



Complete Summary

GUIDELINE TITLE

Control of pain in adults with cancer. A national clinical guideline.

BIBLIOGRAPHIC SOURCE(S)

Scottish Intercollegiate Guidelines Network (SIGN). Control of pain in adults with cancer. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2008 Nov. 71 p. (SIGN publication; no. 106). [264 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline will be considered for review in three years. Any updates to the guideline in the interim period will be noted on [Scottish Intercollegiate Guidelines Network \(SIGN\) Web site](#).

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
CONTRAINDICATIONS
QUALIFYING STATEMENTS
IMPLEMENTATION OF THE GUIDELINE
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Pain in patients with cancer

GUIDELINE CATEGORY

Management
Screening
Treatment

CLINICAL SPECIALTY

Anesthesiology
Family Practice
Internal Medicine
Nursing
Oncology
Pharmacology
Physical Medicine and Rehabilitation
Psychology
Radiology
Surgery

INTENDED USERS

Advanced Practice Nurses
Nurses
Occupational Therapists
Pharmacists
Physical Therapists
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians

GUIDELINE OBJECTIVE(S)

To provide recommendations based on current evidence for best practice in the management of pain in adult patients who have cancer

Note: The guideline includes advice mainly concerning pain secondary to the cancer, but many of the principles outlined are applicable to coexisting painful conditions and pain secondary to treatment of the cancer.

TARGET POPULATION

Patients aged 12 and over with pain due to cancer

Note: This guideline excludes the treatment of pain in children under the age of 12.

INTERVENTIONS AND PRACTICES CONSIDERED

1. Patient issues
 - Effective communication
 - Multidisciplinary approach to care that includes spiritual, psychological and emotional impact of pain
 - Patient education and support
2. Psychosocial issues
 - Routine screening for psychological distress
 - Cognitive behavior therapy (CBT)
 - Biopsychosocial approach that addresses patient adherence
3. Assessment of pain
 - Clinical history and physical examination

- Pain assessment tools (e.g., McGill Pain Questionnaire, Brief Pain Inventory, self-assessment and observational pain scales)
- 4. Principles of pain management
 - World Health Organization (WHO) cancer pain relief program
 - WHO analgesic ladder
- 5. Treatment with non-opioid drugs
 - Paracetamol and/or non-steroidal anti-inflammatory drugs (NSAIDs)
 - Bisphosphonates
 - Antidepressants
 - Anticonvulsants
 - Other analgesics
- 6. Treatment with opioid drugs
 - Choice of opioid (e.g., morphine or diamorphine)
 - Administration of opioid (e.g., orally, continuous subcutaneous infusion, transdermal administration)
- 7. Non-pharmacological treatment
 - Radiotherapy
 - Cementoplasty
 - Anaesthetic interventions
 - Complementary therapies (considered but not recommended)

MAJOR OUTCOMES CONSIDERED

- Pain control
- Development of further pain
- Functional ability
- Quality of life
- Adverse effects of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Quantitative Search Parameters

The literature review for this guideline addressed a set of key questions defined by the guideline development group (*see Annex 3*). Searches were carried out for the period 1997 – June 2007. Databases used were the Cochrane Database of Systematic Reviews, Cochrane Controlled Trials Register, CINAHL, Embase, Medline, NEED, and PsycINFO. A search of key terms and key sites was also carried out on the Internet. A copy of the Medline version of the main strategy is available in the "Supporting materials" section of the SIGN website (<http://www.sign.ac.uk/guidelines/published/support/index.html>). Members of the guideline development group contributed additional literature.

The searches identified 2,570 papers of potential interest. Of these 386 were identified as having the potential to form part of the evidence base and were reviewed in detail.

Janssen-Cilag and Napp Pharmaceuticals were approached and provided information in relation to specific questions relating to opioid dosing and conversion ratios. This information is available for perusal on request to SIGN.

Identifying Qualitative Evidence

A literature search was carried out covering the databases CINAHL, Embase, Medline, and PsycINFO for the period 2000 to September 2006. This search focused on the identification of qualitative literature relevant to the experience of cancer pain. A copy of this search strategy is available in the "Supporting materials" section of the SIGN website (www.sign.ac.uk/guidelines/published/support/index.html).

The initial result from this search was 325 references. A sift of the results aimed at removing clearly irrelevant papers and focusing on research journals reduced this number to 224 references.

Two pairs of reviewers independently reviewed this list of abstracts to identify relevant papers reducing the number of relevant papers to 93. Only 28 of these papers were common to two pairs of reviewers.

