SIGN 50

A guideline developer's handbook

Scottish Intercollegiate Guidelines Network

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First published 2008
Revised edition published 2019

Complying with international standards

SIGN seeks to ensure that its methodology complies with international standards as far as possible within our resources. Although there are now a number of published standards for guideline development methodology, SIGN regards AGREE II (Appraisal of Guidelines for Research and Evaluation; www.agreetrust.org) as the most evidence based of these. The sections in SIGN 50 that address each criterion are identified below.

		Section
Scope and purpose		
1	The overall objective(s) of the guideline should be specifically described.	8.2
2	The health question(s) covered by the guideline should be specifically described.	4.3
3	The population (patients, public, etc) to whom the guideline is meant to apply should be specifically described.	8.2
Stakeholder involvement		
4	The guideline development group should include individuals from all relevant professional groups.	2
5	The views and preferences of the target population (patients, public, etc.) should be sought.	11.2
6	The target users of the guideline should be clearly defined.	8.2
Rigour of development		
7	Systematic methods should be used to search for evidence.	4
8	The criteria for selecting the evidence should be clearly described.	4.3, 4.4
9	The strengths and limitations of the body of evidence are clearly described.	5
10	The methods for formulating the recommendations should be clearly described.	6
11	The health benefits, side effects and risks should be considered in formulating the recommendations.	6.2
12	There should be an explicit link between the recommendations and the supporting evidence.	6.2
13	The guideline should be externally reviewed by experts prior to publication.	7.1
14	A procedure for updating the guideline should be provided.	9
Clarity of presentation		
15	The recommendations should be specific and unambiguous.	6.3, 8.2
16	The different options for management of the condition or health issue should be clearly presented.	6.3, 8.2
17	Key recommendations should be easily identifiable.	6.5, 8.2
Applicability		
18	The guideline should describe facilitators and barriers to its application.	10
19	The guideline should provide advice and/or tools on how the recommendations can be put into practice.	10
20	The potential cost implications of applying the recommendations should be considered.	6.2
21	The guideline should present monitoring and/or auditing criteria.	8.2
Editorial independence		
22	The views of the funding body should not influence the content of the guideline.	1.6
23	Competing interests of guideline development group members should be recorded and addressed.	1.7

Contents

1 Introduction

1.1 Aim and structure of this manual

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. 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.

A secondary aim of this manual is to be transparent about the methods used to develop SIGN guidelines, and to 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.

1.1.1 Review and updating of this manual

This manual was issued in 2019. 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. Comments on either content or presentation of this document are welcome and should be sent to the SIGN Executive, Gyle Square, 1 South Gyle Crescent, Edinburgh, EH12 9EB, email: sign@sign.ac.uk

1.1.2 Summary of updates, by section

1	Introduction	Minor update
2	The guideline development group	Minor update
3	Selection of guideline topics	Updated
4	Systematic literature review	Minor update
7	Consultation and peer review	Minor update
8	Presentation and publication	Minor update
9	Updating published guidelines	New
10	Implementation	Minor update
11	Involving patients and the public	Minor update

1.2 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 NHSScotland, although SIGN retains editorial independence in relation to the guidelines it produces.

The role of guidelines has been described variously over the past two decades. A recent definition of clinical practice guidelines (CPGs) states "CPGs are able to enhance clinician and patient decision making by clearly describing and appraising the scientific evidence and reasoning (the likely benefits and harms) behind clinical recommendations, making them relevant to the individual patient encounter".[3]

The accepted criteria for validity of guidelines were first set out as the "essential elements of good guidelines" by the US Institute of Medicine in 1990.[4] 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."[4] These attributes have formed the basis of SIGN methodology.

The AGREE (Appraisal of Guidelines for Research and Evaluation) guideline appraisal instrument identifies criteria by which the quality of guideline development may be judged. The AGREE II criteria are reproduced in the introductory material to this manual, with links to those manual sections that explain how SIGN addresses each criterion. The full appraisal instrument can be downloaded from the AGREE website: www.agreetrust.org

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 NHSScotland.

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 for healthcare professionals in their practice. However, there is a role for national facilitation of local guideline implementation activities, and this is discussed in section 10.

1.4 Medico-legal implications of SIGN guidelines

Although there has been ongoing discussion about the legal status of clinical guidelines, 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.

To clarify the legal position, all SIGN guidelines carry the following statement of intent:

> This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results.

> The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at through a process of shared decision making with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be documented in the patient's medical records at the time the relevant decision is taken.

1.5 Organisation of the Scottish Intercollegiate Guidelines Network

Since its establishment in 1993, SIGN has been a collaborative initiative; a network of clinicians and other healthcare professionals, including all the medical specialties, nursing, pharmacy, dentistry, allied health professions, public partners and Healthcare Improvement Scotland (HIS).

The overall structure of the organisation is shown in Figure 1-1.

Figure 1-1: The structure of SIGN
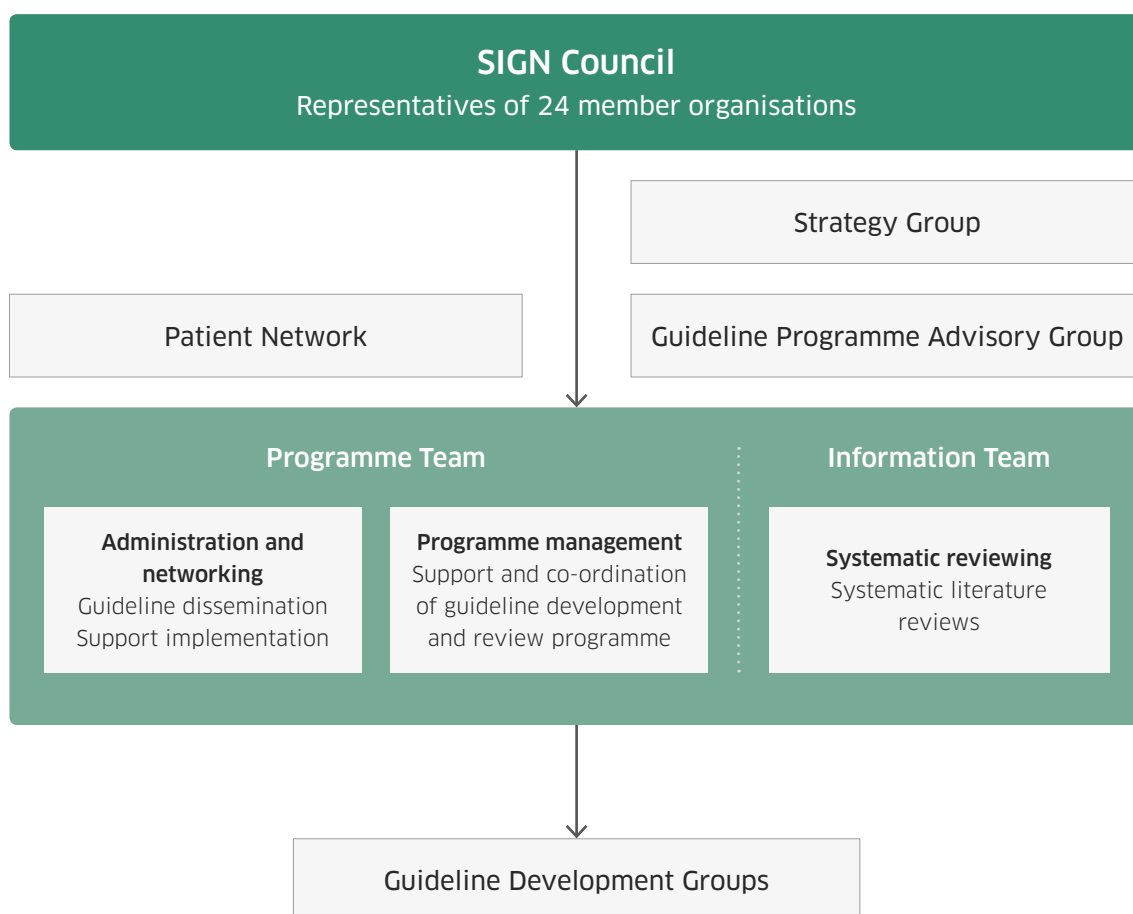
1.5.1 SIGN Council

SIGN Council is the policymaking body for SIGN with overall responsibility for methodology and editorial policy. Although SIGN forms part of the Evidence Directorate at HIS, SIGN is editorially independent from HIS and the Scottish Government which ultimately funds HIS.

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. Public partners are identified from an open call for interested individuals.

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 and all provide input into the selection of topics for guideline development and the composition of guideline development groups. The current membership of SIGN Council is noted on the SIGN website.

1.5.2 SIGN Executive

The SIGN Executive is a Programme Team working closely with the Knowledge and Information Team. Together 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. Expert input is also provided by Health Service Researchers and Health Economists. All staff are employees of Healthcare Improvement Scotland.

1.6 Funding

Core funding from Healthcare Improvement Scotland supports the SIGN Executive, expenses associated with individual guideline development projects (meeting and literature costs) and the costs of printing and distributing published SIGN guidelines.

Members of SIGN guideline development groups do not receive any payment for their participation, although independent practitioners are entitled to claim locum payments and travel expenses. Patient representatives can also claim travel, subsistence, child care/carer expenses and any other reasonable out of pocket 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, under an agreement with the Scottish Government Health and Social Care Directorate.

1.7 Influence of financial and other interests

It has been recognised that financial interests in, or close working relationships with, pharmaceutical companies may have an influence on the interpretation of evidence from clinical studies.

It is not possible to completely eliminate any possible bias from this source, nor even to quantify the degree of bias with any certainty. SIGN requires that all those involved in the work of guideline development should declare all financial and non-financial interests, whether direct or indirect, annually for as long as they are actively working with the organisation.

This includes all of the following:

- SIGN Council and subcommittee members and deputies
- SIGN Executive staff
- speakers at SIGN events
- guideline development group members
- peer reviewers
- all who submit proposals to SIGN.

By being explicit about the influences to which contributors are subjected, SIGN acknowledges the risk of bias and makes it possible for guideline users or reviewers to assess for themselves how likely it is that the conclusions and guideline recommendations are influenced by a biased interpretation of the evidence.

Signed copies are retained by the SIGN Executive and are available on the SIGN website.

Full details of the declarations of interest policy are available on the SIGN website.

1.8 References

1 Scottish Office. Clinical Resources and Audit Group. Clinical guidelines: report by a working group. Edinburgh: Scottish Office; 1993.

2 Petrie J, Grimshaw J, Bryson A. The Scottish Intercollegiate Guidelines Network Initiative: getting validated guidelines into local practice. Health Bull (Edin) 1995;53:354-8.

3 Field M, Lohr K. Institute of Medicine Committee to Advise the Public Health Service on Clinical Practice Guidelines. Clinical practice guidelines: directions for a new program. Washington (DC): National Academy Press; 1990.

4 Institute of Medicine. Standards for developing trustworthy clinical practice guidelines (CPGs). Washington: IoM; 2011.

2 The guideline development group

2.1 Composition of the guideline development group

There is international agreement that guideline development groups should be multidisciplinary in their composition, with representation from all relevant professional groups, and participation of patients, carers and appropriate voluntary organisations.[1,2] This facilitates ownership of both the guideline development process and the resulting recommendations.

At the outset of a new guideline development project the SIGN Executive, in discussion with all relevant bodies, aims to bring together a group which will fulfil the following parameters:

- multidisciplinary, with all relevant clinical specialties represented alongside lay input
- relevant to current care practice, with a balance between members actively involved in day to day delivery of health care with topic experts and academics where appropriate. Ideally membership should represent the range of care or treatment settings related to the clinical condition (eg primary, secondary and tertiary care centres)
- encompasses the range of skills and expertise required for the specific project. Specialists other than clinicians may be recruited when necessary, for example health economists *(see section 6.2.6)*, social workers
- geographically representative, including participants from across Scotland both from urban centres and rural locations.

Meeting this aim requires an iterative process of seeking nominations, issuing invitations and refining membership depending on the interests and availability of individuals whose participation is sought.

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 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".[3] 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.[4,5] A clear relationship between the perceived status of a group member and their level of contribution to group discussions was identified. Although their areas of expertise will vary, members of the guideline development group have equal status on the group and are supported by the Chair and SIGN Programme Manager to participate.

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 a manageable group size for effective decision making. An example of the mix of skills present in a typical guideline group is shown in Figure 2-1.

2.2 Responsibilities of guideline development group members

2.2.1 Guideline group Chair

The role of the guideline development group Chair is crucial to ensure that the group functions effectively and achieves its aims.[6] Chairs of guideline development groups must be sensitive to pre-existing interprofessional tensions and hierarchies and ensure that all members of the group feel able to contribute fully to the guideline development process.

A guideline development group Chair needs to be 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.[4,5,7]

Figure 2-1: Membership of SIGN 127: Management of perinatal mood disorders guideline development group

Chair:
Consultant Perinatal Psychiatrist, Glasgow

Group members:
Consultant Liaison Psychiatrist, Kilmarnock
Consultant in Community Psychiatry, Stirling
Consultant Perinatal Psychiatrist, Livingston
Consultant Psychiatrist, Aberdeen
Consultant in Obstetrics and Gynaecology, Dundee
General Practitioner, Dundee
Lay Representative, Edinburgh
Manager, Postnatal Depression Voluntary Service, Edinburgh
Mental Health Nurse Practitioner, Larbert
Midwife with Specialist Interest in Perinatal Mental Health, Perth
Nurse Consultant, Perinatal Mental Health, Glasgow
Public Health Nurse, Bothwell
Quality and Audit Development Advisor, Royal College of Midwives, London
Senior Lecturer, Edinburgh
Senior Worker, Postnatal Depression Services, Edinburgh
Service Manager, Primary Care Mental Health Team, Glasgow
Senior Pharmacist, Edinburgh
Pharmacist, Inverness
Evidence and Information Scientist, SIGN
Programme Manager, SIGN

2.2.2 SIGN team

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.

