Appendix A: Service delivery – developing review questions, evidence reviews and synthesis

The scope should identify key areas that the guidance will cover. There are various types of review question that may be considered for service guidance; for example, these may cover:

- the content, configuration or integration of services, including the allocation of:
    - medical equipment or tools
    - staff, such as:
        - skills, mix and experience of staff
        - training requirements of staff
        - staffing levels (numbers and staff mix)
- access to services for patients, including:
    - the availability of services
    - the uptake of services
- timing and delivery of services, including:
    - diagnosis
    - treatment
    - transfer and referral
    - waiting times
- location of services, in terms of:
    - setting for delivery
    - economies of scales
    - geographic variation
- Feasibility, with regard to:
    - resource constraints (including capacity, queues and waiting lists)
    - policy constraints.

The questions will compare possible service configurations, which may be existing variations to current services (national and international variations) or a proposed service configuration, with a current service configuration with respect to effectiveness and cost effectiveness.

Key outcomes of service delivery questions are likely to include measures of:

- service effectiveness:
    - health outcomes, including health-related quality of life
    - process outcomes (both directly and indirectly linked to outcomes)
    - compliance rates of staff
    - system failures
- service experience:
    - patient experience
    - family or carer experience
    - staff experience
- service resource use:
    - staff
    - equipment
    - time
    - costs
- service efficiency/optimisation:
    - cost effectiveness (cost–utility analysis)
    - cost consequence
    - cost saving
    - cost minimisations
- service equity (including health and geographical inequalities).

A key difference for service guidance compared with other guidelines is that, to adequately address the question, it is necessary to explore the underlying health and/or service concern first, and then assess the effectiveness of the various health service interventions in addressing this underlying issue. This requires an iterative approach to developing the review questions. The first step is to develop questions to explore the underlying problem, followed by developing questions around potential solutions and service models.

These types of review questions will often require the consideration of supplementary methodological approaches for identifying, assessing, synthesising and interpreting the evidence.

Evidence reviews will be iterative, with new searches and/or analysis being planned depending on the outcome of the initial reviews. For example, a search for studies exploring the effectiveness of a particular intervention may not produce any results. The next step would be to consider whether to search for evidence for a similar condition or another healthcare system. Alternatively, primary data may need to be identified or requested to inform recommendations. The guideline committee and NICE staff with responsibility for quality assurance should be consulted on the suitability of different types of evidence for developing recommendations.

Estimates of the relative effectiveness of service delivery interventions

It is helpful to distinguish between two general types of service delivery questions. One type concerns different pathways of care, different service configurations, interventions to be managed by different types of staff, whether a 'care team' approach is needed, and so on. These are questions for which trial evidence could in principle be found. For these kinds of questions, standard approaches to evidence identification and synthesis (for example, those described in this guideline manual and on the NICE Decision Support Unit website) could, in principle, be used. However, for service guidance it is unlikely that one type of study or piece of evidence will be sufficient to inform recommendations. Therefore non-standard approaches to evidence synthesis will also need to be considered to enable the guideline committee to develop recommendations. Two specific problems that will often need to be addressed are:

- uncertainty about the quality and relevance of existing evidence on outcomes
- the need to consider evidence on process, intermediate or surrogate outcomes, such as uptake of services or compliance, rather than (or in addition to) evidence on outcomes.

A second type of service delivery issue relates to questions about the feasibility of providing access to services and procedures, or making them available within a certain time frame, rather than whether the services or procedures are effective. In these questions, estimates of the effect of providing the service, compared with not providing it, are needed for decision-making, whether based on cost-effectiveness analysis or on other criteria.

It should be emphasised that some service delivery guidance may present a combination of both access and availability issues as well as standard effectiveness issues.

Guidance on how to approach both kinds of problem, as well as on using consensus techniques when estimates based on published data cannot be obtained, is given in the following sections.

Finding studies that provide unbiased estimates of the effectiveness of service interventions is often difficult, for the following reasons:

- Service delivery interventions are inherently 'variable'. Even with a standard protocol, the precise way in which they are implemented at different sites or by different people is necessarily situation- and/or individual-dependent. This could be manifested by centre effects in multicentre trials.
- The relative benefit of a new intervention over 'standard' or pre-existing care is likely to depend on the 'intensity' of the current care. For example, the beneficial effect of a new patient reminder system on the uptake of screening for breast cancer depends on what the current arrangements are, and on current uptake. For example, the effect of introducing a reminder system in the USA, where there is no systematic screening programme, will be quite different from the effect of adding the reminder system to existing infrastructure in the UK. In other words, results from studies carried out within other healthcare systems might not be easily generalised to the UK.

In these circumstances a standard systematic review is likely to identify a range of studies on interventions that are similar to the interventions being considered, but not necessarily the same, or which are described variably with respect to their components. In this case, the guideline committee will need to consider carefully fidelity and applicability issues, and ensure these are accounted for in the 'committee discussion' section of the guidance.

In most cases, the expert opinion of the guideline committee will be used to explore and estimate any impacts on the confidence in the results of such evidence, but quantitative methods for elicitation can be used. If quantitative methods for eliciting are to be used, the NICE Guidelines Technical Support Unit (TSU) should be

contacted for advice on methods and on which types of evidence could be searched for.

Evidence on uptake and compliance outcomes

In some service delivery evaluations, measures of service uptake, patient satisfaction or compliance of health service staff are recorded, rather than data on clinical outcomes for patients. This is typically the case, for example, when the intervention is directed at changing staff behaviour or patient referral routes.

Such evidence can be used when analysing the effectiveness or cost effectiveness of a service delivery intervention, but only if there is also an estimate available – from whatever source – of the underlying effect of the procedure or treatment. It is then possible to combine estimates of the efficacy or effectiveness of the intervention with estimates of the effectiveness of the service delivery intervention in ensuring that the intervention is implemented. It is possible to combine evidence from trials reporting process outcomes alone, trials reporting outcomes alone, and trials reporting both.

The NICE TSU can be consulted for advice on how the two kinds of evidence can be combined within a single modelling framework.

Estimates of relative effectiveness for questions about access and availability

For questions about access and availability, there is a particular difficulty in deriving an estimate of relative effectiveness, over and above those described in the previous section. This would be the case, for example, where a procedure such as endoscopy for upper gastrointestinal bleeding is indicated. The question is not about whether endoscopy should be done, but whether or not the procedure can be safely delayed (for example, at night or at weekends) in patients whose symptoms suggest they are at lower risk.

Studies based on individual patient 'audit' data that relate outcomes to treatment parameters while controlling for patient characteristics are difficult to interpret. This is because patients in whom the treatment was withheld or delayed are always likely to be those who were considered to be at lower risk.

It is likely that better estimates of the effectiveness of such interventions can be derived from nationally collected data in which between-unit variation in outcomes, or

variation between different time periods, can be related to the local policies and practices (for example, staffing levels) in operation at the time. For example, mortality rates within 1 or 2 days of hospital admission could be compared between weekends and weekdays, and hospitals where weekend cover was the same as weekday cover could also be compared with those where it is not. There are a number of examples where comparisons of this type have been published, for example by 'Dr Foster'. Although these surveys avoid the problems of individual audit data, they are still observational and the use of aggregated data introduces further potential biases. The design of the data collection, and the analysis and interpretation of the data obtained, requires major input from clinical epidemiologists, expert clinicians, methodologists, operational research experts and people with relevant operational experience in the NHS.

A service delivery issue that is quite often examined in this way is the relationship between performance indicators and 'volume' (that is, number of cases seen per year). Such data are also used to establish 'institutional rankings'. Data of this type tend to show considerable overdispersion: in other words, there is far more variation between units than would be expected by chance. To determine whether individual units are performing at a level that requires some intervention, control charts can be used. There are also methods and processes for interpreting the relationships between performance and volume and the need to take into account general between-unit variation when trying to infer causal effects.

Appendix B: Approaches to additional consultation

An additional consultation for a guideline is considered only on an exceptional basis and is additional to the routine stakeholder consultations (see section 10.1 of the manual). Additional consultation is a targeted engagement exercise to obtain a range of views and experiences, either to inform the evidence and draft recommendations, or to test the feasibility of implementing the draft recommendations or their relevance and acceptability to those affected by the guideline. This appendix outlines approaches that could be used when additional consultation is needed involving specific groups of professionals or people using services and carers. Additional consultation may be conducted during guideline development or at the same time as the public consultation on the draft guideline.

Points to consider include:

- deciding whether additional consultation is needed
- aim of additional consultation
- commissioning process
- obtaining ethical approval
- the proposal
- reporting findings.

This appendix also describes how findings from an additional consultation are used to finalise the recommendations.

Deciding whether additional consultation is needed

Reasons for additional consultation will vary depending on the topic, and may become apparent at different stages of guideline development. They might include a new area for NICE guidelines during update, a lack of evidence on the views and experiences of people using services, or concerns raised by key stakeholders.

Sometimes health and social care inequalities or impacts on equality are a particular concern, for example, people affected by the guideline find it difficult to engage with health and social care services.

Sometimes a particularly complex topic needs a whole system approach. Configuration of services may be central to the efficacy of a set of recommendations and input from a particular group of health and social care practitioners may be needed.

Occasionally a guideline includes an area of rapidly changing practice, with publication of evidence lagging behind change. It may be necessary to test the draft recommendations with frontline practitioners, or providers or commissioners of services.

In some exceptional cases, the developer may commission an additional consultation with people affected by the guideline to obtain:

- their views on specific aspects of the guideline, review questions or issues raised by the committee
- their views and experiences of relevant health and social care services.

The developer may also wish to commission an additional consultation with people affected by the guideline to test the relevance and acceptability of selected draft recommendations. This may be undertaken at the stakeholder consultation stage (see also section 10.1 of the manual), or earlier in the process to validate emerging draft recommendations.

Examples of how guidelines have used the methods described above include:

- Young people with life-limiting and life-threatening conditions were asked for their views and opinions on selected review questions, including their preferences for place of care, information and communication provision, personalised care planning, and psychological care (Report, appendix L, NICE guideline on end of life care for infants, children and young people with life-limiting conditions).
- In the absence of evidence, the developer worked with Alder Hey Children's Hospital to survey children about their views and experiences of sedation for diagnostic and therapeutic procedures. Trust staff obtained real-time feedback via hand-held touch screen computers which young children can use (chapter 7, full guideline on sedation in children and young people).

- People in prison were consulted on their experiences of prison health services to help refine draft recommendations. The developer commissioned User Voice to conduct focus groups with a range of serving prisoners, including people with disabilities, women, older people, long- and short-term prisoners, and those with a history of substance misuse (appendix v, NICE guideline on physical health of people in prison).
- Children and young people on the autistic spectrum were consulted on emerging draft recommendations (developed from a qualitative literature review) for improving access to and experience of care. The purpose was to validate findings where appropriate and to allow feedback on areas in which the children and young people felt that the qualitative literature was either not representative of their views or that evidence was missing (chapter 4, section 5.2, full guideline on management of autism in children and young people).
- Healthcare professionals working in neonatology and midwives across the country were consulted on the consensus bilirubin thresholds for managing babies 38 weeks or more gestational age with hyperbilirubinaemia. (addendum to NICE guideline on jaundice in newborn babies under 28 days) The additional consultation was conducted during the development of the guideline before public consultation. The aim of the additional consultation was to seek validation from healthcare professionals and midwives on the consensus bilirubin thresholds for managing babies 38 weeks or more gestational age with hyperbilirubinaemia before wider public consultation.
- Due to a lack of published evidence, additional consultation with adult and paediatric neurologists, general practitioners and other healthcare professionals was conducted during guideline development to run a 1-round modified Delphi to gain consensus on signs and symptoms associated with suspected neurological conditions presented in primary care (NGXX Suspected neurological conditions, publication date: to be confirmed).

Aim of additional consultation

The aim of an additional consultation must be clearly stated in the proposal for NICE as well as in the guideline methods. The aim could include, for example:

- obtaining expert view or opinions, or testing the feasibility of recommendations with policy makers, commissioners, health and social care providers and practitioners
- identifying barriers and facilitators to implementing recommendations with policy makers, commissioners, health and social care providers and practitioners
- obtaining users' views and experience of health and social care services to fill evidence gaps
- obtaining users', and their families' or carers', experience and views to fine-tune the recommendations.

These are just a few examples. Developers should consult NICE staff with responsibility for quality assurance for initial discussion as soon as the need for additional consultation is identified. If the work is likely to involve people using services or their carers, the developer should also discuss their plans with NICE public involvement staff, who can advise on options and methods for involving people affected by the guideline, including targeted consultation to obtain their views. They can also signpost to external resources and sources of more specialist advice.

Agreeing who should be commissioned to do the work

Once the aim of additional consultation is agreed, the developer should then discuss the commissioning process with NICE staff with responsibility for quality assurance. Additional consultation may be conducted by the developer or by an external contractor.

When the decision is made to commission an external contractor, the developer and NICE should consider an academic or research organisation, or an organisation that works with people affected by the guideline and has research expertise. This organisation should be separate from the team involved in compiling evidence reviews for the guideline and the committee, unless there are exceptional circumstances. For example, specific expertise in the topic or access to specialist networks is needed. However, the team may be asked to help the contractor, for example, by generating a list of participants.

The contractor should have a good record of qualitative or participatory research and, ideally, should have experience in the topic area, as well as expertise in working with people affected by the guideline.

The developer should document the reasons for the additional consultation, with a proposal including the methods to be used, and the anticipated time and 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.

If an external contractor is commissioned, the commissioning process should follow NICE's Standing Financial Instructions. This involves developing a project specification, issuing invitations to tender and selecting a contractor based on clear and auditable criteria.

Obtaining ethical approval

In principle, additional consultation falls into the category of 'service evaluation' and so is outside the remit of NHS research ethics committees. However, NICE, the developer and external contractor (if commissioned) should consider the ethical issues each time an additional consultation is planned to ensure appropriate expertise, and that policies and procedures are in place for the safety and welfare of participants. If there is any doubt, the developer or external contractor should consult the National Research Ethics Service. The developer or external contractor (if commissioned) is responsible for seeking ethical approval, if required.

For topics covering children and young people, NICE's patient and public involvement policy includes a set of principles for involving them and has an appendix about safeguarding. The National Research Ethics Service should also be consulted for topics covering children and young people and other vulnerable groups such as adults with learning disabilities or frail older people.

The proposal

The proposal for the additional consultation should include information on the:

- aim and objectives
- recruiting participants

- methods used
- analysis of data
- feedback mechanism

The proposal and the final report of the additional consultation should be included as part of the guideline or guideline appendices.

The developer or the external contractor (if commissioned) should agree with NICE the approaches and methods to use, including a summary of the issues to be covered. Similarly, the methodology and any questions or support materials used must be developed and agreed with NICE. For example, NICE should:

- be briefed by the developer or external contractor (if commissioned) in detail before work begins
- agree final documents and comment on draft recruitment letters
- help develop topic guides (for example, summaries of the recommendations and key questions for discussion)
- agree sampling frames and samples, and other supporting materials
- discuss how to get participants from key groups involved, including people who work with or are from seldom heard groups or those who share characteristics protected under equality legislation
- have access to transcripts of all data
- discuss and agree techniques for data analysis and themes for data presentation
- comment on the additional consultation report before the final draft is submitted.

Aim and objectives

The aim of the additional consultation should be clearly stated in the proposal. The proposal should also state the expected outputs, for example, the final report may summarise themes from participants' views, which would be used to inform or fine-tune the final recommendations.

Recruiting participants

The developer and external contractor (if commissioned) should consider the recruitment strategy carefully, taking into account the purpose of the additional consultation, the topic, the groups, the range of views required, and other relevant issues.

If the purpose of the consultation is to test the feasibility of implementing recommendations, participants should be chosen to represent a broad range of stakeholder groups in the statutory, non-statutory and voluntary sectors, where applicable. This may include people who work with the target populations covered by the guideline and other users of the guideline, such as health and social care practitioners, commissioners, policy makers, people using services, and if appropriate their families or carers. Participants do not have to be from an organisation that is registered as a NICE stakeholder.

When planning an additional consultation with children and young people, school holidays and exam schedules should be taken into account.

