



*National Institute for  
Health and Clinical Excellence*

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# **Interventional Procedures Programme**

**Methods guide**

## **Interventional Procedures Programme methods guide**

**Issued: June 2007**

This booklet describes the methods that NICE uses to assess interventional procedures.

The booklet is available from the NICE website ([www.nice.org.uk](http://www.nice.org.uk)) or from the NHS Response Line (phone 0870 1555 455; quote reference number N1278).

### **National Institute for Health and Clinical Excellence**

MidCity Place  
71 High Holborn  
London  
WC1V 6NA

[www.nice.org.uk](http://www.nice.org.uk)

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# 1 Introduction

## 1.1 Background

The National Institute for Health and Clinical Excellence (NICE) is the independent organisation responsible for providing national guidance on promoting good health and preventing and treating ill health. Further details about the Institute and its programmes of work are available in 'A guide to NICE', which can be downloaded from the NICE website ([www.nice.org.uk/guidetonic](http://www.nice.org.uk/guidetonic)).

NICE produces guidance on the use of new and existing medicines, treatments and procedures within the NHS, including the efficacy and safety of interventional procedures. Assessment of the efficacy and safety of interventional procedures is carried out by the Institute's Interventional Procedures (IP) Programme, which comprises the Interventional Procedures Advisory Committee (IPAC or 'the Committee') and a Programme team, which carries out technical tasks and project management. The Programme team is employed by NICE. All members of the Committee are independent. Although the IP Programme mostly investigates new procedures, it may also examine an established procedure if there is uncertainty about its efficacy and/or safety.

This guide describes the principles and methods used to assess interventional procedures. The methods are designed to ensure that robust guidance for the NHS is developed in an open, transparent and timely way that allows appropriate input from consultees and other stakeholders. This guide is intended to be complementary to the 'Interventional Procedures Programme manual' ('IP Programme manual') ([www.nice.org.uk/ipprogrammemanual](http://www.nice.org.uk/ipprogrammemanual)).

A glossary of terms used in this document is provided on page 35.

## 1.2 Aims of the Interventional Procedures Programme

The IP Programme assesses the efficacy and safety of interventional procedures, with the aim of protecting patients and helping clinicians, healthcare organisations and the NHS to introduce procedures appropriately. By reviewing evidence, consulting widely, facilitating data collection and analysis, and providing guidance on the efficacy and safety of interventions, the Programme enables clinical innovation to be conducted responsibly. No interventional procedure is entirely free from risk; the Programme gauges the extent of risks and benefits and makes recommendations in terms of their implications.

NICE issues guidance on interventional procedures to ensure that:

- patients and carers are reassured that new interventional procedures are being assessed to protect patient safety, and that they have access to information about procedures

- clinicians, healthcare organisations and the NHS will be supported in the process of introducing new procedures
- innovation is fostered by facilitating data collection and analysis, arranging systematic reviews, recommending training and providing advice on the efficacy and safety of new procedures.

### 1.3 Remit of the Interventional Procedures Programme

The remit of the IP Programme is outlined in the ‘Supplemental directions to the National Institute for Clinical Excellence in relation to interventional procedures’ which amended the NHS Act 1977. This was set out in more detail for the NHS as follows: WHC(2003)58, May 2003 (Wales); HSC2003/011, November 2003 (England); NHS HDL(2004)04, January 2004 (Scotland); HSS(PPMD)/(NICE)01/06 June 2006 (Northern Ireland). NICE’s interventional procedures guidance applies in all four UK countries.

To fall within the remit of the IP Programme, a notified interventional procedure must:

- involve an incision or a puncture or entry into a body cavity, or the use of ionising, electromagnetic or acoustic energy, and
- be available within the NHS or be about to be used for the first time in the NHS, outside formal research, and
- be either not yet generally considered standard clinical practice, or a standard clinical procedure, the safety or efficacy of which has been called into question by new information.

### 1.4 Key methodological issues considered in this guide

Assessment of procedures within the IP Programme consists of several phases. The following are addressed in this guide:

- development of the scope for procedures that fall within the Programme’s remit
- identification, selection and collation of appropriate evidence and commentary (including specialist advice and lay input)
- assessment of the evidence
- consideration of the evidence and commentary by the Committee
- formulation of provisional recommendations by the Committee
- consultation and consideration of consultees’ comments
- formulation of final recommendations by the Committee.

Several other issues relating to the function and processes of the Programme (such as assessing whether a notified procedure falls within the Programme’s remit) are covered by the ‘IP Programme manual’.

## 2 Developing the scope

An interventional procedure that is notified to the Institute is assessed by the IP team to determine whether it falls within the remit of the Programme. (For further details of the notification process, see the 'IP Programme manual'.) Procedures that fall within the Programme's remit are then scoped in preparation for assessment.

### 2.1 Introduction

The purpose of scoping is to provide a framework for the assessment of a procedure. The scope defines the issues of interest as clearly as possible and sets the boundaries for the work to be undertaken by the IP Programme team and the Committee. This is done by defining the clinical questions that the overview (see the glossary and section 4.1) will attempt to answer.

In preparing the scope, the Programme team seeks advice from Specialist Advisers to the Programme (see the glossary and section 3.2.4.1) and IPAC members.

Appropriate IPAC members are also consulted on the draft scope. If there is no specialist IPAC member for the specialty of the procedure under consideration, a Specialist Adviser is consulted.

### 2.2 Standard approach to scoping

The Institute undertakes an initial scoping exercise by conducting a preliminary search of the literature to establish a scope that sets out the following:

- notified procedure title, and proposed procedure title (if a different title is thought necessary – see section 2.3)
- proposed lay description
- notified indication (patient indications and population), where applicable
- proposed indication (patient indications and population), where applicable (if different indications are thought necessary – see section 2.3)
- the notified comparator
- the proposed comparator
- relevant safety and efficacy outcomes
- category of notifier
- disease area(s)
- specialty area(s)

- relevant specialist societies
- relevant patient organisations
- related NICE guidance
- special issues relating to the procedure.

Where appropriate, the scope also includes brief details of other considerations that could form part of the assessment of the procedure. These may include:

- details of specific patient subgroups
- highlighting where procedures are notified for more than one indication
- identification of issues regarding the available evidence base (for example, emerging key trials)
- procedures that can be performed with more than one device
- information about the timing of regulatory approval of the technologies and related policy developments, such as NICE clinical guidelines or national service frameworks.

## 2.3 Scoping complex notifications

Scoping sometimes identifies that the notification cannot be accepted in its original form, but suggests how useful guidance could be developed. This can include the following situations.

- A procedure is notified with an imprecise name or spelling, or one that is atypical in UK practice. As there is no universally recognised nomenclature for interventional procedures, the Programme's technical team may rename the notified procedure on the advice of Specialist Advisers or the specialist IPAC member.
- A procedure is notified with a name that is device specific (for example, 'Device X for indication Y' instead of 'Procedure Z for indication Y'). Because the Programme does not evaluate devices (this is the remit of the Medicines and Healthcare products Regulatory Agency), the name of the procedure is revised to avoid reference to either specific devices or trade names.
- A procedure is notified for an imprecise or atypical indication. For example, the indication might be a symptom of a disease (such as pruritus) rather than the disease itself (chronic liver disease). The Programme's technical team may revise the procedure–indication pair in order to produce appropriate guidance.
- A procedure is notified for more than one distinct indication. In this case it is normal practice for the procedure to be 'split' and for one piece of guidance to be produced for each indication.