The SIGN team supporting each guideline development must ensure that clinical knowledge and expertise is appropriately applied to the interpretation of the evidence base and that all group members have the opportunity to actively contribute when the drafting of guideline recommendations is being undertaken.

2.2.3 Guideline development group members

Guideline development group members in turn must make a full commitment to the group and the tasks involved in guideline development, and are 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, whilst maintaining confidentiality around the content of discussions undertaken within the group.

The approximate life span of each guideline development group varies depending on whether it is a new project (around 29 months), an update (around 15 months) or a minor revision (3–6 months). For a full guideline project, groups meet on average once every two to three months, although subgroups may meet more frequently.

2.3 References

1 Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting and evaluation in health care. Cmaj 2010;182(18):E839-42.

2 Qaseem A, Forland F, Macbeth F, Ollenschlager G, Phillips S, van der Wees P. Guidelines International Network: toward international standards for clinical practice guidelines. Ann Intern Med 2012;156(7):525-31.

3 Grimshaw J, Eccles M, Russell I. Developing clinically valid practice guidelines. J Eval Clin Pract 1995;1(1):37-48.

4 Pagliari C, Grimshaw J. Impact of group structure and process on multidisciplinary evidence-based guideline development: an observational study. J Eval Clin Pract 2002;8(2):145-53.

5 Pagliari C, Grimshaw J, Eccles M. The potential influence of small group processes on guideline development. J Eval Clin Pract 2001;7(2):165-73.

6 Shekelle PG, Woolf SH, Eccles M, Grimshaw J. Clinical guidelines: developing guidelines. BMJ 1999;318(7183):593-6.

7 Atkins L, Smith JA, Kelly MP, Michie S. The process of developing evidence-based guidance in medicine and public health: a qualitative study of views from the inside. Implement Sci 2013;8:101.

3   Selection of guideline topics

3.1   Proposing a topic

Producing evidence-based clinical practice guidelines is a time and resource intensive process. To make best use of these resources, 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.[1,2] There must also be robust evidence of effective practice on which to base guideline recommendations.

Developing a guideline with a broad scope is not only time consuming and costly but also requires considerable specialist input. The SIGN proposal form, which was adapted and developed from a published topic proposal template,[3] focuses on the important but challenging areas where uncertainty exists or the evidence requires careful evaluation.

Any group or individual may propose a guideline topic to SIGN. The proposal form is available from the SIGN Executive or can be downloaded from the SIGN website *(see section 3.1.1)*.

When submitting a proposal form, the following information must be included on the proposal form:

- Details of the group(s) or institution(s) supporting the proposal.
- A brief background to the clinical topic which will be addressed by the proposed guideline, including the burden of the condition and areas of uncertainty in management of the condition.
- Evidence of variation in practice in the management of the condition, and in health outcomes.
- An indication of the benefits likely to arise from the development and successful implementation of the guideline. This should include the potential to improve current clinical practice and important health outcomes, as well as the impact on resources.
- Key areas of concern for patients, carers and/or the organisations that represent them.
- A definition of the patient group to which the guideline will apply. This should include consideration of whether any specific social or minority groups are likely to be particularly affected, either favourably or adversely, by changes in healthcare provision in the topic area under consideration.
- 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.
- An indication of the healthcare professionals who could potentially be involved in developing the guideline.
- Details of any existing guidelines or systematic reviews in the field.
- Links with existing policies and initiatives that could aid implementation.
- A declaration of interests.

3.1.1   Proposals from patients, carers, voluntary organisations and members of the public

A topic proposal form designed for patients, carers, voluntary organisations and members of the public can be downloaded from the patient involvement section of the SIGN website. Proposers are supported by the SIGN Patient Involvement Advisor and SIGN Public Partners to complete the application, and healthcare professionals are sought to give a clinical perspective on the proposal. The completed proposals are processed in the same way as the standard application.

The procedure for application and selection of new topics is illustrated in Figure 3-1.

3.2 Topic selection process

3.2.1 Screening topics

When a group or individual proposes a guideline topic to SIGN their suggestion is discussed initially by the SIGN Senior Management Team (SMT). SMT uses the following criteria to assess the topic:

- Is this an appropriate clinical topic for a SIGN guideline? (considering whether the topic is clinical, its breadth and the need for the guideline as identified in the proposal)
- Is there a suitable alternative product which would address this topic? (considering whether other Healthcare Improvement Scotland products could better address the topic)
- Has this topic been considered before and rejected? (reasons for rejection would be reviewed and assessed for current applicability).

If the proposed topic meets the selection criteria the proposal moves onto the next stage of the process.

Topic proposals under consideration can be found on the SIGN website.

3.2.2 Scoping topics

As part of the preparatory work done by SIGN, 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.

The scoping search aims to identify guidelines, Health Technology Assessments (HTAs), Cochrane reviews and other systematic reviews that exist in the topic of interest by searching a number of different sources.

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.

3.2.3 Selecting and prioritising topics

SIGN has limited resources for guideline development. As a result it is important to identify and prioritise topics which best meet the needs of NHSScotland and ensure effective use of those resources.

For information on the current SIGN programme, see the SIGN website.

The Guideline Programme Advisory Group (GPAG) is a subgroup of SIGN Council and oversees development of proposals for new guidelines or for reviewing existing guidelines. When considering topics, GPAG also takes into account the work programmes of other parts of Healthcare Improvement Scotland, for example, development of standards and improvement programmes, as well as other guideline developers, in particular NICE (the National Institute for Health and Care Excellence) in England and Wales, to avoid potential duplication of effort.

GPAG meets three times a year and considers new proposals on a rolling basis. Proposers are invited to present their proposals to GPAG.

GPAG uses a proforma to screen proposals for their suitability as a guideline topic. The proforma allows GPAG to identify the extent to which the proposal fulfils the criteria listed in section 3.2.4, make an assessment of the extent of the evidence on which the guideline could be based and consider whether the benefits that are likely to accrue from successful implementation of the guideline recommendations would outweigh the efforts required to develop it.

Figure 3-1: Selection of new topics for SIGN guideline development
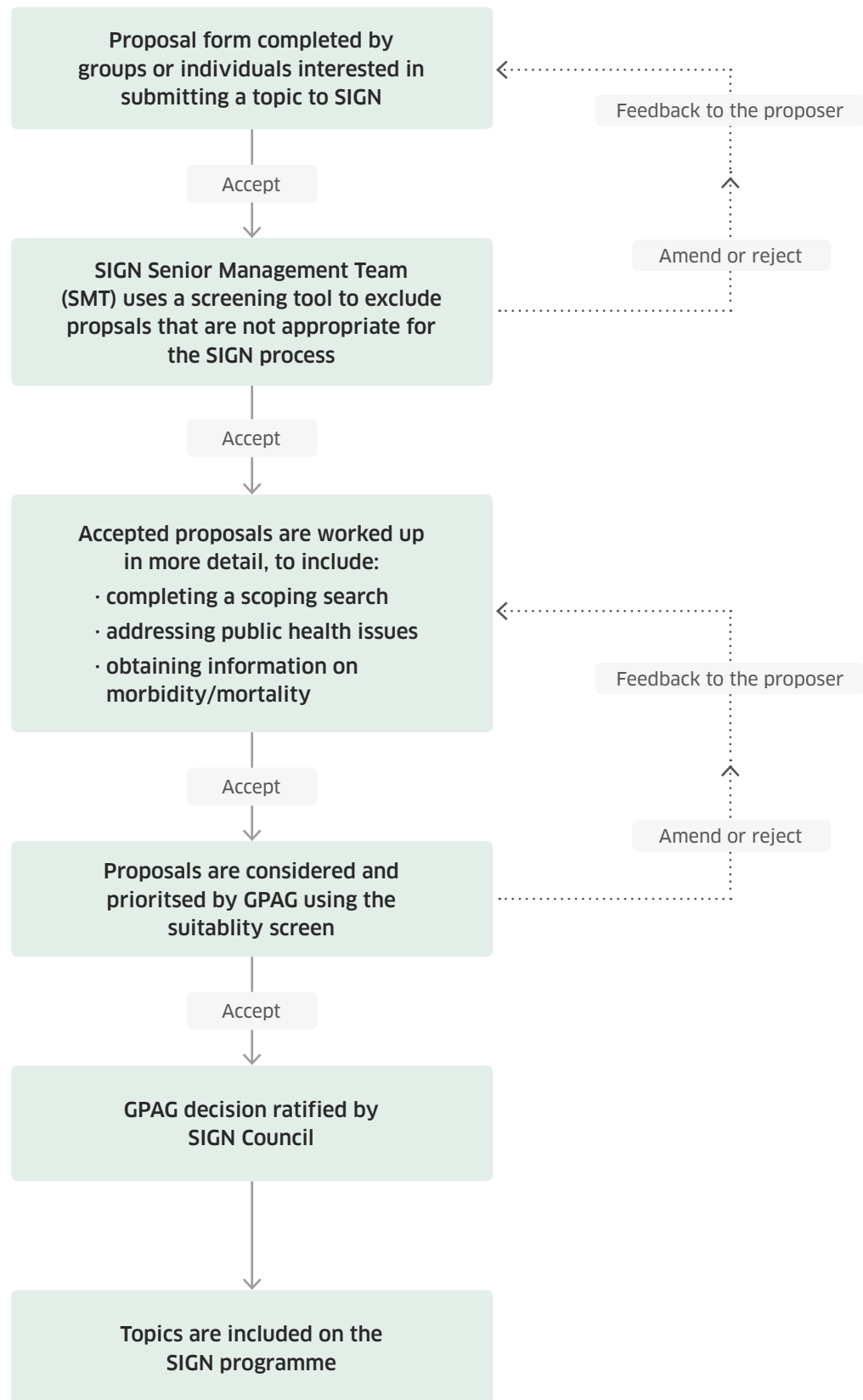
3.2.4 Criteria for selection of topics

There is a lack of evidence to guide choice of criteria and methods for prioritising topics, although the criteria used by guideline development organisations are broadly similar.[2] 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 health outcomes, and the potential to improve outcome. The following criteria are considered by SIGN in selecting and prioritising topics for guideline development:

• clinical priority areas for NHSScotland
• 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
• the perceived need for the guideline, as indicated by a network of relevant stakeholders.

3.3 Guidelines in need of update

In addition to proposals for new guideline topics, GPAG also considers guidelines that are deemed to be in need of update, either through:

• scheduled scoping three years after publication *(see section 9.1)*, or
• a request from a group or individual to make a change to a published guideline *(see section 9.3)*.

3.3.1 Scheduled scoping

Once GPAG has reviewed the summary of the 3-year scope and consultation and agrees with a recommendation to update a guideline, it is accepted onto the programme without the need to be ratified by SIGN Council. This allows updates to take place in a timely way and keeps the guideline current.

3.3.2 Requests for a change to a published guideline

To allow SIGN to be reactive to the needs of healthcare professionals in NHSScotland, small changes to published guidelines are agreed by GPAG rather than SIGN Council and accepted onto the programme according to current capacity and workload.

If scoping suggests that the request does not meet the criteria for a small change, GPAG will consider whether the body of new evidence warrants a full review. If this is the case, GPAG will request a full proposal from the proposer which is then processed as described in section 3.2.

3.4 Accepting topics onto the SIGN work programme

Using the information from new topic proposals and taking into account SIGN's work capacity, GPAG makes recommendations to SIGN Council about which proposals should be accepted onto the work programme and which should be rejected.

SIGN Council is responsible for approving guideline topic proposals that have been recommended by GPAG as suitable candidates for the SIGN guideline development programme. Council is presented with the guideline proposals and the proformas summarising the suitability screening results and the subsequent discussions of the Guideline Programme Advisory Group before making a decision on which topics should be included in the SIGN programme.

3.5   References

1   Oxman AD, Schunemann HJ, Fretheim A. Improving the use of research evidence in guideline development: 2. Priority setting. Health Res Policy Syst 2006;4:14.

2   Schunemann HJ, Wiercioch W, Etxeandia I, Falavigna M, Santesso N, Mustafa R, et al. Guidelines 2.0: systematic development of a comprehensive checklist for a successful guideline enterprise. CMAJ 2014;186(3):E123-42.

3   Estonian Handbook for Guidelines Development. Estonia: World Health Organization; 2011.

4 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.[1,2] SIGN guidelines are therefore produced using a considered judgement process informed by systematic reviews of 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".[3]

The SIGN approach is to carry out a systematic review of the evidence for each key question (KQ) to be addressed in the guideline. Evidence tables are produced as supporting documents and the essential elements of systematic review are met in that the literature is:

*   identified according to an explicit search strategy
*   selected according to defined inclusion and exclusion criteria
*   evaluated against consistent methodological standards.

All stages of the review process are thoroughly documented *(see below)*.

The benefits of the SIGN approach derive from the close involvement of guideline development group members with the synthesis of the evidence base, allowing them to apply their 'considered judgment' when deriving recommendations *(see sections 5 and 6)*, and from encouraging a sense of ownership of the guideline amongst all those involved in the process.