Equality issues should be fully considered when choosing participants. This may mean getting a representative spread of practitioners or people using services, but it may also mean focusing on participants from seldom heard groups or people with recent experience of working with them. When testing the feasibility of implementing recommendations, the approach should be based on the content of the draft recommendations, whether or not they refer to the whole population or subgroups, and service delivery and policy issues.

Different sampling methods may be used to recruit participants. Sampling should be guided by the topic and will depend on the:

- stakeholder groups identified as being responsible for taking action
- the make-up of the population affected by the guideline
- scope
- research questions
- inclusion criteria for the evidence reviews.

'Snowballing' (gathering participants via other participants or networks) and purposive or other non-random techniques may be used to ensure all relevant groups are represented.

Random sampling (randomly selecting participants from the relevant groups) or quota sampling (selecting a fixed number of participants, randomly or purposively from these groups) may be useful for large-scale surveys. Random and quota

sampling may also be useful where there are a large number of potential participants, but there are not enough of them in each relevant geographical area.

The proposal should explicitly state the groups of participants to be recruited, the recruitment strategy, including sampling method, the number of participants to be recruited, considerations of consent, confidentiality and data protection. The developer or external contractor (if commissioned) should ensure the sampling frame and sample take account of equality issues. It should be agreed with NICE.

Methods used

Additional consultation is a targeted engagement exercise to obtain a range of views and experiences either to inform the evidence and draft recommendations, or to test the feasibility of implementing the draft recommendations or their relevance and acceptability to those affected by the guideline. Additional consultation can involve a number of approaches and methods. NICE, the relevant committee and the developer or external contractor should consider the choice of methods carefully, taking into account the topic, the groups involved and other issues. When involving people affected by the guideline, the methods and materials used should be tailored to the age, ability and culture of participants. Additional consultation may include the use of groups, 1-to-1 or paired in-depth interviews or surveys. In some cases – for example, if a range of groups are involved – a combination of approaches may be used.

Group-based methods

Group-based methods include focus groups, participative workshops and 'virtual' (electronic) groups. These may be appropriate when:

- potential participants have clear 'professional identities' and the 'field' is well established
- the developer (with support from NICE) can contact enough people in a geographical region to set up a focus group or workshop
- the issues discussed are unlikely to be confidential or sensitive and anonymity will not be necessary.

The developer or external contractor (if commissioned) may also want to consider the following:

- more than 1 participative workshop or focus group or 'virtual' (electronic) group could be convened; these should take place in more than 1 geographical region and will normally be a half day but may take up to a day; if it is not feasible to organise this many workshops or groups, the decision on how many should be convened must be agreed with NICE
- if it suits the needs of the project, separate participative workshop or focus group or 'virtual' (electronic) group can be arranged for different practitioner or user groups; this will depend on the number of participants and should be agreed with NICE
- for some topic areas, researchers may be included in the additional consultation; in such cases, a separate meeting should be convened for them, using the same processes; this should be agreed with NICE
- topic guides, prompts or supporting materials (such as the draft recommendations and the key areas of concern) must be developed in collaboration with, and agreed by, NICE
- if the purpose of the additional consultation is to test the feasibility of implementing guideline recommendations, a member of the NICE field team should attend at least 1 meeting.

1-to-1 or paired in-depth interviews

Interviews may be carried out face-to-face, by telephone or online. They may be appropriate when:

- it is not possible to get groups together because the topic is a relatively new area, the number of possible participants is limited or there are geographical or time constraints
- the issues discussed are likely to be confidential or sensitive and anonymity may be needed
- in-depth responses are needed.

Interviews may be structured or semi-structured, depending on the topic and the groups involved. Semi-structured interviews allow complex or difficult issues to be

explored and so are likely to be more useful than a fixed-format interview. They should focus on, for example, areas in which views and experiences are needed, or the draft recommendations.

Individual or paired interviews are usually more expensive to set up than group work, and the need for in-depth or individual contact should be weighed against the available resources at the planning stage.

Surveys

Group-based methods and 1-to-1 or paired interviews are the best way to find out opinions. But they are not suitable in all circumstances, for example, because of the sensitivity of the topic, confidentiality issues, or difficulties in recruiting participants. In such cases, surveys that use semi-structured and open-ended questions could be more appropriate. Surveys may be carried out by telephone, online, on paper or by using vote casting or polling.

Surveys gather opinions in a quick and less obtrusive manner than group-based approaches and interviews. The responses can also be quantified. But surveys do not allow the same depth of exploration and, generally, should only be used if other methods are unsuitable. Formal consensus methods such as Delphi survey and RAND appropriateness could be modified for the survey if appropriate.

Analysis of data

There are different ways of analysing data from additional consultation, depending on the methods used for data collection. Some descriptive summary statistics should be provided, for example, characteristics of participants and attendance or response rates.

Group-based methods and interviews are likely to generate qualitative data. Analysis may be performed using qualitative research software, or by hand, but the method should be fully reported in the proposal and the final report.

Qualitative data can be broken down into common and consistent themes for each of the questions asked, using, for example, a content analysis approach. Usually, 1 researcher should prepare an initial analysis, which should be verified by ‘blind’ coding and sorting of a sample of the transcript by a second researcher. For

examples of this kind of analysis, see part 3 (chapters 7 to 13) of Silverman (2004) or Ritchie and Spencer (1993).

Once the analysis is complete, participants' quotes may be selected to illustrate each theme. These quotes should be coded to keep participants anonymous and to allow the quotes to be distinguished. Where transcripts are processed, ensure confidentiality and data protection are fully considered. As with data from clinical trials, transcripts should be kept for at least 5 years (see www.ct-toolkit.ac.uk).

Surveys are likely to involve a mixture of quantitative and qualitative data. Quantitative data may be analysed and presented using summary statistics. These could be generated using various statistical software or calculators. Where informal consensus methods such as Delphi survey and RAND appropriateness have been modified for the survey, specific analytical methods, for example, thresholds for agreement, should be stated in the proposal and the final report.

The developer or external contractor (if commissioned) should ensure the methods for analysing the data are discussed and agreed with NICE.

Feedback mechanism

The developer should ensure that all participants receive feedback on their contribution or the findings of the consultation and how this information has been used. For commissioned work, the external contractor should agree with the developer a process for giving feedback to all participants. Providing feedback to participants should be specified in contracts. This may include an evaluation exercise, a follow-up session or sharing interim findings via email.

Reporting and using the findings

The final report of the additional consultation should follow the same structure as the proposal. It should include sections on aim and objectives, recruiting participants, methods used, analysis of data and all the findings from the additional consultation.

These findings should be used to inform the guideline recommendations. The developer may present a summary of all the findings to the committee, and the committee should use this information to refine and prioritise the recommendations before or after the public consultation, depending on when the additional consultation

is conducted. How the summary findings are used to inform committee's decision-making should be documented in the committee's discussion of the evidence.

Both the proposal and the final report of the additional consultation should be available as appendices on publication of the guideline.

Further information

References and further reading

Green J, Thorogood N (2004) Qualitative methods for health research: qualitative methods for health. London: Sage

Kelly MP, Chambers J, Huntley J et al. (2004) Method 1 for the production of effective action briefings and related materials. London: Health Development Agency

Lightfoot J, Sloper P (2002) Having a say in health: guidelines for involving young patients in health services development. University of York: Social Policy Research Unit

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Shaw C, Brady L-M, Davey C (2011) Guidelines for research with children and young people. London: National Children's Bureau

Silverman D, editor (2004) Doing qualitative research: a practical handbook. London: Sage

Tashakkori A, Teddlie C (2002) Handbook of mixed methods in social and behavioural research. London: Sage

Appendix C: Key roles and responsibilities of committee members

The committee chair

The committee chair is required to attend a specific induction session (see section 3.7 of the manual) ideally before guideline committee meeting number 1.

The chair needs an understanding of NICE's guideline development process, and may have some background knowledge about the guideline topic but should not have any direct interests (in accordance with the NICE declarations of interest policy) that relate to the areas within the scope of the guideline. The chair signs off the equality impact assessment at scoping and final guideline stages. The chair ensures that the committee takes full account of the evidence in developing recommendations and considers the analysis and interpretation of the evidence prepared by the developer. Shortlisting and interviews of committee members will be undertaken by the committee chair or vice-chair.

To facilitate the effective working of the committee, the chair:

- may be involved in developing the scope and setting boundaries for the work
- helps to plan the committee meetings
- runs the committee according to the principles set out in the Terms of Reference and Standing Orders
- establishes a climate of trust and mutual respect among members
- provides opportunities for all members, including members with additional needs, to contribute to the discussions and activities of the committee.

The chair also gives committee members if requested feedback and comment, on an annual basis, on their contribution for revalidation purposes or personal development. The chair is given feedback and comment on their own contribution on an annual basis from a senior member of NICE staff if requested. The developer may also provide feedback on an ongoing basis or as required.

All committee members

Committee members are expected to:

- Review and abide by the Terms of Reference and Standing Orders for guideline committees.

- Contribute constructively to meetings and have good communication and team-working skills; this should include a commitment to considering the needs of people using services, family members and carers.
- Use their background knowledge and experience of the guideline topic to advise the developer on carrying out systematic reviews and economic analyses.
- Read all relevant documentation and make constructive comments and proposals at (and between) committee meetings.
- Work with the developer and other members of the committee to develop, prepare and write the rationales for the recommendations.
- Work with the developer and other members of the committee to write up the committee's discussion of the evidence.
- Work with other members of the committee to develop recommendations based on the evidence or on consensus if evidence is poor or lacking.
- Help ensure that the guideline as a whole, and particularly the recommendations, is worded sensitively (for example, that people using services or population groups are treated as people, not as objects of assessments or interventions).
- Advise the developer on how to identify best practice in areas for which research evidence is absent, weak or equivocal.
- Consider, with other members of the committee, the feasibility of the recommendations and highlight any potential implementation issues to NICE. This may provide contextual information or inform resource impact assessment and potentially other implementation activity, including the identification of examples from practice or external support resources to assist people using the guideline (see chapter 12 of the manual).
- Agree, with other members of the committee, the minutes of committee meetings.

Committee members are not routinely expected to:

- carry out review of the evidence
- search the literature
- write up the evidence.

Additional roles for lay members of committees

Lay members of the committee have the same roles and responsibilities as other committee members, but they are also often able to offer specific expertise to:

- help ensure that review questions include issues that are important to people using services, their family members and carers, or the community affected by the guideline
- raise awareness of grey literature (for example, surveys of people using services) that highlights issues that may be relevant to the work of the committee
- indicate the extent to which published evidence has measured and taken into account outcomes that are considered important by people using services, their family members and carers, or the community affected by the guideline
- highlight areas where the guideline may need to acknowledge the choice and preferences of people using services, their family members and carers, or the community affected by the guideline
- help ensure that recommendations address issues and concerns of people using services, their family members and carers, and the public (where relevant)
- advise on the practicality of implementing the guideline (for example, medicines adherence)

Appendix D: Guideline committee Terms of Reference and Standing Orders

Terms of reference

General

1. The committee will operate as an advisory committee to NICE's Board.

2. The committee will advise NICE on:

- any development of review questions from key issues in the scope
- how to identify best practice in areas where research evidence is absent, weak or equivocal
- the effectiveness, and cost effectiveness of interventions, actions and measures to improve the health and social care of the public
- opportunities and challenges that may be faced in implementing the recommendations that might require additional resources or implementation efforts at a local level.

3. The committee will throughout guideline development:

- develop a guideline for the relevant audiences in accordance with the agreed process and methods manual
- submit its recommendations to NICE's Guidance Executive, which will have powers delegated by the Board to consider and approve the recommendations
- be accountable to the NICE director (or delegated senior member of the NICE team) responsible for the guideline
- be collectively responsible for its recommendations
- acknowledge that the intellectual property of content arising from the guideline development process belongs to NICE
- follow NICE's equality policy and take account of socioeconomic factors and their influence on health and ill health
- adhere to NICE's principles on social value judgements.

4. Individual committee members will:

- declare all relevant interests, sign a declaration of interest form and inform NICE of any additions or changes to declared interests

throughout the development process, in accordance with the declaration of interests policy for NICE advisory committees

- sign a confidentiality agreement with NICE relating to any information designated confidential by NICE, such as academic or commercial-in-confidence material or sensitive personal data.

Membership

5. Committee members will be appointed by the developer, and committee membership will reflect both the spread of interests and expertise required for the business of the committee and NICE's values of equality and diversity.

6. The chair and members of the committee will be appointed in accordance with NICE's policy on recruitment and selection to advisory bodies.

7. Committee members will be drawn from the NHS, local government, the academic community and other areas, as appropriate, as agreed by the developer and NICE staff with responsibility for guideline quality assurance. They will include practitioners, commissioners and providers, people using services, their family members and carers, and advocates.

8. The committee will have a minimum of 7 voting members with additional members agreed on a topic-by-topic basis according to need. Each committee will have a chair. Topic-specific committees may have a topic adviser, and will include professional and practitioner members, and lay members. Standing committees will have core members and topic expert members. All committee members are selected for their expertise and not as representatives of their organisations.

9. Co-opted members may be included as additional members of a committee for 1 or more specific meetings. Co-opted members are part of the committee, join in discussion and contribute to formulating the recommendations. However, they are not full members, do not have voting rights and do not count towards the quorum.

10. Expert witnesses may be invited to attend and advise the committee on specific topics and can be drawn from a wide range of areas as appropriate. They are invited to present their evidence in the form of expert testimony and are asked to provide a written paper, or to agree a summary of their evidence recorded by the developer.

They also help the committee to consider and interpret the evidence, but they are not members of the committee so they should not be involved in the final decisions or influence the wording of the recommendations. Expert witnesses have no voting rights and do not count towards the quorum.

Standing orders

General

11. These Standing Orders describe the procedural rules for managing the work of the committee as agreed by NICE. The committee will act as an advisory body to NICE. Nothing in these Standing Orders shall limit compliance with NICE's Standing Orders so far as they are applicable to these Bodies.

12. The appointment of advisory committees is at the discretion of the Board subject to any direction as may be given by the Secretary of State.

13. Members of the committee shall be bound by these Standing Orders and will be expected to abide by the 7 principles for the conduct of public life as recommended by the Nolan Committee, which are:

- selflessness
- integrity
- objectivity
- accountability
- openness
- honesty
- leadership.

14. Other members who may be co-opted to the committee from time to time at the discretion of the committee shall be subject to the same principles.

15. Behaviour by committee members and attendees at committee meetings such as bullying, harassment and victimisation is unacceptable to NICE. NICE is committed to taking the necessary action to ensure that such behaviour does not occur, and to taking the appropriate action in the event that it does occur.

16. For **topic-specific committees**, the chair and members of the committee will be appointed for the duration of the development of the guideline. Alternatively, a standing chair will be appointed for an initial period of up to 3 years. This may be extended by mutual agreement to a further term of up to 3 years and up to a maximum term of office of 10 years.

17. For **standing committees**, the chair and core members will be appointed for an initial period of up to 3 years. This may be extended by mutual agreement to a further term of up to 3 years and up to a maximum term of office of 10 years.

18. For standing committees, when a committee member is appointed chair of the committee of which they are a member, it will count as a new appointment.

19. For standing committees, the topic expert members are usually recruited for a specific guideline, but may be appointed for up to 3 years so that they can work on subsequent guidelines. They are recruited in accordance with NICE's policy on committee recruitment.

20. The removal or substitution of committee members and the general constitution of an advisory committee shall be at the discretion of NICE.

21. All reasonable facilities shall be provided for members to ensure that they have the opportunity to participate fully and equitably in the business of committees.

Interpretation

22. During the course of a committee meeting, the chair of the committee can suspend the meeting to seek advice from senior members of NICE with responsibility for guideline quality assurance on the final interpretation of the Standing Orders.

23. Statements of committee members made at meetings shall be relevant to the matter under discussion at the time and the decision of the chair on questions of order, relevancy and interpretation (including conflicts of interest) shall be final.

Chairs and vice-chairs

24. Meetings will be conducted by the chair or in their absence, an officially appointed vice-chair or a nominated deputy.

25. The vice-chair will be appointed in accordance with NICE's policy on committee recruitment.

26. The vice-chair's appointment will be for the duration of guideline development for topic-specific committees, or for a three year term for standing committees.

