Healthcare Improvement Scotland

SIGN
Scottish Intercollegiate Guidelines Network

50

SIGN 50
A guideline developer's handbook

Revised edition
November 2011

NHS Quality Improvement Scotland (NHS QIS) is committed to equality and diversity. This guideline has been assessed for its likely impact on the six equality groups defined by age, disability, gender, race, religion/belief, and sexual orientation.

For the full equality and diversity impact assessment report please see the "published guidelines" section of the SIGN website at **www.sign.ac.uk/guidelines/published/numlist.html**. The full report in paper form and/or alternative format is available on request from the NHS QIS Equality and Diversity Officer.

Scottish Intercollegiate Guidelines Network

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January 2008

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SIGN consents to the photocopying of this guideline for the purpose of implementation in NHSScotland

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Meeting the agree appraisal criteria

SIGN methodology complies with the criteria used by the AGREE (Appraisal of Guidelines for Research and Evaluation in Europe) to identify good quality guidelines. The chapters of this manual that describe how SIGN addresses each criterion are identified below.

		SIGN 50 chapter
Scope and purpose		
1.	The overall objective(s) of the guideline should be specifically described.	9.1
2.	The clinical question(s) covered by the guideline should be specifically described.	6.3
3.	The patients to whom the guideline is meant to apply should be specifically described.	9.1
Stakeholder involvement		
4.	The guideline development group should include individuals from all the relevant professional groups.	5
5.	The patients' views and preferences should be sought.	4
Rigour of development		
6.	Systematic methods should be used to search for evidence.	6
7.	The criteria for selecting the evidence should be clearly described.	6.3, 6.4
8.	The methods used for formulating the recommendations should be clearly described.	7.1
9.	The health benefits, side effects and risks should be considered in formulating the recommendations.	7.2
10.	There should be an explicit link between the recommendations and the supporting evidence.	7.2
11.	The guideline should be externally reviewed by experts prior to publication.	8.2
12.	A procedure for updating the guideline should be provided.	3.4
Clarity of presentation		
13.	The recommendations should be specific and unambiguous.	9.1
14.	The different options for diagnosis and/or treatment of the condition should be clearly presented.	9.1
15.	Key recommendations should be easily identifiable.	7.2.3
Applicability		
16.	The target users of the guideline should be clearly defined.	9.1
17.	The potential organisational barriers in applying the recommendations should be discussed.	10
18.	The potential cost implications of applying the recommendations should be considered.	7.4
19.	The guideline should be supported with tools for application.	10
20.	The guideline should present key review criteria for monitoring and audit purposes	9.1, 9.7
21.	The guideline should be piloted among end users.	8.1
Editorial independence		
22.	The guideline should be editorially independent from the funding body.	1.1
23.	Conflicts of interest of guideline development members should be recorded.	2.4

1 Introduction

1.1 CLINICAL GUIDELINES AND SIGN

The Scottish Intercollegiate Guidelines Network (SIGN) was established in 1993 by the Academy of Royal Colleges and their Faculties in Scotland, to develop evidence based clinical guidelines for the National Health Service in Scotland.[1,2] Since January 2005, SIGN has been part of NHS Quality Improvement Scotland, though under the transfer agreement with the Academy SIGN retains editorial independence in relation to the guidelines it produces.

Clinical practice guidelines have been defined as "*systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances*".[3] They are designed to help practitioners assimilate, evaluate and implement the ever increasing amount of evidence and opinion on best current practice. Clinical guidelines are intended as neither cookbook nor textbook but, where there is evidence of variation in practice which affects patient outcomes and a strong research base providing evidence of effective practice, guidelines can assist healthcare professionals in making decisions about appropriate and effective care for their patients.

The accepted criteria for validity of guidelines have evolved from the 'essential elements of good guidelines' identified by the US Institute of Medicine in 1990.[3] These recommended 'attributes of good guidelines' included validity, reliability, clinical applicability, clinical flexibility, clarity, multidisciplinary process, scheduled review, and documentation. The recommendations were underpinned by the twin themes of credibility and accountability: "*The link between a set of guidelines and the scientific evidence must be explicit, and scientific and clinical evidence should take precedence over expert judgement.*" SIGN's original Criteria for Appraisal of Clinical Guidelines for National Use,[4] and the more recent AGREE (Appraisal of Guidelines, Research and Evaluation for Europe) guideline appraisal instrument[5] are based on these founding principles of guideline development.

The AGREE criteria are reproduced in the introductory material to this manual, with links to those manual chapters that explain how SIGN addresses each criterion. The only area where SIGN does not comply with the AGREE criteria is in relation to the piloting of guidelines. The full appraisal instrument can be downloaded from the AGREE website: **www.agreetrust.org**

1.2 AIM AND STRUCTURE OF THIS MANUAL

This is the third revision of SIGN 50, previous versions having been issued in 2002 and 2004. SIGN methodology has continued to develop and since the previous version of this manual there have been significant developments in the procedures for reviewing guidelines, the involvement of patients and carers, and extending the range of evidence considered.

The principal aim of this manual is to provide a reference tool that may be used by individual members of guideline development groups as they work through the development process. Guidelines are intended for use by healthcare practitioners who are inevitably busy, with limited time available to read publications such as guidelines. Rather than overload every guideline with methodological details, SIGN 50 outlines the key elements of the development process common to all SIGN guidelines. Only where aspects of the topic under consideration require a variation from the standard process will these be reported in the guidelines themselves.

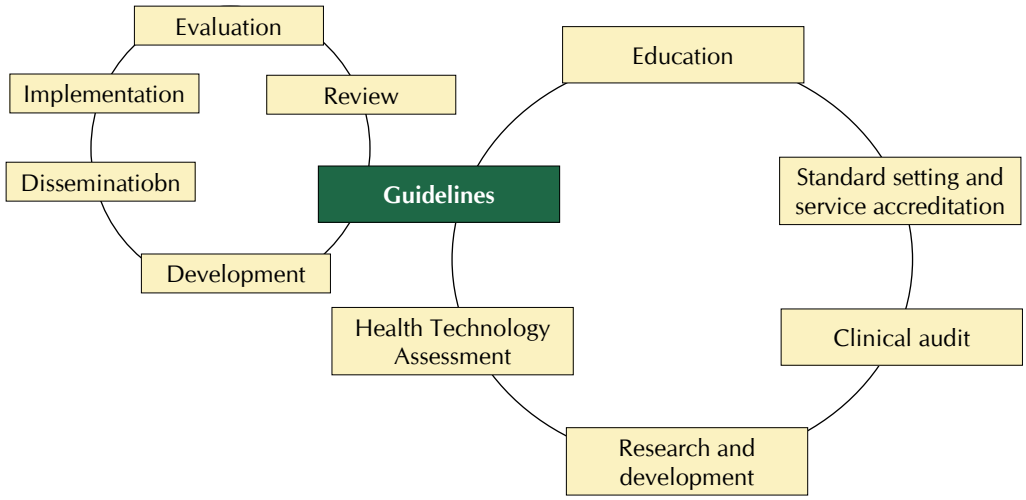
Guideline developers have an increasing obligation to be transparent about the methods they have used to develop their guideline. A secondary aim of this manual is to allow users to see how SIGN guidelines are developed, and instil confidence that the potential biases of guideline development have been addressed adequately, and that the recommendations are both internally and externally valid, and feasible for practice.

SIGN 50 is structured to follow the guideline development process from beginning to end, taking each step in turn. It starts with the context of guideline development in Scotland, and progresses from first proposal of a new topic to final publication and implementation of the guideline. Hyperlinks are provided in the text to guide the user to related topics where there is overlap between different chapters.

1.3 GUIDELINES IN CONTEXT

Guideline development, implementation, and review should be seen not as a linear process, but as a cycle of interdependent activities. These in turn are part of a range of complementary activities to translate evidence into practice, set and monitor standards, and promote clinical excellence in NHSiS, as illustrated in Figure 1.

Figure 1: Guideline and audit cycles



Guidelines frequently look at medicines, interventions and technologies that are also the subject of individual review with authorities responsible for approving their use in the NHS. In this respect SIGN takes account of the reviews carried out by the Scottish Medicines Consortium (SMC) and the National Institute for Health and Clinical Excellence (NICE). The close relationship between SIGN and other parts of NHS Quality Improvement Scotland facilitates these processes. The highest standards of patient care and improved outcomes are the ultimate goal.

Guidelines can achieve better treatment outcomes and care for patients, but local ownership of the implementation process is crucial to success in changing practice. For this reason, SIGN is responsible for the development of national guidelines and their implementability, but not directly for their implementation into practice. This is a responsibility of each individual NHS Board, and is now reinforced by the twin 'levers' of clinical governance and the standard setting and review components of NHS Quality Improvement Scotland. However, there is a role for national facilitation of local guideline implementation activities, and this is discussed in **Chapter 10.**

Links with local and national audit projects are also an essential part of guideline implementation, and SIGN has been working closely with the Information and Statistics Division (ISD) to develop the audit component of guidelines and, where possible, to develop minimum datasets to facilitate prospective audit. This is discussed in **Chapter 9.**

1.4 MEDICO-LEGAL IMPLICATIONS OF SIGN GUIDELINES

The potential medico-legal implications of clinical guidelines have been of ongoing concern to medical practitioners since the establishment of a Scottish national guideline development programme was first proposed. Dr Pamela Abernethy of Simpson and Marwick WS, one of the leading Scottish experts on medical negligence, provided an initial paper on the legal implications of guidelines to SIGN and NHS Scotland in December 1995.[6] In this paper she concluded that clinical guidelines do not rob clinicians of their freedom, nor relieve them of their responsibility to make appropriate decisions based on their own experience and according to the particular circumstances of each patient. It is stressed that the standard of care required by law derives from customary and accepted practice rather than from the imposition of practices through clinical guidelines.

Dr Abernethy refers to the 1955 case of Hunter v Hanley as establishing the standard of care required under Scottish Law and describes the three-step test used to establish the liability of a healthcare professional where it is alleged that (s)he has deviated from normal practice. The Central Legal Office (CLO) advised SIGN in 2006[7] that the Hunter v Hanley test is still the appropriate test in Scotland for liability for clinical negligence, ie it must be established that the course the healthcare professional has adopted "is one which no professional man of ordinary skill would have taken if he had been acting with ordinary care". This test was developed further by the Bolam test, ie a healthcare professional is not guilty of negligence if "he has acted in accordance with a practice accepted as proper by a responsible body of men skilled in that particular art". A healthcare professional may therefore defend a charge of negligence with evidence that (s)he acted in conformity with the practice accepted by another body of opinion. The test applied by the Court is therefore based on what is actually done in practice rather than on a prescription of what should be done as proposed by guidelines.

Dr Abernethy states also that customary and accepted practice will be established in court by introduction of expert testimony. Although clinical guidelines will not be introduced as a substitute for expert testimony, they may be referred to by an expert witness as evidence of such customary and accepted practice. The CLO has advised SIGN that this is still the case.

The Hunter v Hanley test has been developed since 1995 by the 1997 case of Bolitho v City and Hackney Health Authority. This case introduced a more critical approach to the evidence supplied by expert witnesses and provided that where it can be demonstrated that professional opinion is not capable of withstanding logical analysis, the judge would be entitled to determine that the opinion was not reasonable or responsible.

The CLO advice to SIGN following this case is that the opinions of medical experts may not be regarded as final and authoritative.[7] Although a defendant may present expert opinion that his practice was sound, the judge may look at additional evidence to determine whether the practice was in fact logical. It may be that evidence based guidelines will be referred to as part of that additional evidence and the court may require to know why such guidelines were not followed and the reasoning behind the decision not to follow them. There is consequently greater potential for clinical guidelines to have a greater role in identifying the standard of care.

In addition to this legal development in the determination of the duty of care, the origins of some guidelines which have been produced since 1995 may be relevant in the future in determining their legal status. There is an argument that some guidelines produced by organisations such as SIGN and NICE could come to be regarded as authoritative guidance in view of the robust methods used in their production and also in view of the national status of these organisations.

Some established national guidelines may be referred to by the court at present as a starting point from which to consider a healthcare professional's conduct. The Hunter v Hanley test does of course still apply in determining the standard of care and at present such guidelines do not set the standard of care. (This is stated in each SIGN guideline).

If the law were to develop in the future to accredit a more authoritative status to guidelines of this nature, the burden of proof, in the opinion of some commentators, may move to the healthcare professional where such a guideline is not adhered to. Instead of the plaintiff being required to prove that the healthcare professional failed to provide a minimum standard of care in accordance with the Hunter v Hanley Test, the healthcare professional may be required to prove that the care met the required standard of the Hunter v Hanley test although the guideline has not been applied. This is, however, only conjecture and at present the burden of proof remains with the plaintiff.

The CLO has advised SIGN that there has to date been no reference to SIGN guidelines in any reported cases of medical negligence.[7]

It is important to emphasise that SIGN guidelines are intended as an aid to clinical judgement not to replace it. Guidelines do not provide the answers to every clinical question, nor guarantee a successful outcome in every case. The ultimate decision about a particular clinical procedure or treatment will always depend on each individual patient's condition, circumstances and wishes, and the clinical judgement of the healthcare team.

Guidelines are, however, intended to address variation in practice. While there is no compulsion to implement any SIGN guideline or individual recommendations, NHS Boards, clinical teams, and individual practitioners in primary and secondary care should all be able to define the standard of care which they provide, and to justify if necessary why these do not meet nationally agreed recommendations.

1.5 REVIEW AND UPDATING OF THIS MANUAL

It is intended that *SIGN 50* should be a 'living' publication, continually revised to reflect future developments in SIGN methodology. For this reason the definitive version of this handbook is that published on the SIGN website. Printed versions are produced for use as required by SIGN guideline development groups.

Comments on either content or presentation of this document are welcome and should be sent to the SIGN Executive, Elliott House, 8 -10 Hillside Crescent, Edinburgh EH7 5EA. Email: **sign@sign.ac.uk**

2 Organisation of guideline development

2.1 THE SCOTTISH INTERCOLLEGIATE GUIDELINES NETWORK

The Scottish Intercollegiate Guidelines Network (SIGN) was established in 1993 by the Conference (later, the Academy) of Royal Colleges and their Faculties in Scotland, to develop evidence based clinical guidelines for the National Health Service in Scotland.[2] This followed the publication of a report by the Clinical Resource and Audit Group (CRAG) which highlighted the need for national, evidence based clinical guidelines to be developed by "the Royal Colleges, the specialist associations of the healthcare professionals and relevant educational bodies".[1]

SIGN has evolved significantly since 1993 but remains a collaborative initiative - a network of clinicians, patients' representatives and other healthcare professionals, including all the medical specialties, nursing, pharmacy, dentistry, professions allied to medicine, and NHS management. Patients are represented on SIGN by Voluntary Health Scotland and lay representation. The current membership of SIGN Council is noted on the website: **www.sign.ac.uk**

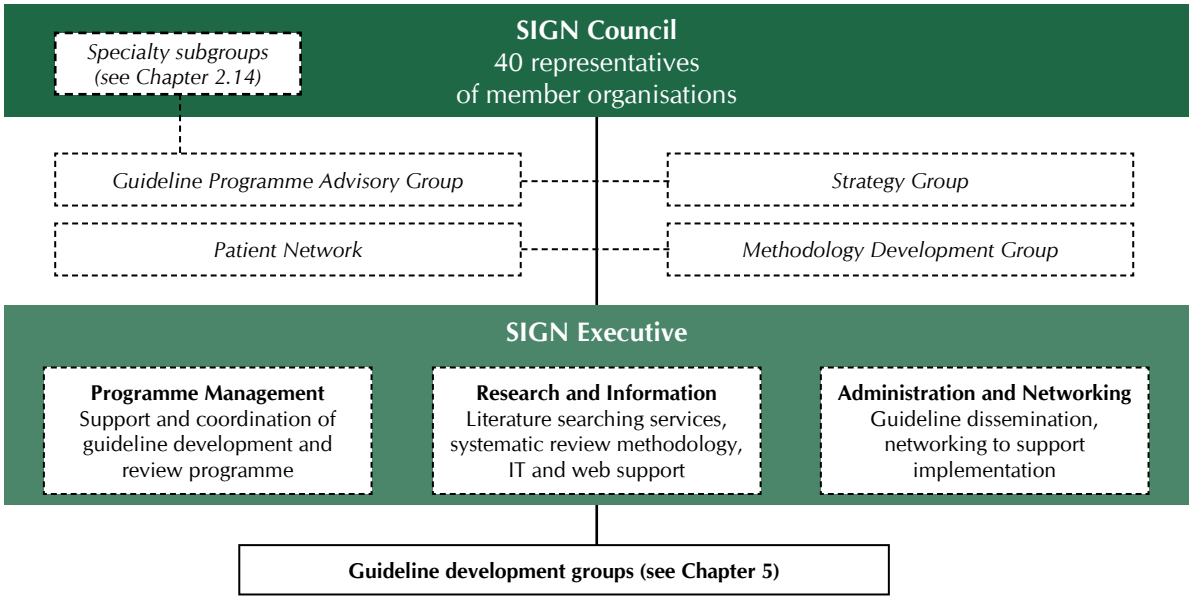
2.1.1 SIGN COUNCIL

SIGN Council is the policy making body for SIGN with overall responsibility for topic selection, methodology, and editorial policy. Members of SIGN Council are nominated by a particular Royal College or other professional organisation or committee, but also represent their specialty or discipline in a wider sense and consult widely with other specialist societies in their field. SIGN also works closely with other parts of its parent body, NHS Quality Improvement Scotland, as well as other relevant national groupings and agencies within NHSScotland.

Members of SIGN Council determine the overall direction of SIGN's development and play a key role in shaping the SIGN guideline programme. Some are also actively involved in aspects of the guideline development process - as members of Advisory Groups, or on the editorial group for specific guidelines, or as chairs or members of individual guideline development groups - and all provide input into the selection of topics for guideline development and the composition of guideline development groups **(see Chapters 4 and 5).**

The structure of SIGN is illustrated in Figure 2

Figure 2 STRUCTURE OF SIGN



2.1.2 STRATEGY GROUP

The Strategy Group is chaired by the Vice-Chair of SIGN Council and provides a strategic monitoring and advisory role for SIGN. Among the specific functions of the group are:

- To discuss and develop emerging strategies for SIGN to be presented to SIGN Council
- To advise on the development of SIGN's business plan
- To monitor SIGN's performance in relation to the business plan
- To discuss relevant issues raised by SIGN Council or the SIGN Executive and advise on actions to be taken.

Membership of the group is made up of five elected voting members of SIGN Council, (one of whom must be a lay representative and at least two current holders of medical or dental qualifications and are members of Royal Colleges or their Faculties in Scotland) plus representation from other parts NHS Quality Improvement Scotland. Meetings are also attended by the Chair of SIGN, Executive Secretary to SIGN Council, and members of the SIGN Senior Management Team.

2.1.3 GUIDELINE PROGRAMME ADVISORY GROUP (GPAG)

GPAG oversees the guideline development programme. Specific functions include:

- Monitoring progress of the programme
- Advising the SIGN Executive regarding any concerns they may have with the development of specific guidelines
- Directing SIGN Council specialty subgroups as they seek nominations for new topics
- Selecting appropriate proposals for new topics for discussion by Council from the full list of proposals submitted to the SIGN Executive.

Membership of the group consists of:

- Programme Director (Chair)
- Chair of SIGN Council (ex-officio)
- Director (ex officio)
- A child health representative on SIGN Council
- A General Practice representative on SIGN Council
- Leads of the SIGN Council specialty subgroups
- A nursing representative on SIGN Council
- The pharmaceutical representative on SIGN Council
- A representative of the other parts of NHS Quality Improvement Scotland.

Meetings are also attended by the Executive Secretary to SIGN Council.

2.1.4 SPECIALTY SUBGROUPS (SSGS)

There are five specialty subgroups of SIGN Council, one in each of the NHS priority areas (cancer, children, cardiovascular disease, mental health) plus one covering primary care. The role of each subgroup is to advise on the selection of new topics, to support implementation of guidelines in their topic area, and to network with others to promote guideline use.

Membership of each group is made up of members of SIGN Council (who are asked to volunteer for the group closest to their subject interest) plus one or two representatives from other organisations with a particular interest in the topic of the SSG. All groups should include a patient representative.

2.1.5 METHODOLOGY DEVELOPMENT GROUP (MDG)

The Methodology Development Group advises the SIGN Executive on the most appropriate ways of developing the SIGN guideline development methodology and provides advice and methodological support for guideline development groups. Methods of meeting these objectives include:

- Monitoring external developments in guideline development methodology, and evaluating their relevance to SIGN
- Reviewing internal developments in SIGN methodology and ensuring they are applied consistently
- Acting as an editorial board for SIGN 50
- Acting as arbitrators where guideline developers are unable to agree on the interpretation or grading of specific pieces of evidence.

All decisions or proposals from the Methodology Development Group must be ratified by SIGN Council before they are fully implemented.

Membership of the Methodology Development Group consists of:

- Quality and Information Director (Chair)
- Chair of SIGN Council (ex-officio)
- Director (ex officio)
- Three members of SIGN Council
- Programme Director
- Patient Involvement Officer
- Representation from other parts of NHS Quality Improvement Scotland
- SIGN Economics Adviser
- Up to four external (ie not directly involved in the work of SIGN) participants with knowledge or expertise in specific aspects of research methodology.

Meetings of the Committee are attended by the Executive Secretary to SIGN Council.

2.1.6 SIGN EXECUTIVE

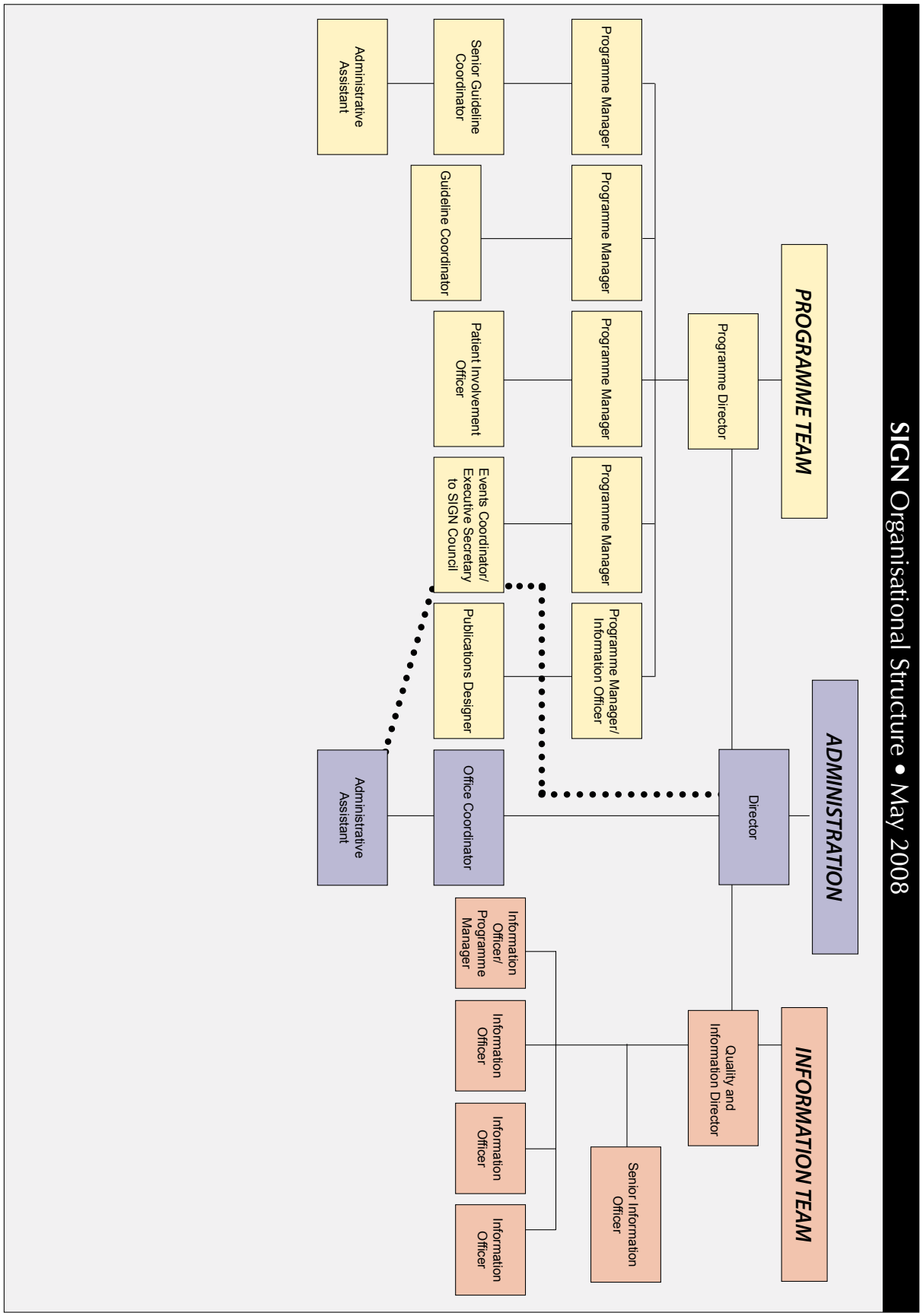
The SIGN Executive are the staff employed to run the organisation. They are responsible for the implementation of decisions taken by SIGN Council and its subgroups, and for delivering the guideline programme to time and on budget. All staff are employees of NHS Quality Improvement Scotland and as such are also required to work closely with other parts of that organisation, and to comply with their policies and procedures with the specific exception of those areas where responsibility has been retained by SIGN Council **(see Chapter 2.1.1).** A staff tree of the current SIGN staff is shown in Figure 3.