## 3 Evidence and commentary

Evidence (mainly from the published peer-reviewed literature) and commentary (from Specialist Advisers or consultees) is considered by the Committee at two stages in the assessment of a procedure: first to formulate provisional recommendations for consultation, and second to arrive at the Committee's final recommendations. This section deals primarily with the evidence that the Committee uses to make its provisional decision, which is mainly, although not exclusively, from published sources. In this guide, 'commentary' refers to the variety of opinion, published data and information from unpublished sources that may be relevant to a procedure.

This section describes how relevant evidence on efficacy and safety is identified (section 3.1) and selected (section 3.2). It also describes the way in which the most relevant evidence is highlighted for presentation to the Committee (section 3.3).

The presentation of evidence to the Committee after consultation (including patient commentary) is described in section 5.7.

### 3.1 Identification of efficacy and safety evidence

#### 3.1.1 Introduction

Selection of evidence for the IP Programme is based on the following key principles.

- The IP process considers only efficacy and safety.
- It does not assess cost effectiveness.
- Depending on the circumstances, either active treatment or sham (placebo) is the preferred standard in assessing the efficacy and safety of a procedure.
- Detailed recommendations on different indications and patient subgroups are not usually possible.
- The timescale for producing guidance is short (details are given in the 'IP Programme manual').

The nature of the IP Programme's remit means that many interventional procedures notified to the Institute are new, and thus published evidence is often limited in both volume and quality. Randomised controlled trials (RCTs) are often not available; non-randomised controlled trials and case series studies may therefore be the main sources of data for some procedures.

In order to allow rapid review of the literature, the clinical question(s) are derived from the 'population, intervention, comparator, outcome' (PICO) framework (see the glossary). For IP guidance, the population is the population of patients with the relevant indication, and the intervention is the procedure under consideration. The preferred comparator is the best standard treatment; however, such comparative evidence is rarely available for emerging interventional procedures.

Evidence and commentary about the efficacy and safety of a procedure are gathered from the following sources:

- a rapid review of the published literature, based on an explicit search
- information from Specialist Advisers in specialties associated with the procedure
- knowledge of expert IPAC members.

For selected procedures, the following sources of evidence may also be used:

- information from databases or registers of the procedure
- a systematic review of the literature commissioned by the Institute.

### 3.1.2 Literature search

The available evidence is presented to the Committee in the form of an overview. This is a compilation and analysis of the studies found during the literature search.

The literature search is carried out by the Institute's Information Services (IS) team and aims to identify as much evidence on the procedure as possible, using a comprehensive and exhaustive search strategy but on a limited number of sources. Development of the search strategy is an iterative process, whereby changes are made to the strategy according to the results retrieved, based on discussions between the IS team and the Programme's technical team.

Because of the nature of procedures notified to the IP Programme, there are rarely directly relevant thesaurus headings (MeSH, Emtree; see the glossary); often a given procedure has no 'established' terminology and is referred to in a variety of ways by different centres or researchers. For this reason, the use of free-text searches (words in titles and abstracts) may be more important, and appropriate synonyms, abbreviations and alternative spellings are sought and used extensively in the search strategy.

The search focuses on being able to identify relevant background information, systematic reviews, health technology assessments (rarely available) and, most importantly, primary research and ongoing/newly reported research in the form of conference proceedings and current research.

The following searches are conducted against the sources and methodology set out below.

#### 3.1.2.1 Background information

- General Internet search
- The Australian Safety and Efficacy Register of New Interventional Procedures (ASERNIP-S)
- US Food and Drug Administration (FDA)

#### 3.1.2.2 Systematic reviews and health technology assessments

- Cochrane Database of Systematic Reviews (CDSR)
- Database of Abstracts of Reviews of Effects (DARE)
- Health Technology Assessment database

#### 3.1.2.3 Primary research evidence

- Cochrane Central Register of Controlled Trials (CENTRAL)
- EMBASE
- Medline
- Medline In-process and other non-indexed citations (Premedline)
- Cumulative Index to Nursing and Allied Health Literature (CINAHL)

#### 3.1.2.4 Ongoing research databases

Databases including the following are used:

- National Research Register
- Controlled Trials Registry

#### 3.1.2.5 Conference proceedings

Because many of the procedures considered by the IP Programme are very new, searching through conference proceedings can yield useful results. The British Library Inside Conferences (BLIC) database and websites of the major relevant professional bodies (UK and abroad) are searched for recent conference proceedings.

#### 3.1.2.6 Other sources of evidence

Other subject-specific databases may be searched, depending on the subject area.

#### 3.1.2.7 Use of methodological filters

Methodological filters such as the Cochrane highly sensitive search strategy are seldom used. This is because the evidence base is rarely large enough to warrant such restrictions and because, at the time of assessment by the IP Programme, interventional procedures have rarely

been assessed in controlled trials. However, for some procedures, where perhaps the efficacy of an established procedure is being called into question by new information, a filter based on study design may be applied. A filter for safety outcomes may be applied for some procedures where there is a large body of evidence that includes systematic reviews, and where complications (morbidity) have been identified as a particular concern.

#### 3.1.2.8 Language restrictions

Searches include publications in any language. Where a large body of evidence is available in English, selection is usually limited to English-language publications. Translation into English of full articles published in languages other than English is requested by the technical team if the outcomes reported in the non-English literature differ in nature from those reported in the English-language literature, or are reported with substantially different frequencies – particularly for safety outcomes. Such translations are treated in exactly the same way as English-language studies (that is, they are included in the evidence summary table of the overview if they are considered to be among the most valid and relevant studies).

#### 3.1.2.9 Date restrictions

Date restrictions are not normally used when searching for interventional procedures. They are applied only in particular situations, for example, where a technology has evolved, where there is an exceptionally large amount of literature, or where a good-quality systematic review or health technology assessment exists that has not excluded studies on the basis of study design. In this latter case, the search would be restricted to studies published after the year of publication of the most recent study included in the review or assessment.

#### 3.1.2.10 Timeliness

The literature search is conducted as close to the relevant IPAC meeting as possible, to ensure timeliness of the search. If there are any delays to the assessment of the procedure, a further search (using the same search terms) is conducted shortly before the relevant IPAC meeting in case new literature has emerged.

## 3.2 Selection of evidence for presentation to the Committee

The initial screening of studies eligible for the overview is done using abstracts downloaded from electronic databases. A study is eligible for inclusion if it includes patients with the appropriate indication, describes the relevant intervention and reports efficacy and safety outcome data. If a study cannot be reasonably excluded on the basis of the abstract alone, its eligibility is assessed using the full text of the publication.

Once all the studies identified in the literature search have been assessed for eligibility, the reference lists of the eligible studies are checked for other studies that may not have been identified by the search strategy. If a considerable number of potentially eligible studies is identified through this process, then the original search strategy is modified and the search is repeated.

### 3.2.1 Inclusion of eligible papers in the overview

The main purpose of evidence selection is to identify the studies that are most valid and relevant for detailed presentation to the Committee. Evidence is presented to the Committee in the form of an overview with a summary table for the most relevant evidence, and an appendix which includes other studies in less detail.