27. In standing committees, if a committee member has been appointed to vice–chair from within the committee, the new term will count against the 10-year total. For example, if a member serves one 3-year term and is then appointed to vice-chair for another 3-year term, this will be regarded as having served 6 years as a member of the committee.

28. The chair, or the vice-chair or deputy nominated by the chair in the chair's absence, may take action on behalf of the committee outside of scheduled committee meetings when urgent decisions are required and it is impracticable to convene a special meeting of the committee.

29. In committee meetings, the chair:

- ensures that committee members declare any new conflicts of interest that have arisen since their last declaration and handles any conflicts as they arise, in line with the declaration of interests policy for NICE advisory committees
- steers the discussions according to the agenda
- keeps the group discussion unified and discourages disruption or dominance by any members
- encourages constructive debate, without forcing agreement
- prevents repetitive debate
- summarises the main points and key decisions from the debate
- signs off meeting minutes once approved by the committee.

30. The chair must ensure that NICE's equality policy and principles on social value judgements are adhered to. The chair approves the equality impact assessment at scoping and final guideline stages.

31. The chair approves the draft guideline before sign-off by NICE, and advises the developer on responses to stakeholder comments as appropriate.

Voting

32. The decisions of the committee will normally be arrived at by a consensus of committee members present. Voting will only be used for decision-making in exceptional circumstances. Before a decision to move to a vote is made, the chair will, in all cases, consider whether continuing the discussion at a subsequent meeting is likely to lead to consensus.

33. Voting will be anonymous and decisions determined by a simple majority of non-conflicted committee members present at a quorate meeting.

34. The chair of the committee will be included in the vote, and in the event of there being an equality of votes the chair will have a second, casting vote.

35. Only committee members present at the meeting will be eligible to vote. There will be no proxy voting.

36. Co-opted members, expert witnesses, developer staff, NICE staff and observers will not be eligible to vote.

Quorum

37. The quorum is set at 50% of the full membership of the committee, in accordance with paragraph 3 in the membership section of these terms of reference, and includes both core and topic expert members and the chair (but excludes co-opted members, expert witnesses, developer staff, NICE staff and observers). The quorum should be rounded up to the next whole number when there is an odd number of committee members.

38. No recommendations should be confirmed unless the meeting is quorate. This provision also applies if a member is excluded because of a conflict of interest and as a result membership falls below the quorum. At the discretion of the chair on advice from a senior member of NICE staff, a meeting may proceed if it is not quorate on the basis that any recommendations formulated or decisions made are considered draft and are shared with the full committee for comment and approval.

39. The balance of the committee are such that even if the meeting is quorate, an appropriate spread of members' interests should be represented at each meeting. It is also important that for standing committees the mix of core and topic expert members is appropriate, and topic expert members are not in a majority. If, in the view of the chair, the spread of interests is insufficient for the business under consideration, the meeting or part of the meeting may be suspended or adjourned until a later date.

Collective responsibility

40. All members of the committee shall abide by the principle of collective responsibility, stand by the recommendations of the committee and not speak against them in public.

41. Members of the committee are not permitted to submit comments as stakeholders during the consultation on the draft guideline (see chapter 10 of the manual). If a committee member is involved with a registered stakeholder organisation, they should not submit comments during the consultation on behalf of that organisation – someone else in the organisation should draft and submit the comments.

Confidentiality

42. On appointment, committee members (including co-opted members) will be required to sign a confidentiality agreement with NICE relating to any information designated confidential by NICE such as academic or commercial-in-confidence material or sensitive personal data.

43. Confidential papers and confidential information disclosed in committee deliberations should not be discussed with colleagues who are not members of the committee, with other organisations, the media, or members of the committee who are excluded from discussions because of a conflict of interest.

44. If committee members are asked by external parties – including stakeholders or their professional organisation – to provide information about the work of the committee, they should discuss the request with the developer. They should also declare this at the next committee meeting. Any enquiries from the media should be

directed immediately to NICE's enquiry handling team (nice@nice.org.uk) and the developer.

45. Co-opted members, expert witnesses and observers invited by the committee will sign a confidentiality form if confidential information is included in meeting papers, or if attending part of a meeting where confidential information is being discussed.

Arrangements for meetings

46. NICE will ensure that committee meetings take place in venues that are accessible to, and have facilities for, disabled people.

47. Meetings of the Committee shall be held at such times and places as are deemed necessary to facilitate the conduct of its business.

48. Committee members may also be required to attend a working group that may be associated with the committee and will be expected to contribute to virtual discussions and occasional teleconferences as appropriate.

49. Developers shall determine which aspects shall appear on every agenda in advance of each meeting.

50. Any other business shall be discussed at the discretion of the chair.

51. Meetings will normally begin at 10:00 am and finish no later than 5:00 pm unless otherwise advised.

52. Committee members will be expected to attend for the full day unless agreed in advance with the chair or unless they have declared a conflict of interest to 1 or more discussions.

53. Laptops and other devices are to be used in a committee meeting by members solely to conduct the business of the meeting.

54. The developer will make all reasonable attempts to agree each meeting date well in advance and committee members are expected to keep proposed dates free until they are confirmed.

Access by members of the public

55. When committee meetings are open to the public, the following provisions will apply.

56. Public access will be enabled to meetings of standing committees; topic-specific committees will be held in private.

57. If considered necessary because of the confidential nature of the business to be transacted, the agenda for meetings held in public will be divided into 2 parts. Part 1 will be open to the public and part 2 will be closed to the public to enable the committee to discuss confidential information whereupon Standing Orders 61 and 65 will apply.

58. Only members of the committee and NICE staff, co-opted members, observers invited by NICE, and the developer will be present for part 2 of the meeting. However, at the discretion of the chair, experts such as practitioners, people using services, their family members or carers, and manufacturers may be invited to remain in order to discuss confidential or personal medical information that was not discussed in part 1. Once the information concerned has been discussed, the experts will leave the meeting and will take no further part in its deliberations.

59. Usually 20 working days before each committee meeting held in public, a public notice of the time and place of the meeting, along with the public part of the agenda, shall be displayed on NICE's website. The final agenda will be displayed on the NICE website usually 5 working days before the meeting.

60. The public and representatives of the press shall be allowed access to observe all formal meetings of the committee for part 1 of the agenda but shall not be entitled to ask questions or otherwise engage in the business of the committee.

61. The public and representatives of the press shall be excluded from part 2 of the committee meeting upon the chair moving the following motion:

- "That representatives of the press and other members of the public be excluded from the remainder of this meeting having regard to the confidential nature of the business to be transacted, publicity in which

would be prejudicial to the public interest" [section 1(2) Public Bodies (Admissions to Meetings) Act 1960].

62. Notwithstanding the above, the chair will have the discretion to adjourn the meeting at any time if the presence of the public or representatives of the press is considered prejudicial to the effective conduct of the business of the meeting upon moving the following motion:

- 'That in the interests of public order the meeting adjourn for (the period to be specified by the chair) to enable the Committee to complete business without the presence of the public' [section 1(8) Public Bodies (Admission to Meetings) Act 1960].

Other observers

63. NICE staff and invited guests (for example, visiting academics) may attend committee meetings as observers, with the permission of the chair.

64. Observers do not need to register via NICE's website. Observers should not sit with members of the public and should not enter into committee discussions unless invited to do so by the chair.

65. Observers can attend part 2 of meetings held in public if the chair and centre director agree. Observers who are not NICE or developer staff or are not commissioned to provide a service to NICE should sign a confidentiality agreement if they wish to attend a topic-specific committee meeting or part 2 of a meeting held in public.

Minutes

66. The draft minutes of the committee meetings shall be drawn up and submitted to the next meeting for approval by the committee. The minutes of the final committee meeting will be circulated and approved by email.

67. The approved minutes will be published on NICE's website subject to the redaction of any confidential or otherwise exempt material within 20 working days of approval.

Declarations of interest

68. Anybody applying to be a member of a NICE advisory committee must declare any interests as part of the application process, in line with the declaration of interests policy for NICE advisory committees.

69. All standing committee members must make an annual declaration of interests in line with the declaration of interests policy for NICE advisory committees.

70. All committee members must declare in writing before and orally at the start of each committee meeting any interests that are relevant, or could be perceived to be relevant, to the work of the committee. Declarations of interest will be recorded in the minutes and published on the NICE website.

71. During the course of the meeting, if a conflict of interest arises with matters under consideration, the member concerned must withdraw from the meeting, or part thereof, as appropriate.

72. Experts invited to provide expert testimony, and co-opted members will make a declaration of interest before committee meetings and in accordance with declaration of interests policy for NICE advisory committees. This declaration will be reaffirmed again at the start of each meeting. These will be recorded in the minutes and published on the NICE website.

73. Co-opted members will not be able to take part in a meeting if they have a conflict of interests. Expert witnesses may still be asked to give their evidence if they have a conflict of interest, but this will be at the discretion of the developer and NICE staff with a responsibility for quality assurance.

Suspension of Standing Orders

74. Except where this would contravene any statutory provision, any 1 or more of the Standing Orders may be suspended at any meeting. This should be agreed with the developer and NICE staff with responsibility for quality assurance, and a simple majority of those present and eligible to participate should vote in favour of the suspension.

75. Any decision to suspend Standing Orders shall be recorded in the minutes of the meeting.

76. No formal business may be transacted while Standing Orders are suspended.

77. NICE's Audit Committee shall review all decisions to suspend Standing Orders.

Petitions

78. Petitions from the public will not be received directly by or responded to by the committee. Anyone wishing to present a petition will be directed to NICE staff with responsibility for guideline quality assurance.

Recording of meetings

79. The recording of proceedings or the taking of pictures at committee meetings by public attendees is not allowed.

80. The recording of meetings is permitted by the developer where agreed by the committee, and for the purposes of facilitating guideline development or promoting transparency. Recordings will be deleted on approval of the meeting minutes.

Record of attendance

81. A record will be kept of committee members' attendance at committee meetings via the minutes.

82. Members of standing committees are expected:

- to attend at least 75% of their committee's meetings during a 12-month period
- not to miss more than 2 consecutive committee meetings.

83. Members of topic-specific committees are expected:

- to attend all of their committee's meetings.

84. If committee members are unable to attend a committee meeting, deputies are not permitted.

85. Members who are unable to meet either of these expectations may be asked to stand down from the committee in accordance with Standing Order 20.

86. If a committee member is unable to fulfil their duties (for example, because of illness), another recruitment process may be considered to replace that person.

Terms of Reference

78. Committee members must comply with the Terms of Reference that set out the scope of the committee's work and its authority.

Review of Terms of Reference and Standing Orders

85. These Terms of Reference and Standing Orders will be reviewed every 3 years.

Appendix E: Code of conduct for committee members

This code sets out the responsibilities of NICE and the committee, and the principles of transparency and confidentiality. The following principles should be read alongside the Terms of Reference and Standing Orders.

Key principles of guideline development

NICE's guideline development process:

- uses the best available evidence and robust and transparent methods to develop recommendations that are clearly written
- involves people affected by the guideline (including stakeholder organisations that represent the interests of people using services, their family members and carers, and the community, bodies that represent professionals and practitioners working in health and social care, local authorities, providers and commissioners of care and services, commercial industries and research bodies)
- advances equality based on NICE's social value judgements
- considers the feasibility of implementing the recommendations.

Each committee should ensure that its guideline is developed in line with these requirements. It should also ensure that the guideline cross-refers to or incorporates any relevant recommendations from NICE's other guidance programmes (for example, technology appraisal or interventional procedure guidance) as set out in the guideline scope (see chapter 8 of the manual). It should also consider recommendations from relevant national policy. The committee should also follow the principles set out in NICE's principles on social value judgements and adhere to NICE's equality policy.

Status of committee members

Committee members are appointed to a committee by virtue of their relevant experience or because they have specific technical skills or knowledge. If members are from stakeholder organisations, NICE and the committee assume that these members bring this perspective to the group, but are not representing their organisations. For topic-specific committees, chairs and members are appointed for the period of development of a guideline. Standing committee chairs and core members are appointed for a 3-year period, with membership subject to renewal for

a period of up to 10 years. Topic expert members of standing committees are appointed for the period of development of a guideline.

Committee members are co-authors of the guideline although the intellectual property of content arising from the guideline development process belongs to NICE. As such, they should respect the rights of NICE both to publish the final guideline and associated products (for example, products to support implementation) and they should notify NICE of any proposed publications related to their work on the guideline.

Responsibilities of NICE and committee members

NICE undertakes to ensure that:

- the committee is properly resourced to produce the guideline
- all members of the committee are provided with appropriate access to available resources
- the support needs of all members of the committee are met to enable them to contribute fully to the work of the committee
- appropriate training is offered to committee members to enable them to play a full part in the development of the guideline
- committee members are provided with feedback and comment on their contribution when requested for revalidation or personal development
- technical support is provided during the development of the guideline.

Committee members undertake to:

- set aside enough time to attend committee meetings and properly inform the development of the guideline through their personal and professional knowledge
- raise any concerns about process or details in the draft guideline with the committee, and try to resolve these issues within the committee, with support from the developer
- contribute positively to the work of the committee and the development of the guideline
- take full account of the evidence in developing recommendations

- consider the analysis and interpretation of evidence prepared by the evidence review team
- act in a professional manner, show good manners and be courteous to colleagues and staff at all times (committee members should behave in a polite, efficient and respectful manner and without bias or favour, using the highest standards of conduct expected in public life and service while on NICE duty)
- be impartial and honest in the conduct of their official business, use public funds entrusted to them to the best advantage of NICE and do nothing that is deliberately intended to damage the confidence of the public or stakeholders in NICE
- ensure that there is rigorous adherence to NICE's social value judgements and equality policy
- read and adhere to NICE's policies on hospitality, declarations of interest and travel and subsistence.

Transparency

NICE believes that its guidelines will be more meaningful if those who are intended to benefit from them and those who have the responsibility for implementing them have had the opportunity to be involved in their development.

The guideline development process is designed to be transparent. However, information and discussions may be restricted when material has been provided under agreement of commercial or academic confidentiality. There is therefore a need for arrangements that protect the confidentiality of documents and discussions. In order to protect confidentiality, NICE expects committee members:

- to regard the discussions held in any closed committee sessions as confidential
- not to discuss confidential papers and confidential information disclosed in committee discussions with colleagues who are not members of the committee, colleagues within their own organisation, other organisations, the media, or members of the committee who are excluded from discussions because of a conflict of interest

- to respect the confidentiality of documents supporting published or in development NICE guidance, including guidance from other NICE programmes, if such documents are received by the committee.

Bullying, harassment and victimisation are unacceptable. NICE is committed to taking the necessary action to ensure that they do not occur, or if they do occur that they are dealt with appropriately.

Appendix F: Suggested sources for scoping

Type of information	Source
NICE guidance and products	• NICE website – published and in development
Other guidance and standards	• Evidence Search (NICE Evidence Services) • Trip Database • Clinical Knowledge Summaries • Websites of national organisations (e.g. NHS England, Public Health England, Social Care Institute for Excellence (SCIE)) • Royal college/professional body websites • Charity, and other community and voluntary sector websites (including equality organisations, for example, Race Equality Foundation's Better Health briefings) • Patient and service user organisation websites (NICE's Public Involvement Programme (PIP) can advise further)
Guidelines, reviews and economic evaluations	• Cochrane Database of Systematic Reviews (CDSR) • Scottish Intercollegiate Guideline Network (SIGN) • The Campbell Collaboration • Database of Abstracts of Reviews of Effects (DARE) – last updated Dec 2014 • Health Technology Assessment (HTA) database – last updated October 2016 • International Guideline Library • Guidelines International Network • US National Guidelines Clearinghouse • Health Evidence • National Institute for Health Research Health Technology Assessment Programme • Prospero • NHS Economic Evaluation Database (NHS EED) – last updated Dec 2014 • Bibliographic databases (where required)
Information on current practice	• Care Quality Commission • Regulation and Quality Improvement Authority

	• NHS Digital • MHRA • National Clinical Audit and Patient Outcomes Programme (NCAPOP) • National Audit Office • NHS England • NHS Improvement • Nuffield Trust • Bibliographic databases (where required)
Information on the experiences of patients, service users and carers, or the target population	• Websites/databases of people's experiences of health and social care (for example, Healthtalk.org, Youthhealthtalk.org, PatientVoices Healthwatch) The Patient Experience Library, National Voices • Patient and service user organisation websites (NICE's PIP can advise further) • Bibliographic databases (where required)
Policy and legislation	• Government and other policy websites (for example, legislation.gov.uk) • Regulatory authority websites (for example, General Dental Council, General Medical Council)
Statistics	• Faculty of Public Health • NHS Digital • UK Data Service • Office for National Statistics • Disease-specific statistics, for example, CancerStats • Patient registries (for example, UK Cystic Fibrosis Registry)

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Appendix G: Sources for evidence reviews

The selection of sources to search for evidence reviews should be determined by the subject of the review question and the type of evidence sought (see chapter 5 of the manual).

