

# Appropriateness of colonoscopy in Europe (EPAGE II)

## Functional bowel disorders: pain, constipation and bloating

### Authors

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### Institutions

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**submitted** 17 June 2008

**accepted after revision**  
5 December 2008

### Bibliography

**DOI** 10.1055/s-0028-1119625

Endoscopy 2009; 41:  
234–239 © Georg Thieme  
Verlag KG Stuttgart · New York  
ISSN 0013-726X

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**Background and study aims:** To summarize the published literature on assessment of appropriateness of colonoscopy for the investigation of functional bowel symptoms, and report appropriateness criteria developed by an expert panel, the 2008 European Panel on the Appropriateness of Gastrointestinal Endoscopy, EPAGE II.

**Methods:** A systematic search of guidelines, systematic reviews and primary studies regarding the evaluation and management of functional bowel symptoms was performed. The RAND/UCLA Appropriateness Method was applied to develop appropriateness criteria for colonoscopy for these conditions.

**Results:** Much of the evidence for use of colonoscopy in evaluation of chronic abdominal pain, and/or constipation and/or abdominal bloating is modest. Major limitations include small numbers of patients and lack of adequate characterization of these patients. Large community-based follow-up studies are needed to enable better definition of the natural history of patients with func-

tional bowel disorders. Guidelines stress that alarm features ("red flags"), such as rectal bleeding, anemia, weight loss, nocturnal symptoms, family history of colon cancer, age of onset > 50 years, and recent onset of symptoms should all lead to careful evaluation before a diagnosis of functional bowel disorder is made. EPAGE II assessed these symptoms by means of 12 clinical scenarios, rating colonoscopy as appropriate, uncertain and inappropriate in 42% (5/12), 25% (3/12), and 33% (4/12) of these, respectively.

**Conclusions:** Evidence to support the use of colonoscopy in the evaluation of patients with functional bowel disorders and no alarm features is lacking. These patients have no increased risk of colon cancer and thus advice on screening for this is not different from that for the general population. EPAGE II criteria, available online (<http://www.epage.ch>), consider colonoscopy appropriate in patients of > 50 years with chronic or new-onset bowel disturbances, but not in patients with isolated chronic abdominal pain.

### Introduction

Several definitions have been used to describe chronic constipation, using features such as type and consistency of stools, frequency of bowel movements and duration of symptoms (chronic/acute) [1–4]. Nonacute/chronic lower abdominal pain relies on patients' subjective sensations (onset, duration) [5]. Bloating refers both to a subjective sensation and to the objective abdominal distension. We used 3 months' duration as a cutoff point for these three nonspecific abdominal symptoms.

The definition of irritable bowel syndrome (IBS) is complex and has been subject to considerable modification over the years. (For the Rome III criteria see **Table e1**; for a comparison of the Rome II and III criteria see **Table e2**). **Table A** gives definitions related to lower abdominal func-

tional bowel disorders as used by EPAGE II. IBS is a disorder characterized by abdominal pain or discomfort associated with defecation and/or a change in bowel habits (diarrhea and/or constipation), and by features of disordered defecation [2], with characteristic symptoms being present during the previous 3 months and with onset > 6 months previously [2].

The prevalence of constipation in the general population [6–8] ranges from 2% to 30%. Women seem to be more frequently affected than men (female-to-male ratio 2:1). Bloating is experienced at least once a month in 16% of healthy individuals [9]. In the general population, about 10%–30% of adults have symptoms consistent with IBS, and most studies show a preponderance of females [10–13]. There are many reasons why a patient might experience symptoms such as

Term	Definition
Uncomplicated	None of following: melena, hematochezia, hemoccult-positive stools, unexplained iron-deficiency anemia, weight loss.
Lower abdominal pain	Pain or discomfort below the umbilicus, with or without bloating.
Empirical inflammatory bowel syndrome (IBS) therapy	At least 2 weeks of daily treatment with fiber (psyllium- or methylcellulose-containing preparations) or antispasmodics (dicyclomine, propantheline, hycosamine, loperamide, diphenoxylate). Empirical therapy does not allow prediction of endoscopic lesions; therefore, it does not appear in the matrix though widely used in clinical practice.
Risk factors for colorectal cancer	Personal history of colorectal cancer (CRC) or colorectal adenomas, inflammatory bowel disease (IBD) Or: Family history of a first-degree relative with CRC or colorectal adenomas, familial polyposis syndrome, hereditary nonpolyposis colorectal cancer (HNPCC) syndrome
Lower GI investigations	Sigmoidoscopy or barium enema since onset of lower abdominal pain or within past 5 years
Barium enema	Double-contrast technique.
Sigmoidoscopy	Flexible tube (60 cm)
Constipation therapy	At least 2 weeks of daily treatment with fibers (psyllium- or methylcellulose-containing preparations)
Constipation	Two or more of the following symptoms for at least 3 months: 2 or fewer bowel movements per week, hard stools more than 25 % of the time, straining more than 25 % of the time, or incomplete evacuation more than 25 % of the time
Chronic bowel disturbances	Change in bowel habits (mainly constipation) with/without bloating of at least 3 months' duration.
New-onset bowel disturbances	Change in bowel habits of < 3 months duration (excluding isolated diarrhea which is dealt with in the companion article about diarrhea)

