



## Complete Summary

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### GUIDELINE TITLE

Management of obstructive sleep apnoea/hypopnoea syndrome in adults. A national clinical guideline.

### BIBLIOGRAPHIC SOURCE(S)

Scottish Intercollegiate Guidelines Network (SIGN). Management of obstructive sleep apnoea/hypopnoea syndrome in adults. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2003 Jun. 35 p. (SIGN publication; no. 73). [158 references]

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## SCOPE

### DISEASE/CONDITION(S)

Obstructive sleep apnoea/hypopnoea syndrome

Note: The guideline is not intended to exhaustively cover all causes of excessive daytime sleepiness in adults nor does it deal with central sleep apnoea or specifically with snoring.

### GUIDELINE CATEGORY

Diagnosis  
Evaluation  
Treatment

### CLINICAL SPECIALTY

Family Practice  
Internal Medicine  
Otolaryngology

Pulmonary Medicine  
Sleep Medicine  
Surgery

#### INTENDED USERS

Advanced Practice Nurses  
Allied Health Personnel  
Nurses  
Physician Assistants  
Physicians

#### GUIDELINE OBJECTIVE(S)

To produce recommendations which can be used to aid patients, general practitioners (GPs), secondary care physicians, and surgeons to recognize the symptoms of obstructive sleep apnoea/hypopnoea syndrome, to prioritise referral requests, to understand how sufferers may be investigated and which treatment modalities are currently available

#### TARGET POPULATION

Males and females over the age of 16 years with obstructive sleep apnoea/hypopnoea syndrome

#### INTERVENTIONS AND PRACTICES CONSIDERED

##### Diagnosis

1. Epworth Sleepiness Scale (ESS)
  - Referral to a sleep centre
    - Multiple Sleep Latency Test (MSLT)
    - Maintenance of wakefulness test (MWT)
2. Physical examination
3. Diagnostic Tools
  - Recommended:
    - Sleep studies
    - Polysomnography (PSG)
    - Oximetry
  - Considered but not recommended:
    - Flow volume loops
    - Radiological imaging
    - Questionnaires
    - Nasendoscopy under sedation

##### Treatment

1. Behavioural interventions
  - Weight loss
  - Smoking cessation
  - Avoidance of alcohol and sedatives or sleeping tablets

- Change of sleeping position
- 2. Non-surgical interventions
  - Continuous positive airway pressure (CPAP)
  - Bi-level positive airway pressure for patients with ventilatory failure
  - Intra-oral devices
- 3. Pharmacological interventions (not recommended)
- 4. Surgical interventions
  - Uvulopalatopharyngoplasty (UPPP) or laser-assisted uvulopalatopharyngoplasty (LAUP) is considered but not recommended
  - Tracheostomy
  - Other surgical techniques including mandibular advancement, suprahyoid testing, bariatric (weight reducing) surgery, and nasal surgery (not recommended)

#### MAJOR OUTCOMES CONSIDERED

- Severity of obstructive sleep apnoea/hypopnoea syndrome (OSAHS) using apnoea/hypopnoea index (AHI) or respiratory disturbance index (RDI)
- Sleepiness measures (cognitive function, vigilance, mood)
- Vitals including blood pressure, heart rate, oxygen saturation
- Effectiveness of diagnostic tools (sleep studies, polysomnography)
- Cost effectiveness of treatment
- Patient driving/quality of life

## METHODOLOGY

#### METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

#### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence base for this guideline was synthesised in accordance with Scottish Intercollegiate Guidelines Network (SIGN) methodology. A systematic review of the literature was carried out using an explicit search strategy devised by a SIGN Information Officer in collaboration with members of the guideline development group.

Internet searches were carried out on the Web sites of the Canadian Practice Guidelines Infobase, the New Zealand Guidelines Programme, the UK Health Technology Assessment Programme, the US National Guidelines Clearinghouse, and the US Agency for Healthcare Research and Quality. Searches were also carried out using Google and OMNI search engines, and all suitable links followed up.

Database searches were carried out on the Cochrane Library, Embase, Medline, and Psychological Abstracts. With the exception of the Cochrane Library, all searches were restricted to the period 1991 to 2000. The Medline

version of the main search strategies is available on the SIGN Web site, in the section covering supporting material for published guidelines.

The main searches were supplemented by material identified by individual members of the development group.

