Complete Summary

GUIDELINE TITLE

Management of colorectal cancer. A national clinical guideline.

BIBLIOGRAPHIC SOURCE(S)

Scottish Intercollegiate Guidelines Network (SIGN). Management of colorectal cancer. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2003 Mar. 47 p. (SIGN publication; no. 67). [256 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline was issued in 2003 and will be reviewed periodically as required to reflect new evidence.

Any amendments to the guideline will be noted on the Scottish Intercollegiate Guidelines Network (SIGN) Web site.

COMPLETE SUMMARY CONTENT

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

DISEASE/CONDITION(S)

- Colorectal cancer
- Hereditary non-polyposis colorectal cancer (HNPCC)
- Familial adenomatous polyposis (FAP)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Prevention
Risk Assessment
Screening
Treatment

CLINICAL SPECIALTY

Colon and Rectal Surgery
Family Practice
Gastroenterology
Internal Medicine
Nursing
Oncology
Pathology
Radiology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Hospitals
Nurses
Patients
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Public Health Departments
Utilization Management

GUIDELINE OBJECTIVE(S)

- To encourage measures to reduce the risk of developing colorectal cancer in the general population and in high risk groups
- To encourage early diagnosis in the general population and in high risk groups
- To improve the consistency of referral patterns
- To improve all aspects of the management of colorectal cancer patients in order to improve overall and disease-free survival and health-related quality of life

TARGET POPULATION

- The general population and those in high risk groups for developing colorectal cancer in Scotland
- Patients with colorectal cancer, including hereditary non-polyposis colorectal cancer (HNPCC) and familial adenomatous polyposis (FAP)

INTERVENTIONS AND PRACTICES CONSIDERED

Prevention/Screening

1. Eat five or more portions of fruits and vegetables a day
2. Take at least 30 minutes of physical activity, such as brisk walking, on most days
3. Encouragement not to smoke
4. Colonoscopy with mucosal biopsies and biopsy of any suspicious lesions
5. Sigmoidoscopy
6. Discussion of gynaecological screening for endometrial and ovarian cancer*
7. Upper gastrointestinal endoscopy*
8. Consideration for screening for other cancers*

* Also recommended for high-risk patients suspected of having hereditary non-polyposis colorectal cancer [HNPCC]

Note: Hormone replacement therapy specifically to prevent colorectal cancer is not recommended

Diagnosis

1. Family history
2. Thorough abdominal and rectal examination
3. Referral to specialist, such as clinical genetics, surgery
4. Colonoscopy
5. Double contrast barium enema
6. Double contrast barium enema and flexible sigmoidoscopy
7. Computed tomography (CT) pneumocolon
8. Pre-operative imaging of liver and chest for patients undergoing elective surgery for colorectal cancer
9. Intraoperative liver ultrasound or postoperative imaging for patients requiring emergency surgery
10. Pathological reporting of colorectal cancer resection specimens, including tumour differentiation, staging, margins, and extramural vascular invasion

Treatment

1. Venous thromboembolism prophylaxis
2. Antibiotic prophylaxis
3. Total mesorectal excision (TME) surgery
4. Colectomy (partial or total with ileorectal anastomosis)
5. Proctocolectomy with or without ileoanal reconstruction
6. Adjuvant chemotherapy or chemotherapy synchronous with radiotherapy, such as intermittently infused fluorouracil and folinic acid (FUFA); continuous fluorouracil (5-FU); or bolus FUFA
7. Adjuvant radiotherapy
8. Combination chemotherapy, including oxaliplatin
9. Raltitrexed**
10. Second-line treatment with irinotecan
11. Palliative radiotherapy
12. Medical management with analgesics, antiemetics and antisecretory drugs to relieve the symptoms of bowel obstruction
13. Follow up care

** Raltitrexed is not recommended as a first line therapy but may be considered as an alternative in patients intolerant of 5-FU regimens or in whom 5-FU is contraindicated due to cardiotoxicity

Note: Patients with Dukes' B tumours of the colon or rectum should not be treated routinely with adjuvant chemotherapy

Note: Portal vein chemotherapy should not be used as the sole regimen in postoperative adjuvant treatment

Note: The addition of levamisole or interferon alpha to FUFA chemotherapy as adjuvant treatment is ineffective in colorectal cancer and should not be considered

