-slice spiral CT of coronary arteries be used as replacement for conventional invasive coronary angiography?

In patients suspected of cow's milk allergy, should skin prick tests rather than an oral food challenge with cow's milk be used for diagnosis and management?

In adults receiving care in non-specialist settings, should serum or plasma cystatin C rather than serum creatinine concentration be used for diagnosing and managing renal impairment?

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, for example, 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 test-and-treat 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.

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 may predict outcomes (including suicide, non-fatal repetition, other psychosocial outcomes) from self-harm?
>
> Which people having neoadjuvant chemotherapy or chemoradiotherapy for rectal cancer do not need surgery?

A review question about prognosis is best answered using a prospective cohort study with multivariate analysis. Case–control studies and cross-sectional 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 clinical prediction models for individual prognosis or diagnosis

Clinical prediction models are developed to help healthcare professionals estimate the probability or risk that a specific disease or condition is present (diagnostic prediction models) or that a specific event will occur in the future (prognostic prediction models). These models are used to inform decision-making. They are usually developed using a multivariable prediction model – a

mathematical equation that relates multiple predictors for a particular person to the probability of or risk for the presence (diagnosis) or future occurrence (prognosis) of a particular outcome. Other names for a prediction model include risk prediction model, predictive model, prognostic (or prediction) index or rule, and risk score.

Diagnostic prediction models can be used to inform who should be referred for further testing, whether treatment should be started directly, or to reassure patients that a serious cause for their symptoms is unlikely. Prognostic prediction models can be used for planning lifestyle or treatment decisions based on the risk for developing a particular outcome or state of health in a given period.

Clinical prediction model studies can be broadly categorised into those that develop models, those that validate models (with or without updating the model) and those that do both. Studies that report model development aim to derive a prediction model by selecting the relevant predictors and combining them statistically into a multi-variable model. Logistic and Cox regression are most frequently used for short-term (for example, disease absent versus present, 30-day mortality) outcomes and long-term (for example, 10-year risk) outcomes, respectively. Studies may also focus on quantifying how much value a specific predictor (for example, a new predictor) adds to the model.

Quantifying the predictive ability of a model using the same data from which the model was developed (often referred to as apparent performance) tends to overestimate performance. Studies reporting the development of new prediction models should always include some form of validation to quantify any optimism in the predicted performance (for example, calibration and discrimination). There are 2 types of validation: internal validation and external validation. Internal validation uses only the original study sample with methods such as bootstrapping or cross-validation. External validation evaluates the performance of the model with data not used for model development. The data may be collected by the same investigators or other independent investigators, typically using the same predictor and outcome definitions and measurements, but sampled from a later period (temporal or narrow validation). If validation indicates poor performance, the model can be updated or adjusted on the basis of the validation data set. For more information on validating prediction models, see Steyerberg et al. 2001, 2003, 2009; Moons et al. 2012; Altman et al. 2009; and Justice et al. 1999.

Well-known clinical prediction models include QCancer, GerdQ, Ottawa Ankle Rules, and the Alvarado Score for diagnosis; and for prognosis, QRISK2, QFracture, FRAX, EuroScore, Nottingham Prognostic Index, the Framingham Risk Score and the Simplified Acute Physiology Score.

For more information, see the TRIPOD statement and the TRIPOD statement: explanation and

elaboration.

Although assessing predictive accuracy is important for establishing the usefulness of a clinical prediction model, the value of a clinical prediction model lies in how useful it is in guiding treatment or management decisions, or the provision of services, and ultimately in improving outcomes. Review questions aimed at establishing the value of a clinical prediction model in practice, for example, to compare outcomes of people who were identified from a clinical prediction model (in combination with a management strategy) with outcomes of people who were identified opportunistically (in combination with a management strategy) can be structured in the same way as questions about interventions.

Box 4.6 Examples of review questions on clinical prediction models

Diagnostic prediction models

Which scoring tools for signs and symptoms (including Centor and FeverPAIN) are most accurate in predicting sore throat caused by group A beta-haemolytic streptococcus (GABHS) infection in primary care?

What are the accuracy, clinical utility and cost effectiveness of clinical prediction models/tools (clinical history, cardiovascular risk factors, physical examination) in evaluating stable chest pain of suspected cardiac origin?

Prognostic prediction models

What risk tool best identifies people with multimorbidity who are at risk of unplanned hospital admission?

What risk tool best identifies people with type 2 diabetes who are at risk of reduced life expectancy?

Which risk assessment tools are the most accurate in predicting the risk of fragility fracture in adults with osteoporosis or previous fragility fracture?

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 and the type of evidence that will best inform the question.

In some circumstances, specific questions should be formulated about the views and experience of people using services, family members or carers and the public. 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:

- 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)
- information and support needs specific to the topic
- 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 guidelines on patient experience in adult NHS services, service user experience in adult mental health, people's experience in adult social care services, 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. The PICo (Population, Interest, Context) framework and the SPIDER framework are

examples of frameworks that can be used to structure review questions on the views or experiences of people using or providing services, family members or carers or the public.

Box 4.7 Examples of review questions on the views or experiences of people using or providing services, family members or carers or the public

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?
What information and support should be offered to children with atopic eczema and their families and carers?
What are the views and experiences of health, social care and other practitioners about home-based intermediate care?

A review question about the views or experiences of people using or providing services, family members or carers or the public could be answered using qualitative studies or cross-sectional surveys (or both) , although information on views and experiences is also becoming increasingly available as part of some 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 call for evidence (see section 5.5), or approaching experts 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 an additional 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 appendix B.) The developer should document the reasons, 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 reasons 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 or what are the different core components of services and how different components could be re-configured.

Box 4.8 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 the following outcomes: 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?

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, including observational evidence (including real world evidence), experimental and qualitative evidence. Other types of questions on service delivery are also likely to be answered using evidence from study types other than RCTs. For example, in order to determine whether an intervention will work for a particular subgroup or setting, we might want to know how the intervention works, which will require evidence of the relevant underlying mechanisms.

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 chapter 7 and appendix A may be used. Such methods should be agreed with NICE staff with responsibility for quality assurance and should be clearly documented in the 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 incidence or prevalence of a condition would provide baseline data for further evidence synthesis, 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.

Box 4.9 Examples of review questions that might benefit from an epidemiological review

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 is the incidence of Lyme disease in the UK?

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 review on associations. 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 review on associations – may be needed to establish the epidemiological factors associated with any positive or negative behaviours or outcomes.

Box 4.10 Examples of review questions that might benefit from a review on associations

What factors are associated with children's or young people's physical activity and how strong are the associations?
What physiological and aetiological factors are associated with coeliac disease?
What physical, environmental and sociological factors are associated with the higher prevalence of multiple sclerosis in European countries?

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 should be 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 and refinement of logic models (see section 2.3) 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 can include both quantitative and qualitative evidence. Sometimes, 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 of services (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 users, stakeholders, practitioners, commissioners or the public
- theories of, or reasons for, associations between interventions and outcomes.

Examples of the types of review questions that could be 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). 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?

Existing systematic reviews

Often reviews of quantitative or qualitative studies (secondary evidence) already exist (for example, those developed by internationally recognised producers of systematic reviews such as Cochrane, the Campbell Collaboration and the Joanna Briggs Institute among others). 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 may be of particular value as sources of evidence (see appendix H for checklists to assess risk of bias or quality of studies when developing guidelines). Some reviews may be 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 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 may have undertaken additional analyses (such as individual patient data analyses). 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).

Systematic 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 systematic review can also help to identify some of the limitations or difficulties associated with a topic, for example, through a critical appraisal of the limitations 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.

High-quality systematic reviews that are directly applicable to the guideline review question can be used as a source of 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, PICO, inclusion and exclusion criteria) of the review are sufficiently similar to the review protocol of the guideline review question. 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) 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 topic and the review question, other sources of relevant evidence such as reports, audits, and service evaluation may be included. This should be agreed with NICE staff with responsibility for quality assurance before proceeding. The quality, reliability and applicability of the evidence is assessed according to standard processes (see appendix H).

See also chapter 8 on linking and using evidence from non-NICE 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 to 7), rather than duplicating the methodology stated here. It should include the components outlined in appendix I.

When a guideline is updating a published guideline, the protocol from the published guideline, if available, should be used to outline how the review question would be addressed. Information gathered during surveillance and scoping of the guideline should also be added. This might include new interventions and comparators, and extension of the population.

Process for developing the review protocol

The review protocol should be drafted by the developer, with input from the guideline committee, 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.

All review protocols should be registered on the PROSPERO database before the completion of data extraction. The review protocol, principal search strategy (see sections 5.2 and 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 draft guideline goes out for consultation. 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 and updated on the PROSPERO database.

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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. Literature searches should be systematic, transparent and reproducible to minimise 'dissemination biases'. 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 or systematic review software. The methods for undertaking scoping searches are described in chapter 2. For information on searching for economic evidence, see chapter 7.

NICE encourages the use of search methods that balance recall and precision. 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. When the guideline is an update, the approach can also be informed by searches for the existing guideline and subsequent surveillance review. Searching includes:

- tailoring the search approach to the eligibility/inclusion criteria of the review question, as specified in the review protocol
- 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 wider range of sources consider other question frameworks and search approaches, including the use of supplementary searching techniques.

The Cochrane handbook for systematic reviews of interventions and the Campbell Collaboration's searching for studies methods guide offer good overviews of literature searching (Lefebvre et al. 2011; Kugley et al. 2017). The SuRe Info resource also provides research-based advice on information retrieval for systematic reviews and is updated twice a year.

5.2 Search protocols

Search protocols should be developed by the information specialist and agreed with the other members of the developer's team before undertaking a systematic search. Search protocols are part of the review protocol (see appendix I), which is signed off by the committee. When developing search protocols, the information specialist may ask the committee for expert advice (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:

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

5.3 Sources

Searches should include a mix of bibliographic 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, and other potentially relevant sources that could be considered. It is important to ensure adequate coverage of the relevant literature and to search a range of sources, but there should be clear reasons, 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 following should be prioritised for searching:

- the Cochrane Central Register of Controlled Trials (CENTRAL)
- the Cochrane Database of Systematic Reviews (CDSR)
- Embase
- MEDLINE
- the Medicines and Healthcare products Regulatory Agency (MHRA) – for drug safety information.

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)
- HealthTalk.

For service delivery questions, some of the evidence may be in the form of modelling studies published in journals related to operational research, statistical and mathematical methods rather than in health journals. These are less likely to be indexed in healthcare databases such as MEDLINE, and consideration should be given to sources likely to retrieve this evidence.

The following sources may be useful for service delivery questions:

- Science Citation Index
- HMIC

- Social Care Online or Social Policy Online
- Kings Fund.

Evidence may also be primary data needed to inform parameters identified in the design-oriented conceptual model. For information on searching for model inputs, see chapter 7.

For some review questions, for example, where evidence is likely to be published in non-journal sources, it may be appropriate to search for grey literature. Useful sources of grey literature include:

- HMIC
- OpenGrey
- CORE.

Reports from organisations such as the European Medicines Agency and the US Food and Drug Administration may also be of value. The Canadian Agency for Drugs and Technology in Health (CADTH) Grey Matters may also be useful for identifying sources for grey literature, as may web search tools, such as NICE Evidence Search and Trip. Topic experts on the committee may also be able to suggest appropriate sources for grey literature.

A list is provided in appendix G as a starting point for identifying potential relevant sources.

5.4 Developing search strategies

Devising a search strategy

The approach to devising and structuring search strategies should be informed by the review question. For example, the PICO (population, intervention, comparator and outcome) or the SPICE (setting, perspective, intervention, comparison, evaluation; Booth 2006) framework can be used to structure a search strategy for an intervention question. For other types of question, other frameworks may be more suitable. It may also be appropriate for the search framework to differ from that of the review question, and the choice should reflect the question type and search approach. Davies (2011) undertook a review of possible frameworks and SuRe Info has a useful summary of alternatives to PICO which have been evaluated. When using a framework, 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.

Some topics are complex, for example, where search requirements evolve as evidence is identified and it is important to balance recall and precision. One approach, when the relevant literature for a question is less well defined or indexed, is to use a multi-stranded method. 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.

Another approach is to use an iterative and/or 'stepped' method. Searching is done in several stages, with each search taking into account the evidence that has already been retrieved. Searching in stages allows the reviewers to review the most relevant, high-quality information first. It also gives the opportunity to stop searching, omitting some steps if this is felt appropriate for the topic. Additional steps are added if the developer decides that the quantity or quality of the evidence already gathered is not sufficient. It may also be appropriate to add an additional search step to identify literature published between the final search date of a study and its inclusion in a systematic review. If the developer then finds there are topics of interest not covered by existing reviews, it would be appropriate to carry out additional searching on specific topics. A decision to use a stepped or iterative approach should be agreed by the developer and NICE staff with responsibility for quality assurance because it can affect timelines.

Some topics may have multiple information needs, for example, sometimes indirect evidence is needed for network meta-analyses. This may involve developing iterative searches for a set of relevant comparators as opposed to a search for pre-determined comparators (Hawkins et al. 2009). This type of searching can be time consuming and the developer should agree a decision to do this with NICE staff with responsibility for quality assurance. Searching for observational data for service delivery questions can also be very time consuming. Registry data can be a source of estimates of treatment effects, but if the committee cannot estimate the extent or direction of any biases, the value of the data is greatly reduced and the usefulness of searching is low.

For some types of review question, for example, questions for which qualitative research is more appropriate, it may not be necessary to identify all the literature on a topic. The objective may be to reach theoretical saturation, where any additional studies identified merely support the existing line of argument, rather than identify all relevant studies. In this context, it may be possible to undertake searches which are more precise. The search approaches for this type of evidence have been reviewed and summarised by Booth (2016) and can be used to guide practice.

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 a single search that covers all the interventions, although this approach may retrieve a large number of studies.

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 databases will have indexing terms and some databases will contain records which have not yet been indexed. Also, 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. For a guideline that is being updated, previous search strategies, including surveillance searches, should be reviewed and used to inform search strategy design. New or changed terms should be identified, as well as any changes to indexing terms. This also applies when an existing review, for example, a Cochrane review, is being updated to answer a review question. Known key studies can be a useful source to identify search terms, but additional sources such as reports, guidelines, and topic-specific websites or topic experts can also be helpful.