Each pair of reviewers was then asked to identify themes that emerged from the joint list of selected papers, and to pick out papers that they thought represented the key issues underlying each theme. These papers were reviewed for methodological quality using the Critical Appraisals Skills Programme (CASP) checklist developed by the Public Health Resource Unit, Oxford. At the conclusion of this process nine papers are included as evidence, split into three themes: communication, existentialism, and relationships.

Literature Search for Patient Issues

At the start of the guideline development process, a SIGN Information Officer conducted a literature search for qualitative and quantitative studies that addressed patient issues of relevance to cancer pain. The search was run in Medline, Embase, CINAHL and PsycINFO, and the results were summarised and presented to the guideline development group for consideration when forming key questions that underpin the guideline.

The literature focused on themes including anxiety/depression, alternative treatments, barriers to pain management, breakthrough pain, care delivery, caregiver issues, communication, coping styles, health professional education, pain tools, patient beliefs, psychological issues, quality of life and symptom control. Many of these are addressed in either the narrative review or other sections of the guideline.

A copy of the Medline version of the patient search strategy is available in the "Supporting materials" section of the SIGN website (<http://www.sign.ac.uk/guidelines/published/support/index.html>).

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, or RCTs with a low risk of bias

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

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

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

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

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

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

4: Expert opinion

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

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

this assessment will affect the level of evidence allocated to the paper, which will in turn influence the grade of recommendation that it supports.

The methodological assessment is based on a number of key questions (see Annex 3 of the original guideline document) that focus on those aspects of the study design that research has shown to have a significant influence on the validity of the results reported and conclusions drawn. These key questions differ between study types, and a range of checklists is used to bring a degree of consistency to the assessment process. Scottish Intercollegiate Guidelines Network (SIGN) has based its assessments on the MERGE (Method for Evaluating Research and Guideline Evidence) checklists developed by the New South Wales Department of Health, which have been subjected to wide consultation and evaluation. These checklists were subjected to detailed evaluation and adaptation to meet SIGN's requirements for a balance between methodological rigour and practicality of use.

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

Evidence Tables

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

Additional details can be found in the companion document titled "SIGN 50: A Guideline Developers' Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50]), available from the [SIGN Web site](#). (See also the "Availability of Companions Documents" field in this summary.)

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Synthesising the Evidence

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

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

Considered Judgment

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

Under the heading of considered judgment, guideline development groups 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
- Directness of application to the target population for the guideline
- Clinical impact (i.e., the extent of the impact on the target patient population, and the resources needed to treat them.)
- Implementability (i.e., how practical it would be for the NHS in Scotland to implement the recommendation.)

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

Additional detail about SIGN's process for formulating guideline recommendations is provided in Section 6 of the companion document titled "SIGN 50: A Guideline Developers' Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50], available from the [SIGN Web site](#)).

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendation

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

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

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

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

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

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

Extrapolated evidence from studies rated as 2++

D: Evidence level 3 or 4; *or*

Extrapolated evidence from studies rated as 2+

Good Practice Points: Recommended best practice based on the clinical experience of the guideline development group

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The national open meeting is the main consultative phase of Scottish Intercollegiate Guidelines Network (SIGN) guideline development, at which the guideline development group presents its draft recommendations for the first time. The national open meeting for this guideline was held on 23 April 2007 and was attended by 203 representatives of all the key specialties relevant to the guideline. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

Peer Review

All SIGN guidelines are reviewed in draft form by independent expert referees, who are asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. A number of general practitioners (GPs) and other primary care practitioners also provide comments on the guideline from the primary care perspective, concentrating particularly on the clarity of the recommendations and their assessment of the usefulness of the guideline as a working tool for the primary care team. The draft is also sent to a lay reviewer in order to obtain comments from the patient's perspective. The comments received from peer reviewers and others are carefully tabulated and discussed with the chairman and with the guideline development group. Each point must be addressed and any changes to the guideline as a result noted or, if no change is made, the reasons for this recorded.

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

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 full-text guideline document.*

The grades of recommendations (A–D) and levels of evidence (1++, 1+, 1-, 2++, 2+, 2-, 3, 4) are defined at the end of the "Major Recommendations" field.

Psychosocial Issues

Psychological Distress

B - Comprehensive chronic pain assessment should include routine screening for psychological distress.

A - Cognitive behaviour therapy should be considered as part of a comprehensive treatment programme for those with cancer related pain and resulting distress and disability.

Psychological Factors and Adherence to Treatment

D - Patient beliefs concerning pain should be assessed and discussed as part of a comprehensive, biopsychosocial cancer pain assessment.