Note: Bolus 5-FU regimens are not recommended as routine first line chemotherapy for advanced disease

Note: Immune modulation should not be used routinely in the management of advanced colorectal cancer

MAJOR OUTCOMES CONSIDERED

- Incidence of colorectal cancer
- Mortality and survival rates
- Physical, psychological, social, and sexual impact following colorectal cancer surgery
- Patient characteristics, including age, risk factors, and symptoms
- Sensitivity of diagnostic tests
- Relative risks or operative morbidity and cancer recurrence
- Pathological information, such as tumour differentiation, staging, margins, and extramural vascular invasion
- Toxicity and side effects of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence base for this guideline was synthesised in accordance with the Scottish Intercollegiate Guideline Network (SIGN) methodology. A systematic review of the literature was carried out using an explicit search strategy devised by the SIGN Information Officer in collaboration with members of the guideline development group. The search for systematic reviews and meta-analyses covered the Cochrane Library, MEDLINE, EMBASE, CINAHL and HEALTHSTAR databases, and the internet, from January 1990 to January 2001. The search for randomised controlled trials, cohort studies, case control studies, and cross-sectional surveys covered the Cochrane Library, MEDLINE, PUBMED, EMBASE, CANCERLIT and CINAHL databases, and the internet, from January 1993 to January 2001. The evidence base was updated during the course of development

of the guideline, and the search was supplemented by reviewing references identified from papers from the searches and from personal databases of the guideline development group members. The MEDLINE version of the search strategies used can be viewed on the SIGN Web site.

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 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

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 "SIGN 50: A Guideline Developers' Handbook." (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 synthesizing the evidence base to form graded guideline recommendations is illustrated 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.

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 group 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 <u>not</u> 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.

Grade A: At least one meta-analysis, systematic review of randomized controlled trials (RCTs), or randomized controlled trial 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

Grade 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+

Grade 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 rate as 2++

Grade 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

A national open meeting is the main consultative phase of the Scottish Intercollegiate Guidelines Network (SIGN) guideline development, at which the guideline development group presents their draft recommendations for comment. The national open meeting for this guideline was held in October 2001 and was attended by 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 reviewed in draft form by a panel of 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.

The guideline was then reviewed by an Editorial Group comprising relevant specialty representatives on SIGN Council, to ensure that the peer reviewers' comments had been addressed adequately and that any risk of bias in the guideline development process as a whole had 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 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.

Prevention and Screening

Diet and Excess Weight

B - The population of Scotland should be advised to maintain a body mass index of 18.5-25 kg/m^2 throughout life.

C - Individuals in Scotland should be advised to eat five or more portions of fruits and vegetables a day, in line with the current guidance from the Health Education Board for Scotland.

B - The population of Scotland should be encouraged to take at least 30 minutes of physical activity (such as brisk walking) on most days, citing decreased colorectal cancer risk as one of the reasons.

B - The population of Scotland should be encouraged not to smoke, citing decreased colorectal cancer risk as one of the reasons.

B - The use of hormone replacement therapy specifically to prevent colorectal cancer is not recommended.

D -

- Patients with left-sided colitis or pancolitis of 10 years duration should undergo three yearly colonoscopy with mucosal biopsies and biopsy of any suspicious lesions.
- The frequency of examination should increase to yearly when the disease has been present for 20 years, or when indeterminate dysplasia has been diagnosed.

D - Colectomy should be performed for high grade dysplasia, and considered for low grade dysplasia.

D -

- Patients who have undergone colonoscopic polypectomy for adenomas should be offered follow up colonoscopy.
- If one or two adenomas <1 cm are found at colonoscopy, a repeat colonoscopy should be performed at five years. If this is normal, colonoscopic surveillance may cease.
- If there are three or more adenomas, or at least one $\geq$1 cm, or at least one showing severe dysplasia, repeat colonoscopy should be performed at three years. If surveillance colonoscopy is subsequently normal on two consecutive occasions, it may cease.

The Impact of Colorectal Cancer on Patients and Their Families

Interventions to Alleviate the Impact of Colorectal Cancer

D - Information about local support services should be made available to both the patient and their relatives.

B - Clinicians must be aware of the potential for physical, psychological, social and sexual problems after all colorectal cancer surgery, including sphincter-saving operations.