Comprehensively identifying search terms may present challenges. For example, for public health, social care or implementation 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 (Alpi 2005, Papaioannou et al. 2010).

A further challenge may arise from websites or certain databases having limited search functionality. It may be necessary to simplify the search strategy, using fewer search terms or undertaking multiple searches of the same resource with different search term combinations.

It may be helpful to use frequency analysis or text mining to develop the search strategy (Stansfield et al. 2017, Hausner et al. 2012). Tools such as PubReMiner and Medline Ranker can help, either by highlighting search terms that might not otherwise be apparent, or by flagging terms of high value when exhaustive synonym searching is unfeasible or inadvisable. This is a rapidly developing area,

but in principle NICE supports the use of such technologies to inform search development.

Limits and filters

Searches should be limited to studies reported in English. When there are likely to be animal studies in the evidence base, these can be excluded from the search results in some databases.

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). When the guideline is an update, searches may be limited by date, but only if appropriate (for example, the inclusion/exclusion criteria for the update are the same as for the existing guideline). 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. For some databases, restricting the search by date is difficult. When this is the case, searches can be run without date limits, using reference management or systematic review software to separate new results. 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, to ensure the search strategy is transparent and reproducible.

Other search filters relating to age, setting, geography, and health inequalities 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. This resource also includes critical appraisal tools, which can be used for filter selection. Additionally, McKibbon (2009) reviews the performance of 38 randomised controlled trial filters. Both sources may be useful when choosing a filter. 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. Alternative methods for refining a search to achieve an adequate balance of recall and precision should be used when filters are not

appropriate.

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 recall 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, with reference lists being used to identify these.

Supplementary search techniques should follow the same principles of transparency, rigour 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 developer or committee may believe that there is relevant evidence in addition to that identified by the searches. In these situations, the developer may invite stakeholders, and possibly also other relevant organisations or individuals with a significant role or interest (see section 3.5 on expert witnesses), to submit evidence. A call for evidence is issued directly to registered stakeholders and via the NICE website. Examples and details of process are included in appendix J. Confidential information should be kept to an absolute minimum.

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

Quality assuring the literature search is an important step in guideline development. Studies have shown that errors do occur (Sampson 2006). Although developed specifically for Cochrane reviews, the Methodological Expectations of Cochrane Intervention Reviews (MECIR) may be useful to guide practice. They set out the components which can ensure that the identification of the evidence base is comprehensive, transparent and reproducible (Higgins et al. 2016).

For each search (including economic searches), the principal database search strategy should be quality assured by a second information specialist to maintain a consistently high standard for identifying the evidence. A checklist should be used to ensure clarity and consistency when quality assuring search strategies. An example is the PRESS 2015 Guideline Evidence-Based Checklist (McGowan et al. 2016).

Each time the principal database strategy is adapted for use in another database, it is good practice for it to be peer reviewed by a second information specialist to ensure quality and consistency is maintained.

As part of quality assurance, there is also an opportunity to undertake an audit of search results to analyse how the evidence for the guideline was identified. Using the final list of included studies, it is possible to determine the contribution of individual sources and search techniques. This can provide valuable data for informing the search approach for future surveillance and guideline updates.

5.8 Reference management

Electronic records of the references retrieved by searches should be stored using systematic review software such as EPPI-Reviewer or reference management software such as EndNote. Records can be exported from bibliographic databases and imported automatically into the software using import filters.

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.

Thorough documentation facilitates future surveillance and updating, and there are several published guides that cover this, including MECIR and the PRISMA checklist (Moher 2009).

Documenting the search begins with creating the search protocol (see section 5.2). If using an emergent 'stepped' approach, initial search strategies, key decision points and the reasons for subsequent search steps should be clearly documented in the search protocol.

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:

- details of search approach with reasons (this should include any notable differences between the searches for an existing guideline and those for an update of the guideline)
- 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/specific segment
- names of any non-database sources searched and number of citations retrieved
- search strategies for all sources and number or citations retrieved (these should be annotated to explain any decisions on included and excluded terms which are not self-explanatory)
- details of any supplementary searching undertaken, including the reasons
- 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 (including economics searches) 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. Searching PubMed or OVID's MEDLINE Epub Ahead of Print at this stage, in addition to MEDLINE, is useful to identify 'ahead-of-print' citations.

A decision to re-run searches will be taken by the developer and members of NICE staff with a quality assurance role.

If undertaken, searches should be re-run at least 6 to 8 weeks before the final committee meeting before consultation.

If evidence is identified after the last cut-off date for searching but before publication, a judgement 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

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6 Reviewing research evidence

Reviewing evidence is an explicit, systematic and transparent process that can be applied to both quantitative (experimental and observational) 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 summarise the evidence and its limitations so that the committee can interpret the evidence and make appropriate recommendations, even where there is uncertainty.

Evidence identified during literature searches and from other sources (see chapter 5) should be reviewed against the review protocol to identify the most appropriate information to answer the review questions. The evidence review process used to inform guidelines must be explicit and transparent and involves 6 main steps:

- writing the review protocol (see section 4.5)
- identifying and selecting relevant evidence
- critical appraisal
- extracting and synthesising the results
- assessing quality/certainty in the evidence
- interpreting the results.

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

6.1 Identifying and 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 all data, whether fully or partially published studies or unpublished data supplied by stakeholders. Care should be taken to ensure that multiple reports of the same study are identified and ordered in full text to ensure that data extraction is as complete as possible, but study participants are not double counted in the analysis.

Published studies

Titles and abstracts of the retrieved citations should be screened against the inclusion criteria defined in the review protocol, and those that do not meet these should be excluded. A percentage (at least 10%, but possibly more depending on the review question) should be screened independently by 2 reviewers (that is, titles and abstracts should be double-screened). The percentage of records to be double-screened for each review should be specified 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 against a pre-specified threshold (usually 90% agreement, unless another threshold has been agreed and documented). If agreement is lower than the pre-specified threshold, the reason should be explored and a course of action agreed to ensure a rigorous selection process. A further proportion of studies should be double-screened to validate this new process until appropriate agreement is achieved.

Once the screening of titles and abstracts is complete, full versions of the selected studies should be obtained for assessment. As with title and abstract screening, a percentage of full studies should be checked independently by 2 reviewers, with any differences being resolved and additional studies being assessed by multiple reviewers if sufficient agreement is not achieved. 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 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. Reasons for study exclusion need to be sufficiently detailed (for example, 'editorial/review' or 'study population did not meet that specified in the review protocol').

Priority screening

Priority screening refers to any technique that uses a machine learning algorithm to enhance the efficiency of screening. Usually, this involves taking information on previously included or excluded papers, and using this to order the unscreened papers from those most likely to be included to those least likely. This can be used to identify a higher proportion of relevant papers earlier in the

screening process, or to set a cut-off for manual screening, beyond which it is unlikely that additional relevant studies will be identified.

There is currently no published guidance on setting thresholds for stopping screening where priority screening has been used. Any methods used should be documented in the review protocol and agreed in advance with NICE staff with a quality assurance role. Any thresholds set should, at minimum, consider the following:

- the number of references identified so far through the search, and how this identification rate has changed over the review (for example, how many candidate papers were found in each 1,000 screened)
- the overall number of studies expected, which may be based on a previous version of the guideline (if it is an update), published systematic reviews, or the experience of the guideline committee
- the ratio of relevant/irrelevant records found at the random sampling stage (if undertaken) before priority screening.

Ensuring relevant records are not missed

Regardless of the level of double-screening, and whether or not priority screening was used, additional checks should always be made to reduce the risk that relevant studies are not identified. These should include, at minimum:

- checking reference lists of included systematic reviews, even if these reviews are not used as a source of primary data
- checking with the guideline committee that they are not aware of any relevant studies that have been missed
- looking for published papers associated with key trial registry entries or published protocols.

It may be useful to test the sensitivity of the search by checking that it picks up known studies of relevance.

Conference abstracts

Conference abstracts seldom contain enough information to allow confident judgements about the quality and results of a study, but they may 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. The investigators may be contacted if additional information is needed to complete the quality assessment.

Sometimes conference abstracts can be a good source of other information. For example, they can point to published studies that have been missed, they can indicate how much evidence has not yet been fully published (and so guide calls for evidence), and 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 (such as drug safety updates from the Medicines and Healthcare products Regulatory Agency [MHRA]). Legislation and policy does not need quality assessment in the same way as other evidence, given the nature of the source. 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. Confidential information should be kept to a minimum, and 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 most likely to be important.

6.2 Assessing quality of evidence: critical appraisal, analysis, and certainty in the findings

Introduction

Assessing the quality of the evidence for a review question is critical. It requires a systematic process of assessing potential biases through considering both the appropriateness of the study design and the methods of the study (critical appraisal) as well as the certainty of the findings (using an approach, such as GRADE).

Options for assessing the quality of the evidence should be considered by the developer. The chosen approach should be discussed and agreed with NICE staff with responsibility for quality assurance, where the approach deviates from the standard (as described below). The agreed approach should be documented in the review protocol (see appendix I) together with the reasons for the choice. If additional information is needed to complete the data extraction or quality assessment, study investigators may be contacted.

Critical appraisal of individual studies

Every study should be appraised using a checklist appropriate for the study design (see appendix H for checklists). If a checklist other than those listed is needed or the one recommended as first choice is not used, the planned approach should be discussed and agreed with NICE staff with responsibility for quality assurance and documented in the review protocol.

Before starting the review, the criteria from the checklist (if not all) that are likely to be the most important indicators of biases for the review question should be agreed. These criteria will be useful in guiding decisions about the overall risk of bias of each individual study.

Sometimes, a decision might be made to exclude certain studies or to explore any impact of bias through sensitivity analysis. If so, the approach should be specified in the review protocol and agreed with NICE staff with responsibility for quality assurance.

Criteria relating to key areas of bias may also be useful when summarising and presenting the evidence (see section 6.4). Topic-specific input (for example, from committee members) may be needed to identify the most appropriate criteria to define subgroup analyses, or to define inclusion in a review, for example, the minimum biopsy protocol for identifying the relevant population in cancer studies.

For each criterion that might be explored in sensitivity analysis, the decision on whether it has been

met or not, and the information used to arrive at the decision, should be recorded in a standard template for inclusion in an evidence table (see appendix H for examples of evidence tables).

Each study included in an evidence review should preferably be critically appraised by 1 reviewer and checked by another. Any differences in critical appraisal should be resolved by discussion or recourse to a third reviewer. Different strategies for critical appraisal may be used depending on the topic and the review question.

Data extraction

Characteristics of data should be extracted to a standard template for inclusion in an evidence table (see appendix H). Care should be taken to ensure that newly identified studies are cross-checked against existing studies to avoid double-counting. This is particularly important where there may be multiple reports of the same study.

Analysing and presenting results for studies of interventions

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

There are several ways of summarising and illustrating 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: a forest plot needs data derived from the same (or justifiably similar) outcomes and measures.

Head-to-head data that compares the effectiveness of interventions is useful for a comparison between 2 active management options. Comparative studies are usually combined in a meta-analysis where appropriate. A network meta-analysis is an analysis that can include trials that compare the interventions of interest head-to-head and also trials that allow an indirect comparison via a common third intervention.

The same principles of good practice for evidence reviews and meta-analyses should be applied when conducting network meta-analyses. The reasons for identifying and selecting the randomised controlled trials (RCTs) should be explained, including the reasons for selecting the treatment

comparisons. The methods of synthesis should be described clearly in the methods section of the evidence review.

When multiple competing options are being appraised, a network meta-analysis should be considered. The data from individual trials should also be documented (usually as an appendix). If there is doubt about the inclusion of particular trials (for example, because of concerns about limitations or applicability), a sensitivity analysis in which these trials are excluded should also be presented. The level of consistency between the direct and indirect evidence on the interventions should be reported, including consideration of model fit and comparison statistics such as the total residual deviance, and the deviance information criterion (DIC). Results of further inconsistency tests, such as those based on node-splitting, should also be reported, if available. Results from direct comparisons may also be presented alongside network meta-analyses to help validate the overall effect sizes obtained; ideally this will be the results from direct pairwise comparisons.

When evidence is combined using network meta-analyses, trial randomisation should typically be preserved. If this is not appropriate, the planned approach should be discussed and agreed with NICE staff with responsibility for quality assurance. A comparison of the results from single treatment arms from different RCTs is not acceptable unless the data are treated as observational and appropriate steps are taken to adjust for possible bias and increased uncertainty.

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

To promote transparency of health research reporting (as endorsed by the EQUATOR network), evidence from a network meta-analysis should usually be reported according to the criteria in the modified PRISMA-NMA checklist in appendix K.

Evidence from a network meta-analysis can be presented in a variety of ways. The network should 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 documents developed by the NICE Technical Support Unit.

There are a number of approaches for assessing the quality, or confidence in outputs derived from network meta-analysis that have recently been published (Phillippo et al. 2017, Caldwell et al. 2016, Purhan et al. 2014, Salanti et al. 2014). The strengths and limitations of these approaches and their application to guideline development are currently being assessed.

Analysing and presenting results of studies of diagnostic test accuracy

Information on methods of presenting and synthesising results from studies of diagnostic test accuracy is being developed by Cochrane and the GRADE working group. The quality of the evidence should be based on the critical appraisal criteria from QUADAS-2 (see appendix H). If meta-analysis is not possible or appropriate, there should be a narrative summary of the results that were considered most important for the review question.

Evidence on diagnostic test accuracy may be summarised in tables or presented as Receiver Operating Characteristic curves (**ROC curves**). Meta-analysis of results from a number of diagnostic accuracy studies can be complex. Relevant published technical advice (such as that from Cochrane) should be used to guide reviewers.

Analysing and presenting results of studies of prognosis or clinical prediction models

There is currently no general consensus on approaches for synthesising evidence from studies on prognosis or prediction models. A narrative summary of the quality of the evidence should be given, based on the quality appraisal criteria from the quality assessment tool used (for example, PROBAST [for clinical prediction models], or QUIPS [for simple correlation/univariate regression analyses], see appendix H). Characteristics of data should be extracted to a standard template for inclusion in an evidence table (see appendix H). Methods for presenting syntheses of evidence on prognosis and prediction models are being developed by the GRADE working group.