The following list is not exhaustive and other sources may be appropriate. To aid the selection of sources, the databases have been listed according to the primary focus of the subject coverage, but note many databases cover more than one subject.

The sources listed in appendix F should also be considered for evidence review searches.

Databases

Biomedical

- British Nursing Index (BNI)
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Cochrane Database of Systematic Reviews (CDSR)
- Cumulated Index to Nursing and Allied Health Literature (CINAHL)
- Database of Abstracts of Reviews of Effects (DARE) – last updated December 2014
- Embase
- Health Technology Assessment (HTA) – last updated October 2016
- MEDLINE/MEDLINE in Process

Economics

- EconLit
- NHS Economic Evaluation Database (NHS EED) – last updated December 2014
- CEA Registry
- Paediatric Economic Database Evaluation (PEDE)
- Health Technology Assessment (HTA) database
- ScHARR Health Utilities Database (HUD)
- Websites of HTA agencies
- RePEc (Research Papers in Economics)

Education

- British Education Index (BEI)
- Educational Information Resources Center (ERIC)

Management

- Health Business Elite
- Health Management Information Consortium (HMIC)

Psychology

- PsycINFO

Sociology and social care

- Applied Social Science Index and Abstracts (ASSIA)
- CareKnowledge
- Social Care Online
- Social Policy and Practice
- Social Science Citation Index
- Social Services Abstracts
- Social Welfare Portal (British Library)
- Sociological Abstracts

Other

- Allied and Complementary Medicine (AMED)
- Campbell Collaboration
- Database of Promoting Health Effectiveness Reviews (DoPHER)
- Physiotherapy Evidence Database (PEDro)
- SportDiscus
- Transport
- Trials Register of Promoting Health Interventions (TRoPHI)
- Greenfile

Websites

- Websites of national organisations, e.g. Care Quality Commission, Department of Health, NHS England, Public Health England, MHRA
- Websites of professional bodies and other organisations relevant to the topic

- Websites of research institutes and consultancies relevant to the topic
- NICE Evidence Search
- Trip
- Kings Fund
- OpenGrey
- European Medicines Agency
- US Food & Drug Administration
- Healthtalk.org
- Youthhealthtalk.org
- The Patient Experience Library
- National Voices
- Ipsos MORI
- Joseph Rowntree Foundation
- School for Social Care Research
- OPM
- Personal Social Services Research Unit (PSSRU)
- Picker Institute
- Social Policy Research Institute
- Websites of other organisations for people using services, including the target population, family members and carers

Conference abstracts

- Embase
- British Library Inside Conferences (BLIC)
- Google Scholar
- Conference websites relevant to the topic

Ongoing trials

- ClinicalTrials.gov
- EudraCT
- ISRCTN Registry
- WHO ICTRP

Institutional and thesis repositories

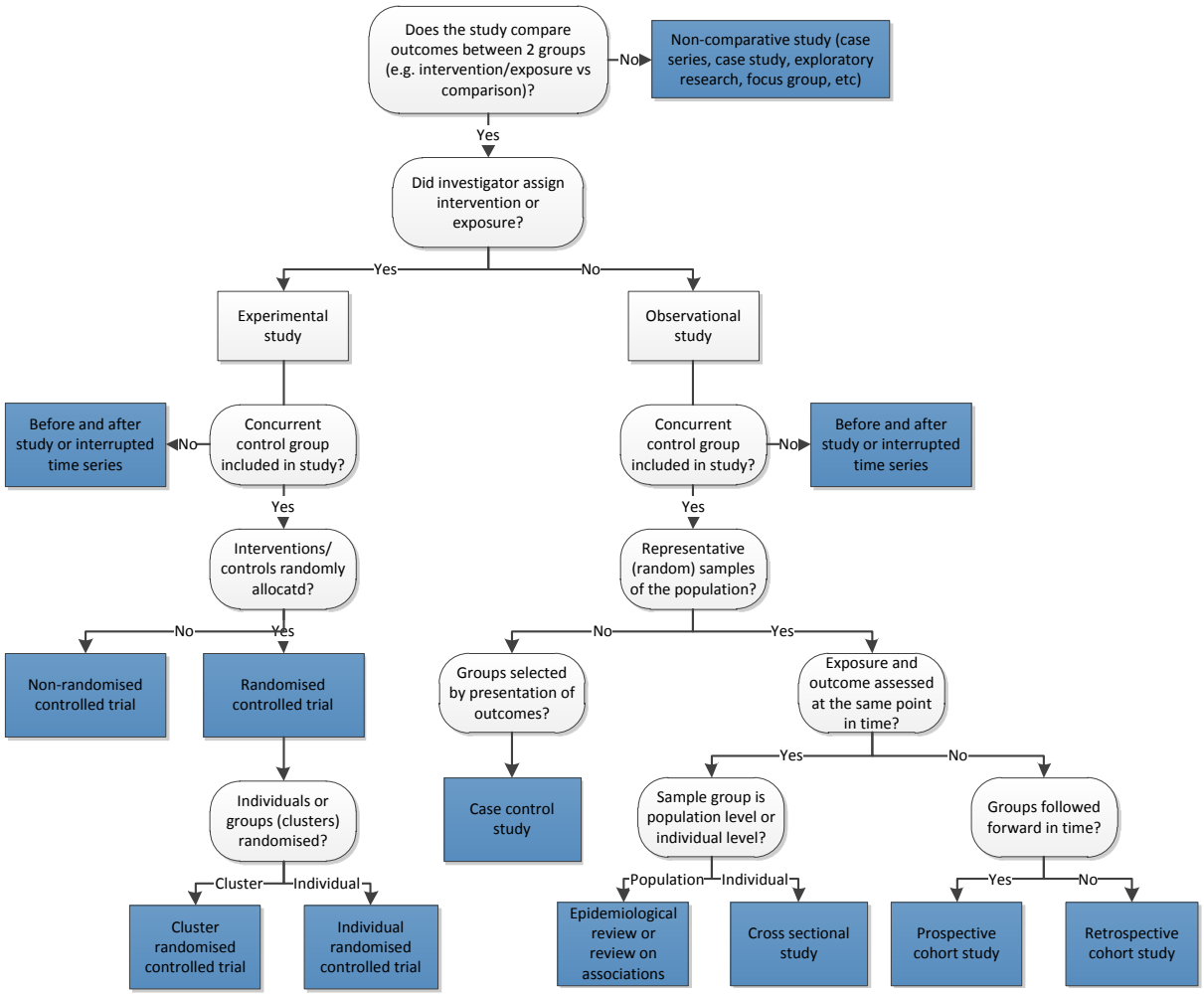
- CORE
- OpenDOAR (The Directory of Open Access Repositories)
- EThOS (British Library)
- Open Access Theses and Dissertations (OATD)

Appendix H Appraisal checklists, evidence tables, GRADE and economic profiles

This aims to give examples of checklists that can be used to assess risk of bias or quality of studies when developing guidelines. NICE has some preferred checklists as a result of external collaborations and the endorsement of GRADE. These preferred checklists are indicated in this appendix. However, where the preferred checklist is not appropriate to address a particular review question, other appropriate checklist should be used according to the specific review question. The reasons for using other non-preferred checklists should be provided in the review protocol (see section 4.5 in the manual). The checklist should allow assessment of those features considered important – these may be study design specific or specific to the topic. As such, additional items may need to be included, or minor modification made. Where this is the case, this should be documented, and agreed with members of NICE staff with responsibility for quality assurance.

Algorithm for classifying quantitative (experimental and observational) study designs

The algorithm below can be used to classify quantitative study designs and guide decisions about which checklist should be used.



Quantitative review question

Appraisal checklists: Intervention studies - systematic reviews and meta-analyses

(Preferred) ROBIS http://www.bristol.ac.uk/media-library/sites/social-community-medicine/robis/robisguidancedocument.pdf

Amstar www.amstar.ca

DSU NMA methodology checklist http://scharr.dept.shef.ac.uk/nicedsu/wp-content/uploads/sites/7/2016/03/TSD7-reviewer-checklist.final_.08.05.12.pdf

CASP systematic review checklist
http://docs.wixstatic.com/ugd/dded87_a02ff2e3445f4952992d5a96ca562576.pdf

Appraisal checklists: Diagnostic test accuracy, clinical prediction and prognostic studies - systematic reviews and meta-analyses

(Preferred) ROBIS http://www.bristol.ac.uk/media-library/sites/social-community-medicine/robis/robisguidancedocument.pdf

Appraisal checklists: Intervention studies - randomised controlled trials (individual or cluster)

(Preferred) Cochrane RoB tool (2.0)
https://sites.google.com/site/riskofbiastool/welcome/rob-2-0-tool

Effective Practice and Organisation of Care (EPOC) RoB Tool (for randomised trial)

http://epoc.cochrane.org/resources/epoc-resources-review-authors

(Note: for complex interventions, consider the EPOC RoB Tool)

CASP RCT checklist
http://docs.wixstatic.com/ugd/dded87_40b9ff0bf53840478331915a8ed8b2fb.pdf

Appraisal checklists: Intervention studies – Non-randomised studies

A) Non-randomised controlled trials (also called clinical controlled trials)

(Preferred) Cochrane ROBINS-I
https://sites.google.com/site/riskofbiastool//welcome/home

Effective Practice and Organisation of Care (EPOC) RoB Tool (for studies with a control group) http://epoc.cochrane.org/resources/epoc-resources-review-authors

(Note: for complex interventions, consider the EPOC RoB Tool)

GATE - Effective Public Health Practice Project Quality assessment tool for quantitative studies

B) Cohort study

(Preferred) Cochrane ROBINS-I
https://sites.google.com/site/riskofbiastool//welcome/home

Effective Practice and Organisation of Care (EPOC) RoB Tool (for studies with a control group) http://epoc.cochrane.org/resources/epoc-resources-review-authors

(Note: for complex interventions, consider the EPOC RoB Tool)

CASP cohort study checklist
http://docs.wixstatic.com/ugd/dded87_e37a4ab637fe46a0869f9f977dacf134.pdf

Newcastle-Ottowa scale (for cohort study)
http://www.ohri.ca/programs/clinical_epidemiology/nosgen.pdf

Downs & Black checklist for measuring quality
http://jech.bmj.com/content/52/6/377.abstract

Quality assessment for quantitative studies www.ephpp.ca/tools.html

GRACE www.graceprinciples.org

C) Case control study

(Preferred) CASP case control checklist
http://docs.wixstatic.com/ugd/dded87_63fb65dd4e0548e2bfd0a982295f839e.pdf

Effective Practice and Organisation of Care (EPOC) RoB Tool (for studies with a control group) http://epoc.cochrane.org/resources/epoc-resources-review-authors

Newcastle-Ottowa scale (for cohort study)
http://www.ohri.ca/programs/clinical_epidemiology/nosgen.pdf

Downs & Black checklist for measuring quality
http://jech.bmj.com/content/52/6/377.abstract

D) Controlled before-and-after study

(Preferred) Effective Practice and Organisation of Care (EPOC) RoB Tool (for before-and-after study) http://epoc.cochrane.org/resources/epoc-resources-review-authors

E) Interrupted time series

(Preferred) Effective Practice and Organisation of Care (EPOC) RoB Tool (for interrupted time series study) http://epoc.cochrane.org/resources/epoc-resources-review-authors

F) Cross sectional study

(Preferred) JBI checklist for cross sectional study
https://joannabriggs.org/assets/docs/critical-appraisal-tools/JBI_Critical_Appraisal-Checklist_for_Analytical_Cross_Sectional_Studies.pdf

AXIS http://bmjopen.bmj.com/content/6/12/e011458

G) Historical controlled/retrospective cohort study

(Preferred) Cochrane ROBINS-I
https://sites.google.com/site/riskofbiastool//welcome/home

Effective Practice and Organisation of Care (EPOC) RoB Tool (for studies with a control group) http://epoc.cochrane.org/resources/epoc-resources-review-authors

(Note: for complex interventions, consider the EPOC RoB Tool)

CASP cohort study checklist
http://docs.wixstatic.com/ugd/dded87_e37a4ab637fe46a0869f9f977dacf134.pdf

Newcastle-Ottowa scale (for cohort study)
http://www.ohri.ca/programs/clinical_epidemiology/nosgen.pdf

H) Case series (uncontrolled longitudinal study)

(Preferred) Institute of Health Economics (IHE) checklist for case series
http://www.ihe.ca/publications/ihe-quality-appraisal-checklist-for-case-series-studies

JBI checklist for case series https://joannabriggs.org/assets/docs/critical-appraisal-tools/JBI_Critical_Appraisal-Checklist_for_Case_Series.pdf

NIH tool for case series studies https://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardiovascular-risk-reduction/tools/case_series

Appraisal checklists: Diagnostic test accuracy studies

Note: This is for diagnostic test accuracy (DTA) review (using cross sectional study, cohort study or case control study design) where a typical 2x2 table is used to collect data on TP, FP, TN, FN. No univariate or multivariate regression analysis is conducted.

(Preferred) QUADAS-2 http://www.bristol.ac.uk/population-health-sciences/projects/quadas/quadas-2/

CASP diagnostic test accuracy checklist
http://docs.wixstatic.com/ugd/dded87_3815f02af1b34c21b8c3b2b5020024c3.pdf

Appraisal checklists: Clinical prediction studies for a prognosis or diagnosis

Note: This is for clinical prediction rule/model (CPM) for a prognosis or a diagnosis (see TRIPOD statement for classifications: https://www.equator-network.org/reporting-guidelines/tripod-statement/), these studies often used cohort, cross sectional and case control study design accompanied by multivariate regression modelling.

Examples for CPM for a prognosis: QAdmission, PREDICT, risk-prediction model for falls, etc.

Examples for CPM for a diagnosis: QCancer, QRISK, Framingham Risk Score, etc.

(Preferred) PROBAST – In development

CASP clinical prediction rule checklist
http://docs.wixstatic.com/ugd/dded87_a2f74f6cd2f24bd684bb26efe7ad7196.pdf

Cochrane CHARMS

http://methods.cochrane.org/sites/methods.cochrane.org.prognosis/files/public/uploads/CHARMS%20checklist.pdf

Appraisal checklists: Prognostic studies

Note: this is for simple association studies for particular risk factor(s)/variable(s) and its associations with a prognosis (with simple correlational analysis or univariate regression analysis). These studies often used cohort, cross sectional and case control study design.

(Preferred) QUIPS checklist

http://methods.cochrane.org/sites/methods.cochrane.org.prognosis/files/public/uploads/QUIPS%20tool.pdf

Appraisal checklists: Prevalence/incidence studies or epidemiological studies

(Preferred) JBI checklist for prevalence studies

https://joannabriggs.org/assets/docs/critical-appraisal-tools/JBI_Critical_Appraisal-Checklist_for_Prevalence_Studies.pdf

Appraisal checklists: Other quantitative studies

A) Cross sectional survey/survey questionnaire study

(Preferred) CEBM checklist https://www.cebma.org/wp-content/uploads/Critical-Appraisal-Questions-for-a-Survey.pdf

Boynton & Greenhalgh checklist (see Box A.4)

http://onlinelibrary.wiley.com/doi/10.1002/9780470987407.app2/pdf

The BMJ checklist

http://www.bmj.com/content/suppl/2004/05/27/328.7451.1312.DC1

Roever checklist https://www.omicsonline.org/open-access/critical-appraisal-of-a-questionnaire-study-ebmp-1000e110.php?aid=70356

B) Other studies on associations (other than for clinical diagnosis and prognosis)

Note: examples: the relationship between gender, age and exercise; the relationship between city/non-city dwelling and aggressive driving behaviour; the relationship between social economic status and sedentary lifestyle, etc. These studies usually used cohort, cross sectional and case control study design.