Methods and Sources of Communication

B - Listening and explaining skills can be improved by high quality courses, and all healthcare professionals in cancer care should undergo such training.

B - Healthcare professionals in cancer care should consider giving either written summaries or audio-tapes of consultations to people who have expressed a preference for them.

Involving the Patient in the Decision-Making Process

D - Healthcare professionals should respect patients' wishes to be involved when making plans about their own management.

D - Patients should be given clear information about the potential risks and benefits of treatment, in order that they can make choices.

Genetics

Family History of Colorectal Cancer

C - A three generation family history should be taken from all individuals with colorectal cancer.

D - Individuals at moderate risk of developing colorectal cancer on the basis of their family history should be offered a single colonoscopy at 30-35 years and again at 55 years.

Table 1 in the original guideline document provides criteria for screening individuals at risk of colorectal cancer by risk level (e.g., high, moderate, low)

Individuals with a High Risk Family History of Colorectal Cancer (Including Hereditary Non-polyposis Colorectal Cancer [HNPCC])

C - Referral of individuals with a high risk of developing colorectal cancer should be made to the local clinical genetic service for consideration of mismatch repair gene mutation analysis.

C - Individuals carrying a mismatch repair gene mutation or fulfilling high risk criteria for HNPCC should be offered endoscopic screening starting in the twenties if possible and repeated every two to three years, taking into account the patient's general condition and uptake.

Familial Adenomatous Polyposis (FAP)

C - Patients with clinically diagnosed FAP should be referred to the local clinical genetic service for APC gene mutation analysis.

C - Individuals at risk of FAP, determined either by a positive family history or on the basis of mutation analysis, should be offered colonoscopy every two to three years and yearly sigmoidoscopy.

C -

- Patients with FAP should be offered proctocolectomy with or without ileoanal reconstruction or total colectomy with ileorectal anastomosis once adenomas have developed.
- Subsequent management should include lifelong surveillance of the residual rectum where appropriate and regular upper gastrointestinal endoscopy to detect duodenal adenomas or malignancy.

Primary Care and Referral

Important Symptoms of Colorectal Cancer

C - Patients over the age of 50 years with any of the following symptoms over a period of six weeks should be urgently and appropriately investigated:

- Rectal bleeding with a change in bowel habit to looseness or increased frequency
- Rectal bleeding without anal symptoms
- Palpable abdominal or rectal mass
- Intestinal obstruction

C - All patients with iron-deficiency anaemia (Hb <11g/dl in men or <10g/dl in postmenopausal women) without overt cause should be thoroughly investigated for colorectal cancer.

Strategies to Reduce Delay in Diagnosis of Colorectal Cancer

D - Patient groups at risk of colorectal cancer, especially those over 50 years of age, should be informed about significant symptoms and encouraged to seek medical attention early should they develop such symptoms.

D - General practitioners should perform a thorough abdominal and rectal examination on all patients with symptoms suspicious of colorectal cancer.

D - When a patient presents with suspicious symptoms or signs, they should be urgently investigated and referred to a surgical unit with a declared interest in colorectal cancer.

Diagnosis

Endoscopy

D - Colonoscopy is recommended as a very sensitive method of diagnosing colorectal cancer, enabling biopsy and polypectomy.

Double Contrast Barium Enema

B - Double contrast barium enema may be employed as a sensitive, safe alternative to colonoscopy.

B - Where the sigmoid colon is not well visualised, e.g., in the presence of severe diverticular disease, double contrast barium enema should be combined with flexible sigmoidoscopy.

Computed Tomography (CT) Pneumocolon

D - Where the radiological expertise and equipment exist, a CT pneumocolon is recommended as a sensitive test for colorectal cancer.

Surgery

Preoperative Staging

B -

- All patients undergoing elective surgery for colorectal cancer should have preoperative imaging of the liver and chest.
- In patients requiring emergency surgery intraoperative liver ultrasound or postoperative imaging is acceptable.

C - Complete colonic examination by colonoscopy, CT pneumocolon or barium enema should be carried out, ideally preoperatively, in patients with colorectal cancer.

Preoperative Preparation

A - Patients undergoing surgery for colorectal cancer should have:

- Venous thromboembolism prophylaxis
- Antibiotic prophylaxis consisting of a single dose of antibiotics providing both aerobic and anaerobic cover given within 30 minutes of induction of anaesthesia

Prophylaxis measures should be taken as outlined in the appropriate Scottish Intercollegiate Guideline Network (SIGN) guidelines.