#### NUMBER OF SOURCE DOCUMENTS

Not stated

#### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

#### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

##### Levels of Evidence

1++: High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

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

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

2++: High quality systematic reviews of case control or cohort or studies; high quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

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

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

3: Non-analytic studies, e.g. case reports, case series

4: Expert opinion

#### METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses  
Systematic Review

#### DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The Scottish Intercollegiate Guidelines Network (SIGN) carries out comprehensive systematic reviews of the literature using customized search strategies applied to a number of electronic databases and the Internet. This is often an iterative process whereby the guideline development group will carry out a search for existing guidelines and systematic reviews in the first instance and, after the results of this search have been evaluated, the questions driving the search may be redefined and focused before proceeding to identify lower levels of evidence.

Once papers have been selected as potential sources of evidence, the methodology used in each study is assessed to ensure its validity. SIGN has developed checklists to aid guideline developers to critically evaluate the methodology of different types of study design. The result of this assessment will affect the level of evidence allocated to the paper, which in turn will influence the grade of recommendation it supports.

Additional details can be found in the companion document titled "An Introduction to the SIGN Methodology for the Development of Evidence-based Clinical Guidelines" (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50]). Available from the [SIGN Web site](#).

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

### Expert Consensus

## DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The process for synthesising the evidence base to form graded guideline recommendations is illustrated in the companion document "An Introduction to the SIGN Methodology for the Development of Evidence-based Clinical Guidelines" (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50]). Available from the [Scottish Intercollegiate Guidelines Network \(SIGN\) Web site](#).

Evidence tables should be compiled, summarizing all the validated studies identified from the systematic literature review relating to each key question. These evidence tables form an important part of the guideline development record and ensure that the basis of the guideline development group's recommendations is transparent.

In order to address how the guideline developer was able to arrive at their recommendations given the evidence they had to base them on, SIGN has introduced the concept of considered judgement.

Under the heading of considered judgement, guideline development groups are expected to summarise their view of the total body of evidence covered by each evidence table. This summary view is expected to cover the following aspects:

- Quantity, quality, and consistency of evidence

- Generalisability of study findings
- Applicability to the target population of the guideline
- Clinical impact (i.e., the extent of the impact on the target patient population, and the resources need to treat them.)

Guideline development groups are provided with a pro forma in which to record the main points from their considered judgement. Once they have considered these issues, the groups are asked to summarise their view of the evidence and assign a level of evidence to it, before going on to derive a graded recommendation.

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

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

On occasion, there is an important practical point that the guideline developer may wish to emphasise but for which there is not, nor is their likely to be, any research evidence. This will typically be where some aspect of treatment is regarded as such sound clinical practice that nobody is likely to question it. These are marked in the guideline as "good practice points." It must be emphasized that these are not an alternative to evidence-based recommendations, and should only be used where there is no alternative means of highlighting the issue.

#### RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

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

A: At least one meta-analysis, systematic review of randomised controlled trials (RCTs), or RCT rated as 1++ and directly applicable to the target population; or

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

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

Extrapolated evidence from studies rated as 1+ or 1+

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

Extrapolated evidence from studies rated as 2+

D: Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+

## COST ANALYSIS

### Economic Analysis of Continuous Positive Airway Pressure (CPAP) Usage

Patients with undiagnosed obstructive sleep apnoea/hypopnoea syndrome (OSAHS) are heavy users of the healthcare system. Expenditure on undiagnosed patients is approximately twice that of age and gender matched controls. This difference extends back over 10 years prior to the diagnosis of OSAHS being made.

Treatment with continuous positive airway pressure (CPAP) reduces these costs with evidence of decreased hospitalisation due to cardiovascular and pulmonary disease. Hospitalisation and other costs associated with road traffic accidents are also reduced in those using CPAP therapy. Overall mean hospitalization days per year decreased with CPAP use.

There is a need for more studies on the cost effectiveness of CPAP and other treatments for OSAHS. One study carried out in 1994 has estimated that CPAP resulted in an average gain of 5.4 Quality Adjusted Life Years (QALYs) at a cost of Canadian \$3,400 to \$9,800/QALY gained, equivalent to £1,500 to £4,400. A British study suggests a cost of £3,200/QALY gained over a five year period. These do not include any benefits that would be expected to accrue from a decrease in blood pressure (BP) or road traffic accident decrease with CPAP treatment. These studies indicate a cost-effectiveness ratio in line with other routinely funded procedures within the NHS, but more studies are needed to confirm this (see Annex 2 in the original guideline document).

## METHOD OF GUIDELINE VALIDATION

External Peer Review

Internal Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

A national open meeting is the main consultative phase of Scottish Intercollegiate Guidelines Network (SIGN) guideline development, at which the guideline development group present their draft recommendations for the first time.

The national open meeting for this guideline was held on 3 April 2001 and was attended by 77 representatives of all the key specialties relevant to the guideline. The draft guideline was also available on the SIGN web site for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

The guideline was also reviewed in draft form by independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline.