**Table A** Definitions related to lower abdominal functional bowel disorders.

chronic constipation and/or lower abdominal pain and/or bloating [14–17].

Thus the main difficulty is to differentiate between organic and functional disorders. Although diagnostic colonoscopy may be useful for such patients, its appropriateness is questioned [18,19].

In April 2008, a multidisciplinary European expert panel convened in Montreux, Switzerland, to discuss and develop criteria for the appropriate use of colonoscopy. The RAND Appropriateness Method was chosen for this purpose, because it allows the development of appropriateness criteria based on published evidence and supplemented by explicit expert opinion. A detailed description of the application of the RAND Appropriateness Method, including the literature search process, is published separately in a companion article in this issue [20].

This article presents the literature review on the appropriateness of colonoscopy in functional bowel disorders (chronic constipation and/or pain and/or bloating) that was provided to the panelists before the panel meeting, to support their ratings of appropriateness of use of colonoscopy in such circumstances; their ratings are also reported here. This updates a previous literature review published in 1999 [21].

The present chapter refers to diagnostic colonoscopy only. Patients considered here for colonoscopic evaluation would have no risk factor for colorectal cancer (CRC), except for age, and none of the following so-called alarm or “red flag” symptoms: hematochezia; positive fecal occult blood test (FOBT); anemia; personal/family history of colon cancer; personal/family history of inflammatory bowel disease; weight loss of  $\geq 5$  kg; severe, persistent constipation that is unresponsive to treatment; recent-onset constipation in an elderly patient without any evidence of a possible primary cause; abdominal pain/discomfort associated with exercise, movement, urination, or menstruation; fever; presence of an abdominal mass; or HIV/AIDS [22–25]. A companion article deals with chronic diarrhea including occasional

isolated patients with functional diarrhea. The following disorders are also not considered in this article: diverticular disease, diverticulitis, metabolic conditions, and drug artifacts.

## Methods



The literature review process included a systematic search of websites issuing guidelines and of Medline (1997–February 2008) to select published guidelines, systematic reviews, and primary studies assessing the use of colonoscopy in patients with functional bowel disorders. With the exception of certain relevant articles, the literature published before 1997 is presented in the previous literature review [21].

As mentioned above, the application of the RAND/UCLA Appropriateness Method is described in detail in a companion article in this issue [20]. Briefly, this process is a formal explicit expert panel method that allows classification of each indication into one of the following categories of appropriateness: inappropriate; uncertain; appropriate; appropriate and necessary (that is, the indication mandates the procedure).

To simplify the graphical presentation of the appropriateness results, these four categories were consolidated into two clusters: “Appropriate” (including “appropriate,” and “appropriate and necessary”) and “Not appropriate” (comprising “inappropriate” and “uncertain”). In addition to simplification and enhanced clarity of presentation, the rationale for this choice was that in many instances in the case of a nonappropriate scenario, whether it be uncertain or inappropriate, the decision for not proposing the colonoscopy should be specifically discussed and shared with the patient. All clinical indications and their ratings are available on the EPAGE website ([www.epage.ch](http://www.epage.ch)).

## Results

### Literature review

Eight primary studies investigating the diagnostic yield of colonoscopy in patients presenting chronic constipation and/or abdominal pain and/or bloating and published between 1997 and February 2008 were identified; 21 guidelines published over the same period on the use of colonoscopy in such patients were retrieved.