C - Patients should receive education about the range of pain control interventions available to them.

Assessment of Pain

What is Pain?

For the purposes of this guideline, pain has been defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."

A comprehensive assessment of pain should consider the following domains:

- Physical effects/manifestations of pain
- Functional effects (interference with activities of daily living)
- Psychological factors (level of anxiety, cultural influences, fears, effects on interpersonal relationships, factors affecting pain tolerance, (see Table below))
- Spiritual aspects

Table. Factors Affecting Pain Tolerance

Aspects That Lower Pain Tolerance	Aspects That Raise Pain Tolerance
Discomfort	Relief of symptoms
Insomnia	Sleep
Fatigue	Rest, or paradoxically, physiotherapy
Anxiety	Relaxation therapy
Fear	Explanation/support
Anger	Understanding/empathy
Boredom	Diversional activity
Sadness	Companionship/listening
Depression	Elevation of mood
Introversion	Understanding of the meaning and significance of the pain
Social abandonment	Social inclusion
Mental isolation	Encouragement to express emotions

Adapted from Twycross R, Lack S. Symptom control in far advanced cancer: pain relief London: Pitman; 1983.

Why Assess Pain?

D - Prior to treatment an accurate assessment should be performed to determine the cause, type and severity of pain, and its effect on the patient.

Who Should Assess Pain?

D - The patient should be the prime assessor of his or her pain.

How Should Pain Be Assessed?

D - Patients with cancer pain should have treatment outcomes monitored regularly using visual analogue scales, numerical rating scales or verbal rating scales.

C - Self assessment pain scales should be used in patients with cognitive impairment, where feasible.

C - Observational pain rating scales should be used in patients who cannot complete a self assessment scale.

Principles of Pain Management

B - Patients should be given information and instruction about pain and pain management and be encouraged to take an active role in their pain management.

World Health Organization (WHO) Cancer Pain Relief Programme

D - The principles of treatment outlined in the WHO cancer pain relief programme should be followed when treating pain in patients with cancer.

Using the WHO Analgesic Ladder

B - A patient's treatment should start at the step of the WHO analgesic ladder appropriate for the severity of the pain.

B - Prescribing of analgesia should always be adjusted as the pain severity alters.

D - Analgesia for continuous pain should be prescribed on a regular basis, not 'as required'.

D - Appropriate analgesia for breakthrough pain must be prescribed.

Treatment with Non-Opioid Drugs

Paracetamol and Non-Steroidal Anti-Inflammatory Drugs

A - Patients at all stages of the WHO analgesic ladder should be prescribed paracetamol and/or a non-steroidal anti-inflammatory drug unless contraindicated.

A - Patients taking non-steroidal anti-inflammatory drugs who are at high risk of gastrointestinal complications should be prescribed either misoprostol 800 mcg/day, standard dose proton pump inhibitors or double dose histamine-2 receptor antagonists as pharmacological prophylaxis.

Bisphosphonates

B - Bisphosphonates should be considered as part of the therapeutic regimen for the treatment of pain in patients with metastatic bone disease.

Antidepressants and Anticonvulsants

A - Patients with neuropathic pain should be given either a tricyclic antidepressant (*e.g., amitriptyline or imipramine*) or anticonvulsant (*e.g., gabapentin, carbamazepine or phenytoin*) with careful monitoring of side effects.

Cannabinoids

A - Cannabinoids are not recommended for the treatment of cancer pain.

Treatment with Opioid Drugs

Choice of Opioid

Mild to Moderate Pain (Step 2 of the WHO Ladder)

D - For mild to moderate pain, (*score 3-6 out of 10 on a visual analogue scale or a numerical rating scale*) weak opioids such as codeine should be given in combination with a non-opioid analgesic.

Moderate to Severe Pain (Step 3 of the WHO Ladder)

D - Oral morphine is recommended as first line therapy to treat severe pain in patients with cancer.

D - Diamorphine is recommended as first line subcutaneous therapy to treat severe pain in patients with cancer.

Breakthrough Pain

D - Patients with moderate or severe breakthrough pain should receive breakthrough analgesia.

D - When using oral morphine for breakthrough pain the dose should be one sixth of the around the clock morphine dose and should be increased appropriately whenever the around the clock dose is increased.

Patients with Renal Impairment

C - In the presence of reduced kidney function all opioids should be used with caution and at reduced doses and/or frequency.

Administration of Opioids

D - Continuous subcutaneous infusion of opioids is simpler to administer and equally as effective as continuous intravenous infusion and should be considered for patients unable to take opioids orally.