As a final quality control check, the guideline is reviewed by an Editorial Group comprising the relevant specialty representatives on SIGN Council to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Note from the Scottish Intercollegiate Guidelines Network (SIGN) and National Guideline Clearinghouse (NGC): In addition to these evidence-based recommendations, the guideline development group also identifies points of best clinical practice in the original guideline document.

The strength of recommendation grading (A-D) and level of evidence (I++-4) are defined at the end of the "Major Recommendations" field.

#### Diagnosis

C - All patients who have suspected sleep apnoea and their partners should complete an Epworth questionnaire to subjectively assess the degree of pretreatment sleepiness.

#### Diagnostic Tools

B - Limited sleep studies to assess respiratory events are an adequate first-line method of diagnostic assessment for obstructive sleep apnoea/hypopnoea syndrome (OSAHS).

#### Treatment

## Behavioural Interventions

C - Weight loss should be encouraged in all patients with obesity contributing to their OSAHS. Attempts at weight loss should not delay the initiation of further treatment. Weight loss should also be encouraged as an adjunct to continuous positive airway pressure (CPAP) or intra-oral devices as it may allow discontinuation of therapy.

## Non-Surgical Interventions

### CPAP

A - CPAP is the first choice therapy for patients with moderate or severe OSAHS that is sufficiently symptomatic to require intervention.

C - Persistent low CPAP use (less than two hours per night) over six months, following efforts to improve patient comfort, should lead to a review of treatment.

B - Bi-level ventilation should not be used routinely in OSAHS but should be reserved for patients with ventilatory failure.

### Intra-Oral Devices

A - Intra-oral devices are an appropriate therapy for snorers and for patients with mild OSAHS with normal daytime alertness.

B - Intra-oral devices are an appropriate alternative therapy for patients who are unable to tolerate CPAP.

D - The use of intra-oral devices should be monitored following initiation of therapy to allow device adjustment and assessment of OSAHS control and symptoms.

## Pharmacological Therapy

A - Pharmacological therapy should not be used as first line therapy for OSAHS.

## Surgical Intervention

B - Use of uvulopalatopharyngoplasty (UPPP) or laser-assisted uvulopalatopharyngoplasty (LAUP) for the treatment of OSAHS is not recommended.

D - Patients being offered palatal surgery should be informed of the risk of difficulty with CPAP use if they later develop OSAHS.

## Effects of Treatment on driving and quality of life

A - CPAP should be considered for the improvement of driving ability in patients with severe OSAHS as it reduces daytime sleepiness.

Definitions:

Grades of Recommendation

A: At least one meta-analysis, systematic review of randomised controlled trials (RCTs), or RCT rated as 1++ and directly applicable to the target population; or

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

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

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

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

Extrapolated evidence from studies rated as 2++

D: Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+

Levels of Evidence

1++: High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

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

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

2++: High quality systematic reviews of case control or cohort studies; high quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

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

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

3: Non-analytic studies, e.g. case reports, case series

4: Expert opinion

CLINICAL ALGORITHM(S)

None provided

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Reduced daytime sleepiness
- Improved driving performance
- Improved quality of life
- Reduced blood pressure
- Improved mood

POTENTIAL HARMS

Side Effects for Continuous Positive Airway Pressure (CPAP)

Major side effects of CPAP use (e.g., significant epistaxis, paranasal sinusitis) are rare, but minor side effects (rhinitis, nasal bridge sores, discomfort, claustrophobia, abdominal bloating, noise) are common. Nasal symptoms are usually due to mouth leaks causing high flows of cool air through the nose. Attempts should be made to reduce these using chin straps or full face masks. In a few patients nasal corticosteroids can be useful. A heated humidifier may help to improve comfort and compliance.

## QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guideline is not intended to be construed or to serve as a standard of medical 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. These parameters of practice should be considered guidelines only. Adherence to them 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 regarding a particular clinical procedure or treatment plan must be made by the doctor, following discussion of the options with the patient, in light of 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 fully documented in the patient's case notes at the time the relevant decision is taken.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation of national clinical guidelines is the responsibility of each National Health System (NHS) Trust and is an essential part of clinical governance. It is acknowledged that every Trust cannot implement every guideline immediately on publication, but mechanisms should be in place to ensure that the care provided is reviewed against the guideline recommendations and the reasons for any differences assessed and, where appropriate, addressed. These discussions should involve both clinical staff and management. Local arrangements may then be made to implement the national guideline in individual hospitals, units and practices, and to monitor compliance. This may be done by a variety of means including patient-specific reminders, continuing education and training, and clinical audit.