Professional healthcare qualifications are not a requirement for any SIGN staff positions, and there is an extensive mix of skills among the Executive staff, including:

- Critical appraisal (teaching and doing)
- Desk top publishing
- Editing
- Events management
- Graphics design
- Management of small group processes
- Patient involvement
- Project management
- Systematic literature searching
- Web design.

Day to day management is the responsibility of the **Senior Management Team (SMT)**. This team is made up of the three Directors, plus the Chair and Vice-Chair of SIGN Council. SMT meets regularly to resolve problems and to discuss the allocation of resources to the different parts of the guideline development programme.

Figure 3: Staff tree, SIGN Executive



2.2 FUNDING FOR GUIDELINE DEVELOPMENT

Funding from NHS Quality Improvement Scotland supports the SIGN Executive, expenses associated with individual guideline development projects (eg online search costs, library and copyright fees to obtain copies of articles for review, guideline development group meeting expenses), and the costs of printing and distributing published SIGN guidelines.

As of April 2007, the funding for SIGN was around £1 million. It is important to note that this funding does not include the majority of the professional time involved in guideline development. Members of SIGN guideline development groups do not receive any payment for their participation, although General Medical and Dental Practitioners are partially reimbursed through locum payments and travel expenses to enable them to attend guideline development group meetings. The expenses of other members of SIGN guideline development groups are met by their employing NHS Boards and universities, which make an important contribution to the SIGN initiative in this way. The expenses of any members of guideline development groups who are unable to reclaim these from their employers for any reason (eg patient representatives) are met by SIGN.

Additional sources of income for the SIGN initiative are the sale of guidelines to individuals and organisations outwith NHSScotland and a small amount made from training courses and consultancy work in the UK and overseas.

2.3 TIMESCALE FOR GUIDELINE DEVELOPMENT

The time taken to develop a SIGN guideline varies widely according to the scope of the topic under consideration, the volume of relevant literature to be critically appraised, the amount of feedback received during the consultative phases of development and, most importantly, the competing pressures on the time of members of guideline development groups. The average time taken by recent guideline development groups is illustrated in Figure 2.3 (see also Figure 9).

Figure 4: Average timescale for SIGN guideline development

2.4 INFLUENCE OF FINANCIAL AND OTHER INTERESTS

It has been recognised for some time that financial interests in, or close working relationships with pharmaceutical companies has an influence on the interpretation of evidence from clinical studies. This can affect both guideline developers and guideline users.

It is not possible to completely eliminate any possible bias from this source, nor even to quantify the degree of bias with any certainty. Despite some doubts as to how effective an answer it is, most organisations have chosen to address this problem by asking those involved in producing clinical guidelines to declare any financial or other interests related to their work on the guideline. By being explicit about the influences to which the authors are subjected, guideline producers acknowledge the risk of bias and make it possible for guideline users or reviewers to assess for themselves how likely it is that the conclusions and guideline recommendations are based on a biased interpretation of the evidence.

SIGN has taken the view that all those involved in the work of guideline development should declare all financial interests, whether direct or indirect, annually for as long as they are actively working with the organisation. An example of the form to be completed by all concerned is presented in **Annex A** to this document.

These forms are completed annually by all members of the following groups.

- SIGN Council and subgroups
- SIGN Executive
- All members of guideline development groups
- All individuals contributing peer review comments.

Signed copies are retained by the SIGN Executive and can be inspected by any interested party at the SIGN offices.

3 Selection of guideline topics

3.1 THE SIGN PROGRAMME

The experience of SIGN and other guideline developers has shown that selection of appropriate topics for guideline development is crucial. Guidelines should address a specific healthcare need and there should be an expectation that change is possible and desirable and that, if the guidelines are followed, there is potential to improve the quality of care and/or patient outcomes. There must also be robust evidence of effective practice on which to base guideline recommendations.

SIGN has limited resources for guideline development. As a result it is important to identify topics which are most amenable to guideline development. Likewise, when a published guideline is due for review it must be judged against potential new topics for inclusion in the SIGN programme.

3.2 CRITERIA FOR SELECTION OF TOPICS

Guideline topics selected for inclusion in the SIGN programme are chosen on the basis of the burden of disease, the existence of variation in practice, and the potential to improve outcome. The following criteria are considered by SIGN in selecting and prioritising topics for guideline development:

- Areas of clinical uncertainty as evidenced by wide variation in practice or outcomes.
- Conditions where effective treatment is proven and where mortality or morbidity can be reduced.
- Iatrogenic diseases or interventions carrying significant risks.
- Clinical priority areas for NHSScotland: presently these are coronary heart disease and stroke, cancer, and mental health. The strategic aims of NHSScotland are also considered. These are improving health and tackling inequalities, especially with regard to children and young people, developing primary and community care and reshaping hospital services.
- The perceived need for the guideline, as indicated by a network of relevant stakeholders.

For information on the current SIGN programme, see the SIGN website: **www.sign.ac.uk**

3.3 TOPIC SELECTION PROCESS

Any group or individual may propose a guideline topic to SIGN. In addition, the five SIGN specialty subgroups (SSGs) may suggest new topics for consideration **(see Chapter 2.1.4** for details of the SSGs).

The Chair of each SSG represents SIGN Council on the Guideline Programme Advisory Group (GPAG), which oversees development of proposals for new guidelines or for reviewing existing guidelines. This ensures that there is appropriate communication and interaction between the specialty subgroups, as most topics are relevant to more than one specialty. The Group also has representatives from other parts of NHS Quality Improvement Scotland. This should ensure that, wherever possible, SIGN's programme and the programmes of clinical standards and health technology assessments will be complementary. GPAG will also consider the work programme of other guideline developers, in particular guidelines that have been commissioned by NICE (the National Institute for Health and Clinical Excellence) in England and Wales, to avoid potential duplication of effort.

Specialty subgroups consider all new proposals, prioritise them using a suitability screening and scoring tool and submit their prioritised lists of potential guideline topics to the Guideline Programme Advisory Group. The suitability screening tool identifies the extent to which the proposal fulfils the criteria listed in **chapter 3.2**, makes an assessment of the extent of evidence on which to base the guideline and considers whether the benefits that were likely to accrue from successful implementation of the guideline recommendations would outweigh the efforts required to develop it.

GPAG will look at the combined scores from each SSG and using this information, together with the professional judgment of the group, and taking into account SIGN's work capacity, will make recommendations to SIGN Council about which proposals should be accepted onto the work programme and which should be rejected. Topics ranked highest are included in SIGN's proposed programme, depending on capacity. Proposals which are not ranked sufficiently highly to be accepted on to the programme will be reconsidered at the next topic prioritisation meeting alongside new and review topics. If the proposal still receives a low ranking on its second reading it will be returned to the SIGN specialty subgroup for reconsideration or revision.

SIGN Council dedicates one meeting each year to approving guideline topic proposals that have been recommended by GPAG as suitable candidates for the SIGN guideline development programme. Council is presented with fully worked up guideline proposals and a summary of the suitability screening results and the subsequent discussions of the Guideline Programme Advisory Group.

The final step is for the resulting topics to be forwarded to NHS Quality Improvement Scotland for approval for inclusion in the work programme before incorporation into the SIGN programme.

3.3.1 APPLICATION PROCEDURE

SIGN uses a two-stage application procedure. The initial application is made using a short, single-page application form. When a group or individual proposes a guideline topic to SIGN, their suggestion is discussed initially by the SIGN Senior Management Team (SMT). SMT use a set of defined criteria to assess whether or not the topic is an appropriate one for a SIGN guideline. If the proposed topic has the potential to meet the selection criteria the proposer is asked to complete a second, more detailed, application form.

As part of the preparatory work done before a guideline proposal is considered by the SSGs and submitted to the Guideline Programme Advisory Group, a scoping search is carried out. This is a very broad search of the literature relevant to the condition that is to be the topic of the guideline. No attempt is made to focus on specific questions at this stage. The intention is only to establish the general extent of the literature in the clinical area to see if there is likely to be sufficient good quality evidence to make an evidence based guideline feasible.

Firstly, a check is made to see if any other good quality guidelines have been produced on the subject by searching the following websites:

Guidelines International Network **(www.g-i-n.net)**

National Library for Health Guidelines finder **(www.library.nhs.uk/guidance/)**

National Guideline Clearinghouse **(www.guideline.gov)**

National Institute for Clinical Excellence **(www.nice.org.uk)**

In addition, a search for existing systematic reviews is carried out. This covers reviews produced by the Cochrane Collaboration and those covered by the databases of the Centre for Reviews and Dissemination at the University of York **(www.crd.york.ac.uk/crdweb/)**

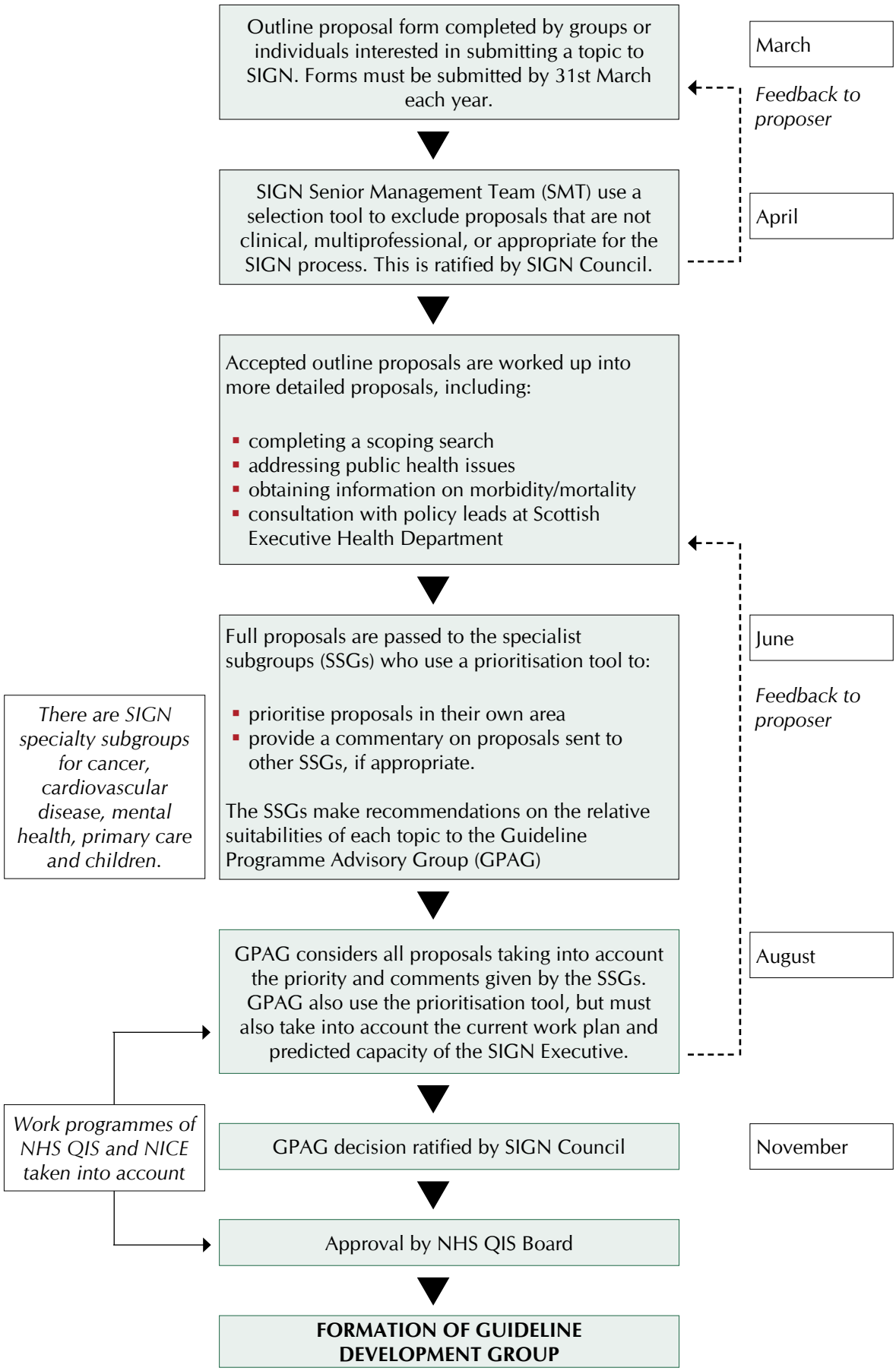
From this scoping search a report is prepared summarising the available evidence, emphasising the outcomes from systematic reviews and whether these have been positive or have identified significant work that remains to be done.

SIGN's standard guideline application form requests the following information:

1. A summary of the clinical problems and outcomes to be addressed.
2. Details of the group(s) or institution(s) supporting the proposal.
3. A brief background to the clinical topic which will be addressed by the proposed guideline.
4. Evidence of variation in practice in the management of the condition.
5. An indication of the benefits likely to arise from the development and successful implementation of the guideline.
6. A definition of the patient group to which the guideline will apply. This should include consideration of whether any specific social groups or minorities are likely to be particularly affected, either favourably or adversely, by changes in healthcare provision in the topic area under consideration.
7. A definition of the aspects of management of the clinical condition which the proposed guideline will address and an indication as to whether the guideline will apply to primary or secondary care, or both.
8. An indication of the healthcare professionals potentially involved in developing the guideline.
9. An indication of the size and strength of the evidence base which is available to support recommendations on effective practice, citing key supporting papers.
10. Details of any existing guidelines or systematic reviews in the field.

The procedure for selection of new topics for SIGN guidelines is illustrated in Figure 3.1. The application form to request consideration by SIGN of a specific guideline topic and the full guideline proposal form are available from the SIGN Executive or can be downloaded from the SIGN website: **www.sign.ac.uk**

*Figure 5: S*election of new topics for SIGN guideline development



SECTION 3.4 UPDATED NOVEMBER 2011

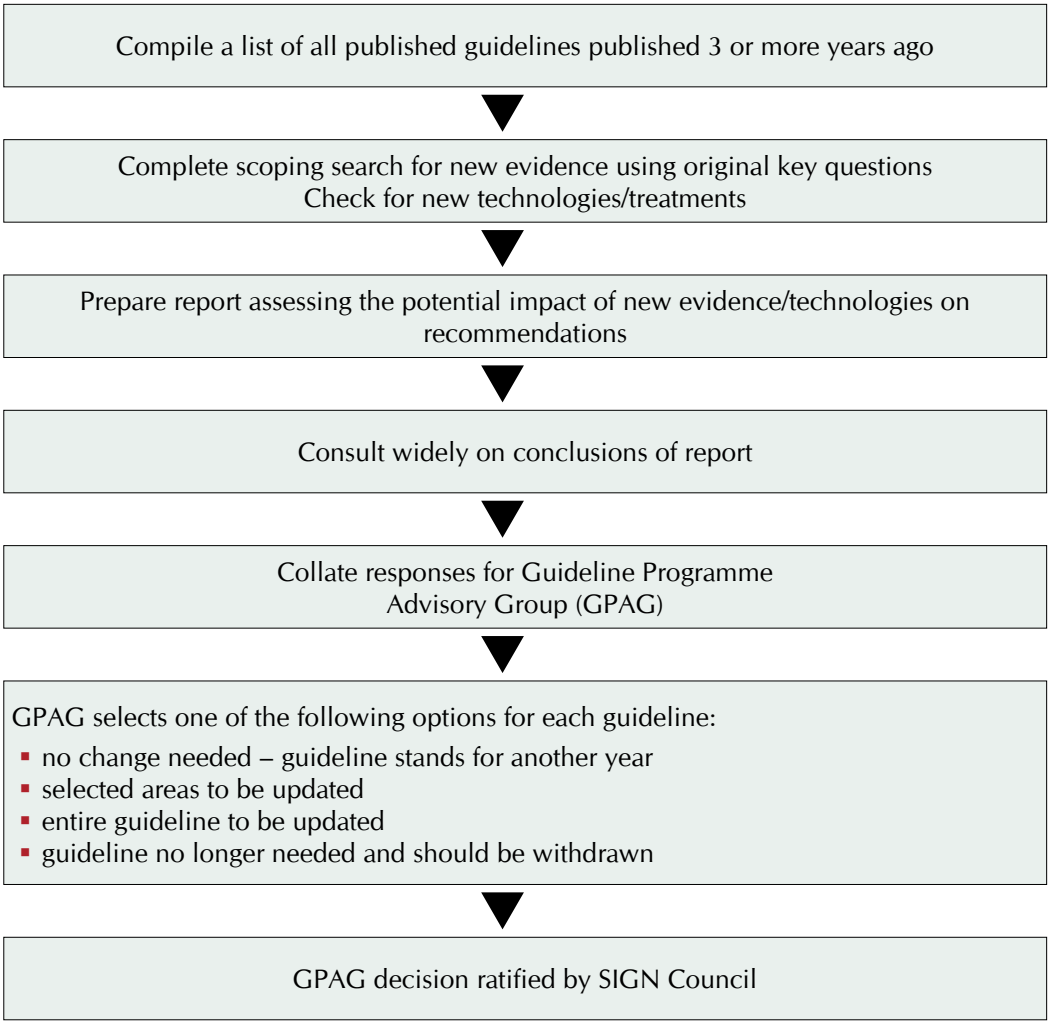
3.4 UPDATING PUBLISHED GUIDELINES

3.4.1 SCHEDULED UPDATES

SIGN has made a commitment to consider whether or not published guidelines need to be reviewed after a period of three years and all SIGN guidelines carry a statement indicating that they will be considered for review three years after publication. A full review of a guideline after a fixed time period is not always appropriate as new evidence is published at different rates in different fields. It also imposes a workload for future years that may not be achievable in practice. A further factor that will influence the decision on whether and how to review a guideline is the emergence of any evidence of inequality in access to services between different social groups that can be addressed through guideline recommendations.

3.4.2 UPDATE PROPOSALS

Figure 6: Selection of guidelines for updating



When a guideline is considered for updating, there are four possible outcomes:

- the guideline, as it stands, will be revalidated for a further year
- the guideline will undergo a complete review
- the guideline will undergo a partial or selective review
- the guideline will be withdrawn.

A fifth option, which is likely to be applicable in only a small number of cases, is to make the guideline into a 'living guideline'. This option involves keeping the evidence under constant review and updating the guideline on a regular basis. A three year trial project using this process for the asthma guideline (produced in conjunction with the British Thoracic Society) is nearing completion, and evaluation of this project will influence the extent of future use of this approach to guideline updating.

As a first step, an update search is carried out looking for evidence based guidelines, HTAs, and systematic reviews produced since publication of the last version of a guideline. These searches are based on the key questions and search strategies used in the original guideline.

Results are presented in the form of summaries of the findings of the papers that have been identified. These searches include an element of horizon scanning to see if there are new treatments or technologies that should be considered as part of the update.

The search results are incorporated into a report that summarises the new evidence and looks at how it will impact on the recommendations made in the existing guideline. This report will also note any new areas or key questions that have emerged since the previous publication.

The review report is then widely circulated for comment within NHSScotland, to Royal Colleges and other professional bodies (through their representatives on SIGN Council), to relevant patient organisations, and to other organisations providing guidance or advice to the NHS in any part of the UK. Responses to this consultation are gathered and presented to the Guideline Programme Advisory Group. On the basis of these reports combined with input from their professional networks GPAG then makes recommendations to SIGN Council on which guidelines should be updated, and whether a full or selective update is appropriate.

At their November meeting, SIGN Council will agree which guidelines are to be updated and prioritise the updates along with new guideline proposals for addition to the SIGN guideline programme. Information on the status of guidelines due for updating, or currently being updated, is provided on the SIGN website: **www.sign.ac.uk**

3.4.3 SELECTIVE UPDATE PROCEDURE

When a guideline has been accepted for a selective update, the process for carrying out the update will be largely the same as that described elsewhere in this manual. The principal difference is that the update will focus on those chapters of the original guideline that have been identified as being in need of updating. The same methodological principles apply, though the nature of the chapters being reviewed may necessitate a slightly different composition from the original guideline group. If a chapter on surgical interventions is a major part of an update, for example, the guideline group is likely to include more surgeons and theatre staff than (say) pharmacists or home care workers.

The process begins with a review of the patient literature. This will feed into a review of patient issues (see Chapter 4) that seeks to establish whether any new issues have emerged since the last version of the guideline.

Unlike new topics, where the main literature searches do not get underway until the key questions have been established by the guideline group, literature searches for systematic reviews and randomised controlled trials are started while the guideline group is being assembled. These searches are based on the recommendations in the chapters of the guideline that have been identified as being in need of updating. They seek to update and build on the evidence base used in the original guideline. The only new questions that may be addressed are any arising from the patient issues search, or that arose from new developments identified during the process of authorising the update.

Once searches are completed, the Information Officer working with the guideline group will carry out a preliminary sift to remove irrelevant material. The Chair or a designated alternative from the new guideline group will carry out a second sift to remove any further papers seen as clinically irrelevant or inappropriate. The remaining papers will be obtained for review and shared among guideline group members for critical appraisal. The Information Officer will extract relevant data from those papers deemed acceptable by the group, and produce evidence tables.

From this point the processes used will be the same as those used for a new guideline. A possible exception is the need for a national meeting. Here the guideline group may decide whether or not the proposed changes are sufficiently far reaching as to justify such wide consultation. If a national meeting is not held, the first draft of the guideline is published on the SIGN website for a fixed period, during which time potentially interested parties will be alerted to its presence and invited to submit comments.

3.4.4 LIVING GUIDELINES

As with a selective update, the process for updating a living guideline will be largely the same as that described elsewhere in this manual. The main difference is that a living guideline will be developed on a rolling programme of regular updates. The frequency of updating will depend on the rate at which new evidence is emerging, but will normally be annual or biennial. GDG membership will be relatively constant, but only subgroups of the GDG with an interest in the topics under review will be actively involved in the development process at any time. A steering group consisting of the chairs of the subgroups and other relevant individuals will oversee guideline development and ensure consistency of approach across the subgroups year on year.

Each update will focus on those areas of the original guideline where new evidence has been identified. The same methodological principles apply and literature searches are based on a series of existing key questions. They seek to update and build on the evidence base used in the original guideline and subsequent updates. The only new questions that may be addressed are any arising from the patient issues search, or that arose from new developments identified during the process of scoping the update.

Once searches are completed, considered judgements will be reviewed against the updated evidence base. The text and recommendations of the guideline will be revised to take account of any new evidence and flagged as being revised. The other processes used will be the same as those used for a new guideline. A possible exception is, as with a selective update, the need for a national meeting. SIGN currently develops only one living guideline, the British guideline on the management of asthma in collaboration with the British Thoracic Society (BTS). Every year the updated draft of this guideline is presented at one of the BTS biennial meetings, as well as being published on the SIGN and BTS websites for a fixed period, during which time comments are invited.