D - Advice on stability of commonly used drug combinations for continuous subcutaneous infusion should be available to staff who prepare these infusions.

D - Advice on the use of other combinations should be taken from palliative care specialists.

D - Patients with stable pain on oral morphine should be prescribed a once or twice daily modified release preparation.

D - Patients with stable pain on oral oxycodone should be prescribed a twice daily modified release preparation.

Non-Pharmacological Treatment

Radiotherapy for Relieving Pain in Patients with Bone Metastases

B - All patients with pain from bone metastases which is proving difficult to control by pharmacological means should be referred to a clinical oncologist for consideration of external beam radiotherapy or radioisotope treatment.

Cementoplasty

D - Patients with bone pain from malignant vertebral collapse proving difficult to control by pharmacological means should be referred for consideration of vertebroplasty where this technique is available.

D - Patients with bone pain from pelvic bone metastases proving difficult to control by pharmacological means and reduced mobility should be considered for percutaneous cementoplasty.

Anaesthetic Interventions

B - Interventions such as coeliac plexus block and neuraxial opioids should be considered to improve pain control and quality of life in patients with difficult to control cancer pain.

Definitions:

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, or RCTs with a low risk of bias

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

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

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

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

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

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

4: Expert opinion

Grades of Recommendation

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

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

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

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

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

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

Extrapolated evidence from studies rated as 2++

D: Evidence level 3 or 4; *or*

Extrapolated evidence from studies rated as 2+

Good Practice Points: Recommended best practice based on the clinical experience of the guideline development group

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The specific type of supporting evidence is explicitly identified in each section of the guideline.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of pain in adult patients who have cancer leading to improvement in functional ability and quality of life

POTENTIAL HARMS

Non-steroidal Anti-inflammatory Drugs (NSAIDs)

- The most common serious adverse effects of NSAIDs are due to ulceration of the gastrointestinal (GI) tract. The following have been shown to increase the risk of upper GI toxicity when NSAIDs are prescribed:
 - Increasing age (>65 years)
 - Previous peptic ulcer disease, particularly if complicated with haemorrhage or perforation
 - Comorbid medical illness
 - Smoking
 - Type of NSAID (e.g., ketoprofen, ketorolac and piroxicam are associated with a high risk of serious gastrointestinal toxicity relative to other NSAIDs)
 - Increasing NSAID dose
 - Use of multiple NSAIDs
 - Combined use of NSAIDs and other drugs which could increase the risk of ulceration or bleeding such as corticosteroids, anticoagulants (e.g., warfarin), selective serotonin-reuptake inhibitors or antiplatelet agents (e.g., aspirin)
 - Existing renal, cardiac or hepatic impairment.
- Cyclooxygenase-2 (COX-2) selective inhibitors (e.g., celecoxib, etoricoxib, lumiracoxib and parecoxib) can cause serious, and sometimes fatal GI reactions. Randomised controlled trials have shown that COX-2 selective inhibitors demonstrate an increased risk of thrombotic cardiovascular adverse reactions, particularly myocardial infarction (MI) and stroke.

Bisphosphonates

Osteonecrosis of the jaw (ONJ) is a complication occurring in patients treated with bisphosphonates, especially the aminobisphosphonates. The most significant predisposing factors were found to be:

- Use of aminobisphosphonates with increasing risk over time of exposure and higher doses
- History of trauma, dental surgery, or dental infection. Sixty percent had some form of dento-alveolar surgery resulting in non-healing of the surgical site and necrosis of the bone.

Opioids

- Use of the WHO analgesic ladder has been shown to be effective in managing pain in about three quarters of patients with cancer. Despite dose titration and appropriate management of predictable side effects, a minority of patients at step 3 of the WHO ladder have inadequate pain relief, persistent unacceptable side effects, or a combination of the two. There is an increasing tendency in clinical practice to switch between opioids but the rationale for this in individual patients is not always clear, appropriate or well documented.
- Individuals with renal impairment are at an increased risk for opioid toxicity. In patients with poor or deteriorating kidney function, the following are of considerable importance to prevent or manage toxicity:
 - Choice of opioid
 - Consideration of dose reduction and/or an increase in the dosage interval
 - Change from modified release to an immediate release oral formulation
 - Frequent clinical monitoring and review

See the original guideline document for information on toxicity specific to the opioid being considered.

Antidepressants and Anticonvulsants

Some patients experience adverse effects.