4.1 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 methods 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. Whereas other literature searches carried out for the guideline attempt to answer focused key questions by filtering out the volume of irrelevant evidence, the patient search is deliberately as broad and inclusive as possible. It focuses entirely on the health condition that is being considered, and makes no attempt to concentrate on any social group or class. As the reviewer develops themes from the literature, they will pay particular attention to anything that suggests there are population groups that are disadvantaged and ensure their interests are specifically considered by the guideline development group. The results of this search are presented to the guideline development group to inform the setting of key questions. Further details can be found in section 11.

The use of this literature search is discussed in more detail in SIGN 100: A handbook for patient and carer representatives.[4]

4.2 Using existing guidelines

As more good-quality guidelines are being produced by other agencies, SIGN is making use of the evidence base underlying guidelines produced elsewhere for use in NHSScotland.

The guidelines identified in the scoping search carried out for the guideline proposal will be presented to an early meeting of the guideline development group to allow it to consider the context of evidence-based guideline recommendations in the relevant area.

Guidelines are evaluated using the AGREE II instrument and must be shown to have followed an acceptable methodology before they can be considered for use by SIGN guideline developers.

There is a range of possible ways in which published guidelines can be used in relation to SIGN guidelines.

- There is an existing guideline that addresses some of the SIGN key questions, or there is a well-produced guideline that is now out of date. If the guideline development group can access the original evidence tables used to develop that guideline, these can be updated and reviewed before being used to form the basis for new recommendations. For example, NICE evidence tables were used by the group developing SIGN 115 on management of obesity. In this case, the evidence is rated according to the scheme used by the source guideline.
- There is an existing guideline that addresses some of the questions in the proposed guideline, but it is not possible to obtain the evidence tables. In this case the guideline can be included in the body of evidence, as low quality evidence (all guidelines are rated at level 4; *see section 5*) supporting new recommendations
- There is an existing guideline that addresses some aspect of the guideline topic and which can be referred to as an alternative. For example, SIGN 111 on management of hip fracture in older people refers to British Orthopaedic Society guidelines for secondary prevention of fragility fractures rather than tackling the topic anew.
- There are existing guidelines addressing a very specialist area where expertise or resources are limited, and the specialist topic has general applicability. For example SIGN 88 on management of bacterial urinary tract infections references prescribing guidance produced by the Health Protection Agency and the Infectious Diseases Society of America.

In all cases the guideline development group must decide on the best way forward that will address clinical need while avoiding duplication and waste of resources.

4.3 Defining key questions

SIGN guideline development groups break down the guideline remit into a series of structured key questions using the **PICO** format as shown below.[5,6]

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 should be defined including age group and gender.

Consideration should also be given to issues of equity, ensuring that any particular subgroup of the patient population that has particular needs in relation to the topic under review has those needs specifically addressed. This should take account not just of the needs of that population, but any evidence of differences in effectiveness of interventions between equality groups.

It is worth emphasising here that, where clinically important, questions should be addressed even if it is not thought there will be any good evidence. If there is in fact no good evidence, highlighting it as an area for research allows guideline users to appreciate important gaps in the evidence base and may provide priorities for future research. Dealing with uncertainties of this kind will be addressed in the section of this manual covering the later stages of the considered judgment process *(see section 6)*.

The **interventions** (which in this context includes diagnostic tests, risk factors, risk exposure or treatments with medical devices or drugs) 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** may include placebo/no treatment, and comparison with other therapies. It should be borne in mind that, where there is an existing treatment, comparison with placebo or no treatment is not ethically acceptable.

Outcomes must be clearly specified, ideally at the stage of setting the key questions but certainly before making judgments about the quality of evidence. 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 expected to influence decisions about healthcare.

Critical outcomes are those on which the overall quality of evidence for a KQ is based. These are the key outcomes on which a healthcare professional would be expected to base a treatment decision. In osteoporosis, for example, prevention of fracture is likely to be seen as a critical outcome. The number of critical outcomes should be kept low, preferably less than seven per KQ.

Important outcomes are those that a healthcare professional is likely to take into account when making treatment decisions, but which are not the ultimate aim of the intervention under consideration. Often, these will be surrogates for the critical outcome. In the osteoporosis example, improved bone mineral density may be seen as an important outcome as it is a widely accepted surrogate for reduced fracture risk.

In some areas there is a large number of reported outcomes. Some of these are likely to be peripheral to treatment decisions and can be largely ignored in the process of developing guideline recommendations.

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). **Patient important outcomes** should be explicitly considered along with more narrowly defined clinically important outcomes. It is particularly important to include any potential harm associated with the intervention under review so that a balanced view can be taken at the considered judgment stage.

As part of the question setting process, a set of inclusion and exclusion criteria should be drawn up and saved as part of the record of the review. This will provide guidance at a later stage when studies are being selected for review.

Inclusion criteria will include definition of the topic and may include such factors as duration of therapy, drug dosage, and frequency of treatment. Other factors include any geographic or language limits, the types of trials that will be accepted, and date range to be covered. Any equality groups that are expected to have specific needs in relation to the question being addressed should be specified.

Exclusion criteria are likely to be more variable. They are, however, essential in that they help sift out irrelevant studies from the (often very large) initial search result.

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. While a large number of key questions allows the guideline to have a more comprehensive scope, or to address issues in more detail, it will incur a very high workload for the developers. Care must be taken to ensure this is kept within limits that will allow the guideline to be completed within the agreed timescale. Keeping the number of questions to a minimum is particularly important in areas that are particularly rich in literature, as each question will require review of a large number of studies.

Deciding the key questions is entirely the responsibility of the guideline development group which must apply its knowledge and experience to ensuring the questions address the key issues in the area to be covered by the guideline, supported by SIGN and Healthcare Improvement Scotland staff. The Evidence and Information Scientist working with the group will provide guidance on question formatting, and ensure they are likely to produce useable results. They will also work with the Patient and Public Involvement Adviser to ensure that the key questions address appropriately the issues identified through the patient consultation exercise.[4]

Once the questions have been agreed they form the basis of the literature searches to be undertaken by an Evidence and Information Scientist. These searches will focus on the patients, interventions, and (sometimes) comparison parts of the question. Additional references provided by group members or other interested parties may be included for consideration in the evidence base but must be evaluated on the same basis as all other studies and must still meet the same inclusion criteria *(see section 4.5)*.

4.4 Identifying and selecting the evidence

The literature search must focus on the best evidence available to address each key question. SIGN uses a set of standard search filters that identify:

- systematic reviews (including meta-analyses)
- randomised controlled trials
- observational studies
- diagnostic studies
- economic studies.

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 following sources:

- Cochrane Library
    - for reviews: the Cochrane Library
    - for RCTs: Cochrane Central Register of Controlled Trials (CENTRAL)
- Medline
- Embase
- Internet sites relevant to the topic (including patient organisations)
- WHO International Clinical Trials Registry Platform.

Specialised databases such as CINAHL, ERIC or PsycINFO will only be searched for questions specific to their area of coverage.

SIGN does not undertake hand searching of key journals as part of the literature review.

The period that the literature search covers will depend on the nature of the clinical topic under consideration, and will be discussed with the guideline group. For a rapidly developing field a five-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 available to members of guideline development groups to review.

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 publication of the guideline.

Before any studies are acquired for evaluation, the search output is sifted to eliminate irrelevant material. Results are sifted in two stages. A preliminary sift of each search result is carried out by an Evidence and Information Scientist, normally by the individual that carried out the search. Studies that are clearly not relevant to the key questions or not the type of study being considered at this stage (eg observational studies when the focus is on controlled trials) are eliminated. Abstracts of remaining studies are then examined and any that clearly do not meet the agreed inclusion and exclusion criteria are also eliminated at this stage. In cases of doubt, the Evidence and Information Scientist will leave abstracts in the output file at this stage.

A final sift is carried out by at least one member of the guideline development group, who will apply clinical judgment to reject any studies that do not meet the pre-agreed criteria. These will include clinical criteria, but may also consider issues such as size of the study, relevance to practice in the UK, etc. Only when all stages of search result sifting have been completed will the remaining studies be acquired for evaluation.

4.5   Evaluating the literature

Once studies have been selected as potential sources of evidence, the methodology used in each study is assessed to ensure its validity.

The methodological assessment is based on a number of criteria that focus on those aspects of the study design that research has shown to have a significant effect on the risk of bias in the results reported and conclusions drawn. These criteria differ between study types, and a range of checklists is used to bring a degree of consistency to the assessment process. The SIGN checklist for systematic reviews is based on the AMSTAR tool,[7,8] while that for RCTs is based on an internal project carried out in 1997.[9] Checklists for observational studies are based on the MERGE (Method for Evaluating Research and Guideline Evidence) checklists developed by the New South Wales Department of Health,[10] which have been subjected to wide consultation and evaluation. The checklist for diagnostic accuracy studies is based on the QUADAS programme.[11]

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 available on the SIGN website.

The assessment process inevitably involves a degree of subjectivity. The extent to which a study meets a particular criterion, for example 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 and, inevitably, the judgment of the individual reviewers.

The methodology of studies selected for full consideration will be evaluated by at least two people with experience in carrying out such appraisals. Normally this will be the Evidence and Information Scientists but other Healthcare Improvement Scotland staff and guideline group members may be involved. The subjective nature of critical appraisal makes double checking essential to minimise the chance of bias and to ensure consistency. Where reviewers cannot agree on the overall quality of a study the SIGN Programme Manager will arbitrate. This only applies to studies being actively considered as evidence. There is no need to seek agreement for studies that are not to be included. Only studies reviewed using this process can be used as evidence to support a recommendation in the guideline.

4.6 References

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5   Assessing the quality of evidence

5.1   Introduction

The previous section of this handbook sets out how individual studies are identified and assessed for methodological rigour. The next step in the guideline development process is to examine the body of evidence associated with each specific key question.

One of the factors likely to influence a practitioner's decision to implement a recommendation is the degree of confidence that they have in it; that is how certain they are that following the recommendation will produce the expected improvement in outcome for their patients. Not only does this certainty relate to the degree of confidence in the size of effect of an intervention in relation to specific important outcomes, but it also encompasses other issues such as patient preferences and the availability of resources to support introduction of a new intervention. For this reason the guideline development group has to consider both the overall quality of the supporting evidence and the other factors that might influence the strength of the recommendation.

If a reviewer evaluates a guideline using the AGREE instrument they will expect both of these aspects to be clearly addressed. These aspects also need to be addressed properly to comply with the standards set out by the Institute of Medicine.[1]

5.2   Presenting the evidence

This section of the manual considers the practical issues involved in presenting the evidence to the guideline development group. It relates to the SIGN solution, although there are a number of ways of doing this.[3]

5.2.1   Existing systematic review

It is a fundamental principle that each recommendation should be based on a systematic review of the literature. For many questions systematic reviews will already exist, and in these cases the guideline development groups are provided with a complete systematic review plus an evidence table summarising more recent studies. Where there are multiple existing reviews, an evidence table summarising the findings of all existing reviews, is provided.

In these circumstances the quality of the studies included in the systematic review has already been established by the systematic reviewers, and, the guideline development group can move on to consider its conclusions *(see section 6)*.

Consideration of the evidence in relation to different outcomes is considerably simplified if a summary of findings (SoF) table is available.[4] Any SoF produced as part of a systematic review should be included in the material submitted to the guideline group. If they are not included in a systematic review, the authors may be contacted to see if SoF tables are available.

5.2.2   Internally conducted reviews

A completed evidence table based on an internally conducted systematic review of the literature will be provided for all questions. These will either update existing reviews or provide a review of all relevant literature. Each evidence table will include methodological evaluation of and data extracted from each individual study relevant to a specific key question. Study results will be reported on a per outcome basis wherever possible.

An example of a completed evidence table records appears in Figure 5-1.

5.3 Considering the quality of evidence

SIGN is committed to following the principles of the GRADE methodology which complies with the standards covered in section 5.1. The process for assessing the overall quality of evidence using GRADE (Grading of Recommendations, Assessment, Development and Evaluations), is described in the Journal of Clinical Epidemiology (JCE) series on GRADE.[2]

From this point in the process the guideline development group is looking at a body of evidence for each question; the collection of studies that help answer the question. This raises a number of issues beyond the methodological quality of the individual studies.

The evaluation of a body of evidence should be completed before deciding what to recommend in the guideline. The focus here is on the quality of the available evidence, not what conclusions may be drawn from it.[2]

The evidence identified in a systematic review of the published literature is first summarised in an evidence table *(see Figure 5-1)* The features described in the following sections are then reviewed and commented on in part A of the considered judgment form *(see Figure 5-2)*.

In summary, at the end of this stage of the process, the guideline development group will have agreed on the overall quality of the evidence for all critical outcomes for the key questions being addressed.

5.3.1 How reliable are the studies in the body of evidence?

The first issue to be considered is the risk of bias in the studies that make up the body of evidence related to a particular question. The methods used for the assessment of risk of bias in individual studies are outlined in section 4 of this manual.

5.3.2 Are the studies consistent in their findings?

Also known as heterogeneity, this aspect looks at all the studies relating to a particular outcome to see if they all point in the same direction (ie all support or reject the course of action being considered). Sometimes it is very clear that evidence is consistent, but at other times this is far from the case. Sometimes there are clinical reasons to explain this and these will be discussed by the guideline development group. The issue that is of concern here, however, is statistical heterogeneity.

