



**Associazione
Italiana di
Epidemiologia**

**Disposizioni in materia di responsabilità
professionale del personale sanitario:
il problema delle linee guida**

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Art. 5

(Buone pratiche clinico-assistenziali e raccomandazioni previste dalle linee guida)

1. *Gli esercenti le professioni sanitarie, ... , si attengono, alle buone pratiche clinico-assistenziali e alle raccomandazioni previste dalle linee guida* elaborate dalle società scientifiche iscritte in apposito elenco le linee guida sono inserite nel Sistema nazionale per le linee guida (SNLG) e pubblicate nel sito internet dell'Istituto superiore di sanità.

Art. 6

(Responsabilità penale dell'esercente la professione sanitaria).

1. Agli effetti di quanto previsto dal primo comma, ***è esclusa la colpa grave quando, ..., sono rispettate le buone pratiche clinico-assistenziali e le raccomandazioni previste dalle linee guida***

Preambolo

- Se le linee guida diventano causa di ***esclusione della colpa grave*** e quindi di non punibilità, devono:
 - essere **rigorose** (attenersi a quanto la ricerca scientifica ha dimostrato)
 - essere periodicamente **aggiornate**
 - **coprire tutte le principali condizioni cliniche** (e di sanità pubblica)

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1. Gli esercenti le professioni sanitarie, ... , si attengono, alle buone pratiche clinico-assistenziali e alle raccomandazioni previste dalle ***linee guida elaborate dalle società scientifiche iscritte in apposito elenco*** le linee guida sono inserite nel Sistema nazionale per le linee guida (SNLG) e ***pubblicate nel sito internet dell'Istituto superiore di sanità.***

Cosa sono, oggi, le linee guida?

- Raccomandazioni di comportamento clinico
- elaborate mediante un processo di revisione sistematica della letteratura e delle opinioni di esperti
- con lo scopo di aiutare i medici e i pazienti a decidere le modalità assistenziali più appropriate in specifiche situazioni cliniche

(Institute of Medicine)

Linee guida

- Le linee guida sono documenti molto complessi:
 - devono sintetizzare tutta l'evidenza degli studi di qualità (evitando quelli di cattiva)
 - e trasformare le sintesi in raccomandazioni attraverso un percorso rigoroso e trasparente
 - considerare la complessità scientifica e disciplinare, e gli interessi dei cittadini e del sistema sanitario
 - ed esplicitare la forza di ogni raccomandazione

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SIGN 126 • Diagnosis and management of colorectal cancer

A national clinical guideline

December 2011 • Revised October 2015

Evidenza scientifica

KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

LEVELS OF EVIDENCE

1 ⁺⁺	High quality meta-analyses, systematic reviews of 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
	High quality systematic reviews of case control or cohort studies
2 ⁺⁺	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, eg case reports, case series
4	Expert opinion

Graduazione delle raccomandazioni

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

- | | |
|-------------------------------------|---|
| <input checked="" type="checkbox"/> | Recommended best practice based on the clinical experience of the guideline development group |
|-------------------------------------|---|

3.1 DIET AND EXCESS WEIGHT

Diet has long been regarded as the most important environmental influence in colorectal cancer and this is reflected in the volume of observational studies testing the dietary hypothesis. There are, however, two major problems in the interpretation of observational studies. Firstly, diet is related to other aspects of lifestyle that may influence risk, and secondly, people eat food rather than nutrients. In consequence, it is difficult to identify the specific components of diet that influence risk. The second expert report of the World Cancer Research Fund and the American Institute of Cancer Research has brought together the available literature through systematic review and, where possible, meta-analyses.²

3.1.1 WEIGHT

Both body fatness and abdominal fatness are categorised as convincing factors for developing colorectal cancer.² In Caucasian populations the normal range of body mass index (BMI) is between 18.5 and 25 kg/ m².

D Maintaining a BMI close to the lower end of the normal range is advised for the general population to reduce the risk of developing colorectal cancer.

