

ESMO Congress:

European Guidelines for Quality Assurance on Colorectal Cancer Screening and Diagnosis

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Wien: October 1, 2012



Centro di Riferimento per l'Epidemiologia
e la Prevenzione Oncologica in Piemonte

Conflict of interest

- Advisory board meeting for Colorectal Cancer Screening in January 2011, as a paid expert, on colorectal cancer blood screening assay, organised by the Roche Diagnostics Ltd.
- Formal permission by the employer, the S. Giovanni University Hospital of Turin.

- According to the most recent estimates by the International Agency for Research on Cancer (IARC) colorectal cancer (CRC) is the most common cancer in Europe with 432 000 new cases in men and women reported annually. It is the second most common cause of cancer deaths in Europe with 212 000 deaths reported in 2008. Worldwide CRC ranks third in incidence and fourth in mortality with an estimated 1.2 million cases and 0.6 million deaths annually.

- In the 27 Member States of the European Union (EU), CRC ranks first in incidence and second in mortality in both sexes, with approximately 334 000 new cases and 149 000 deaths estimated for men and women combined in 2008. Even in those Member States in the lower range of age-standardised rates of CRC, the burden of disease is significant compared to other regions of the world. CRC is therefore an important health problem across the EU.

- Screening is an important tool in cancer control in countries with a significant burden of CRC, provided the screening services are of high quality. The EU recommends population-based screening for breast, cervical and colorectal cancer using evidence-based tests with quality assurance of the entire screening process including diagnosis and management of patients with screen-detected lesions.



**European guidelines for quality assurance in colorectal
cancer screening and diagnosis** *First Edition*



European Commission



Directorate-General for
Health & Consumers



European guidelines for quality assurance in colorectal cancer screening and diagnosis

First Edition

Editors

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European guidelines for quality assurance in colorectal cancer screening and diagnosis. First Edition Executive summary

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European Guidelines for Quality Assurance in Colorectal Cancer Screening – first edition *

Volume 1 – 10 Chapters, 386 pages

- Introduction
- Organisation
- Evaluation
- FOBT
- Endoscopy
- Training
- Pathology
- Clinical Management
- Surveillance
- Communication

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Volume 2 – Evidence 1.000 pages, 500 tables of evidence

PROCESS

1. Definition of clinical questions and PICOS by the authors
2. Literature search, evidence tables and summary documents by the literature group
3. Chapter drafts based on the literature search results
4. Circulation of the drafts and meetings with chapters authors, editorial board and literature group to check and share the contents of the chapters and the format
5. External review and web consultation
6. Final revision and editing by the authors and the EB

QUESTIONS FORMULATION

All authors of the chapters have been invited to define, for each heading and subheading, **one or more relevant clinical question** to be answered by searching the literature

They have been also invited to compile the **PICOS**

P: characteristics of patients

I: intervention to be assessed

C: comparison

O: relevant outcomes

S: study designs to be considered

CLINICAL QUESTION 2

What are the levels of diagnostic reproducibility of the pathological features:

- dysplasia
 - villousness
- in colorectal adenomas?

PICOS

- **P**: Asymptomatic people detected with polyps or symptomatic patients
- **I**: Pathological diagnosis of dysplasia or villousness
- **C**: Not applicable
- **O**: Diagnostic reproducibility/concordance
- **S**: (Systematic reviews of) diagnostic accuracy; cross-sectional studies, population studies; case series

SEARCH METHOD

- We contacted experts in the field to retrieve papers relevant to this issue. We also performed a search
- on MedLine using the following two strategies:
- (("Reproducibility of Results"[Mesh]) OR ("Sensitivity and Specificity"[Mesh])) AND ((dysplasia OR villousness) AND (colorectal adenoma)) AND ((Humans[Mesh])). Reproducibility of results (Mesh) AND colorectal neoplasms (Mesh) AND adenoma (Mesh).