Results may be presented as tables. Reviewers should be wary of using meta-analysis to summarise results unless the same factor has been examined across all studies and the same outcome measured. It is important to explore whether all likely confounding factors have been accounted for, and whether the metrics used to measure exposure (or outcome) are universal. When studies cannot be pooled, results should be presented consistently across studies (for example, the median and ranges of predictive values). For more information on prognostic reviews, see Collins 2015 and Moons 2015.

Analysing and presenting results of qualitative evidence

Qualitative evidence occurs in many forms and formats and so different methods may be used for synthesis and presentation (such as those described by Cochrane). As with all data synthesis, it is important that the method used to evaluate the evidence is easy to follow. It should be written up in clear English and any analytical decisions should be clearly justified. Critical appraisal of qualitative evidence should be based on the criteria from the Critical Appraisal Skills Programme (CASP; see appendix H).

In most cases, the evidence should be synthesised and then summarised in GRADE-CERQual. If synthesis of the evidence is not appropriate, a narrative summary may be adequate; this should be agreed with NICE staff with responsibility for quality assurance. 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 may be appropriate.

The simplest approach to presenting qualitative data in a meaningful way is to analyse the themes (or 'meta' themes) in the evidence tables and write second level themes 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 a number of ways, and each may be appropriate depending on the question type, and the evidence identified. 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 (Glaser and Strauss 1967). Other potential techniques include meta-ethnography (Noblit and Hare 1988) and meta-synthesis (Barroso and Powell-Cope 2000), but expertise in their use is needed.

Certainty or confidence in the findings of analysis

The certainty or confidence in the findings should be presented at outcome level using GRADE or GRADE-CERQual (for individual or synthesised studies). If this is not appropriate, the planned approach should be discussed and agreed with NICE staff with responsibility for quality assurance. It should be documented in the review protocol (see appendix I) together with the reasons for the choice.

Certainty or confidence in the findings by outcome

Before starting an evidence review, the outcomes of interest which are either 'critical' or 'important' to people using services and the public for the purpose of decision-making should be identified. The reasons for prioritising outcomes should be documented in the evidence review. This should be done before starting the evidence review and clearly separated from discussion of the evidence, because there is potential to introduce bias if outcomes are selected when the results are known. An example of this would be choosing only outcomes for which there were statistically significant results.

The committee discussion section should also explain how the importance of outcomes was considered when discussing the evidence. For example, the committee may have found evidence on important outcomes but none on critical outcomes. The impact of this on the final recommendation should be clear.

GRADE and GRADE-CERQual assess the certainty or confidence in the review findings by looking at features of the evidence found for each 'critical' and 'important' outcome or theme. GRADE is summarised in box 6.2, and GRADE-CERQual in box 6.3.

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

GRADE 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 extent of differences between the population, intervention, comparator for the intervention and outcome of interest across studies
- imprecision – the extent to which confidence in the effect estimate is adequate to support a particular decision
- other considerations – publication bias, the degree of selective publication of studies.

Box 6.3 GRADE-CERQual approach to assessing the confidence of evidence for qualitative studies

GRADE-CERQual assesses the following features for the evidence found for each 'critical' and each 'important' outcome or finding:

- methodological limitations – the internal validity of the evidence
- relevance – the extent to which the evidence is applicable to the context in the review question
- coherence – the extent of the similarities and differences within the evidence
- adequacy of data – the extent of richness and quantity of the evidence.

The certainty or confidence of evidence is classified as high, moderate, low or very low. In the context of NICE guidelines, it can be interpreted as follows:

- **High** – further research is very unlikely to change our recommendation.
- **Moderate** – further research is likely to have an important impact on our confidence in the estimate of effect and may change the strength of our recommendation.
- **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 recommendation.
- **Very low** – any estimate of effect is very uncertain and further research will probably change the recommendation.

The approach taken by NICE differs from the standard GRADE and GRADE-CERQual system in 2 ways:

- it also integrates a review of the quality of cost-effectiveness studies (see chapter 7)
- 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. The GRADE working group continues to refine existing approaches and to develop new approaches. Developers should check the GRADE website for any new guidance or systems when developing the review protocol. Any substantial changes, made by the developer, to GRADE should be agreed with NICE staff with responsibility for quality assurance before use.

GRADE or GRADE-CERQual tables summarise the certainty in the evidence and data for each critical and each important outcome or theme and include a limited description of the certainty in the evidence. GRADE or GRADE-CERQual tables should be available (in an appendix) for each review question(s).

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 criteria specified in the review protocol should be included in the evidence tables. 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, and record these where reported, as specified in the review protocol. Review inclusion and exclusion criteria should also take the relevant groups into account, as specified in the review protocol.

Equalities should be considered during the drafting of the reviews. Equality considerations should be included in the data extraction process and should be recorded in the committee discussion section if they were important for decision-making.

6.4 Summarising evidence

Presenting evidence

The following sections should be included in the evidence review:

- an introduction to the evidence review

- summary of the evidence identified, in either table or narrative format
- evidence tables (usually presented in an appendix)
- full GRADE or GRADE-CERQual profiles (in an appendix)
- evidence statements (if GRADE [or a modified GRADE approach], or GRADE-CERQual is not used)
- results from other analysis of evidence, such as forest plots, area under the curve graphs, network meta-analysis (usually presented in an appendix).

The evidence should usually be presented separately 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, and data extraction and presentation should still apply.

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

Summary of the evidence

A summary of the evidence identified should be produced. The content of this summary will depend on the type of question and the type of evidence. It should also identify and describe any gaps in the evidence.

Short summaries of the evidence should be included with the main findings. These should:

- summarise the volume of information gleaned for the review question(s), that is, the number of studies identified, included, and excluded (with a link to a PRISMA selection flowchart, in an appendix)
- summarise the study types, populations, interventions, settings or outcomes for each study related to a particular review question.

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, study design (for example, RCT, case–control study) and setting (for example, country)
- funding details (if known)
- population (for example, source and eligibility)
- intervention, if applicable (for example, content, who delivers the intervention, duration, method, dose, mode or timing of delivery)
- comparator, if applicable (for example, content, who delivers the intervention, duration, method, dose, 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 if summarising a systematic review/meta-analysis)
- inadequately reported data, missing data or if data have been imputed (include method of imputation or if transformation is used)
- overall comments on quality, based on the critical appraisal and what checklist was used to make this assessment.

If data are not being used in any further statistical analysis, or are not reported in GRADE tables, effect sizes (point estimate) with confidence intervals should be reported, or back calculated from the published evidence where possible. If confidence intervals are not reported, exact p values (whether or not significant), with the test from which they were obtained, should be included. When confidence intervals or p values are inadequately reported or not given, this should be

stated. Any descriptive statistics (including any mean values and degree of spread such as ranges) 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 assessment of potential biases should also be presented. When study details are inadequately reported, or absent, 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)
- study aim, study design and setting (for example, country)
- funding details (if known)
- population or participants
- 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
- overall comments on quality, based on the critical appraisal and what checklist was used to make this assessment.

Evidence statements

Full GRADE or GRADE-CERQual tables that present both the results of the analysis and describe the confidence in the evidence should normally be provided (in an appendix).

If GRADE or GRADE-CERQual is not appropriate for the evidence review, evidence statements should be included. Examples of where evidence statements may be needed are review questions covering prognosis/clinical prediction models (where data cannot be pooled), review questions covering service delivery, or where formal consensus approaches have been taken to answer a review question.

Evidence statements should provide an aggregated summary of all of the relevant studies or analyses, regardless of their findings. They should reflect the balance of the evidence, and its strength (quality, quantity and consistency, and applicability). Evidence statements should summarise key aspects of the evidence but should also highlight where there is a lack of evidence (note that this is different to evidence for a lack of effect).

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 is effective or ineffective, or is inconclusive
- the size of effect and associated measure of uncertainty
- whether the evidence is applicable to people affected by the guideline and contexts covered by the guideline.

Structure and content of evidence statements

If evidence statements are presented, 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 should identify the sources of evidence and their quality in brief descriptive terms and not just by symbols. Each statement should also include summary information about the:

- content of the intervention, management strategy (for example, what, how, where?) and comparison, or factor of interest
- population(s), number of people analysed, and setting(s) (for example, country)
- 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.

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).

An evidence statement indicating where no evidence is identified for a critical or important outcome should be included.

Terminology of evidence statements

A set of standardised terms for describing the strength of the evidence is given in box 6.4. However, the evidence base for each review may vary, so the developer should define how these terms have been used.

Box 6.4 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…'.

Weak evidence: 'There was weak evidence from 1 controlled before and after study'.

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 cohort study'.

Inconsistent evidence: 'The quality of the evidence is mixed'.

Further commentary may be needed on the variability of findings in different studies. For example, when the quality of studies reporting the same outcome varies. 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.

The terms should not be used to describe other aspects of the evidence, such as applicability or

direction 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 or association 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.

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

Evidence statements for quantitative evidence

An example of an evidence statement from a prognostic review is given in box 6.5. The example has been adapted from the original and is for illustrative purposes only:

Box 6.5 Example of an evidence statement from a prognostic review

Association between communication and contraceptive use

There is moderate evidence from 3 UK cross-sectional studies[1,2,3] (n=254), 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 an increase in actual condom use at first sex (OR 2.67 [95% CI 1.55 to 4.57]). Another study[3] found that not talking to a partner about protection before first sexual intercourse was associated with an increase in teenage pregnancy (OR 1.67 [1.03 to 2.72]). And, another study[2] found small positive 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

Abbreviations: OR, odds ratio; CI, confidence interval.

Evidence statements for qualitative evidence

Evidence statements for qualitative studies or synthesis of qualitative studies 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. Instead statements should summarise the evidence, its context and quality, and the consistency of key findings and themes across studies (meta-themes). Areas where there is little (or no) coherence should also be summarised. An example of an evidence statement developed from qualitative data is given in box 6.6.

Box 6.6 Example of an evidence statement developed from qualitative data

Association between education and childcare

Two UK studies[1,2] and 1 Dutch study[3] (n=542) reported the views of teenage mothers. In 1 study[1] of mothers interviewed in a family planning clinic and 1 study[2] of mothers' responses 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

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6.5 References and further reading

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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. 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 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's principles on 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'). In general, the committee should be increasingly certain of the cost effectiveness of a recommendation as the cost of implementation increases.

Common types of health economic analysis are summarised in box 7.1.

Box 7.1 Types of economic analysis

- Cost-minimisation analysis: a determination of the least costly among alternative interventions that are assumed to produce equivalent outcomes
- Cost-effectiveness analysis (CEA): a comparison of costs in monetary units with outcomes in quantitative non-monetary units (for example, reduced mortality or morbidity)
- Cost–utility analysis (CUA): a form of cost-effectiveness analysis that compares costs in monetary units with outcomes in terms of their utility, usually to the patient, measured in QALYs
- Cost–consequence analysis: a form of cost-effectiveness analysis that presents costs and outcomes in discrete categories, without aggregating or weighting them
- Cost–benefit analysis (CBA): a comparison of costs and benefits, both of which are quantified in common monetary terms

The committee may require more robust evidence on the effectiveness and cost effectiveness of recommendations that are expected to have a substantial impact on resources. Economic analysis must be done when there is no robust evidence of cost effectiveness to support these recommendations. Any uncertainties must be offset by a compelling argument in favour of the recommendation. However, the cost impact or savings potential of a recommendation should not be the sole reason for the committee's decision.

Resource impact is considered in terms of the additional cost or saving above that of current practice for each of the first 5 years of implementing the guideline. Resource impact is defined as substantial if:

- implementing a single guideline recommendation in England costs more than £1 million per year **or**
- implementing the whole guideline in England costs more than £5 million per year.

The aim is to ensure that the guideline does not introduce a cost pressure into the health and social care system unless the committee is convinced of the benefits and cost effectiveness of the recommendations.

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. Health economic input in guidelines typically involves 2 stages. The first is a literature review of published economic 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 approaches such as adapting existing economic models or building new 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 and personal social services [PSS] 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 and PSS 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). This should

be agreed with NICE before any economic evaluation is conducted.

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 funded by the NHS and PSS with health outcomes	Interventions funded by the public sector with health and non-health outcomes	Interventions funded by the public sector 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; for PSS include only care that is funded by NHS (such as 'continuing healthcare' or 'funded nursing care')	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 and/or informal carers)	All health effects on individuals. For local government and other settings, where appropriate, non-health effects 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 (base case) 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[3] is the preferred measure of health-related quality of life in adults		
Measure of non-health effects	Not applicable	Where appropriate, to be decided on a case-by-case basis	Capability or social care-related quality of life measures where an intervention results in both health and capability 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, particularly for public health interventions 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] QALY is a measure of health effects based on patient-reported changes in health-related quality of life, and combines both quantity and health-related quality of life into a single measure of health gain. [3] See NICE position statement on the EQ-5D-5L Abbreviations: PSS, personal social services; QALY, quality-adjusted life year.	

Interventions funded by the NHS and PSS with health outcomes

For decision problems where the intervention evaluated is solely commissioned by the NHS and does not have a clear focus on non-health outcomes, the reference case for 'interventions funded by the NHS and PSS with health outcomes' should be chosen.

More details on methods of economic evaluation for interventions with health outcomes in NHS and PSS 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.

All relevant NHS and PSS costs that change as a result of an intervention should be taken into account. Important non-NHS and PSS costs should also be identified and considered for inclusion in sensitivity analysis, or to aid decision-making. These may include costs to other central government departments and local government. Service recommendations are likely to have additional costs, which include implementation costs not usually included in the analysis and costs to other government budgets, such as social care. Implementation costs should be included in a sensitivity

analysis, where relevant, while costs to other government budgets can be presented in a separate analysis to the base case.

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

Interventions funded by the public sector with health and non-health outcomes

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 funded by the public sector with health and non-health outcomes' should be chosen. For the base-case analysis, a cost–utility analysis should be done using a cost per QALY (quality-adjusted life year) where possible.

This reference case may be most appropriate for public health interventions paid for by an arm of government, and would consider all the costs of implementing the intervention, and changes to downstream costs. In some cases, the downstream costs are negative, and refer to cost savings. For example, an intervention such as increasing physical activity, whose effects may include preventing 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 workplace interventions), the perspective on costs should be discussed and agreed with NICE staff with responsibility for quality assurance.