3.1.2 DIET

The consumption of foods containing dietary fibre, such as pulses and relatively unprocessed cereals, may help to decrease the risk of colorectal cancer.² The consumption of fruit and non-starchy vegetables may also decrease the risk, although the evidence is limited and merely suggestive.² The Scottish Government strategy also encourages people to eat 400 g (14 oz) of fruit and vegetables (in five portions) per day and cancer.² In Caucasian populations the normal range of body mass index (BMI) is between 18.5 and 25 kg/ m².

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3.1.2 DIET

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The consumption of red meat and processed meat are convincing risk factors for colorectal cancer. Red meat should be restricted to less than 500 g (18 oz) per week. Processed meat should be avoided.²

D The general population should be advised to:

- eat at least five portions (400 g or 14 oz) of non-starchy vegetables and fruits each day and to eat relatively unprocessed cereal with every meal
- keep consumption of red meat to less than 500 g (18 oz) per week and avoid processed meat.

3.2 ALCOHOL

Alcohol consumption is a convincing risk factor for colorectal cancer in men and a probable risk factor in women.² The risk is highest for those who consume more than 30 g of alcohol per day (equivalent to 100 g of pure alcohol).

villous features or high-grade dysplasia also fall into this category, provided that they have been completely resected (whole not piecemeal).²⁸

4

Patients with ≥ 5 small adenomas, or ≥ 3 adenomas with at least one ≥ 1 cm in size are at high risk, and should undergo colonoscopy at one year.²²

4

Surveillance colonoscopy should not routinely continue beyond the age of 75 years, as the lead time for an adenoma to progress to a cancer is similar to the life expectancy at that age.²²

4

The performance of high-quality colonoscopy is vitally important. The accurate detection of adenomas is dependent upon a slow and careful examination of the colonic mucosa, including behind folds. Incomplete removal of polyps is associated with an increased risk of interval cancers. The site of large, sessile polyps, particularly if removed piecemeal, should be tattooed with India Ink and re-examined at three months.²²

4

A meta-analysis of four randomised controlled trials (RCTs) has suggested that chromoendoscopy using pancolonoscopic indigo-carmin dye spraying may improve the detection of small or flat lesions (both adenomatous and hyperplastic). Methodology was not consistent between the studies, however, the cost of dye and the increased procedure time might limit the usefulness of this approach in clinical practice.²⁹

1⁺⁺

- D** Patients who have undergone colonoscopic polypectomy for adenomas should be offered follow-up colonoscopy based on risk stratification.
- D** Patients with one or two adenomas < 1 cm in size without high-grade dysplasia are at low risk and only require follow-up colonoscopy at five years if other factors indicate the need for further surveillance. If no polyps are found, further surveillance is not required.
- D** The presence of either 3-4 small adenomas (< 1 cm), or one adenoma > 1 cm in size confers an intermediate risk, and surveillance colonoscopy should be undertaken at three years. If surveillance colonoscopy is subsequently normal on two consecutive occasions, it may cease.
- D** Patients with ≥ 5 small adenomas, or ≥ 3 adenomas with at least one polyp ≥ 1 cm in size are at high risk, and should undergo colonoscopy at one year.
- ✓** The accurate detection of adenomas is dependent upon the performance of high-quality colonoscopy.

7.4 PSYCHOLOGICAL CONSEQUENCES OF SCREENING

The long term effects of screening, such as reassurance in cases of false negative tests or increased distress in anxious individuals, have not been studied.

TME eliminates the inherent risk of involved lymph nodes as long as the margin is greater than 1 mm. This circumferential margin is also an independent risk factor for the development of distant metastases and mortality and can be accurately predicted by the use of MRI.^{80,106} It is unlikely that tumours of the upper rectum will benefit from total excision of the mesorectum, as long as the principles of careful dissection in the plane immediately outside the mesorectum are applied.¹⁰⁷ The low anastomosis necessitated by TME results in poorer functional results than a higher anastomosis, and should be avoided unless doing so would compromise adequate mesorectal excision.¹⁰⁸ It is also important to preserve the autonomic nerves in the pelvis to minimise bladder and sexual dysfunction.¹⁰⁹