SUMMARY DOCUMENT

A **SUMMARY DOCUMENT** has been prepared for each clinical question reporting:

- **PICOS** question
- **Methods:** Search strategy used
- **Results:** n. and types of retrieved studies, summary of their characteristics and results, methodological quality
- **Conclusions** and **overall level of evidence**

LEVEL OF EVIDENCE

A grading of level of evidence was used and reported in each evidence table and summary documents

I: many randomized controlled trials (RCTs) or systematic reviews (SRs) of RCTs

II: one RCT

III: prospective cohort studies or SRs of cohort studies

IV: retrospective case-controls studies or SRs of case controls studies, time series analysis

V: case series; before after studies without control group, cross sectional surveys

VI: expert opinion

STRENGTH OF THE RECOMMENDATIONS

- A** intervention strongly recommended for all patients
- B** intervention recommended
- C** intervention to be considered but with uncertainty about its impact
- D** intervention not recommended
- E** intervention strongly not recommended

Recommendations (N= 279) by levels of evidence and strength

	Levels of evidence						
Strength of recommendation		I	II	III	IV	V	VI
	A	12	13	23		4	69
	B	13	11	17	2	9	62
	C		3	6	4	4	18
	D		1	5		2	1
	E						
	Total	25	28	51	6	19	150

*including recommendations reported just once

Example of recommendations' list-

chapter 5

Endoscopic technique

- There should be local policies and processes in place to optimise sedation and patient support in order to maximise tolerance and minimise risk of complications (**I - B**).^{5.4.4}
- Policies on the use of sedation must take into account historical context, the impact on the patient experience and costs (**I - B**).^{5.1.3}
- Carbon dioxide insufflation is recommended for colonic endoscopic procedures (**I – A**).^{5.4.4}
- Carbon dioxide insufflation should be avoided in patients with COPD, known CO₂ retention or reduced pulmonary function (**VI – A**).^{5.4.4}

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Summary Table of performance standards in colorectal cancer screening

	Indicator ¹	Acceptable level	Desirable level
1	Invitation coverage ^{Rec 3.7; Sect 3.3.1}	95%	>95%
2	Uptake rate ^{Rec 3.8; Sect 3.3.1}	>45%	>65%
3	Rate of inadequate FOBT ^{Rec 3.9; 4.21; Sect 3.3.2; 4.3.4}	<3%	<1%
4	Maximum time between test and receipt of result should be 15 days ^{Rec 3.15; Sect 3.3.4}	>90%	
5	Rate of referral to follow-up colonoscopy after positive test ^{Rec 3.10; Sect 3.3.2, 3.3.3}	90%	>95%
6	Maximum time between referral after positive screening (any modality) and follow-up colonoscopy should be 31 days ^{Rec 3.16, 5.19; Sect 3.3.4, 5.3.5}	>90%	>95%
7	Compliance with follow-up colonoscopy after positive FS ^{Rec 3.14; Sect 3.3.2, 3.3.3}	85%	>90%
8	Rate of complete colonoscopies. Follow-up and screening colonoscopies to be recorded separately ^{Rec 3.11; Rec 5.41; Sect 3.3.2, 3.3.3, 5.4.5.1}	>90%	>95%
9	Time interval between positive colonoscopy/FS and definitive management should be within 31 days ^{Rec 3.17, 8.2; Sect 3.3.4, 8.2}	>95%	
10	Endoscopists participating in a CRC screening programme should perform a minimum no. of procedures per year ^{Rec 5.38; Sect 5.4.5.1}	300	>300
11	Biopsies and lesions identified in the screening programme and the subsequent resection specimen should be reported on a proforma ^{Rec 7.11; Sect 7.6.5.2, 7.8}	>90%	
12	Rate of high-grade neoplasia reported by pathologists in a colonoscopy screening programme ^{Rec 7.21; Sect 7.7}	<5%	
13	Rate of high-grade neoplasia reported by pathologists in a FOBT screening programme ^{Rec 7.21; Sect 7.7}	<10%	

¹ Sect (superscript) refers to the section/s of the Guidelines dealing with the respective indicator.

Rec (superscript) refers to the number of the corresponding recommendation in the Guidelines.

QUALITY ASSURANCE IN PATHOLOGY

Recommendations

7.1 Due to the improved diagnostic reproducibility of the revised Vienna classification, use of this classification in a format modified for lesions detected in screening is recommended to ensure consistent international communication and comparison of histopathology of biopsies and resection specimens **(IV – B)**.

Only two grades of colorectal neoplasia (low grade and high grade) should be used, to minimise intraobserver and interobserver error **(V - B)**.

The terms intra-mucosal adenocarcinoma or in-situ carcinoma should not be used **(VI - B)**.