Selection is straightforward for many procedures because the number of studies judged to be relevant is small and they are all presented in the evidence summary table.

For some procedures, however, selecting the studies to include in the overview – and for further appraisal in the evidence summary table – may be a complex and difficult task, because some studies have to take priority over others, on the basis of a judgement about their relevance and validity. A particular difficulty arises when there is a disproportionate number of published studies in relation to:

- different subgroups of patients treated with the same procedures
- different devices used for the same procedure, or technical variations of a procedure
- different outcomes (for example, some studies reporting only efficacy and some only safety outcomes; some studies reporting quality-of-life outcomes, others not).

In this context, the Programme's technical team may take the following actions.

- Prioritise a particular subgroup of studies, chosen to provide a balanced view of the evidence.
- Propose splitting the overview, so that more than one piece of guidance is produced. This approach has to be considered alongside the need for effective use of Programme resources and Committee time, and potential usefulness to the NHS.

In general, studies that are designed and executed in a way that is most likely to minimise bias are included in the evidence summary table. A number of checks are used to establish whether the right studies have been selected for inclusion, including using the expertise and knowledge of the Specialist Advisers, the notifier of the procedure, the specialist Committee member and, ultimately, consultees who respond to the consultation for the procedure.

The treatment effect of a technology can, in essence, be summarised as the difference between the health state or quality of life that would be experienced on average by patients receiving the technology, and the health state or quality of life of the same group were they to receive standard treatment and/or sham (placebo). The following criteria are considered when selecting evidence on safety and efficacy for presentation in the overview.

#### 3.2.1.1 General quality considerations

Quality of evidence relates to the methods used to minimise bias within a study design and in the conduct of a study – see also section 4.3.3.

### 3.2.1.2 Study design

Levels of evidence are a convenient way to summarise study design according to its capacity to minimise bias. The highest value has traditionally been placed on evidence from meta-analysis of RCTs or one or more well-designed and executed RCTs. However, the level of evidence is only one dimension when considering validity and relevance. In some instances, non-randomised studies may be more informative about outcomes, particularly safety outcomes.

### 3.2.1.3 Study size

Assuming that other considerations about study type and methods are equal, priority is usually given to studies that include larger numbers of patients. This is important in order to provide accurate estimates of efficacy and safety, and to optimise the possibility of identifying less frequent safety outcomes.

### 3.2.1.4 Follow-up length and completeness

Assuming that other considerations about study type and size are equal, priority is usually given to studies with longer and more complete follow-up. This is particularly relevant for assessing efficacy and safety in the context of certain conditions (such as cancer and conditions that cause long-term disability) and for procedures relating to implantable materials or devices. Prolonged follow-up is also important to detect rare adverse events following procedures.

### 3.2.1.5 Patient-focused outcomes

Patient-focused, as opposed to surrogate, outcomes are considered particularly important when judging the efficacy of a procedure. For example, evidence that a procedure reduces tumour size carries less weight than evidence about clinical benefits such as enhanced survival and/or improved quality of life.

Because safety is an important issue, studies that systematically report adverse events are sought.

Safety outcomes are often not well addressed in randomised trials. Large numbers of treated patients are required to reliably detect uncommon yet serious adverse events. Large case series, surveys and registers may provide valuable information, and case reports of rare complications may also prove useful and are given prominence, particularly when there is concern about the potential for rare but important complications. Although these sources often lack denominator data to substantiate incidence calculations, they provide qualitative information that can be highly relevant. This is particularly the case for serious adverse events that occur in the treatment of conditions with an otherwise good prognosis.

## 3.2.2 Procedures for which no comparator (controlled) data are reported

Sometimes all of the evidence for a given procedure relates to non-comparative studies (for example, originating from case series studies). In these circumstances, selected evidence about key efficacy and safety outcomes of likely comparator procedures may be presented. If no available comparators exist, then key aspects of natural history (such as survival rates at different time intervals if untreated) may be presented.

## 3.2.3 Inclusion of unpublished data

### 3.2.3.1 Efficacy data

Efficacy data that have not been published or accepted for publication by peer review are not normally selected for presentation to the Committee. Conference abstracts are not normally considered adequate to support decisions on efficacy and are not generally selected for presentation in the overview. If an abstract report relates to a major and potentially relevant study, then efforts are made to obtain a peer-reviewed paper of the findings at the earliest possible opportunity.

### 3.2.3.2 Safety data

Data on safety, at however immature a stage, may arise from abstracts, manufacturers, Specialist Advisers' reports and other miscellaneous sources. The Programme team will always bring such data to the Committee's attention, regardless of source, when safety issues relating to serious adverse events are identified.

## 3.2.4 Commentary

### 3.2.4.1 Specialist Advisers

The process by which Specialist Advisers are identified is described in the 'IP Programme manual'.

Specialist Advisers have an essential role in the process of assessing interventional procedures, their knowledge and opinion providing supplementary evidence that may be absent from the scientific literature.

In order to minimise the potential for bias in evidence presented to the Committee, Specialist Advisers are sought from a range of backgrounds, including clinicians with varying degrees of experience in performing the procedure and those who have not been involved in performing the procedure but who have expert knowledge of the relevant specialist field.

The opinion of Specialist Advisers is sought on the following issues:

- controversy between specialties over the procedure
- how novel or well established the procedure is, or whether it is a minor variation on current practice
- interventions that could be considered as comparators
- potential adverse events associated with the procedure
- uncertainties or concerns about the efficacy or safety of the procedure
- suggested efficacy and safety outcomes for audit
- training or facilities required to perform the procedure safely
- current research or registers
- current and likely future impact of the procedure on the NHS.

The Specialist Advisers' responses are presented in full to the Committee, and help to inform its recommendations. Specialist Advisers are required to declare any conflicts of interest, following NICE's policy on declaration of conflicts of interest.

#### 3.2.4.2 Evidence from manufacturers

Although some interventional procedures involve the use of a particular device, the IP Programme does not evaluate the device itself. Therefore, formal submissions from manufacturers are not used routinely in the assessment of procedures, although any peer-reviewed evidence offered by manufacturers is considered.

#### 3.2.4.3 Contributions from patients to the development of recommendations

NICE is aware that patients who have been treated with specific procedures have a unique insight that may be of value to the Committee in formulating its recommendations. NICE is committed to taking this into account in the assessment of interventional procedures, and the outcome of NICE's work in this area will be incorporated into future amendments to, and updates of, the IP Programme's guides.

### 3.2.5 Systematic review

In some situations, the standard IP Programme assessment of a procedure is not appropriate, or is insufficient for the Committee to issue definitive guidance; in these situations a systematic review is requested. This may happen when:

- there is too much relevant evidence to present to the Committee in the evidence summary table, and/or
- evidence is conflicting, and/or



- the impact of the procedure is thought to be potentially important.

In these situations, a systematic review from the Review Body for Interventional Procedures may be requested to inform the development of guidance (see the 'IP Programme manual'). The request may be initiated by the Institute itself, or by the Committee.

### 3.3 Presentation of the evidence to the Committee

The main aim of evidence selection is to highlight the most valid and relevant studies for detailed presentation to the Committee, as part of the evidence summary table in the overview of the procedure. The evidence is often limited, and for some procedures it may be possible to present all the available evidence in the evidence summary table. However, on occasion there may be a considerable number of studies that are potentially relevant (see section 3.2.1 above). If this is the case, the following issues are considered in deciding which studies to prioritise for detailed presentation:

- randomised or non-randomised evidence (randomised takes precedence)
- study size (larger takes precedence)
- length of follow-up (longer takes precedence)
- completeness of follow-up (greater takes precedence)
- in the context of duplicate publications, timeliness and size (the more recent and larger study takes precedence).