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2++
4

Large cohort studies demonstrate that patients undergoing abdominoperineal excision of the rectum rather than anterior resection are more likely to develop local recurrence after the surgery and that this is related to a higher likelihood of circumferential margin involvement.¹¹⁰ The newly developed technique of extralevator abdominoperineal excision which produces a cylindrical resection specimen has been shown to be associated with a lower rate of circumferential margin involvement than the conventional approach and is therefore likely to be associated with lower local recurrence rates.^{111,112}

2+

C Mesorectal excision is recommended for 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 When an abdominoperineal excision of the rectum is required for very low rectal cancers which cannot be adequately excised by a total mesorectal excision, then an extralevator approach to abdominoperineal excision of the rectum is recommended.

✓ Extralevator abdominoperineal excision of the rectum leads to a large perineal defect that is challenging to close, and the involvement of plastic surgeons should be considered.

Prevention

General population advice:

- D Maintain a BMI close to the lower end of the normal range.
- D Eat at least five portions of vegetables and fruits each day and eat relatively unprocessed cereal with every meal. Keep consumption of red meat to less than 500 g per week and avoid processed meat.
- D Limit alcohol consumption to no more than two drinks (four units) per day for men and one drink (two units) per day for women.
- B Avoid smoking
- D Be physically active (equivalent to brisk walking) for a minimum of 30 minutes five days a week is recommended for the whole population.

Screening

- D All patients with ulcerative colitis or Crohn's colitis of 10 years duration should undergo a screening colonoscopy.
- D Chromoendoscopy with pan-colonic dye-spraying and targeted biopsy of abnormal areas is advised for detecting dysplasia. If chromoendoscopy is not used, 2-4 random biopsies should be taken from every 10 cm of the colon. In addition to biopsies of any suspicious areas.
- D Surveillance colonoscopies should be performed yearly, 3-yearly or 5-yearly according to risk-stratification.
- D Colectomy should be performed for high-grade dysplasia, cancer, any dysplasia-associated lesion/mass that cannot be entirely resected endoscopically, and low-grade dysplasia confirmed by two expert gastrointestinal pathologists.
- D Patients who have undergone colonoscopic polypectomy for adenomas should be offered follow-up colonoscopy based on risk stratification.
- D Patients with one or two adenomas <1 cm in size without high-grade dysplasia are at low risk and only require follow-up colonoscopy at five years. If other factors indicate the need for further surveillance. If no polyps are found, further surveillance is not required.
- D The presence of either 3-4 small adenomas (<1 cm), or one adenoma >1 cm in size confers an intermediate risk, and surveillance colonoscopy should be undertaken at three years. If surveillance colonoscopy is subsequently normal on two consecutive occasions, it may cease.
- D Patients with ≥ 5 small adenomas, or ≥ 3 adenomas with at least one polyp ≥ 1 cm in size are at high risk, and should undergo colonoscopy at one year.

Impact of colorectal cancer on patients and their families

- 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.
- D Patients should be given clear information about the potential risks and benefits of treatment, in order that they can make choices.
- ✓ All patients, newly diagnosed or with a suspected diagnosis of colorectal cancer, should have access at diagnosis to a clinical nurse specialist for support, advice and information.
- ✓ All patients who may require stoma formation (permanent or temporary) should be referred and assessed by a stoma nurse specialist before admission

Genetics

- B Individuals at risk or known to be carrying a CRC syndrome gene mutation should be offered colonic screening according to the BSG/ACPGBI guidelines.
- D Family history should be used to inform decision making about colonoscopic screening in asymptomatic individuals.