Statistical heterogeneity can only be established through meta-analysis. Often these analyses will provide statistics to indicate the degree of heterogeneity The most commonly quoted is the χ^2 (chi squared) statistic.[6] If this is below 40, inconsistency is not likely to be a problem. Over 90 and it is a very serious issue for consideration. In between these values, you need to consider possible explanations for the variation in results and how they might influence the size of effect in the Scottish population.[7]

In the context of SIGN guideline development, such calculations will normally only be available through published meta-analyses.

5.3.3 Are the studies relevant to our target population?

This is often referred to as directness of evidence, but can also be referred to as applicability or external validity. In this context it relates to how directly applicable the evidence is to NHSScotland.[8] Guidelines should indicate where the studies used as evidence were conducted, if not by listing all the countries involved, at least indicating which parts of the world the evidence came from. For example:

"The main work on this topic has been carried out in Europe and the UK."

"Most of the evidence in this area comes from the US-based Framingham study".

Studies carried out in the UK are likely to be directly applicable to the target population for a SIGN guideline. For studies carried out elsewhere some thought has to be given to what factors, if any, might influence relevance of the results in our target population.[9] Studies of diagnosis of heart disease, for example, may be seen as directly relevant no matter where they are conducted as the underlying biology of the condition should be the same. If the studies relate to the risk of heart disease however, applicability may be more problematic.

Examples of factors that can influence the applicability of evidence include:

- variations in baseline risk
- differences in genetic makeup of the population
- differences in culture or lifestyle between populations
- differences in how care is delivered, or availability of technologies or resources
- different outcomes measured in studies to those that the guideline development group see as being of critical importance
- differences in how the intervention(s) studied is/are administered to patients in Scotland
- use of indirect (surrogate) outcomes
- indirect rather than direct comparison of outcomes.

It is worth highlighting that the last two points above relate to different forms of indirectness. Surrogate outcomes reflect a situation where it is difficult or impossible to accurately measure the effect of an intervention on the final patient important outcome. In that case an alternative outcome that can be shown to be related to the important outcome may be measured instead. An example of this is in osteoporosis where studies often report the impact of interventions on bone mineral density, when in fact the outcome of interest is the degree of fracture risk. Increased bone density is associated with a reduced risk of fracture, hence its use as a measure of treatment effect.

The second issue arises where there are no head-to-head comparisons of different options for treatment. It may be, for example, that there is no comparison of A versus B, but there are trials of A versus C and B versus C. In this situation evidence may be addressed through a process referred to variously as indirect comparison reviews, mixed treatment comparisons, or network meta-analyses.[10] These analyses are always indirect, and given their nature are unlikely to give a precise result.

Situations where there is a mix of direct and indirect evidence are the most difficult to judge. The guideline development group has to look at the body of evidence and see where most of the data comes from. If it is clearly from direct evidence there should not be a problem.

In some cases it may be that the group has to consider different subpopulations within the overall body of evidence. People of Asian origin living in the UK, for example, are known to have an increased risk of Type 2 diabetes at an earlier age than the white population. Any evidence in this area would need to take account of the risk difference when considering whether or not it was direct. It may be preferable to ask the question independently for different groups where situations like this are suspected to see if there is direct evidence for any specific group of patients.

5.3.4 How sure are we that estimates of the size of effect are reliable?

This is often referred to as precision of the estimate of effect. It relates to how confident the user can be in any estimate of the size of the effect to be expected from an intervention or exposure. Precision around an effect estimate is usually presented as 95% confidence intervals.[11]

Trial results are commonly reported in terms of relative effect or relative risk. Wherever possible, estimates of absolute risk or benefit should also be used along with the appropriate confidence intervals.

5.3.5 Are we sure we have all the relevant evidence?

This question relates to publication bias, where only some study results (usually the positive ones) have been reported. Unfortunately it is not usually possible to establish the presence or absence of publication bias, and reviewers can only indicate if it is likely or unlikely.

Published reviews should include an assessment by the authors of the likelihood of publication bias.

For internal reviews carried out by SIGN staff, it may be assumed that the literature searches coupled with the knowledge of the guideline development group members have covered the majority of the available literature. Some papers may have been missed, but there will not be any systematic bias in the search results. SIGN searches do not cover unpublished material, and it is a matter of judgment for the guideline development group to decide if there is likely to be a substantial body of unpublished literature that might influence the results.

Note: Data and comments in the following figures have been adapted from documents used in a published guideline. They have, however, been amended for illustrative purposes and should not be taken as accurate and complete summaries of the evidence in this area.

Figure 5-1: Example pages from an evidence table

Guideline topic: Breast cancer	
Question:	KQ03: In patients with BC (men, premenopausal women, postmenopausal women) with an inoperable tumour/unsuitable for breast-conserving surgery, what is the evidence that neoadjuvant chemotherapy is effective and what is the optimal regimen?

Cuppone, F, Bria, E, Carlini, P, Milella, M, Felici, A, Sperduti, I, et al.
Taxanes as primary chemotherapy for early breast cancer: Meta-analysis of randomized trials (*Cancer: 2008 113 238-46*)

Study type / evidence level	Study details/limitations	Patient characteristics	Interventions
Meta-analysis/ RCT **Evidence level: +**	*Countries:* *Centres:* *Setting:* *Funding sources:* Not stated *Dropout rates:* *Study limitations:*	*Total no. patients:* 2,455 *Patient characteristics:* Operable breast cancer stage II and III – otherwise not well defined *Inclusion criteria:* Searched till October 2007 *Exclusion criteria:*	Combination taxane and anthrycycline
Notes:	The primary endpoint is pCR. The included trials use different definitions of pCR (unlisted). A similar criticism exists for other endpoints such as response rate although breast-conservation rate should be robust. Thorough search of the literature. Poor reporting of populations characteristics of the included studies. No quality appraisal carried out. Sensitivity analysis carried out for sequential taxane schedule showing higher probability of acheiving a pCR. Author's comment on the heterogeneity of the studies, including populations, sample size and treatment duration. **Author's conclusions:** The combination of taxanes and anthracyclines as neoadjuvant chemotherapy for early breast cancer improved the chance of achieving higher breast-conserving surgery rates and pathologic complete response rates. This main conclusion followed from the evidence presented, but did not clearly acknowledge limitations of the evidence discussed by the review authors, so it may not be entirely reliable.		
Outcome Measures/results	*Primary:* pathological complete response (any definition), rate of breast-conserving surgery *Secondary:* clinical complete and partial response, rate of node-negative disease after treatment, rate of grade 3/4 neutropenia, DFS, OS	Data for primary endpoints were available for 7 RCTs. The rate of BCS was significantly higher for patients receiving taxanes, with an AD of 3.4% (P=5.012), which translates into 29 patients NNT, without significant heterogeneity. The rate of pCR was higher for patients receiving taxanes (not statistically significant). In the sensitivity analysis, patients receiving taxanes as a sequential schedule had a significant higher probability to achieve pCR, with an AD of 2.4% (P=5.013), which translates into 41 patients NNT, without significant heterogeneity. Patients receiving taxanes as a concomitant schedule had a significantly higher probability to achieve BCS, with an AD of 5.3% (P=5 .027), which translates into 19 patients NNT, without significant heterogeneity. The complete response rate was significantly higher in the taxane arms, regardless of the adopted strategy, with an AD ranging from 6.7% to 15.5%.	

Figure 5-1: Example pages from an evidence table (continued)

Gianni, L, Baselga, J, Eiermann, W, Guillem Porta, V, Semiglazov, V, Lluch, A, et al.
Feasibility and tolerability of sequential doxorubicin/paclitaxel followed by cyclophosphamide, methotrexate, and fluorouracil and its effects on tumor response as preoperative therapy (Clinical Cancer Research: 2005 11 8715-21)

Study type/ evidence level	Study details/limitations	Patient characteristics	Interventions
Randomised controlled trial **Evidence level:+**	*Countries:* Spain, Italy, Russia, Poland, Estonia, Hungary, Austria, Czech Rep *Centres:* *Setting:* *Funding sources:* Healthcare Industry, Bristol Meyers Squibb *Dropout rates:* *Study limitations:*	*Total no. patients:* 1,355 *Patient characteristics:* 20% had tumours >4 cm, more than half were aged over 50. *Inclusion criteria:* Women with primary operable breast tumour >2 cm (T2-T3, N0-N1, M0) *Exclusion criteria:*	Primary systemic therapy v CMF/doxorubicin followed by CMF or CMF/doxorubicin/paclitaxel followed by CMF
Notes:	In multivariate analysis only estrogen receptor (ER) status was significantly associated with pathologic complete response (odds ratio for ER negative, 5.77; 95% confidence interval, 3.49 to 9.52; P<0.0001). Neoadjuvant chemotherapy induced a significant axillary downstaging (P<0.001), and breast-sparing surgery was feasible in 65% versus 34% (P<0.001). Not a blinded trial. No ITT. **Author's conclusions:** Doxorubicin/paclitaxel followed by CMF is feasible, safe, and well tolerated. Given as PST, it is markedly active, allowing for breast-sparing surgery in a large fraction of patients.		
Outcome measures/results	Toxicity, adverse events	Grade 3 or 4 National Cancer Institute toxicities were low (<5%) in all arms. Neuropathy was more frequent in the paclitaxel-containing arms (grade 2, 20.5% versus 5.0%; grade 3, 1.3% versus 0.2%). At 31 months of follow-up, asymptomatic drop of left ventricular ejection fraction was similar in all arms, whereas symptomatic cardiotoxicity was recorded in three patients (0.5%) in A and in three patients (0.3%) in B plus C. PST induced clinical complete plus partial remission in 78%,with an in-breast pathologic complete response rate of 23% and an in-breast plus axilla pathologic complete response rate of 20%. In the multivariate analysis, only estrogen receptor (ER) status was significantly associated with pathologic complete response (odds ratio for ER negative, 5.77; 95% confidence interval, 3.49-9.52; P<0.0001). PTS induced a significant axillary downstaging (P<0.001), and breast sparing surgery was feasible in 65% versus 34% (P<0.001).	

Figure 5-1: Example pages from an evidence table (continued)

Huober, J, von Minckwitz, G, Denkert, C, Tesch, H, Weiss, E, Zahm, DM, et al.
Effect of neoadjuvant anthracycline-taxane-based chemotherapy in different biological breast cancer phenotypes: Overall results from the gepartrio study
(Breast Cancer Research & Treatment: 2010 124 133-40)

Study type/ evidence level	Study details/limitations	Patient characteristics	Interventions
Cohort study **Evidence level: +**	*Countries:* *Centres:* *Setting:* *Funding sources:* Not stated *Dropout rates:* *Study limitations:*	*Total no. patients:* 2,090 *Patient characteristics:* Operable or LABC *Inclusion criteria:* Women with Operable or LABC *Exclusion criteria:*	TAC
Notes:	Exploring association of clinico-pathological variables with response - all patients received the same chemotherapy for the first part of the trial. Independent factors for mid-course response and pCR were: young age, non-T4 tumors, high grade, and hormone receptor status, the strongest single predictive factor. Grading and age can identify subgroups within the luminal and triple negative patients who have an increased benefit from NACT. These are useful data to answer question of benefit in different populations (ER+ v ER –; HER2+ v HER2-; PR+ v PR-) Evaluated as a cohort; evaluation of prerandomised cohort from Gepartrio trial. No control group. Large number lost to follow-up. **Author's Conclusion:** Grading and age can identify subgroups within the luminal and triple negative patients who have an increased benefit from NACT.		
Outcome measures/results	pathological clinical response	The overall pCR rate, defined as no invasive residuals in breast and axilla, was 20.5%. The highest pCR rate of 57% was observed in patients below 40 years of age with triple negative or grade 3 tumors. Independent factors for mid-course response and pCR were: young age, non-T4 tumors, high grade, and hormone receptor status, the strongest single predictive factor. Within the biological subtypes, grading was an independent factor to predict pCR for luminal tumors, clinical tumor stage for the HER2 like tumors and age for the triple negative ones. Grading gave independent information for mid-course response within the triple negative group. No factor predicted mid-course response within the other groups.	

Figure 5-2: Example of considered judgment

◉ **Considered judgement**	
Key question: KQ03 In patients with BC (men, premenopausal women, postmenopausal women) with an inoperable tumour/unsuitable for breast conserving surgery, what is the evidence that neoadjuvant chemotherapy is effective and what is the optimal regimen?	
A: Quality of evidence	
1. How reliable are the studies in the body of evidence? *(see SIGN 50, section 5.3.1, 5.3.4)* *If there is insufficient evidence to answer the key question go to section 8.*	
Comment here on any issues concerning the quantity of evidence available on this topic and its methodological quality. Please include citations and evidence levels.	**Evidence level**
Neoadjuvant chemotherapy vs surgery/adjuvant chemotherapy There is a Cochrane review (van de Hage, 2009), comprising 14 studies, which randomised 5,500 women. High quality meta-analysis, which shows no heterogeneity in OS or LRR across the trials.	1++
Duration of chemotherapy There are 3 RCTs comparing different chemotherapy durations. RCTs consistently show increased pCR and a trend towards increased BCS for 6 cycles v 3 cycles (Reitsamer 2005, Steger 2007) or 6 cycles v 4 cycles (Han 2009).	1+
Taxanes vs non-taxanes There is 1 meta-analysis with no significant heterogeneity (Cuppone 2008), 2 systematic reviews (Nowak 2004, Trudeau 2005) and a meta-analysis of 7 trials conducted in a single institution (Mazouni 2007)	1++ 1+ 1-
Herceptin in Her2 positive There is 1 Cochrane review (Moja 2012), showing no heterogeneity and, in particular, no heterogeneity compared with adjuvant trials.1 meta-analysis (Valachis 2011) and surgical outcomes of the Noah trial have been recently reported separately (Semiglazov 2011).	1++ 1+
Subtypes There are 2 well conducted RCTs (Gianni 2005 & Huober 2010), which report on outcome (using pCR as a surrogate marker) depending on biological subtype. There is a pooled analysis of 8 German RCTs, (von Minckwitz 2011) reporting the relationship of biological subtype to pCR.	1++ 1+ 2+
2. Are the studies consistent in their conclusions? *(see SIGN 50, section 5.3.2)*	
Comment here on the degree of consistency demonstrated by the evidence. Where there are conflicting results, indicate how the group formed a judgement as to the overall direction of the evidence.	
Overall there does not appear to be any significant inconsistency between the trials.	
3. Are the studies relevant to our target population? *(see SIGN 50, section 5.3.3)*	
For example, do the studies: • *include similar target populations, interventions, comparators or outcomes to the key question under consideration?* • *report on any comorbidities relevant to the target population?* • *use indirect (surrogate) outcomes* • *use indirect rather than direct comparison of outcomes*	
The trial results and interventions are applicable to the Scottish population.	
4. Are there concerns about publication bias? *(see SIGN 50, section 5.3.5)*	
Comment here on concerns about all studies coming from the same research group, funded by industry etc	
Van de Hage comments that publication bias may be possible. No publication bias reported in the Moja review. Not commented on in Cuppone review.	