In practice, subjective judgements sometimes have to be made, informed by these considerations. Under these circumstances, a second opinion is always sought from another member of the technical team, and any disagreement about the inclusion or exclusion of a particular study is resolved by consensus. If consensus is not possible, a third opinion from another member of the technical team, usually more senior, is also sought. The person offering the third opinion makes the final decision.

The remaining eligible studies that have not been included in the evidence summary table are listed in an appendix, giving brief details of each study and its outcomes. The aim of this appendix is to give a broader overall picture of the procedure and to reinforce the fact that the studies included in the evidence summary table are the most reliable and valid amongst a larger literature. The appendix allows more studies to be listed without making the overview excessively large. It is possible, however, that other potentially relevant studies may not be included in the appendix because they were not identified by the literature search.

Studies that do not contain clinical information on efficacy and safety outcomes (for example, review articles, animal studies or studies reporting on physiological outcomes) are not taken into consideration and are not presented in the overview.

## 4 Analysis of evidence

This section describes how the evidence is analysed and assessed by the Programme team for presentation to the Committee.

### 4.1 The overview

The Programme team prepares an overview of the evidence for each procedure, which forms the basis of the Committee's decision making. The overview normally comprises:

- a lay description of the procedure and the condition being treated
- an initial narrative section that outlines the indications for the procedure, other current treatment options for the relevant condition, and a brief description of what the procedure involves; this section usually includes key aspects of the natural history of the relevant condition
- a narrative summary of key efficacy outcomes (as reported in the reviewed literature)
- a narrative summary of key safety outcomes (as reported in the reviewed literature)
- the evidence summary table, which includes an outline of the design and findings of the included studies
- a narrative summary of comments received from Specialist Advisers about the procedure and its efficacy and safety
- a critical appraisal that highlights specific methodological issues or concerns about the evidence, as perceived by the Programme's technical team
- appendices detailing:
  - the search strategy used for the literature review, and the date of the search
  - studies that met the selection criteria for inclusion but which were not included in the evidence summary table, including reasons for non-inclusion
  - other NICE guidance relevant to the procedure.

The overview is written in language intended to be understood by any healthcare professional without specialist knowledge of a particular procedure or disease area. This is consistent with the Programme's aim of providing advice about the efficacy and safety of interventional procedures to non-expert healthcare professionals and their NHS organisations.

## 4.2 Principles adopted in development of the overview

Studies included in the overview will often have used different terminology to report identical or similar outcomes. For example, erectile dysfunction may also be described as male sexual dysfunction or impotence; insomnia might also be called sleep disturbance. In the absence of a universally accepted nomenclature of signs and symptoms, the Programme team may opt to 'translate' specific signs and symptoms to more widely used or reported terms. The original term is introduced, with an explanation about its subsequent substitution to aid readability and comparisons between studies.

In the overview, the usual way to refer to a quantified outcome expressed as a rate is:  $x\%$  ( $r/n$ ) where  $x$  denotes a percentage value, and  $r$  and  $n$  denote numerator and denominator values, respectively. If a denominator is less than 11, the rate is given as a fraction ( $r/n$ ), without a percentage value. In studies where only  $x\%$  is provided in the primary study report, the  $r/n$  is not usually calculated from assumed values.

Confidence intervals around rate values are not usually calculated, unless they are judged relevant; they may be included in the overview if reported in the primary report and considered relevant.

Statistical comparisons are usually appropriate when comparative data are reported (RCTs or non-randomised controlled trials). When a comparative outcome reported in the studies is judged important for inclusion in the overview, the  $p$  value reported in the primary study is also reported. If no significance level is reported, this is indicated by 'Not reported' or 'NR'.

## 4.3 Evidence summary table

The evidence summary table included in the overview comprises 'Study details', 'Efficacy outcomes', 'Safety outcomes' and 'Comments' (brief critical appraisal) columns.

### 4.3.1 Study details

The column is usually structured as follows (details are included where provided by the primary study report):

- reference (first author – surname and initials – and year)
- study type/design, that is:
  - health technology assessment or systematic review (of RCTs or non-RCT studies)
  - RCT
  - non-randomised controlled trial
  - case series
  - case report

- country (or countries) where study was conducted
- study period
- study sample size (total number of patients and, when relevant, number of patients treated with the procedure of interest)
- population (age, sex and other relevant demographic data)
- indications (exclusion and inclusion criteria, including disease types and subtypes, pathological subtypes, subgroups divided by disease severity scores, as applicable; concomitant medication, if and when relevant)
- technique (details of procedure performed) and comparator (where relevant)
- follow-up period (mean or median where stated)
- details of any conflict of interest declared by the authors of the report.

### 4.3.2 Efficacy and safety outcomes

These two columns present the efficacy and safety outcomes reported in the studies in the most clear and helpful way. Outcomes may be grouped under subheadings where appropriate.

### 4.3.3 Critical appraisal of the evidence ('Comments')

Critical appraisal comments identify issues that might have an influence on the strength of evidence (study type, quality of study and statistical analysis), effect size and relevance (outcomes).

While a number of critical appraisal checklists exist, it is difficult to be prescriptive about using such lists because the relative importance of the dimensions will vary according to the intervention, the indication and the available evidence.

The following issues may be commented upon by the IP analyst when reporting on a primary study or systematic review of primary studies:

- completeness of follow-up for any studies involving post-procedure follow-up; reasons for loss to follow-up; selection of patients for particular outcome assessment
- patient accrual/recruitment method (for example, whether accrual of participants was continuous)
- previous training of operators carrying out the procedure
- previous volume of experience of operators or of participating unit(s) with the procedure
- relevance of outcomes measured

- validity and reproducibility of the measurement of outcomes (for example, blinding)
- appropriateness of analysis (for example, intention-to-treat analysis)
- general considerations about validity and generalisability of the studies, as and when appropriate
- inclusion of the same patients in more than one study
- multiple reporting of a single study.

## 5 The Committee's assessment of the evidence on efficacy and safety

This section describes how the Committee weighs the evidence presented to it. In particular, it explores specific factors underpinning the Committee's consideration of efficacy (section 5.5) and safety (section 5.6).

It also describes how evidence and commentary received as part of the consultation process is considered by the Committee when producing its final recommendations.

### 5.1 Introduction

The Committee makes recommendations about the procedure on the basis of the available evidence relating to its efficacy and safety. Both efficacy and safety may be affected by certain variables about which published evidence provides little or no helpful information. The individual operator and the different devices used to perform procedures are often important in this context.

### 5.2 The operator

For many procedures, the outcomes are influenced by the training, experience and aptitude of the operator. This applies particularly to procedures that require great technical skill, such as complex laparoscopic operations. Many procedures are said to have a 'learning curve'; this may affect outcomes in published series used as evidence, as well as the outcomes for clinicians who start doing procedures de novo. Specialist Advisers are a valuable source of advice about procedures that present particular technological challenges and/or for which special training is desirable. These considerations may influence the Committee's recommendations about the procedure, and are often translated into recommendations about training.