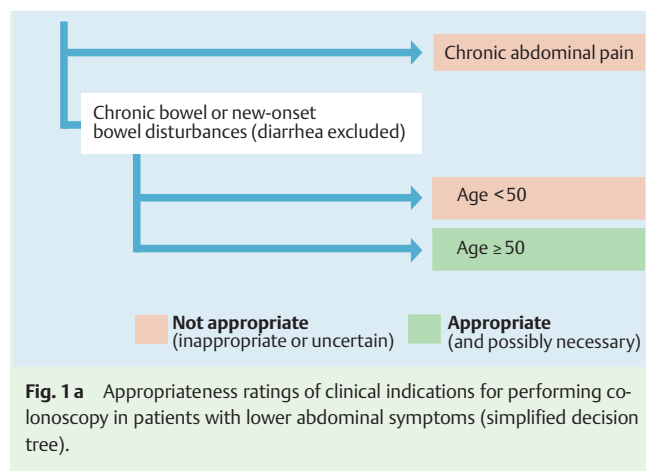
Primary studies [26–33] (see also [34]) investigating the diagnostic yield of colonoscopy in patients presenting such symptoms show very variable rates, with a variety of findings in 10% to 70% of the cases (Table e3). Guidelines [17, 22–25, 35–50] (Table e4) show no clear consensus on the role of colonoscopy in the diagnosis of patients presenting chronic constipation and/or lower abdominal pain and/or bloating. Patient groups presenting such nonspecific symptoms tend to be classified according to age and whether or not they have associated alarm symptoms and/or “red flags” for organic disease. Lower gastrointestinal endoscopic evaluation would then be justified for patients ≥ 50 years with recent-onset complaints or for any patients with complaints associated with alarm features. There is no clear consensus on whether the initial procedure in patients presenting these nonspecific symptoms should be a sigmoidoscopy or a colonoscopy.

In patients presenting with chronic constipation and/or lower abdominal pain and/or bloating, practitioners might principally consider performing a colonoscopy to exclude colorectal cancer (CRC). In primary studies [51–61], chronic constipation thus does not unequivocally appear to constitute an indicator or a risk factor for colonic neoplasia (Table e5). The literature does not give a clear indication as to whether individuals presenting with chronic constipation and/or abdominal pain and/or bloating should be considered “asymptomatic” thus being eligible for “colorectal cancer screening,” or “symptomatic” thus justifying the search for a potential colonic pathology [26]. Some CRC screening/surveillance guidelines [35, 36, 47] do mention chronic constipation and/or lower abdominal pain and/or bloating as possible symptoms likely to raise concern about the presence of CRC, while most of them do not [62–71]. The prevalence of organic disease such as CRC or inflammatory bowel disease (IBD) is not elevated in patients with IBS, compared with that in a control population [38]. Only the French guidelines from ANAES [35] recommend that a total colonoscopy be performed to identify a potential colonic neoplasia in patients with nonspecific abdominal symptoms of recent onset and which are unresponsive to treatment, if symptoms appear > 50 years of age, or if symptoms appear < 50 years of age and if symptomatic treatment does not have positive results.

### EPAGE II appropriateness criteria

The panelists assessed lower abdominal symptoms (chronic constipation/abdominal pain/bloating) in three categories: chronic abdominal pain only, chronic bowel disturbances, and new-onset bowel disturbances (see Table A for definitions used by the panel). Patients with known inflammatory bowel disease, anemia, or positive FOBT were explicitly excluded from this set of scenarios.

Out of 463 indication scenarios presented to the panel, 12 pertained to these symptoms; in 5/12 scenarios colonoscopy was



considered appropriate, in 3/12 uncertain, and in 4/12 it was considered inappropriate. Fig. 1 a is a color-coded presentation of the results in a clustered dichotomy of “Not appropriate” (inappropriate or uncertain), versus “Appropriate” (appropriate or both appropriate and necessary). Isolated chronic abdominal pain was considered not appropriate for colonoscopy, as well as chronic or new-onset bowel disturbances in patients younger than 50 years. Chronic or new-onset bowel disturbances in those over 50 years of age were appropriate and potentially necessary (i.e. mandating) indications.

Fig. e1b presents appropriateness criteria in more detail. With isolated chronic abdominal pain, colonoscopy is considered inappropriate in individuals younger than 50 years, and of uncertain appropriateness in individuals 50 years or older. Patients with chronic bowel disturbances (i.e. mainly constipation under 50 years) are not considered appropriate candidates for colonoscopy under 50 years. In contrast to isolated abdominal pain, change in bowel habits of at least 3 months’ duration is deemed appropriate for colonoscopy in patients aged 50 years or more. In patients under 50 years with new-onset bowel disturbances (new onset constipation with/without bloating, excluding diarrhea), panelists strongly disagreed, resulting in an “uncertain” rating. In contrast, patients with similar complaints but aged 50 years or more are all considered appropriate candidates for colonoscopy. If the procedure had never been performed previously, or was done 5 years or more previously, then colonoscopy was even deemed necessary (mandatory) in this clinical situation.

