NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Developing NICE guidelines: the manual

31 October 2014

18 January 2022

5 Identifying the evidence: literature searching and evidence submission

5.1 Introduction

The systematic identification of evidence is an essential step in developing NICE guideline recommendations.

This chapter sets out how evidence is identified at each stage of the guideline development cycle. It provides details of the systematic literature searching methods used to identify the best available evidence for NICE guidelines. It also provides details of associated information management processes including quality assurance (peer review) [see quality assurance in the section on who is involved in the introduction chapter], re-running searches, and documenting the search process.

NICE's searching methods are informed by the chapter on searching & selecting studies in the Cochrane Handbook for Systematic Reviews of Interventions and the Campbell Collaboration's searching for studies guide. The Summarized Research in Information Retrieval for HTA (SuRe Info) resource also provides research-based advice on information retrieval for systematic reviews.

NICE's literature searches are designed to be systematic, transparent, and reproducible, and minimise dissemination bias. Dissemination bias may affect the results of reviews and includes publication bias and database bias.

We use search methods that balance recall and precision. When the need to reduce the number of studies requires pragmatic search approaches that may increase the

risk of missing relevant studies, the context and trade-offs are discussed and agreed within the development team and made explicit in the reported search methods.

A flexible approach to identifying evidence is adopted, guided by the subject of the review question (see the chapter on developing review questions and planning the evidence review), type of evidence sought, and the resource constraints of the evidence review. Often an evidence review will be an update of earlier NICE work, therefore the approach can be informed by previous searches and surveillance reviews.

5.2 Searches during guideline scoping and surveillance

Scoping searches

Scoping searches are top-level searches to support scope development. The purpose of the searches is to investigate the current evidence around the guideline topic, and to identify any areas where an evidence review may be beneficial and any research gaps. The results of the searches are used to draft the scope of the upcoming guideline and to inform the discussions at scoping workshops (if held). Scoping searches do not aim to be exhaustive.

In some cases, scoping searches are not required when it is more efficient to use the surveillance review (see the chapter on the scope).

The sources searched at scoping stage will vary according to the topic of the guideline, type of review questions the guideline will seek to address, and type of evidence sought. Each scoping search is tailored using combinations of the following types of information:

- NICE guidance and guidance from other organisations
- policy and legislation guides
- key systematic reviews and epidemiological reviews
- economic evaluations
- current practice data, including costs and resource use and any safety concerns
- views and experiences of people using services, their family members or carers, or the public

- other real-world health and social care data (for example audits, surveys, registries, electronic health records, patient-generated health data), if appropriate
- summaries of interventions that may be appropriate, including any national safety advice
- statistics (for example on epidemiology, natural history of the condition, service configuration or national prevalence data).

All scoping searches are fully documented and if new issues are identified at a scoping workshop, the search is updated. A range of possible sources considered for scoping searches is provided in the appendix on suggested sources for scoping.

Health inequalities searches

The purpose of these searches is to identify evidence to help inform the scope, health inequalities briefing, or the equality and health inequalities assessment (EHIA). They help identify key issues relevant to health inequalities on the topic, for example covering protected characteristics, groups experiencing or at risk of inequalities, or wider determinants of health.

The searches involve finding key data sources, such as routinely available national databases, audits or published reports by charities, non-governmental bodies, or government organisations. Quantitative and qualitative studies might be needed.

Surveillance searches

Surveillance determines whether published recommendations remain current. The searches are tailored to the evidence required. This may include searches for new or updated policies, legislation, guidance from other organisations, or ongoing studies in the area covered by the evidence review

If required, published evidence is identified by searching a range of bibliographic databases relevant to the topic. Surveillance searches generally use the same core set of databases used during the development of the original evidence review. A list of sources is given in the appendix on sources for evidence reviews.

The search approach and sources will vary between topics and may include:

- population and intervention searches

- focused searches for specific question areas
- forward and backward citation searching.