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6 Making recommendations

6.1 Introduction

Earlier sections of this manual cover the identification and evaluation of evidence relating to specific key questions. By this point of the process the guideline development group knows how much evidence there is (or is not) available to help answer their questions. Though there is clearly room for debate about some issues, a framework of basic rules for identifying and appraising evidence has been in place. The process now moves on to an area where there is more scope for opinion to guide the final conclusion.

A newcomer to the field of evidence-based guidelines may wonder what place opinion has in applying evidence. For an explanation, we need to go back to a basic definition of evidence-based medicine (EBM). In the introduction to their landmark book on EBM,[1] David Sackett and his co-authors defined it as:

"...the integration of best research evidence with clinical expertise and patient values".

So far, we have dealt with gathering the research evidence. What now needs to happen is for clinical expertise and patient values, among other things, to be applied to that evidence to arrive at a recommendation that is in line with the evidence, is practical to deliver, and takes account of patient preferences. In other words a recommendation that is likely to be implemented and to be acceptable to patients.

This section is based on the Evidence to Decision (EtD) tool developed as part of the DECIDE project,[2] which is in turn based on the work of the GRADE group.[3,4]

6.1.1 Strong versus weak

Before going further, it is worth focusing on the outcome of a GRADE decision-making process. It is to produce a recommendation that is rated as either strong or weak (which, in the SIGN implementation of GRADE, we will refer to as 'conditional' recommendations).

A strong recommendation is made where:

- the evidence is of high quality *(see section 5)*
- estimates of the effect of an intervention are precise (ie there is a high degree of certainty that effects will be achieved in practice)
- there are few downsides of therapy
- there is a high degree of acceptance among patients.

A conditional recommendation is made where:

- there are weaknesses in the evidence base
- there is a degree of doubt about the size of the effect that can be expected in practice
- there is a need to balance the upsides and downsides of therapy
- there are likely to be varying degrees of acceptance among patients.

6.2 Evidence to recommendation

The following sections are based on DECIDE EtD frameworks. At the time of writing these were at an advanced stage of development, but may be further refined. This chapter will be updated periodically in the light of further developments in the DECIDE work and experience of applying these principles in SIGN guidelines.

It is worth keeping in mind at all times that fundamental to this approach to guideline development is the issue of transparency. Different guideline developers will allocate greater or fewer resources to developing their guidelines, and the detail of the work they do will vary accordingly. The important point in all that follows is to be clear about what was actually done at each stage of the process. Justifications can be provided if thought necessary, but the key point is to produce a structured summary of the complete process that reviewers or guideline users can check when they are considering implementation of the guideline.

6.2.1 Is this question a priority?

Given that a question has survived through the processes of topic selection and key question setting, it might be taken as read that it is a priority. The intention here, however, is to indicate why the question is being addressed.

- What risks will be reduced?
- To what extent is there a need to improve on current treatments?
- How many patients are likely to be affected?
- Could improvement in this condition reduce the risk/impact of common comorbid conditions?

These are some of the types of issue to be addressed here.

Members of the guideline development group have a key role to play as they will be aware of the main issues that make a question important, as well as some of the key information that will illustrate that importance. Their knowledge may be supplemented by evidence from official data, published sources, or research studies.

6.2.2 How sure are we that any given option will work?

At this point the guideline development group relies on the summarised evidence produced at the previous stage in the process *(see section 5)*. The factors described in the following sections are then considered in part B of the **considered judgment form** *(see Figure 6-1)* to allow recommendations to be formed from the evidence.

Ideally this table can be taken from a summary of findings (SoF), but this is unlikely to be available in every case. For those key questions where an SoF is not available, an alternative short format presenting non-pooled results (for example, an evidence table) will suffice. The guideline development group should focus on (for each outcome):

- outcome
- impact
- number of studies
- quality/certainty of the body of evidence.

6.2.3 Balancing benefits and harms

Fundamental to making any recommendation is the need to ensure that any benefit to the patient outweighs, preferably by a substantial margin, any risks or harms associated with the treatment.

In order to make such judgments, the guideline development group has to have a clear understanding of how substantial the expected benefits of an intervention are likely to be in practice. They also need to consider how substantial the downsides are. These may range from physical side effects to an increased risk of developing additional health problems. The evidence supporting benefits will often come from stronger study designs than that supporting harms. This makes judgments more difficult, but it is nonetheless essential to explicitly consider the size of effect for both sides of the balance. A detailed presentation of the evidence from a summary of findings or similar table *(see section 5.3)* is essential when making such decisions.

Once the size of all effects has been established, a judgment must be made as to whether the benefits outweigh the harms. This is not just a clinical judgment but must take into account patient values *(see section 6.2.4)* if a realistic assessment is to be achieved.

6.2.4   How do patients value the different outcomes?

For a recommendation to be implemented effectively, it is important that the outcomes are sufficiently valued by patients for them to be willing to adhere to the treatment. The science of assessing patient values and preferences, however, remains largely undeveloped.[6] When developing guideline recommendations, the focus should be on questions where the application of values is likely to affect outcomes and should rely on practical and achievable methods.

In the case of venous leg ulcers, for example, there is strong evidence that using compression stockings is an effective treatment, and the higher the compression the better the results. Compression stockings have various drawbacks, however, and some patients either cannot or will not tolerate the highest levels of compression. It then becomes a question of balancing these preferences against the risk of larger or longer lasting ulcers. A recommendation based entirely on trial evidence without taking into account patient preferences is unlikely to be widely adhered to, and therefore ineffective.

Assessing patient values and preferences can focus on the extent to which they are likely to follow a recommended course of action, though there is some evidence that wider social values can play a part in such decisions.[7] A first step should be to consult patient representatives on the guideline development group, and through them a wider body of patient opinion.

If time and resources allow, a literature search can be carried out looking specifically for information on patient values in relation to the question being addressed. It is worth noting that there is an increasing literature on patient values related to specific conditions.

If acceptability of a recommendation to patients is seen as critical to its effective implementation, and no clear idea of patient views has been identified by the above methods, it may be necessary to run a series of focus groups to establish patient values and preferences.

6.2.5   Equity

Under the **Equality Act 2010** all public bodies in Scotland are required to take into account the needs of equality groups. This applies to all guidelines and other publications produced by SIGN. The equality groups identified in the Act are:

- age
- disability
- gender reassignment
- marriage and civil partnership
- race
- religion or belief
- sex
- sexual orientation.

Guideline groups are therefore required by law, as well as good practice, to consider whether any recommendations they make will have a differential impact on any of these groups.

Some aspects of equality issues have been addressed earlier in this manual *(see sections 4.3 and 5.3.3)*. At this later stage in the process, it may be necessary to analyse the evidence for specific subgroups of the population to see if and how it differs from the main results. If there are substantial differences it will be necessary to make separate recommendations for these subgroups taking these differences into account.

Apart from issues of social equity, subgroups may need to be considered for clinical reasons such as specific comorbidities, or issues around polypharmacy where separate recommendations may be required for these groups.

6.2.6 Costs and benefits

There are two aspects to the consideration of costs and benefits in relation to guideline recommendations.[8,9]

The first relates to cost effectiveness of a single proposed intervention, and involves assessing the incremental cost of applying the new intervention compared to current practice and relating it to the net benefit of the intervention. In many cases this will not be a major issue, but where it is an assessment should be made to ensure introduction of the new approach is worthwhile. This may be achieved through a review of the existing literature, or through economic modelling. For these issues to be addressed adequately a health economist should be available to advise the group on which questions are likely to require an assessment, and if possible to conduct that assessment and report the results to the group prior to their making a recommendation.

The second issue relates to the resources required to implement a recommendation across the NHS in Scotland. Again, this may not be an issue in a lot of cases but where very expensive treatments or interventions requiring substantial investment in equipment or changes to working practices are involved an assessment of the cost impact is important if the guideline is to be implemented.

In this second case the cost assessment may not influence specific recommendations directly, but should be produced along with the guideline to inform decision makers who need to allocate resources within individual health boards. If the potential cost is very high and may not be achievable in the short term, a 'next best' option may be recommended in the guideline. The guideline should, however, always identify the most cost-effective option, with the 'next best' as an interim option only.

6.3 Making recommendations

It is not possible for SIGN or any other guideline organisation to advise or direct a guideline group as to the conclusions they should reach. All that can be asked is that the group considers all the issues and uses a transparent process to reach their conclusion.

Usually the guideline development group forms recommendations through a process of informal consensus facilitated by the SIGN Programme Manager. Since the recommendations are explicitly linked to the body of consistent evidence, agreement is generally reached. When it is not possible to reach consensus in this way, independent interpretation of the evidence may be sought. In addition the Programme Manager may seek advice from the Editorial Group or SIGN senior management team (SMT) depending on the nature of the disagreement. SMT will discuss how to progress the issues with the Programme Manager, Chair, members of the guideline development group and external experts as appropriate. The outcomes of these discussions are recorded in the supporting documentation for the guideline, for example in the considered judgement form *(see Figure 5-2)* and meeting minutes, and in the guideline itself if necessary.

Balancing all the issues described above is a matter of considerable complexity, and presents a challenge to any guideline group. High quality evidence from well conducted studies should lead to a strong recommendation, but relating the trial populations to the target population of a guideline and taking into account issues of cost and patient acceptability may lead to a recommendation that is much weaker than first thought. Equally, there will be circumstances where the evidence is flawed but there are few or no downsides to treatment and the clinical importance of the topic is such that a strong recommendation is justifiable.

Particularly where considerations of equity or comorbidity are involved, the guideline development group may have to make more than one recommendation; one for each subgroup discussed.

In all situations, however, the overall judgment of the guideline development group can only lead to one of the five possible conclusions shown in Table 6-1, each related to a particular form of recommendation.

Table 6-1: Forms of recommendation

Judgment	Recommendation
Undesirable consequences clearly outweigh desirable consequences	Strong recommendation against
Undesirable consequences probably outweigh desirable consequences	Conditional recommendation against
Balance between desirable and undesirable consequences is closely balanced or uncertain.	Recommendation for research and possibly conditional recommendation for use restricted to trials
Desirable consequences probably outweigh undesirable consequences	Conditional recommendation for
Desirable consequences clearly outweigh undesirable consequences	Strong recommendation for

Whatever the conclusion, the published guideline and supporting documentation should contain a justification for the recommendation highlighting the supporting evidence and the factors that have been taken into account when arriving at a conclusion.

Where decisions are particularly complex, such a justification may be quite lengthy. In these cases the full justification can be included in supporting material with a shortened version included in the published guideline.

Recommendations are differentiated from other text in the published guideline by presenting as a single paragraph in bold text. A capital 'R' is used alongside to emphasise that the associated text is a recommendation.

R | **Patients with larger tumours may be considered for oncoplastic surgery instead of mastectomy.**

Figure 6-1: Example of considered judgment

B: Evidence to recommendations

5. Balancing benefits and harms *(see SIGN 50, section 6.2.2, 6.2.3)*

Comment here on the potential clinical impact of the intervention/action – eg magnitude of effect; balance of risk and benefit.

What benefit will the proposed intervention/action have?
Describe the benefits. Highlight specific outcomes if appropriate.

Neoadjuvant chemotherapy vs surgery/adjuvant chemotherapy
There is sufficient evidence to indicate that neoadjuvant chemotherapy is associated with higher rates of breast conservation than adjuvant chemotherapy, with no difference in overall survival or locoregional recurrence rates, providing surgery is part of the treatment pathway. In total, 5,500 patients treated in 14 studies, with median follow-up of 18-124 months were included. The meta-analysis concluded that OS was equivalent for preoperative chemotherapy versus adjuvant chemotherapy (HR 0.98 (95% CI 0.87 to 1.09, p=0.67). There were increased breast-conservation rates with neoadjuvant chemotherapy but there were associated increased locoregional recurrence rates. However, if surgery was included, even in cases of complete response, locoregional recurrence rates were equivalent (HR 1.12 (95% CI 0.92 to 1.37, p=0.25). Patients who achieve pathological complete response show improved survival, compared with patients with residual disease (HR 0.48 (95% CI 0.33 to 0.69, p<104).