Productivity costs should usually be excluded from both the reference-case and 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 and/or informal carers will be included. Non-health effects may also be included. When required, the perspective will be widened to include 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, the reference case on 'interventions with a social care focus' should be chosen. For the base-case analysis, a cost–utility analysis should be done using a cost per QALY approach where possible.

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). The value of unpaid care may also be included in sensitivity analysis, or to aid decision-making. The value of unpaid care should be set at the market value of paid care. Productivity costs should usually be excluded from both the reference-case and 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 and/or informal carers. When required, the perspective may be widened to include 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 effects 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 principal search strategy (see

section 5.4), including search strategies for health economic evidence, 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 chapter 5 about identifying the evidence 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). At the initial scoping stage, it may be efficient to limit any searches of databases that are sources for NHS economic evaluation database (EED) to studies indexed after December 2014 when the searches to identify studies for NHS EED ceased.

Economic evaluations of social care interventions may be published in journals that are not identified through standard searches. Pragmatic searches based on references of key articles and contacting authors should be considered for identifying relevant papers.

Further systematic search to identify economic evaluations

For some review questions a full systematic search, covering all appropriate sources (appendix G), should be performed to identify all relevant economic evaluations. There are several methods for identifying economic evaluations and the developer should choose the appropriate method and record the reasons for the choice in the search protocol.

- All relevant review questions could be covered by a single search using the population search terms, combined with a search filter where appropriate, to identify economic evaluations and health-state utility data.

- Another approach may be to use the search strategies derived with/from the review question(s) combined with a search filter(s) to identify economic evaluations and health-state utility data. If using this approach, it may be necessary to adapt strategies in some databases to ensure adequate sensitivity (Wood et al. 2017).
- Another option is to identify economic evaluations and quality-of-life data alongside screening for evidence for effectiveness. Further guidance on searching for economic evaluations is available from SuRe Info.

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). It 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 each 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 (see box 7.1) 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; but non-comparative costing studies (such as econometric, efficiency, simulation, micro-costing and resource use, and time-series) may be included for some service delivery questions. Sometimes, 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 developer in consultation with NICE staff with responsibility for 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 should be used to appraise published economic evaluations, as

well as unpublished papers, such as studies submitted by registered stakeholders and academic papers that are not yet published. 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 applicability of evidence to the NICE decision-making context (usually the reference case), 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). Lower-quality 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 in the guideline.

Summarising and presenting results for economic evaluations

Cost-effectiveness or net benefit estimates from published or unpublished studies, or from original 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, costs, effects, 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. Original economic analyses should only be performed if an existing analysis cannot 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 needed 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 at least 6 weeks before the guideline goes out for consultation (see section 4.5). The reasons 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
- economic evidence is available to support recommendations that are likely to lead to substantial costs.

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 original 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 original 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).

Developing conceptual models linked to topic areas or review questions may help the health economist to decide what key information is needed for developing effectiveness and cost-effectiveness analyses (see chapter 2 for details). Models developed for public health and service delivery topics are likely to relate to several review questions, so most recommendations will be underpinned by some form of modelled analysis.

The choice of model structure is a key aspect of the design-oriented conceptual model. Brennan's

taxonomy of model structures (Brennan et al. 2006) should be considered for guidance on which types of models may be appropriate to the decision problem.

Even if a fully modelled analysis is not possible, there may be value in the process of model development, because this will help to structure committee discussions. For example, a model might be able to demonstrate how a change in service will affect demand for a downstream service or intervention.

For service delivery questions, the key challenge is linking changes in service to a health benefit. This obviously poses a challenge when conducting health economic analyses, but it will also be difficult finding high-quality evidence of effectiveness. Modelling using scenario analysis is usually needed to generate the health effects used within the health economic analyses. Because of the considerable resource and health impact of any recommendations on service delivery, its cost effectiveness must be considered, either analytically or qualitatively (see appendix A).

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.

The structure of any economic model should be discussed and agreed with the committee early in guideline development. The reasons for the structure of the model should be clear. Potential alternatives should be identified and considered for use in sensitivity analysis. If existing economic models are being used, or are informing a new analysis, the way these models are adapted or used should be clear.

For service delivery questions, any analysis will need to consider resource constraints. These might be monetary, but might also be resources such as staff, beds, equipment and so on. However, affordability should not be the sole consideration for service recommendations; the impact of any proposed changes on quality of care needs to be considered.

Before presenting final results to a committee for decision-making, all economic evaluations should undergo rigorous quality assessment and validation to assess inputs, identify logical, mathematical and computational errors, and review the plausibility of outputs. The HM Treasury's review of quality assurance of government models (2013) provides guidance on developing the environment and processes required to promote effective quality assurance. This process should be documented.

Quality assurance of an economic evaluation may take various forms at different stages in development, as detailed in the HM Treasury Aqua Book (2015). It can range from basic steps that should always occur, such as disciplined version control, extensive developer testing of their own model, and independent testing by a colleague with the necessary technical knowledge, to external testing by an independent third party and independent analytical audit of all data and methods used. For developer health economists testing their own evaluation, or those of others ('model busting'), useful and practical validation methods include:

- 1-way and *n*-way sensitivity analyses, including null values and extreme values (Krahn et al. 1997)
- ensuring that the model results can be explained, for example, the logic and reason underlying the effect of a particular scenario analysis on results
- ensuring that predictions of intermediate endpoints (for example, event rate counts) and final endpoints (for example, undiscounted life expectancy) are plausible, including comparison 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 et al. 1996 and Husereau et al. 2013) to ensure that reporting of methods and results is transparent. For time horizons that extend beyond 10 years, it may be useful to report discounted 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:

- endpoints 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 cost or outcome, with each strategy compared with the next non-dominated alternative in ranking. Comparisons with a common baseline intervention should not be used for decision-making, although should be included in the incremental analysis, if it reflects a relevant option.

Any comparison of interventions in an economic model that are not based on head-to-head trial comparisons should be carefully evaluated for the between-study heterogeneity, and potential for modifiers of treatment effect should explored. Limitations should be noted and clearly discussed in the guideline.

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 (see box 7.1 for examples). 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 effects are expressed as 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 can consider all the relevant health and non-health effects of an intervention across different sectors and reports them without aggregation. A cost–consequences analysis that includes most or all of the potential outcomes of an intervention will be more useful than an analysis that only reports 1 or 2 outcomes.

A cost–consequences analysis is useful when different outcomes cannot be incorporated into an index measure. 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 effects 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 effects 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 effects that can be quantified.

All effects (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 effects 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 effects of an intervention cannot often be considered equal to those of the status quo.

Cost–benefit analysis considers health and non-health effects 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 and 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 effects 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 effectiveness 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 measurement of changes in health-related quality of life should be reported directly from people using services (or their carers). 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, using a choice-based valuation method such as the time trade-off or standard gamble. The QALY is the measure of health effects preferred by NICE, and the EQ-5D is NICE's preferred instrument to measure health-related quality of life in adults.

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 the relevant clinical studies included in the clinical evidence review, EQ-5D data can be sourced 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, published mapped EQ-5D data should be used, or they may be estimated by mapping other health-related quality-of-life measures or health-related effects observed in the relevant studies to the EQ-5D if data are available. 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.

In some circumstances, EQ-5D data may not be the most appropriate or may not be available. Qualitative empirical evidence on the lack of content validity for the EQ-5D should be provided, demonstrating that key dimensions of health are missing. This should be supported by evidence that shows that EQ-5D performs poorly on tests of construct validity and responsiveness in a particular patient group. This evidence should be derived from a synthesis of peer-reviewed literature. In these circumstances, alternative health-related quality of life measures may be used and must be accompanied by a carefully detailed account of the methods used to generate the data, their validity, and how these methods affect the utility values.

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 to 12 years is available, but a validated UK valuation set is not yet available.

As outlined in NICE's guide to the methods of technology appraisal 2013 and an accompanying position statement on use of the EQ-5D-5L valuation set (2017), the EQ-5D 5-level (5L) valuation set is not currently recommended for use by NICE. Guideline developers should:

- Use the 3L valuation set for reference-case analyses, where available.
- If data are available to allow mapping of EQ-5D-5L data to 3L, use the mapping function developed by van Hout et al. (2012) when several mapping functions are available (Hernandez

- Alava et al. 2017), for consistency with the current guide to the methods of technology appraisal.

The QALY remains the most suitable measure for assessing the impact of services, because it can incorporate effects from extension to life and experience of care. It can also include the trade-offs of benefits and adverse events. However, if linking effects to a QALY gain is not possible, links to a clinically relevant or a related outcome should be considered. Outcomes should be optimised for the lowest resource use. The link (either direct or indirect) of any surrogate outcome, such as a process outcome (for example, bed days), to a clinical outcome needs to be justified. However, when QALYs are not used, issues such as trade-offs between different beneficial and harmful effects need to be considered.

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 and Social Care 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 measure for Older people) or ICECAP-A (Investigating Choice Experiments for the Preferences of Older People CAPability measure for Adults) instruments may be considered by NICE when developing methodology in the future. If an intervention is associated with both health- and non-health-related effects, it may be helpful to present these elements separately.

Economic analysis for interventions funded by the NHS and PSS with health outcomes

Economic analyses conducted for decisions about interventions with health outcomes funded by the NHS and PSS 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 funded by the public sector with health and non-health outcomes

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 effects 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. However, for the base-case analysis, a cost–utility analysis should be undertaken using a cost per QALY approach where possible.

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. However, for the base-case analysis, a cost–utility analysis should be undertaken using a cost per QALY approach where possible.

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 outcome, cost and utility data from the best available published sources.

The reference case across all perspectives (table 7.1) states that evidence on effects should be obtained from a systematic review. Some inputs, such as costs, may have standard sources that are appropriate, such as national list prices or a national audit, but for others appropriate data will need to be sourced.

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.

Although it is desirable to conduct systematic literature reviews for all such inputs, this is time-consuming and other pragmatic options for identifying inputs may be used. Informal searches should aim to satisfy the principle of 'saturation' (that is, to 'identify the breadth of information needs relevant to a model and sufficient information such that further efforts to identify more information would add nothing to the analysis' (Kaltenthaler et al. 2011). Studies identified in the review of evidence on effects should be scrutinised for other relevant data, and attention should be paid to the sources of parameters in analyses included in the systematic review of published economic evaluations. Alternatives could include asking committee members and other experts for suitable evidence or eliciting their opinions, for example, using formal consensus methods such as

the Delphi technique or the nominal-group technique. If a systematic review is not possible, transparent processes for identifying model inputs should be reported; the internal quality and external validity of each potential data source should be assessed and their selection justified. If more than 1 suitable source of evidence is found, consideration should be given to synthesis and/or exploration of alternative values in sensitivity analyses. Further guidance on searching and selecting evidence for key model inputs is available from Kaltenthaler et al. (2011) and Paisley (2016).

Data from registries and audits may be used to inform both estimates of effectiveness and any modelling, particularly for service delivery questions. To obtain such data, it may be necessary to negotiate access with the organisations and individuals that hold the data, or to ask them to provide a summary for inclusion in the guidance if published reports are insufficient. Any processes used for accessing data will need to be reported in the health economic plan and in the guideline. Given the difficulties that organisations may have in extracting audit data, such requests should be focused and targeted: for example, identifying a specific audit and requesting results from the previous 3 years.

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.

Some information on unit 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's reference costs (provider perspective). Information on resource impact costings can be found in NICE's methods guide on resource impact assessment. 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.

In cases where current costs are not available, costs from previous years should be adjusted to present value using inflation indices appropriate to the cost perspective, such as the hospital and community health services (HCHS) index and the PSS pay and prices index, available from the PSSRU report on unit costs of health and social care or the Office for National Statistics (ONS)

consumer price index.

Wherever possible, costs relevant to the UK healthcare system should be used. However, in cases where only costs from other countries are available these should be converted to Pounds Sterling using an exchange rate from an appropriate and current source (such as HM Revenue and Customs or Organisation for Economic Co-operation and Development).

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 and Social Care, the analyses should include the costs associated with the scheme. If the price is not listed on eMIT, then the current price listed on the British National Formulary (BNF) should be used. For medicines that are predominantly dispensed in the community, 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.

Preference-based 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. When searching bibliographic databases for health-state utility values, specific techniques outlined in Ara (2017) and Golder et al. (2005) and Papaioannou et al. (2010) may be useful, and specific search filters have been developed that may increase sensitivity (Arber et al. 2017). The provision of quality-of-life data should be guided by the health economist at an early stage during guideline development so that the information specialist can adopt an appropriate strategy. Resources for identifying useful utility data for economic modelling are the dedicated registries of health-state

utility values such as ScHARRHUD and Tufts CEA Registry and the technical support documents 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 effects 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 health 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 type of parameter and the method of its estimation. 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 unsuitable, 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. NICE considers that it is usually appropriate to discount costs and health effects at the same annual rate of 3.5%.

Sensitivity analyses using 1.5% as an alternative rate for both costs and health effects may be presented alongside the reference-case analysis, particularly for public health guidance. 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.

Local considerations

For service delivery questions, cost-effectiveness analyses may need to account for local factors, such as the expected number of procedures and the availability of staff and equipment at different

times of the day, week and year. Service delivery models may need to incorporate the fact that each local provider may be starting from a different baseline of identified factors (for example, the number of consultants available at weekends). It is therefore important that these factors are identified and considered by the committee. Where possible, results obtained from the analysis should include both the national average and identified local scenarios to ensure that service delivery recommendations are robust to local variation.

Service failures

Service designs under consideration might result in occasional service failure – that is, where the service does not operate as planned. For example, a service for treating myocardial infarction may have fewer places where people can be treated at weekends compared with weekdays as a result of reduced staffing. Therefore more people will need to travel by ambulance and the journey time will also be longer. Given the limited number of ambulances, a small proportion may be delayed, resulting in consequences in terms of costs and QALYs. Such possible service failures should be taken into account in effectiveness and economic modelling. This effectively means that analyses should incorporate the 'side effects' of service designs.

Service demand

Introducing a new service or increasing capacity will often result in an increase in demand. This could mean that a service does not achieve the predicted effectiveness because there is more demand than was planned for. This should be addressed either in the analysis or in considerations.

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 effects

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.'