(Preferred) Newcastle-Ottowa scale
www.ohri.ca/programs/clinical_epidemiology/oxford.asp

Cochrane EPOC risk of bias tool (for studies with a controlled group)
http://epoc.cochrane.org/resources/epoc-resources-review-authors

Downs & Black checklist for measuring quality
http://jech.bmj.com/content/52/6/377.abstract

Quality assessment for quantitative studies www.ephpp.ca/tools.html

Qualitative review question

Note: CERQual (http://www.cerqual.org/publications/) is for qualitative evidence synthesis and presentation after quality assessment of individual studies has been conducted.

(Preferred) CASP qualitative checklist
http://docs.wixstatic.com/ugd/dded87_29c5b002d99342f788c6ac670e49f274.pdf

Cochrane qualitative checklist http://methods.cochrane.org/qi/supplemental-handbook-guidance

JBI checklist for qualitative research https://joannabriggs.org/assets/docs/critical-appraisal-tools/JBI_Critical_Appraisal-Checklist_for_Qualitative_Research.pdf

Quality Framework: Cabinet Office checklist for social research
http://webarchive.nationalarchives.gov.uk/20140402165901/http://www.civilservice.gov.uk/wp-content/uploads/2011/09/a_quality_framework_tcm6-7314.pdf

(Note: consider the Cabinet Office checklist if the study is specific for qualitative 'evaluation' concerned with the development and implementation of social policy, programmes and practice)

Appraisal checklists: economic evaluations

This checklist can be used to determine whether an economic evaluation provides evidence that is useful to inform the decision-making of the Committee (see chapter 7). It judges the applicability of the study and the limitations.

The robustness of the study results to methodological limitations may sometimes be apparent from reported sensitivity analyses. If not, judgement will be needed to assess whether a limitation would be likely to change the results and conclusions. The judgements should be recorded and presented in the guideline. The 'comments' column in the checklist should be used to record reasons for these judgements, as well as additional details about the studies where necessary.

If this checklist is not considered appropriate, other economic evaluation checklists, such as CHEERS, can be used.

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

Checklist: economic evaluations

Study identification Include author, title, reference, year of publication		
Guidance topic:		**Question no:**
Checklist completed by:		
Section 1: Applicability (relevance to specific review questions and the NICE reference case as described in section 7.5) This checklist should be used first to filter out irrelevant studies.	**Yes/partly/no/unclear/NA**	**Comments**
1.1 Is the study population appropriate for the review question?		

1.2 Are the interventions appropriate for the review question?		
1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?		
1.4 Are the perspectives for costs appropriate for the review question?		
1.5 Is the perspective for outcomes appropriate for the review question?		
1.6 Are all future costs and outcomes discounted appropriately?		
1.7 Are QALYs, derived using NICE's preferred methods, or an appropriate social care-related equivalent used as an outcome? If not, describe rationale and outcomes used in line with analytical perspectives taken (item 1.4 above).		
1.8 If applicable, are costs and outcomes from other sectors fully and appropriately measured and valued?		
1.9 **Overall judgement:** Directly applicable/partially applicable/not applicable There is no need to use section 2 of the checklist if the study is considered 'not applicable'.		
Other comments:		
Section 2: Study limitations (the level of methodological quality) This checklist should be used once it has been decided that the study is sufficiently applicable to the context of the guideline	**Yes/partly/no/unclear/NA**	**Comments**
2.1 Does the model structure adequately reflect the nature of the topic under evaluation?		
2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?		
2.3 Are all important and relevant outcomes included?		
2.4 Are the estimates of baseline outcomes from the best available source?		
2.5 Are the estimates of relative intervention effects from the best available source?		
2.6 Are all important and relevant costs included?		

2.7 Are the estimates of resource use from the best available source?		
2.8 Are the unit costs of resources from the best available source?		
2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?		
2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?		
2.11 Has no potential financial conflict of interest been declared?		
2.12 **Overall assessment:** Minor limitations/potentially serious limitations/very serious limitations		
Other comments:		

If the economic evaluation is a cost-benefit analysis [CBA], the following questions should also be addressed:

1. Are money-costs and 'benefits' which are savings of future money-costs evaluated?

2. Have all important and relevant costs and outcomes for each alternative been quantified in money terms?
If not, state which items were not quantified, and the likely extent of their importance in terms of influencing the benefit/cost ratio.

3. Has at least 1 of net present value, benefit/cost ratio and payback period been estimated?

4. Were any assumptions of materiality made? That is, were any items where costs and/or benefits were sufficiently small that their addition to the analysis would not have changed any recommendations in the guidelines?

Cost-consequences analysis [CCA] is used primarily for public health and social care interventions which report a diverse range of outcomes in discrete categories that cannot be aggregated into a single metric. It may also be used to either supplement a cost-utility analysis [CUA], where important relevant outcomes would be excluded,

or as a necessary first step to conducting a CBA. If the economic evaluation is a CCA, the following questions should also be addressed:

1. Have all important and relevant costs and outcomes for each alternative been quantified, where appropriate?
If not, state which items were not quantified.
Were they still used in the CCA and how were they used?

2. Were any assumptions of materiality made to restrict the number of consequences considered? That is, were any items where costs and/or benefits were sufficiently small that their addition to the analysis would not have changed any recommendations in the guidelines?

3. Was any analysis of correlation between consequences carried out to help control for double counting?

4. Was there any indication of the relative importance of the different consequences by a suggested weighting of them?

5. Were there any theoretical relationships between consequences that could have been taken into account in determining weights?

6. Were the consequences considered one by one to see if a decision could be made based on a single consequence or a combination of a small number of consequences?

7. Were the consequences considered in subgroups of all the consequences in the analysis to see if a decision could be made based on a particular subgroup?

Notes on use of the checklist: economic evaluations

For all questions:

- answer ‘yes’ if the study fully meets the criterion
- answer ‘partly’ if the study largely meets the criterion but differs in some important respect
- answer ‘no’ if the study deviates substantively from the criterion

- answer ‘unclear’ if the report provides insufficient information to judge whether the study complies with the criterion
- answer ‘NA (not applicable)’ if the criterion is not relevant in a particular instance.

For ‘partly’ or ‘no’ responses, use the comments column to explain how the study deviates from the criterion.

Section 1: Applicability

1.1 Is the study population appropriate for the review question?

The study population should be defined as precisely as possible and should be in line with that specified in the guidance scope and any related review protocols.

This includes consideration of appropriate subgroups that require special attention. For many interventions, the capacity to benefit will differ for participants with differing characteristics. This should be explored separately for each relevant subgroup as part of the base-case analysis by the provision of estimates of effectiveness and cost effectiveness. The characteristics of participants or communities in each subgroup should be clearly defined and, ideally, should be identified on the basis of an a priori expectation of differential effectiveness or cost effectiveness as a result of biologically, sociologically or economically plausible known mechanisms, social characteristics or other clearly justified factors.

Answer ‘yes’ if the study population is fully in line with that in the review questions and if the study differentiates appropriately between important subgroups. Answer ‘partly’ if the study population is similar to that in the review questions but: (i) it differs in some important respects; or (ii) the study fails to differentiate between important subgroups. Answer ‘no’ if the study population is substantively different from that in the review questions.

1.2 Are the interventions/services/programmes appropriate for the review question?

All relevant alternatives should be included, as specified in the guidance scope and any related review protocols. These should include routine and best practice in UK settings, existing NICE guidance and other feasible options.

Answer ‘yes’ if the analysis includes all options considered relevant for the review question, even if it also includes other options that are not relevant. Answer ‘partly’ if the analysis omits 1 or more relevant options but still contains comparisons likely to be useful for the guidance. Answer ‘no’ if the analysis does not contain any relevant comparisons.

1.3 Is the system in which the study was conducted sufficiently similar to the current UK context?

This relates to the overall structure of the system within which the interventions were delivered. For example, an intervention might be delivered on a residential basis in one country whereas in the UK it would be provided in the community. This might significantly influence the use of resources and costs, thus limiting the applicability of the results to a UK setting. In addition, old UK studies may be severely limited in terms of their relevance to current practice.

Answer ‘yes’ if the study was conducted within the UK and is sufficiently recent to reflect current practice. For non-UK or older UK studies, answer ‘partly’ if differences in the setting are unlikely to substantively change the cost-effectiveness estimates. Answer ‘no’ if the setting is so different that the results are unlikely to be applicable in the current UK context.

1.4 Are the perspectives for costs appropriate for the review question?

The appropriate perspective will depend on the reference case that is relevant for a particular guideline or review question (see NICE Chapter 7 of the guidelines manual), essentially the decision-making perspective determines the range of costs that should be included in the analysis. For example, the perspective in the reference case for 'Interventions with health outcomes funded by the NHS is an NHS and PSS perspective. Productivity costs and costs borne by patients and carers that are not reimbursed by the NHS or PSS are usually excluded from this reference case (or any other NICE reference case). Answer ‘yes’ if the perspective used is appropriate for the review question; also answer ‘yes’ if the study has taken a wider perspective, but the results are presented in such a way that the cost effectiveness can be calculated from the appropriate perspective. Answer ‘partly’ if the study has taken a wider or narrower perspective than that in the appropriate reference case, but the additional/omitted costs are small in relation to the total expected costs and are considered unlikely to change the cost-effectiveness result. Answer ‘no’ if the

perspective is not appropriate, or the perspective taken is wider or narrower than that specified in the appropriate reference case and these costs are considered significant and likely to change cost-effectiveness.

1.5 Is the perspective for outcomes appropriate for the review question?

The appropriate perspective for outcomes will depend on the reference case that is relevant for a particular guideline or review question consistent with an objective of maximising benefits from available public sector resources:

- Interventions funded by the NHS with health outcomes: All direct health effects, whether for individuals directly affected or, when relevant, other people (often other family members or carers). Non-health effects: not applicable.

- Interventions funded by the public sector with health and non‑health outcomes: All health effects on individuals. Non-health effects: where deemed appropriate (decided on case-by-case basis, for example for local government and other non-health settings).

- Interventions funded by the public sector with a social care focus: Effects on people for whom services are delivered (people using services and/or carers). Non-health effects: Capability or social care quality of life measures where an intervention results in both capability or social care and health outcomes.

Answer 'yes' if the analysis includes all related effects and excludes non-related effects (or if such effects can be excluded from the results). Answer 'partly' if the analysis excludes some related effects or includes some non-related effects but these are small and unlikely to change the cost-effectiveness results. Answer 'no' if the analysis excludes significant effects or includes significant non-related effects that are likely to change the cost-effectiveness results.

1.6 Are all future costs and outcomes discounted appropriately?

The need to discount to a present value is widely accepted in economic evaluation, although the specific rate is variable across jurisdictions and over time. NICE considers that it is usually appropriate to discount costs and effects at the same rate.

The annual rate of 3.5%, based on the recommendations of the UK Treasury for the discounting of costs, should be applied to both costs and effects. Sensitivity analyses using rates of 1.5% for both costs and effects may be presented alongside the reference-case analysis, particularly for public health interventions.

Answer ‘yes’ if both costs and effects are discounted at 3.5% per year (or at another rate considered appropriate). Answer ‘partly’ if costs and effects are discounted at a rate similar to the rate considered appropriate (for example, costs and effects are both discounted at 3% per year where the appropriate rate is 3.5% or the intervention assessed is public health and a discount rate of 1.5% has been applied to both costs and effects). Answer ‘no’ if costs and/or effects are not discounted, or if they are discounted at a rate (or rates) different from the rate considered appropriate (for example, 5% for both costs and effects, or 6% for costs and 1.5% for effects where the appropriate rate is 3.5%). Note in the comments column what discount rates have been used. If all costs and effects accrue within a short time (roughly a year), answer ‘NA’.

1.7 Are QALYs derived using NICE’s preferred methods, or an appropriate social care-related equivalent used as an outcome?

The QALY is a measure of a person’s length of life weighted by a valuation of their health-related quality of life (HRQoL) over that period. For review questions where the QALY is not be the most appropriate measure of effects, other measures based on social care-related quality of life or capability may be used.

Answer ‘yes’ if the effectiveness of the intervention is measured using QALYs and they are derived using EQ-5D administered to people with the condition or receiving the intervention/comparator with the UK population utility value set applied, or an appropriate social care-related equivalent; answer 'partly' if the effectiveness of the intervention is measured using QALYs but derived using methods not in line with NICE preferred methods; answer ‘no’ if QALYs or a social care-related equivalent are not used. Use the comments column to describe the measure of effects used. There may be circumstances when QALYs or a social care-related equivalent measure cannot be obtained or where the underlying assumptions are considered inappropriate. In such situations answer ‘no’, but consider retaining the study for appraisal. Similarly, answer ‘no’ but retain the study for appraisal if it does not

include appropriate measures of effects but is still thought to be useful for Committee decision-making: for example, if the evidence indicates that an intervention might be dominant, and estimates of the relative costs of the interventions from a cost-minimisation study are likely to be useful. When economic evaluations not using appropriate measures of effects are retained for full critical appraisal, use the comments column to note why.

1.8 Are costs and outcomes from other sectors fully and appropriately measured and valued?

Studies can include costs accruing to other sectors of the economy or benefits gained by these sectors. Not all of these benefits can be translated into measures of effects (for example, the ability to return to work earlier). Answer 'yes' if all relevant costs and benefits have been included, if they are appropriately measured and if they are appropriately valued. Answer 'partly' if omissions are not material and answer 'no' if some major cost or benefit is omitted, is improperly measured or improperly valued. Use the comments column to describe costs and outcomes relating to other sectors.

1.9 Overall judgement

Classify the applicability of the economic evaluation to the guideline, the current UK situation and the context for NICE guidance as 1 of the following:

- **Directly applicable** – the study meets all applicability criteria, or fails to meet 1 or more applicability criteria but this is unlikely to change the conclusions about cost effectiveness.
- **Partially applicable** – the study fails to meet 1 or more of the applicability criteria, and this could change the conclusions about cost effectiveness.
- **Not applicable** – the study fails to meet 1 or more of the applicability criteria, and this is likely to change the conclusions about cost effectiveness. Such studies would usually be excluded from further consideration and there is no need to continue with the rest of the checklist.

Section 2: Study limitations

2.1 Does the model structure adequately reflect the nature of the topic under evaluation?

This relates to the choice of model and its structural elements (including cycle length in discrete time models, if appropriate). Model type and its structural aspects should be consistent with a coherent theory of the needs under evaluation. The selection of care pathways, whether individual states or branches in a decision tree, should be based on the underlying biological, sociological or economic processes of the topic under study and the potential impact (benefits and adverse consequences) of the interventions of interest.

Answer 'yes' if the model design and assumptions appropriately reflect the condition and interventions of interest. Answer 'partly' if there are aspects of the model design or assumptions that do not fully reflect the condition or interventions but these are unlikely to change the cost-effectiveness results. Answer 'no' if the model omits some important aspect of the condition or intervention and this is likely to change the cost-effectiveness results. Answer 'NA' for economic evaluations based on data from a study which do not extrapolate intervention outcomes or costs beyond the study context or follow-up period.

2.2 Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?

The time horizon is the period of analysis of the study: the length of follow-up for participants in a trial-based evaluation, or the period of time over which the costs and outcomes for a cohort are tracked in a modelling study. This time horizon should always be the same for costs and outcomes, and should be long enough to include all relevant costs and outcomes relating to the intervention. A time horizon shorter than lifetime could be justified if there is no differential mortality effect between options, and the differences in costs, social care-related quality of life or other relevant outcomes relate to a relatively short period.

Answer 'yes' if the time horizon is sufficient to include all relevant costs and outcomes. Answer 'partly' if the time horizon may omit some relevant costs and outcomes but these are unlikely to change the cost-effectiveness results. Answer 'no' if the time horizon omits important costs and outcomes and this is likely to change the cost-effectiveness results.

2.3 Are all important and relevant outcomes included?

All relevant outcomes should include direct effects relating to harms from the intervention as well as any potential benefits.

Answer ‘yes’ if the analysis includes all relevant and important harms and benefits. Answer ‘partly’ if the analysis omits some harms or benefits but these would be unlikely to change the cost-effectiveness results. Answer ‘no’ if the analysis omits important harms and/or benefits that would be likely to change the cost-effectiveness results.