Duration of chemotherapy
A randomised trial of 4 vs 6 cycles epirubicin and docetaxel (Han 2009) of 176 patients showed pCR 11% vs 24% (p=0.047) with a trend to higher clinical response and higher breast conservation. A randomised trial of 3 vs 6 cycles epirubicin and docetaxel (Reitsamer 2005) of 45 patients showed pCR 10% vs 36% (p=0.045) with a trend to increase breast conservation. A randomised trial of 3 vs 6 cycles epirubicin and docetaxel (Steger 2007) of 292 patients showed pCR 7.7% vs 18.6% (p=0.045) with a trend to increased breast conservation.

Taxanes vs non-taxanes
There is sufficient evidence to indicate that breast-conservation rates and rates of pathological complete response (pCR) are higher in patients treated with a combination of anthracycline and taxane-based neoadjuvant chemotherapy, compared with non-taxane based chemotherapy. Cuppone review – 7 RCTs in the meta-analysis, including concomitant or sequential administration, either docetaxel or paclitaxel used as the taxane (ie the treatment regimes are quite heterogeneous). 2455 patients in total. BCS significantly higher with a taxane (absolute difference 3.4%, p=0.12). There was a trend to higher pCR for patients treated with taxanes, which reached statistical significance in patients receiving sequential anthracyclines/taxanes (AD 2.4%, p=0.013). The Mazouni pooled analysis of 7 consecutive neoadjuvant chemotherapy trials conducted at MD Anderson (1079 patients in total) indicated higher pCR in patients receiving a taxane (29% vs 15% in ER negative patients, p<0.001 and 8.8% vs 2.0% in ER positive patients, p<0.001).

Herceptin in Her2 positive
There is sufficient evidence to indicate that patients with Her-2 positive (Her2 3+ or Her2 2+ FISH amplified) breast cancer, receiving neoadjuvant chemotherapy, should receive herceptin, either as adjuvant treatment or with non-anthracycline-based neoadjuvant chemotherapy. In patients with Her2 positive disease, adjuvant or neoadjuvant herceptin leads to improved DFS and OS. The Cochrane review (Moja 2012) of 8 studies (neoadjuvant/adjuvant studies combined) which included 11991 patients. This showed improved OS (HR 0.66, 95% CI 0.57-0.77, p<0.00001) and improved DFS (HR 0.060, 95% CI 0.50-0.71, p<0.00001) with no heterogeneity of effect between adjuvant and neoadjuvant administration of herceptin. A meta-analysis (Valachis) of 5 trials with 515 patients showed higher pCR rates (RR 1.85, 95% CI 1.39-2.46, p<0.001). Data on rate of BCS was available in 4 trials (280 patients). For these patients, no difference was seen in rate of BCS (OR 0.98, 95% CI 0.80-1.19, p=0.82). The NOAH trial (Semiglazov 2011) has reported a higher rate of BCS in patients with locally advanced breast cancer receiving neoadjuvant Herceptin in addition to chemotherapy (23% vs 13%).

Figure 6-1: Example of considered judgment (continued)

Subtypes

In the ECTO trial (Gianni 2005) ER negativity was significantly associated with pCR (odds ratio for ER negative 5.77, 95% CI 3.49 to 9.52, p<0.0001). In the GEPARTRIO study (Huober 2010), association of clinico-pathological variables with response was explored (not randomised). The strongest single predictive factor for pCR was ER and PR negativity (odds ratio 3.08, 95% CI 2.32 to 4.09, p<0.001).

What harm might the proposed intervention/action do?
Describe the benefits. Highlight specific outcomes if appropriate.

Neoadjuvant chemotherapy vs surgery/adjuvant chemotherapy

van de Hage found no significant difference between adjuavant and neoadjuvant chemotherapy for postoperative complications, nausea/vomiting or alopecia. Events of leucopenia and infections (RR 0.69, 95% CI 0.56 to 0.84, p= 0.0003) were significantly lower with neoadjuvant chemotherapy

Duration of chemotherapy

Han showed no similar rates of toxicity (grade ¾ neutropenia, febrile neutropenia and mucositis) for 3 vs 6 cycles. Reitsamer did not report on toxicity. Steger reported no differences in haematological, GI, neurological, cardiac or other serious toxicities between the 2 groups.

Taxanes vs non-taxanes

The Cuppone, Mazouni and Nowak reviews did not report toxicity. Trudeau reported increased haematological toxicity, including neutropenia and febrile neutropenia, with taxane-containing regimes. There was no evidence of significant difference in other adverse events, other than peripheral neurotoxicity.

Herceptin in Her2 positive

A combined analysis of neoadjuvant and adjuvant trials (Moja) reported a significantly increased risk of congestive heart failure (RR 5.11, 90% CI 3.00 to 8.72, p<0.00001) and left ventricular ejection fraction decline (RR 1.83, 90% CI 1.36 to 2.47, p=0.0008) when Herceptin is added to chemotherapy. There was no difference in haematological toxicities.

6. Impact on patients *(see SIGN 50, section 6.2.4, 6.2.5)*

Is the intervention/action acceptable to patients and carers compared to comparison? Consider benefits vs harms, quality of life, other patient preferences (refer to patient issues summary).

Are there any common comorbidities that could have an impact on the efficacy of the intervention?

The use of adjuvant chemotherapy in patients with breast cancer at moderate/high risk of disease recurrence reduces the risk of relapse and improves survival. The use of adjuvant trastuzumab in patients with Her-2 positive breast cancer reduces the risk of relapse and improves survival. Health care professionals and patients place high value on these outcomes.

Neoadjuvant chemotherapy +/- trastuzumab is associated with higher rates of breast conservation than adjuvant chemotherapy, with no difference in overall survival or locoregional recurrence rates, providing surgery is part of the treatment pathway. In addition, there is no evidence of any significant difference between toxicity of neoadjuvant or adjuvant chemotherapy.

Patients and health care professionals place high value on recurrence/survival outcomes and, in suitable patients, increased breast conservation rates.

Figure 6-1: Example of considered judgment (continued)

7. Feasibility *(see SIGN 50, section 6.2.6)*	
Is the intervention/action implementable in the Scottish context? Consider existing SMC advice, cost effectiveness, financial, human and other resource implications.	
Neoadjuvant chemotherapy +/- trastuzumab is generally well tolerated and the regimes used are similar to adjuvant chemotherapy. Patients with inoperable breast cancer are, by definition, incurable and therefore treatment that renders such a patient operable and potentially curable is cost effective. Breast conservation is less morbid than mastectomy and, arguably, offers improved quality of life and neoadjuvant chemotherapy with this aim is, therefore, cost effective. In line with SMC/NICE recommendations	

8. Recommendation *(see SIGN 50, section 6.3)*

What recommendation(s) does the guideline development group agree are appropriate based on this evidence?

*'**Strong**' recommendations should be made where there is confidence that, for the vast majority of people, the intervention/action will do more good than harm (or more harm than good). The recommendation should be clearly directive and include '**should/ should not**' in the wording.*

*'**Conditional**' recommendations, should be made where the intervention/action will do more good than harm, for most patients, but may include caveats eg on the quality or size of the evidence base, or patient preferences. Conditional recommendations should include '**should be considered**' in the wording.*

Neoadjuvant chemotherapy should be considered for all patients with breast cancer whose disease is either inoperable but localised to the breast/loco-regional lymph node groups, or high T/N stage, or where the only surgical option is mastectomy and downstaging might offer the patient the opportunity for breast conservation.	***Strong***
Anthracycline-taxane based chemotherapy combinations increase the rate of breast conservation rates and pCR rates, compared with anthracycline-alone regimes and should be considered for all patients receiving neoadjuvant chemotherapy.	***Strong***
Trastuzumab should be offered to patients with Her-2 postitive breast cancer, either as adjuvant treatment or with non-anthracycline-based neoadjuvant chemotherapy.	***Strong***
Anthracyclines and trastuzumab should be avoided or used with extreme caution in patients with cardiac comorbidity. In less fit patients, the benefits of chemotherapy +/- trastuzumab are more likely to be outweighed by the potential harms and treatment should only recommended after careful consideration.	***Strong***

Briefly justify the strength of the recommendation
In patients with breast cancer, where disease is either inoperable, higher stage or there is the possibility of increasing breast conservation rates, the likelihood of doing good outweighs the likelihood of doing harm.

9. Recommendations for research

List any aspects of the question that have not been answered and should therefore be highlighted as an area in need of further research.
Studies into the efficacy of therapies for men with breast cancer are required.

6.4   Good practice points and consensus recommendations

Good Practice Points (GPP) are intended to assist guideline users by providing short pieces of advice which may not have an evidence base, but which are seen as essential to good clinical practice.

Examples of acceptable GPPs:

- Healthcare professionals should refer to the WHO medical eligibility criteria for contraceptive use prior to offering contraceptive advice to women with diabetes.
- Healthcare professionals should signpost patients to self-help resources, identified and recommended by local pain services, at any point throughout the patient journey.

If the group feels strongly that they want to make a recommendation even though there is no significant evidence, this should be done as a weak recommendation based on very-low quality evidence. Note that there must be some evidence of opinion supporting the recommendation from outside the guideline group. If no such evidence exists, formal methods should be used to develop a consensus-based recommendation which will be clearly identified as such within the guideline by a statement accompanying the recommendation.

The methods used to reach consensus may vary between guideline groups. Whatever method is used, it is essential that it is described either in an Annex to the guideline or as a supporting document linked to the guideline on the SIGN website.

6.5   Key recommendations

The guideline group will identify a small number of key recommendations to be listed in a separate section of the guideline *(see section 8)*. These key recommendations are identified by the guideline development group as the recommendations that, in order to improve patient outcomes, should be prioritised for implementation. They appear in the main text as well as section 2 of the guideline, and will appear in the Quick Reference Guide and associated app.

A consensus-based recommendation may be included as a key recommendation.

6.6   References

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7 Consultation and peer review

7.1 Consulting on draft guidelines

SIGN seeks feedback on a draft version of a new guideline from the wider health and social care community through:

- open consultation
- a national open meeting
- peer review.

The benefits of consultation 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, and the feasibility of implementing the proposed recommendations.

2. The wider community has the opportunity to contribute to and influence the form of the final guideline, generating a sense of ownership over the guideline across geographical and disciplinary boundaries.

7.1.1 Open consultation

The draft guideline is available on the SIGN website for a month and widely publicised to professional and patient representative groups most likely to have an interest in the topic. Comments can be submitted by individuals or corporate, commercial, professional or societal groups. Comments are only accepted if accompanied by a declaration of interests from the reviewer.

All feedback is compiled into a consultation report for consideration by the guideline development group *(see section 7.1.4)*.

7.1.2 National open meeting

During the open consultation, SIGN may hold a national open meeting to discuss the draft recommendations of each guideline. The guideline development group presents its preliminary conclusions and draft recommendations and encourages further feedback through discussion at the meeting, on social media and via the online consultation. It provides an opportunity for two-way learning. Delegates are made aware of the latest evidence and proposed recommendations, and the guideline development group gains an insight into how the draft guideline is interpreted. It also allows for any controversial areas to be highlighted and discussed.

SIGN national open meetings are widely publicised and are usually attended by between 75 and 300 healthcare professionals and others interested in the guideline topic, including patient and carer representatives, from across Scotland. The meeting is advertised to the same groups as the open consultation and via social media. Particular efforts are made to ensure that all equality groups with a potential interest in the topic are represented. For updates to existing guidelines, national open meetings are only held if the content of the guideline has significantly changed. Otherwise, the guideline is made available for open consultation on the SIGN website for one month. No consultation meeting is held for published guidelines that are undergoing a small change *(see sections 9.3 and 9.4)*. In this case the revised section of the guideline is sent directly to appropriate expert reviewers *(see section 7.1.3)*.

7.1.3   Peer review

All SIGN guidelines are reviewed in draft form by referees, who are not members of the guideline development group, selected for their expertise and to reflect the multidisciplinary nature of the guideline. The draft is also sent to at least two lay reviewers in order to obtain comments from the patient's perspective. Reviewers are asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline.

Comments from peer reviewers will not be considered unless an accompanying declaration of interests has also been submitted. The comments received from peer reviewers are compiled in the consultation report and discussed by the guideline development group *(see section 7.1.4).*

7.1.4   Consultation report

All submissions from the open consultation and peer review are compiled in a consultation report, which lists the reviewers' names, designations and any conflict of interests. The guideline development group addresses each comment and makes changes to the draft guideline, or records reasons for no change in the report. The consultation report is published alongside the guideline.

7.2   Editorial review

As a final quality control check prior to publication, the guideline and the consultation report are reviewed by the SIGN Editorial Group, consisting of the SIGN Chair, Programme Lead and representatives of SIGN Council. The Editorial Group ensures that each point raised at consultation has been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The full editorial and consultation phase is illustrated in Figure 7-1.