### 5.3 The device

Some procedures require the use of a particular device. This introduces important variables that need to be taken into account in the Institute's guidance.

- Evidence may only be available for a particular device or devices, even though others may be in use.

- New devices may be introduced into the market at any time during the development of the guidance, or after it has been published.
- The technology of devices may advance rapidly. This means that both efficacy and safety outcomes reported in the published literature may not accord with 'current practice' using technologically more advanced devices; further technological progress may alter outcomes still further.

The Committee is mindful of these issues; it makes recommendations based on the available evidence, bearing in mind that it is evaluating the procedure rather than a specific device. The IP guidance may refer to the potentially important influence of different devices on the safety and/or efficacy of the procedure, or to rapid technological developments described by the Specialist Advisers, manufacturers or other sources.

## 5.4 Comparisons with other procedures

The remit of the IP Programme is to consider efficacy and safety. Comparison of a procedure's efficacy with that of established procedures is appropriate when they are used to treat the same condition. This applies also to safety: the frequency and gravity of complications of any established procedure are used as a benchmark against which the complications associated with a new procedure are judged.

Comparison of efficacy is straightforward when randomised studies of established and new procedures are available. The aim of such comparison is to ensure that a new procedure works at least as well as established treatments; evidence of superior efficacy is neither necessary nor usually an expectation. A new procedure may have other advantages, such as being less invasive and/or allowing more rapid recovery.

Any comparison of safety is also aimed at establishing whether the safety profile is at least comparable to that of existing treatments.

Frequently, direct comparisons are not available; in these situations judgements about the efficacy and safety of a new or established procedure need to be made indirectly and/or on the basis of the opinions of Specialist Advisers.

A particular difficulty can be encountered when published data about an established procedure are limited. For some common and well-established procedures, there is little evidence of their efficacy for certain indications or of their safety profile, in particular concerning the incidence of uncommon but serious complications.

## 5.5 Decisions about efficacy

Outcome measures directly relevant to patients and their quality of life are given precedence when making decisions relating to efficacy.

### 5.5.1 Consideration of benefits

The Committee considers the nature of the benefits, their magnitude, the ways in which they can be assessed and their duration. All these criteria need to be judged in the context of the natural history of the condition being treated or investigated, and compared with outcomes following the other available treatment options.

In addition, there needs to be evidence of benefit that is judged sufficient to justify submitting a patient to the procedure and its risks. Minor improvements in outcome measures that do not seem to translate into real clinical improvements will not support a decision that a procedure is efficacious.

### 5.5.2 Outcome measures

Evidence of improved survival, reduced morbidity or improved quality of life carry more weight in decision making than surrogate outcomes (such as those shown by imaging or a biochemical marker). The Committee may identify outcome measures that it considers to be particularly appropriate and suggest these for future research and audit.

### 5.5.3 Consideration of placebo response

In some situations there are no studies that compare an active treatment with a sham procedure and/or standard treatment. In these cases the Committee may issue guidance recommending that comparative studies be performed.

## 5.6 Decisions about safety

No procedure is completely 'safe'; all interventions are associated with risks of one kind or another. Decisions relating to safety need to be made in the context of the natural history of the condition being treated or investigated, and the alternative treatments available.

It is important to point out the difference between a recommendation based on the Committee's assessment that the evidence on safety is adequate (see section 6.2.1) and the concept that a procedure is 'safe'. If the Committee considers that evidence on safety is adequate in quantity and quality, this means that there were sufficient data to inform a decision about safety. A procedure may nevertheless be associated with significant risks of serious complications, but enough is judged to be known about those complications and their frequency to make a decision and to construct recommendations about the use of the procedure.



### 5.6.1 Magnitude and frequency of reported adverse events

When making judgements about safety, both the magnitude (seriousness) and frequency of adverse events need to be considered. A low risk of very damaging complications is generally considered to be a more significant safety issue than a high risk of minor complications. The most important consideration is that patients (or their parents or carers, when appropriate) should be informed and should understand the risks when offered the procedure. This always means telling them the known risks, but in addition it may mean telling them that there is uncertainty about the frequency (risk) of complications – in particular uncommon and serious ones.

### 5.6.2 Quantity of evidence on safety outcomes

The number of reported cases considered adequate to make or support a decision relating to the safety of a procedure is influenced by:

- the natural history of the condition
- the prevalence of the condition
- the expectation of likely adverse events.

For a procedure that is used to treat a rare but rapidly fatal condition, safety data may be considered adequate on the basis of only a few reported cases. In contrast, when considering a procedure for a common condition that is not a serious threat to health and when theoretical concerns have been raised about the possibility of an uncommon but serious complication of the procedure, very large numbers of well-reported cases may be required for its safety to be judged adequately.

### 5.6.3 Quality of evidence on safety outcomes

Decisions relating to safety are strongly influenced by the completeness with which adverse events appear to have been reported in the available studies and case series. Some studies make clear that safety outcomes have not been reported at all, whereas other studies have obviously presented complications in great detail (to the extent that some of those outcomes may be judged as expected sequelae of the procedure). Particular difficulties arise in making decisions about safety in the following circumstances.

- Studies do not report any adverse events but fail to make clear whether none occurred, or whether events were simply not recorded or reported.
- Specialist Advisers refer to specific theoretical complications as matters for concern (and even cite anecdotal complications known to them) but there are no reports of these complications in the published literature; this suggests that the published reports may be inadequate.

- The frequency of adverse events varies markedly between studies.
- Several different devices may be used for the procedure and these are examined differently in the available evidence; that is, different devices may have been examined in different studies and there may be no data on others.

In making decisions relating to safety, the Committee generally adopts a risk-averse approach, preferring to take account of higher complication rates and advice that raises concerns rather than low complication rates (when studies vary) and more optimistic advice. This approach is particularly pertinent when considering procedures for chronic conditions with good overall prognosis.

#### **5.6.4 Impact of adverse events on patients' quality of life**

The Committee tries to take account of the impact of complications on patients' quality of life, informed by their own clinical knowledge and by advice from both patients and specialists. Lay members of the Committee are in a position to make particular contributions in this context. It is recognised that the methodology for evaluating patients' experience in the context of a rapid review of evidence needs further development.

#### **5.6.5 Influence of particular clinicians or teams on the safety of procedures**

The experience and training of clinicians undertaking a procedure may influence the frequency of adverse events, particularly for procedures said to be associated with a steep learning curve. This is discussed in section 5.2 above.

#### **5.6.6 Long-term safety concerns**

Some procedures pose risks of adverse events which only present in the longer term. These may either be suggested by the nature of the procedure (for example, insertion of a prosthesis) or be raised by Specialist Advisers. Lack of long-term safety data is a frequent problem. If there is uncertainty or concern about long-term safety in the context of the condition being treated, the Committee may decide that the safety data are altogether inadequate. If the risk of delayed adverse events is only theoretical or sufficiently remote, the decision made may be simply to advise reporting of these, if and when they occur, in order to inform future practice.

#### **5.6.7 Other safety considerations compared with alternative (comparator) treatments**

Some new procedures have the advantages of being less invasive and traumatic than established alternatives, with the potential for lesser morbidity and shorter length of hospital stay, and greater patient acceptability. These factors may be judged pertinent by the Committee.