Perioperative Blood Transfusion

B - If a patient undergoing colorectal cancer surgery is deemed to require a blood transfusion, this should not be withheld on account of a possible association with increased risk of cancer recurrence.

Techniques in Colorectal Cancer Surgery

B - Mesorectal excision is recommended for most rectal cancers where the patient is fit for radical surgery. The mesorectal excision should be total for tumours of the middle and lower thirds of the rectum, and care should be taken to preserve the pelvic autonomic nerves wherever this is possible without compromising tumour clearance.

C - With a low rectal anastomosis, consider giving a defunctioning stoma.

C - With a low rectal anastomosis after total mesorectal excision (TME), consider a colopouch.

Local Excision of Colorectal Cancers

C - The relative risks of operative morbidity and recurrence must be carefully weighed and explained fully to the patient so that an informed decision can be made regarding local excision and rectal cancer.

C - Further surgery for pedunculated polyp cancers is indicated if:

- There is histological evidence of tumour at, or within 1 mm of, the resection margin
- There is lymphovascular invasion
- The invasive tumour is poorly differentiated

Management of Malignant Colonic Obstruction

C - Mechanical large bowel obstruction should be distinguished from pseudo-obstruction before surgery.

C - Patients with malignant obstruction of the large bowel should be considered for immediate resection.

A - If immediate reconstruction after resection is deemed feasible, segmental resection is preferred for left-sided lesions.

D - Where facilities and expertise are available, colonic stenting should be considered.

Surgery for Advanced Disease

D - Patients with liver and lung metastases should be considered for resection or, in the case of liver disease, in situ ablation.

D - In patients with advanced local or recurrent disease, careful consideration should be given to surgical excision or palliative intraluminal procedures.

Specialisation and Work Load in Colorectal Cancer Surgery

B - Surgery for colorectal cancer should only be carried out by appropriately trained surgeons whose work is audited. Low rectal cancer surgery should only be performed by those trained to carry out total mesorectal excision.

Pathology

Important Pathological Parameters

B - Pathological reporting of colorectal cancer resection specimens should include information on:

- Tumour differentiation
- Staging (Dukes' and tumour, node, metastasis [TNM] systems)
- Margins (peritoneal and circumferential resection margin [CRM])
- Extramural vascular invasion.

See Annex 1 in the original guideline document for definitions of tumor staging.

Reporting in Colorectal Cancer

B - All reporting of colorectal cancer specimens should be done according to or supplemented by the Royal College of Pathologists' minimum data set.

Chemotherapy and Radiotherapy

Adjuvant Chemotherapy

A - Patients with Dukes' C tumours of the colon or rectum should be considered for adjuvant chemotherapy.

A - Patients with Dukes' B tumours of the colon or rectum should not be treated routinely with adjuvant chemotherapy.

B - Portal vein chemotherapy should not be used as the sole regimen in postoperative adjuvant treatment.

A - The addition of levamisole or interferon alpha to fluorouracil and folinic acid (FUFA) chemotherapy as adjuvant treatment is ineffective in colorectal cancer and should not be considered.

A - The recommended adjuvant regimen in patients with Dukes' C tumours is bolus FUFA, administered over five days every four weeks. The duration of treatment should be six months.

C - The schedule of FUFA given once weekly for 30 weeks used in the QUASAR (QUick And Simple And Reliable) trial may be an acceptable option for certain patients.

Adjuvant Radiotherapy

A - Preoperative radiotherapy, planned with three or four fields, should be considered in patients with operable rectal cancer.

C - When postoperative radiotherapy is indicated, a schedule of 45 Gy in 25 fractions over five weeks is recommended. Patients should not be treated with parallel opposed fields; a planned technique with three or four fields should be used.

C - Chemotherapy should be given synchronously with the radiotherapy using one of the following three regimens:

- Intermittently infused FUFA (Bosset)
- Continuous fluorouracil (Lokich) or
- Bolus FUFA

Chemotherapy for Metastatic Disease

A - All patients with metastatic colorectal cancer should be considered for chemotherapy.

A - Bolus 5-fluorouracil (5-FU) regimens are not recommended as routine first line chemotherapy for advanced disease.