3.4.5 WITHDRAWING GUIDELINES

From time to time it is necessary to consider withdrawing guidelines which are outdated or no longer relevant. Proposals to withdraw guidelines are submitted initially to the Guideline Programme Advisory Group and if it agrees with the proposal it is submitted to SIGN Council for final approval. Once it has been agreed to withdraw a guideline, all versions of the text and any associated material will be removed from the SIGN website. The list of published guidelines will be amended to show the guideline as withdrawn, with a note of the reason for withdrawal and reference to any alternative sources of advice. Guidelines may be withdrawn for any of the following reasons.

- Superceded by a more recent or more comprehensive guideline
- Evidence that the guideline is fully complied with by NHSScotland, and has become accepted practice
- Emergence of new treatments or preventive measures that render the guideline irrelevant.

3.4.6 MONITORING AND INTERIM UPDATES

All comments received on published SIGN guidelines, or information on important new evidence in the field, or evidence of impacts on equality groups are fed back to the guideline development group, either for immediate response or for more detailed consideration on review of the guideline. Any updates to the guideline which might be required in the interim period prior to review are noted on the SIGN website.

4 Involving patients and their representatives

4.1 PATIENT INVOLVEMENT IN GUIDELINE DEVELOPMENT

The term *patients* is used throughout this chapter as a generic term to describe patients, carers, lay representatives and those who represent and/or support patients in the voluntary sector.

Patient involvement is 'the appropriate, active participation of patients, carers and patient representatives as partners in their own care and in the planning, monitoring and development of health services.[8] The potential contribution of patient representatives has been recognised for some time, as well as the difficulties in making that contribution effective.[9]

Patients may have different perspectives on healthcare processes, priorities, and outcomes from those of health professionals. The involvement of patients in guideline development is therefore important to ensure that guidelines reflect their needs and concerns. The purpose of patient involvement is to ensure that the guideline addresses issues that matter to them and that their perspectives are reflected in the guideline. Patients can identify issues that may be overlooked by health professionals, can highlight areas where the patient's perspective differs from the views of health professionals, and can ensure that the guideline addresses key issues of concern to patients.

Patient representatives on guideline development groups can remind the other group members of the limitations of the scientific findings in respect of age, disability,, gender, ethnicity, race, sexual orientation, quality of life and life circumstances such as accessibility. They help to ensure that the group gives consideration to the specific needs of particular ethnic or social groups - information and communication needs, for example. Factors such as age and gender may have an influence over choice of treatment setting – eg males may be less likely to access GP services - and patient representatives can remind the group of this.

A wide range of other issues can be drawn out by patient representatives to make sure a guideline addresses the needs of all those affected by a condition. The influence of religion/belief on compliance with treatment -. eg complying with a recommended diet or medication, or a different approach to STI screening being required for people in prison and those who are homeless.

Patient representatives can also assist the group on the use of clear and sensitive language in the guideline.

4.2 IDENTIFYING PATIENTS' VIEWS

4.2.1 LITERATURE SEARCH

SIGN has developed a literature search strategy to identify both qualitative and quantitative studies that reflect patients' experiences and preferences in relation to the clinical topic **(see Chapter 6.1).** This search is performed at least three months prior to the first group meeting to ensure adequate time to obtain relevant papers and summarise their findings for presentation at the first guideline group meeting.

The types of studies identified generally include patients' views on:

- positive and negative experiences of the condition, including diagnosis, medication and other treatments, follow-up care and quality of life
- unfulfilled needs
- information needs and preferences
- participation in decision making about treatment
- overall satisfaction with care received.
- A copy of the Medline version of the patient search strategy is available on the SIGN website **www.sign.ac.uk**

4.2.2 PATIENT ORGANISATIONS AND SIGN PATIENT NETWORK

SIGN writes to the organisations and charities that aim to represent and/or lobby for patients at least four months before the first meeting of the guideline development group, asking them to inform SIGN of the issues they think the guideline should address. A form is supplied to enable them to structure their feedback in a useful way and, importantly, to indicate the source(s) of their suggestions (eg telephone help line data, surveys).

SIGN also writes to members of the Patient Network asking them which issues they think the guideline should address. The Patient Network is a database of patient, carer and other user representatives. The Network includes contacts for both individuals and organisations, including NHS Board Designated Directors for patient and public involvement, equality and diversity group stakeholders (for example,eg REACH community health project), previous and current patient representatives on SIGN guideline development groups, representatives from patient advocacy services, representatives from patient support organisations, and representatives from relevant Scotland wide groups.

4.2.3 OTHER NHS ORGANISATIONS

SIGN writes to various other NHS organisations at least four months before the first meeting of the guideline development group to find out if any local research on patient views has been performed. This might include, for example, patient focus groups to help in the redesign of services, or questionnaire studies to gauge levels of patient satisfaction with existing services. Reports such as this tend not to be published even though they are in the public domain and can be very useful as a snap shot into current patient issues and concerns regarding particular NHS services and treatments.

4.2.4 DIRECT FEEDBACK FROM USERS OF THE SERVICE

Where published evidence is scarce and inadequate feedback from patient organisations has been received, patient and carer views may be sought via direct contact with users of the service. Techniques employed to date have included focus groups with patients in different regions of Scotland, attending patient support group meetings, and SIGN organised meetings for patients and carers. All of these approaches have provided valuable information that has been fed back directly to guideline groups to influence the remit and key questions underpinning the guideline. Often the guideline development group identifies a need for further input from patients and carers at a later stage of the guideline development process. Focus groups can be carried out and the findings used to complement the scientific evidence.

Running focus groups requires expert facilitation. Views are sought from both men and women of different age groups, in both rural and urban communities. Special efforts are made to include those who are socially excluded and may be less likely to join a local or national organisation. SIGN does this by working with healthcare professionals, local community groups and schools who can help identify people to take part.

4.2.5 PRESENTING THE FINDINGS

The Patient Involvement Officer reviews the results of the patient literature search, and seeks to identify common themes that emerge from the literature. These themes are then integrated with the issues that emerge from the other approaches described above presented at the first meeting of the guideline development group by the Patient Involvement Officer.

The group is asked to take cognisance of these issues when it drafts its key questions. Once a first draft of the key questions has been prepared, the Information Officer working with the group along with the Patient Involvement Officer compares the questions with the issues highlighted through the consultative process and highlights any that have not been included in the key questions. At a subsequent group meeting the results of this comparison are presented to the group, and they are asked to consider whether the questions should be revised.

Guideline groups are not obliged to take on board all the issues raised through the patient consultative process, but they are expected to give explicit reasons if they choose to omit particular topics that have arisen from this source.

4.3 RECRUITMENT OF PATIENTS TO GUIDELINE DEVELOPMENT GROUPS

SIGN recruits a minimum of two patient representatives to guideline development groups by inviting nominations from the relevant "umbrella", national and/or local patient focused organisations in Scotland. Where organisations are unable to nominate, patient representatives are sought via other means, eg from consultation with health board public involvement staff. Where patients have been consulted directly (eg if a focus group has been held) this may also provide a source of possible future patient and carer representatives.

Details of the role of the patient representatives, the support they will be given, the commitment required and useful attributes for representatives are provided to allow informed nominations to be made.

4.4 ROLE OF PATIENT REPRESENTATIVES ON GUIDELINE DEVELOPMENT GROUPS

Although their areas of expertise will vary, members of the guideline development group have equal status on the group. A key role for patient and carer representatives is to ensure that patient views and experiences inform the group's work. This includes:

- ensuring that key questions are informed by issues that matter to patients
- identifying outcome measures they think are important for each key question
- considering the extent to which the evidence presented by group members has measured and taken into account these outcome measures
- identifying areas where patients' preferences and choices may need to be acknowledged n the guideline
- making sure that the degree to which the evidence addresses patients' concerns is reflected in the guideline
- helping to write the Information to Patients chapter of the guideline, including identifying sources of further information
- raising awareness of patient issues at the National Open Meeting by preparing a presentation ssisting SIGN with the identification of voluntary organisations and charities to invite to the National Open Meeting
- helping to ensure that the guideline is sensitively worded (for example treating patients as people and not as objects of tests or treatments)
- identifying individuals to take part in the peer review process
- assisting SIGN with the collection of patient views eg by helping to prepare questions for focus groups
- helping SIGN with consultation arrangements
- appraising literature (if the individual chooses to do so)
- raising awareness of the SIGN guideline among members of their support group and members of the public.

No formal qualifications are needed but it may be helpful if patient representatives have some of the following:

- experience of the guideline condition (eg as someone who has, or has had the condition, or a carer or relation of someone who has or has had the condition)
- an understanding of the experiences and needs of a wider network of patients (eg as a member of a patient support group)
- time to commit to the work of the group (eg attending meetings, background reading, commenting on drafts)
- some familiarity with medical and research language (although members of the guideline group should help with specific technical terms)
- willingness to feed in the views of patient/carer groups not represented on the guideline group
- ability to be objective
- good communication and team working skills.

4.5 SUPPORT FOR PATIENT REPRESENTATIVES ON GUIDELINE DEVELOPMENT GROUPS

SIGN supports patient representatives by:

- delivering introduction to SIGN training for patient representatives
- offering telephone and email support
- inviting new patient representatives to join the SIGN Patient Network
- providing clear guidance on their roles and responsibilities within the group
- ensuring opportunities to attend training events are open to all guideline development group members
- inviting patient representatives to informal events.

In addition, SIGN is exploring the development of other types of support for patient representatives including the production of a patient handbook and CD-ROM, introducing a "buddy" system, and the development of a critical appraisal course aimed specifically at lay representatives.

The Chair of each guideline development group is asked to support patient representatives by:

- ensuring patient representatives are fully engaged with the group
- addressing the group if contributions by patient representatives are not acknowledged appropriately
- welcoming and encouraging contributions from patient representatives.

4.6 WIDER CONSULTATION WITH PATIENTS AND CARERS

Further patient and public participation in guideline development is achieved by involving patients, carers and voluntary organisation representatives at the National Open Meeting which is held to discuss each draft guideline **(see Chapter 8.1).** The meetings are advertised widely and are free of charge.

Patient representatives are invited to take part in the peer review stage of each guideline and specific guidance for lay reviewers has been produced.

Members of the SIGN patient network are also invited to comment on draft documents such as patient versions of guidelines, patient chapters of guidelines and other literature aimed at patients.

5 The guideline development group

5.1 COMPOSITION OF THE GUIDELINE DEVELOPMENT GROUP

One of the US Institute of Medicine's strongest recommendations for 'good guidelines' was that the process of developing guidelines should include participation by representatives of key groups and disciplines affected.[3] Farmer has also stressed that guidelines should not be developed by academics and senior clinicians insulated from the day to day pressures involved in providing medical care, warning that "Unless a guideline accurately reflects the routine working practices of most doctors it will act only as a gold standard to be admired."[10]

A Canadian Medical Association workshop held in 1992 to establish the principles on which to base the formulation of individual clinical practice guidelines also recommended that clinical practice guidelines should be developed by physicians in collaboration with representatives of those who will be affected by the specific intervention(s) in question, including relevant physician groups, patients, and other health care providers as appropriate.[11] Studies have shown that the balance of disciplines within a guideline development group has considerable influence on the guideline recommendations.[12, 13] Establishing a multidisciplinary guideline development group is therefore important to ensure that:

- all relevant groups are represented, providing expertise from all stages in the patient's journey of care
- all relevant scientific evidence will be located and critically evaluated
- practical problems with using the guideline will be identified and addressed
- stakeholder groups will see the guideline as credible and will cooperate in implementation.[14,15]

Following the acceptance of a guideline proposal into the SIGN development programme **(see Chapter 3)**, the SIGN Executive discusses which specialties and professions should be represented on the guideline development group with the topic proposer(s), with advice from the appropriate Specialty Subgroup(s) and SIGN Council. This ensures that all of the relevant professions in Scotland can input into and feel ownership over the guideline development process.

SIGN guideline development groups vary in size depending on the scope of the topic under consideration, but generally comprise between 15 and 25 members. There is necessarily a trade-off between the number of organisations or specialties that should be represented on the guideline development group, and achieving the optimum group size for effective decision making. Care is also taken to ensure that the group is balanced geographically, with representatives from across Scotland.

In putting together a guideline development group, SIGN is aware of the many psychosocial factors, including the problems of overcoming professional hierarchies that can affect small group processes. Grimshaw (1995) states: "To ensure that guidelines achieve their full potential… requires a programme of research and development that accords at least as much thought to the psychology of group dynamics as the science of systematic reviews".[15] Research into the progress and functioning of SIGN's own guideline development groups has shown the impact of professional or status differences on members' contributions to group discussions.[16,17] A clear relationship between the perceived status of a group member and their level of contribution to group discussions was identified. This may be difficult to avoid, as members with highest status often have the greatest amount of research expertise, which is of great benefit when interpreting evidence. Care is therefore taken to offer support to those who may feel at an initial disadvantage compared with the group's "experts" **(see Chapter 5.2).** This begins with selecting a balanced group that is not "top heavy" and a chairperson with an awareness of these hierarchies and with skills in facilitating full participation by all group members.

The process for establishing SIGN guideline development groups is illustrated in Figure 7. The membership of a typical guideline development group is shown in Figure 8.

Figure 7: Establishing the guideline development group

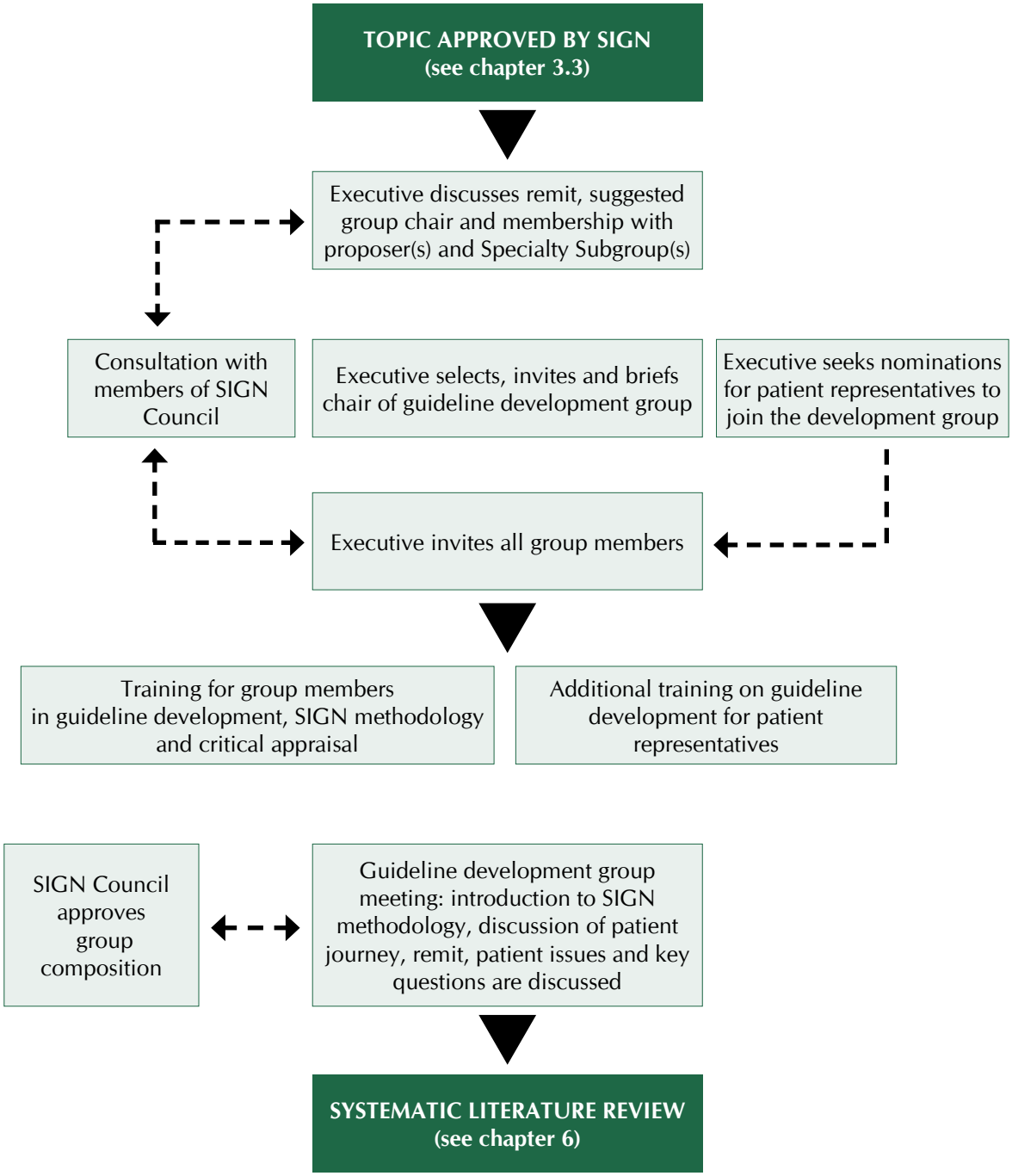


Figure 8: Membership of the SIGN peripheral arterial disease guideline development group

Chairman: Professor of Epidemiology, Public Health Sciences, Edinburgh

Group members:

Consultant Vascular Surgeon, Aberdeen

Consultant Vascular Surgeon, Dunfermline

General Practitioner, Beith

Health Economist, Glasgow

Clinical Nurse Specialist, Edinburgh

Vascular Liaison Nurse, Glasgow

Vascular Liaison Nurse, Inverness

Vascular Nurse, Stirling

Patient representative, Glasgow

Patient representative, Penicuik

Chief Pharmacist, Dundee

Senior Vascular Physiotherapist, Inverness

Superintendent Physiotherapist, Glasgow

Professor of Vascular Medicine, Dundee

Public Health Lecturer, Edinburgh

Specialist Registrar in Public Health, Edinburgh

Vascular Radiologist, Edinburgh

Vascular Technologist, Glasgow

SIGN Programme Manager

SIGN Information Officer

5.2 RESPONSIBILITIES OF DEVELOPMENT GROUP MEMBERS

SIGN's experience in coordinating the work of over 100 guideline development groups has shown that the role of the group leader is crucial to ensure that the group functions effectively and achieves its aims.[18] Chairs of guideline development groups must be sensitive to pre-existing inter-professional tensions and hierarchies and ensure that all members of the group feel able to contribute fully to the guideline development process.

The most successful guideline development groups have a Chair who is aware of and constantly attentive to small group processes (eg how the group interacts and communicates, decision making processes and chairing strategies). The Chair must be prepared to overcome potentially serious difficulties by careful negotiation.[16,17]

The SIGN Programme Manager assigned to each guideline helps the Chair to identify potential barriers to successful group work, to plan and progress the guideline development project, and acts as facilitator at group meetings. Some SIGN guideline development groups are co-chaired by the SIGN Programme Manager and the group leader in order to help reduce potential conflicts.

Guideline development group members in turn must make a full commitment to the group and the tasks involved in guideline development, and be responsible for indicating areas of concern to the Chair. Guideline development group members should also bear in mind that they represent both a geographical region and a specialty or professional group, and must be prepared to consult with colleagues to ensure that the widest possible range of views are considered.

Each guideline development group requires a mix of the following skills:

- clinical expertise (eg medical, surgical, nursing etc.)
- other specialist expertise (eg health economics, social services)
- practical understanding of problems faced in the delivery of care
- communication and team working skills
- critical appraisal skills.

A healthcare professional joining a guideline development group is not expected to be an expert in all of these areas. Many group members may feel they have only one or two of these skills, but at some point in the development of the guideline, their knowledge and experience will be invaluable.

Many potential development group members are concerned that their critical appraisal skills may not be sufficient to complete the systematic review of the literature. To address this, SIGN runs a range of training seminars in critical appraisal skills that all group members are encouraged to attend. In addition, guideline development groups are also supported throughout the development process by the SIGN Executive. The Programme Manager and Information Officer assigned to each guideline development group give regular presentations on SIGN methodology, and will also ensure that methodological checks are correctly applied and that the development process itself is fully documented.

The life span of each guideline development group is approximately 28 months, with groups meeting on average once every two months, although groups may form subgroups which meet more frequently. The development timetable of a typical guideline, and the associated tasks, is shown in figure 9. Guideline development groups are supported by the SIGN Executive.

The work commitment of the healthcare professionals and patients who take part in the development of a SIGN guideline is significant and should be recognised before accepting an invitation to join such a group. In addition to taking on the responsibility of representing both a geographical region and a specialty group, group members need to pledge a considerable amount of their time to guideline development. Prospective guideline development group members are encouraged to attend critical appraisal training prior to joining a group to ensure that they understand the commitment they are about to undertake.

Figure 9: Timetable for guideline development

Months 1-3	▪ Define remit of guideline ▪ Attend critical appraisal training ▪ Plan development process ▪ Share relevant knowledge and experience ▪ Identify key questions/terms for literature search (with advice from SIGN Information Officer ▪ Discuss requirements of systematic literature review	***Prepare group and finalise remit:*** **3 months**
Months 1-10	▪ Review abstracts to select papers for detailed review ▪ Clarify criteria used to select or reject papers ▪ Detailed literature review, grading and synthesis of evidence (often undertaken in subgroups)	***Literature search and appraisal: 10 months***
Months 11-15	▪ Draft recommendations derived from evidence review ▪ Draft guideline prepared ▪ National open meeting held to present and discuss draft recommendation	***Draft guideline: 5 months***
Months 16-25	▪ Feedback from national meeting incorporated into draft guideline. Draft is edited by group with assistance from SIGN Executive ▪ Guideline sent for external peer review ▪ Feedback from external reviewers incorporated into draft guideline	***Post national meeting review; Peer review 10 months***
Months 26-28	▪ Review by SIGN Editorial Group ▪ Publication and dissemination	***Final editing***

6 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.[19,20] 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".[21]

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 Chapter 7)**, and from encouraging a sense of ownership of the guideline amongst all those involved in the process.

6.1 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.

The use of this literature search is discussed in more detail in **Chapter 4.2**

6.2 USING EXISTING GUIDELINES

The guidelines identified in the scoping search carried out for the original guideline proposal **(see Chapter 3.4)** will be presented to an early meeting of the guideline development group to allow it 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 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 NHSScotland, 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 its own review.

As more good quality guidelines are being produced by other agencies, SIGN is considering use of the ADAPTE instrument [22,23] to adapt guidelines produced elsewhere for use in NHSScotland. A trial of this process started in April 2007, looking at the guideline on obesity produced by the National Institute for Health and Clinical Excellence.

6.3 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 using the PICO format:

Patients or population to which the question applies

Intervention (or diagnostic test, exposure, risk factor, etc.) being considered in relation to these patients

Comparison(s) to be made between those receiving the intervention and another group who do not receive the intervention

Outcome(s) to be used to establish the size of any effect caused by the intervention.

The **Patients** or **population** to be covered by the literature searches is largely defined by the presence of the particular condition that the guideline will cover. It should be made clear at this stage, however, which age groups are to be covered. For searching the main medical databases these can be split into:

- Neonates < 1 month
- Infants up to 2 years
- Pre-school children aged 3-5 years
- Children aged 6-12
- Adolescents 13-18 years
- Adults 19-45 years
- Middle aged 46-64
- Aged 65-79 years
- Elderly 80 + years

Consideration should also be given as to whether any particular ethnic or social groups have particular needs in relation to the topic under review. If it is thought that any group needs particular consideration in relation to a key question (people of African origin who have sickle cell disease, for example, may need a different approach to antibiotic treatment) the needs of these groups should be specifically addressed in the key questions and subsequent literature searches.

It is worth emphasising here that questions should be addressed even if it is not thought there will be any good evidence. If there is in fact no good evidence, then highlighting it as an area for research is a useful outcome in itself.

Exclusion of any group from the population covered by the guideline should be identified when setting the key questions, and reasons given for their exclusion.

The **Interventions** (which in this context includes diagnostic tests, risk factors, risk exposure) must be specified clearly and precisely. The only exception is in drug therapy where drug classes should be used in preference to specific agents unless there is a clear reason for focusing on a named agent.

The decision on **Comparisons** is mostly between placebo / no treatment, or comparison with alternative therapies. It should be borne in mind that where there is an existing treatment comparisons with placebo or no treatment are not ethically acceptable.