Figure 7-1: Consultation and peer review phases of guideline development
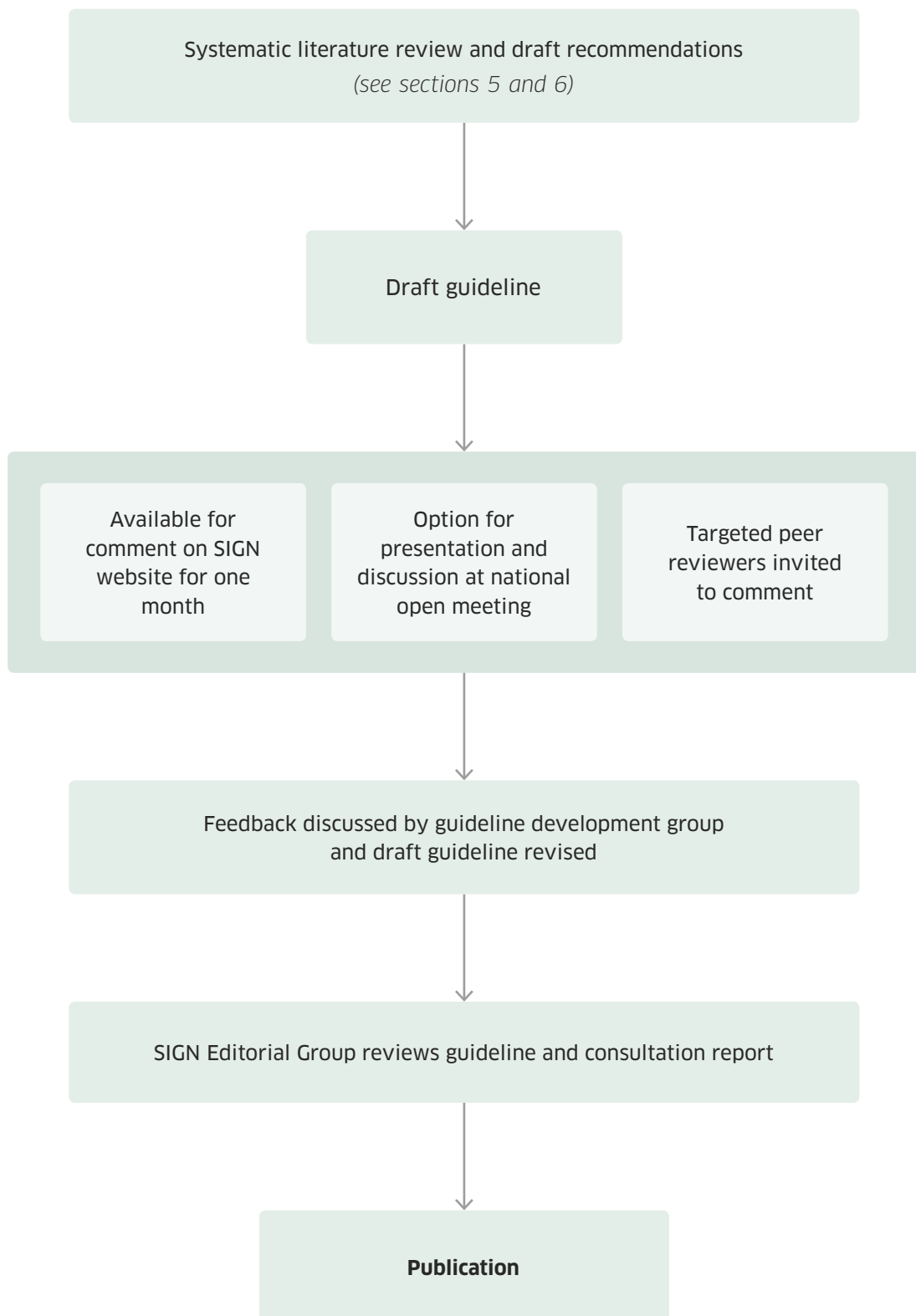
8 Presentation and publication

8.1 Presentation of the guideline

There is little information available on the effect that style and presentation have on the adoption and utility of guidelines. Clarity of definitions, language, and format, is likely to be important. Guidelines should, therefore, be written in unambiguous language and should define all terms precisely. The most appropriate 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 on methods of presentation. This is an additional function of the extensive peer review process to which all SIGN guidelines are subject *(see section 7)*.

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 sections 4, 5 and 6, guideline development groups will find that most of the required information will then be produced in a structured, accessible format, ready to slot into the guideline template.

8.2 Content of the guideline

8.2.1 Introduction

Each SIGN guideline has an introduction, outlining the need for the guideline, including evidence of variation in practice and the potential for the guideline to improve patient care. There is also a short summary of the patient perspective. The remit of the guideline is carefully defined, detailing definitions, the patient population, including common comorbidities, and target users of the guideline. The key clinical questions covered in the guideline are detailed in an Annex with clear reference to the section to which the question refers and where methodological limitations of the evidence base are discussed. A statement of intent makes clear the purpose of the guideline.

8.2.2 Evidence and recommendations

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 section:

- A clear statement of the issue under consideration
- An 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 quality of evidence and key references). This should provide the justification for the recommendation to follow; that is, the evidence for improved patient outcome resulting from the recommended action or for harms or contraindications relating to treatment options *(see section 5)*
- The recommendations that the group has derived from this evidence *(see section 6)*
- A brief discussion of any practical points (eg resource/geographical considerations to be taken into account in the discussion of local guidelines for implementation), or 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, a 'good practice point' may be presented alongside the recommendations.

8.2.3 Key recommendations

The guideline development group highlights a small number of recommendations, which may include good practice points, as the key recommendations that should be prioritised for implementation. It is important to note that the key recommendations will not necessarily be those with the strongest supporting evidence, but those considered by the guideline development group as having the greatest potential impact on patient care *(see section 6)*.

8.2.4 Information for patients

All SIGN guidelines include a 'Provision of information' section, which gives examples of the information patients and carers may find helpful at the key stages of the patient journey. The information in this section is provided for use by health and care professionals when interacting with patients and carers and for guiding the production of locally-produced information materials. The issues highlighted in this section are informed by:

- patient views gathered earlier in the development process *(see sections 4.1 and 11)*
- discussion with patient representatives on the development group
- input from other guideline development group members.

In cases where there are strong and diverse views among patients, focus groups may be used to identify the most widely-needed information that patients require.

This section also includes details of appropriate help lines, support groups and reading materials.

8.2.5 Implementation resources

During the development of the guideline, the development group identifies or develops tools and activities that will aid implementation of the guideline *(see section 10)*. Resource implications of implementing the key recommendations and key points for audit are also developed as part of an implementation strategy for the guideline *(see section 10)*.

8.2.6 Guideline development

Brief details of the systematic review on which the guideline recommendations are based are provided, with full details of the main search strategy available on the SIGN website. Stakeholder involvement is demonstrated through listing the guideline development group members, specialist peer reviewers and others commenting at the consultation stage of guideline development, and the SIGN Editorial Group.

8.2.7 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 section 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.

8.2.8 Review and updating

A plan for updating the guideline and details of any updates since publication are listed.

8.3 Publishing the guideline

All SIGN guidelines are available free of charge on the SIGN website. Updates including any corrections are made to the electronic version of the guideline, which is the definitive version at all times.

The search strategy and register of interests declared by the guideline development group, and consultation report are published alongside the guideline. A report of any updates is also available. Other supporting material may include:

- implementation resources, eg patient pathways, costing tools
- patient resources, eg booklets, sample leaflets
- learning resources, eg slide sets, on-line tutorials.

8.3.1 Quick reference guide

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.

8.3.2 Guideline App

The SIGN guideline app for iPhone, iPad and Android phones and tablets contains QRGs of recently published SIGN guidelines. The QRG content is enhanced with material from the main guideline and online resources, linked to the SIGN website. Each new SIGN QRG is available as an update through the Apple App Store or Google Play Store as it is published.

The app features keyword search, bookmarking, and a function allowing the user to attach a PDF of the guideline they are interested in to an email message.

8.3.3 Patient booklets

SIGN patient versions of guidelines are lay translations of the clinical guidelines. The patient versions of guidelines are intended to supplement or support discussions between professionals and patients. They should always be 'handed' to patients to allow them the opportunity to ask questions to help them with decision making. While they are not intended to be general health education material, each booklet provides brief background information on the condition and signposts patients to further sources of information. They are intended to:

- help patients, service users and carers understand what the latest evidence supports around diagnosis, treatment and self care
- empower people to participate fully in decisions around management of their condition in discussion with healthcare professionals
- highlight to people where there are areas of uncertainty.

The content and presentation of the patient booklets are based on strategies developed during SIGN's participation in the DECIDE collaboration.[1,2]

These booklets include:

- context: who the information is for
- a brief summary of the condition
- a summary of tests, treatments and procedures recommended in the guideline
- how professionals can support people to help themselves
- details on where people and their families can find more information about the condition, and
- how guidelines are produced.

As part of SIGN's commitment to the equality agenda of NHSScotland, patient versions of guidelines can be produced in languages other than English upon receipt of requests from users. Languages covered include those community languages identified by Scottish Government, Gaelic, or British Sign Language (BSL). Large print versions can also be made available.

8.4 References

1   Fearns N, Graham K, Johnston G, Service D. Improving the user experience of patient versions of clinical guidelines: user testing of a Scottish Intercollegiate Guideline Network (SIGN) patient version. BMC Health Serv Res 2016;16:37.

2   Fearns N, Kelly J, Callaghan M, Graham K, Loudon K, Harbour R, et al. What do patients and the public know about clinical practice guidelines and what do they want from them? A qualitative study. BMC Health Serv Res 2016;16:74.

9 Updating published guidelines

As medical practice continues to develop and new options for treatment become available, guidelines inevitably fall behind current evidence for best practice. They must therefore be kept under review and updated when necessary.[1-4]

The currency of guidelines is categorised in a traffic light system on the SIGN website in the following way:

✅ current (within three years of publication or over three years old and revalidated)

❓ over three years old and not revalidated

❗ over seven years old and not revalidated

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. Updates can apply either to sections of guidelines, or in some circumstances to individual recommendations. Processes have to be in place to address all of these possible options.[5]

9.1 Scoping for the need to update

SIGN considers 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 literature review is carried out to establish if there are previous or ongoing projects in Healthcare Improvement Scotland on the same topic. Searches also cover other UK guidelines, the Cochrane Library for systematic reviews, NIHR for HTAs and ECRI for evidence reports. A report is prepared, supplemented by comments received since publication of the guideline, outlining the potential impact of any new evidence on the recommendations in the guideline. During consultation, the group responsible for developing the guideline, or a wider group of healthcare professionals, is asked to consider the potential impact of the new evidence on the guideline. The report and recommendations on the need to update the guideline is made available to GPAG *(see section 3.3)*.

The outcome of the report will be one of four options:

- **Revalidate** if no evidence was identified that would change recommendations
- **Update** if there is new evidence that would change recommendations in some areas of the guideline
- **Request a proposal** for a new guideline if the new evidence would change many of the existing guideline's recommendations
- **Withdraw** the guideline if the new evidence renders it unsafe or obsolete.

9.2 Updating a guideline

If the scoping process carried out three years after publication confirms the need for an update *(see section 9.1)*, the process for carrying out the update is largely the same as that described elsewhere in this manual. The principal difference is that the update will focus on those sections of the original guideline that have been identified, through the scoping, as being in need of updating. The same methodological principles apply, although the nature of the sections being reviewed may necessitate a slightly different composition from the original guideline group. If, for example a section on surgical interventions is a major part of an update, the guideline group is likely to include more surgeons and theatre staff than say pharmacists or allied health professionals.

The guideline group must decide whether or not the proposed changes are sufficiently far reaching as to justify the need for a national meeting. 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 *(see section 7.1).*

9.3 Requests for a change to a published guideline

All comments received on published SIGN guidelines, or information on important new evidence in the field, or evidence of impacts on equality groups is considered, either for immediate response or for more detailed consideration on review of the guideline.

Individuals commenting on published guidelines are invited to complete a small change proposal form, which can be downloaded from the SIGN website. Once received, small change proposals are processed alongside full proposals *(see section 3.3.2).*

GPAG considers proposals for small changes to published guidelines on a rolling basis and guidelines will be updated if a proposal meets the following criteria:

- new evidence substantially changes a small number of recommendations in the guideline (corresponding to no more than two related key questions) OR
- a specific issue such as a new drug therapy or national issue such as a new government policy will give rise to a new key question AND
- the nature of the update may not warrant assembling a multidisciplinary group.

9.4 Making a small change to a guideline

When GPAG decides that a guideline is in need of a small change *(see section 3.3.2)*, the process for this is largely the same as that described for updating a guideline *(see section 9.2)*, although the scope of the update is much narrower and the timescale shorter. The level of involvement of a guideline development group and extent of consultation will depend on the nature of the changes to the guideline.

9.5 Recording updates to a guideline

Any updates to the guideline made in the period prior to review are recorded in the update report which can be found in the supplementary material section for the guideline on the SIGN website. The update report provides details of any requests from stakeholders to update the guideline (or other triggers, such as a change in drug marketing authorisation), the decision from GPAG on whether or not the update is warranted, when the update was published and the nature of the update.

9.6 Living guidelines

As with an update to a guideline, the process for updating a living guideline is largely the same as that described elsewhere in this manual. The main difference is that a living guideline is 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.

Each update focuses on those areas of the currrent 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 arise from new developments identified during the process of scoping the update.

Once searches are completed, if new evidence has been identified to change a recommendation or to add a new topic, the text and recommendations of the guideline are revised. The updates are summarised in the published guideline. The other processes used will be the same as those used for a new guideline. A possible exception is, as with an update, the need for a national meeting.

9.6.1 Living guideline on the management of asthma

SIGN has only developed one living guideline, the British guideline on the management of asthma in collaboration with the British Thoracic Society (BTS). Updated drafts of this guideline were presented at one of the BTS biannual meetings, as well as being published on the SIGN and BTS websites for a fixed period, during which time comments were invited.