Searches usually focus on randomised controlled trials and systematic reviews, although other study types will be considered where appropriate, for example for diagnostic questions.

The search period starts at either the end of the search for the last update of a guideline evidence review, or at the last search date for any previous surveillance check. Where appropriate, living evidence surveillance could be set up to continuously monitor the publication of new evidence over a period of time until impact reaches the threshold for actions. For more information on NICE guideline recommendation surveillance, see the chapter on ensuring that guideline recommendations are current and accurate.

5.3 Searches during guideline development

Search protocols

Search protocols form part of the wider guideline review protocol (see the appendix on the review protocol template). They pre-define how the evidence is identified and provide a basis for developing the search strategies.

Once the final scope of the guideline is agreed, the information specialist develops the search protocols and agrees them with the development team before the searching for evidence begins.

A search protocol includes the following elements:

- approach to the search strategy, tailored to the review question and eligibility criteria
- sources to be searched
- plans to use any additional or alternative search techniques, when known at the protocol development stage, and the reasons for their use
- details of any limits to be applied to the search
- references to any key papers used to inform the search approach.

Sources

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

For most searches there are key sources that are prioritised, and other potentially relevant sources that can be considered. It is important to ensure adequate coverage of the relevant literature and to search a range of sources. However, there are practical limits to the number of sources that can be searched in the standard time available for an evidence review.

The selection of sources varies according to the requirements of the review question.

Clinical intervention sources

For reviews of the effectiveness of clinical interventions the following sources are prioritised for searching:

- the Cochrane Central Register of Controlled Trials (CENTRAL)
- the Cochrane Database of Systematic Reviews (CDSR)
- Embase
- MEDLINE.

Clinical safety sources

In addition to the sources searched for clinical interventions, the following should be prioritised for clinical safety review questions:

- MHRA drug safety updates
- National patient safety alerts.

Antimicrobial resistance sources

For reviews of antimicrobial resistance, the following sources should be prioritised:

- UK Health Security Agency's English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report
- UK Health Security Agency's antimicrobial resistance local indicators.

Cost-effectiveness sources

For reviews of cost effectiveness, economic databases are used in combination with general bibliographic databases, such as MEDLINE and Embase (see appendix G on sources for economic reviews).

Economic evaluations of social care interventions may be published in journals that are not identified through standard searches. Targeted searches based on references of key articles and contacting authors can be considered to identify relevant papers.

Topic-specific sources

Some topics we cover may require the use of topic-specific sources. Examples include:

- PsycINFO (psychology and psychiatry)
- CINAHL (nursing and allied health professions)
- ASSIA (Applied Social Sciences Index and Abstracts)
- HealthTalk, and other sources to identify the views and experiences of people using services, carers and the public
- social policy and practice
- social care online
- sociological abstracts
- transport database
- Greenfile (environmental literature)
- HMIC (Health Management Information Consortium).

Searching for model inputs

Evidence searches may be needed to inform design-oriented conceptual models. Examples include precise searches to find representative NHS costs for an intervention or finding out the proportion of people offered an intervention who take up the offer.

Some model inputs, such as costs, use national sources such as national list prices or national audit data. In some cases, it may be more appropriate to identify costs from the academic literature. Further advice on methods to identify model inputs are

also informed by Paisley (2016) and Kaltenhaler et al. (2011). See also the chapter on incorporating economic evaluation

Real-world data

Information specialists can identify sources of real-world data (such as electronic health records, registries, and audits) for data analysts to explore further. The Health Data Research Innovation Gateway can be used to identify datasets. The NICE real-world evidence framework (2022) has additional guidance on searching for and selecting real-world data sources.

Grey literature

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

- HMIC (Health Management Information Consortium)
- GOV.uk
- TRIP database
- social policy and practice
- Canadian Agency for Drugs and Technology in Health (CADTH) Grey Matters resource.

Committee members may also be able to suggest additional appropriate sources for grey literature.

A list containing potential relevant sources is provided in the appendix on sources for evidence reviews.