It is important to specify **Outcomes** in advance, and to think of these in terms of what outcomes will influence the views of guideline group members as to how effective a particular intervention is. For some questions there will be a wide range of outcomes used in the literature, and if useful comparisons are to be made across studies it must be made clear which of these outcomes are important.

As far as possible outcomes should be objective and directly related to patient outcomes (eg length of time to next cardiovascular incident or survival time, rather than just reductions in blood pressure). It is also important to include outcomes that are important to patients, rather than focusing entirely oin clinical outcomes.

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

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 its knowledge and experience to ensuring the questions address the key issues in the area to be covered by the guideline. The Information Officer working with the group will provide guidance on the formatting of the questions, and ensure they are in a format likely to produce useable results. They will also ensure that the key questions address most, if not all, the issues identified through the patient consultation exercise **(see Chapter 4.2).**

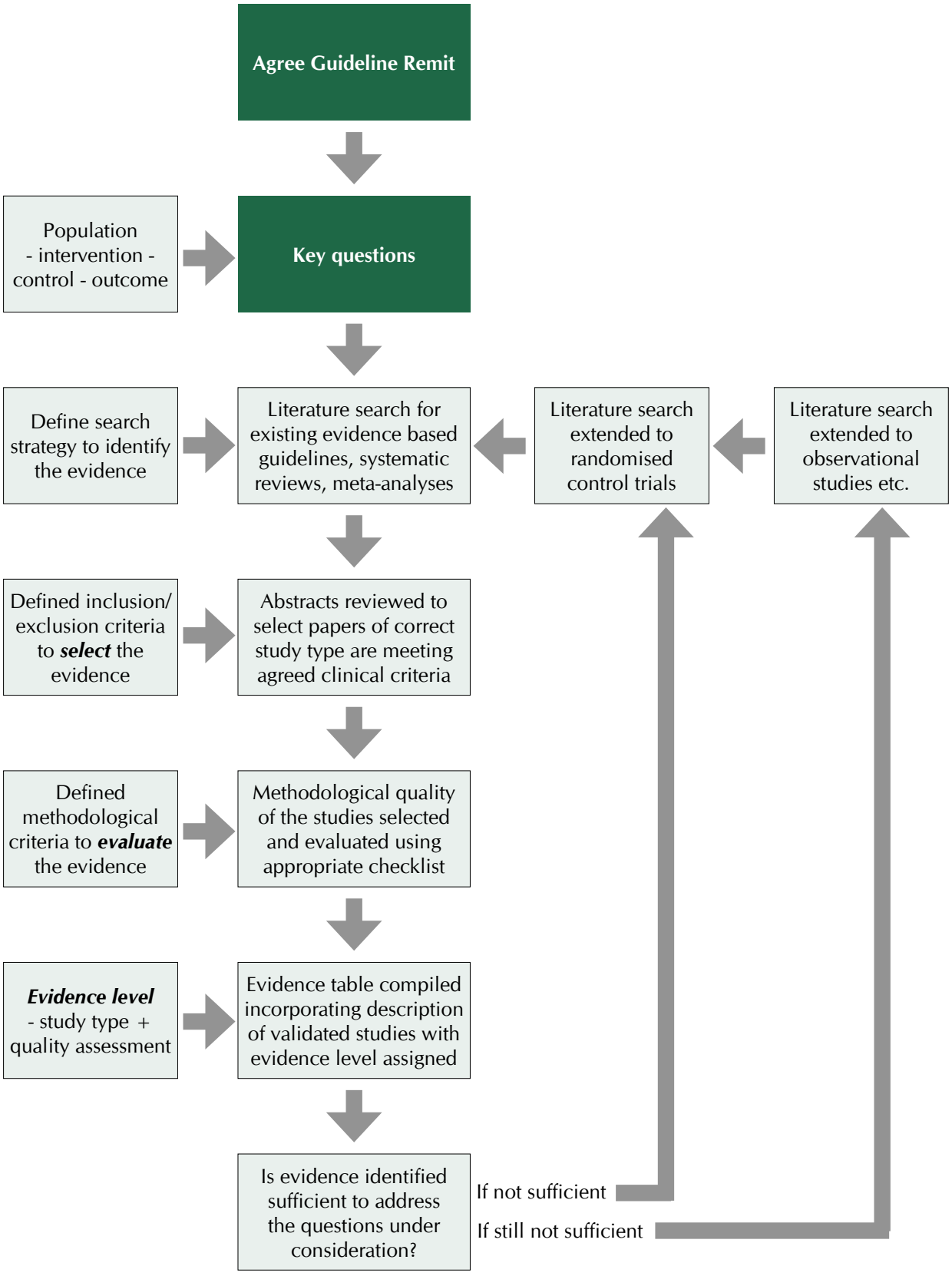
6.4 IDENTIFYING AND SELECTING THE EVIDENCE

The literature 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 Annex B).** SIGN uses a set of standard search filters that identify:

- Systematic reviews.
- Randomised controlled trials.
- Observational studies
- Diagnostic studies
- Economic studies.

These search filters are available from the SIGN website. The systematic literature review procedure is illustrated in Figure 10.

Figure 10: Systematic literature review



In order to minimise bias and to ensure adequate coverage of the relevant literature, the literature search must cover a range of sources. As a minimum, SIGN requires searches to cover the Cochrane Library, Embase, Medline, NHS Economic Evaluations Database (NEED) and the Internet. It is expected that in most cases the search will also cover additional sources specific to the topic under review.

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 5 or 10-year limit to the search may be appropriate, whereas in other areas a much longer time frame might be necessary.

All the main search strategies are subject to an independent review by an Information Scientist based elsewhere in NHS Quality Improvement Scotland.

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.

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 website at the time of the National Meeting associated with the guideline. This strategy will remain on the wWebsite 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 also be 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 specific clinical or other exclusion 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.

All sifting is carried out according to an agreed protocol setting out the criteria used to select papers for inclusion or elimination from the process.

In practice, a single search does not 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. Information Officers take an iterative approach to the task, 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. This iterative process is illustrated in Figure 10.

6.5 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 Chapter 7).**

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 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,[24] 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 – eg 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 individuals. Any differences in assessment should then be discussed by the full group. Where differences cannot be resolved, an independent reviewer will arbitrate to reach an agreed quality assessment.

7 Forming guideline recommendations

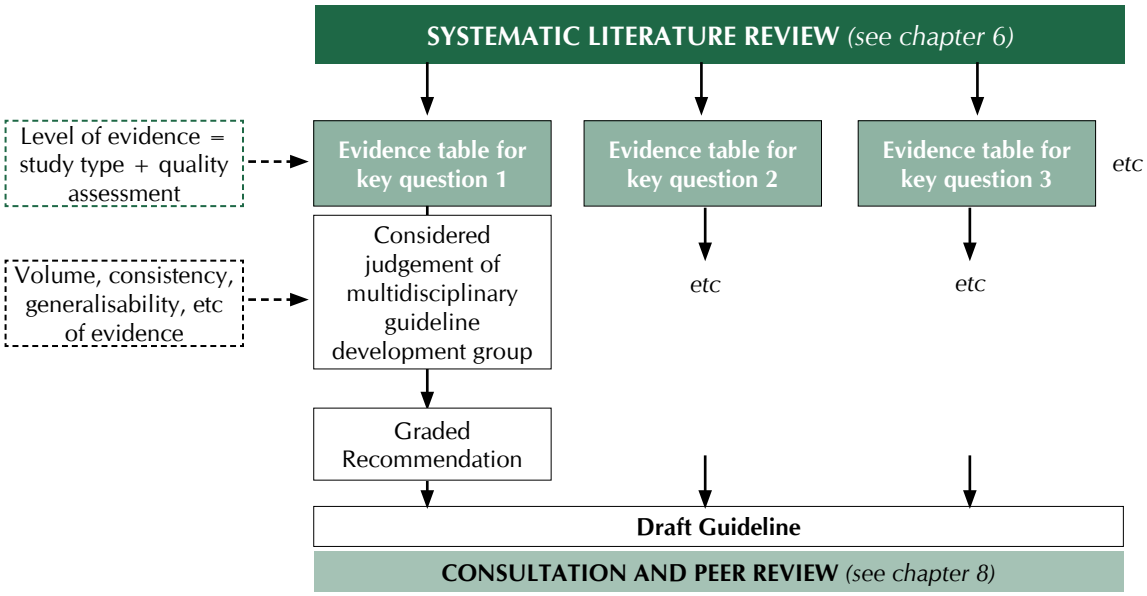
7.1 SYNTHESISING THE EVIDENCE

Guideline recommendations are graded to differentiate between those based on strong evidence and those based on weak evidence. This judgement is made on the basis of an (objective) assessment of the design and quality of each study (as discussed in **Chapter 6**) and a (perhaps more subjective) judgement on the consistency, clinical relevance and external validity of the whole body of evidence. The aim is to produce a recommendation that is evidence based, but which is relevant to the way in which health care is delivered in Scotland and is therefore *implementable*.

It is important to emphasise that the grading does not relate to the *importance* of the recommendation **(see also Chapter 7.2.3)**, but to the strength of the supporting evidence and, in particular, to the predictive power of the study designs from which these data were obtained. Thus, the grading assigned to a recommendation indicates to users the likelihood that, if that recommendation is implemented, the predicted outcome will be achieved.

The process for synthesising the evidence base to form graded guideline recommendations is illustrated in Figure 11.

Figure 11: Forming guideline recommendations



Evidence tables are compiled by SIGN Executive staff based on the quality assessments of individual studies provided by guideline development group members. The tables summarise all the validated studies identified from the systematic literature review relating to each key question. They are presented in a standard format to make it easier to compare results across studies, and will present separately the evidence for each outcome measure used in the published studies. These evidence tables form an essential part of the guideline development record and ensure that the basis of the guideline development group's recommendations is transparent. An example evidence table is shown in **Annex D.**

7.2 CONSIDERED JUDGEMENT

It is rare for the evidence to show clearly and unambiguously what course of action should be recommended for any given question. Consequently, it is not always clear to those who were not involved in the decision making process how guideline developers were able to arrive at their recommendations, given the evidence they had to base them on. In order to address this problem, SIGN has introduced the concept of **considered judgement**.

Under the heading of considered judgement, guideline development groups summarise their view of the total body of evidence covered by each evidence table. This summary view is split into three parts.

7.2.1 JUDGING THE LEVEL OF EVIDENCE

In the first chapter, the guideline group comments on:

- Quantity, quality, and consistency of evidence
- External validity (generalisability) of studies.
- Directness of application to the target population for the guideline.

At this point the guideline group is asked to note the overall **levels of evidence** addressing this specific key question.

7.2.2 JUDGING THE IMPACT OF THE EVIDENCE

For the next step, the guideline group is asked to consider other factors that may influence its eventual grading of a recommendation. These factors are:

- Any evidence of potential harms associated with implementation of a recommendation.
- Clinical impact (ie the extent of the impact on the target patient population, and the resources required by NHSScotland to treat them in accordance with the recommendation)
- Whether, and to what extent, any equality groups may be particularly advantaged or disadvantaged by the recommendations made.
- Implementability (ie how practical it would be for NHSScotland to implement the recommendation).

The group are finally asked to summarise its view on all of these issues, both the quality of the evidence and its potential impact, before making a graded recommendation. This summary should be succinct, and taken together with its views of the level of evidence represent the first draft of the text that will appear in the guideline immediately before a graded recommendation.

7.2.3 IDENTIFYING KEY RECOMMENDATIONS

Finally, the group is asked to consider the **importance** of the recommendation(s) it has just made. Importance is not necessarily related to strength of evidence, but should reflect the extent to which the group believes the recommendation will impact on the health status or quality of life of the patients concerned.

Where the group has indicated that a recommendation is a **key recommendation**, it is asked to provide a justification for why this recommendation should be highlighted in the final guideline. All key recommendations will be identified as such in the published guideline, and will appear in the Quick Reference Guide.

Guideline development groups are provided with a pro forma in which to record the main points from their considered judgement. An example of this form and the associated notes for users is included in **Annex C**.

7.3 LEVELS OF EVIDENCE AND GRADES OF RECOMMENDATION

SIGN formerly used the levels of evidence developed by the US Agency for Health Care Policy and Research (AHCPR, now the US Agency for Health Research and Quality, AHRQ).[25] As a number of limitations were becoming apparent in that system, a review was carried out and new levels of evidence and associated grades of recommendation were developed. Following extensive consultation and international peer review, the new grading system was introduced in Autumn 2000.[26, 27] The current grading system is shown in **Annex B.**

The assignment of a level of evidence should involve all those on a particular guideline development group or subgroup involved with reviewing the evidence in relation to each specific question. The allocation of the associated grade of recommendation should involve participation of all members of the guideline development group. Where the guideline development group is unable to agree a unanimous recommendation, the difference of opinion should be formally recorded and the reasons for dissent noted.

On occasion, guideline development groups find that there is an important practical point that they wish to emphasise but for which there is not, nor is there likely to be, any research evidence. This will typically be where some aspect of treatment is regarded as such sound clinical practice that nobody is likely to question it (it could be regarded as "clinical common sense"). These are shown in the guideline as Good Practice Points (GPP), and are marked ☑.

It must be emphasised that these are **not** an alternative to evidence based recommendations. Indeed, the existence of any evidence relating to a key question, however low quality it might be, excludes the possibility of using a good practice point to make a recommendation relating to that question.

Examples of how GPPs might be used include:

- Emphasising the importance of patient participation in decision making about specific procedures.
- Providing advice on the management of specific surgical procedures for which there is an evidence based recommendation
- Advising caution where there is perceived risk of harm but no available direct evidence of such harms.

The revised grading system is intended to place greater weight on the *quality* of the evidence supporting each recommendation, and to emphasise that the *body of evidence* should be considered as a whole, and not rely on a single study to support each recommendation. It is also intended to allow more weight to be given to recommendations supported by good quality observational studies where RCTs are not available for practical or ethical reasons. Through the considered judgement process guideline developers are also able to downgrade a recommendation where they think there are important inconsistencies in the evidence base, evidence is not generalisable, not directly applicable to the target population, or for other reasons is perceived as being weaker than a simple evaluation of the methodology would suggest.

7.4 RESOURCE IMPLICATIONS

(This chapter is undergoing a separate detailed review and will be added shortly.)

7.5 CURRENT AREAS FOR DEVELOPMENT

The SIGN Methodology Development Group was established to consider new developments in guideline methodology, and to attempt to answer specific questions on methodological issues. It is currently looking at the following questions:

Qualitative studies as evidence: Qualitative methods are increasingly being used to inform practice in some aspects of medical care. At present, there is no mechanism for incorporating such studies in the evidence base. Some progress has been made on methods of identifying qualitative studies, and in evaluating their methodological quality. The use of qualitative evidence to identify issues of concern to patients, and to help identify key questions to be addressed in the guideline is becoming an established part of SIGN methodology. A pilot exercise looking at the formal inclusion of qualitative evidence in developing a SIGN guideline has been carried out[28] and will form the basis of future developments in this area.

Revision of the grading system: The grading system described in Chapter 7.3 is an improvement on the previous system, but still has weaknesses that need to be addressed.[29] SIGN has been participating in the international GRADE project aimed at developing a methodologically sound system that can be applied across countries and cultures.[30, 31]

Whether and to what extent the GRADE approach should be adopted by SIGN is under discussion, but whatever is decided there remains a problem in dealing with different types of evidence. GRADE addresses evidence of effectiveness where it is possible to clearly quantify benefits and harms. In other questions addressed by guidelines evidence is more likely to be presented in narrative form. As the grading system develops, means of dealing with both types of evidence in a rigorous manner will be required. Whatever changes are made are likely to be evolutionary rather than revolutionary in nature.

8 Consultation and peer review

8.1 NATIONAL OPEN MEETING

The AGREE instrument suggests that guidelines should be pilot-tested prior to publication. SIGN considers that the pilot-testing phase is more appropriately carried out at a local level as part of the local implementation process, as testing the feasibility of implementation in one environment may not be applicable to another. However, as an early stimulus to this process, SIGN holds a national open meeting to discuss the draft recommendations of each guideline. This takes place whilst the guideline is still in development and gives the guideline development group the opportunity to present its preliminary conclusions and draft recommendations to a wider audience. The benefits of the national open meeting are twofold:

1. the guideline development group obtains valuable feedback and suggestions for additional evidence which group members might consider, or alternative interpretation of that evidence
2. the participants are able to contribute to and influence the form of the final guideline, generating a sense of ownership over the guideline across geographical and disciplinary boundaries.

SIGN national open meetings are widely publicised and are usually attended by between 150 and 300 healthcare professionals and others interested in the guideline topic, including patient representatives, from across Scotland. Advertising of the meetings is targeted on those professional and patient representative groups most likely to have an interest in the topic. Particular efforts are made to ensure that all equality groups with a potential interest in the topic are represented.

The meetings are registered for CPD (Continuing Professional Development) and for EPASS (Educational Providers Accreditation Scheme Scotland) accreditation. The draft guideline is also available on the SIGN website for a month at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

The national open meeting is the main consultative phase of SIGN guideline development. Although the draft guideline is circulated to Directors of Public Health and to a number of health service organisations at a later stage, this is more as a courtesy to inform them of the likely content of the final guideline than for consultation.

8.2 PEER REVIEW

All SIGN guidelines are reviewed in draft form by independent expert referees, who are asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. A number of GPs and other primary care practitioners also provide comments on the guideline from the primary care perspective, concentrating particularly on the clarity of the recommendations and their assessment of the usefulness of the guideline as a working tool for the primary care team. The draft is also sent to at least two lay reviewers in order to obtain comments from the patient's perspective.

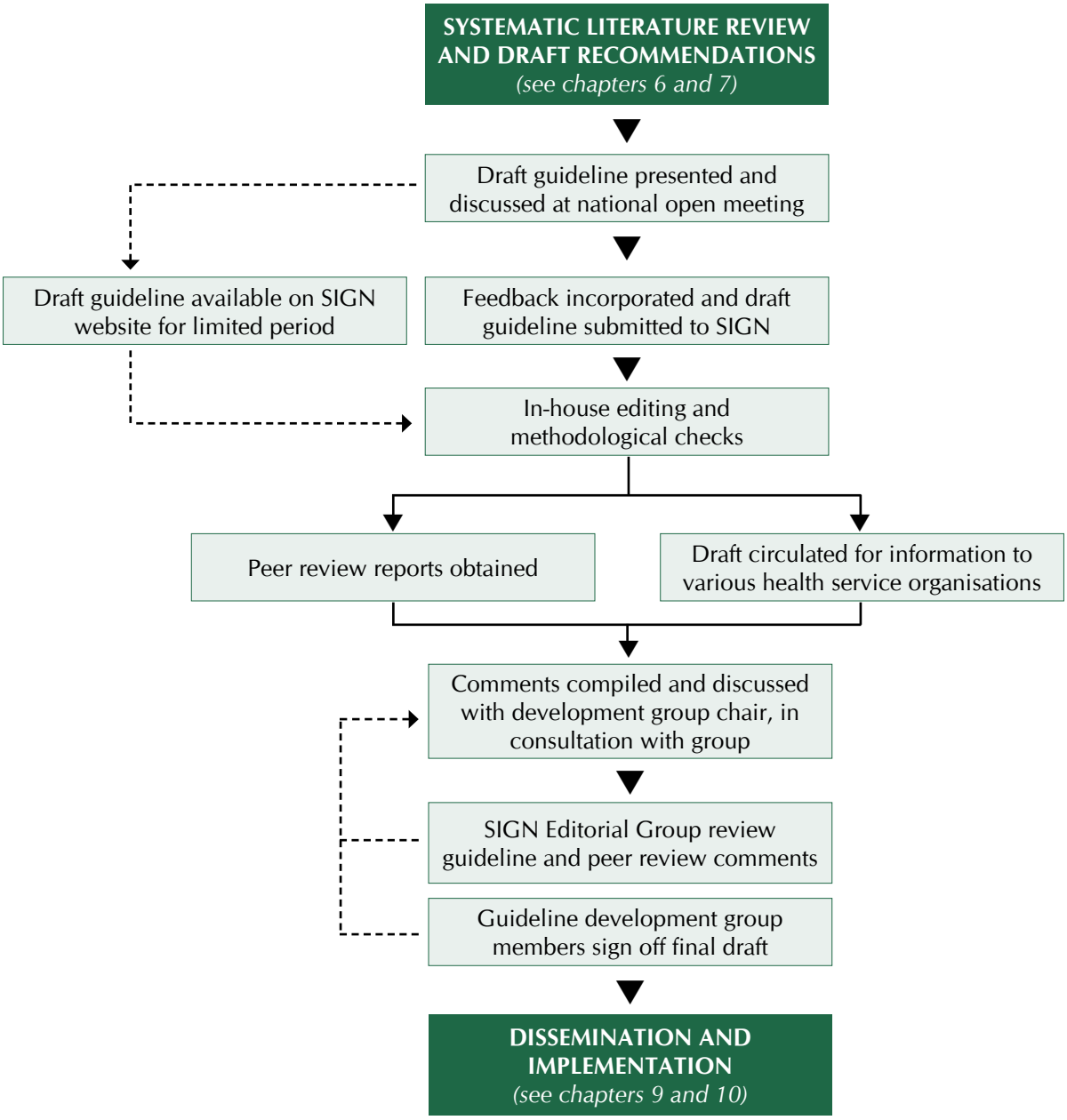
It should be noted that all reviewers are invited to comment as individuals, not as representatives of any particular organisation or group. Corporate interests, whether commercial, professional, or societal have an opportunity to make representations at the national meeting stage where they can send representatives to the meeting or provide comment on the draft produced for that meeting. Peer reviewers are asked to complete a declaration of interests form.

The comments received from peer reviewers and others are carefully tabulated and discussed with the Chair and with the guideline development group. Each point must be addressed and any changes to the guideline as a result noted or, if no change is made, the reasons for this recorded.

As a final quality control check prior to publication, the guideline and the summary of peer reviewers' comments are reviewed by the SIGN Editorial Group for that guideline to ensure that each point has been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. Each member of the guideline development group is then asked formally to approve the final guideline for publication.

The full editorial and consultation phase is illustrated in Figure 12. This process of extended consultation greatly enhances the validity of the final SIGN guideline and increases the likelihood that the guideline will be implemented successfully into local practice for the benefit of patients.

Figure 12: Consultation and peer review



9 Presentation and dissemination

9.1 CONTENT AND PRESENTATION OF THE GUIDELINE

Guidelines with a wide range of styles and formats have been shown to be effective in changing practice. Whilst there is little information available on the effect that style and presentation have on the adoption of guidelines, clarity – of definitions, language, and format – is obviously important. Guidelines should, therefore, be written in unambiguous language and should define all terms precisely. The best format for presenting guidelines will vary depending on the target group(s), the subject matter, and the intended use of the guideline. Ideally, end users should be consulted regarding the most appropriate method of presentation for them. This is an additional function of the extensive peer review process to which all SIGN guidelines are subject **(see Chapter 8).**

Each SIGN guideline includes an introduction, outlining the need for the guideline (including evidence of variation in practice) and defining carefully the remit of the guideline, including the patient and practitioner groups to which it applies. Within the main body of the guideline, the structure should as far as possible reflect the development process that the guideline development group has followed, ie (for each chapter):

- A clear statement of the question/issue under consideration.
- A brief explanation of the treatment options available.
- A summary of the conclusions drawn from the critical appraisal of the evidence (the evidence statement, annotated with the level of evidence and key references). This should provide the justification for the recommendation to follow – ie the evidence for improved outcome resulting from the recommended action.
- The recommendations that the group has derived from this evidence (graded according to the strength of the supporting evidence).
- A brief discussion of any practical points (eg resource/geographical considerations to be taken up in the discussion of local guidelines for implementation), or outstanding treatment options for which there is no evidence (the last should be stated clearly).
- Finally, if the group feels it is important to give guidance in any of these latter areas where there is no suitable evidence, a "good practice point" may be presented.

Having a well developed and defined template for presentation of the final guideline can greatly facilitate the development process, enabling guideline development groups to plan at the outset what type of information will be required and also to envisage what format the content will take. By following the model for systematic review and formation of guideline recommendations outlined in chapters 6 and 7, guideline development groups will find that most of the required information will then be produced in a structured, accessible fomat, ready to slot into the guideline structure.