## 5.7 Assessment of evidence and commentary obtained at consultation

### 5.7.1 Updated evidence and commentary

During the consultation period, an updated literature search is conducted to find any further evidence that may have been published since the first Committee meeting. Relevant studies that meet the initial inclusion criteria are presented to the Committee to be considered for inclusion in an updated overview. The Committee may decide to include any such studies in the final overview, which is updated by the technical team before final publication of the guidance. This forms the final body of evidence on which the Committee's recommendations are based.

Comments received at consultation frequently include suggestions for further evidence to be considered by the Committee. These may include published or unpublished studies, which are prioritised using the same criteria as outlined in section 3.2.1 above.

### 5.7.2 Patients, carers and the public

Commentary on patients' experiences of the procedure is considered by the Committee in formulating its final recommendations, particularly when issues are raised that are not reported in the published literature. The Committee particularly encourages the submission of statements on efficacy and safety outcomes that are of importance to patients. Descriptions of the benefits or harms of procedures that may only be identified by patients are also of interest, particularly those relating to quality of life, for example:

- comparing life before and after the procedure
- changes induced by the effects of the procedure itself (side effects)
- experience of disease progression with and without the procedure.

Patients' contributions may also provide valuable perspectives on:

- living with the condition
- outcomes that patients value most from the procedure
- the difference the procedure may make to:
  - the physical well-being of patients (symptoms, pain, mobility, disability)
  - lifestyles and the choices that matter to patients and carers (impact on daily activities, work, hobbies, social life, relationships)
  - the psychological health of patients/carers (for example, mood, anxiety, distress)
  - the balance between quality of life and length of life (if appropriate)
  - the various treatment choices that matter to patients and carers.

## 6 Nature and style of recommendations

This section describes the types of recommendations that the Committee can make, and outlines factors considered in making these recommendations. It also describes and defines various terms commonly used in the recommendations.

### 6.1 Introduction

The stated aims of the IP Programme are to protect patients; to support clinicians, hospitals and the NHS; and to foster safe innovation. When introducing new procedures that may benefit both current and future patients, there is some tension between the principles of protecting patients and fostering safe innovation. Undue restriction in the use of a procedure when there is uncertainty about its safety or efficacy could deny patients access to potentially important clinical benefits. In making its recommendations, the Committee's aim is to steer a course between the extremes of obstructing use of a procedure for fear of harm, and allowing its unrestricted use in the expectation of benefit. If the evidence is inadequate or leaves room for uncertainty, recommendations need to allow patients access to a procedure, but with appropriate safeguards.

For any clinician using a new procedure, normal good practice includes informing the hospital management, informing patients clearly and auditing outcomes thoroughly. These principles are translated into guidance as recommendations that clinicians wishing to use a procedure with inadequate or uncertain evidence should do the following.

- Inform their clinical governance lead. This is often the medical director of the hospital. The clinical governance lead is the nominated officer bearing responsibility.
- Make special arrangements for consent. This means following all the normal good practice guidance for consent published by the Department of Health and, in addition, informing patients about the newness of the procedure, the clinician's own experience with it, and any particular uncertainties. Special arrangements for consent should include giving patients thorough written information. (Use of NICE's 'Understanding NICE guidance' is recommended – see next paragraph.)
- Make special arrangements to audit and review their results. This means keeping detailed and accurate records of all patients who have the procedure, including all adverse events and outcome measures of efficacy. These data should be reviewed at appropriate intervals and practice should be changed if the results suggest a need to do so.

The obverse of these recommendations – when evidence on the efficacy and safety of a procedure is deemed adequate – is that clinicians should observe normal arrangements for governance, consent and audit. These arrangements include a clear description of the procedure (including options for anaesthesia if appropriate), its intended benefits, the risks, and information about recovery after the procedure. The normal process of informed consent should also include explanation of the prognosis of the condition without treatment, and alternative treatment options that are available. There is an expectation that clinicians will provide explicit written advice about the procedure. The Institute provides information for patients that explains the guidance produced by NICE ('Understanding NICE guidance'); this is not intended to be detailed advice about the procedure, which should be provided by the clinician(s) responsible for the patient.

## 6.2 Main types of recommendations made by the Committee

### 6.2.1 'Normal' arrangements

In order for a procedure to be recommended for use with normal arrangements, the evidence should be adequate in the following respects.

- It should be valid, relevant and of good quality.
- It should be available in sufficient quantities for the Committee to make a positive decision.
- It should be sufficiently consistent in nature.
- It should demonstrate benefits within an appropriate time of the procedure (short- and/or long-term efficacy). It may not be practical to obtain long-term efficacy evidence for some recently introduced procedures, in which case specific recommendations may be made about the need for more data on long-term outcomes. When long-term safety issues seem relevant, data on these should be adequate or the need for reporting on long-term safety outcomes may be stipulated.
- For a procedure to be recommended for use with normal arrangements, it should also be demonstrated that the frequency and severity of adverse effects of the procedure are similar to, or less than, those of any comparable and established procedures. In exceptional circumstances, the frequency and severity of adverse events may be greater, but this would normally only lead to a recommendation for 'normal arrangements' in the context of much greater benefit: that is, in reasonable proportion to the severity of the condition being treated and the size of clinical benefit obtained; and acceptable in the context of the natural history of the condition.

## 6.2.2 'Special' arrangements

In instances where any of the above conditions are not fulfilled, recommendations are made for clinicians to use the procedure only with special arrangements for consent and/or audit and/or research. It is also stipulated that the clinical governance leads of trusts should be notified. This recommendation is often made when the procedure is considered to be emerging practice in the NHS.

## 6.2.3 'Research only'

In some circumstances, the Committee recommends that the procedure should be carried out only in the context of formal research studies approved by a research ethics committee. This recommendation is often made where:

- the procedure is still considered to be experimental in nature
- the level of uncertainty about the efficacy and/or safety evidence is such that it is considered to be in the best interest of patients to recommend controlled investigation of the procedure under the scrutiny and protection of a research ethics committee
- resolution of substantial uncertainties about its efficacy and/or safety would be fundamental to its routine use.

## 6.2.4 'Should not be used'

The Committee may recommend this for a procedure where the evidence suggests that it has no efficacy and/or poses unacceptable safety risks.

# 6.3 Formulating recommendations

## 6.3.1 Teams and units

It is sometimes recommended that a procedure should only be performed in the context of a particular type of clinical team or unit. Recommendations of this kind are usually based on the opinions of Specialist Advisers or comments received from the consultation, and must take the following factors into account.

- Some procedures can be skillfully done by clinicians of different specialties.
- Appropriate team members and adequate facilities are usually more important than geographical location or particular named hospitals.

- Specialist teams may require members to contribute to patient selection, counselling, carrying out the procedure, dealing with unexpected problems, care during recovery, adjuvant treatments and rehabilitation. Recommendations may stipulate that particular team members are considered essential. They may state that the team 'should include' particular specialists, but recognise that different specialists may make up appropriate teams in different units. Supporting services to deal with potential problems arising from a procedure do not necessarily need to be on the same site, provided that appropriate arrangements are in place to access such services without delay if the need arises.

Recommendations are not normally made about the number of procedures (or similar procedures) that should be carried out regularly or should have been performed previously by a clinician or unit, even though this is sometimes suggested during consultation. It is recognised that some units will be starting to use a procedure de novo and that they may not initially be able to perform substantial numbers. The important issues are appropriate training and thorough audit within a clinical governance framework, both during the introduction phase of the procedure and thereafter.