2.4 Are the estimates of baseline outcomes from the best available source?

The sources and methods for eliciting baseline probabilities should be described clearly. These data can be based on ‘natural history’ (outcomes in the absence of intervention), sourced from cohort studies. Baseline probabilities may also be derived from the control arms of experimental studies. Sometimes it may be necessary to rely on expert opinion for particular parameters.

Answer ‘yes’ if the estimates of baseline outcomes reflect the best available evidence, for example as identified from a recent well-conducted systematic review of the literature. Answer ‘partly’ if the estimates are not derived from the best available estimate but are likely to reflect outcomes for the relevant group of people in England (for example, if they are derived from a large UK-relevant cohort study). Answer ‘no’ if the estimates are unlikely to reflect outcomes for the relevant group of people in England.

2.5 Are the estimates of relative intervention effects from the best available source?

Evidence on outcomes should be obtained from a systematic review with meta-analysis where appropriate.

The methods and assumptions that are used to extrapolate short-term results to final outcomes should be clearly presented.

Answer ‘yes’ if the estimates of the effect of intervention appropriately reflect all relevant studies of the best available quality, as identified through a recent well-conducted systematic review of the literature. Answer ‘partly’ if the estimates of the effect of intervention are not derived from a systematic review but are similar in

magnitude to the best available estimates (for example, if the economic evaluation is based on a single large study with effects similar to pooled estimates from all relevant studies). Answer ‘no’ if the estimates of the effect of intervention are likely to differ substantively from the best available estimates.

2.6 Are all important and relevant costs included?

Costs related to the topic of interest and incurred in additional years of life gained as a result of intervention should be included in the base-case analysis. Costs that are considered to be unrelated to the topic or intervention of interest should be excluded. If introduction of the intervention requires additional infrastructure to be put in place, consideration should be given to including such costs in the analysis.

Answer ‘yes’ if all important and relevant resource use and costs are included given the perspective and the research question in the economic study under consideration. Answer ‘partly’ if some relevant resource items are omitted but these are unlikely to affect the cost-effectiveness results. Answer ‘no’ if important resource items are omitted and these are likely to affect the cost-effectiveness results.

2.7 Are the estimates of resource use from the best available source?

It is important to quantify the effect of the interventions on resource use in terms of physical units (for example, days in care or contacts with practitioners) and valuing those effects in monetary terms using appropriate prices and unit costs. Evidence on resource use should be identified systematically. When expert opinion is used as a source of information, any formal methods used to elicit these data should be clearly reported.

Answer ‘yes’ if the estimates of resource use appropriately reflect all relevant evidence sources of the best available quality, as identified through a recent well-conducted systematic review of the literature. Answer ‘partly’ if the estimates of resource use are not derived from a systematic review but are similar in magnitude to the best available estimates. Answer ‘no’ if the estimates of resource use are likely to differ substantively from the best available estimates.

2.8 Are the unit costs of resources from the best available source?

Resources should be valued using the prices relevant to the agencies that deliver the interventions. A first point of reference in identifying costs and prices should be any current official listing published by relevant government departments.

When the acquisition price paid for a resource differs from the public list price, the public list price should be used in the base-case analysis. Sensitivity analysis should assess the implications of variations from this price. When cost data are taken from the literature, the methods used to identify the sources should be defined. When several alternative sources are available, a justification for the costs chosen should be provided and discrepancies between the sources explained. When appropriate, sensitivity analysis should have been undertaken to assess the implications for results of using alternative data sources.

Answer ‘yes’ if resources are valued using up-to-date prices relevant to the appropriate sectors. Answer ‘partly’ if the valuations of some resource items differ from current relevant unit costs but this is unlikely to change the cost-effectiveness results. Answer ‘no’ if the valuations of some resource items differ substantively from current relevant unit costs and this is likely to change the cost-effectiveness results.

2.9 Is an appropriate incremental analysis presented or can it be calculated from the data?

An appropriate incremental analysis is one that compares the expected costs and outcomes of one intervention with the expected costs and outcomes of the next-best non-dominated alternative.

Standard decision rules should be followed when combining costs and effects, and should reflect any situation where there is dominance or extended dominance. When there is a trade-off between costs and effects, the results should be presented as an incremental cost-effectiveness ratio (ICER): the ratio of the difference in mean costs to the difference in mean outcomes of a technology or intervention compared with the next best alternative. Where benefits are expressed as QALYs, in addition to ICERs, expected net monetary or health benefits can be presented using values placed on a QALY gained of £20,000 and £30,000. However, it may not be possible to place such values on other measures of benefits that are used in public health and social care economic evaluation.

For cost-consequences analyses, appropriate incremental analysis can only be done by selecting one of the consequences as the primary measure of effectiveness, providing the consequences are independent of one another.

Answer ‘yes’ if appropriate incremental results are presented, or if data are presented that allow the reader to calculate the incremental results. Answer ‘no’ if: (i) simple ratios of costs to effects are presented for each alternative compared with a standard intervention; or (ii) if options subject to simple or extended dominance are not excluded from the incremental analyses.

2.10 Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?

There are a number of potential selection biases and uncertainties in any evaluation (trial- or model-based) and these should be identified and quantified where possible. There are 3 types of bias or uncertainty to consider:

- Structural uncertainty – for example in relation to the categorisation of different states of capability/wellbeing/health and the representation of different pathways of care. These structural assumptions should be clearly documented and the evidence and rationale to support them provided. The impact of structural uncertainty on estimates of cost effectiveness should be explored by separate analyses of a representative range of plausible scenarios.
- Source of values to inform parameter estimates – the implications of different estimates of key parameters (such as estimates of relative effectiveness) must be reflected in sensitivity analyses (for example, through the inclusion of alternative scenarios). Inputs must be fully justified, and uncertainty explored by sensitivity analysis using alternative input values.
- Parameter precision – uncertainty around the mean capability/wellbeing/health and cost inputs in the model. Distributions should be assigned to characterise the uncertainty associated with the (precision of) mean parameter values. Probabilistic sensitivity analysis is preferred, as this enables the uncertainty associated with parameters to be simultaneously reflected in the results of the model. In non-linear decision models – when there is not a straight-line relationship between inputs and outputs of a model (such as Markov models) – probabilistic methods provide the best estimates of mean costs and outcomes.

Simple decision trees are usually linear. The mean value, distribution around the mean, and the source and rationale for the supporting evidence should be clearly described for each parameter included in the model. Evidence about the extent of correlation between individual parameters should be considered carefully and reflected in the probabilistic analysis. Assumptions made about the correlations should be clearly presented.

Answer 'yes' if an extensive sensitivity analysis was undertaken that explored all key uncertainties in the economic evaluation. Answer 'partly' if the sensitivity analysis failed to explore some important uncertainties in the economic evaluation. Answer 'no' if the sensitivity analysis was very limited and omitted consideration of a number of important uncertainties, or if the range of values or distributions around parameters considered in the sensitivity analysis were not reported.

2.11 Has no potential financial conflict of interest been declared?

The British Medical Journal (BMJ) defines competing interests for its authors as follows: 'A competing interest exists when professional judgment concerning a primary interest (such as patients' welfare or the validity of research) may be influenced by a secondary interest (such as financial gain or personal rivalry). It may arise for the authors of a BMJ article when they have a financial interest that may influence, probably without their knowing, their interpretation of their results or those of others.'

Whenever a potential financial conflict of interest is possible, this should be declared.

Answer 'yes' if the authors declare that they have no financial conflicts of interest. Answer 'no' if clear financial conflicts of interest are declared or apparent (for example, from the stated affiliation of the authors). Answer 'unclear' if the article does not indicate whether or not there are financial conflicts of interest.

2.12 Overall assessment

The overall methodological study quality of the economic evaluation should be classified as 1 of the following:

- **Minor limitations** – the study meets all quality criteria, or fails to meet 1 or more quality criteria but this is unlikely to change the conclusions about cost effectiveness.
- **Potentially serious limitations** – the study fails to meet 1 or more quality criteria, and this could change the conclusions about cost effectiveness.
- **Very serious limitations** – the study fails to meet 1 or more quality criteria, and this is highly likely to change the conclusions about cost effectiveness.

Supporting references

Husereau D, Drummond M, Petrou S, et al. Consolidated health economic evaluation reporting standards (CHEERS)—Explanation and elaboration: A report of the ISPOR health economic evaluations publication guidelines good reporting practices task force. Value Health 2013;16:231-50.

National Institute for Health and Clinical Excellence (2008) Social value judgements: principles for the development of NICE guidance (second edition). London: National Institute for Health and Clinical Excellence

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

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

Appraisal checklists: generic

There may be some reviews where it is not helpful to use different checklists for the different study designs (for example, in a complex mixed methods review). In such cases, a single checklist that can be applied to different study designs may be used.

Shepherd J, Kavanagh J, Picot J et al. (2010) The effectiveness and cost-effectiveness of behavioural interventions for the prevention of sexually transmitted infections in young people aged 13–19: a systematic review and economic evaluation. Health Technol Assess 14(7) Appendix 5

Taylor BJ, Dempster M, Donnelly M (2007) Grading gems: appraising the quality of research for social work and social care. British Journal of Social Work 37: 335

Examples of evidence tables

This section includes examples of evidence tables for those study designs that are expected to be used in the evidence reviews for NICE guidelines.

Below are examples of the type of information and data NICE requires in table format in evidence reviews. It is not possible to provide a fixed template for all evidence tables that will suit all topics. The range, type, quantity and quality of evidence identified will inevitably vary and these tables are presented as examples only of how information and data should be presented.

If additional analysis or additional calculation (e.g. calculating numbers needed to treat, odds ratios, risk ratios) of data is required and feasible, these must be clearly noted as ‘calculated by the review team’.

Example of an evidence table for systematic reviews

Title: (review question)

Bibliographic reference	Review design	Study quality	Review search parameters	Review population and setting	Intervention(s)	Outcomes and methods of analysis	Results	Limitations	Additional comments
			Sources *Methods of searching* *Dates* *Inc/exc criteria* *Number of studies*	*Details (demographics)* *Missing information*	*Intervention in detail (who, where, when)* *Controls/comparator also in detail*		*Objective/ subjective* *Time points* *Health inequalities impact*	*Identified by authors* *Identified by developers*	*Source of funding*

The detailed information under each heading should be agreed at the review protocol stage and be consistently completed across the review. The italicised text above is provided as an example of the types of information that could be included. The required information is specified below.

[1] Bibliographic reference: authors, year, article title, journal, volume, pages.

[2] Review type: for example, systematic review with meta-analysis.

[3] Number of studies: total number of studies included in the review.

[4] Study characteristics: characteristics relevant to the area of interest: study design, other restrictions.

[5] Intervention: treatment, service, procedure or test studied. If important for the study, specify duration of treatment.

[6] Setting: the settings where the interventions was delivered (for example care homes).

[7] Comparison: alternative treatment or ‘standard care’.

[8] Outcome measures: list all outcome measures defined in the review protocol, including associated harms.

[9] Results: for example, summary effect size from a meta-analysis.

[10] Source of funding: for example the Department of Health or Economic and Social Research Council. Also detail the role of funding organisations.

[11] Quality assessment: Document any concerns about quality which can be used to provide an overall assessment of the review (e.g. rating from quality checklist) for the use in GRADE assessment or other overall assessment (e.g. ++, +, - if used).

[12] Additional comments: additional characteristics and/or interpretations of the review that the reviewer wishes to record. These might include important flaws and limitations in the review not identifiable from other data in the table, and additional questions or issues that will need to be considered but do not figure in the results tables in the review

Example of an evidence table for intervention studies

Title: (review question)

Bibliographic reference	Study type	Study quality	Intervention	Comparator	Method of allocation	Setting	Number of participants	Participant characteristics	Length of follow-up	Methods of analysis	Outcomes/ Results	Limitations	Additional comments
			Intervention in detail (who, where, when)		*Methods use to minimize confounders*	*Country* *Location*	*Power information* *Method of recruitment*	*Information on representativeness*	*Loss to follow-up*	*ITT or completer* *Adjustments for baseline differences*	*Objective/ subjective* *Time points* *Health inequalities impact*	*Identified by authors* *Identified by developers*	*Evidence gaps* *Further research identified*

The detailed information under each heading should be agreed at the review protocol stage and be consistently completed across the review. The italicised text above is provided as an example of the types of information that could be included. The required information is specified below.

[1] Bibliographic reference: authors, year, article title, journal, volume, pages.

[2] Study type: for example, randomised controlled trial, cohort or case-control studies.

[3] Number of participants: total number of participants included in the study, including number of participants in each arm, with inclusion and exclusion criteria. Also record the numbers of participants who started and completed the study.

[4] Participant characteristics: characteristics relevant to the area of interest: age, sex, ethnic origin, condition status and comorbidity.

[5] Intervention: treatment, service, procedure or test studied. If important for the study, specify duration of treatment.

[6] Setting: the settings where the interventions was delivered (for example care homes).

[7] Comparison: alternative treatment or ‘standard care’.

[8] Length of follow-up: the length of time that participants take part in the study for, from first staging treatment until either a pre-specified end-point or the end of the data-gathering phase is reached. If the study is stopped earlier than originally planned for any reason, this should be noted here.

[9] Outcome measures: list all outcome measures defined in the review protocol, including associated harms.

[10] Effect size: for example, raw data from the study that allow further analyses, as required. Give confidence intervals whenever possible.

[11] Source of funding: for example the Department of Health or Economic and Social Research Council. Also detail the role of funding organisations.

[12] Quality assessment: Document any concerns about quality which can be used to provide an overall assessment of each study (e.g. rating from quality checklist) for use in GRADE assessment

[13] Additional comments: additional characteristics and/or interpretations of the studies that the reviewer wishes to record. These might include important flaws and limitations in the study not identifiable from other data in the table, and additional questions or issues that will need to be considered but do not figure in the results tables in the study

Example of an evidence table for studies of diagnostic test accuracy

Title: (review question)

Bibliographic reference	Study type	Study quality	Type of test (index test)	Reference standard	Number of participants	Prevalence	Participant characteristics	Sensitivity and specificity or raw data for 2x2 table	Other metrics: Positive and negative likelihood ratios and/or Positive and negative predictive values	Additional comments

The detailed information under each heading should be agreed at the review protocol stage and be consistently completed across the review. The italicised text above is provided as an example of the types of information that could be included. The required information is specified below.

[1] Bibliographic reference: authors, year, article title, journal, volume, pages.

[2] Study type: for example, cross-sectional, cohort or case–control studies.

[3] Study quality: note particular strengths and weaknesses.

[4] Number of participants: total number of patients included in the study, with inclusion and exclusion criteria.

[5] Prevalence: proportion of people with the disease in the population at risk.

[6] Participant characteristics: characteristics relevant to the area of interest: age, sex, ethnic origin, comorbidity, disease status, community- or hospital-based.

[7] Type of test (index test): description of the diagnostic test used in the study. Specify the test threshold where applicable.

[8] Reference standard: used as a measure of outcome. Specify if it is a 'gold standard' or 'current best practice'.

[9] Sensitivity: proportion of individuals classified as positive by the gold (or reference) standard who are correctly identified by the study test.
Specificity: proportion of individuals classified as negative by the gold (or reference) standard who are correctly identified by the study test.

Raw data for 2x2 table: study data collected from tests to calculate sensitivity, specificity, positive and negative likelihood ratios, and positive and negative predictive values (see example table below)

		Disease or outcome	
		Present	Absent
Test	+	a (true positive)	b (false positive)
	−	c (false negative)	d (true negative)

[10] Positive likelihood ratio: the likelihood of having the disease, as opposed to not having the disease, having tested positive for it (an estimate of the amount by which a positive test result increases the probability of actually having the disease that was tested for). Negative likelihood ratio: the likelihood of having the disease, as opposed to not having the disease, having tested negative for it (an estimate of the amount by which a negative test result decreases the probability of having the disease that was tested for).

[11] Positive predictive value: proportion of individuals with a positive test result who actually have the disease.
Negative predictive value: proportion of individuals with a negative test result who do not have the disease.

[12] Source of funding: government funding (for example, NHS), voluntary/charity (for example, Wellcome Trust), pharmaceutical company; and the role of funding organisations.