Criteria for cancer polyps removal

- 7.7 Sub-staging of T1 cancers should be performed to determine the risk of residual disease. Consideration should be given to the appropriate method, which may vary depending on the morphology of the lesion (Kikuchi/Haggitt or measurement). For non-polypoid lesions the Kikuchi stage and for pedunculated lesions Haggitt are currently recommended **(VI - C)**. High-risk features for residual disease such as lack of margin clearance (≤ 1 mm), poor differentiation and lymphatic and vascular invasion should be reported **(V - B)**. The multidisciplinary team should be consulted on whether or not surgical resection of pT1 adenocarcinoma is recommended; if surgical resection is recommended, consideration should be given to obtaining an opinion from a second histopathologist as variation exists in evaluating high-risk features **(VI - A)**.^{Sect 7.5.3}

Detected lesions - Italy 2009

	Initial test	Following tests
Screened subjects	631,460	824,562
Carcinomas	1,464	1,041
% of cancer polyps	27.3%	24.4%
Advanced adenomas	6,930	6,205

% of cancer with stage	72%	71%
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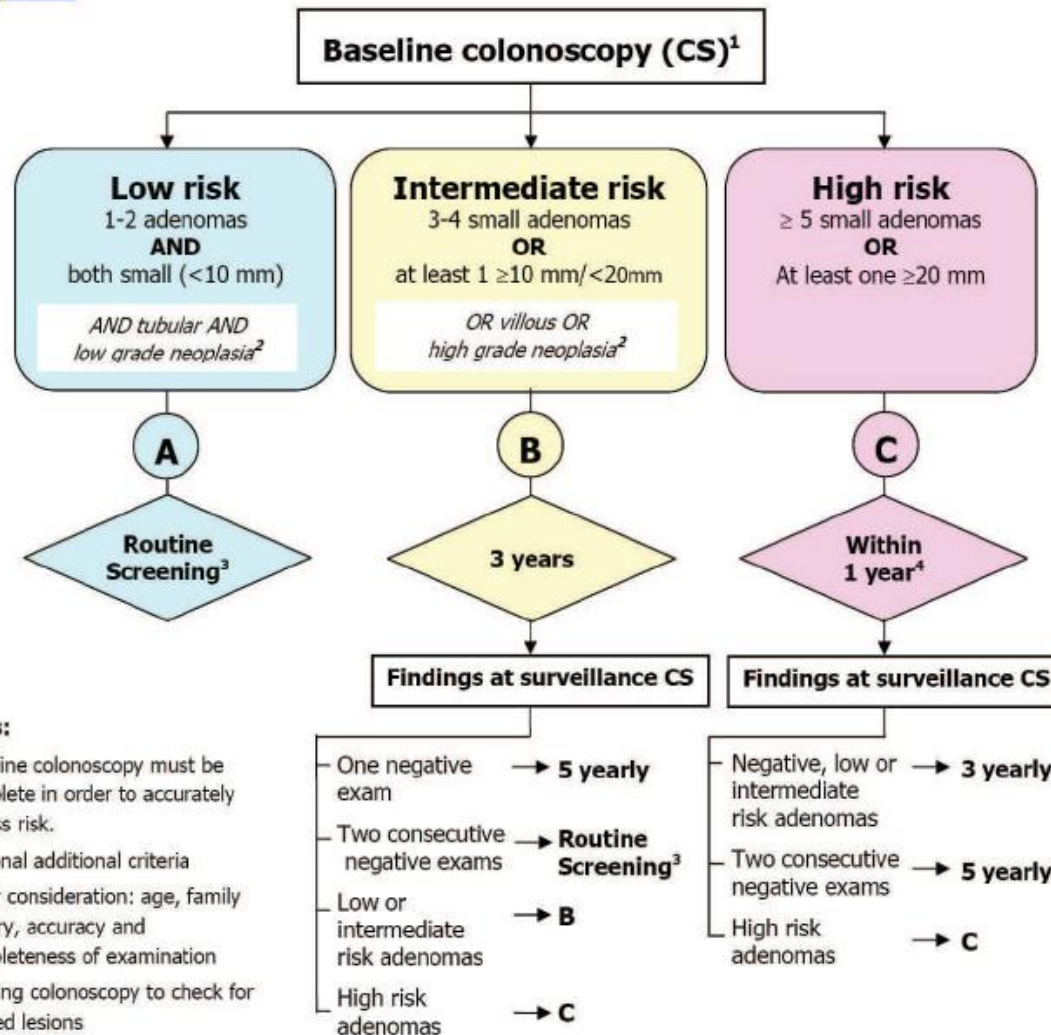
Treatment: endoscopy polypectomy only (71%)

	Mean	10°-90° percentiles
All carcinomas	12,1%	0 – 26%
pT1 Carcinomas	27,2%	0 – 46%
Advanced adenomas	95,7%	89 - 100%

Figure 9.1: Recommended surveillance following adenoma removal. (For explanation see Recommendations 9.1–9.20 and Sections 9.3–9.5)



COLONOSCOPIC SURVEILLANCE FOLLOWING ADENOMA REMOVAL (EU 2010)



Notes:

¹ Baseline colonoscopy must be complete in order to accurately assess risk.