When assessing the cost-effectiveness of competing courses of action, the committee should not give particular priority to any intervention or approach that is currently offered. In any situation where 'current practice', compared with an alternative approach, generates an ICER above a level that would normally be considered cost effective, the case for continuing to invest in it should be carefully considered, based on similar levels of evidence and considerations that would apply to an investment decision. The committee should be mindful of whether the intervention is consuming more resource than its value is contributing based on NICE's cost per QALY threshold.

Equity considerations

In the reference case, an additional QALY should receive the same weight regardless of any other characteristics of the people receiving the health benefit.

The estimation of QALYs, as defined in the reference case, implies a particular position regarding

the comparison of health gained between individuals. Therefore, in the reference case, an additional QALY is of equal value regardless of other characteristics of the individuals, such as their socio-demographic characteristics, their age, or their level of health. The guideline committee has discretion to consider a different equity position, and may do so in certain circumstances and when instructed by the NICE Board (see below).

End of life considerations

In the reference case, the committee will regard all QALYs as being of equal weight. However, the committee can accept analysis that explores a QALY weighting that is different from that of the reference case when an intervention concerns a 'life-extending treatment at the end of life'.

For a 'life-extending treatment at the end of life', all of the following criteria must be met:

- the treatment is indicated for patients with a short life expectancy, normally less than 24 months **and**
- there is enough evidence to indicate that the treatment has the prospect of offering an extension to life, normally of a mean value of at least an additional 3 months, compared with current NHS treatment.

In addition, the committee will need to be satisfied that:

- the estimates of the extension to life are sufficiently robust and can be shown or reasonably inferred from either progression-free survival or overall survival (taking account of trials in which crossover has occurred and has been accounted for in the effectiveness review) **and**
- the assumptions used in the reference case economic modelling are plausible, objective and robust.

When the conditions described above are met, the committee should consider:

- the impact of giving greater weight to QALYs achieved in the later stages of terminal diseases, using the assumption that the extended survival period is experienced at the full quality of life anticipated for a healthy person of the same age **and**
- the magnitude of the additional weight that would need to be assigned to the QALY benefits in this patient group for the cost effectiveness of the technology to fall within the normal range of maximum acceptable ICERs, with a maximum weight of 1.7.

Non-health effects

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 all the health and relevant non-health effects 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 monetarised health effects and all relevant non-health effects.

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 effects. The way that the sets of consequences have been implicitly weighted

should be recorded as openly, transparently and 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, although attention needs to be given to any weightings used, particularly with reference to the NICE reference case and NICE's principles on social value judgements.

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 one intervention is more effective but also more costly than another, then the ICER should be considered. If one 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 (see the section on cost–utility analysis). 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 effects 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 effects 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, which should be presented in the guideline. 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

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8 Linking to other guidance

This chapter describes how guidelines link to other NICE guidance in the topic area and to guidance from other developers.

Related NICE guidelines and guidance on health technologies should be identified during scoping of a guideline (see chapter 2), or when checking if a guideline needs updating (see chapter 13). This includes identifying any related guidance or guidelines in development, as well as those that are published.

When a guideline topic covers guidance on health technologies that is published or in development, NICE staff with a quality assurance role work closely with NICE staff from the health technologies team to agree the approach to take.

8.1 Related NICE technology appraisal guidance

A guideline committee cannot usually publish its own recommendations on health technologies covered by published or in development health technologies guidance. In rare cases, technology appraisal guidance will be updated in the guideline (see below).

Technology appraisal being developed or updated alongside the guideline

When a technology appraisal is developed at the same time as a related NICE guideline, development should ideally be coordinated so that the appraisal recommendations are published in time for a link to be included in the consultation draft of the guideline. This is not always possible (for example, if the technology has not yet received a marketing authorisation). In this case, the guideline consultation draft should link to the appraisal consultation document or final appraisal determination. If guideline committee members wish to comment on the appraisal, they do this through the developer (see the technology appraisal process guide).

The guideline committee chair and the developer may attend relevant appraisal committee meetings as advisers, but do not take part in the formal decision-making.

Updating technology appraisal guidance in a guideline

If there is evidence that a technology appraisal needs updating, the NICE technology appraisals team follow the process in the technology appraisal process guide.

In rare cases, a technology appraisal is updated as part of guideline development, if the criteria in

the policy on updating technology appraisals in clinical guidelines are met.

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 useful. If so, they 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 assesses cost effectiveness (performs an economic analysis) 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 modifying or building on the architecture of an existing economic analysis from the technology appraisal. If so, this should be discussed with a member of NICE staff with responsibility for quality assurance during development of the economic plan.

New medicines

A first assessment of a new medicine or a significant new indication for an existing medicine is usually carried out as a technology appraisal. However, in exceptional circumstances a first assessment can be carried out using the guideline development process, as long as this has been agreed by both the Department of Health and Social Care and the company.

New technology appraisal referral during development of the guideline

When a new related technology appraisal is referred after the guideline has started development, and will be developed alongside the guideline, NICE's technology appraisals team informs the developer and NICE staff with responsibility for guideline quality assurance.

Referring to technology appraisals in recommendations

When related technology appraisal guidance is identified, the usual approach is for the guideline to make a recommendation to follow the technology appraisal recommendations with a link to where these appear in the NICE Pathway (everything NICE has said on the topic). If needed, a brief explanation can be included in the guideline recommendation, for example, if it covers the sequencing of treatments recommended in technology appraisals. Any explanation needs to be agreed with the technology appraisals team at NICE.

In rare cases, technology appraisal recommendations may be included in the guideline, for example, if this is essential for readability or there is a need to highlight specific recommendations.

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 methods described in this manual. 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.

8.2 Related NICE guidelines

Related published or in development NICE guidelines should be identified by the developer at the scoping stage, or by the NICE surveillance team when checking if a guideline needs updating (see chapter 13). 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 link 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 link to recommendations in a published guideline, this will be specified in the scope.

Similar review question covered in another guideline

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 link to the recommendations in the published guideline or to draft new recommendations, based on the evidence review for the published guideline.

In these cases, the committee should discuss and document whether:

- the review question in the guideline in development is similar enough to the question addressed in the published guideline
- the evidence base underpinning any recommendations is unlikely 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.

If the committee agree that the evidence review is relevant for the guideline in development, they consider the recommendations based on the evidence review.

There are 3 options in these circumstances and these are described below.

Link to the recommendations in the other guideline

If the committee are happy to accept the intent and exact wording of the recommendations, and understand that any future changes (for example, as part of an update) would also apply to their guideline, then the guideline will link to the recommendations in the published guideline. If needed, a recommendation can be added to the guideline explaining anything users will need to take into account when applying the recommendations from the published guideline (for example, if some parts of a recommendation do not apply to the population or setting covered by the new guideline). The committee's discussion and decision should be documented clearly in the guideline. This should include areas of agreement and difference with the committee for the published guideline (for example, in terms of key considerations – balance of benefits and harms or costs, and interpretation of the evidence).

Linking to other guidelines is preferred to copying recommendations into the guideline in development. In rare cases, recommendations may be copied into the guideline, for example, if this is essential for readability or there is a need to highlight specific recommendations.

Use the evidence review to make new recommendations

If the committee considers that the intent and wording of the published recommendations are not appropriate for their guideline, or they are not prepared to agree that any updates to recommendations would also apply to their guideline, they may make new recommendations based on the existing evidence review. When evidence reviews from another guideline are used to develop new recommendations, the decision should be made clear in the methods section of the guideline, and their independent interpretation and discussion of the evidence should be documented in the discussion section. The evidence reviews from the published guideline (including review protocol, search strategy, evidence tables and full evidence profiles [if available]) should be included in the guideline. They then become part of the whole evidence base for the guideline, and are updated as needed in future updates of the guideline.

Request a new evidence review

If the review question is not considered similar enough or the evidence review is not considered appropriate, the committee may request that a new evidence 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 agreed by NICE staff with responsibility for quality assurance, and documented in the methods section and the discussion section for the review question.

8.3 Related interventional procedures guidance

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

Any related published IP guidance should be identified during the scoping of a guideline or by the surveillance review. The approach depends on whether the recommendation in the IP guidance is for 'standard' (previously known as '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 'standard' arrangements.

If IP guidance on a procedure relevant to a guideline starts development during development of the guideline, the IP programme will send the finalised scope(s) for the procedure(s) to NICE staff with responsibility for quality assurance of the guideline.

IP guidance with recommendations for 'standard' arrangements

Review question is not justified

If the scoping group for a guideline decides that IP guidance for which 'standard' arrangements (previously known as normal arrangements) are recommended is relevant to the guideline but does not justify a review question, the guideline simply links to the IP guidance in the NICE Pathway. 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 is justified

If the scoping group for a new guideline considers that IP guidance with 'standard' arrangements is likely to justify a review question, this is highlighted in the scope for the guideline. For example, comparisons of clinical and cost effectiveness could be included if there is IP guidance covering several procedures for the same condition. The IP team is contacted by NICE staff with responsibility for guideline quality assurance during scoping to seek their input on the proposed approach.

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).

If a guideline is being updated and the surveillance review identifies that IP guidance with 'standard' arrangements is likely to justify a review question in the updated guideline, this is highlighted in the surveillance report.

When a review question in a guideline relates to IP guidance, the IP guidance remains active unless the IP team and NICE staff with responsibility for guideline quality assurance have identified reasons why not. 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 the recommendations 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 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 link to the IP guidance in the NICE Pathway, and the NICE webpage for the IP guidance will include a link to the guideline.

Other approaches

If NICE staff with responsibility for guideline quality assurance and the IP team agree that a different approach is needed, they present a paper to NICE's Guidance Executive. Decisions to take other approaches are made on a case-by-case basis. Examples include:

- Appraisal of the evidence indicates that a procedure with IP guidance is not effective, and the guideline recommends that it should not be used.
- There is considerable uncertainty about the clinical or cost effectiveness of a procedure.
- The guideline committee makes a 'research only' recommendation for a procedure with published IP recommendations for 'standard' arrangements.

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 area of a review question, the IP team is notified for potential review of the IP guidance. If the guidance is reviewed and the procedure's status is changed to 'standard' arrangements, the developer considers the procedure's effectiveness and cost effectiveness. If the procedure retains its 'special' arrangements status, the guideline should link to the IP guidance in the NICE Pathway.

IP guidance 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. 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, the IP team informs the developer and NICE staff with responsibility for guideline quality assurance that the notified procedure is relevant to the guideline. The guideline can link to the IP guidance when it is published.

8.4 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 appraisal of the guideline development process because this has already been assessed by NICE. However, the evidence reviews in the guideline will still need to be critically appraised (using checklists in appendix H) to ensure that the quality of the evidence is appropriate for deriving NICE recommendations.

Published guidelines produced by organisations not accredited by NICE are assessed for quality using the AGREE II instrument or the AGREE global rating scale 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, and a summary of the assessment included in the evidence review. 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 as being of high quality using the appropriate methodology checklist (see appendix H)
- accompanied by a GRADE table, GRADE-CERQual table or evidence statement and evidence table(s)
- 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 another organisation should not be quoted or linked to, unless the organisation's process has been accredited by NICE and the evidence reviews have been critically appraised to verify quality.

8.5 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 Writing the guideline

During development of the guideline, the developer and committee will write:

- the recommendations
- recommendations for research
- the rationale for the recommendations, and their likely impact on practice
- the context for the guideline – such as the need for the guideline, or the reason for updating an existing guideline
- summaries of evidence supporting shared decision-making, if there are preference-sensitive decision points in the guideline
- information about changes to published recommendations (if the guideline is an update)
- structured summaries of the committee's discussions
- summaries of the evidence – with details of analysis and any modelling
- the methods used for guideline development – highlighting the reasons for options taken, and any deviations from the methods and processes described in this manual.

For publication, the recommendations, recommendations for research, rationale for the recommendations and likely impact, context, and any summaries of evidence supporting shared decision-making are presented in a 'web version'. The committee's discussion and evidence are presented as PDFs in separate evidence reviews, along with the methods used during guideline development. Exactly how we organise and present the information is likely to change in future.

9.1 Interpreting the evidence to make recommendations

Assessment and interpretation of the evidence to inform guideline recommendations is at the heart of the work of the committee. 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, and the committee's discussions and debate (see chapter 3). Sometimes recommendations are made because of a legal duty or the consequences of not following a course of action are extremely serious. If there is a legal duty, the recommendation should refer to supporting documents and should build on the law or statutory guidance rather than simply repeating it.

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 strength and quality of the evidence is assessed for both internal and external validity, but also requires interpretation. Evidence also needs to be assessed in light of any conceptual framework.

As soon as the committee has discussed the evidence, they should start drafting recommendations. They should decide what action to recommend and keep in mind which sectors (including which practitioners or commissioners within those sectors) should act on the recommendations. The record of the committee's discussion should explain clearly how they moved from the evidence to each recommendation, and document how any issues influenced their decision-making. In line with the GRADE principles on 'evidence to decisions', summaries of the discussions 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 (see Alonso-Coello et al. 2016, Schünemann 2016).

Findings from several evidence reviews may be integrated into a single summary of the committee's discussions if they relate to the same recommendation or group of recommendations.

For each group of recommendations, the committee should briefly explain their rationale for making the recommendations and record their views on any likely impact of the recommendations on practice or services.

Quality of the evidence

The committee is presented with GRADE tables, GRADE-CERQual tables or (if GRADE or GRADE-CERQual is not used) evidence statements. These 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 reviews are a fair summary of the evidence and should discuss any uncertainty, including the presence, likely magnitude and direction of potential biases.

GRADE tables, GRADE-CERQual tables or the summary of the committee's discussion should include the committee's view of the directness (or applicability) of the evidence to people affected by the guideline and the setting.

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 controlled experimental conditions), effectiveness (the extent to which a specific intervention, when used under 'real world' circumstances, does what it is intended to do) or both. Often the distinction between the 2 is not 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 details of the committee's discussion of the relative position of interventions within a pathway of care or service model.

The committee should also assess whether, when recommending an intervention, they are able to recommend stopping other interventions because they have been superseded by the new one.

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 at the same time as 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. 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 the committee's discussion of the relative position of an intervention in a care pathway or service model, based on cost effectiveness.