The guideline should also include key points for audit (accompanied where possible with a recommended minimum data set: **see Chapter 9.7)**, suggested outcome measures, recommendations for further research, and information for patients and carers **(see Chapter 9.5**). Brief details of the systematic review on which the guideline recommendations are based is also provided, although the majority of this information is made available for reference on the SIGN website.

9.2 RECOMMENDATIONS FOR RESEARCH

SIGN guidelines themselves may act as a stimulus to research. An important subsidiary outcome of the guideline development process is in highlighting gaps in the evidence base and guidelines contain a chapter or annex listing the guideline development group's recommendations for research. The review of a guideline is an opportunity to discover whether any of the gaps in the evidence base have been filled

9.3 QUICK REFERENCE GUIDES AND KEY MESSAGES

Each SIGN guideline is published with an accompanying Quick Reference Guide (QRG). This provides a summary of the key recommendations and other information from the guideline, often following a loosely algorithmic format illustrating the recommended care pathway. The Quick Reference Guides are normally printed on the back cover of the guideline and as a separate leaflet, and have proved very popular with practitioners. It is important to note that the 'key' recommendations will not necessarily be the highest grade of recommendations (ie those with the strongest supporting evidence) but those considered by the guideline development group as having the greatest potential impact on patient care **(see Chapter 7.2.3).**

9.4 ELECTRONIC PUBLISHING

All SIGN guidelines and quick reference guides, along with any updates to guidelines, are available free of charge on the SIGN website: **www.sign.ac.uk**. With advances in access to technology, and the increasing importance of currency of information, these electronic versions are now the definitive versions of SIGN guidelines. Paper copies will continue to be produced, but it is anticipated that the number of copies printed will be substantially reduced in coming years.

9.5 INFORMATION FOR PATIENTS

All SIGN guidelines now include an 'information for patients and carers' chapter, which highlight those issues where patients and their families will most likely require information to help them understand and cope with the diagnosis, treatment options and possible outcomes. This chapter is targeted at health professionals, to help them produce local evidence based information materials although patients and carers themselves may also find this chapter useful. The issues highlighted in this chapter are informed by the:

- results of patient views gathered earlier in the development process (see **Chapter 4.2)**
- patient representatives on the development group,
- other guideline development group members.

This chapter also includes appropriate general background explanations to the clinical condition and details of appropriate help lines, support groups and reading materials.

SIGN has introduced patient versions of the guidelines. These patient versions are lay translations of the clinical guidelines and are intended to act as a tool for healthcare professionals to use when discussing management and treatment options with patients and their families. SIGN plans to carry out an evaluation of these and if results are positive they will become integrated with SIGN methodology.

As part of SIGN's commitment to the equality agenda of NHS Scotland, versions of guidelines (either full or patient versions) can be produced in the nine community languages identified by the Scottish Government, in large print, or in Signing in response to specific requests from users.

9.6 DISSEMINATION

Guidelines must obviously be made as widely available as possible in order to facilitate implementation and SIGN guidelines are distributed free of charge throughout the NHS Scotland. However, distribution of printed guidelines alone has been shown to be ineffective in achieving change in practice: guidelines are more likely to be effective if they are disseminated by an active educational intervention, and implemented by patient-specific reminders relating directly to professional activity. Distribution of SIGN guidelines in NHS Scotland is organised within each NHS Board by local distribution coordinators, who are often also responsible for facilitating implementation.

SIGN has initiated a review of its publication and dissemination processes with a view to improving the targeting of guidelines to those health care professionals most likely to find them useful.

9.7 LINKS WITH AUDIT

Development, dissemination and implementation of a guideline should be monitored and evaluated through clinical audit. During the development of the guideline, the development group identifies key points for audit. These should allow the implementation of the guideline recommendations and the impact of these on the processes and, where possible, the outcomes of care to be measured objectively. Often these process and outcome indicators are presented in the form of a minimum data set. SIGN has recently been collaborating with the Information and Statistics Division (ISD) and the Scottish Government to produce national datasets specific to guideline topics.

Clinical audit of guidelines can provide valuable information for standard setting and service accreditation. SIGN guidelines provide the evidence base for many of the national standards developed and monitored by NHS Quality Improvement Scotland. This joint approach to producing evidence based guidelines, which contain national datasets, which in turn are used to set clinical standards that are audited, should, in theory at least, improve the quality of health care delivered. Audit in turn is able to inform guideline reviews and further improve the implementation of specific recommendations.

10 Implementation

10.1 GETTING GUIDELINES INTO PRACTICE

To achieve the objective identified in Chapter 1.1 "to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances"1 it is important not only to develop valid guidelines by a sound methodology, but also to ensure the implementation of the evidence based recommendations. As one of a range of tools to help health care professionals and organisations to improve clinical effectiveness and patient outcomes **(see Chapter 1.3)**, guidelines provide an opportunity for practitioners to improve shared clinical decision-making, increase team working, expand their evidence based knowledge, and reduce variation in practice. They can also enable professionals to keep up to date and to assess their own clinical performance against the recommendations for best practice.

However, there is often a gap between the development of guidelines, as set out in the previous chapters of this handbook, and their implementation into practice. Just as guidelines themselves help provide a bridge between research and practice, this chapter outlines the strategies that can assist practitioners, and health services to bridge the gap between guideline development and implementation

10.2 IDENTIFYING BARRIERS TO IMPLEMENTATION

There are two types of barriers to the implementation of guidelines: those internal to the guideline itself, and the external barriers relating to the clinical environment and particular local circumstances. Potential external barriers to guideline implementation include:

- Structural factors (eg financial disincentives)
- Organisational factors (eg inappropriate skill mix, lack of facilities or equipment)
- Peer group (eg local standards of care not in line with desired practice)
- Individual factors (eg knowledge attitudes, skills)
- Professional-patient interaction (eg problems with information processing).

SIGN addresses the internal barriers by developing guidelines according to a highly respected methodology, described in detail in the earlier chapters. For successful implementation, the external barriers also need to be assessed and implementation strategies developed to address them.

10.3 IMPLEMENTATION INITIATIVES

Implementation of guidelines is a local responsibility and many local initiatives have already been successful in overcoming these barriers to implementation. Most clinical governance support teams in NHS Boards now have audit and clinical effectiveness facilitators with some resources to help local implementation. This is an opportunity to encourage team working and co-operation within primary and secondary care and at the interface between them.

Although its remit is limited to guideline development, SIGN seeks to facilitate guideline implementation with a number of approaches. These include wide dissemination of the guidelines at no cost to the practitioner, awareness raising initiatives and using electronic publishing to improve the availability of guidelines.

SIGN's guideline distribution policy **(see Chapter 9.6)** encourages Boards to take responsibility for local dissemination, which further promotes local awareness and opportunities for local implementation. SIGN uses the media to promote the publication of guidelines when appropriate. Members of SIGN Council are also actively involved in promoting guidelines and developing projects.

Initiatives both nationally and locally have taken into account evidence on the effectiveness of different strategies to implementation: "evidence based medicine requires evidence based implementation".[32] Implementing guidelines is not simple or straightforward. Difficulties often centre on the need for personal, organisational or cultural change.[33] However, such change is being carried through in many areas of clinical practice and information to support a local evidence based strategy is available from a variety of sources.

The Cochrane Effective Practice and Organisation of Care (EPOC) group has published a summary of 44 systematic reviews of implementation interventions, giving an indication of the most effective approaches[34] as summarised in Figure 9. The authors were quick to point out that there are "no magic bullets". Each implementation strategy is effective under certain circumstances, and a multifaceted approach is most likely to achieve change. The approach should be tailored to suit local circumstances taking into account any particular potential barriers. It is important to build in support and incentives and to consider the resources needed for successful implementation.

Figure 10.1: Effectiveness of interventions to promote implementation

Variable effectiveness	Largely effective
Audit and feedback	Reminders
Local consensus conferences	Educational outreach (for prescribing)
Opinion leader	Interactive educational workshops
Patient mediated interventions	Multi-faceted interventions

A more recent HTA review of dissemination and implementation strategies suggests that the evidence for educational outreach is equivocal and that dissemination of educational materials may have greater impact than originally considered and that multifaceted intervention comparison is problematic. The review makes it clear that there is an imperfect evidence base to support decisions about dissemination and implementation and therefore any strategy should always take account of local circumstances

Figure 10.2, adapted from Palmer and Fenner[35] and the Effective Health Care Bulletin,[34] illustrates how each strategy can be used to form part of a local implementation strategy.

10.4 PRACTICAL STEPS

The first step in this process is to prioritise the topic for the team. This may be decided by the NHS Board through their Local Health Plan, or a local service or practice may identify a priority clinical area in which they wish to examine care and identify areas for improvement. It is important to recognise that clinical teams can only tackle one guideline at a time for an active implementation strategy. Indeed it may be that only certain key recommendations within the guideline are prioritised for implementation. However the clinical team should identify the strengths and weaknesses of present provision and not merely choose those areas that are most easily implementable. It is encouraging to identify what is being done well but also important to identify where services could be improved ensuring that any changes that are planned are achievable.

Figure 10.2: Implementation strategies

Method	*Effectiveness*	*Local considerations*
Written materials	Variable findings; at best, small effect	Whilst impact is small, could be used to raise awareness of the guideline through materials or through medical journals or local publications. Useful in combination with other strategies.
Audit and feedback	Sometime effective; small to moderate effect but potentially important	This could be a valuable starting point to provide baseline information from which to develop an implementation strategy.
Education (group)	Variable effects which improve when the influence of peers is included	Identify a local multiprofessional group who can be supported with education from experts or by attending workshops or conferences. Facilitation at practice/unit level is helpful.
Education (individual)	More effective than other educational initiatives	Targeting stakeholders through individual education centred on the topic, or more general implementation issues. Consideration needs to be given to cost.
Opinion leaders	Mixed effects	Identify local and national opinion leaders and consider how they might be involved.
Product champions	No conclusive evidence	Identifying product champions might highlight innovative methods for implementation.
Academic detailing / educational outreach	Effects are small to moderate but of potential importance	Could be incorporated with individual education approach and written materials.
Mass media	May have a positive influence on how health services are used	Take advantage of mass media coverage and additionally local media sources.
Patient-mediated interventions	No conclusive research evidence	Consider local patients, consumer and pressure groups so that involvement is part of strategy at the outset
Continuous quality improvement	No conclusive research evidence	Local audit/clinical governance/ effectiveness departments should always be included in any implementation strategy.
Financial incentives	Some appear to influence practice, but not all	This may only be available for some professional groups and would depend on the nature of the guideline, eg financial support for audit, prescribing incentives.

Policy / regulation	No conclusive research evidence	National standards drawn up by NHS QIS are supported by clinical guidelines and can be influential in supporting local implementation
Reminder systems	Computerised records have supported the implementation of guidelines. Manual reminder systems were effective in many, but not all studies	Implementation may prompt a review of the record keeping system and may initiate developments such as multiprofessional integrated care pathways. Computerised decision support is being developed.
Internet / online databases	No conclusive research evidence	If local services are networked this could form a useful medium for communication and information sources
Combinations of methods	Appear to be more effective than any one intervention on its own	Importantly, a local strategy needs to consider which of the above and in what combination such strategies may be helpful

Figure 10.3 outlines the likely steps that a local implementation group might take, adapted from the Royal College of Nursing Guidelines[36] and the SPICEpc (Scottish Programme for Improving Clinical Effectiveness in Primary Care) project **(www.ceppc.org/spice/index.shtml).**

Figure 10.3: Practical steps towards guideline implementation

Step 1

Decide who will lead and coordinate the team and identify stakeholder representatives for the implementation group. It is often helpful to have a key facilitator for this process. The team should be multiprofessional in composition.

Step 2

Determine the current position. It is essential to be aware of current practice and to identify where changes need to be made. It is helpful to audit current clinical practice. It is also important to review the local environment considering people, systems, structures and internal and external influences. Through this process it is possible to identify potential barriers and facilitators to implementation.

Step 3

Prepare the people and the environment for guideline implementation. It is important to ensure that the professionals are receptive with a positive attitude to the initiative and have the skills and knowledge to carry out the procedures. This requires time, enthusiasm and commitment with good communication and offers of tangible help. It is important also to involve patient groups in planning the initiative so they are involved from the outset and can influence the way that the guideline is implemented into local services. It is important to take into account patient preferences and views eg Scottish Health Council publications, local surveys. In preparing the environment it may be necessary to acquire new equipment or change forms or access services in a different way. It may be possible to consider the inclusion of reminder notes or computer assisted reminders.

Step 4

Decide which implementation techniques to use to promote the use of the clinical guidelines in practice. This should take into account the potential barriers already identified and use the research evidence on effective strategies.

Step 5

Pulling it all together. This requires an action plan for the improvement process. It requires everyone to agree the aims with a named person responsible for the action plan; a time scale identified with contingency plans to deal with any problems along the way.

Step 6

Evaluate progress through regular audit and review with feedback to the team. Rewarding achievements is important. Plans may be required to be modified in the light of difficulties or surprises found during the implementation process. It is always important though to celebrate successes and aim for small achievable steps along the way to improve the quality of patient care.

10.5 MONITORING IMPLEMENTATION

Monitoring of guideline implementation is one of the responsibilities of NHS Quality Improvement Scotland (NHS QIS). NHS QIS clinical standards focus on clinical issues and are evidence based, although levels and types of evidence vary. Where possible they are based on standards drawn from SIGN and other evidence based guidelines as well as good practice statements.

Annex A

Register of interests – fictitious example

Having read the attached SIGN Policy on Declaration of Competing Interests I declare the following competing interests for the previous year, and the following year. I understand that this declaration will be retained by the SIGN Administrator for 5 years, and made available for public inspection at the SIGN Office

Signature:				
Name:	Lindsay Brown			
Relationship to SIGN:	Member of Guideline Development Group on bronchiolitis			
Personal interests				
This section relates to interests of the person concerned. For their partners or close relatives, interests are restricted to employment in, or share holdings in, healthcare organisations. **Specific interests are those which relate to a topic or remit of the particular guideline. Non specific interests are those which are otherwise relevant to the work of SIGN.**				
Remuneration from employment				
	Name of Employer and Post held	**Nature of Business**	**Self or partner / relative**	**SPECIFIC?**
Details of Employment held which may be significant to, or relevant to, or bear upon the work of SIGN	Consultant Bogside NHS Trust Sales Representative for Ultra (antiviral drug) Aviemore Pharmaceuticals PLC	Medical Practitioner Manufacture of antiviral drugs used in paediatric conditions	Self Partner	No Yes
Remuneration from self-employment				
	Name of Business	**Nature of Business**	**Self or partner / relative**	**SPECIFIC?**
Details of self-employment held which may be significant to, or relevant to, or bear upon the work of SIGN	Bogside Physiotherapy Practice	Private physiotherapy practice	Daughter	Yes

Remuneration as holder of paid office				
	Nature of Office held	**Organisation**	**Self or partner / relative**	**SPECIFIC?**
Details of office held which may be significant to, or relevant to, or bear upon the work of SIGN	Organist, St Elsewhere's Church	Church of St Elsewhere	Self	No
Remuneration as a director of an undertaking				
	Name of Undertaking	**Nature of Business**	**Self or partner / relative**	**SPECIFIC?**
Details of directorship held which may be significant to, or relevant to, or bear upon the work of SIGN	Bogside Private Hospice	Non executive Director	Self	No
Remuneration as a partner in a firm				
	Name of Partnership	**Nature of Business**	**Self or partner / relative**	**SPECIFIC?**
Details of Partnership held which may be significant to, or relevant to, or bear upon the work of SIGN	Bogside Computer Games Ltd	Software development	Brother	No
Shares and securities				
	Description of organisation	**Description of nature of holding** (value need not be disclosed)	**Self or partner / relative**	**SPECIFIC?**
Details of interests in shares and securities in commercial healthcare companies, organisations and undertakings	Mega oxygen Supplies PLC	Shares	Self	Yes
	Glastonbury Pharmaceuticals PLC	Shares	Partner	No
Remuneration from consultancy or other fee paid work commissioned by, or gifts or support from, commercial healthcare companies, organisations and undertakings				
	Nature of work	**For whom undertaken and frequency**	**Self or partner / relative**	**SPECIFIC?**
Details of consultancy or other fee paid work which may be significant to, or relevant to, or bear upon the work of SIGN	Consultancy	Ozone Inc (manufacturer of ventilators) 2 days / year	Self	Yes
	Lecturing on terminal care	Lecture fee paid by Exit Inc. (once only)	Self	No

Details of gifts which may be significant to, or relevant to, or bear upon the work of SIGN	Personal computer	Exit Inc.	Self	No
Details of support to attend meetings / conferences which may be significant to, or relevant to, or bear upon the work of SIGN	Travel and conference fees to attend annual paediatric respiratory forums	Ozone Inc	Self	Yes
Non-financial interests				
	Description of interest	**Self or partner / relative**	**SPECIFIC?**	
Details of non-financial interests which may be significant to, or relevant to, or bear upon the work of SIGN	Member of Bronchosupport, Bogside (charitable support group)	Self	Yes	
Non personal interests				
This chapter relates to support from healthcare companies to departmental / employer / business for research and audit activities, travel and subsistence for conferences, etc.				
	Name of company, organisation or undertaking	**Nature of interest**	**Self or partner / relative**	**SPECIFIC?**
Details of non-personal support from commercial healthcare companies, organisations or undertakings.	Universal Pharmaceuticals PLC	Departmental support for research nurse (2 sessions / week) performing clinical trials of physiotherapy in bronchiolitis	Self	Specific
	Nairn Pharmaceutics PLC	Departmental support for Registrar's travel to meeting of European Society of Palliative Care (Self, non specific)	Self	Non specific
DATE RECEIVED AT SIGN:				

Annex B

Key to evidence statements and grades of recommendations

LEVELS OF EVIDENCE

1++ High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias

1+ Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias

1- Meta-analyses, systematic reviews, or RCTs with a high risk of bias

2++ High quality systematic reviews of case control or cohort studies

High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2+ Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2- Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3 Non-analytic studies, eg case reports, case series

4 Expert opinion

GRADES OF RECOMMENDATION

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 1++ or 1+

C A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 2++

D Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+

GOOD PRACTICE POINTS

☑ Recommended best practice based on the clinical experience of the guideline development group.

Annex C

METHODOLOGY CHECKLIST 1: SYSTEMATIC REVIEWS AND META-ANALYSES			
Study identification (*Include author, title, year of publication, journal title, pages*)			
Guideline topic:		Key Question No:	
Checklist completed by:			
SECTION 1: INTERNAL VALIDITY			
In a well conducted systematic review		**In this study this criterion is::**	
1.1	The study addresses an appropriate and clearly focused question.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.2	A description of the methodology used is included.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.3	The literature search is sufficiently rigorous to identify all the relevant studies.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.4	Study quality is assessed and taken into account.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.5	There are enough similarities between the studies selected to make combining them reasonable.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	How well was the study done to minimise bias? Code + +, +, or –		
2.2	If coded as +, or – what is the likely direction in which bias might affect the study results?		

SECTION 3: DESCRIPTION OF THE STUDY Please print answers clearly		
3.1	What types of study are included in the review? *(Highlight all that apply)*	RCT CCT Cohort Case-control Other
3.2	How does this review help to answer your key question? *Summarise the main conclusions of the review and how it relates to the relevant key question. Comment on any particular strengths or weaknesses of the review as a source of evidence for a guideline produced for the NHS in Scotland.*	

NOTES ON THE USE OF METHODOLOGY CHECKLIST 1: SYSTEMATIC REVIEWS AND META-ANALYSES

Section 1 identifies the study, the reviewer, the guideline for which the paper is being considered as evidence, and the key question(s) it is expected to address. The reviewer is asked to consider a series of aspects of study design and to make a judgement as to how well the current study meets each criterion. Each relates to an aspect of methodology that research has shown to be likely to influence the conclusions of a study.

For each question in this section you should use one of the following to indicate how well it has been addressed in the study:

- Well covered
- Adequately addressed
- Poorly addressed
- Not addressed (i.e. not mentioned, or indicates that this aspect of study design was ignored)
- Not reported (i.e. mentioned, but insufficient detail to allow assessment to be made)
- Not applicable.

1.1 The study addresses an appropriate and clearly focused question.

Unless a clear and well defined question is specified in the report of the review, it will be difficult to assess how well it has met its objectives or how relevant it is to the question you are trying to answer on the basis of the conclusions.

1.2 A description of the methodology used is included.

One of the key distinctions between a systematic review and a general review is the systematic methodology used. A systematic review should include a detailed description of the methods used to identify and evaluate individual studies. If this description is not present, it is not possible to make a thorough evaluation of the quality of the review, and it should be rejected as a source of Level 1 evidence. (Though it may be useable as Level 4 evidence, if no better evidence can be found.)

1.3 The literature search is sufficiently rigorous to identify all the relevant studies.

A systematic review based on a limited literature search – e.g. one limited to Medline only – is likely to be heavily biased. A well conducted review should as a minimum look at Embase and Medline, and from the late 1990s onward, the Cochrane Library. Any indication that hand searching of key journals, or follow up of reference lists of included studies were carried out in addition to electronic database searches can be taken as evidence of a well conducted review.

1.4 Study quality is assessed and taken into account.

A well conducted systematic review should have used clear criteria to assess whether individual studies had been well conducted before deciding whether to include or exclude them. If there is no indication of such an assessment, the individual papers included in the review must be obtained and their methodology evaluated.

1.5 There are enough similarities between the studies selected to make combining them reasonable.

Studies covered by a systematic review should be selected using clear inclusion criteria. These criteria should include, either implicitly or explicitly, the question of whether the selected studies can legitimately be compared. It should be clearly ascertained, for example, that the populations covered by the studies are comparable; that the methods used in the investigations are the same; that the outcome measures are comparable; and the variability in effect sizes between studies is not greater than would be expected by chance alone.

Section 2 relates to the overall assessment of the paper. Question 2.1 asks you to rate the methodological quality of the study, based on your responses in Section 1 and using the following coding system:

+ +

All or most of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought **very unlikely** to alter.

+

Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought **unlikely** to alter the conclusions.

-

Few or no criteria fulfilled. The conclusions of the study are thought likely or very likely to alter.

The code allocated here, coupled with the study type, will decide the level of evidence that this study provides.

Question 2.2 asks you to indicate whether a review with poor or relatively poor methodology is likely to overstate or understate any effect identified.

Section 3 asks you to identify the types of study covered by the review, and to provide a brief summary of the conclusions of the review as well as your own view of its strengths and weaknesses, and how it will help to answer the key question.

METHODOLOGY CHECKLIST 2: RANDOMISED CONTROLLED TRIALS			
Study identification (Include author, title, year of publication, journal title, pages)			
Guideline topic:		Key Question No:	
Checklist completed by:			
SECTION 1: INTERNAL VALIDITY			
In a well conducted RCT study…		***In this study this criterion is:***	
1.1	The study addresses an appropriate and clearly focused question.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.2	The assignment of subjects to treatment groups is randomised	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.3	An adequate concealment method is used	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.4	Subjects and investigators are kept 'blind' about treatment allocation	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.5	The treatment and control groups are similar at the start of the trial	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.6	The only difference between groups is the treatment under investigation	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.7	All relevant outcomes are measured in a standard, valid and reliable way	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?		
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.10	Where the study is carried out at more than one site, results are comparable for all sites	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable

SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise bias? Code + +, +, or –	
2.2	If coded as +, or – what is the likely direction in which bias might affect the study results?	
2.3	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	
2.4	Are the results of this study directly applicable to the patient group targeted by this guideline?	
SECTION 3: DESCRIPTION OF THE STUDY *(The following information is required to complete evidence tables facilitating cross-study comparisons. Please complete all sections for which information is available).* PLEASE PRINT CLEARLY		
3.1	How many patients are included in this study? Please indicate number in each arm of the study, at the time the study began.	
3.2	What are the main characteristics of the patient population? *Include all relevant characteristics - e.g. age, sex, ethnic origin, comorbidity, disease status, community/hospital based*	
3.3	What intervention (treatment, procedure) is being investigated in this study? *List all interventions covered by the study.*	
3.4	What comparisons are made in the study? Are comparisons made between treatments, or between treatment and placebo / no treatment?	
3.5	How long are patients followed-up in the study? *Length of time patients are followed from beginning participation in the study. Note specified end points used to decide end of follow-up (e.g. death, complete cure). Note if follow-up period is shorter than originally planned.*	
3.6	What outcome measure(s) are used in the study? *List all outcomes that are used to assess effectiveness of the interventions used.*	
3.7	What size of effect is identified in the study? *List all measures of effect in the units used in the study - e.g. absolute or relative risk, NNT, etc. Include p values and any confidence intervals that are provided.*	
3.8	How was this study funded? *List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.*	
3.9	Does this study help to answer your key question? *Summarise the main conclusions of the study and indicate how it relates to the key question.*	

NOTES ON THE USE OF METHODOLOGY CHECKLIST 2: RANDOMISED CONTROLLED TRIALS

Section 1 identifies the study, the reviewer, the guideline for which the paper is being considered as evidence, and the key question(s) it is expected to address. The reviewer is asked to consider a series of aspects of RCT design and to make a judgement as to how well the current study meets this criterion. Each relates to an aspect of methodology that research has shown makes a significant difference to the conclusions of a study.