² Optional additional criteria

³ Other consideration: age, family history, accuracy and completeness of examination

⁴ Clearing colonoscopy to check for missed lesions

Surveillance following adenomas removal

- 9.3 **Low risk.** Patients with only one or two small (<10 mm) adenomas are at low risk, and should be returned to the screening programme **(III - A)**.^{Sect 9.3.1}
- 9.4 **Intermediate risk.*** Patients with three or four small adenomas or at least one adenoma of size ≥ 10 mm and <20 mm are at intermediate risk **(III - A)** and should be offered surveillance at 3-yearly intervals **(II - A)**. After one negative exam, the interval can be extended to 5 years **(V - C)**. After two consecutive normal exams, the patient can return to routine screening **(VI - C)**.^{Sect 9.3.2; 9.4.1}

* Some programmes may wish to include small (<10 mm) adenomas with a villous component or with high grade neoplasia² in this group **(III - C)**.^{Sect 9.2.2.3; 9.3.1}

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* Some programmes may wish to include small (<10 mm) adenomas with a villous component or with high grade neoplasia² in this group **(III - C)**.^{Sect 9.2.2.3; 9.3.1}

Surveillance following adenomas removal

- 9.5 **High risk.** If either of the following is detected at any single examination (at baseline or follow-up): 5 or more adenomas, or an adenoma ≥ 20 mm, the patient is at high risk and an extra examination should be undertaken within 12 months, to check for missed synchronous lesions, before initiating 3-yearly surveillance (**III - B**). After two consecutive normal exams, the interval can be extended to 5-yearly (**V - C**). In the absence of evidence on the safety of stopping surveillance in the high risk group, surveillance should continue, taking into account Recommendations 9.10 and 9.11 (**VI - C**).^{Sect 9.3.3; 9.4.1}

Stopping surveillance

9.10 The decision to undertake each colonoscopic surveillance examination should depend not only on adenoma characteristics, but also on the patient's age and wishes, and the presence of significant co-morbidity. The patient status should be established prior to attendance for each examination **(VI - A).Sect 9.4.2**

9.11 The cut-off age for stopping surveillance is usually 75 years, but this should also depend upon patient wishes and co-morbidity **(VI - A).Sect 9.4.2**

9.12 Following cessation of surveillance, individuals should be returned to the population screening programme **(VI - C).Sect 9.4.2**

Family History

9.13 Recommendations should not differ for patients with a family history who are found to have adenomas, unless it is suspected that they have one of the dominantly inherited conditions.

(III - B).Sect 9.2.3.2

Thank you for the attention

Chapter 5 Endoscopy

To help in the planning of location of endoscopic services for screening, the following five levels of competency are proposed.

- **Level 0:** The operator does not remove any lesions, referring on all patients with any detected lesions. The operator will be able to biopsy lesions, and pathological material may inform the decision to refer. Basic level of competency for diagnostic FS but not recommended for screening FS.
- **Level 1:** Removing lesions <10 mm in diameter at FS. Rationale: larger lesions will indicate a need for colonoscopy and can be removed when the colonoscopy is performed. Tissue is required from smaller lesions to decide whether colonoscopy is necessary. Thus any person performing FS screening should have this level of competency.
- **Level 2:** Removing polypoid and sessile lesions <25 mm providing there is good access. All colonoscopists should have this level of competency.
- **Level 3:** Removing smaller flat lesions (<20 mm) that are suitable for endoscopic therapy, larger sessile and polypoid lesions, and smaller lesions with more difficult access. Some flat lesions <20 mm with poor access might be unsuitable for this level. Any person doing colonoscopy for positive FOBT in a screening programme should have this level of competency.
- **Level 4:** Removing large flat lesions or other challenging polypoid lesions that might also be treated with surgery. This is the type of lesion that would not be removed at the first colonoscopy because of time constraints, if applicable, or because the surgical option needs to be discussed with the patient. If the patient chooses to have endoscopic therapy, then he/she should be referred to a level 4 competent endoscopist. This level of competency would be expected of only a small number of regionally based colonoscopists.

Stage distribution at diagnosis

Stage	FIT		Programs FS (n=23)
	First test (n=1052)	Following tests (n=740)	
I	35,5	42,3	56,5
I*	8,9	10,1	17,4
II	29,9	21,1	8,7
III-IV	25,7	26,5	17,4

*cancer polyps, endoscopically (only) removed