CONTRAINDICATIONS

CONTRAINDICATIONS

All cyclooxygenase-2 (COX-2) selective inhibitors are contraindicated for patients with established ischaemic heart disease, peripheral arterial disease or cerebrovascular disease.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data

available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

- The extent of risk for osteonecrosis of the jaw (ONJ) in patients taking oral bisphosphonates has not been determined. There are no data available to suggest that discontinuation of bisphosphonates for patients requiring invasive dental treatment reduces the risk of osteonecrosis of the jaw. The clinical judgement of the treating clinician should guide the management plan based on the individual risks/benefits for the patient.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation of national clinical guidelines is the responsibility of local National Health Service (NHS) Board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements may then be made to implement the national guideline in individual hospitals, units and practices.

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

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

End of Life Care
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Scottish Intercollegiate Guidelines Network (SIGN). Control of pain in adults with cancer. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2008 Nov. 71 p. (SIGN publication; no. 106). [264 references]

ADAPTATION

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

DATE RELEASED

2000 Jun (revised 2008 Nov)

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: Professor John Welsh, Professor of Palliative Medicine, (*Chair*) Beatson Oncology Centre, Glasgow; Dr Esther Murray, Consultant Clinical Psychologist in Psychosocial Oncology, Ayrshire Central Hospital; Dr Lesley Colvin, Consultant Anaesthetist, Western General Hospital, Edinburgh; Ms Marguerite Connolly, District Nursing Sister, NHS Grampian; Dr Paul Cormie, MacMillan Lead General Practitioner (Cancer and Palliative Care), NHS Borders; Dr David Craig, Consultant Clinical Psychologist, Southern General Hospital, Glasgow; Dr John Currie, Consultant Anaesthetist, Royal Hospital for Sick Children, Glasgow; Professor Marie Fallon, St Columba's Hospice Chair of Palliative Medicine, Institute of Genetics and Molecular Medicine, Edinburgh Cancer Research Centre, Western General Hospital, Edinburgh; Dr Graeme Giles, Consultant in Palliative Medicine, Strathcarron Hospice, Denny; Mr Adam Gillespie, Lay Representative, Glasgow; Reverend Tom Gordon, Chaplain, Marie Curie Hospice, Edinburgh; Mr Robin Harbour, Quality and Information Director, SIGN; Dr Derek Jones, Lecturer in Occupational Therapy, Queen Margaret University,

Edinburgh; Ms Linda Kerr, Clinical Nurse Specialist in Palliative Care, Ayr Hospital; Ms Alison MacRobbie, Palliative/Community Care Pharmacist, NHS Highland; Ms Jane Mair, Community Cancer Support Nurse, Inverurie; Dr Moray Nairn, Programme Manager, SIGN; Dr Kathleen Sherry, Consultant in Palliative Medicine, The Ayrshire Hospice, Ayr; Ms Janet Trundle, Macmillan Specialist Pharmacist in Palliative Care, NHS Greater Glasgow and Clyde; Ms Gillian Wilson, Lay Representative, Dunbar

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All members of the guideline development group made declarations of interest and further details of these are available on request from the Scottish Intercollegiate Guidelines Network (SIGN) Executive.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline will be considered for review in three years. Any updates 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: Control of pain in adults with cancer. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network, 2008 Nov. 12 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:

- Cancer pain. Booklet for patients and carers. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network, 2009. 36 p. 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 summary was completed by ECRI on January 3, 2002. The information was verified by the guideline developer as of February 4, 2002. This summary was updated on May 3, 2005 following the withdrawal of Bextra (valdecoxib) from the market and the release of heightened warnings for Celebrex (celecoxib) and other nonselective nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on May 20, 2005, following the U.S. Food and Drug Administration advisory on Aredia (pamidronate disodium) and Zometa (zoledronic acid). This summary was updated by ECRI on June 16, 2005, following the U.S. Food and Drug Administration advisory on COX-2 selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI Institute on January 29, 2009. The updated information was verified by the guideline developer on February 4, 2009.

COPYRIGHT STATEMENT

Scottish Intercollegiate Guidelines Network (SIGN) guidelines are subject to copyright; however, SIGN encourages the downloading and use of its guidelines for the purposes of implementation, education, and audit.

Users wishing to use, reproduce, or republish SIGN material for commercial purposes must seek prior approval for reproduction in any medium. To do this, please contact sara.twaddle@nhs.net.

Additional copyright information is available on the [SIGN Web site](#).

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC

Inclusion Criteria which may be found at
<http://www.guideline.gov/about/inclusion.aspx>.

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

© 1998-2009 National Guideline Clearinghouse

Date Modified: 3/2/2009