Developing search strategies

The approach to devising and structuring search strategies is informed by the review protocol. The PICO (population, intervention, comparator and outcome) or SPICE (setting, perspective, intervention, comparison, evaluation) frameworks may be used to structure a search strategy for intervention review questions. For other types of review questions, alternative frameworks may be more suitable.

It is sometimes more efficient to conduct a single search for multiple review questions, rather than conducting a separate search for each question.

Some topics may not easily lend themselves to PICO- or SPICE-type frameworks. In these cases, it may be better to combine multiple, shorter searches rather than attempting to capture the entire topic using a single search. This is often referred to as multi-stranded searching.

In some instances, for example where the terminology around a topic is diffuse or ill defined, it may be difficult to specify the most appropriate search terms in advance. In these cases, an iterative approach to searching can be used.

In an iterative approach, searching is done in several stages, with each search considering the evidence that has already been retrieved (for example, see Booth et al. 2020). Searching in stages allows the reviewers to review the most relevant, high-quality information first and then make decisions for identifying additional evidence if needed.

Decisions to use iterative approaches are agreed by the development team and staff with responsibility for quality assurance because it can affect timelines.

Updating previous work

Where high-quality review-level evidence is available on a topic, the review team may choose to update or expand this previous work rather than duplicating the existing findings. In these cases, the original review searches are re-run and expanded to account for any differences in scope and inclusion criteria between the original review and the NICE update.

Cost-effectiveness searches

There are several methods that can be used to identify economic evaluations:

- All relevant review questions can be covered by a single search using the population search terms, combined with a search filter, to identify economic evidence.

- The search strategies for individual review questions can be combined with search filters to identify economic evidence. If using this approach, it may be necessary to adapt strategies for some databases to ensure adequate sensitivity.
- Economic evidence can be manually sifted while screening evidence from a general literature search (so no separate searches are required).

The rationale for the selected approach is recorded in the search protocol.

Where searches are needed to populate an economic model, these are usually conducted separately.

Identifying search terms

Search terms usually consist of a combination of subject headings and free-text terms from the titles and abstracts of relevant references.

When identifying subject headings, variations in thesaurus and indexing terms for each database should be considered, for example MeSH (Medical Subject Headings) in MEDLINE and Emtree in Embase. Not all databases have indexing terms and some contain records that have not yet been indexed.

Free-text terms may include synonyms, acronyms and abbreviations, spelling variants, old and new terminology, brand and generic medicine names, and lay and medical terminology.

For a guideline that is being updated, previous search terms, including those from surveillance searches, are reviewed and used to inform new search terms. New or changed terms are identified, as well as any changes to indexing terms. This also applies when an existing review, for example a Cochrane review, is being updated to answer a review question.

Key studies can be a useful source of search terms, as can reports, guidelines, topic-specific websites, committee members and topic experts.

Some websites and databases have limited search functionality. It may be necessary to use fewer search terms or do multiple searches of the same resource with different search term combinations.

It may be helpful to use frequency analysis or text mining to develop the search-term strategy. Tools such as PubReMiner and Medline Ranker can help, either by highlighting search terms that might not otherwise be apparent, or by flagging terms of high value when exhaustive synonym searching is unfeasible or inadvisable.

Search limits

The application of limits to search strategies will reflect the eligibility criteria in the review protocol. Typically, English language limits, date limits, removal of animal studies, and the exclusion of conference abstracts are usually done as a matter of routine.

Search filters

A search filter is a string of search terms with known (validated) performance. When a particular study design is required for a review question, relevant search filters are usually applied to literature search strategies.

Other search filters relating to age, setting, geography, and health inequalities are also applied as relevant. The most comprehensive list of available search filters is the search filter resource of the InterTASC Information Specialists' SubGroup. This resource also includes critical appraisal tools, which are used for filter selection.