The panelists did not consider response to irritable bowel syndrome therapy as an important factor when taking decisions about appropriateness of colonoscopy.

All the clinical indications and their ratings are available online (<http://www.epage.ch>), where answering a few clinical questions allows the appropriateness score for each indication to be obtained.

### Conclusions

Primary studies evaluating the appropriateness of colonoscopy in patients presenting nonspecific symptoms such as chronic constipation and/or lower abdominal pain and/or bloating are of modest quality. Most of them are retrospective case series without control groups. The variations among results can be explained by the heterogeneity in measured outcomes, study design, samples, definitions, indications for colonoscopy and/or in-

clusion criteria, which may also reflect the discrepancies in and the evolution of the definitions, and the still unknown etiologies of these nonspecific symptoms. Direct comparisons of results between studies, as well as generalization and recommendations for all individuals with chronic constipation and/or abdominal pain and/or bloating are therefore difficult. Guidelines on these topics must therefore be interpreted with caution since they are mainly based on modest evidence and on expert opinion. The complaints dealt with in this article are difficult to define clinically and often overlap, but are extremely frequent: chronic constipation and/or lower abdominal pain and/or bloating are mainly indicators of functional disease. This review of the published literature highlights the fact that, despite the modest quality of the evidence, and although the presence of these symptoms probably does not enhance the pick-up rate of CRC per se, recommendations tend to consider screening purposes associated with clinical symptoms as a reason for performing colonoscopy. The notion of alarm symptoms ("red flags") is used to differentiate between symptoms of functional disease in which colonoscopy probably is of little help, and symptoms of organic disease in which colonoscopy would be appropriate. Colonoscopic evaluation may thus be justified for patients aged  $\geq 50$  years with recent-onset complaints (chronic constipation and/or abdominal pain and/or bloating) or for any patients with such complaints in association with alarm symptoms.

The EPAGE II panel considered chronic as well as new-onset changes in bowel habits in patients aged  $\geq 50$  years to be appropriate indications for performing colonoscopy. In contrast, isolated pain is not deemed to be an appropriate indication whatever the patients' age. New-onset bowel disturbances at  $\geq 50$  years are necessary (i.e. mandating) indications for colonoscopy. The EPAGE II panel results show the importance of the cutoff age of 50 years for the decision as to whether colonoscopy should be performed in patients with lower abdominal symptoms such as abdominal pain, constipation, and bloating.

## Acknowledgments

The authors gratefully acknowledge the selfless commitment and invaluable contribution of the expert panel members, who made this project possible: Lars Agr us (SE), Christoph Beglinger (CH), Peter Bytzer (DK), Michel Delvaux (FR), Volker F. Eckardt (DE), Peter D. Fairclough (UK), Fran ois Lacaine (FR), Olivier Le Moine (BE), Vicente Lorenzo Z niga Garcia (ES), Giorgio Minoli (IT), Matijs E. Numans (NL), Daniel Oertli (CH), John O'Malley (UK), Alastair Windsor (UK). The authors warmly thank Susan Giddons for her invaluable assistance in the administration of the expert panel process, as well as in the meticulous preparation of the manuscripts.

## Appendix: The EPAGE II Study Group

See page 205.

**Competing interests:** None

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**Fig. e1b** Appropriateness ratings of clinical indications for performing colonoscopy in patients with lower abdominal symptoms (full decision tree).

**Table e1** Functional bowel disorders: Rome III definitions (adapted from [2]).

**Table e2** Comparison between the Rome II and Rome III definitions of functional bowel disorders.

**Table e3** Studies investigating the diagnostic yield of colonoscopy in patients presenting with chronic constipation and/or abdominal pain and/or bloating (1997 – February 2008).

**Table e4** Guidelines/reviews issuing recommendations on the appropriateness of colonoscopy for diagnostic purposes in chronic constipation and/or abdominal pain and/or bloating.

**Table e5** Guidelines/reviews issuing recommendations on the appropriateness of colonoscopy for diagnostic purposes in chronic constipation and/or abdominal pain and/or bloating.

**Table e6** Studies investigating the association between chronic constipation and colorectal cancer (1997 – February 2008).