Use of indirect evidence

Sometimes when there is no evidence directly relevant to a specific population or setting, indirect

evidence from other populations or settings may be considered. 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 indirect evidence must be considered carefully by the committee, with explicit consideration of the features of the condition or interventions that allow extrapolation to a different context or population. This also applies when extrapolating findings from evidence in different care settings (for example, between primary and secondary care). The committee should consider and document any similarities in case mix, staffing, facilities and processes, and any limitations.

Availability of evidence to support implementation (including evidence from practice)

The committee should also judge to what extent it will be feasible to put the recommendations into practice. They can use expert oral or written testimony, the experience of committee members or results from other approaches (see chapter 10 and appendix B) if these have been used. They may also be able to draw on qualitative studies or other forms of evidence relating to organisational and political processes where appropriate.

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 resources to 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 endpoints.

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 inductive or deductive reasoning:

- inductive because it involves using what is known (the evidence) while accepting that there is uncertainty about what is reasonably expected to happen as a consequence of implementing a recommendation
- deductive when it is drawn from theory or methodological principles that are generally held to be true so that any logical conclusion will be true.

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 judgements they make. The committee may also draw on 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 frameworks or logic models that have been used to inform the guideline because these may help to identify any practical issues involved with a recommendation that will change practice.

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), and how the recommendations address areas highlighted in the equality impact assessment. 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)
- any groups of people might find it impossible or unreasonably difficult to receive or access 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 efficacy or effectiveness for an intervention is either lacking or too low quality for firm conclusions to be reached, the committee has several options. It may:

- make a 'consider' recommendation based on the limited evidence (see section 9.2)
- decide not to make a recommendation, and make a recommendation for research (see section 9.4)
- recommend that the intervention is used only in the context of research
- recommend not to offer the intervention.

Factors the committee should consider before making a 'do not offer' recommendation include:

- The intervention should have no reasonable prospect of providing cost-effective benefits to people using services.
- Stopping the intervention is not likely to cause harm for people currently receiving it.

Factors the committee should consider before issuing 'only in research' recommendations include:

- The necessary research can realistically be set up or is already planned, or people using services are already being recruited for a study.
- The intervention should have a reasonable prospect of providing cost-effective benefits to people using services.
- There is a real prospect that the research will inform future NICE guidelines.

The principles for wording recommendations described in section 9.2 should be used, reflecting the strength of the evidence. The committee's discussion and the rationale should be documented fully.

Strength of recommendations

The concept of the 'strength' of a recommendation (Guyatt 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. Similarly, if the committee believes that the vast majority of practitioners or commissioners and people using services would not choose a particular intervention if they considered the evidence in the same way as the committee, a negative recommendation can be made (that is, 'Do not offer'). This is generally the case if the harms clearly outweigh the benefits for most people, or the intervention is not 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, or people have different preferences and values. In these circumstances, the recommendation is generally weaker, although it may be possible to make stronger recommendations for specific groups of people. The committee should also discuss making negative recommendations in such situations if they believe most people are particularly likely to experience no benefit or experience harm, but that there may be a benefit for some. Be as specific as possible about the circumstances (for example, 'Do not offer…, unless…') or population.

NICE reflects the strength of the recommendation in the wording (see section 9.2). NICE uses 'offer' (or words such as 'measure', 'advise', 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.

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. This is because that course of action has been judged to be an inefficient use of limited resources, with the population as a whole gaining fewer benefits than from alternative (cost-effective) courses of action. In some cases though, considerations about equity may also affect the decision whether to recommend the intervention (see section 7.6).

The committee's view of the strength of a recommendation should be clear from its discussions, and reported in the guideline.

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 structured 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: people using services and the wider public should be informed of their options and be involved in decisions about their care.

There are 3 NICE guidelines specifically on the experience of people using services: patient experience in adult NHS services, service user experience in adult mental health and people's experience in adult social care services. These include general recommendations on the principles of person-centred care, such as communication and providing information, which should not be restated in topic-specific guidelines.

However, recommendations on person-centred care can be included in topic-specific guidelines if there is evidence of specific need for the topic.

9.2 Wording the recommendations

This section gives the principles of writing recommendations. For more on NICE style, see the style guide and writing for NICE.

Focus on the action and what readers need to know

Recommendations should be clear about what needs to be done, without the reader having to read the committee's discussion of the evidence. When writing recommendations, keep in mind a reader asking, 'What does this mean for me?'

Include only one action per recommendation or bullet point, and use direct instructions wherever possible because these are easier to follow. Recommendations often start with a verb such as 'offer' (or 'do not'), 'consider', 'measure', 'advise', 'discuss', 'ask about'.

Exceptions to this principle include:

- Recommendations that specify who should take action, or cover service organisation. For example, 'A multidisciplinary team should provide care'.
- Recommendations that use 'must' or 'must not' (because of a legal duty or a very serious consequence of not following the recommendation).
- Recommendations to take different actions in different circumstances or for different populations. For example, it is often clearer to start with details of the population covered by

- the recommendation.

Think carefully about how much detail to include. Recommendations should be specific about interventions. But this needs to be balanced against the need to be clear and concise. Including a lot of detail can reduce the impact and make it harder for users to identify the most important actions.

Generally, avoid making recommendations about basic good practice unless there is evidence of poor practice or variation in practice.

Be clear about who should be offered an intervention, but don't spell this out in every recommendation if it is obvious from the context. Similarly, readers need to know which sections of the guideline they need to act on. Clear subheadings can help here, for example, by spelling out the setting where the recommendations apply (for example, 'first treatment', 'in primary care' or 'in care homes').

The content and measurability of any related NICE quality standard will be affected by the clarity and precision of recommendation wording. If possible, be clear when interventions should take place, and include the reasoning in the rationale and discussion sections.

Reflect the strength of the recommendation

The 'strength' of a recommendation (see section 9.1) should be reflected in the consistent wording of recommendations within and across guidelines.

In recommendations on activities or interventions that should (or should not) be offered, use directive language such as 'offer' (or 'do not offer'), 'advise', or 'ask about'. In keeping with the principles of shared decision-making, people may choose whether or not to accept what they are offered or advised.

If there is a closer balance between benefits and harms (activities or interventions that could be used), use 'consider'.

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.

Box 9.1 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 offered

- Offer a trial of supervised pelvic floor muscle training of at least 3 months' duration as a first 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.
- Do not offer lamotrigine to treat mania.
- Do not offer tigecycline to treat diabetic foot infections, unless other antibiotics are unsuitable.

Recommendations for activities or interventions that could be offered

- Consider pelvic MRI to assess the extent of deep endometriosis involving the bowel, bladder or ureter.
- Consider referring people to other behavioural support services within the local health and care network (for example, to voluntary or community services) for interventions that are not available in the pharmacy.

Use 'person-centred', precise, concise, clear English

Person-centred language

Use language that is person centred, and acknowledges the experience of people who are directly affected by the recommendations (and family members, carers or advocates), and their role in decision-making. Generally use verbs such as 'offer' and 'discuss' in recommendations, rather than

'prescribe' or 'give'. Use 'people' or 'people with [condition]' (or 'people using services', or 'patients') rather than 'individuals', 'service users', 'cases' or 'subjects'.

Clarity and consistency

Using clear, consistent wording is an important part of NICE's 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. More information is available in the NICE style guide and our guide to writing recommendations.

Use bullet lists and tables if they help to make recommendations easier to follow. Make sure there is a clear link back to the evidence and the committee's discussion for all information in a table.

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

Do not give dosages routinely

Readers are expected to refer to a medicine's summary of product characteristics (SPC) for details of dosages for licensed indications. 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. Information about dosage can be found in the BNF or BNF for Children as well as the SPC. SPCs can be found in the Electronic Medicines Compendium.

Dosage information for off-label use of a licensed medicine will usually not be included in the SPC (see below). If off-label use is being recommended, check whether there is any relevant dosage information in the BNF or BNF for Children for the particular population or indication it is being recommended for. If there is none, NICE staff with responsibility for guideline quality assurance will liaise with the BNF.

Off-label use of licensed medicines

Using a UK licensed medicine outside the terms of its marketing authorisation is classed as off-label use.

Recommendations are usually about the uses of medicines for which the regulatory authority has granted a marketing authorisation, either in the UK or under the European centralised authorisation procedure (often referred to as the licensed indications). 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. For example, 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 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.

The guideline developer and committee should check recommended uses of a medicine against the licensed indications listed in the SPC. If the medicine does not have a UK marketing authorisation for the use being recommended (off-label use), add the following standard footnote to the recommendation:

At the time of publication ([month year]), [name of drug or drug class] 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.

Recommendations on medical devices, including off-label use

Using a CE-marked device outside its instructions for use is classed as off-label use.

Recommendations are usually about the use of devices within the terms of the instructions for their use. However, there are clinical situations in which the off-label use of a device may be judged by the prescriber and patient to be in the best interests of the patient. For example, off-label use may be recommended when using a device outside the time period specified in the instructions for use.

The Medicines and Healthcare products Regulatory Agency (MHRA) has issued guidance on the off-label use of medical devices. The guideline developer and committee should check the instructions for use of a device and if the device is being recommended for off-label use, include

this information in this standard footnote to the recommendation:

At the time of publication (Month year), not all devices with a CE mark for [intended purpose] are intended by the manufacturer for use as recommended here. The healthcare professional should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. MHRA's advice remains to use CE-marked devices for their intended purpose where possible. See guidance on off-label use of a medical device for more information.

9.3 Supporting shared decision-making

Identify preference-sensitive decision points

Guidelines should include information to support shared decision-making between people and their health or social care practitioners (see NICE's recommendations on supporting people to make decisions about their care in patient experience in adult NHS services, service user experience in adult mental health and people's experience in adult social care services). The committee should identify any recommendations where someone's values and preferences are likely to be particularly important in their decision about the best course of action for them.

When identifying these recommendations committees should take account of people's autonomy and right to make individual decisions, in line with NICE's social value judgements. They should, however, ensure that their recommendations represent an effective use of health and social care resources and so would not disadvantage other people using the services (see section 4.3 of NICE's social value judgements).

These 'preference-sensitive decision points' occur when the committee recommends 2 or more options for investigation, treatment or care that deliver similar outcomes but:

- they have different types of harms and benefits which people may value differently **or**
- the likelihood of the harms or benefits may differ **or**
- the practicalities of the options are different (for example, the choice is between medicine and surgery, or the requirements for monitoring differ) **or**
- some people may consider the overall risks of harms for any of the options outweigh the overall benefits compared with no treatment.

Alternatively, a preference-sensitive decision point may occur if the choice between an

investigation, treatment or care option and 'no treatment' is finely balanced.

When to identify preference-sensitive decision points

In some cases, preference-sensitive decision points might be apparent at the scoping stage of a guideline. In other cases, the committee will identify them when reviewing the evidence. This is the same evidence used to make the recommendations, and no additional evidence searches or syntheses are needed.

For updates, the committee only needs to identify decision points in the areas of the guideline being updated.

Summarise information to support decisions

When a preference-sensitive decision point is identified, the committee should create a summary of the evidence that will appear in the guideline. This is to make it easy for professionals and practitioners to compare the options and discuss them with the person.

This summary should set out information about the options clearly and simply. It should usually include the option of no treatment or investigation. This could include brief information, for each option, about:

- **efficacy or effectiveness**: how well something is likely to work for particular outcomes or circumstances and for particular subgroups of people
- **safety**: the risk of short- or long-term harms, and any contraindications
- **practical factors relevant to people using services**: people's experience of treatment or care – for example, ease of use (route of administration for medicines), monitoring requirements, side effects, or impact on quality of life
- **quality and certainty of the evidence**: an overall judgement about the quality of the underlying evidence for each option.

In some cases, NICE will develop additional decision aids (see chapter 12).

9.4 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 recommendations for research.

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. The committee should select up to 5 key recommendations for research that are likely to inform future decision-making (based on a systematic assessment of gaps in the current evidence base). Methods such as value of information analyses can be useful in this process. They can also make other recommendations for research. These will be listed in the guideline after the key recommendations for research but will be of lower priority. 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 NICE 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 as similar as possible to the NICE Pathway. They should also consider the links with existing pathways to help integrate the new topic into NICE Pathways.

9.6 References and further reading

Alonso-Coello P, Oxman AD, Moberg J et al. for the GRADE working group (2016) GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 2: Clinical practice guidelines. BMJ 353: i2089

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

Guyatt GH, Oxman AD, Vist GE et al. for the GRADE working group (2008) GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 336: 924 (see also the GRADE website)

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-based medicine and health technology assessment. Social Theory and Health 10:1–19

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Scottish Intercollegiate Guidelines Network (2015) 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

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 are notified of the consultation dates in advance via the guideline page on the NICE website, and are reminded by email. (See register as a stakeholder for more information.)

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 (recommendations, rationales, committee discussions, evidence reviews and methods) is posted on the NICE website for consultation with registered stakeholders. Stakeholders can register at any point during guideline development. NICE informs registered stakeholders that the draft is available, via email and through its promotional channels, 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 the potential equality impact. NICE also asks stakeholders to comment on recommendations identified as likely to substantially increase costs, and their justification, and to consider whether any other draft recommendations are expected to add substantial costs. Questions related to implementation may also be included to identify practitioners who are already implementing the draft recommendations, or resources that could be fed into the NICE endorsement scheme.

Consultation usually lasts for 6 weeks. A 4-week consultation may be used for partial updates of guidelines 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 deadline.

Comments should be constructed as reasoned argument and be submitted for the purpose of improving the draft guideline. NICE reserves the right not to respond to comments that are hostile or inappropriate.

Stakeholders should make sure that any confidential information or information that the owner would not wish to be made public is clearly underlined and highlighted. 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. Tobacco companies and those who speak for them or are funded by them (collectively referred to as 'tobacco organisations') cannot register as stakeholders. This is in line with NICE's obligation under Article 5.3 of the WHO Framework Convention on Tobacco Control (FCTC) to protect public health policies from the commercial and other vested interests of the tobacco industry. Tobacco organisations are simply referred to as 'respondents' and any comments received during consultation are reviewed for factual inaccuracy claims and are made public along with any responses.

Approaches to additional consultation

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.

For example, it may be important to explore 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.

It may also be important to test draft recommendations directly with people using services, and where appropriate their families or carers.