Economics-related filters

A variety of search filters of relevance to cost effectiveness are available. These include filters for economic evaluations, quality of life data, and cost-utilities data. It may be necessary to use more than 1 filter to identify relevant data. In addition, it may be appropriate to add geographic search filters, such as those for the UK or Organisation for Economic Co-operation and Development (OECD) countries, to retrieve economic studies relevant to the UK or OECD (Ayiku et al. 2017, 2019, 2021).

Use of machine learning-based classifiers

Machine learning-based classification software has been developed for some study types (for example the Cochrane RCT classifier, Thomas et al. 2020). These classifiers apply a probability weighting to each bibliographical reference within a set of search results. The weighting relates to the reference's likelihood to be a particular

study type, based on a model created from analysis of known, relevant papers. The weightings can then be used to either order references for screening or be used with a fixed cut-off value to divide a list of references into those more likely to be included, and those that can be excluded without manual screening.

We support the use of machine classifiers if their performance characteristics are known, and if they improve efficiency in the search and screening process. However, caution is needed when using classifiers, because they may not be as effective if used on data that is different to the type of data for which they were originally developed. For example, the Cochrane RCT classifier is reported to have over 99% recall for health studies but showed “unacceptably low” recall for educational research (Stansfield et al. 2022).

Priority screening, a type of machine classifier that orders references for manual sifting based on previous sifting decisions, is considered in the chapter on reviewing evidence.

Additional search techniques

Additional search techniques are used alongside database searching when it is known, or reasonably likely, that relevant evidence is not indexed in bibliographic databases, or when it will be difficult to retrieve relevant evidence from databases in a way that adequately balances recall and precision. Additional search techniques include forward and backward citation searching, journal hand-searches and contacting experts and stakeholders.

Existing reviews may provide an additional source of primary studies, with reference lists being used as an indirect method of identifying primary research.

Various tools, including Citationchaser and Web of Science, are available to speed up the process of citation searching. These may not be as comprehensive as manual reference list checking (due to limitations of the underlying data sources), but the trade-off in terms of speed is generally acceptable.

All search techniques should follow the same principles of transparency, rigour and reproducibility as other search methods.

If possible, additional search techniques should be considered at the outset and documented in the search protocol (see the section on search protocols). They should also be documented in the supporting appendices for the final evidence review.

5.4 Health inequalities and equality and diversity

All searches aim to be inclusive. This may mean not specifying any population groups.

Searches should avoid inadvertently excluding relevant groups. For example, if the population group is older people, a search for older people should pick up subpopulations such as disabled older people.

Additional search strategies may be needed to target evidence about people with protected characteristics or people experiencing or at risk from other inequalities.

Searches may need to be developed iteratively to ensure coverage of the health inequalities issues or evidence on the impacts of an intervention on equality.

Appropriate terminology for the search should be used, considering how language has evolved.

5.5 Quality assurance

Quality assuring the literature search is an important step in guideline development. Studies have shown that errors do occur.

For each search (including economic searches), the initial MEDLINE search strategy is quality assured by a second information specialist. A checklist is used to ensure clarity and consistency when quality assuring search strategies. An example is the PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement.

The information specialist carrying out the quality assurance process also considers how appropriate the overall search approach is to the parameters of the evidence review (for example, the time available to carry out the review). The quality assurance comments are recorded and the information specialist who conducted the search should respond to the comments and revise the search strategy as needed.

Search strategy translations across the remaining databases are also checked by a second information specialist to ensure that the strategies have been adapted appropriately, in accordance with the interfaces and search functionality of the sources used.

5.6 Documenting the search

Details of the evidence search are included as appendices to the individual evidence reviews. They are published for consultation alongside the draft evidence review and included in the final version.

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

We use the PRISMA-S: an extension to the PRISMA statement for reporting literature searches in systematic reviews to inform search reporting. The search documentation is an audit trail that allows the reader to understand both the technical aspect of what was done (such as which sources were searched; what platform was used and on what date; any deviations from the original search protocol) and the underlying rationale for the search approach where this may not be immediately apparent.

