

## 5 Systematic literature review

Guidelines based on a consensus of expert opinion or on unsystematic literature surveys have been criticised as not reflecting current medical knowledge and being liable to bias.<sup>1</sup> <sup>2</sup> SIGN guidelines are therefore based on a systematic review of the evidence. Systematic review is defined as "*an efficient scientific technique to identify and summarise evidence on the effectiveness of interventions and to allow the generalisability and consistency of research findings to be assessed and data inconsistencies to be explored*".<sup>3</sup>

The SIGN approach leads to guidelines that are essentially the direct product of the systematic review. There is no separate report of the review or its conclusions, though all the stages of the review process are thoroughly documented (see below). Because the reviews are largely undertaken by members of SIGN guideline development groups working part time on the project, and within a limited timescale, their coverage of the literature may be more limited than those carried out by dedicated systematic review groups such as the Cochrane Collaboration. Nevertheless, the essential elements of systematic review are met:

- the literature is identified according to an explicit search strategy
- selected according to defined inclusion and exclusion criteria
- evaluated against consistent methodological standards.

The benefits of the SIGN approach derive from the close involvement of guideline developers with the synthesis of the evidence base, allowing them to apply their *considered judgement* when deriving recommendations (see section 6), and from encouraging a sense of ownership of the guideline amongst all those involved in the process.

### 5.1 ADDRESSING PATIENT ISSUES IN THE LITERATURE SEARCH

Incorporating the patient's perspective from the beginning of the development process is essential if it is to influence the coverage of the final guideline. One of the measures used to achieve this is to conduct a specific search on patient issues in advance of the first meeting of the guideline development group. This search is designed to cover both quantitative and qualitative evidence, and is not limited to specific study designs. It is carried out over the same range of databases and sources as the main literature review, but will normally include both nursing and psychological literature even where these are not seen as particularly relevant to the later searches of the medical literature.

Once this search has been carried out, the results are sifted to identify those papers relevant to the guideline topic. Wherever possible the methodology of these papers is evaluated using standard checklists (see Section 5.4). The final results of this search and evaluation process are categorised into themes that highlight the main issues of concern to patients. These themes are then presented to the guideline development group as a means of ensuring that the key questions they specify take account of patient concerns.

### 5.2 DEFINING KEY QUESTIONS

The training in critical appraisal and guideline development offered to members of SIGN guideline development groups encourages them to break down the guideline remit into a series of structured key questions that clearly identify the *population* concerned, the *intervention* (or diagnostic test, etc.) under investigation, the type of *control* used, and the *outcome measures* used to measure the effectiveness of the interventions. These questions

then form the basis of the literature search, which is undertaken by a SIGN Information Officer.

The range of key questions may be influenced by existing guidelines. The guideline section of the scoping search carried out for the original guideline proposal (see *Section 3*) will be updated and extended to cover material found in Embase and Medline and the results presented to an early meeting of the guideline development group to allow them to consider what has been done already.

In some cases good quality, directly relevant guidelines will have been produced on some of the issues that fall within the remit of the new guideline. In these circumstances reference will be made to the existing guidelines rather than repeating work that has already been completed. All guidelines must be evaluated using the AGREE instrument (see *Annex A*) and be shown to have followed an acceptable methodology before they can be considered for use in this way.