Key points for audit are identified in the original guideline document.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better  
Living with Illness

### IOM DOMAIN

Effectiveness  
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Scottish Intercollegiate Guidelines Network (SIGN). Management of obstructive sleep apnoea/hypopnoea syndrome in adults. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2003 Jun. 35 p. (SIGN publication; no. 73). [158 references]

## ADAPTATION

Not applicable: The guideline was not adapted from another source.

## DATE RELEASED

2003 Jun

## GUIDELINE DEVELOPER(S)

Scottish Intercollegiate Guidelines Network - National Government Agency  
[Non-U.S.]

## SOURCE(S) OF FUNDING

Scottish Executive Health Department

## GUIDELINE COMMITTEE

Not stated

## COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Guideline Development Group: Dr Tom Mackay (Chairman), Consultant Respiratory Physician, Sleep Centre, Edinburgh Royal Infirmary; Dr Steve Banham, Consultant Respiratory Physician, Glasgow Royal Infirmary; Miss Alison Beattie, Senior Dietitian, Department of Nutrition and Dietetics, Perth Royal Infirmary; Dr Roger Carter, Principal Scientist, Glasgow Royal Infirmary; Dr Alistair Dorward, Consultant Physician, Royal Alexandra Hospital, Paisley; Dr Heather Engelman, Senior Research Fellow, Sleep Centre, Edinburgh Royal Infirmary; Professor Colin Espie, Clinical Psychologist, Glasgow University; Mrs Jean Gall, Chair, Scottish Association for Sleep Apnoea; Mr Robin Harbour, Quality and Information Director, Scottish Intercollegiate Guidelines Network (SIGN); Sister Carol Hoy, Senior Specialist Sleep Nurse, Sleep Centre, Edinburgh Royal Infirmary; Dr Peter Hutchison, General Practitioner, Dumfries; Dr William Kinnear, Consultant Physician, University Hospital, Nottingham; Mr Jim McDonald, Consultant Orthodontist, Edinburgh; Dr Moray Nairn, Programme Manager, SIGN; Dr Janet Pollock, Consultant Anaesthetist, Southern General Hospital, Glasgow; Dr Michal Scullion, General Practitioner, Alexandria; Dr Robin Smith, Consultant Respiratory Physician, Ninewells Hospital, Dundee; Professor John Stradling, Consultant Respiratory Physician, Churchill Hospital, Oxford; Mr Paul White, Consultant Otolaryngologist, Ninewells Hospital, Dundee

## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All members of the Scottish Intercollegiate Guidelines Network (SIGN) guideline development groups are required to complete a declaration of interests, both personal and non-personal. A personal interest involves payment to the individual concerned (e.g., consultancies or other fee-paid work commissioned by or shareholdings in the pharmaceutical industry); a

non-personal interest involves payment which benefits any group, unit or department for which the individual is responsible (e.g., endowed fellowships or other pharmaceutical industry support). Details of the declarations of interest of any guideline development group member(s) are available from the Scottish Intercollegiate Guidelines Network executive.

#### ENDORSER(S)

British Thoracic Society

#### GUIDELINE STATUS

This is the current release of the guideline.

Any amendments to the guideline in the interim period will be noted on [Scottish Intercollegiate Guidelines Network \(SIGN\) Web site](#).

#### GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [Scottish Intercollegiate Guidelines Network \(SIGN\) Web site](#).

#### AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Quick reference guide: Management of obstructive sleep apnoea/hypopnea syndrome in adults. A national clinical guideline. Scottish Intercollegiate Guidelines Network, 2003. 2 p. Available in Portable Document Format (PDF) from the [Scottish Intercollegiate Guidelines Network \(SIGN\) Web site](#).
- SIGN 50: A guideline developer's handbook. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network. (SIGN publication; no. 50). Available from the [SIGN Web site](#).
- Appraising the quality of clinical guidelines. The SIGN guide to the AGREE (Appraisal of Guidelines Research & Evaluation) guideline appraisal instrument. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network, 2001. Available from the [SIGN Web site](#).

#### PATIENT RESOURCES

The following is available:

- Information for discussion with patients and carers. In: Management of obstructive sleep apnoea/hypopnea syndrome in adults. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2003 Jun. 50 p. (SIGN publication; no. 73).

Electronic copies: Available in Portable Document Format (PDF) from the [Scottish Intercollegiate Guidelines Network \(SIGN\) Web site](#).

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

## NGC STATUS

This NGC summary was completed by ECRI on April 26, 2004. The information was verified by the guideline developer on July 15, 2004.

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If you wish to replicate or reproduce guidelines, or if you have a commercial interest in any aspect of the guidelines, you must first obtain agreement from SIGN. To do this, please contact [sign@rcpe.ac.uk](mailto:sign@rcpe.ac.uk).

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