[13] Quality assessment: Document any concerns about quality which can be used to provide an overall assessment of each study (e.g. QUADAS-2) for use in GRADE/modified GRADE assessment

[14] Additional comments: additional characteristics and/or interpretations of the studies that the reviewer wishes to record. These might include important flaws in the study not identifiable from other data in the table, and additional questions or issues that will need to be considered but do not figure in the results tables in the study (for example, if a test is one of a sequence of tests; if its utility was determined).

Example of an evidence table for prognostic studies or clinical prediction rule/model for prognosis or diagnosis

Title: (review question)

Bibliographic reference	Study type	Study quality	Prognostic factor(s) or risk factor(s) or sign(s)/symptom(s)	Number of participants	Participant characteristics	Length of follow-up	Outcome measures	Results	Additional comments

The detailed information under each heading should be agreed at the review protocol stage and be consistently completed across the review.

The italicised text above is provided as an example of the types of information that could be included. The required information is specified below.

[1] Bibliographic reference: authors, year, article title, journal, volume, pages.

[2] Study type: for example, cohort, nested cohort, case series.

[3] Study quality: note particular strengths and weaknesses.

[4] Number of participants: total number of patients included in the study, including number and proportion of patients with prognostic factors or risk factor(s), or sign(s) and symptom(s), with inclusion and exclusion criteria. Also record numbers of patients who started and completed the study.

[5] Participant characteristics: characteristics relevant to the area of interest: age, sex, ethnic origin, comorbidity, disease status, community- or hospital-based. Include method used to select participants.

[6] Prognostic factors or risk factor(s) or sign(s)/symptom(s): include details of method of measurement.

[7] Length of follow-up: the length of time that patients take part in the study for, from entry until either a pre-specified end-point (for example, death, specified length of disease-free remission) or the end of the data-gathering phase is reached. If the study is stopped earlier than originally planned for any reason, this should be noted here.

[8] Outcome measures: all outcome measures should be listed, with each on a separate line.

[9] Results: odds ratio or adjusted odds ratio or relative risk or hazard ratio associated with the prognostic factor of interest or risk factor(s) or sign(s)/symptom(s), absolute risk of event in baseline group; time-to-event analysis. For clinical prediction rule/model for diagnosis results may be reported as accuracy metrics (e.g. sensitivity, specificity, +LR, -LR, PPV, NPV, etc.).

[10] Source of funding: government funding (for example, NHS), voluntary/charity (for example, Wellcome Trust), pharmaceutical company; and the role of funding organisations.

[11] Quality assessment: Document any concerns about quality which can be used to provide an overall assessment of each study (e.g. rating from quality checklist) for use in GRADE/modified GRADE assessment

[12] Additional comments: additional characteristics and/or interpretations of the studies that the reviewer wishes to record. These might include important flaws in the study not identifiable from other data in the table, and additional questions or issues that will need to be considered but do not figure in the results tables in the study.

Example of an evidence table for qualitative studies

Title: (review question)

Reference		Research parameters				Population	Results	Limitations	Additional comments
Bibliographic reference	**Study quality**	**Research question**	**Theoretical approach**	**Data collection**	**Method and process of analysis**	**Population and sample collection**	**Key themes**		
							Quotes, where helpful or illustrative		

The detailed information under each heading should be agreed at the review protocol stage and be consistently completed across the review. The italicised text above is provided as an example of the types of information that could be included. The required information is specified below.

[1] Bibliographic reference: authors, year, article title, journal, volume, pages.

[2] Research question: what were the research questions?

[3] Theoretical approach: what theoretical approach (for example, grounded theory, interpretive phenomenological analysis) does the study take (if specified)?

[4] Data collection: how were the data collected? Give details of:

- methods
- by whom
- when.

[5] Method and process of analysis: what methods were used to analyse the data (for example, constant comparative method)?

[6] Population and sample collection: what population was the sample recruited from? Include the following information:

- how they were recruited (for example, specify the type of purposive sampling)
- how many participants were recruited
- specific exclusion criteria
- specific inclusion criteria.

[7] Settings: The settings where the qualitative study was undertaken.

[8] Key themes: list all relevant to this review (with illustrative quotes if available).

[9] Source of funding: for example the Department of Health or Economic and Social Research Council, and the role of funding organisations.

[10] Quality assessment: Document any concerns about quality which can be used to provide an overall assessment of each study (e.g. rating from quality checklist) for use in CERQual assessment.

[11] Limitations: both those identified by the authors and those identified by the reviewer.

[12] Evidence gap and/or recommendations for future research.

Example of an evidence table for economic evaluation studies

Bibliographic reference	Study type	Study quality	Setting	Intervention	Comparator	Number of participants	Participant characteristics	Methods of analysis	Results	Limitations	Additional comments
		Applicability	*Country* *Setting* *Location*	*Intervention in detail (who, where, when)*	*As for intervention*		*Source population*	*Type of economic analysis* *Data sources Time horizon* *Discount rates* *Perspective* *Measures of uncertainty*	*Objective/ subjective* *Time points* *Health inequalities impact* *Primary results* *Secondary analysis* *Modelling method*	*Identified by authors* *Identified by developers*	*Source of funding* *Evidence gaps* *Further research identified*

The detailed information under each heading should be agreed at the review protocol stage and be consistently completed across the review.

The italicised text above is provided as an example of the types of information that could be included. The required information is specified below.

Please complete for all headings and note where data is 'Not reported' or 'Not applicable'.

[1] Bibliographic reference: authors, year, article title, journal, volume, pages.

[2] Study type: for example, randomised controlled trial with economic evaluation.

[3] Number of participants: total number of participants included in the study, including number of participants in each arm, with inclusion and exclusion criteria. Also record the numbers of participants who started and completed the study.

[4] Participant characteristics: characteristics relevant to the area of interest: age, sex, ethnic origin, condition status and comorbidity.

[5] Intervention: treatment, service, procedure or test studied. If important for the study, specify duration of treatment.

[6] Setting: the settings where the interventions was delivered (for example care homes).

[7] Comparison: alternative treatment or 'standard care'.

[8] Length of follow-up: the length of time that participants take part in the study for, from first staging treatment until either a pre-specified end-point or the end of the data-gathering phase is reached. If the study is stopped earlier than originally planned for any reason, this should be noted here.

[9] Outcome measures: list all outcome measures defined in the review protocol, including associated harms.

[10] Effect size: for example, raw data from the study that allow further analyses, as required. Give confidence intervals whenever possible.

[11] Source of funding: for example the Department of Health or Economic and Social Research Council. Also detail the role of funding organisations.

[12] Quality assessment: Document any concerns about quality with respect to the limitations and applicability to provide an overall assessment of each study assessment

[13] Additional comments: additional characteristics and/or interpretations of the studies that the reviewer wishes to record. These might include important flaws and limitations in the study not identifiable from other data in the table, and additional questions or issues that will need to be considered but do not figure in the results tables in the study

GRADE profile and economic evidence profile

This aims to give examples of profiles that can be used when developing guidelines. The decision about which information to be included in the profile should be made as part of the review protocol development. The profile should include features considered important – these may be study design specific or specific to the topic. As such, additional items may need to be included, or minor modification made. Where this is the case, this should be documented, greed with the NICE QA team.

Worked example of a GRADE profile

Review question: Should duloxetine vs placebo be used for painful diabetic neuropathy?

Quality assessment							*No. of patients*		*Effect*		*Quality*	*Importance*
No. of studies	*Design*	*Risk of bias*	*Inconsistency*	*Indirectness*	*Imprecision*	*Other considerations*	*Duloxetine*	*Placebo*	*Relative (95% CI)*	*Absolute*		
Patient-reported 30% pain reduction (follow-up 12 weeks)												
2[1]	Randomised trials	No serious risk of bias	Serious[2]	No serious indirectness	No serious imprecision	None	220/327	111/215	RR 1.33 (0.95 to 1.88)	17 more per 100 (from 3 fewer to 45 more)	Moderate	Critical
No. of withdrawals due to adverse effects (follow-up 12 weeks)												
4[3]	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	113/906	21/448	RR 2.63 (1.68 to 4.12)	8 more per 100 (from 3 more to 15 more)	High	Critical
Dizziness (adverse effects) (follow-up 12 weeks)												
3[6]	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision[5]	None	90/674	26/332	RR 1.81 (1.17 to 2.79)	6 more per 100 (from 1 more to 14 more)	Moderate	Critical
GI disturbances (adverse effects) (follow-up 12 weeks)												
2[8]	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious imprecision[5]	None	28/332	8/217	RR 2.53 (1.13 to 5.67)	6 more per 100 (from 0 more to 17 more)	Moderate	Important
Any adverse effects (non-specified) (follow-up 12 weeks)												
1[9]	Randomised trials	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious imprecision[10]	None	86/106	78/109	RR 1.13 (0.98 to 1.32)	9 more per 100 (from 1 fewer to 23 more)	Low	Critical

[1] Gao et al. (2010); Wernicke et al. (2006).

[2] Substantial heterogeneity, random-effect model was used. Potential sources of heterogeneity: i) Gao et al. (2010) – ITT data available, used flexible dose between 30 mg and 120 mg, non-pharmaceutical company funded; ii) Wernicke et al. (2006) – only per-protocol data available, combined 2 fixed doses (60 mg and 120 mg), pharmaceutical company funded.

[3] Gao et al. (2010); Goldstein et al. (2005); Raskin et al. (2005); Wernicke et al. (2006).

[4] Substantial heterogeneity, random-effect model was used. Potential sources of heterogeneity: i) Gao et al. (2010) – used flexible dose between 30 mg and 120 mg, non-pharmaceutical company funded; ii) Goldstein et al. (2005), Raskin et al. (2005) and Wernicke et al. (2006) – combined different fixed doses (20 mg, 60 mg and 120 mg), pharmaceutical company funded.

[5] Confidence interval crossed 1 end of default MID.

[6]Gao et al. (2010); Goldstein et al. (2005); Wernicke et al. (2006).

[7] Gao et al. (2010); Goldstein et al. (2005).

[8] Gao et al. (2010); Wernicke et al. (2006).

[9] Gao et al. (2010).

[10] Confidence interval crossed both ends of default MID.

Abbreviations: CI, confidence interval; GI, gastrointestinal; ITT, intention to treat; MID, minimal important difference; RR, relative risk.

Example of an uncompleted GRADE profile

Quality assessment							***No. of patients***		***Effect***		***Quality***	***Importance***
No of studies	***Design***	***Risk of bias***	***Inconsistency***	***Indirectness***	***Imprecision***	***Other considerations***	.	.	***Relative (95% CI)***	***Absolute***		
X												
X												
X												
X												
X												
X												
[References, abbreviations and other footnotes].												

Worked example of an economic evidence profile

Adapted from Crohn's disease: management in adults, children and young people (NICE clinical guideline 152).

Systematic review of economic evaluations of budesonide for maintenance of remission in Crohn's disease

Study	*Limitations*	*Applicability*	*Other comments*	*Incremental*			*Uncertainty*
				Costs	*Effects*	*Cost effectiveness*	
Noble 1998 Budesonide controlled ileal release versus no maintenance therapy	Potentially serious limitations[1,2]	Partially applicable[3]	Study employed a Markov decision-analytic model with a 1-year time horizon	£115	0.017 QALYs[5]	£6,981 per QALY gained	Incremental cost effectiveness ratio (ICER) decreases significantly if the cost of surgery is increased.
National Clinical Guideline Centre model Oral budesonide versus no maintenance therapy[4]	Potentially serious limitations[2]	Directly applicable	Study employed a Markov decision-analytic model with a 2-year time horizon	£477[6] £150[7]	0.012 QALYs[6] 0.012 QALYs[7]	£40,392 per QALY gained[6] £15,070 per QALY gained[7]	No treatment most cost-effective option when baseline risk of relapse decreased. In the probabilistic sensitivity analysis (PSA), probability of budesonide being the most cost-effective treatment at willingness-to-pay threshold of £20,000 per QALY gained ranged from 0 to 8%

[1] Modelling was undertaken over a short time horizon and no probabilistic sensitivity analysis was conducted.

[2] Specific costs and disutilities of drug-related adverse events could not be explicitly modelled. Adverse events were captured by modelling treatment-specific withdrawal rates. This may have overestimated the cost effectiveness of maintenance treatment.

[3] The cost-effectiveness model was designed to reflect the management of Crohn's disease in the Swedish healthcare setting. Although a cost per QALY estimate was reported, it was not based on health-related quality of life values elicited from patients.

[4] The NCGC model compared a number of different maintenance treatments.

[5] Figures may differ because of rounding off.

[6] Conservative 4-line model. Conservative treatment effects were used and people relapsing while on azathioprine maintenance treatment had a different induction sequence.

[7] Conservative three-line model. Conservative treatment effects were used and people were assumed to have the same 6 induction sequence regardless of maintenance treatment.

Example of an uncompleted economic evidence profile

Study	***Limitations***	***Applicability***	***Other comments***	***Incremental***			***Uncertainty***
				Costs	***Effects***	***Cost effectiveness***	
.							
.							
.							
.							
.							
[References, abbreviations and other footnotes].							

Notes on use of economic evidence profiles

The economic evidence profile includes columns for the overall assessments of study limitations and applicability as identified using an appropriate checklist. There is also a comments column to note particular issues that the Committee should consider when assessing the economic evidence. Footnotes should be used to explain the reasons for quality assessments.

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

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

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

If results are available for 2 or more subgroups, these should be presented in separate economic evidence profile tables or as separate rows within a single table.

Costs and cost-effectiveness estimates should only be presented for appropriate incremental comparisons; that is, where an intervention is compared with the next most expensive non-dominated option. If comparisons are relevant only for some groups of the population (for example, people who cannot tolerate 1 or more of the

other options, or for whom 1 or more of the options is contraindicated), this should be stated in a footnote to the economic evidence profile.

Appendix I Review Protocol Template

- Add title of the review question, the review question number (from the work plan) and the relevant section of the scope (it is invaluable to be able to match the review question across the protocols, work plan, health economic plan and meeting agendas).
- Create a separate review protocol for each review question. Amend fields in this template according to the type of review question.
- Instructions for completing the template are in blue and should be deleted when no longer needed (including this text).

ID	Field	Content	Developer comments *(delete before publication)*	QA comments *(delete before publication)*
0.	PROSPERO registration number	[Complete this section with the PRSOSPERO registration number once allocated]		
1.	Review title	[Give the working title of the review. Ideally the title should state succinctly the interventions or exposures being reviewed and the associated health or social problems. Where appropriate, the title should use the PI(E)COS structure to contain information on the Participants, Intervention (or Exposure) and Comparison groups, the Outcomes to be measured and Study designs to be included.		

		Acronyms may be included in titles, but should not be used alone without expansion unless they are regarded as more usual than the expansion (e.g. HIV).]		
2.	Review question	[State the question(s) to be addressed by the review, clearly and precisely.]		
3.	Objective	[What is the objective of the review? Is any rationale/ detail of what is known necessary?]		
4.	Searches	[Give details of the sources to be searched, search dates (from and to), and any restrictions (e.g. language or publication period). The full search strategy is not required, but may be supplied as a link or attachment. List all sources that will be used to identify studies for the review. Sources include (but are not limited to) bibliographic databases, reference lists		

		of eligible studies and review articles, key journals, trials registers, conference proceedings, Internet resources and contact with experts and manufacturers.] The following databases will be searched: [Amend if required] • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Cumulated Index to Nursing and Allied Health Literature (CINAHL) • Database of Abstracts of Reviews of Effectiveness (DARE) • Embase • MEDLINE/MEDLINE in Process • ClinicalTrials.gov • Current Controlled Trials • United Kingdom Clinical Research Network's (UKCRN) Portfolio Database		

		• NHS EED Searches will be restricted by: • [Date limitations] • [English language] • [Human studies] • [Any other filters] Other searches: • [Reference searching] • [Citation searching] • [Inclusion lists of systematic reviews] • [Websites] The searches will be re-run 6 weeks before final submission of the review and further studies retrieved for inclusion. Full search strategies for all databases will be published in the final review.		