Documenting the search begins with creating the search protocol (see the section on search protocols). If using an iterative or emergent stepped approach, initial search strategies, key decision points and the reasons for subsequent search steps are clearly documented in the search protocol and final evidence review. When using a proprietary search engine such as Google, whose underlying algorithm adapts to different users, the search is reported in a way that should allow the reader to understand what was done.

5.7 Re-running searches

Searches undertaken to identify evidence for each review question (including economics searches) may be re-run before consultation or before publication. For example, searches are re-run if the evidence changes quickly, there is reason to

believe that substantial new evidence exists, or the development time is longer than usual.

A decision to re-run searches is taken by the development team and staff with responsibility for quality assurance.

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

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

5.8 Calls for evidence from stakeholders

Stakeholders' role in providing evidence

In some topic areas or for some review questions, staff with responsibility for quality assurance, the development team or the committee may believe that there is relevant evidence in addition to that identified by the searches. In these situations, the development team may invite stakeholders, and possibly also other relevant organisations or individuals with a significant role or interest (see 'expert witnesses' in the section on other attendees at committee meetings in the chapter on decision-making committees), to submit evidence. A call for evidence is issued directly to registered stakeholders on the NICE website. Examples and details of process are included in the appendix on call for evidence and expert witnesses. Confidential information should be kept to an absolute minimum.

5.9 References and further reading

Ayiku L, Levay P, Hudson T et al. (2017) The medline UK filter: development and validation of a geographic search filter to retrieve research about the UK from OVID medline. Health Information and Libraries Journal 34(3): 200–216

Ayiku L, Levay P, Hudson T et al. (2019) The Embase UK filter: validation of a geographic search filter to retrieve research about the UK from OVID Embase. Health Information and Libraries Journal 36(2): 121–133

Ayiku L, Hudson T, Williams C et al. (2021) The NICE OECD countries' geographic search filters: Part 2-validation of the MEDLINE and Embase (Ovid) filters. Journal of the Medical Library Association 109(4): 583–9

Booth A, Briscoe S, Wright JM (2020) The “realist search”: a systematic review of current practice and reporting. Research Synthesis Methods 11: 14–35

Canadian Agency for Drugs and Technologies in Health (2019) Grey Matters: a practical tool for searching health-related grey literature [online; accessed 24 July 2023]

Glanville J, Lefebvre C, Wright K (editors) (2008, updated 2017) The InterTASC Information Specialists’ Subgroup Search Filters Resource [online; accessed 24 July 2023]

Kaltenthaler E, Tappenden P, Paisley S (2011) NICE DSU Technical support document 13: identifying and reviewing evidence to inform the conceptualisation and population of cost-effectiveness models [online; accessed 24 July 2023]

Kugley S, Wade A, Thomas J et al. (2017) Searching for studies: a guide to information retrieval for Campbell systematic reviews. Oslo: The Campbell Collaboration

Lefebvre C, Glanville J, Briscoe S et al. Chapter 4: Searching for and selecting studies. In: Higgins JPT, Thomas J, Cumpston M et al. (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021). Cochrane, 2021

McGowan J, Sampson M, Salzwedel DM et al. (2016) PRESS Peer Review of Electronic Search Strategies: 2015 guideline statement. Journal of Clinical Epidemiology 75: 40–6

National Institute for Health and Care Excellence (2022) NICE real-world evidence framework [online; accessed 24 July 2023]

Paisley S (2016) Identification of key parameters in decision-analytic models of cost-effectiveness: a description of sources and a recommended minimum search requirement. Pharmacoeconomics 34: 597–8

Rethlefsen M, Kirtley S, Waffenschmidt S et al. (2021) PRISMA-S: an extension to the PRISMA statement for reporting literature searches in systematic reviews. Systematic Reviews 10: 39

Stansfield C, Stokes G, Thoman J (2022) Applying machine classifiers to update searches: analysis from two case studies. Research Synthesis Methods 13: 121–33

Summarized research for Information Retrieval in HTA (SuRe Info) [online; accessed 24 July 2023]