9.7 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 GPAG 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.

Guidelines may be withdrawn for any of the following reasons:

- superseded 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
- the guideline is over 10 years old.

9.8 References

1   Alonso-Coello P, Martinez Garcia L, Carrasco J, Sola I, Qureshi S, Burgers J, et al. The updating of clinical practice guidelines: insights from an international survey. Implement Sci 2011;6:107.

2   Lyratzopoulos G, Barnes S, Stegenga H, Peden S, Campbell B. Updating clinical practice recommendations: is it worthwhile and when? International Journal of Technology Assessment in Health Care 2012;28(1):29-35.

3   Martinez Garcia L, Arevalo-Rodriguez I, Sola I, Haynes RB, Vandvik PO, Alonso-Coello P, et al. Strategies for monitoring and updating clinical practice guidelines: a systematic review. Implementation Science 2012;7:109.

4   Schunemann HJ, Wiercioch W, Etxeandia I, Falavigna M, Santesso N, Mustafa R, et al. Guidelines 2.0: systematic development of a comprehensive checklist for a successful guideline enterprise. CMAJ 2014;186(3):E123-42.

5   Becker M, Neugebauer EAM, Eikermann M. Partial updating of clinical practice guidelines often makes more sense than full updating: a systematic review on methods and the development of an updating procedure. Journal of Clinical Epidemiology 2014;67(1):33-45.

10 Implementation

10.1 Getting guidelines into practice

To achieve the objectives set out in section 1.2 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 healthcare professionals and organisations to improve clinical effectiveness and patient outcomes, 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 sections of this handbook, and their implementation into practice. Just as guidelines help provide a bridge between research and practice, this section 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. SIGN addresses the internal barriers by developing guidelines according to a robust methodology, described in detail in the earlier sections. Potential external barriers to guideline implementation include:

- Structural factors (eg budget constraints, significant service redesign required)
- 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)
- Patient perceptions and treatment preferences
- Professional-patient interaction (eg problems due to language or social origin, mental health issues)
- Disadvantaged patient populations (eg poverty, homelessness).

Disadvantaged populations are known to have poorer health and health care and external barriers to implementation contribute to inequalities in health care. For successful implementation, and to achieve the aim of reducing variation in practice, external barriers also need to be assessed and implementation strategies developed to address them.[1]

10.3 Implementation support strategies

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.

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".[2] Implementing guidelines is not simple or straightforward. Difficulties often centre on the need for personal, organisational or cultural change.[3] 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 as summarised in Figure 10-1.[4] The authors emphasised 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. Characteristics of the patient population and any potential health inequities also need to be considered. 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	Multifaceted interventions

A Health Technology Assessment (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.[5] The review makes it clear that there is an imperfect evidence base to support decisions about dissemination and implementation and that any approach should always take account of local circumstances.

Stakeholder consultation showed what type of support healthcare professionals in NHSScotland would like to aid implementation of SIGN guidelines.[6] Results of the survey fell into the following four key domains, which form the basis for our implementation support; improving SIGN processes, awareness raising and education, networking and implementation support resources.

10.3.1 Improving processes

Robust dissemination

Guidelines must be made as widely available as possible in order to facilitate implementation. SIGN Quick Reference Guides and patient booklets are distributed free of charge throughout NHSScotland. Our focus is on electronic distribution and all SIGN guidelines can also be downloaded free of charge from the SIGN website. The Quick Reference Guides are available on the SIGN guideline Smartphone app.

Dissemination of SIGN guidelines in NHSScotland is organised within each NHS board by local distribution co-ordinators, who are responsible for disseminating guidelines across their board. The distribution co-ordinators are notified of all new guidelines and updates to published guidelines and given an opportunity to order Quick Reference Guides to distribute within their board. It is important to maintain a strong relationship with the distribution co-ordinators and keeping contact

details up to date is key to a robust dissemination process. Notification of new guidelines is also sent to the Royal Colleges in Scotland, the chairs of NHS boards, the chief executives of NHS boards, the chief scientist's office, other guideline development organisations, postgraduate college deans and voluntary organisations listed in the guideline.

Copies of all SIGN publications are deposited with the British Library and the Agency for Legal Deposit.

10.3.2 Awareness raising and education

Awareness raising activities

An important element of implementation is making people aware of the guideline and its recommendations. SIGN staff, lay representatives, guideline development group members and SIGN Council members raise awareness by presenting at conferences, workshops and educational events.

SIGN often publishes guideline summaries in medical journals, which allows a much wider audience to be made aware of SIGN and its latest recommendations.

Local clinical champions

Having a powerful clinical champion can be an effective way to raise awareness of a guideline. Clinical champions have a high profile, are widely respected, have a good understanding of policy and have local contacts. SIGN supports clinical champions, usually guideline development group members, to take a leading role in supporting implementation of specific guidelines in their area.

Patients as champions for change

Patients are a powerful agent for change in the health service. Guidelines are published with an accompanying patient and carer version of the guideline and by being aware of a clinical guideline, patients can ask for their care to be in line with the latest recommendations. Making use of connections with patient groups and voluntary organisations also affords more opportunities to raise awareness of guidelines.

Lay representatives on guideline development groups are supported to raise awareness at conferences and other events.

Education and training modules

SIGN has worked with NHS Education for Scotland and the Royal College of Physicians and Surgeons of Glasgow to develop training modules based on guidelines. By linking these to Continuous Professional Development, healthcare professionals are encouraged to complete the training.

10.3.3 Networking

Linking with existing networks and projects

In many areas of clinical practice, there are existing professional networks and/or national projects that aim to improve the quality of care and to put evidence into practice. Examples include Managed Clinical Networks (MCNs) for cancer, coronary heart disease (CHD) and epilepsy.

Building relationships with the various professional networks, Scottish Government, NHS Education for Scotland and others as part of a wider cohesive approach to improving patient care should facilitate implementation. For example, the stroke guideline was developed in co-ordination with revision of the clinical standards, the production of key performance indicators and the production of a resource calculator.

10.3.4 Implementation support resources

Each guideline development group develops tools or signposts useful resources that will support implementation. An implementation resource is any tool or activity that contributes towards putting the recommendations into practice. They are generally targeted towards recommendations that will have the maximum impact on patient care and can include:

Algorithms, care pathways and integrated care pathways

Algorithms and care pathways describe the typical journey of care and provide a visual representation of a group of recommendations. They can be a useful tool for people wishing to implement a change in practice and can be used for educational purposes. Similarly, integrated care pathways, by their design, can ensure that specific recommendations are implemented in practice.

Resource implication tools

Where a key recommendation is likely to result in significant resource changes a resource implications calculator or costing tools can be developed to help NHS boards identify the potential costs and savings of implementation.

Datasets

Datasets that support the implementation of key recommendations are often included with guidelines. Wherever possible SIGN works with other agencies to support the incorporation of recommendations in national datasets and audit tools.

Electronic decision support tools

Incorporating recommendations into local electronic decision-support systems is an efficient way to assist implementation. For example, some referrals made via the Scottish Care Information (SCI) Gateway are based on SIGN recommendations for referral, which are embedded in the system.

Other tools

Other simple tools such as posters highlighting key recommendations, audit proforma, easily accessible and editable lists of the recommendations, slide sets and case studies may also be developed with each guideline and made available on the SIGN website.

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. In fact it may be that only certain key recommendations within the guideline are prioritised for implementation. The clinical team, however, 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 outlines the likely steps that a local implementation group might take, adapted from the Royal College of Nursing Guidelines[7] and the SPICEpc (Scottish Programme for Improving Clinical Effectiveness in Primary Care) project (www.ceppc.org/spice/index.shtml).

Figure 10-2: Practical steps towards guideline implementation

Step 1

Decide who will lead and co-ordinate 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 multidisciplinary 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 to also 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. Patient preferences and views eg local surveys should be taken into account. 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 and 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   References

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2. Grol R, Grimshaw J. Evidence-based implementation of evidence-based medicine. Jt Comm J Qual Improv 1999;25(10):503-13.

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4. University of York. NHS Centre for Reviews and Dissemination. Getting evidence into practice. Effective Health Care Bulletin 1999; 5:

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11 Involving patients and their representatives

11.1 Patient involvement in guideline development

The term patients is used throughout this section as a generic term to describe patients, service users, carers, members of the public and those who represent and/or support them in the voluntary sector.

INVOLVE, a UK government-funded programme to support active public involvement in NHS, public health and social care research, defines involvement as research being carried out 'with' or 'by' members of the public, rather than 'to', 'about' or 'for' them; the term 'public' includes patients, potential patients, carers and people who use health and social care services, as well as organisations that represent people who use these services.[1]

Many national organisations and experts recognise the importance and value of involving patients in the development of guidelines to help meet the needs of the population, foster healthcare choices and ensure guidelines are acceptable for use.[2,3] The potential contribution of patient representatives has been recognised for some time, as well as the difficulties in making that contribution effective.[4]

Patients may have different perspectives on health and social care processes, priorities, and outcomes from those of professionals. The involvement of patients in guideline development is therefore important to ensure that guidelines are more tailored and responsive to patients. 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 bring an 'expert' insight into guidelines because of their experience of living with conditions or using services. They can identify issues that may be overlooked by professionals, can highlight areas where the patient's perspective differs from the views of professionals, and can ensure that the guideline addresses key issues of concern to patients.

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 adherence to treatment, for example complying with a recommended diet or medication, or a different approach to sexually transmitted infection (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.

11.2 Identifying patients' views

11.2.1 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 section 4.1)*. This search is performed at least three months prior to the first group meeting to ensure adequate time to obtain relevant articles 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 making decisions about treatment
* overall satisfaction with the care received.

A copy of the Medline version of the patient search strategy is available on the SIGN website.

11.2.2 Patient organisations and the SIGN patient and public involvement 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 and Public Involvement Network asking them which issues they think the guideline should address. The Patient and Public Involvement Network is a database of patient, service user, carer and public 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 (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.

11.2.3 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 through direct contact with users of the service. Engagement techniques used 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. Views are sought from 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 professionals, local community groups and schools who can help identify people to take part.

Groups are run as workshops with a specific focus and require expert facilitation. A note-based analysis of discussions is carried out and a summary of the findings is prepared.

11.2.4 Presenting the findings

The Public Involvement Advisor reviews the results of the patient literature search, and seeks to identify common themes that emerge from the literature. A theme is recorded for each literature paper and a subject bibliography is created. These themes are used alongside the findings that emerge from the other engagement approaches described and are presented at the first meeting of the guideline development group by the Public Involvement Advisor.

The group is asked to take account of these issues when it drafts the key questions. Once a first draft of the key questions has been prepared, the Evidence and Information Scientist working with the group, along with the Public Involvement Advisor, compare the questions with the issues highlighted through the consultative process and highlight 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.

11.3 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 through other means, for example from consultation with Scottish Health Council 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.

11.4 Role of patients 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 outcomes 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 outcomes
- identifying areas where patients' preferences and choices may need to be acknowledged in the guideline
- making sure that the degree to which the evidence addresses patients' concerns is reflected in the guideline
- helping to write the 'Provision of information' section of the guideline, including identifying sources of further information
- raising awareness of patient issues at the national open meeting by preparing a presentation (with support from SIGN) and speaking at this meeting
- assisting SIGN with the identification of voluntary organisations, charities and individuals to invite to the national open meeting
- helping to ensure that the guideline is sensitively worded (eg 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
- raising awareness of the SIGN guideline with their own networks.

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)
- a willingness to become familiar with medical terms and phrases
- a willingness to feed in the views of patient/carer groups not represented on the guideline group
- the ability to put views across clearly, constructively and sensitively, taking into account other people's responsibilities, views and expertise
- the ability to be objective
- good communication and team working skills.

11.5 Support for patient representatives on guideline development groups

SIGN supports patient representatives by:

- delivering 'Introduction to SIGN' training, based on SIGN 100: A handbook for patient and carer representatives for patient representatives[5]
- offering telephone and email support
- inviting new patient representatives to join the SIGN Patient and Public Involvement 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, including patient representatives
- inviting patient representatives to informal events.

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.

11.6 Wider consultation with patients and carers

Further patient and public participation in guideline development is achieved by involving patients, service users, carers and voluntary organisation representatives at the national open meeting which is held to discuss each draft guideline *(see section 7.1.2)*. The meetings are advertised widely and are free of charge.

Patients, service users, carers and voluntary organisation representatives are invited to take part in the peer review stage of each guideline and specific guidance for them has been produced.

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

11.7 References

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12 Development of the manual

12.1 Introduction

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of Healthcare Improvement Scotland.

SIGN published its first methodology manual, "Clinical guidelines: criteria for appraisal for national use" in 1995, setting set out the draft criteria by which it would appraise clinical guidelines for recommendation for national use in Scotland. "SIGN Guidelines: An introduction to SIGN methodology for the development of evidence-based clinical guidelines" was published in 1999 to reflect developments in the SIGN methodology. The current manual was first published in 2008 and has undergone revisions in 2011, 2014, 2015 and 2019.

12.2 The development group

Development of this manual was supported by the SIGN Executive and Healthcare Improvement Scotland staff members.

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All members make yearly declarations of interest. A register of interests is available on the SIGN Executive page on the website www.sign.ac.uk

12.3   Editorial review

As a final quality control check, the manual is reviewed by an editorial group comprising the members of SIGN Council Strategy Group. All members of SIGN Council make yearly declarations of interest. A register of interests is available on the SIGN Council Membership page of the SIGN website www.sign.ac.uk

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