5.	Condition or domain being studied	[Give a short description of the disease, condition or healthcare domain being studied. This could include health and wellbeing outcomes e.g. Type 2 diabetes. Physical activity in children.]		
6.	Population	Inclusion: [Give summary criteria for the participants or populations being studied by the review. For example children and or adults, line of treatment, previous treatment, severity of condition. The preferred format includes details of both inclusion and exclusion criteria.] Exclusion: [Give summary criteria for the participants or populations being studied by the review. For example children and or adults, line of treatment, previous treatment, severity of condition. The preferred format includes		

		details of both inclusion and exclusion criteria.]		
7.	Intervention/Exposure/Test	[Give full and clear descriptions or definitions of the nature of the interventions or the exposures to be reviewed. This is particularly important for reviews of complex interventions (interventions involving the interaction of several elements). If appropriate, an operational definition describing the content and delivery of the intervention should be given.]		
8.	Comparator/Reference standard/Confounding factors	[Where relevant, give details of the alternatives against which the main subject/topic of the review will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria. Control or comparison interventions should be described in as much detail		

		as the intervention being reviewed. If the comparator is 'treatment as usual' or 'standard care', this should be described, with attention being paid to whether it is 'standard care' at the time that an eligible study was done, or at the time the review is done. Systematic reviews of qualitative studies rarely have a comparator or control; stating 'Not applicable' is therefore acceptable.]		
9.	Types of study to be included	[Give details of the types of study (study designs) eligible for inclusion in the review. If there are no restrictions on the types of study design eligible for inclusion, or certain study types are excluded, this should be stated. The preferred format includes details of both inclusion and exclusion criteria. If different study designs are needed for different parts of the review, this should		

		be made clear. Where qualitative evidence will be incorporated in or alongside a review of quantitative data, this should be stated.]		
10.	Other exclusion criteria	[Add details of any other inclusion/exclusion criteria, with justification. Examples might include language of publication, publication status and study size/number in each arm/exposure.]		
11.	Context	[If relevant, give summary details of the setting and other relevant characteristics which help define the inclusion or exclusion criteria. Include relevant details if these form part of the review's eligibility criteria but are not reported elsewhere in the PROSPERO record. Also include details of any previous guidelines that will be updated by this question]		

12.	Primary outcomes	[Give the pre-specified primary (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria. For systematic reviews of qualitative studies give details of what the review aims to achieve.]		
13.	Secondary outcomes	[List the pre-specified secondary (additional) outcomes of the review, with a similar level of detail to that required for primary outcomes. Where there are no secondary outcomes please state 'None' or 'Not applicable' as appropriate to the review]		
14.	Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements		

		resolved by discussion or, if necessary, a third independent reviewer. If meaningful disagreements are found between the different reviewers, a further 10% of the abstracts will be reviewed by two reviewers, with this process continued until agreement is achieved between the two reviewers. From this point, the remaining abstracts will be screened by a single reviewer to identify potentially eligible studies. The full text of potentially eligible studies will be retrieved will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). Two review authors will extract a random 10% of the data independently, discrepancies will be identified and resolved through discussion (with a third author where necessary). Missing data will be requested from study authors where time and resources allow.		

		[If priority screening is being used add this text in between the two paragraphs above] This review made use of the priority screening functionality within the EPPI-reviewer software. This uses a machine learning algorithm (specifically, an SGD classifier) to take information on features (1, 2 and 3 word blocks) in the titles and abstract of papers marked as being ‘includes’ or ‘excludes’ during the title and abstract screening process, and re-orders the remaining records from most likely to least likely to be an include, based on that algorithm. This re-ordering of the remaining records occurs every time 25 additional records have been screened. Research is currently ongoing as to what are the appropriate thresholds where reviewing of abstract can be stopped, assuming a defined threshold for the proportion of relevant papers it is acceptable to miss on primary screening. As a conservative approach until that research has been completed,		

		the following rules were adopted during the production of this guideline: • at least 50% of the identified abstracts (or 1,000 records, if that is a greater number) are always screened. • After this point, screening will be terminated if [a pre-specified threshold for a number of abstracts] abstracts are screened without a single new include being identified. This threshold is set according to the expected proportion of includes in the review (with reviews with a lower proportion of includes needing a higher number of papers without an identified study to justify termination), and is always a minimum of 250. • A random 10% sample of the studies remaining in the database when the threshold will be additionally screened, to check whether a substantial number of relevant studies have not been correctly classified by		

		the algorithm, with the full database being screened if concerns are identified. As an additional check to ensure this approach does not miss relevant studies, the included studies lists of included systematic reviews will be searched to identify any papers not identified through the primary search.		
15.	Risk of bias (quality) assessment	[Modify as relevant to the types of studies being included] [Individual systematic reviews will be quality assessed using the ROBIS tool, with each classified into one of the following three groups: • High quality – It is unlikely that additional relevant and important data would be identified from primary studies compared to that reported in the review, and unlikely that any relevant and important studies have been missed by the review.		

		• Moderate quality – It is possible that additional relevant and important data would be identified from primary studies compared to that reported in the review, but unlikely that any relevant and important studies have been missed by the review. • Low quality – It is possible that relevant and important studies have been missed by the review. Each individual systematic review will also be classified into one of three groups for its applicability as a source of data, based on how closely the review matches the specified review protocol in the guideline. Studies will be rated as follows: • Fully applicable – The identified review fully covers the review protocol in the guideline. • Partially applicable – The identified review fully covers a		

		discrete subsection of the review protocol in the guideline (for example, some of the factors in the protocol only). • Not applicable – The identified review, despite including studies relevant to the review question, does not fully cover any discrete subsection of the review protocol in the guideline. Individual RCTs and quasi-randomised controlled trials will be quality assessed using the Cochrane Risk of Bias Tool. Cohort studies will be quality assessed using the Cochrane ROBINS-I tool. Each individual study will be classified into one of the following three groups: Low risk of bias – The true effect size for the study is likely to be close to the estimated effect size. Moderate risk of bias – There is a possibility the true effect size for the		

		study is substantially different to the estimated effect size. High risk of bias – It is likely the true effect size for the study is substantially different to the estimated effect size. Each individual study will also be classified into one of three groups for directness, based on whether there are concerns about the population, intervention, comparator and/or outcomes in the study and how directly these variables can address the specified review question. Studies will be rated as follows: Direct – No important deviations from the protocol in population, intervention, comparator and/or outcomes. Partially indirect – Important deviations from the protocol in one of the population, intervention, comparator and/or outcomes. Indirect – Important deviations from the protocol in at least two of the following		

		areas: population, intervention, comparator and/or outcomes.]		
16.	Strategy for data synthesis	[Modify/delete as necessary] Meta-analyses of interventional data will be conducted with reference to the Cochrane Handbook for Systematic Reviews of Interventions (Higgins et al. 2011). Where different studies present continuous data measuring the same outcome but using different numerical scales (e.g. a 0-10 and a 0-100 visual analogue scale), these outcomes will be converted to the same scale before meta-analysis is conducted on the mean differences. Where outcomes measure the same underlying construct but use different instruments/metrics, data will be analysed using standardised mean differences (Hedges' g). A pooled relative risk will be calculated for dichotomous outcomes (using the Mantel–Haenszel method). Both relative and absolute risks will be presented,		

		with absolute risks calculated by applying the relative risk to the pooled risk in the comparator arm of the meta-analysis. Fixed- and random-effects models (der Simonian and Laird) will be fitted for all syntheses, with the presented analysis dependent on the degree of heterogeneity in the assembled evidence. Fixed-effects models are the preferred choice to report, but in situations where the assumption of a shared mean for fixed-effects model are clearly not met, even after appropriate pre-specified subgroup analyses, random-effects results will be presented. Fixed-effects models will not be used if there is: • significant between study heterogeneity in methodology, population, intervention or comparator is identified by the reviewer in advance of data analysis. This decision will be made and recorded before any data analysis is undertaken.		

		• significant statistical heterogeneity in the meta-analysis, defined as $I^2 \geq 50\%$. In any meta-analyses where some (but not all) of the data came from studies at high risk of bias, a sensitivity analysis will be conducted, excluding those studies from the analysis. Results from both the full and restricted meta-analyses will be reported. Similarly, in any meta-analyses where some (but not all) of the data come from indirect studies, a sensitivity analysis will be conducted, excluding those studies from the analysis. Meta-analyses will be performed in Cochrane Review Manager v5.3. GRADE (using GRADEpro) will be used to assess the quality of evidence for the selected outcomes as specified in Developing NICE guidelines: the manual. Data from RCTs will initially be rated as high quality and the quality of the evidence for each outcome will be downgraded or not from this initial point. If non-RCT evidence is included for		

		intervention-type systematic reviews then these will initially be rated as either moderate quality (quasi-randomised studies) or low quality (cohort studies) and the quality of the evidence for each outcome will be further downgraded or not from this point. CERQual will be used to assess data from qualitative studies. Publication bias will be assessed in two ways. First, if evidence of conducted but unpublished studies is identified during the review (e.g. conference abstracts, trial protocols or trial records without accompanying published data), available information on these unpublished studies will reported as part of the review. [Amend if additional approaches to publication bias are undertaken. For example: secondly, where 10 or more studies are included as part of a single meta-analysis, a funnel plot will be produced to graphically assess the potential for publication bias.]		

17.	Analysis of sub-groups	[Give details of any plans for the separate presentation, exploration or analysis of different types of participants (e.g. by age, disease status, ethnicity, socioeconomic status, presence or absence or co-morbidities); different types of intervention (e.g. drug dose, presence or absence of particular components of intervention); different settings (e.g. country, acute or primary care sector, professional or family care); or different types of study (e.g. randomised or non-randomised).]		
18.	Type and method of review	☐ Intervention ☐ Diagnostic ☐ Prognostic ☐ Qualitative		
19.	Language	English		
20.	Country	England		
21.	Anticipated or actual start date	[For the purposes of PROSPERO, the date of commencement for the systematic review can be defined as any point after completion of a protocol		

		but before formal screening of the identified studies against the eligibility criteria begins. A protocol can be deemed complete after formal sign-off by the NICE team with responsibility for quality assurance.		
22.	Anticipated completion date	[Give the date by which the review is expected to be completed. In the absence of an agreed contractual date, a realistic anticipated date for completion should be set. It can be modified should the schedule change. When this date is reached, the named contact will receive an automated email to ask them to provide an update on progress. This field may be edited at any time. All edits will appear in the record audit trail. A brief explanation of the reason for changes should be given in the Revision Notes facility].		

23.	Stage of review at time of this submission	**Review stage**	**Started**	**Completed**		
		Preliminary searches	☐	☐		
		Piloting of the study selection process	☐	☐		
		Formal screening of search results against eligibility criteria	☐	☐		
		Data extraction	☐	☐		
		Risk of bias (quality) assessment	☐	☐		
		Data analysis	☐	☐		

24.	Named contact	**5a. Named contact** [Give name] **5b Named contact e-mail** [Guideline]@nice.org.uk **5c Named contact address** [Give development centres name and full address] **5d Named contact phone number** +44 (0) [number] **5e Organisational affiliation of the review** National Institute for Health and Care Excellence (NICE) and [Insert Development centre]		
25.	Review team members	[Give the title, first name, last name and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong.] From the [Insert Development centre]:		

		• [Tech lead] • [Tech analyst] • [Health economist] • [Information specialist] • [Others]		
26.	Funding sources/sponsor	This systematic review is being completed by the [Insert Development centre] which receives funding from NICE.		
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be		

		recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.		
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are: Chair: [Honorific, Name, Affiliation] Members: [Honorific, Name, Affiliation] [Honorific, Name, Affiliation] [Honorific, Name, Affiliation] etc.		
29.	Other registration details	[Give the name of any organisation where the systematic review title or protocol is registered (such as with The Campbell Collaboration, or The Joanna Briggs Institute) together with any unique identification number assigned. If extracted data will be stored and		

		made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.]		
30.	Reference/URL for published protocol	[Give the citation and link for the published protocol, if there is one.]		
31.	Dissemination plans	The reviewers and guideline committee work with NICE's communications team to disseminate and promote awareness of the guideline at the time of publication and afterwards. Members from the NICE communications team discuss with the reviewers and the committee opportunities for promoting the guideline. Committee members may be asked to take part in such activities. With help from the guideline committee and the developer, they identify how to reach relevant audiences for the guideline, including people using		

		services, carers, the public, practitioners and providers. NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE. NICE may also use other means of raising awareness of the guideline – for example, newsletters, websites, training programmes, conferences, implementation workshops, NICE field team support and other speaking engagements. Some of these may be suggested by guideline 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.		
32.	Keywords	[Give words or phrases that best describe the review.]		
33.	Details of existing review of same topic by same authors	[Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible. NOTE: most NICE reviews will not constitute an update in PROSPERO language. To be an update it needs to be the same review question/search/methodology. If anything has changed it is a new review]		
34.	Current review status	☐ Ongoing ☐ Completed but not published		

		☐ Completed and published ☐ Completed, published and being updated ☐ Discontinued		
35..	Additional information	[Provide any other information the review team feel is relevant to the registration of the review.]		
36.	Details of final publication	[Reference and URL of final guideline]		

Appendix J: Call for evidence

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

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

To simplify copyright considerations, only references or links should be submitted, or details of contacts for unpublished research. The developer will then obtain full copies of all relevant papers or reports, paying a copyright fee if necessary. Copies of full papers, in electronic or hard copy form, should not be submitted in response to a call for evidence.

Submissions of evidence should contain sufficient detail of the methods used to conduct the study to enable NICE to conduct quality assessment.

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

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

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

Confidential information

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

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

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

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

Documenting evidence received in response to a call for evidence

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

Disclosing links with the tobacco industry

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

Box 5.1 Examples of relevant evidence not routinely identified by searches

Ongoing research when an intervention or service is relatively new
Interim study results (not yet published) for longer-term studies
Studies that have been published only as abstracts
Health needs assessments
Protocols
Local pilot studies
Business cases
Financial reports.
Analyses of primary data
Data from patient registries and healthcare databases
Studies of the experiences of people using services, their family members or carers, or practitioners
Data about the off-label use of medicines
Data on harms
Audit data
Implementation case studies
Economic models

Appendix K: Network meta-analysis reporting standards

Reporting of results of network meta-analysis should meet the criteria in the modified version of the PRISMA-NMA checklist specified below. The modified version of the checklist includes only a subset of items in the full checklist that are specifically applicable to reporting the results of network meta-analysis. The full PRISMA-NMA statement with elaborations on each item is reported here:

Hutton B, Salanti G, Caldwell DM et al. (2015) The PRISMA Extension Statement for Reporting of Systematic Reviews Incorporating Network Meta-analyses of Health Care Interventions: Checklist and Explanations. Annals of Internal Medicine 162: 777–84.

Modified PRISMA-NMA checklist (reproduced and modified with permission)

1. Describe the reasons for the review in the context of what is already known, including mention of why a network meta-analysis has been conducted.

2. Specify study characteristics (for example, PICOS, length of follow-up) and report characteristics (for example, years considered, language, publication status) used as criteria for eligibility, giving rationale. Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).

3. Describe methods used to explore the geometry of the treatment network and potential biases related to it. This should include how the evidence base has been graphically summarised for presentation, and what characteristics were compiled and used to describe the evidence base to readers.

4. State the principal summary measures (for example, risk ratio, difference in means). Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses

5. Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to:
    a. Handling of multi-arm trials;
    b. Selection of variance structure;
    c. Selection of prior distributions in Bayesian analyses; and
    d. Assessment of model fit

6. Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address inconsistency when found.

7. Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following:
    a. Sensitivity or subgroup analyses
    b. Meta-regression analyses
    c. Alternative formulations of the treatment network and
    d. Use of alternative prior distributions for Bayesian analyses (if applicable).

8. Provide a network graph of the included studies to enable visualisation of the geometry of the treatment network.

9. Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomised patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure (for example, publication bias).

10. Present results of each meta-analysis done, including confidence/credible intervals. In larger networks, authors may focus on comparisons versus a particular comparator (for example, placebo or standard care). League tables and forest plots may be considered to summarise pairwise comparisons. If additional summary measures were explored (such as treatment rankings), these should also be presented.

11. Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, P values from statistical tests, or summary of inconsistency estimates from different parts of the treatment network.

12. Give results of additional analyses, if done (for example, sensitivity or subgroup analyses, meta-regression analyses, alternative network geometries studied, alternative choice of prior distributions for Bayesian analyses, and so forth).

13. Discuss limitations at study and outcome level (for example, risk of bias), and at review level (for example, incomplete retrieval of identified research, reporting bias). Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (for example, avoidance of certain comparisons).