For each question in this section you should use one of the following to indicate how well it has been addressed in the study:

- Well covered
- Adequately addressed
- Poorly addressed
- Not addressed (i.e. not mentioned, or indicates that this aspect of study design was ignored)
- Not reported (i.e. mentioned, but insufficient detail to allow assessment to be made)
- Not applicable.

1.1 The study addresses an appropriate and clearly focused question

Unless a clear and well defined question is specified, it will be difficult to assess how well the study has met its objectives or how relevant it is to the question you are trying to answer on the basis of its conclusions.

1.2 The assignment of subjects to treatment groups randomised

Random allocation of patients to receive one or other of the treatments under investigation, or to receive either treatment or placebo, is fundamental to this type of study. **If there is no indication of randomisation, the study should be rejected**. If the description of randomisation is poor, the study should be given a lower quality rating. Processes such as alternate allocation, allocation by date of birth, or day of the week attending a clinic are not true randomisation processes and it is easy for a researcher to work out which patients received which treatment. These studies should therefore be classed as Controlled Clinical Trials rather than RCTs.

1.3 An adequate concealment method is used

Allocation concealment refers to the process used to ensure that researchers are unaware which group patients are being allocated to at the time they enter the study. Research has shown that where allocation concealment is inadequate, investigators can overestimate the effect of interventions by up to 40%. Centralised allocation, computerised allocation systems, or the use of coded identical containers would all be regarded as adequate methods of concealment, and may be taken as indicators of a well conducted study. If the method of concealment used is regarded as poor, or relatively easy to subvert, the study must be given a lower quality rating, and can be rejected if the concealment method is seen as inadequate.

1.4 Subjects and investigators are kept 'blind' to treatment allocation

Blinding refers to the process whereby people are kept unaware of which treatment an individual patient has been receiving when they are assessing the outcome for that patient. It can be carried out up to three levels. Single blinding is where patients are unaware of which treatment they are receiving. In double blind studies neither the doctor nor the patient knows which treatment is being given. In very rare cases studies may be triple blinded, where neither patients, doctors, nor those conducting the analysis are aware of which patients received which treatment. The higher the level of blinding, the lower the risk of bias in the study.

1.5 The treatment and control groups were similar at the start of the trial

Patients selected for inclusion in a trial must be as similar as possible. The study should report any significant differences in the composition of the study groups in relation to gender mix, age, stage of disease (if appropriate), social background, ethnic origin, or comorbid conditions. These factors may be covered by inclusion and exclusion criteria, rather than being reported directly. Failure to address this question, or the use of inappropriate groups, should lead to the study being downgraded.

1.6 The only difference between the groups is the treatment under investigation

If some patients received additional treatment, even if of a minor nature or consisting of advice and counselling rather than a physical intervention, this treatment is a potential confounding factor that may invalidate the results. **If groups were not treated equally, the study should be rejected unless no other evidence is available**. If the study is used as evidence it should be treated with caution.

1.7 All relevant outcomes measured in a standard, valid and reliable way

The primary outcome measures used should be clearly stated in the study. **If the outcome measures are not stated, or the study bases its main conclusions on secondary outcomes, the study should be rejected**. Where outcome measures require any degree of subjectivity, some evidence should be provided that the measures used are reliable and have been validated prior to their use in the study.

1.8 What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?

The number of patients that drop out of a study should give concern if the number is very high. Conventionally, a 20% drop out rate is regarded as acceptable, but this may vary. Some regard should be paid to why patients dropped out, as well as how many. It should be noted that the drop out rate may be expected to be higher in studies conducted over a long period of time. A higher drop out rate will normally lead to downgrading, rather than rejection of a study.

1.9 All the subjects are analysed in the groups to which they were randomly allocate (intention to treat analysis)

In practice, it is rarely the case that all patients allocated to the intervention group receive the intervention throughout the trial, or that all those in the comparison group do not. Patients may refuse treatment, or contra-indications arise that lead them to be switched to the other group. If the comparability of groups through randomisation is to be maintained, however, patient outcomes must be analysed according to the group to which they were originally allocated irrespective of the treatment they actually received. (This is known as intention to treat analysis.) If it is clear that analysis was not on an intention to treat basis, the study may be rejected. If there is little other evidence available, the study may be included but should be evaluated as if it were a non-randomised cohort study.

1.10 Where the study is carried out at more than one site, results are comparable for all sites

In multi-site studies, confidence in the results should be increased if it can be shown that similar results were obtained at the different participating centres.

Section 2 relates to the overall assessment of the paper. It starts by rating the methodological quality of the study, based on your responses in Section 1 and using the following coding system:

++

All or most of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought **very unlikely** to alter.

+

Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought **unlikely** to alter the conclusions.

-

Few or no criteria fulfilled. The conclusions of the study are thought **likely or very likely** to alter.

The code allocated here, coupled with the study type, will decide the level of evidence that this study provides.

The aim of the other questions in this section is to summarise your view of the quality of this study and its applicability to the patient group targeted by the guideline you are working on.

Section 3 asks you to summarise key points about the study that will be added to an evidence table at the next stage of the process. **It is important that you complete this section as fully as possible, and include actual data from the study wherever relevant.**

METHODOLOGY CHECKLIST 3: COHORT STUDIES			
Study identification (*Include author, title, year of publication, journal title, pages*)			
Guideline topic:		Key Question No:	
Checklist completed by:			
SECTION 1: INTERNAL VALIDITY			
In a well conducted cohort study...		***In this study the criterion is:***	
1.1	The study addresses an appropriate and clearly focused question.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
SELECTION OF SUBJECTS			
1.2	The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.3	The study indicates how many of the people asked to take part did so, in each of the groups being studied.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.4	The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.5	What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed.		
1.6	Comparison is made between full participants and those lost to follow up, by exposure status.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
ASSESSMENT			
1.7	The outcomes are clearly defined.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.8	The assessment of outcome is made blind to exposure status.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.9	Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable

1.10	The measure of assessment of exposure is reliable.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.11	Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.12	Exposure level or prognostic factor is assessed more than once.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
CONFOUNDING			
1.13	The main potential confounders are identified and taken into account in the design and analysis.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
STATISTICAL ANALYSIS			
1.14	Confidence intervals are provided	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	How well was the study done to minimise the risk of bias or confounding, and to establish a causal relationship between exposure and effect? Code + +, +, or −		
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the exposure being investigated?		
2.3	Are the results of this study directly applicable to the patient group targeted in this guideline?		

SECTION 3: DESCRIPTION OF THE STUDY ***(Note: The following information is required for evidence tables to facilitate cross-study comparisons. Please complete all sections for which information is available).*** **PLEASE PRINT CLEARLY**		
3.1	How many patients are included in this study? *List the number in each group separately*	
3.2	What are the main characteristics of the study population? *Include all relevant characteristics - e.g. age, sex, ethnic origin, comorbidity, disease status, community/hospital based*	
3.3	What environmental or prognostic factor is being investigated in this study?	
3.4	What comparisons are made in the study? *Are comparisons made between presence or absence of an environmental / prognostic factor, or different levels of the factor?*	
3.5	For how long are patients followed-up in the study?.	
3.6	What outcome measure(s) are used in the study? *List all outcomes that are used to assess the impact of the chosen environmental or prognostic factor.*	
3.7	What size of effect is identified in the study? *List all measures of effect in the units used in the study - e.g. absolute or relative risk. Include p values and any confidence intervals that are provided.* ***Note****: Be sure to include any adjustments made for confounding factors, differences in prevalence, etc.*	
3.8	How was this study funded? *List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.*	
3.9	Does this study help to answer your key question? *Summarise the main conclusions of the study and indicate how it relates to the key question.?*	

NOTES ON THE USE OF METHODOLOGY CHECKLIST 3: COHORT STUDIES

The studies covered by this checklist are designed to answer questions of the type "What are the effects of this exposure?", It relates to studies that compare a group of people with a particular exposure with another group who either have not had the exposure, or have a different level of exposure. Cohort studies may be prospective (where the exposure is defined and subjects selected before outcomes occur), or retrospective (where exposure is assessed after the outcome is known, usually by the examination of medical records). Retrospective studies are generally regarded as a weaker design, and should not receive a "++" rating.

Section 1 identifies the study, the reviewer, the guideline for which the paper is being considered as evidence, and the key question(s) it is expected to address. The reviewer is asked to consider a series of aspects of cohort study design and to make a judgement as to how well the current study meets this criterion. Each relates to an aspect of methodology that research has shown to be likely to influence the conclusions of a study

Because of the potential complexity and subtleties of the design of this type of study, there are comparatively few criteria that automatically rule out use of a study as evidence. It is more a matter of increasing confidence in the strength of association between exposure and outcome by identifying how many aspects of good study design are present, and how well they have been tackled. A study that fails to address or report on more than one or two of the questions addressed below should almost certainly be rejected.

For each question in this section you should use one of the following to indicate how well it has been addressed in the study:

- Well covered
- Adequately addressed
- Poorly addressed
- Not addressed (i.e. not mentioned, or indicates that this aspect of study design was ignored)
- Not reported (i.e. mentioned, but insufficient detail to allow assessment to be made)
- Not applicable.

1.1 The study addresses an appropriate and clearly focused question?

Unless a clear and well defined question is specified, it will be difficult to assess how well the study has met its objectives or how relevant it is to the question you are trying to answer on the basis of its conclusions.

1.2 The two groups being studied are selected from source populations that are comparable in all respects other than the factor under investigation.

It is important that the two groups selected for comparison are as similar as possible in all characteristics except for their exposure status, or the presence of specific prognostic factors or prognostic markers relevant to the study in question. **If the study does not include clear definitions of the source populations and eligibility criteria for participants it should be rejected.**

1.3 The study indicates how many of the people asked to take part did so, in each of the groups being studied.

The participation rate is defined as the number of study participants divided by the number of eligible subjects, and should be calculated separately for each branch of the study. A large difference in participation rate between the two arms of the study indicates that a significant degree of selection bias may be present, and the study results should be treated with considerable caution.

1.4 The likelihood that some eligible subjects might have the outcome at the time of enrolment is assessed and taken into account in the analysis?

If some of the eligible subjects, particularly those in the unexposed group, already have the outcome at the start of the trial the final result will be biased. A well conducted study will attempt to estimate the likelihood of this occurring, and take it into account in the analysis through the use of sensitivity studies or other methods.

1.5 What percentage of individuals or clusters recruited into each arm of the study dropped out before the study was completed?

The number of patients that drop out of a study should give concern if the number is very high. Conventionally, a 20% drop out rate is regarded as acceptable, but in observational studies conducted over a lengthy period of time a higher drop out rate is to be expected. A decision on whether to downgrade or reject a study because of a high drop out rate is a matter of judgement based on the reasons why people dropped out, and whether drop out rates were comparable in the exposed and unexposed groups. Reporting of efforts to follow up participants that dropped out may be regarded as an indicator of a well conducted study.

1.6 Comparison is made between full participants and those lost to follow-up, by exposure status.

For valid study results, it is essential that the study participants are truly representative of the source population. It is always possible that participants who dropped out of the study will differ in some significant way from those who remained part of the study throughout. A well conducted study will attempt to identify any such differences between full and partial participants in both the exposed and unexposed groups. Any indication that differences exist, should lead to the study results being treated with caution.

1.7 The outcomes are clearly defined.

Once enrolled in the study, participants should be followed until specified end points or outcomes are reached. In a study of the effect of exercise on the death rates from heart disease in middle aged men, for example, participants might be followed up until death, or until reaching a predefined age. **If outcomes and the criteria used for measuring them are not clearly defined, the study should be rejected**.

1.8 The assessment of outcome is made blind to exposure status

If the assessor is blinded to which participants received the exposure, and which did not, the prospects of unbiased results are significantly increased. Studies in which this is done should be rated more highly than those where it is not done, or not done adequately.

1.9 Where blinding was not possible, there is some recognition that knowledge of exposure status could have influenced the assessment of outcome.

Blinding is not possible in many cohort studies. In order to asses the extent of any bias that may be present, it may be helpful to compare process measures used on the participant groups – e.g. frequency of observations, who carried out the observations, the degree of detail and completeness of observations. If these process measures are comparable between the groups, the results may be regarded with more confidence.

1.10 The measure of assessment of exposure is reliable.

A well conducted study should indicate how the degree of exposure or presence of prognostic factors or markers was assessed. Whatever measures are used must be sufficient to establish clearly that participants have or have not received the exposure under investigation and the extent of such exposure, or that they do or do not possess a particular prognostic marker or factor. Clearly described, reliable measures should increase the confidence in the quality of the study.

1.11 Evidence from other sources is used to demonstrate that the method of outcome assessment is valid and reliable.

The primary outcome measures used should be clearly stated in the study. **If the outcome measures are not stated, or the study bases its main conclusions on secondary outcomes, the study should be rejected.** Where outcome measures require any degree of subjectivity, some evidence should be provided that the measures used are reliable and have been validated prior to their use in the study.

1.12 Exposure level or prognostic factor is assessed more than once

Confidence in data quality should be increased if exposure level is measured more than once in the course of the study. Independent assessment by more than one investigator is preferable.

1.13 The main potential confounders are identified and taken into account adequately in the design and analysis.

Confounding is the distortion of a link between exposure and outcome by another factor that is associated with both exposure and outcome. The possible presence of confounding factors is one of the principal reasons why observational studies are not more highly rated as a source of evidence. The report of the study should indicate which potential confounders have been considered, and how they have been assessed or allowed for in the analysis. Clinical judgement should be applied to consider whether all likely confounders have been considered. If the measures used to address confounding are considered inadequate, the study should be downgraded or rejected, depending on how serious the risk of confounding is considered to be. **A study that does not address the possibility of confounding should be rejected.**

1.14 Confidence intervals are provided

Confidence limits are the preferred method for indicating the precision of statistical results, and can be used to differentiate between an inconclusive study and a study that shows no effect. Studies that report a single value with no assessment of precision should be treated with extreme caution.

Section 2 relates to the overall assessment of the paper. It starts by rating the methodological quality of the study, based on your responses in Section 1 and using the following coding system:

++

All or most of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought **very unlikely** to alter.

+

Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought **unlikely** to alter the conclusions.

-

Few or no criteria fulfilled. The conclusions of the study are thought **likely or very likely** to alter.

The code allocated here, coupled with the study type, will decide the level of evidence that this study provides.

The aim of the other questions in this section is to summarise your view of the quality of this study and its applicability to the patient group targeted by the guideline you are working on.

Section 3 asks you to summarise key points about the study that will be added to an evidence table at the next stage of the process. **It is important that you complete this section as fully as possible, and include actual data from the study wherever relevant.**

METHODOLOGY CHECKLIST 4: CASE-CONTROL STUDIES			
Study identification (*Include author, title, year of publication, journal title, pages*)			
Guideline topic:		Key Question No:	
Checklist completed by:			
SECTION 1: INTERNAL VALIDITY			
In a well conducted case control study...		***In this study the criterion is:***	
1.1	The study addresses an appropriate and clearly focused question	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
SELECTION OF SUBJECTS			
1.2	The cases and controls are taken from comparable populations	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.3	The same exclusion criteria are used for both cases and controls	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.4	What percentage of each group (cases and controls) participated in the study?	Cases: Controls:	
1.5	Comparison is made between participants and non-participants to establish their similarities or differences	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.6	Cases are clearly defined and differentiated from controls	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.7	It is clearly established that controls are non-cases	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
ASSESSMENT			
1.8	Measures will have been taken to prevent knowledge of primary exposure influencing case ascertainment	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.9	Exposure status is measured in a standard, valid and reliable way	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
CONFOUNDING			
1.10	The main potential confounders are identified and taken into account in the design and analysis	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable

STATISTICAL ANALYSIS		
1.11	Confidence intervals are provided	
SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise the risk of bias or confounding? Code + +, +, or –	
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the exposure being investigated?	
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	

SECTION 3: DESCRIPTION OF THE STUDY ***(Note:The following information is required for evidence tables to facilitate cross-study comparisons. Please complete all sections for which information is available).*** **PLEASE PRINT CLEARLY**		
3.1	How many patients are included in this study? *List the number cases and controls separately*	
3.2	What are the main characteristics of the study population? *Include all characteristics used to identify both cases and controls - e.g. age, sex, social class, disease status*	
3.3	What environmental or prognostic factor is being investigated in this study?	
3.4	What comparisons are made in the study? *Normally only one factor will be compared, but in some cases the extent of exposure may be stratified - e.g. non-smokers v. light, moderate, or heavy smokers. Note all comparisons here.*	
3.5	For how long are patients followed-up in the study? *Length of time participant histories are tracked in the study.*	
3.6	What outcome measures are used in the study? *List all outcomes that are used to assess the impact of the chosen environmental or prognostic factor.*	

3.7	What size of effect is identified in the study? *Effect size should be expressed as an odds ratio. If any other measures are included, note them as well. Include p values and any confidence intervals that are provided.*	
3.8	How was this study funded? *List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.*	
3.9	Does this study help to answer your key question? *Summarise the main conclusions of the study and indicate how it relates to the key question.?*	

NOTES ON THE USE OF METHODOLOGY CHECKLIST 4: CASE-CONTROL STUDIES

The studies covered by this checklist are designed to answer questions of the type "What are the factors that caused this event?", and involve comparison of individuals with an outcome with other individuals from the same population who do not have the outcome. These studies start after the outcome of an event, and can be used to assess multiple causes of a single event. They are generally used to assess the causes of a new problem, but may also be useful for the evaluation of population based interventions such as screening.

Section 1 identifies the study, the reviewer, the guideline for which the paper is being considered as evidence, and the key question(s) it is expected to address. The reviewer is asked to consider a series of aspects of cohort study design and to make a judgement as to how well the current study meets this criterion. Each relates to an aspect of methodology that research has shown makes a significant difference to the conclusions of a study.

Case-control studies need to be very carefully designed, and the complexity of their design is often not appreciated by investigators, leading to many poor quality studies being conducted. The questions in this checklist are designed to identify the main features that should be present in a well designed study. There are few criteria that should, alone and unsupported, lead to rejection of a study. However, a study that fails to address or report on more than one or two of the questions addressed below should almost certainly be rejected.

For each question in this section you should use one of the following to indicate how well it has been addressed in the study:

- Well covered
- Adequately addressed
- Poorly addressed
- Not addressed (i.e. not mentioned, or indicates that this aspect of study design was ignored)
- Not reported (i.e. mentioned, but insufficient detail to allow assessment to be made)
- Not applicable.

1.1 The study addresses an appropriate and clearly focused question

Unless a clear and well defined question is specified, it will be difficult to assess how well the study has met its objectives or how relevant it is to the question you are trying to answer on the basis of its conclusions.

1.2 The cases and controls are taken from comparable populations.

Study participants may be selected from the target population (all individuals to which the results of the study could be applied), the source population (a defined subset of the target population from which participants are selected), or from a pool of eligible subjects (a clearly defined and counted group selected from the source population. **If the study does not include clear definitions of the source population it should be rejected.**

1.3 The same exclusion criteria are used for both cases and controls

All selection and exclusion criteria should be applied equally to cases and controls. Failure to do so may introduce a significant degree of bias into the results of the study.

1.4 What percentage of each group (cases and controls) participated in the study?

Differences between the eligible population and the participants are important, as they may influence the validity of the study. A participation rate can be calculated by dividing the number of study participants by the number of eligible subjects. It is more useful if calculated separately for cases and controls. If the participation rate is low, or there is a large difference between the two groups, the study results may well be invalid due to differences between participants and non-participants. In these circumstances, the study should be downgraded, and rejected if the differences are very large.

1.5 Comparison is made between participants and non-participants to establish their similarities or differences

Even if participation rates are comparable and acceptable, it is still possible that the participants selected to act as cases or controls may differ from other members of the source population in some significant way. A well conducted case-control study will look at samples of the non-participants among the source population to ensure that the participants are a truly representative sample.

1.6 Cases are clearly defined and differentiated from controls

The method of selection of cases is of critical importance to the validity of the study. Investigators have to be certain that cases are truly cases, but must balance this with the need to ensure that the cases admitted into the study are representative of the eligible population. **The issues involved in case selection are complex, and should ideally be evaluated by someone with a good understanding of the design of case-control studies. If the study does not comment on how cases were selected, it is probably safest to reject it as a source of evidence.**

1.7 It is clearly established that controls are non-cases

Just as it is important to be sure that cases are true cases, it is important to be sure that controls do not have the outcome under investigation. Control subjects should be chosen so that information on exposure status can be obtained or assessed in a similar way to that used for the selection of cases. If the methods of control selection are not described, the study should be rejected. **If different methods of selection are used for cases and controls the study should be evaluated by someone with a good understanding of the design of case-control studies.**

1.8 Measures will have been taken to prevent knowledge of primary exposure influencing case ascertainment

If there is a possibility that case ascertainment can be influenced by knowledge of exposure status, assessment of any association is likely to be biased. A well conducted study should take this into account in the design of the study.

1.9 Exposure status is measured in a standard, valid and reliable way

The primary outcome measures used should be clearly stated in the study. **If the outcome measures are not stated, or the study bases its main conclusions on secondary outcomes, the study should be rejected.** Where outcome measures require any degree of subjectivity, some evidence should be provided that the measures used are reliable and have been validated prior to their use in the study.

1.10 The main potential confounders are identified and taken into account in the design and analysis

Confounding is the distortion of a link between exposure and outcome by another factor that is associated with both exposure and outcome. The possible presence of confounding factors is one of the principal reasons why observational studies are not more highly rated as a source of evidence. The report of the study should indicate which potential confounders have been considered, and how they have been assessed or allowed for in the analysis. Clinical judgement should be applied to consider whether all likely confounders have been considered. If the measures used to address confounding are considered inadequate, the study should be downgraded or rejected, depending on how serious the risk of confounding is considered to be. **A study that does not address the possibility of confounding should be rejected.**

1.11 Confidence intervals are provided

Confidence limits are the preferred method for indicating the precision of statistical results, and can be used to differentiate between an inconclusive study and a study that shows no effect. Studies that report a single value with no assessment of precision should be treated with extreme caution.

Section 2 relates to the overall assessment of the paper. It starts by rating the methodological quality of the study, based on your responses in Section 1 and using the following coding system:

++

All or most of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought **very unlikely** to alter.

+

Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought **unlikely** to alter the conclusions.

-

Few or no criteria fulfilled. The conclusions of the study are thought **likely or very likely** to alter.

The code allocated here, coupled with the study type, will decide the **level of evidence** that this study provides.

The aim of the other questions in this section is to summarise your view of the quality of this study and its applicability to the patient group targeted by the guideline you are working on.