### 6.3.2 Training

It is expected that consultants should be adequately trained to perform procedures within their specialty. Similarly, it is expected that consultants involved in the delivery of a diagnostic or therapeutic intervention that involves radiation exposure are accredited in its use. Therefore, specific recommendations about training are made only when particular training issues have been raised by Specialist Advisers, comments from consultation or publications. Most often these issues relate to particular technical challenges that may necessitate a level of training, expertise or experience above the norm for a specialist in the relevant discipline. Special knowledge and training may also be needed to use certain devices, including those that deliver energy such as laser, radiofrequency or ultrasound.

In making recommendations about training, the Committee is mindful that specialists have developed procedures de novo and that these procedures have often been adopted quite appropriately by other practitioners using their existing skills. Consultants are, by definition, 'fully trained' in their own specialty. The term 'training', as used in the Committee recommendations, is intended to encapsulate all ways of acquiring knowledge and skills from others, such as mentoring and proctoring.

Where possible, the Committee seeks to identify procedures that require an enhanced level of training and/or experience and to reflect this in their recommendations. Specifying the kind of training required is not possible unless published standards exist or there are training courses that have been recognised and supported by the appropriate professional organisations. If Specialist Advisers are emphatic that specific training is essential, and if no published standards exist, then the Institute may approach professional organisations with a request to publish standards that can be referred to in the guidance. Training and/or standards that are already provided by professional organisations are referenced in the guidance.

For some procedures, specialist training for members of the theatre team other than the operators may also be required and this will be reflected in the guidance.

### 6.3.3 Research

When data on efficacy and/or safety are inadequate, the recommendations usually state that further published outcomes would be helpful, and that the Institute may review the guidance when further evidence is available. The kinds of outcomes that are required are often specified, for example quality-of-life measures or long-term outcomes.

If an appropriate research project is in progress or is nearing the stage of recruitment, a recommendation may be made for clinicians to enter patients into that study. This always involves the Committee making a judgement that the project is both viable and open to recruitment of patients from all clinicians who are likely to want to perform the procedure. If this is the case, a recommendation to enter patients into the study is considered likely to be of benefit to recruitment, and to lead to more rapid accrual of data that will inform further guidance.

The situation is more difficult when additional research data would clearly be of value but where there are no ongoing studies into which clinicians might be recommended to enter patients. This is the most common situation. The practical and procedural obstacles and resource requirements for setting up new clinical research projects are considerable, and the delay between deciding to address a research question and starting to recruit patients may be prolonged.

### 6.3.4 Registers

The Committee may recommend data entry into an appropriate register or database relating to the procedure if one is known to be in operation. This is most often recommended for procedures that receive a recommendation for 'special arrangements' for consent and audit or research. Where a piece of IP guidance recommends special arrangements for audit, the Institute issues audit criteria on publication of the guidance.

### 6.3.5 Other recommendations

Additional recommendations may be made, for example, on whether evidence indicates that certain patient subgroups may derive a greater or lesser benefit or be at a greater or lesser risk from a procedure, and about regulatory issues, such as off-label use of pharmaceutical products as part of the procedure.



## 6.4 Wording of recommendations on efficacy and safety

Recommendations need to take into account efficacy and safety in both the short and the longer term. The relative importance of either short- or long-term outcomes may vary according to the nature of the condition (for example whether it is acute or chronic). Long-term outcomes are particularly important in cancer. Often, explicit statements are made about each of these four aspects (that is, efficacy in the short and long term, and safety in the short and long term). However, sometimes specific reference to each is implicit or unnecessary on the basis of the clinical knowledge, or because long-term follow-up considerations may, by their nature, be inapplicable for certain procedures and conditions. The considerations are outlined below.

### 6.4.1 Short-term efficacy

This is almost always important. A procedure that does not provide benefit in the short term is unlikely to be considered efficacious. Short-term efficacy may sometimes be the only requirement. For example, for a new procedure to treat an acute illness such as appendicitis, the expectation of long-term benefit is implicit once the appendix has been removed and the patient has recovered.

### 6.4.2 Long-term efficacy

This can be a problem for procedures that have not been used for sufficiently long to allow lengthy follow-up studies, so that the evidence on long-term efficacy is small in quantity or of poor quality. Examples of procedures that must have durable results to be considered efficacious are insertion of prosthetic joint components, procedures to relieve urinary or faecal incontinence, and procedures intended to cure cancers.

### 6.4.3 Short-term safety

This is always important and includes complications (morbidity and mortality) during the procedure and shortly afterwards. Interventional specialties commonly use the first 30 days after the procedure as the interval for 'postoperative complications' in reported series.

### 6.4.4 Long-term safety

For some procedures, long-term safety is not an important consideration. This applies, for example, to many techniques used for ablation of the endometrium, tumours or varicose veins. Any adverse events are all likely to occur within a short time of the procedure and are not expected at a later stage. This contrasts with procedures involving insertion of prosthetic material, in which the possibility of adverse events in the long term is almost always relevant.

## 7 Publication of the guidance

Following consultation and the review of updated evidence and commentary (see section 5.7 above), the NICE Guidance Executive receives and considers the draft guidance on behalf of the Board of NICE. NICE then issues the guidance to the NHS in England, Wales and Scotland and the HSS in Northern Ireland. Information for patients is also issued at the same time.

Guidance is published in both printed and electronic form. Each piece of guidance is explained in a document produced by NICE called 'Understanding NICE guidance'. If appropriate, audit criteria are also produced. All documents relating to the guidance are published on the NICE website.

More information about the IP Programme can be found on the NICE website ([www.nice.org.uk/ip](http://www.nice.org.uk/ip)).

## Glossary

### **Abstract (of a published study)**

Summary of a published study, as an introduction to a full scientific paper. Abstracts of scientific papers can usually be retrieved through literature search engines.

### **Abstract (conference)**

Summary of an as-yet unpublished study, presented at a scientific conference. Although such abstracts may be retrievable through literature search engines, they are not peer reviewed, and they do not always result in a subsequent publication. Subsequent publications may differ in content to the original conference abstracts.

### **Adverse event**

An undesirable outcome resulting from a healthcare intervention (including drug or interventional procedure) but not necessarily caused by it. May also be referred to as a 'complication'.

### **Audit**

The evaluation of clinical performance against standards or through comparative analysis, with the aim of informing the management of services. Where a piece of IP guidance recommends special arrangements for audit, the Institute issues audit criteria on publication of the guidance.

### **Bias**

Systematic (as opposed to random) deviation of the results of a study from the 'true' results caused by the way the study is designed or conducted.

### **Case report**

An uncontrolled observational study involving an intervention and outcome in a single patient.

### **Case series**

Report of a number of cases of a given condition, usually covering the course of the condition and the response to treatment. There is no comparison (control) group of patients.

## **CE Mark**

A CE Mark indicates that the manufacturer of a medical device complies with the relevant European Union Directive on safety, quality and performance.

## **Cochrane Library**

A regularly updated electronic collection of evidence-based medicine databases, including the Cochrane Database of Systematic Reviews.

## **Commentary**

Refers to Specialist Adviser opinion, and/or information about an interventional procedure, or to the peer-reviewed literature relating to the interventional procedure of interest.