A - Outside a clinical trial, the choice of an appropriate regimen includes continuous infusional fluorouracil (Lokich), FUFA infusion (de Gramont) or capecitabine.

A - Raltitrexed is not recommended as a first line therapy but may be considered as an alternative in those patients intolerant of 5-FU regimens or in whom 5-FU is contraindicated due to cardiotoxicity.

(Although as efficacious as alternative regimens, raltitrexed is associated with significantly greater toxicity and its benefit to patients who are intolerant to 5-FU or with coronary heart disease should be carefully weighted against the potential harms. This recommendation differs from the HTBS comment (Health Technology Board for Scotland comment. [cited 21 Jan 2003]. Available from http://www.htbs.co.uk/htbsadvice/acomment.asp?did=575) on the NICE appraisal [March 2002] which recommends that the use of raltitrexed is restricted to clinical studies.)

C - Initial combination chemotherapy, including oxaliplatin, should be considered in patients fit for hepatic resection but who have inoperable hepatic metastases that might become resectable on treatment.

A - Carefully selected patients with good performance status, normal liver function tests and no evidence of gastrointestinal obstruction with metastatic colorectal cancer, who have progressive disease despite treatment with 5-FU/FA, should be considered for second line treatment with irinotecan.

A - Immune modulation should not be used routinely in the management of advanced colorectal cancer.

Radiotherapy for Advanced Disease

C - Radiotherapy to convert inoperable rectal cancer into operable disease should be combined with chemotherapy. Suitable regimens include intermittent infusional 5-FU/FA (Bosset), continuously infused 5-FU (Lokich) or bolus 5-FU/FA.

D - Palliative radiotherapy should be considered for patients who have distressing pelvic symptoms from rectal cancer.

Follow up of Patients Treated for Colorectal Cancer

A - Patients who have undergone curative resection for colorectal cancer should undergo formal follow up in order to facilitate the early detection of metastatic disease.

Palliative Care and the Management of Symptoms in Advanced Disease

Symptom Management

D - Medical measures such as analgesics, antiemetics and antisecretory drugs should be used alone or in combination to relieve the symptoms of bowel obstruction.

See Scottish Intercollegiate Guideline Network (SIGN) guideline "Control of Pain in Patients with Cancer" for a more detailed discussion of pain assessment and management.

Definitions

Grades of Recommendations

A - At least one meta-analysis, systematic review of randomised controlled trials (RCTs), or randomised controlled trial 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 rate 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

General Benefits

- Reduction in the risk of developing colorectal cancer in the general population and in high risk groups.
- Early diagnosis of colorectal cancer in the general population and in high risk groups.
- Improvement in the consistency of referral patterns.
- Improvement of all aspects of the management of colorectal cancer patients in order to improve overall and disease-free survival and health-related quality of life.

Specific Benefits

- Colonoscopy is an extremely sensitive diagnostic test for colorectal cancer and has the major advantages of allowing both biopsy and polypectomy and does not involve exposure to ionising radiation.
- Double contrast barium enema is a sensitive, safe, well-tolerated, widely-available method not requiring sedation and has a high completion rate.
- Computed tomography (CT) pneumocolon is a sensitive, well-tolerated method and it provides information outside the colon and rectum that can be used for staging malignant disease (local invasion, liver metastases, lymph node spread, etc.). This technique is particularly useful in frail, immobile, and elderly patients. The radiation dose with modern equipment and best practice can be comparable with conventional barium dose radiation dose levels.
- For liver metastases, preoperative assessment with computed tomography (CT) or magnetic resonance imaging (MRI) is more sensitive than with transabdominal ultrasound, although the most accurate modality appears to be a combination of intraoperative ultrasound and palpation at the time of surgery.
- There is unequivocal evidence from 27 randomised trials and two meta-analyses that adjuvant radiotherapy improves local control in patients undergoing potentially curative resections for rectal cancer. However, the evidence for increased survival is less convincing. Meta-analyses show no overall benefit. Indirect evidence from systematic reviews also suggests that radiotherapy may be more effective if given preoperatively.
- There is evidence from two systematic reviews that chemotherapy for metastatic colorectal cancer can improve survival, and should be considered in all cases. This form of therapy is given with palliative intent, and a major aim should be to alleviate symptoms or delay their onset.