Section 3 asks you to summarise key points about the study that will be added to an evidence table at the next stage of the process. **It is important that you complete this section as fully as possible, and include actual data from the study wherever relevant.**

METHODOLOGY CHECKLIST 5: STUDIES OF DIAGNOSTIC ACCURACY			
This checklist and the associated notes are based on the QADAS tool: Whiting J, Rutjes AW, Dinnes J, Reitsma JB, Bossuyt PM, Kleijnen J. Development and validation of methods for assessing the quality of diagnostic accuracy studies. Health Tech Assess 2004;8(25).			
Study identification (Include author, title, reference, year of publication)			
Guideline topic:		Key Question No:	
Checklist completed by:			
SECTION 1: INTERNAL VALIDITY			
In a well conducted diagnostic study…		***In this study this criterion is***	
1.1	The spectrum of patients is representative of the patients who will receive the test in practice.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.2	Selection criteria are clearly described.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.3	The reference standard is likely to classify the condition correctly.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.4	The period between reference standard and index test is short enough to be reasonably sure that the target condition did not change between the two tests.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.5	The whole sample, or a random selection of the sample, received verification using a reference standard of diagnosis.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.6	Patients received the same reference standard regardless of the index test result.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.7	The reference standard was independent of the index test (i.e. the index test did not form part of the reference standard).	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.8	The execution of the index test was described in sufficient detail to permit replication of the test.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.9	The execution of the reference standard was described in sufficient detail to permit replication of the test.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable

1.10	Index test results were interpreted without knowledge of the results of the reference standard.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.11	Reference standard results were interpreted without knowledge of the results of the index test.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.12	Uninterpretable or intermediate test results are reported.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.13	An explanation is provided for withdrawals from the study.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
SECTION 2: OVERALL ASSESSMENT OF THE STUDY			
2.1	How reliable are the conclusions of this study? **Code + +, +, or –**		
2.2	Were the same clinical data available when test results were interpreted as would be available when the test is used in practice?		
SECTION 3: DESCRIPTION OF THE STUDY (*Note: The following information is required for evidence tables to facilitate cross-study comparisons. Please complete all sections for which information is available).* PLEASE PRINT CLEARLY			
3.1	How many patients are included in this study? *Please indicate number of patients included, with inclusion/exclusion criteria used to select them.*		
3.2	What is the prevalence (proportion of people with the disease being tested for) in the population from which patients were selected?		
3.3	What are the main characteristics of the patient population? *Include all relevant characteristics – e.g. age, sex, ethnic origin, comorbidity, disease status, community/hospital based*		

3.4	What test is being evaluated in this study? *Consider whether the technology being described is comparable / relevant to the test being considered in the guideline. i.e. make sure the test has not been superceded by later developments.*	
3.5	What is the reference standard with which the test being evaluated is compared? *Indicate whether a gold standard, or if not how this standard was validated.*	
3.7	What is the estimated sensitivity of the test being evaluated? (state 95% CI) *Sensitivity = proportion of results in patients with the disease that are correctly identified by the new test.*	
3.8	What is the estimated specificity of the test being evaluated? (state 95% CI) *Specificity = proportion of results in patients without the disease that are correctly identified by the new test*	
3.9	What is the positive predictive value of the test being evaluated? *Positive predictive value = proportion of patients with a positive test result that actually had the disease.*	
3.10	What is the negative predictive value of the test being evaluated? *Negative predictive value = proportion of patients with a negative test result that actually did not have the disease.*	
3.11	What are the likelihood ratios for the test being evaluated? *If not quoted in the study, a number of tools are available that simplify calculation of LRs. Please indicate where results are calculated rather than taken from the study.*	
3.12	How was this study funded? *List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.*	
3.13	Are there any specific issues raised by this study?	

<table>
<tr><th colspan="4">NOTES ON THE USE OF METHODOLOGY CHECKLIST 5: DIAGNOSTIC STUDIES</th></tr>
<tr><td>Section 1</td><td colspan="3">Section 1 identifies the study and makes a series of statements that you can use to assess the internal validity of the study. This is to help you check that the study has been carried out carefully, and that the results reflect the accuracy of the test being evaluated. Each statement covers an aspect that research has shown makes a significant difference to the conclusions of a study.[1]</td></tr>
<tr><td>Statement 1.1</td><td colspan="3">The spectrum of patients is representative of the patients who will receive the test in practice.</td></tr>
<tr><td></td><td>What does this statement mean?</td><td>When does this statement apply?</td><td>Studies should be scored as:</td></tr>
<tr><td></td><td>This statement is about spectrum bias.
You should have a clear idea of the population, or spectrum, of patients you would expect to see in practice, taking into account factors such as disease prevalence and severity, age, and gender.

Different demographic and clinical features between populations may lead to considerable differences in measures of diagnostic accuracy. It is difficult to generalise from reported estimates of diagnostic accuracy if the spectrum of tested patients is not similar to the patients on whom the test will be used in practice.

A description of the spectrum of patients should refer to the severity of the target condition, demographic features, and the presence of differential diagnosis and/or comorbidity. Diagnostic test evaluations should include an appropriate spectrum of patients for the test under investigation. Inclusion criteria for patients should be clearly defined.</td><td>Always applies.</td><td>Well addressed if you believe, based on the information provided by the authors, that the spectrum of patients included in the study was representative of those on whom the test will be used in practice. This judgement should be based on both the method of recruitment and the characteristics of those recruited.

Adequately addressed if it seems likely that the spectrum of patients was representative of those seen in practice but the paper is unclear or lacking some information

Poorly addressed where a group of patients known to have the target disorder are recruited along with a group of healthy controls.</td></tr>
<tr><td colspan="4">These notes are based on the QADAS tool: Whiting J, Rutjes AW, Dinnes J, Reitsma JB, Bossuyt PM, Kleijnen J. Development and validation of methods for assessing the quality of diagnostic accuracy studies. Health Tech Assess 2004;8(25).</td></tr>
</table>

Statement 1.2	**Selection criteria are clearly described**		
	What does this statement mean?	When does this statement apply?	Studies should be scored as:
	Have the authors provided a clear definition of the criteria used to select patients for entry into the study?	Always applies.	**Well covered** if you think that all relevant information regarding how participants were selected for inclusion in the study has been provided. **Adequately addressed** if some information is provided, but not enough to make you confident you understand what the selection criteria were and how they were applied. **Poorly addressed** if some information is provided but you are unclear about what the criteria were or how they were applied. **Not addressed** or **Not reported** if there is no discussion of selection criteria, reject the study.
Statement 1.3	**The reference standard is likely to classify the condition correctly.**		
	What does this statement mean?	When does this statement apply?	Studies should be scored as:
	The reference standard is the method or test used to determine the presence or absence of the target condition. The choice of reference standard depends on the defined target condition and the purpose of the study. To assess the diagnostic accuracy of the new or "index test", results from the index test are compared with results from the reference standard. If no single reference test is available, then careful clinical follow-up, a consensus between observers, or the results of two or more combined tests may be used to determine the presence or absence of the target condition. Estimates of the performance of the index test are based on the assumption that the reference standard that is 100% sensitive and specific. If there are any disagreements between the reference standard and the index test then it is assumed that the index test is incorrect.	Always applies. Your key question may specify the use of a particular reference standard. In this case, exclude all studies that do not use your specified reference standard.	**Well covered** if you believe that the reference standard is likely to classify the target condition correctly. **Adequately addressed** if you think the authors have not fully justified their choice of reference standard. **Poorly addressed** if you do not think that the reference standard was likely to have classified the target condition correctly. **Not addressed** if there is insufficient information to make a judgement.

Statement 1.4	**The period between reference standard and index test is short enough to be reasonably sure that the target condition did not change between the two tests**.		
	What does this statement mean?	When does this statement apply?	Studies should be scored as:
	This statement is about **disease progression bias.** Ideally, results from the index test and the reference standard are collected from the same patients at the same time. Delay between the two measurements could allow either spontaneous recovery or disease progression to occur. The length of time causing such bias will depend on the condition. A delay of a few days is unlikely to be a problem for chronic conditions. For some diseases a delay between tests may be critical. This type of bias may occur in chronic conditions in which the reference standard involves clinical follow-up of several years.	Usually applies	**Well covered.** For rapidly developing conditions, delays of hours to a few days are acceptable. For chronic conditions, disease status is less likely to change rapidly and a delay of weeks is acceptable. **Adequately addressed** if you think the delay is lengthy, but still acceptable. You should decide when you set your key questions what constitutes an acceptable delay. **Poorly addressed.** If you think the period between the performance of the index test and the reference standard was sufficient to allow disease status to change between the performance of the two tests **Not addressed** if insufficient information is provided.
Statement 1.5	**The whole sample, or a random selection of the sample, was verified using a reference standard of diagnosis.**		
	What does this statement mean?	When does this statement apply?	Studies should be scored as:
	This statement is about **partial verification bias**, also known as work-up bias, (primary) selection bias or sequential ordering bias. If only some of the study group receive confirmation of the diagnosis by a reference standard, and the results of the index test influence the decision to perform the reference standard, then biased estimates of test performance may arise. True random selection of patients to receive the reference standard will address this problem.	Generally only occurs when patients are tested by the index test before the reference standard.	**Well addressed** if it is clear that all patients who received the index test went on to receive verification of their disease status using the same reference standard. **Adequately addressed** if the reference standard was not the same for all patients. **Poorly addressed** if not all of the patients who received the index test received verification of their true disease state. **Not applicable** if the reference standard was applied first, and you are confident that verification bias could not have occurred.

Statement 1.6	**Patients received the same reference standard regardless of the index test result.**		
	What does this statement mean?	When does this statement apply?	Studies should be scored as:
	This statement is about **differential verification bias.** This occurs when different reference standards are used to verify the index test results. Different reference standards may vary in their definition of the target condition (e.g. histopathology of the appendix and natural history for the detection of appendicitis). It often occurs when patients testing positive on the index test receive a more accurate, often invasive, reference standard than those with negative test results. The correlation between a particular (negative) test result and being verified by a less accurate reference standard will affect measures of test accuracy in a similar way to partial verification, but less seriously.	Generally only occurs when all patients are tested by the index test before the reference standard.	**Well addressed** if it is clear that all patients who received the index test had their disease status verified using the same reference standard. **Adequately addressed** if the reference standard was not the same for all patients. **Poorly addressed** if some of the patients who received the index test did not have their true disease state verified. **Not applicable** in case-control designs where the order of the tests is reversed (ie reference standard first).

Statement 1.7	**The reference standard was independent of the index test (ie the index test did not form part of the reference standard).**		
	What does this statement mean?	When does this statement apply?	Studies should be scored as:
	This statement is about **incorporation bias**. Incorporation bias may occur when the result of the index test is used to establish the final diagnosis. This will probably increase the agreement between index test results and the reference standard, and hence overestimate the measure of diagnostic accuracy. ***Note****:* knowledge of the results of the index test does not automatically mean that the results are incorporated in the reference standard. For example, a study investigating magnetic resonance imaging (MRI) for diagnosing multiple sclerosis could have a reference standard composed of clinical follow-up, cerebrospinal fluid analysis and MRI. In this case the index test forms part of the reference standard. If the same study used a reference standard of clinical follow-up and the results of the MRI were known when the clinical diagnosis was made but were not specifically included as part of the reference, then the index test does not form part of the reference standard.	Only applies when a composite reference standard is used to verify disease status.	**Poorly addressed** if the index test formed part of the reference standard. **Not applicable** if it is clear that the index test did not form part of the reference standard. ***Note:*** "Poorly addressed" does not refer to whether or not incorporation bias is described or discussed as it may be quite clearly described. "Poorly addressed" refers to the fact that including the index text in the reference standard introduces a potential bias.

Statements 1.8 and 1.9	**The execution of the index test was described in sufficient detail to permit replication of the test.** **The execution of the reference standard was described in sufficient detail to permit replication of the test.**		
	What does this statement mean?	When does this statement apply?	Studies should be scored as:
	A sufficient description of the execution of index test and reference standards is important for two reasons. First, variation in measures of diagnostic accuracy can sometimes be traced back to differences in the execution of index/ reference standards. Second, a clear and detailed description (or references) is needed to implement the test in another setting. If tests are executed in different ways then this could affect test performance. The extent to which this would alter results would depend on the type of test.	Usually applies.	**Well addressed** if the study reports sufficient details to permit replication of the index test and reference standard. **Adequately addressed** if only the bare minimum of information has been provided. **Not reported** if detail is insufficient.
Statements 1.10 and 1.11	**Index test results were interpreted without knowledge of the results of the reference standard.** **Reference standard results were interpreted without knowledge of the results of the index test.**		
	What does this statement mean?	When does this statement apply?	Studies should be scored as:
	This statement is about **review bias.** Review bias is similar to blinding in intervention studies. Interpretation of the results of the index test may be influenced by knowledge of the results of the reference standard, and vice versa. The effect on results will depend on the degree of subjectivity in the interpretation of the test result. The more subjective the interpretation the more likely that the interpreter can be influenced by the results of the index test in interpreting the reference standard, and vice versa.	If the index test is always performed first then interpretation of the results of the index test will usually be without knowledge of the results of the reference standard. If the reference standard is always performed first then the results of the reference standard will be interpreted without knowledge of the index test. In certain situations the results of both the index test and reference standard are blinded in both directions before being interpreted.	**Well addressed** if the study clearly states that the test results (index or reference standard) were interpreted blind to the results of the other test. **Adequately addressed** if you are uncertain of the reliability of the blinding procedure. **Poorly addressed** if you regard the blinding procedure as inadequate. **Not applicable** where test results are entirely objective or tests were carried out in an independent laboratory.

Statement 1.12	**Uninterpretable or intermediate test results are reported**		
	What does this statement mean?	When does this statement apply?	Studies should be scored as:
	A diagnostic test can produce an uninterpretable/ indeterminate/intermediate result with varying frequency, depending on the test. Uninterpretable results are often removed from the analysis which may lead to biased assessment of the test characteristics. Any bias will depend on the correlation between uninterpretable test results and true disease status. If uninterpretable results occur randomly then they should not affect test performance. Whatever the cause of uninterpretable results it is important for them to be reported so that their impact on test performance can be determined.	Always applies.	**Well addressed i**f it is clear that **all** test results are reported. **Poorly addressed** if it is clear that such results occurred, but it is not clear to what extent they have been reported. **Not addressed** if there is no mention of whether such results occurred, or how they were handled.
Statement 1.13	**An explanation is provided for withdrawals from the study.**		
	What does this statement mean?	When does this statement apply?	Studies should be scored as:
	This occurs when patients withdraw from the study before the results of both the index test and reference standard are known. If patients lost to follow-up differ systematically from those who remain, for whatever reason, then estimates of test performance may be biased.	Always applies.	**Well addressed** if it is clear what happened to all patients who entered the study (eg a flow diagram of study participants is reported). **Poorly addressed** if some of the participants who entered the study did not complete it and are not accounted for. **Not reported** if it is not clear whether all patients who entered the study are accounted for.

Statement 1.14	**The same clinical data were available when test results were interpreted as would be available when the test is used in practice.**		
	What does this statement mean?	When does this statement apply?	Studies should be scored as:
	The availability of clinical data (anything relating to the patient that can be obtained by direct observation) during the interpretation of test results may affect estimates of test performance. Such knowledge can influence the test result if it involves an interpretative component. If clinical data will be available when the test is interpreted in practice then it should be available when the test is evaluated.	Does not apply to tests which are fully automated and involve no interpretation, or where the index test is intended to replace other clinical tests.	**Well addressed** if it is clear that the index test was evaluated in circumstances identical to those that apply in routine practice. **Adequately addressed** if there is discussion of any differences between the circumstances of test evaluation and routine practice. **Not reported** if the circumstances of test evaluation and routine practice are not discussed.
Section 2	Section 2 relates to the overall assessment of the paper. It rates the methodological quality of the study, based on the responses in section 1, using the following coding system:		
+ +	**All or most** of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought **very unlikely** to alter.		
+	**Some** of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought **unlikely** to alter the conclusions.		
-	**Few or no** criteria fulfilled. The conclusions of the study are thought **likely or very likely** to alter.		
The code allocated here, coupled with the study type, will decide the **level of evidence** that this study provides.			
Section 3	Section 3 asks for any general comments that you might want to incorporate into an evidence table at the next stage of the process.		

METHODOLOGY CHECKLIST 6: ECONOMIC EVALUATIONS			
Study identification (Include author, title, year of publication, journal title, pages)			
Guideline topic:		Key Question No:	
Checklist completed by:			
SECTION 1: INTERNAL VALIDITY			
In a well conducted economic study...		***In this study this criterion is:***	
1.1	There is a defined and answerable study question	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.2	The economic importance of the question is clear	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.3	The choice of study design is justified	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.4	All costs that are relevant from the viewpoint of the study are included and are measured and valued appropriately	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.5	The outcome measures used to answer the study question are relevant to that purpose and are measured and valued appropriately	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.6	If discounting of future costs and outcomes is necessary, it been performed correctly	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.7	Assumptions are made explicit and a sensitivity analysis performed	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.8	The decision rule is made explicit and comparisons are made on the basis of incremental costs and outcomes	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.9	The results provide information of relevance to policy makers	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable

SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	Is this study an economic evaluation, or a cost analysis?	
2.2	How well was the study conducted? *Code + +, +, or –*	
2.2	Are the results of this study directly applicable to the patient group targeted by this guideline?	

SECTION 3: DESCRIPTION OF THE STUDY ***(The following information is required to complete evidence tables facilitating cross-study comparisons. Please complete all sections for which information is available).*** **PLEASE PRINT CLEARLY**	
3.1	What interventions are evaluated in this study?
3.2	What type of study is it (cost-benefit analysis, cost utility study, etc.)?
3.3	How many patients participated in the study?
3.4	What was the scale of the incremental cost/benefit?
3.5	Is any statistical measure of uncertainty given? *e.g. confidence intervals; p values*
3.4	What are the characteristics of the study population? e.g. age, sex, disease characteristics of the population, disease prevalence.
3.5	What are the characteristics of the study setting? *e.g. rural, urban, hospital inpatient or outpatient, general practice, community*.
3.6	How many groups/sites are there in the study? *If the study is carried out on more than one group of patients, or at more than one site, indicate how many are involved.*
3.7	How was this study funded? List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.
3.8	Does this study help to answer your key question? Summarise the main conclusions of the study and indicate how it relates to the key question.

NOTES ON THE USE OF METHODOLOGY CHECKLIST 6: ECONOMIC EVALUATIONS

Section 1 identifies the study and asks a series of questions aimed at establishing the internal validity of the study under review - i.e. making sure that it has been carried out carefully, and that the results are likely to be reliable and useful. Each question covers an aspect of study design that is known to make a significant difference to the conclusions of a study.

For each question in this section you should use one of the following to indicate how well it has been addressed in the review:

- Well covered
- Adequately addressed
- Poorly addressed
- Not addressed (i.e. not mentioned, or indicates that this aspect of study design was ignored)
- Not reported (i.e. mentioned, but insufficient detail to allow assessment to be made)
- Not applicable.

1.1 There is a defined and answerable study question

As with clinical evaluations, a clearly defined question is essential to allow the user to assess how well the study has met its objectives or how relevant it is to the guideline recommendation to which the results might be applied. For an economic evaluation, the question should contain information on the alternatives under comparison, the viewpoint, and (ideally) the form of economic evaluation being used and the resulting decision rule.

1.2 The economic importance of the question is clear

Not all economic evaluations are equally relevant or important. A comparison between different drugs available to treat the same condition, for example, could influence the choice of drug and possibly the overall cost of treatment. A study of drug therapy versus psychotherapy, on the other hand, could have major implications for the range, type, and extent of resources required to deliver good quality health care in a specific area. A well conducted study will provide some information on how great an impact the results are likely to have on the overall economics of the area of health care to which it relates.

1.3 The choice of study design is justified

The design of the study can have a big impact on the results derived from it. It is therefore important that the study design is clearly identified, and its limitations made clear. Each study design has its own strengths and weaknesses and each may be appropriate under different settings.

The main types of study used for economic evaluations are:

- **Economic evaluation alongside randomised controlled trial.**

In some respects this is a good model as cost and benefit data can be collected in parallel with the clinical data, and is therefore likely to be relevant and applicable. On the other hand, a number of factors are likely to make study results unrepresentative of real practice. More resources are likely to be available in a study setting than in normal practice; patient compliance may be higher than normal; there is unlikely to be scope for economies of scale; etc. The overall result is likely to be higher costs and better outcomes in the trial than are achievable once the treatment is provided on a broader basis.

- **Before and after studies.**

A "before and after study" compares costs and outcomes before the introduction of a new therapy, and after it has been provided for some time. The major problem with this type of study design is the difficulty of attributing any changes purely to the new treatment (high risk of confounding).

- **Comparative studies.**

Two systems are compared in these studies – one with the new intervention, and one that does not have the new intervention but is similar in all other respects. This design is often used in areas where randomised trials are impractical or unethical. The main difficulty is in finding two directly comparable locations or systems and eliminating the possibility of confounding. In some studies comparisons may be made between a real location and an economic model. In all such studies use of sensitivity analysis to assess the reliability of results is essential, and such analyses are particularly important where model comparisons have been used.

- **Modelling of routine data sets.**

For major policy issues, econometric modelling based on data sets such as mortality or health service utilisation can be used to estimate the effect of changes. The general lack of suitable data sets makes this a difficult option to apply in a UK context.

- **Secondary economic evaluations.**

In these evaluations local data is applied to the results of published studies to produce economic evaluations that can be applied in the local context. The scope for applying such methods is limited by the range of published economic studies. Again, the effective use of sensitivity analysis is an essential part of a well designed study.

Whichever type of design is used, the study should make clear why it was chosen, and how any possible weaknesses were addressed.

1.4 *All costs that are relevant from the viewpoint of the study are included and are measured and valued appropriately*

This is a key aspect of study design. Any study that fails to adequately detail how cost information was obtained or estimated should not be used as evidence.

All costs relevant to the study have to be identified, measured, and valued. What constitutes "relevant costs" will depend on the viewpoint of the study. A study looking at the subject from the point of view of the health service, for example, will cover all treatment and related costs. A study taking a societal view will take into account additional costs such as lost working days.

Ideally, opportunity costs (i.e. the extent to which an opportunity to use resources for some other purpose has been given up) should be used and not purely financial costs. Costs are defined as any change (either increase or decrease) in resource use as a result of the study intervention, and measured in appropriate units.

Realistically, many studies will rely on cost data. Likely sources of such data include the financial systems of service providers, scales of charges for provision of services by the private sector, and published cost studies. All sources of cost data have weaknesses, and a well conducted study will indicate how possible uncertainties or weaknesses in the data have been addressed.

1.5 *The outcome measures used to answer the study question are relevant to that purpose and are measured and valued appropriately*

This is a key aspect of study design. Any study that fails to adequately detail how outcomes were measured and (where appropriate) valued should not be used as evidence.

All outcomes should be explicitly identified and measured, even if they are not the prime focus of the study. If, for example, a comparison of two treatment programmes showed no difference in cost effectiveness in terms of life years gained between two treatments, measurement of other factors such as long-term pain or quality of life could help choose between them.

Valuation of outcomes is only required in cost benefit analysis or other types of study where it is necessary to compare costs and outcomes in commensurate units. Even in those cases, valuation is only required where none of the options is dominant (i.e. none is clearly better and cheaper, or worse and more expensive, than the others). Methods of valuation vary considerably, and where they are used, it is essential that the valuation methods are described and associated uncertainties discussed.

1.6 If discounting of future costs and outcomes is necessary, it been performed correctly

In many economic studies some costs or outcomes may not arise at the time of the study, but in the future. A transplant patient, for example, may be able to resume a full life following transplant but will require lifelong drug therapy and periodic follow-up visits to hospital. These future costs and benefits must be taken into account, but should be valued at a lower level than immediate costs and benefits. This is normally done through a process of discounting at a fixed rate per annum.

Take the example of the transplant patient, and assume that following surgery he is going to be permanently reliant on drugs that currently cost £20,000 per annum. Assume also that though the actual amount paid each year remains constant, the value of this amount will decline by 6% per annum. We can now calculate how much the drug will cost in each future year, based on present day values

Year	Future value	Discount factor	Present value
0	£20,000	1	£20,000
1	£20,000	0.943	£18,860
2	£20,000	0.89	£17,800
3	£20,000	0.84	£16,800
4	£20,000	0.793	£15,860

The discount factor is calculated by working out the value of £1 less the decrease in value over the year, so in year one it is 1/1.06, in year 2 it is 0.943/1.06, and so on.