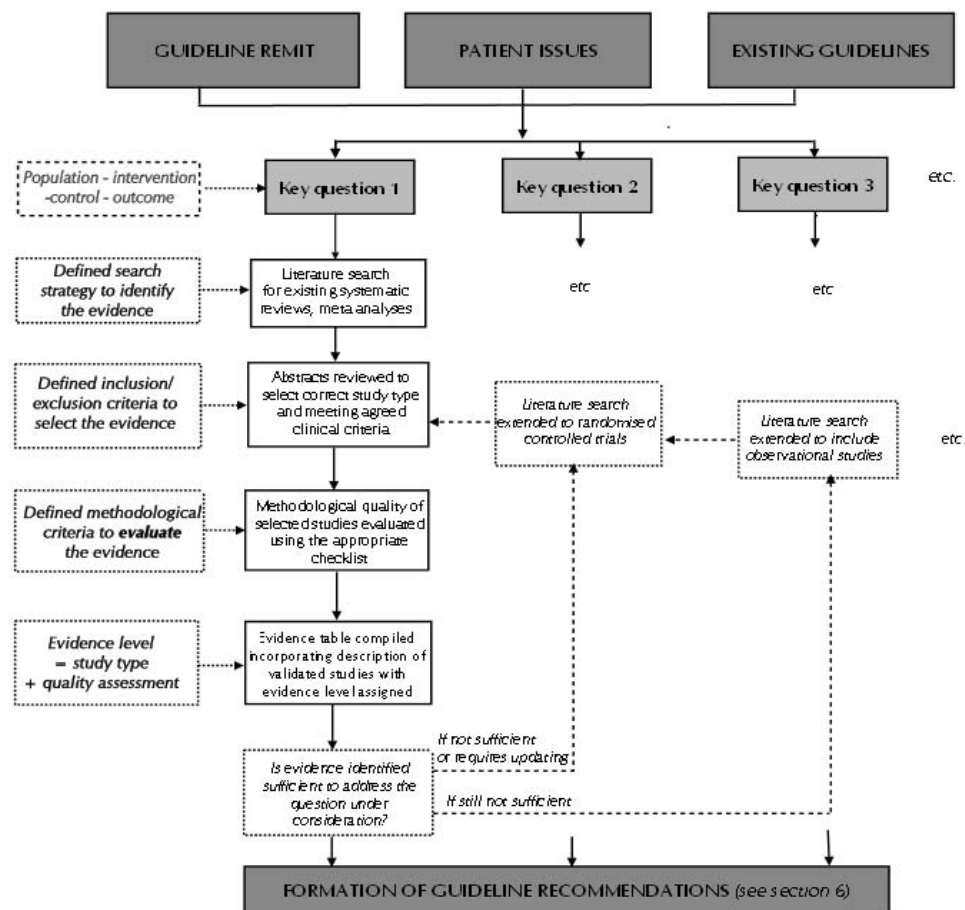
In other cases existing guidelines may not be directly relevant to the NHS in Scotland, or may be found to have methodological weaknesses. If these guidelines are based on a well conducted systematic review, the guideline group may be able to use the evidence base from those guidelines as a starting point for their own review.

Definition of a set of clear and focused clinical questions is fundamental to the successful completion of a guideline development project. It is also important to be realistic about the number of questions that can be addressed in a single guideline if the final product is not to be too large to be useable. A large number of key questions also implies a very high workload for the developers, and care must be taken to ensure this is kept within manageable limits. Where the number of questions reaches 40 or more, serious consideration must be given as to whether the scope of the guideline needs to be redefined.

Deciding the key questions is entirely the responsibility of the guideline development group who must apply their knowledge and experience to ensuring the questions address the key issues in the area to be covered by the guideline.

### 5.3 IDENTIFYING AND SELECTING THE EVIDENCE

Figure 5.1  
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The search must focus on the best available evidence to address each key question, and should ensure maximum coverage of studies at the top of the hierarchy of study types (see section 6). SIGN uses a set of standard search filters that identify:

- Guidelines
- Meta-analyses, and systematic reviews.
- Randomised controlled trials.
- Observational studies
- Diagnostic studies
- Economic studies
- Qualitative studies

These search filters are available from the SIGN Web site ([www.sign.ac.uk](http://www.sign.ac.uk)). The systematic literature review procedure is illustrated in Figure 5.1 and an example protocol documenting all aspects of a literature review is shown in Annex E.