Sometimes additional consultation will be considered because there is a lack of evidence on the views and experiences of people affected by the guideline, or NICE's standard processes need to be adapted or supplemented to incorporate user perspectives. Examples of where this could occur include guidelines covering children and young people, or people with a learning disability or cognitive impairment (see section 3.2 and appendix B for more information).

The main criteria for considering additional consultation are:

- the topic covers novel or sensitive areas **or**
- the evidence, such as evidence on users' views is 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 reasons for the additional 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 reasons and methods should be documented in the guideline.

Additional consultation usually happens at the same time as draft guideline consultation, but can be undertaken earlier (for example, to seek views and experiences of people affected by the guideline when there is a lack of evidence, or to validate selected draft recommendations with people using services, policy makers, commissioners, practitioners and professionals before guideline consultation). Occasionally additional consultation may be needed at more than one stage of

guideline development.

The results of all consultations are considered by the committee. The committee uses this information to refine and prioritise the recommendations after consultation. This includes making them more specific or targeting them at different groups of practitioners, where appropriate.

Further details on approaches to additional consultation are given 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 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, and comments and responses, in confidence 2 weeks before publication (see chapter 11). Comments and responses are made available on the NICE website when the final guideline is published.

NICE reserves the right to summarise and edit comments received during consultations, or not to publish them at all, if we consider the comments are too long, or publication would be unlawful or otherwise inappropriate.

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. Comments received from 'respondents' are reviewed for factual inaccuracy claims and are made public along with any responses.

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 changes agreed by the committee 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 stakeholders' comments. Further changes to the guideline may be needed; the developer continues to maintain an audit trail of all the changes. The NICE Pathway (everything NICE says on a topic in an interactive flowchart) 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
- will lead to a resource impact when implemented.

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 usually 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, the evidence reviews and a copy of the responses to stakeholder consultation comments 2 weeks before publication. This information is confidential until the guideline is published. This step 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, including evidence reviews, methods, NICE Pathway, key messages for the public and most 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 media relations team and, if implementation support projects are planned, the implementation lead 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 and its support tools will be promoted.

Members from the NICE media relations team 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, 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

The media relations team may set up interviews or filming with committee members ahead of the guideline launch or on the day itself. 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 may be 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, and should not answer them without involvement of the media relations team.

A guideline launch is usually accompanied by activity on social media which may include graphics, animations, videos and quotes from key committee members or NICE directors. In most cases, this work will be prepared ahead of the launch.

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. Developers should inform committee members that in such cases, the NICE's media relations team should be notified at the earliest possible opportunity. Any materials developed from guideline content by committee members should be submitted to NICE staff with a quality assurance role. Committee members who wish to publish their materials for a UK audience only may do so under the NICE UK Open Content Licence. This is a self-assessment exercise and no fee is involved. The

international use of NICE content is subject to a formal licensing agreement, but without a fee for those who have contributed to the development of NICE guidance. Please see Reusing our content.

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.

12 Resources to support putting the guideline into practice

12.1 Introduction

Guideline committees consider implementation issues as an integral part of developing a guideline, and take account of comments on the draft guideline. NICE teams work with committees to consider what can be done to address implementation challenges, for example, by producing tools to help people put the guideline into practice, in line with our implementation strategy.

12.2 Tools for planning and resource impact assessment

NICE 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 report and an associated resource impact template are produced for guidelines that will have a substantial resource impact. The template enables a local estimate to be made of the potential costs and savings involved in implementation. If the resource impact is deemed not to be substantial, a 1-page resource impact statement is produced.

12.3 Tools to support decision-making by practitioners and people using services

Visual summaries and quick guides

For some guidelines, there is a need for a visual summary of part of the guideline for health or care practitioners. For example, where practice needs to change, a practitioner needs to make quick decisions, or a specific audience needs support in implementing the recommendations.

Discussions about any visual summary or quick guide should happen as soon as possible. If NICE and the developer agree that a tool of this type will be helpful, the NICE editor will work with the developer to develop it for publication alongside the guideline.

For some topics, a quick guide is produced to help practitioners with putting recommendations into practice (for example, in a care home), or to support people using services to understand what to

expect, and make decisions about their care.

Decision aids

If the committee identifies a preference-sensitive decision point in the guideline (see section 9.3), NICE may develop a decision aid.

Decision aids supplement or support the discussion between the person and their health or care practitioner about a preference-sensitive decision point, rather than replacing it. The person facing the decision can also refer to the aid after their appointment, and discuss it with their family and carers if they wish. NICE decision aids are written in non-technical language and include information about:

- the treatment or care options recommended in NICE guidance
- the aims of treatment or care and how likely the person is to benefit
- possible adverse effects from the treatment or care options and the likelihood of experiencing them
- other issues likely to be important to the person facing the decision (such as additional monitoring requirements and duration of treatment).

Decision aids usually include a visual representation of the likelihood of benefits or harms. They may also include a table to support the person to think about the relative importance to them of different factors in their decision.

If the committee identifies an area where there is a particular need for support with decision-making, the developer should alert NICE staff with responsibility for quality assurance during guideline development. NICE will decide whether to produce a decision aid. This is based on factors such as:

- the value of a visual representation of the chance of benefits or harms
- the complexity of the issues or the number of options the person is choosing between
- whether or not the decision is 'high stakes' with possible life-changing consequences
- whether or not the risks and benefits between options are similar, so that preferences will be the determining factor.

Each decision aid is developed by a project group with expertise in the topic area, including practitioners and people who use health and care services.

12.4 Working with other organisations and endorsing resources

Organisations and individuals, both lay and practitioner, can play a key role in supporting the implementation of the guideline and NICE may work with external partners to help with this.

Implementation resources which have been jointly developed by NICE in collaboration with key national partner organisations, can be co-badged and carry the NICE logo, providing they are approved by a director and the placement of the logo is approved by the communications team.

Organisations other than NICE may produce resources for guideline implementation. These could include implementation and adoption resources, learning modules/educational packages and patient decision aids. These resources can be endorsed by NICE. A guideline should usually only link to externally developed tools and resources when the tools and resources have been endorsed by the NICE endorsement programme. Endorsement confirms that the resources accurately reflect the content of the NICE guideline and can be updated as needed. Endorsed resources do not carry the NICE logo. If developers identify a relevant tool during development of a guideline, they should contact the endorsement team.

NICE also publishes shared learning case studies, which show how organisations have put our recommendations into practice. If developers hear about any examples of good practice, they should contact the shared learning team.

If a guideline is expected to have a significant resource impact or be challenging to implement, the Guideline Resource and Implementation Panel reviews it, and advises on affordability and workforce issues. The panel works with NICE to produce a statement to support implementation; the statement is published alongside the guideline. The panel includes representatives from NICE, NHS England, NHS Improvement and Health Education England, along with topic experts and other national organisations if needed.

12.5 Other NICE implementation support

The following services and resources help to put all NICE guidance and standards into practice:

- The implementation support team at NICE works with national partners to support implementation.

- Members of the NICE field team support local organisations to implement NICE guidance and use quality standards.
- NICE medicines and prescribing associates and the medicines education team use their local networks to deliver specialist support for high-quality, cost-effective prescribing and medicines optimisation.
- NICE publishes reports and a database on uptake of NICE recommendations.
- NICE into practice resources cover the principles of changing practice and practical steps to implement NICE 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.
- NICE's public involvement team works with national and local voluntary and community sector organisations and members of the public to promote the use of our guidance and standards, and support implementation.

We also seek feedback from people who use our guidelines to make them, and any resources to support implementation, as easy to use as possible.

12.6 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

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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

Kneale D, Goldman R, Thomas J (2016) A scoping review characterising the activities and

landscape around implementing NICE guidance [online; accessed 11 October 2018]

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 (surveillance).

13.1 Aims of surveillance

The aim of surveillance is to check that guidelines are up to date. This is done by exploring if there is any new evidence to contradict, reinforce or clarify guideline recommendations. Surveillance also identifies new interventions that may need to be considered within the guideline. Finally, it explores changes in context that may mean modifications are needed, for example, changes in policy, infrastructure, legislation or costs.

NICE has more than 270 published guidelines so the number of checks needed is considerable. A proactive approach is taken that includes reacting to events at any time after guideline publication (for example, publication of a key study) and a standard check every 5 years. Where possible, surveillance of guidelines covering similar populations or settings is undertaken at the same time.

13.2 Reacting to events

Some topic areas are fast moving and this increases the risk of guidelines having out-of-date recommendations. Therefore, NICE maintains an event tracker containing information on key events, such as ongoing studies, that are judged to be relevant to the guideline content. Ongoing studies are identified for the event tracker through the standard check and also through NICE's engagement with the National Institute for Health Research. The event tracker means that NICE can react quickly to changes in the evidence base, by initiating a check of the guideline as soon as the event has occurred. A check does not necessarily mean that the guideline will be updated.

An event that could affect the guideline could include:

- publication of a study that is directly relevant to NICE guidance and has the potential to affect recommendations
- substantial changes in policy or legislation (an example includes changes to the UK physical activity guidelines by the Chief Medical Office)
- development of a related piece of NICE guidance that contradicts recommendations in another NICE guideline

- withdrawal of a drug from the market or a clinically significant drug safety update from the Medicines and Healthcare products Regulatory Authority (MHRA)/Commission on Human Medicines.

This list is not exhaustive and individual events will be considered on a case-by-case basis. Events are identified through constant intelligence gathering, for example, the standard check, the guideline development process and stakeholder correspondence and enquiries.

Process for reacting to events

The NICE surveillance team considers how an event could affect a guideline. If an event is likely to affect guideline recommendations a check is performed before the next scheduled standard check. This involves considering the impact of the event on the guideline recommendations and incorporating feedback from topic experts in the area. The check may include intelligence gathering and literature searches, if needed, involving the same approach as for the standard check.

Checks in response to events do not undergo stakeholder consultation because they focus only on an important event and potentially a small section of a guideline. However, the decisions are communicated on the NICE website.

If NICE's Guidance Executive decides that an update of the guideline is needed after this type of check, registered stakeholders are informed of the planned approach.

13.3 The standard check

The median lifespan of a clinical guideline is 60 months (Alderson et al. 2014). More recent work within NICE incorporating data for public health guidelines supports this conclusion. Therefore, all NICE guidelines will be checked every 5 years using the approach described below.

Topic expert engagement

Topic experts including members of NICE's Expert Advisers Panel are invited to participate in surveillance and provide views about the continued relevance of recommendations. But if their response is limited or further specialist input is needed, we may seek input from other experts, such as government bodies or representatives from a Quality Standards Advisory Committee.

Intelligence gathering

Topic experts are surveyed for their views on the continued relevance of the published guideline

and recommendations, and their knowledge of recent developments in the topic area and any important new evidence since publication of the guideline. Feedback is also sought from internal teams within NICE who have expertise in the topic area under surveillance (for example, where there is a social care or medicines focus in the guideline). We may also ask stakeholders for their views, including organisations representing the interests of patients, people using services, carers and the public.

Additional intelligence might include:

- external queries and comments received since publication of the guideline (these are collated in an issues log for consideration during surveillance)
- related NICE guidance and quality standards (including placeholder statements in NICE quality standards) developed since the guideline was published
- information about guideline implementation, including evidence derived from analysis of primary data on the uptake of recommendations
- information about important ongoing studies in the area covered by the guideline (identified through searches of trial databases)
- changes in licensing status of medicines
- updated or new national policy.

Literature searching

Published evidence is identified through searching a range of bibliographic databases relevant to the topic, which are generally based on those searched for the published guideline. Sources searched may vary depending on the topic. In general, MEDLINE, MEDLINE in Process, Embase, Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials (CENTRAL) would be considered.

Search approaches

The search approach will vary between topics and may depend on priority areas highlighted through topic expert engagement and intelligence gathering. The following search approaches can be used:

- population or population/intervention search as needed for the guideline scope with:

- – randomised controlled trials (RCTs) and systematic reviews as a default
  - if RCTs are not appropriate because of the topic or guideline (for example, purely diagnostic), then other study types will be considered
- focused search(es) for a specific question or a new question, meaning that the study type searched for (RCTs or observational studies) should reflect the type expected to address the question.
- citation search forward/back (this option would be supplemented with either a restrictive full scope search or focused searches).

Other considerations

It may be appropriate to consider setting limits for the searches, which could include, but are not limited to:

- study design using appropriate search filter(s)
- date
- location
- population(s)/subpopulation(s)
- intervention
- service delivery aspect
- prognostic factors.

Search period

The search period will start at the:

- end of the search for the last update of the guideline
- end of the search for the last standard check.

The search date ends on the date the search is conducted.

Decision-making

Proposals on the need to update a guideline include an element of judgement and are based on an assessment of the relevant evidence published since guideline publication (abstracts of primary or secondary evidence), information obtained through intelligence gathering and feedback from stakeholder consultation.

The update proposal will be based on the following options:

- no update (check again in 5 years)
- no update at present but date of next check should be brought forward or pushed back (this decision would be made exceptionally, for example where it is clear that new evidence critical to this decision is due to be published)
- full update (develop replacement guideline)
- partial update (update defined sections of the guideline)
- transferring the guideline to the static list (see section 13.4)
- refreshing the guideline (see section 14.4)
- withdrawing some recommendations or the whole guideline.

When a guideline is being updated, the original scope may be used (unchanged), the original scope may be modified (for example, where new areas have been identified that require an extension to the scope) or a new scope may be developed. See chapters 2 and 14 for further details.

Stakeholder consultation

For all proposals other than a full update, we consult with stakeholders for 2 weeks. There is no stakeholder consultation on the proposal for a full update.

Signing off the final decision

All surveillance proposals go through a validation process at NICE (including sign-off by the associate director and centre director) before approval is sought from NICE's Guidance Executive.

13.4 Static list check

Guidelines are considered static when the recommendations are still current and should continue to be implemented, but are unlikely to change in the foreseeable future (because the evidence base or practice is unlikely to change). Guidelines are only considered static after consultation with stakeholders, and providing the following criteria are met:

- there is a decision not to update following a standard check and no major ongoing research expected to publish before the next standard check **or**
- the guideline is not intervention-based (for example, it focuses on commissioning or implementation) and no major changes to commissioning or service configurations have occurred since guideline publication, or are expected.