Looking at the table, it is clear that working out the cost of the drugs at a fixed rate per annum will give a very different answer to one based on the discounted rate. This is a rather simplified example, but for the purposes of study evaluation it is not necessary to evaluate such calculations in detail – just to be sure that they have been done if the interventions have long term effects, and that there is some justification for the selected discount rate.

1.7 Assumptions are made explicit and a sensitivity analysis performed

Economic evaluation requires assumptions to be made, but if studies are to be useful to others and comparable with other work the assumptions made must be explicit. **If a study appears to make assumptions that are not identified or explained it should not be used as evidence.**

Wherever assumptions have been made, sensitivity analyses should be carried out to see what difference variations in the assumptions would make to the final outcome. Where such analyses are not included in a study, the results should be treated with great caution.

1.8 The decision rule is made explicit and comparisons are made on the basis of incremental costs and outcomes

The decision rule specifies the basis on which a decision about the intervention will be made – e.g. the most cost effective option will be selected. The results of an economic evaluation are normally expressed as the additional cost per additional unit of outcome. If the results are presented in some other way, the study may not be a true economic evaluation but a form of cost study.

Note that this information provides a basis for decision making, but does not represent a decision in itself: the final decision (like the recommendations based on these studies) is likely to be influenced by other factors as well as the economic case.

1.9 The results provide information of relevance to policy makers

Study results should be presented clearly and concisely, in a way that makes it easy for decision makers to interpret the results correctly. Ideally, the limitations of the study should be discussed along with comments on its generalisability.

Section 2 relates to the overall assessment of the paper. It starts by asking a fundamental question about the nature of the study, and whether it is a true economic evaluation. If the paper is a cost study, it will be of little or no value as a source of evidence for guideline recommendations.

The following question asks you to decide how well the study meets the quality criteria overall. This should be based on your assessment of the criteria set out in Section 1, and should use the following scale:

+ +

All or most of the criteria have been fulfilled. Those that have not been fulfilled are **very unlikely** to alter the conclusions or the generalisability of the study.

+

Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or are not adequately described are thought **unlikely** to alter the conclusions or the generalisability of the study.

-

Few or no criteria fulfilled. The conclusions of the study are thought **likely or very likely** to alter.

The final question in this section asks you to consider whether the results of this study are directly applicable to the patient population that the guideline is intended to cover. If it is not, careful consideration must be given to how generalisable the study is and whether it should be considered as part of the evidence base.

Section 3 asks you to summarise key points about the study that will be added to an evidence table at the next stage of the process. **It is important that you complete this section as fully as possible, and include actual data from the study wherever relevant.**

Annex D

METHODOLOGY CHECKLIST 2: RANDOMISED CONTROLLED TRIALS			
Study identification (Include author, title, year of publication, journal title, pages) **Elman, RJ and Bernstein-Ellis, E 1999 The efficacy of group communication treatment in adults with chronic aphasia. Journal of Speech, Language and Hearing Research 42, 411 - 419**			
Guideline topic: **Stroke rehabilitation**		Key Question No: **12**	
Checklist completed by: ***C Mackenzie***			
SECTION 1: INTERNAL VALIDITY			
In a well conducted RCT study...		***In this study this criterion is:***	
1.1	The study addresses an appropriate and clearly focused question.	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.2	The assignment of subjects to treatment groups is randomised	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.3	An adequate concealment method is used	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.4	Subjects and investigators are kept 'blind' about treatment allocation	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.5	The treatment and control groups are similar at the start of the trial	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.6	The only difference between groups is the treatment under investigation	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.7	All relevant outcomes are measured in a standard, valid and reliable way	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed?	**>80%**	
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis)	Well covered Adequately addressed Poorly addressed	Not addressed Not reported Not applicable

SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise bias?	**+**
2.2	If coded as +, or - what is the likely direction in which bias might affect the study results?	**Overestimate of effect**.
2.3	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	**Reasonably so, though with caution given the small subject number**
2.4	Are the results of this study directly applicable to the patient group targeted by this guideline?	**Yes – if same amount and form of treatment used**
SECTION 3: DESCRIPTION OF THE STUDY *(The following information is required to complete evidence tables facilitating cross-study comparisons. Please complete all sections for which information is available).* **PLEASE PRINT CLEARLY**		
3.1	How many patients are included in this study? *Please indicate number in each arm of the study, at the time the study began.*	**24:12 immediate treatment and 12 deferred.**
3.2	What are the main characteristics of the patient population? *Include all relevant characteristics – e.g. age, sex, ethnic origin, comorbidity, disease status, community/ hospital based*	**Single left stroke. Minimum 6 months post onset** **Age 38 – 79. Mixed aphasia types and severity**
3.3	What intervention (treatment, procedure) is being investigated in this study? *List all interventions covered by the study.*	**Group communication intervention in aphasia – 5 hours per week for 4 months**
3.4	What comparisons are made in the study? *Are comparisons made between treatments, or between treatment and placebo / no treatment?*	**Treatment v social contact programme (3 hours per week)**
3.5	How long are patients followed-up in the study? *Length of time patients are followed from beginning participation in the study. Note specified end points used to decide end of follow-up (e.g. death, complete cure). Note if follow-up period is shorter than originally planned.*	**4 months**
3.6	What outcome measure(s) are used in the study? *List all outcomes that are used to assess effectiveness of the interventions used.*	**Linguistic and communicative measures**

3.7	What size of effect is identified in the study? *List all measures of effect in the units used in the study – e.g. absolute or relative risk, NNT, etc. Include p values and any confidence intervals that are provided.*	**Advantage for treated group, with greater changes for more severely affected subjects**
3.8	How was this study funded? *List all sources of funding quoted in the article, whether Government, voluntary sector, or industry.*	**Not stated.**
3.9	Does this study help to answer your key question? *Summarise the main conclusions of the study and indicate how it relates to the key question.*	**Treatment programme effective after 2 months with additional gains after further 2 months. Gains maintained after 4 – 6 week no treatment period. No change during general socialisation period for control group** **Encouraging result as regards language impairment and functional communication measures.** **Further data in relation to broader disability/ handicap issues is in progress. Conclusions must be cautious given small scale of study.**

EVIDENCE TABLE FOR INTERVENTION STUDIES

Question: Which tooth cleaning methods have been shown to be most effective in preventing dental caries and what are the risks and barriers associated with these?

Bibliographic Citation	Study type	Evidence level	Number of patients	Patient characteristics	Intervention	Comparison	Length of Follow-up	Outcome measure	Effect size	Source of funding
Wendt, L. K., Hallonsten, A. L., Koch, G. and Birkhed, D.. Oral hygiene in relation to caries development and immigrant status in infants and toddlers. Scandinavian Journal of Dental Research. 1994:102;269-73.	Cohort Study	+	1 yr olds caries-free = 629 ; 2 year olds caries free = 298 ; 3 year olds caries free = 270	Pre-school children; community-based; Immigrant status = (a) Swed, i.e. at least one parent born in Sweden and (b) Immi, i.e. both parents born outside Sweden. Caries-free at 1 year of age.	Presence of caries + oral health habits	Presence or absence of dental caries, gingivitis and visible plaque.	3 years	Presence or absence of dental caries	Visible plaque at 1 year of age: 29% carious lesions by 2 years, + 54% carious lesions by 3 years.	
General comments: Potential confounding factors not addressed, i.e. gender + heterogeneity of different ethnic groups. Not enough evidence to support a recommendation on its own.										
Verrips, G. H., Kalsbeek, H., Van Woerkum, C. M., Koelen, M. and Kok-Weimar, T. L.. Correlates of toothbrushing in preschool children by their parents in four ethnic groups in The Netherlands. Community Dental Health. 1994:11;233-9.	Survey	+	614 children examined 476 parents interviewed	4 different ethnic groups / Selection by district and ethnic group / Community based	Questionnaire on parental attitudes/beliefs regarding toothbrushing – as predictors of caries risk			Risk factors for dental caries	1. Age at start of brushing as a risk factor: 29% of diff. In scores between Turkish grp. and Dutch and Surinamese (reference group) could be attributed to the role of all potential correlates, i.e. parental habits, attitudes, beliefs etc. 2. Frequency of brushing : Relatively strong relationship between freq. and attitudes and habits (i.e. 54% of difference attributed to these correlates.	

General comments: Selection bias due to 67% of Moroccan respondents being illiterate. No details of how well terminology was explained, e.g. caries, molars etc. Possible recall bias. Importance of health education in advocating frequency of brushing more than once daily + commencement of brushing before 2 yrs. of age.										
Sjogren, K., Birkhed, D. and Rangmar, B.. Effect of a modified toothpaste technique on approximal caries in preschool children. Caries Research. 1995:29;435-41.	RCT	+ +	Baseline = 369 Test groups x 2 = 131 Control groups x 2 = 150	4 to 7 year olds attending clinic	Instruction on use of F-paste with brushing technique	Between treatments + between treatment and control. Baseline and final radiographs	3 years	DMF(S)/ dmf(s)/ salivary F concentration/ + behavioural factors via questionnaire	Total mean dfs (Baseline and at end): Test Groups = 1.5 ; Control groups = 2.01) $p<0.05$. 2. Caries increment (new dfs) Test = 1.14/ Control = 1.55 $p<0.05$ 3.Salivary fl. Concentration – mean = 1.8 times higher in test group than control group ($p<0.01$) + AUC value = 1.9 times higher ($p<0.001$)	Government. Toothpaste/brush manufacturers
General comments: Good ev for brushing with fluoride toothpaste (mechanical action) & importance of decreased use of rinsing water after brushing										
Raitio, M., Mottonen, M. and Uhari, M.. Toothbrushing and the occurrence of salivary mutans streptococci children at day care centers. Caries Research. 1995:29;280-4.	RCT	+ +	Baseline 506; Follow-up 358 ; Took part in both examinations 345.	Age : 1-8 yrs Community-based : Municipal day care centres in Oulu, Finland	Mutans Strep. Tests + reported dental health habits	Before and after intervention + intervention (toothbrushing group) vs. control (no brushing) group	8 months	Positive MS tests. Diff. In dmf values between those with MS and those without.	RR for irregular brushing = 2.1; $p<0.001$ - MS counts for irregular brushers 64.9% vs 46.4% for regular brushers.	not stated
								Assoc. of risk factors with occurrence of MS	MS increased with sweet consumption ($p<0.01$). MS reduced by fluoride tablets ($p<0.02$) MS count and older age ($p<0.01$) / Positive MS test and female sex associated ($p<0.05$).	not stated
General comments: Toothbrushing at day-care centres does not influence salivary MS counts. Incidental finding : Children who brushed irregularly at home had more risk of positive MS test than those brushing teeth daily at home. (MS considered to be most important bacteria involved in dental decay process).										

Holtta, P. and Alaluusua, S.. Effect of supervised use of a fluoride toothpaste on caries incidence in pre-school children. International Journal of Paediatric Dentistry. 1992:2;145-9.	RCT	+	Test group = 87 ; Control group = 87	Community-based (2 nursery schools). Children aged 3-6 yrs from same residential area of average income families. All children receiving regular dental care at Dept. Pedodontics and Orthodontics, Uni. Of Helsinki.	Supervised use of fluoride toothpaste once a day in nursery school	Daily brushing with fluoride toothpaste vs. brushing with no toothpaste in low-caries population	Mean follow-up = 1.4 yrs	Difference in dfs + DFS (mean caries increments) between test and controls.	Mean dfs+DFS – 1.3 (test group) & 2.0 (control) (NS)	
								Number of new carious surfaces	No. of new carious surfaces - 13 children in test group & 25 in control group ($p<0.05$)	
								Number of caries-free children	Stat. significant diff. between test and control groups ($X2 = 4.55$, $p<0.05$)	
General comments: Even in low-caries groups, supervised brushing with fluoride toothpaste >1000ppmF offers benefits & increases no. of caries-free children. Some caution should be exercised in interpreting results of this study due to study design issues but it appears to support the argument for the use of fl. toothpaste in the prevention of dental caries.										
Davies, G. M., Worthington, H. V., Ellwood, R. P., Bentley, E. M., Blinkhorn, A. S., Taylor, G. O. and Davies, R. M.. A randomised controlled trial of the effectiveness of providing free fluoride toothpaste from the age of 12 months on reducing caries in 5 4-year old children. Community Dental Health. 2002:19;131-6.	RCT	++	3731	All age 12 months at commencement/ all aged 5-6 yrs at primary school at clinical examination/ all from areas with high levels of dental caries. Community-based	Provision of free fluoride paste from age 12 mnths to 5.6 yrs.	Effectiveness of two concentrations of fluoride paste (440ppmF and 1450ppmF) + comparison between treatment and placebo	5 year follow-up	Dmft index	1450ppmF confers a 16% reduction in mean dmft compared with control ($p<0.05$). NS difference in mean dmft between 440ppmF group and controls.	Grant from former North Western RHA. 2 authors employed by Colgate-Palmolive
								Prevalence of caries	Prevalence = 50% in 1450ppm group vs. 58% in 440ppm group and control group.	
General comments: High drop out rate (7422 recruited). Importance of fluoride dose when recommending use of fluoride toothpaste.										

Chestnutt, I. G., Schafer, F., Jacobson, A. P. and Stephen, K. W.. The influence of toothbrushing frequency and post-brushing rinsing on caries experience in a caries clinical trial. Community Dentistry & Oral Epidemiology. 1998:26;406-11.	Survey		2621 (No explanation of why 2621 in this study but 4294 in the 3 year trial).	Scottish adolescents (aged 11-12 yrs at outset). 54% male. Participants from non-affluent backgrounds. Setting : Area of generally high deprivation	Use of fluoride dentifrice containing either 1000 or 1500 ppm fluoride	Frequency of toothbrushing + method of post-brushing rinsing. (No comparison between different fluoride concentrations of toothpaste.)	3 years	Caries experience and caries increment, i.e. DMFS values. (+ data collection on oral health habits via questionnaire and interview of subjects at examination)	Association between caries experience and claimed brushing frequency at baseline : DMFS values of 9.66 (Group1), 8.12 (Group 2), 7.36 (Group 3) $p < 0.001$.	Not stated but one author supported by Unilever Dental Research
								Caries experience and caries increment, i.e. DMFS values. (+ data collection on oral health habits via questionnaire and interview of subjects at examination)	Assoc. between caries increment and brushing frequency ($p < 0.01$)	
								Influence of post-brushing rinsing method (i.e. beaker vs. no beaker).	Caries increment with beaker 6.84 ; caries increment without beaker 5.84 ($p < 0.05$).	
General comments: Provides evidence of importance of frequency of brushing but study flawed as a result of being based on reported frequency by participants, i.e. could be misreported causing bias.										

CONSIDERED JUDGEMENT FORM	
Key question: What is the evidence that cardiovascular risk in patients with Type 2 diabetes and nephropathy can be reduced by specific interventions?	Evidence table ref: **3**
1. Volume of evidence Comment here on any issues concerning the quantity of evidence available on this topic and its methodological quality.	
Only two studies have assessed cardiovascular risk reduction in patients with Type 2 diabetes and nephropathy. Both studies were methodologically of good quality, but in only one (the HOPE study) was cardiovascular disease risk reduction the primary endpoint. In the other study (the Steno Study), cardiovascular disease risk reduction was a tertiary endpoint and so the study was not adequately powered to detect a significant difference. None of the major intervention studies of hypoglycaemic therapy, lipid-lowering therapy, anti-hypertensive therapy, smoking cessation or dietary modification have specifically addressed issues of cardiovascular disease risk reduction in patients with Type 2 diabetes and nephropathy. In patients with chronic renal failure and coronary artery disease, no large-scale trials have compared aggressive cardiovascular risk reduction by medical therapy with coronary revascularisation.	
2. Applicability Comment here on the extent to which the evidence is directly applicable to the NHS in Scotland.	
Fully applicable.	
3. Generalisability Comment here on how reasonable it is to generalise from the results of the studies used as evidence to the target population for this guideline.	
Highly reasonable.	
4. Consistency Comment here on the degree of consistency demonstrated by the available of evidence. Where there are conflicting results, indicate how the group formed a judgement as to the overall direction of the evidence	
High degree of consistency - no conflicting results.	
5. Clinical impact Comment here on the potential clinical impact that the intervention in question might have – e.g. size of patient population; magnitude of effect; relative benefit over other management options; resource implications; balance of risk and benefit.	
Large potential impact - large numbers of patients with Type 2 diabetes are likely to be prescribed ACE inhibitor therapy.	
6. Other factors Indicate here any other factors that you took into account when assessing the evidence base.	
None	
7. Evidence statement Please summarise the development group's synthesis of the evidence relating to this key question, taking all the above factors into account, and indicate the evidence level which applies.	**Evidence level**

In patients with Type 2 diabetes and nephropathy: Treatment with the Angiotensin Converting Enzyme (ACE) Inhibitor Ramipril significantly reduces, all-cause mortality, cardiovascular mortality, and cardiovascular events. The effect of ramipril on cardiovascular outcomes appears to be out of proportion to its anti-hypertensive effects. Therapy with Vitamin E does not affect cardiovascular outcomes. There is no direct trial evidence that aggressive management of other cardiovascular risk factors affects cardiovascular outcomes. Evidence from blood pressure and lipid intervention trials in diabetic patients (whose nephropathy status has generally not been documented) would indicate that cholesterol reduction with statin agents and blood pressure reduction are likely to be of benefit in reducing cardiovascular events. Glucose-lowering therapy with metformin may also be of benefit in obese patients without significant impairment of renal function. Coronary angiography (with subsequent revascularisation if coronary artery disease is identified) is often advocated in patients who are being considered for renal replacement therapy. There is no direct trial evidence to support this, nor have any trials compared coronary revascularisation with aggressive medical management of cardiovascular risk factors in such circumstances.	1++ 1++ 4 4
8. Recommendation What recommendation(s) does the guideline development group draw from this evidence? Please indicate the grade of recommendation(s) and any dissenting opinion within the group.	**Grade of recommendation**
Patients with Type 2 diabetes and microalbuminuria should be commenced on therapy with Ramipril. There is no trial evidence that supports the use of other ACE inhibitors, in terms of cardiovascular risk reduction, although a class effect could be anticipated. In patients with Type 2 diabetes and nephropathy, targets for glycaemic control, blood pressure and cholesterol concentrations should be the same as for patients with established cardiovascular disease. Advice on smoking cessation should be given.	**A** **D**

SEARCH PROTOCOL: MANAGEMENT OF CUTANEOUS MALIGNANT MELANOMA

KEY QUESTIONS

A Prevention/Education/Surveillance

1. Is there any evidence that screening patients with increased risk of malignant melanoma is effective?
2. Is there any evidence that primary prevention of malignant melanoma is effective?
3. Is there any evidence that public and /or professional education and early detection campaigns are effective?
4. What evidence is there regarding the information value of leaflets ,booklets and other published media e.g. websites?
5. What is most effective way of achieving early diagnosis at GP/ Primary care level/non-specialist doctors/ PAMS?

B Diagnosis

6. Is there any evidence that early diagnosis makes a difference to outcome
7. Is there evidence of who is most accurate in clinical recognition of melanoma
8. Is the evidence of benefit from non-surgical diagnostic aids e.g. dermatoscopy, computer images
9. What is best form of surgery to make diagnosis of melanoma?
10. What type of minor surgery can be done in primary care ?
11. At what stage is referral appropriate and to which specialty?
12. Is there any evidence that classifying malignant melanoma into histogenetic types influences prognosis or provides useful information?
13. Is there any evidence for value of these or other pathological measures
    - Clark Level
    - Breslow thickness
    - Inflammatory reaction/ regression
    - Radial vs. vertical growth phase
    - Lymphatic/ vascular involvement
    - Measuring surgical clearance
14. Is there any evidence that specialist path reporting is of value in melanoma diagnosis?

C Surgical management

15. What are the best methods of removal of melanoma – width of excision, depth, other techniques e.g. laser?
16. Is there evidence for benefit with individual specialty or multi disciplinary management?
17. What is optimal timing of post excision biopsy surgery?
18. What is the role of SNB in staging?
19. What is evidence for benefit / morbidity with elective / therapeutic lymph node dissection?

D Further management and investigation

20. What is role of non-surgical techniques in treatment of stage 1-3 malignant melanoma?
21. At what point(s) should the patient be staged for secondary disease?
22. What is evidence for different staging methods?

23. What are most appropriate imaging methods to use? MRI vs. Pet vs. CT
24. Is there any evidence that routine follow up is effective? Who should do follow-
25. Is there a role for routine imaging or blood tests in patients being followed up for malignant melanoma?
26. What information is needed for patients and their families to understand and cope with the diagnosis, treatment and outcome?
27. What evidence is there regarding the impact of verbal information from health professionals at initial diagnosis re treatment/ outcomes. How can this be made more effective?
28. Is there evidence that support groups aid patients and relatives to cope?

E Management of metastatic disease

29. What is primary care role in melanoma chemotherapy ?
30. Is there evidence of benefit in chemo-, biochemo- or biotherapy of metastatic melanoma? Is level of morbidity known?
31. Is there any evidence that multidisciplinary care/ specialization influences outcomes?
32. How often should patients being treated for metastatic malignant melanoma be imaged to assess response?
33. What is the role of radiotherapy, isolated limb perfusion or other techniques in metastatic melanoma? (Benefit vs. morbidity)
34. Is there evidence for a requirement for specialist palliative care for malignant melanoma? How best should this be harnessed to rest of melanoma management?

Database coverage:

The following databases will be searched for all or part of the list of key questions:

- Cancerlit
- CINHAL (for some areas)
- Cochrane Library
- Embase
- HEED
- Medline
- NEED

An initial search will be carried out using a search filter to identify guidelines and systematic reviews. Coverage of subsequent searches will depend on the results of this search, and the extent to which results answer the key questions. All searches will cover the period from 1993 onwards for Systematic Reviews in the first instance.

In addition a number of Internet sites will be searched for Systematic Reviews and Existing Guidelines.

- Cancernet
- National Guidelines Clearinghouse
- OMNI/Biome
- Other Medical Search Engines

Search strategies will be based on the following Medline strategy:

1. Exp Melanoma/
2. Melanoma.tw.
3. 1 or 2
4. Exp mass screening/
5. Screen$.tw.

6. Exp Sensitivity and specificity/
7. Family history.tw.
8. Exp Genetic predisposition to disease/
9. Exp Family Health/
10. Early detection.tw.
11. Follow up.tw.
12. Exp Aftercare/
13. Early diagnosis.tw.
14. Exp Palliative care/
15. Exp referral and consultation/
16. Self referral.tw.
17. Referral.tw.
18. Exp diagnostic imaging/
19. MRI.tw.
20. PET.tw.
21. CT.tw.
22. Or/4-21
23. Exp primary prevention/
24. Exp health education/
25. Exp health promotion/
26. Exp patient education/
27. Exp self-help groups/
28. Support group$.tw.
29. Exp Physician-patient relations/
30. Leaflet$.tw.
31. Exp pamphlet/
32. Exp Internet/
33. Booklet$.tw.
34. Exp Mass media/
35. Exp patient care team/
36. Multidisciplinary care.tw.
37. Exp professional education/
38. Professional education.tw.
39. Or/23-38
40. Exp hematologic tests/
41. Blood test$.tw.
42. Dermatoscopy.tw.
43. Exp microscopy/
44. Histogen$.tw.
45. Breslow.tw.
46. Clark level.tw.
47. Inflammatory reaction.tw.
48. Inflammatory regression.tw.
49. Lymphatic involvement.tw.
50. Vascular involvement.tw.
51. Exp lasers/

52. Exp lymph node excision/
53. Lymph node dischapter.tw.
54. Sentinel node biopsy.tw.
55. Radial.tw.
56. Vertical.tw.
57. Surgical clearance.tw.
58. Exp neoplasm staging/
59. Or/40-58
60. Exp biopsy/
61. Punch biopsy.tw.
62. Excision.tw.
63. Exp Surgery/
64. Exp radiotherapy/
65. Exp perfusion, regional/
66. Isolated limb perfusion.tw.
67. Or/60-66
68. 22 or 39 or 59 or 67
69. 68 and 3

Set 69 will be combined with search filters for systematic reviews or other types of study as required.

Exclusions.

Search terms relating to drug or chemotherapy have been specifically excluded as it is expected that they would generate a large number of hits that are not relevant to the topic of this guideline.

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