In order to minimise bias and to ensure adequate coverage of the relevant literature, the literature search must cover a range of sources. The Information Team reviews all search strategies in conjunction with members of the guideline development group. As a minimum, SIGN requires searches to cover the Cochrane Library, Embase, Medline, and the Internet. It is expected that in most cases the search will also cover additional sources specific to the topic under review, and the health economics literature.

The period that the search should cover will depend on the nature of the clinical topic under consideration, and will be discussed with the guideline development group. For a rapidly developing field a 10 or 15-year limit to the search may be appropriate, whereas in other areas a much longer time frame might be necessary.

SIGN does not undertake hand searching of key journals as part of the literature review. It is accepted that this means some relevant trials may be missed, and introduces the possibility of a degree of bias in the process. However, given time and resource constraints, it is not feasible for this to form part of the process. Manual searching of indexes such as *Index Medicus* for papers published prior to the introduction of computerised databases may be necessary in some cases, however, and this will be included in the search process.

A listing of the Medline search strategies used for the guideline, plus notes of any significant variation on other databases, is published on the SIGN Web site ([www.sign.ac.uk](http://www.sign.ac.uk)) at the time of the National Meeting associated with the guideline. This strategy will remain on the Web as part of the supporting material for the guideline when it is published.

Before any papers are acquired for evaluation, sifting of the search output is carried out to eliminate irrelevant material. A preliminary sift of each search result is carried out by staff at the SIGN Executive, normally by the individual that carried out the search. Papers that are clearly not relevant to the key questions are eliminated. Abstracts of remaining papers are then examined and any that are clearly not appropriate study designs, or that fail to meet specific methodological criteria, will be also eliminated at this stage.

A final sift is carried out by one or two individuals from the guideline development group, who will reject other papers that do not meet clinical or other criteria that have been agreed by the development group. Only when all stages of search result sifting have been completed will the remaining papers be acquired for evaluation.

In practice, it is rare for a single search to cover all the questions being addressed within a guideline. Different questions may be best answered by different databases, or may rely on different levels of evidence. Guideline development groups are encouraged to take an iterative approach to the search, carrying out a search for high level evidence in the first instance. After the results of this search have been evaluated, the questions may be redefined and subsequent searches focused on the most appropriate sources and study types.

### 5.4 EVALUATING THE EVIDENCE

Once papers have been selected as potential sources of evidence, the methodology used in each study is assessed to ensure its validity. The result of this assessment will affect the **level of evidence** allocated to the paper, which will in turn influence the **grade of recommendation** that it supports (see section 6).

The methodological assessment is based on a number of key questions that focus on those aspects of the study design that research has shown to have a significant influence on the

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validity of the results reported and conclusions drawn. These key questions differ between study types, and a range of checklists is used to bring a degree of consistency to the assessment process. SIGN has based its assessments on the MERGE (Method for Evaluating Research and Guideline Evidence) checklists developed by the New South Wales Department of Health,<sup>4</sup> which have been subjected to wide consultation and evaluation. These checklists were subjected to detailed evaluation and adaptation to meet SIGN's requirements for a balance between methodological rigour and practicality of use. Copies of these checklists and accompanying notes on their use are included in Annex C.

The assessment process inevitably involves a degree of subjective judgement. The extent to which a study meets a particular criterion – e.g. an acceptable level of loss to follow up – and, more importantly, the likely impact of this on the reported results from the study will depend on the clinical context. To minimise any potential bias resulting from this, each study must be evaluated independently by at least two group members. Any differences in assessment should then be discussed by the full group. Where differences cannot be resolved, an independent reviewer or an experienced member of SIGN Executive staff will arbitrate to reach an agreed quality assessment.

### *References to section 5*

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2. Mulrow C. Rationale for systematic reviews. *BMJ* 1994;309:597-9.
3. Woolf S. Practice guidelines, a new reality in medicine. II: Methods of developing guidelines. *Arch Intern Med* 1992;152:946-52.
4. Liddle J, Williamson M, Irwig L. Method for evaluating research and guideline evidence. Sydney: New South Wales Department of Health; 1996.