## **Comparator**

An alternative treatment against which the intervention under appraisal is compared. The comparator could be standard treatment (including on occasions expectant management or no intervention) or a sham procedure.

## **Confidence interval**

A measure of the uncertainty around the main finding of a statistical analysis. Estimates of quantities, such as the relative risk or the odds ratio comparing an experimental intervention with a control, are usually presented as a point estimate and a 95% confidence interval.

## **Consultee**

An individual or organisation who submits a response to an interventional procedure consultation document.

## **Control**

An explicitly defined comparator against which the effects of an intervention are compared in a clinical study.

## Critical appraisal

The process of assessing and interpreting evidence by systematically considering its validity, results and relevance.

## Device

A piece of equipment used for diagnostic or therapeutic purposes, at times in conjunction with (a) pharmaceutical agent(s).

## Effectiveness (clinical)

An effective procedure is one that produces benefits compared with other interventions that patients value in routine use. To be considered effective, the procedure must have been assessed in more standard clinical settings than is the case for efficacy.

## Efficacy

An efficacious procedure is one that produces a desirable outcome in research conditions.

## EMBASE

Excerpta Medica database. A European database of medical and health research.

## EMTREE

A controlled vocabulary used for EMBASE and other similar databases.

## Evidence

Information on which a decision or guidance is based. Evidence is obtained from a range of sources and methodologies, most usually from peer-reviewed publications.

## Evidence summary table (in overview)

A summary in a tabular format of the design, methods, results and brief critical appraisal of the studies judged to be most valid and relevant in relation to the interventional procedure of interest.

### **Exclusion criteria (primary clinical study)**

Criteria that define individuals who are not eligible to participate in a clinical study.

### **Exclusion criteria (review of primary studies)**

Criteria that define individual primary studies that are not eligible for inclusion in a review.

### **Follow-up**

Observation of clinical study participants over a period of time to measure outcomes under investigation.

### **Generalisability**

The extent to which the results of a study relating to a particular patient population and/or context hold true for other patient populations and/or different contexts.

### **Health technology assessment**

A set of activities that involves the collection, synthesis and analysis of various types of data collected from various sources to address the safety, efficacy, effectiveness and economic implications of a technology.

### **Indication**

A condition that may make a patient eligible for a particular treatment or procedure.

### **Inclusion criteria (literature review)**

Explicit criteria used to decide which studies should be considered as potential sources of evidence.

### **Interventional procedure**

A procedure used for diagnosis or treatment that involves incision, puncture or entry into a body cavity, or the use of ionising, electromagnetic or acoustic energy.

## **Interventional Procedures Advisory Committee (IPAC)**

The Committee is responsible for advising NICE on the safety and efficacy of interventional procedures.

## **Interventional Procedures Guidance**

Guidance on the use of an interventional procedure based on current evidence of its safety and efficacy, issued by NICE after consultation has ended and the Committee has met to discuss comments received at consultation.

## **Learning curve**

The process by and period during which an individual surgeon and/or surgical team achieves proficiency in a particular surgical procedure. It relates mostly to complex and difficult procedures that require subspecialty expertise and skills.

## **Medline**

An online, open-access, searchable electronic database produced by the US National Library of Medicine (NLM).

## **MeSH**

Medical subject headings, the controlled vocabulary used for Medline and certain other US National Library of Medicine MEDLARS databases

## **Meta-analysis**

A statistical technique for combining (pooling) the results of a number of studies that address the same question and report on the same outcomes to produce a summary result. The aim is to derive more accurate and clear information from a large data pool. Meta-analysis is generally more likely than the individual trials to reliably confirm or refute a hypothesis.

## **National Institute for Health and Clinical Excellence (NICE)**

NICE is an independent organisation responsible for providing national guidance on promoting good health and preventing and treating ill health.

## **Non-randomised controlled study**

Any study of an intervention compared with another intervention (whether looking at harm or benefit) that does not use randomisation to allocate patients to comparison groups.

## **Operator**

The individual clinician who performs a procedure – he or she may be a surgeon, interventional radiologist, radiotherapist, interventional physician, etc.

## **Outcome**

The clinical effect that results from exposure to a healthcare intervention.

## **Overview**

A document produced by NICE to inform the Committee about an interventional procedure. It contains information on the indications for the procedure, a description of the procedure, a summary of key points from a rapid review of the literature, and a summary of commentary by the Specialist Advisers.

## **p value**

The probability (ranging from 0 to 1) that the observed results could have occurred by chance. The lower the probability value the more likely that the observed difference is not due to chance.

## **Patient-focused outcome**

Any health outcome that is directly meaningful to the patient (for example survival, mortality, morbidity, quality of life). Such outcomes should be distinguished from surrogate outcomes (defined below).

## **PICO**

An acronym for population, intervention, comparator, outcome – a framework used to define a clinical question.

## **Placebo (sham procedure)**

An inactive substance or interventional procedure administered to a study participant, against which to compare the effects of an active drug or interventional procedure.



## **Randomised controlled trial (RCT)**

A comparative study in which participants are allocated randomly to intervention and control groups, and are followed up to examine differences in outcomes between the groups.

## **Rapid review**

A review of the literature that is systematic but not exhaustive (for example not including direct contact with study authors, or manual searches of journals).

## **Register**

A type of database for observations and related information about a group of patients, a disease or an intervention, for the purpose of analysis.

## **Review Body for Interventional Procedures**

A consortium of two UK universities, commissioned by NICE to undertake systematic reviews on the safety and efficacy of interventional procedures.

## **Risk**

The proportion of participants experiencing the adverse event of interest.

## **Safety**

Refers to adverse effects, such as those that threaten life, require or prolong hospitalisation, or result in permanent disability or subjective symptoms.

## **Search strategy**

The combination of terms used to identify studies in an electronic database such as Medline.

## **Serious adverse event**

An adverse event resulting in death, hospitalisation, prolonged hospital stay or long-term loss of function.

## **Sham (placebo) procedure**

An inactive substance or interventional procedure administered to a study participant, against which to compare the effects of an active drug or interventional procedure.

## **Specialist Adviser**

A person nominated by a relevant professional organisation to advise the IP Programme about procedures that have been notified.

## **Stakeholder**

An individual or organisation with an interest in the Programme's activities and outputs.

## **Surrogate outcome**

An outcome measure that is not of direct clinical importance but may be associated with patient-focused clinical outcomes, such as one based on imaging findings or measurement of a biochemical marker. Should be distinguished from 'patient-focused outcome' (defined above).

## **Systematic review**

A summary of several individual research reports. It is prepared by comprehensive searching for reports eligible for inclusion, unbiased assessment of their validity and methodical comparison of the study quality and findings.

## **Technical team**

Members of the IP Programme team with responsibility for the technical aspects of the assessment process, including scoping the topic, selecting and analysing the evidence that forms the basis of the overview and advising on technical aspects in the consultation documents.

## **'Understanding NICE guidance'**

A document issued by NICE for patients and carers that summarises the recommendations in the NICE guidance in everyday language.

## **Validity**

The degree to which a result (of a measurement or study) is likely to be true and free of bias (systematic errors).



**National Institute for  
Health and Clinical Excellence**

MidCity Place  
71 High Holborn  
London  
WC1V 6NA

[www.nice.org.uk](http://www.nice.org.uk)

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