POTENTIAL HARMS

- There is some radiation associated with the use of double contrast barium enema and a reduced accuracy of the test when used in the presence of sigmoid diverticular disease. However, the radiation dose can be significantly reduced by modern digital technology, and double contrast barium enema can

be combined with flexible sigmoidoscopy in the presence of severe diverticular disease.

- There are some disadvantages to colonoscopy, including the inability to reach the caecum in a variable proportion of cases (5-30%); the use of intravenous (IV) sedation; the inaccuracy associated with the localisation of tumour; and the small but significant risk of complications.
- Computed tomography (CT) pneumocolon cannot detect polyps less than 10 mm. It is not possible to detect or exclude tumours in normally sized lymph nodes.
- The procedure-related mortality is approximately 1 in 5,000 for colonoscopy and 1 in 50,000 for sigmoidoscopy and for double contrast barium enema.
- There is strong evidence of an increase in non-cancer deaths during the first year after treatment in patients irradiated preoperatively, which may, in part, offset any potential survival benefit of improved local control. Further evidence indicates that this excess mortality is related to radiotherapy technique, in particular outmoded regimens which treated large volumes with parallel opposed fields. Trials using three or four field plans to more conservative volumes fail to show any increase in non-cancer deaths.
- A randomised adjuvant trial of raltitrexed compared to fluorouracil and folinic acid was stopped prematurely when drug-related deaths in the raltitrexed arm were double those of the control arm and a greater proportion of patients failed to complete the intended treatment. Some of these problems may be related to the effects of impaired renal function upon toxicity associated with raltitrexed. In patients with metastatic disease, raltitrexed was also associated with an increased incidence of treatment-related death (6%) when compared to the de Gramont and Lokich regimens, although overall survival was similar in each of the three groups. Nevertheless, raltitrexed may be useful in the management of patients with severe coronary artery disease, as it does not, in contrast to the other regimens, induce coronary vasospasm.

CONTRAINDICATIONS

CONTRAINDICATIONS

Chemotherapy may not be appropriate for all patients due to comorbidity or personal preference. In older patients or in patients with significant coexisting illness (e.g., cardiovascular problems) the risks of toxicity may increase and decisions about adjuvant chemotherapy should be based on careful discussion between the patient and oncologist.

QUALIFYING STATEMENTS

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- 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. However, it is advised 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 Service (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.

IMPLEMENTATION TOOLS

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
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Scottish Intercollegiate Guidelines Network (SIGN). Management of colorectal cancer. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2003 Mar. 47 p. (SIGN publication; no. 67). [256 references]

ADAPTATION

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

DATE RELEASED

2003 Mar

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 Robert Steele (Chairman); Mr John Anderson; Dr David Brewster; Professor Frank Carey; Mr Andrew Denholm; Dr Simon Dover; Dr John Drummond; Dr Ewan Forrest; Dr David Goudie; Dr Tim Habeshaw; Dr Duncan Jodrell; Ms Gillian Knowles; Ms Amy Leslie; Dr Pamela Levack; Professor Julian Little; Ms Jill Macintyre; Dr James MacKenzie; Mrs Grace MacLeod; Professor Alastair Munro; Dr Moray Nairn; Dr Mary Porteous; Dr Vicky Save; Mr Duncan Service; Mrs Sandra Teo; Ms Joanne Topalian; Dr Ramsay Vallance

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.

SIGN guideline group members should be able to act as independently of external commercial influences as possible, therefore, individuals who declare considerable personal interests may be asked to withdraw from the group. Details of the declarations of interest of any guideline development group member(s) are available from the SIGN executive.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline was issued in 2003 and will be reviewed periodically as required to reflect new evidence.

Any amendments to the guideline will be noted on the 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 colorectal cancer. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2003 Mar. 2 p. Available in Portable Document Format (PDF) from the Scottish Intercollegiate Guidelines Network (SIGN) Web site.
- SIGN 50: a guideline developers' handbook. Edinburgh (UK): 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 and Evaluation) guideline appraisal instrument. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network, 2001. Available from the SIGN Web site.
- A background paper on the legal implications of guidelines. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network.

PATIENT RESOURCES

The following is available:

- Information for discussion with patients and carers. In: Management of colorectal cancer. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2003 Mar. 47 p. (SIGN publication; no. 67).

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 summary was prepared by ECRI on November 20, 2003. The information was verified by the guideline developer on January 16, 2004.

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