Primary Care and Referral

- B Patients over the age of 40 who present with new onset, persistent or recurrent rectal bleeding should be referred for investigation.
- D For patients under the age of 40 with low-risk features and transient symptoms a watch and wait policy is recommended.
- C Review of the patient by a regional clinical genetics service is recommended for accurate risk assessment if family history of colorectal cancer is the principal indication for referral for investigation.
- B General practitioners should perform an abdominal and rectal examination on all patients with symptoms indicative of colorectal cancer. A positive finding should expedite referral, but a negative rectal examination should not rule out the need to refer.
- B All symptomatic patients should have a full blood count. In cases of anaemia the presence of iron deficiency should be determined.
- B All patients with unexplained iron deficiency anaemia should be referred for endoscopic investigation of upper and lower gastrointestinal tracts.

Diagnosis

- ✓ Where colorectal cancer is suspected clinically, the whole of the large bowel should be examined.

Endoscopy

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

Radiological diagnosis

- C CT colonography can be used as a sensitive and safe alternative to colonoscopy.
- D Minimal preparation CT is an alternative to CT colonography in frail elderly patients.

Initial staging

- D All patients with colorectal cancer should be staged by contrast enhanced CT of the chest, abdomen and pelvis unless the use of intravenous iodinated contrast is contraindicated.
- C MRI of the rectum is recommended for local staging of patients with rectal cancer.
- C Endoluminal US can be used in a complementary role with MRI in staging patients with early rectal cancer.

Positron Emission Tomography

- C In patients with apparently organ-restricted liver or lung metastases (either at primary presentation or during follow up) who are being considered for resection, a PET/CT scan should be considered prior to the administration of cytoreductive chemotherapy. The identification of occult metastatic disease prior to resection or chemotherapy may render resection inappropriate or may alter patient's management.

- D FDG PET/CT should be used in the evaluation of patients with raised tumour marker CEA with negative or equivocal conventional imaging or assessment of possible pelvic recurrence and pre-sacral mass following treatment.

Surgery

Preoperative staging

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

Preoperative preparation

- D Patients undergoing surgery for colorectal cancer should have venous thromboembolism prophylaxis and antibiotic prophylaxis consisting of a single dose of antibiotics providing both aerobic and anaerobic cover given within 30 minutes of induction of anaesthesia.
- B Preoperative mechanical bowel preparation is recommended for patients undergoing restorative rectal resection.

Techniques in colorectal cancer surgery

- C Mesorectal excision is recommended for 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 When an abdominoperineal excision of the rectum is required for very low rectal cancers which cannot be adequately excised by a total mesorectal excision, then an extralevator approach to abdominoperineal excision of the rectum is recommended.
- C It is recommended that colon cancer is treated with radical surgery involving complete mesocolic excision and flush ligation of the colonic vessels.
- C With a low rectal anastomosis, consider giving a defunctioning stoma.
- C With a low rectal anastomosis after TME, consider a colopouch.
- B After a low rectal anastomosis (ie after a TME) a defunctioning stoma should be constructed unless there are compelling reasons not to do so.

Laparoscopic surgery for colorectal cancer

- 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 that have been removed endoscopically 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.
- A Laparoscopic and open surgery can be offered for resection of colorectal cancer.
- 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.

In sintesi...

... c'è ancora molta incertezza nella scienza
medica

Società scientifiche

- Devono partecipare alla elaborazione delle LG
- Ma possono essere *sole attrici* del processo di elaborazione?
- 3 ordini di dubbi:
 - competenze
 - multidisciplinarietà
 - risorse

Società scientifiche

- 3 ordini di dubbi:
 - mancanza di **competenze**: hanno il personale e le competenze metodologiche necessarie?
 - **multidisciplinarietà**: possono assicurare l'integrazione fra discipline, ma soprattutto gli interessi non difesi dalla società scientifiche, per esempio quelli dei cittadini e del sistema sanitario?
 - **risorse**: come possono ottenere risorse per svolgere questa attività? essendo perlopiù finanziate dall'industria del farmaco?

Grazie dell'attenzione!



F Faggiano (presidente), R Pirastu (vicepresidente), E Allara, M Falcone, G Ferrante, B Pacelli, P Schifano, C Senore, M Serinelli

Appello al Senato della Repubblica Italiana:

Le società scientifiche non possono essere lasciate sole nella elaborazione delle linee guida di pratica medica