Following stakeholder consultation, a proposal to add the guideline to the static list may no longer be appropriate if stakeholders have made us aware of:

- relevant research **or**
- pertinent issues that need to be monitored **or**
- information that would impact on the 'no update' proposal.

Any ongoing research would be added to the event tracker to feed into a guideline check process.

Process

Static guidelines are looked at 5 years after they go on the static list and then every 5 years to determine whether they should undergo a standard check. This preliminary check is similar to the standard check but no literature searches are done. Topic experts are asked to supply information on any new published evidence that could affect the recommendations. Information is also gathered from the event tracker. This is likely to highlight the main events that could trigger a standard check and a possible update of the guideline. This process is applied consistently across static list guidelines with key decisions recorded as part of an audit trail. Guidelines are removed from the static list when the preliminary check suggests new evidence may affect the recommendation. They then undergo the standard check as described in section 13.3.

13.5 References and further reading

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and Care Excellence clinical guidelines was about 60 months. Journal of Clinical Epidemiology 67: 52–5

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 Alderson LJ, Alderson P, Tan T (2014) guidelines: how quickly do guidelines become outdated? JAMA 286: 1461–7

14 Updating guidelines

14.1 Scheduling updates

When scheduling updates of guidelines, NICE prioritises topics according to 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). Where possible, 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). Recommendations that are outside the scope of an update may be refreshed (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- or 6-week consultation period, depending on length and complexity (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

Refreshing a guideline allows us to improve the usability of recommendations without changing the intent and therefore without the need for an evidence review or committee input. All refreshing changes are signed off by NICE's Guidance Executive.

Refreshing changes can be made to guideline recommendations even when the surveillance decision is not to update the guideline. All changes to recommendations made as part of the surveillance process should be agreed by the NICE surveillance team (see chapter 13).

When a partial update has been agreed, the publishing team also identifies recommendations that may need refreshing to feed into the scoping process. Occasionally during development of partial updates, additional recommendations that are not part of the update may be identified for refreshing by the committee or the publishing team.

Refreshing might involve:

- amending or adding cross references to other NICE guidance or hyperlinks to other NICE-endorsed tools or resources
- adding or amending a footnote to reflect changes to a medicine's marketing authorisation, to reflect changes in service configuration (for example, a change from primary care trusts to clinical commissioning groups) or a change to an organisation's name
- ensuring recommendations take into account the latest government policy or guidelines, for example, on alcohol consumption

- amending recommendations to reflect the current practice context, for example, removing references to tools or resources that no longer exist
- bringing recommendations in line with NICE's current policy on wording without affecting the intent, for example:
    - reflecting the involvement of people in decisions about their care
    - using person-centred language.

Refreshing changes that are made during scoping and guideline development should be agreed with NICE staff with responsibility for quality assurance.

14.5 Presenting updates

A full update replaces an existing guideline and has a new set of recommendations, a new set of rationale and impact sections, 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 is 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 on a partial update, the developer should check the following:

- All sections have been updated as agreed.
- It is clear which sections have been updated and are open for comment during consultation.
- Recommendations from sections which have not been updated have been checked to determine whether any changes are essential (for example, if a medicine is no longer available).
- Refreshing changes (see section 14.4) to 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 in 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 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 which sections have been updated, and whether the recommendations have been updated or amended.
- The summary of changes to recommendations has been revised in line with the final recommendations.

The NICE Pathway is also updated, and resources to support implementation are checked for current relevance.

14.6 Post-publication changes

Measures are in place throughout the development of a guideline to avoid errors in the collection, synthesis, interpretation or presentation of the evidence as far as possible. On rare occasions errors are found after publication of the guideline, or users may ask for clarification.

Corrections or changes to a published guideline are made if an error or lack of clarity:

- 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.

Errors or clarifications that do not warrant immediate changes to the guideline are logged for consideration when the guideline undergoes surveillance (see chapter 13).

If an error or clarification meets the criteria for changing 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. Resources to support implementation are also amended if necessary. The changes are explained in the guideline and pathway. 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

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.

Case–control study

An observational study to find out the possible cause(s) of a disease or condition. This is done by comparing a group of patients who have the disease or condition (cases) with a group of people who do not have it (controls) but who are otherwise as similar as possible (in characteristics thought to be unrelated to the causes of the disease or condition). This means the researcher can look for aspects of their lives that differ to see if they may have caused the condition.

For example, a group of people with lung cancer might be compared with a group of people the same age who do not have lung cancer. The researcher could compare how long both groups had been exposed to tobacco smoke. Such studies are retrospective because they look back in time from the outcome to the possible causes of a disease or condition.

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).

Cohort study

An observational study with 2 or more groups (cohorts) of people with similar characteristics. One group has a treatment, is exposed to a risk factor or has a particular symptom and the other group does not. The study follows their progress over time and records what happens.

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. A conceptual model has been defined as the abstraction and representation of complex phenomena of interest in some readily expressible form, such that the individual stakeholders' understanding of the parts of the system, and/or the mathematical representation of that system, can be shared, questioned, tested and ultimately agreed.

Confidence interval

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 or count towards quorum. 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

This is a type of economic evaluation in which 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

This is a type of economic evaluation in which 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

This is a type of economic evaluation in which 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-effectiveness analysis is also used as an umbrella term to cover all types of economic evaluation.

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

This is a type of economic evaluation in which 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.

Design-oriented conceptual model

This is an explicit simplification and abstraction of the problem-oriented conceptual model, mediated by what is feasible and by the availability of evidence and data.

Developer

The team responsible for scoping the guideline, identifying and reviewing the evidence, undertaking economic analyses, 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.

Economic evaluation

The comparative analysis of alternative courses of action in terms of both their costs and consequences.

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.

Endorsement

The NICE endorsement programme formally endorses resources produced by external organisations that support the implementation of NICE guidance and the use of quality standards in part or in full.

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 from practice

Information on context and current practice, which could be in the form of published implementation trials, audit data, manuscripts of case studies or service evaluation reports, or accounts from experts.

Evidence review

Identifying and reviewing the evidence, and undertaking economic analyses:

- The information specialist identifies relevant literature to answer the review questions, 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 (including GRADE tables, GRADE-CERQual or evidence statements, if used). 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 Advisers Panel

The Expert Advisers Panel provides a single repository of experts and practitioners (who have been through a robust recruitment process) for the NICE Centre for Guidelines, and can be called upon

to contribute to various guideline development activities, such surveillance reviews and guideline updates.

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.

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.

Full update of a guideline

When a guideline is identified for a full update, the existing guideline with its recommendations, are stood down and a replacement guideline is developed with new recommendations.

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.

GRADE table/GRADE 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).

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 and Social Care 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 between 2 interventions, strategies or programmes in the population of interest divided by the differences in the mean outcomes between the 2 interventions, strategies or programmes 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 trial.

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 a medicines regulator (for example, the Medicines and Healthcare products Regulatory Agency [MHRA] or the European Medicines Agency). It is normally necessary before a medicine can be prescribed or sold.

Markov modelling

A decision-analytic technique that predicts future events occurring in a group over a period of time 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 and Social Care 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

A method often used in systematic reviews to combine results from several studies of the same

test, treatment or other intervention to estimate the overall effect of the treatment.

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 effectiveness, adverse events, diagnostic accuracy, prognosis, quality of life, resource use and 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 3 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 a tool to help find NICE guidance quickly and easily – everything NICE says on a topic in an interactive flowchart.

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

An odds ratio compares the odds of something happening in one group with the odds of it happening in another. An odds ratio of 1 shows that the odds 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 and Social Care 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.

Pragmatic clinical trial

A study comparing health interventions among a randomised, diverse population representing clinical practice, and measuring a broad range of health outcomes. To ensure generalisability, pragmatic trials should represent the intended patients to whom the treatment will be applied as best as possible. (Definition from GetReal glossary)

Problem-oriented conceptual model

This is a simplified, diagrammatic representation of the framework that describes the resources, processes and interactions in the delivery of interventions.

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 year (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 guideline lead is responsible for the development and quality assurance of the guideline (including the scope), and has delegated responsibility for approving the consultation draft, the final guideline, and other documents, before final approval by NICE's Guidance Executive. The guideline lead also advises the chair of the committee and the developer on matters of method and process. Guideline commissioning managers help them with this.
- The NICE clinical, public health or social care adviser is responsible for providing advice during all stages of guideline development.
- 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 assurance of guideline surveillance reflects quality assurance of guideline development. The NICE associate director – surveillance is responsible for ensuring that processes are followed and that decisions to update or not update guidelines are robust and fit for approval by NICE's Guidance Executive.

Quality of life

See Health-related quality of life.

Quality standards

Quality standards set out the priority areas for quality improvement in health and social care. They cover areas where there is variation in care. Each standard includes a set of statements to help improve quality, and information on how to measure progress.

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 recommendations should be confirmed unless the quorum is reached.

Randomised controlled trial

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.

Real world evidence

See the GetReal glossary.

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 organisations (for example, tobacco companies, those who speak for them or are funded by them) with an interest in a particular topic. 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).

Shared learning examples

These show how NICE guidance and standards have been put into practice by a range of health, local government and social care organisations.

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:

- children and young people 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.

Social value judgements

The decisions in NICE guidance are based on the best available evidence. Sometimes the available evidence is not of good quality or can be incomplete, so the committees involved have to make scientific value judgements and social value judgements. Social value judgements take account of society's expectations, preferences, culture and ethical principles when making recommendations.

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.

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.

See also respondent.

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.

Surveillance report

A report that summarises the evidence and intelligence identified through the surveillance process and explains the reasons for updating or not.

Surveillance review

The process of checking whether a guideline needs to be updated. This generally includes consideration of new evidence and intelligence such as topic expert feedback, changes to legislation or policy, and information on implementation.

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.

Update information

October 2018: Major changes from the 2014 guidelines manual are shown below.

Service delivery

Methods for developing recommendations on service delivery have been incorporated into the manual, with information added to the chapters on scoping, searching, evidence submission and economics. We have added a new appendix (appendix A) with detailed advice on developing review questions in this area.

Primary data analytics

NICE is currently exploring the place of primary data analytics in our work and further advice will be shared as this develops.

Chapter 2 – the scope

We encourage developers to list areas where evidence is lacking and details of stakeholders who might provide information in a call for evidence or who might identify expert witnesses.

We are clear that guidelines don't usually include key issues covered by bodies such as the Department of Health and Social Care, NHS England or Public Health England.

We remind developers that guidelines don't usually cover training requirements. However, recommendations may cover the need for specific knowledge and skills for a particular aspect of care.

Chapter 3 – decision-making committees

We encourage developers to think about other related NICE guidance in development and promote cross-representation across committees when topics are closely related.

We include advice for developers about seeking expert testimony from children and vulnerable groups, including use of video recording and giving testimony in private session.

We have made changes to ensure consistency with the updated code of practice for declaring and dealing with conflicts of interest. We have also clarified the involvement of tobacco companies as

respondents rather than stakeholders.

Chapter 4 – developing review questions and planning the evidence review

We indicate that core outcome sets (one source is the COMET database) should be used if suitable based on quality and validity. We give standards for assessing the suitability of core outcome sets.

We include review questions that assess diagnostic prediction models and prognostic prediction models and link to external sources of further advice.

We have included a standard template for review protocols as an appendix (appendix I). Registration of the review protocol on the PROSPERO database is now mandatory.

Chapter 5 – identifying the evidence

We have included new sources, tools and approaches to searching, as well as a new prompt for identifying MHRA safety information.

Chapter 6 – reviewing the evidence

We now recommend GRADE as the first approach to quality assessment for all guidelines, including those covering public health and social care topics. We recommend GRADE-CERQual for qualitative evidence.

Results of the analysis and confidence in the evidence should now be presented as GRADE profiles. Evidence statements should be presented when the GRADE approach is not used.

We now have preferred 'checklists' for assessing the quality of the evidence (see appendix H). Use of any other checklist should be agreed in advance with NICE staff with a quality assurance role.

We now indicate that an agreed proportion of papers should be sifted by 2 analysts (not less than 10%) because duplicate sifting of all papers is time consuming and there are other ways of ensuring that relevant papers aren't missed. We have included details of using a machine learning algorithm for priority screening.

We include advice on the minimum outputs and reporting standards for network meta-analyses (see appendix K) and how these apply to developing NICE guidelines.

Chapter 7 – economic evaluation

For base-case analysis, we recommend a cost–utility analysis using a cost per QALY. This will allow more consistent decisions related to costs.

We have clarified that the same levels of evidence and considerations should be used for disinvestment and investment decisions.

We have added information on end of life criteria in line with technology appraisal methods.

Chapter 8 – linking to other guidance

We advise linking to technology appraisal recommendation in the NICE Pathway rather than incorporating TA recommendations verbatim in a guideline.

We have removed the details on updating technology appraisals within a guideline and have added a link to the policy from the Department of Health and Social Care.

We include advice for developers on what to do when similar review questions are covered in other guidelines. Options include linking to the recommendations in the other guideline, using the evidence review to make new recommendations or doing a new systematic review.

Chapter 9 – writing the guideline

We have simplified advice on writing guidelines, and a separate writing guide with more details and examples will be coming soon.

The section on supporting shared decision-making has been clarified, and includes information on when a separate decision aid could be produced. The writing guide includes more detail on summarising evidence in the guideline to support a professional's discussion with the person making the decision.

We have added new advice on what to do when recommendations are made for the use of CE-marked devices outside their instructions for use. This includes standard footnote wording.

We have clarified advice on recommendations on the off-label use of medicines.

Chapter 10 – validation

We have defined the types of 'additional consultation' that can inform development. There is more information about the changes in appendix B.

Chapter 12 – implementation

Information on how we work and the tools we produce has been updated. A new section on how we work with other organisations, including endorsing resources, has also been added.

We highlight the role of the new Guideline Recommendations Implementation Panel.

Chapter 13 – surveillance

We have focused the process on event-driven checks of guidelines as well as a standard check every 5 years.

We plan themed surveillance of guidelines covering similar populations or settings to ensure that the process is efficient.

We have revised the process for considering whether to remove a guideline from the static list.

We have indicated that we may refresh some recommendations following an event-driven or standard check.

We have added information about the quality assurance of the surveillance process.

Chapter 14 – updating guidelines

We have added a new section on refreshing recommendations, to make minor changes to improve the usability of recommendations without the need for an evidence review or committee input.

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