Appropriateness of colonoscopy in Europe (EPAGE II)
Screening for colorectal cancer

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Background and study aims: To summarize the published literature on assessment of appropriateness of colonoscopy for screening for colorectal cancer (CRC) in asymptomatic individuals without personal history of CRC or polyps, 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 colonoscopy for screening for colorectal cancer was performed. The RAND/UCLA Appropriateness Method was applied to develop appropriateness criteria for colonoscopy in these circumstances.

Results: Available evidence for CRC screening comes from small case-controlled studies, with heterogeneous results, and from indirect evidence from randomized controlled trials (RCTs) on fecal occult blood test (FOBT) screening and studies on flexible sigmoidoscopy screening. Most guidelines recommend screening colonos-copy every 10 years starting at age 50 in average-risk individuals. In individuals with a higher risk of CRC due to family history, there is a consensus that it is appropriate to offer screening colonoscopy at < 50 years. EPAGE II considered screening colonoscopy appropriate above 50 years in average-risk individuals. Panelists deemed screening colonoscopy appropriate for younger patients, with shorter surveillance intervals, where family or personal risk of colorectal cancer is higher. A positive FOBT or the discovery of adenomas at sigmoidoscopy are considered appropriate indications.

Conclusions: Despite the lack of evidence based on randomized controlled trials (RCTs), colonoscopy is recommended by most published guidelines and EPAGE II criteria available online (http://www.epage.ch), as a screening option for CRC in individuals at average risk of CRC, and undisputedly as the main screening tool for CRC in individuals at moderate and high risk of CRC.

Introduction
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Cancer of the colon and rectum (colorectal cancer [CRC]) is one of the most common cancers diagnosed in Western countries and is a major cause of cancer-associated morbidity and mortality [1,2]. In Europe, the annual age-standardized incidence of CRC is 35 and 55 per 100 000 in women and in men respectively [1]. The age distribution of CRC shows a predominance in patients > 50 years with less than 10 % of patients being younger than 50 years [3]. The mean age at diagnosis was found to range from 65 to 71.5 years [4]. CRC is the second major cause of cancer mortality in both women and men. While the survival rate for early-stage cancers is high, the survival rate for those diagnosed with widespread cancer is low.

About 75 % of all new cases of CRC occur in asymptomatic individuals with no known predisposing factor for the disease except age (≥ 50 years old; average risk) [5]. The remaining cases occur in individuals with a family history of CRC or adenomatous polyps, or with a family history of hereditary nonpolyposis colorectal cancer (HNPCC), or with familial adenomatous polyposis (FAP) or attenuated FAP. Screening, which refers to the search for colorectal lesions in asymptomatic patients with no personal history of CRC or adenomas, appears to be the best option available to reduce CRC morbidity and mortality by early detection of CRC in individuals ≥ 50 years old. However, there is debate about the best screening method and about whether colonoscopy should be recommended for CRC screening.

In April 2008, a multidisciplinary European expert panel was convened in Montreux, Switzerland, to discuss and develop criteria for the appropriate use of colonoscopy. This article presents the literature review on screening for CRC in asymptomatic individuals that was provided to

the panelists before the panel meeting to support their ratings of appropriateness of use of colonoscopy for such screening, and also presents the panel's results. It updates the previous literature review and consideration of appropriateness criteria that was published in 1999 [6].

The aim of this review is to assess the effectiveness/appropriateness of colonoscopy for screening for CRC in asymptomatic individuals, at average risk (≥ 50 years old), at slight or moderate risk (with a family history of CRC or adenomatous polyps) and at high risk (with a family history of HNPCC, FAP, or attenuated FAP). The use of colonoscopy for surveillance after polypectomy and after resection of CRC is reviewed in a companion article in this issue.

Method
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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 for CRC screening. With the exception of certain relevant articles, the literature published before 1997 is presented in the previous literature review [6].

The application of the RAND/UCLA Appropriateness Method is described in detail in a companion article in this issue [7]. Briefly, the RAND 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, and appropriate and necessary (that is, mandating colonoscopy). To simplify the graphical presentation of the appropriateness results, these four categories were consolidated into two clusters: "Appropriate" (comprising the categories appropriate, and appropriate and necessary) and "Not appropriate" (comprising the categories 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).

Results: Literature review
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Primary studies on the use of colonoscopy for CRC screening in asymptomatic individuals at average risk

Colonoscopy is usually considered to be the gold standard examination for adenoma and CRC detection. Single-test sensitivity was reported to be 90% for large adenomas and 75% for small adenomas (< 1cm); sensitivity for cancer was > 90% [8]. However, insufficient procedural competence and experience on the part of the endoscopist may impair test performance [9] and recent studies comparing computed tomography colonography with colonoscopy have found greater miss rates for colonoscopy than previously described [10, 11].

The diagnostic yield of CRC screening by colonoscopy in studies published since 1997 is presented in **Table e1** [12 – 23]. In individuals aged ≥ 50 years, rates range from 9% to 16% for adenomas, from 3% to 6% for advanced adenomas, and from 0% to 2.6% for cancer. In individuals aged 40–49, the diagnostic yield is lower (6%–9% for adenomas, 1%–3% for advanced adenomas, < 1% for cancer), while it is higher for individuals aged > 65 years (14%–

43% for adenomas, 12%–13% for advanced adenomas, 1%–3% for cancer). Rates are also lower in women compared with men [13, 14, 17, 19, 23].

No randomized controlled study has evaluated whether screening colonoscopy alone reduces the incidence or mortality from CRC in people at average risk of the disease. There is currently one ongoing randomized controlled trial (RCT) investigating screening colonoscopy versus standard care (study I) and versus annual fecal occult blood test (FOBT) (study II) in patients aged 50 to 69, conducted by Sidney Winawer in the US. Two case-controlled studies and one cohort study on colonoscopy screening for CRC have been published since 1997 [24 – 26], in addition to the two case-controlled studies published in 1995[27, 28] (**Table e2**). In the latter studies [27, 28], men diagnosed with CRC were significantly less likely to have had colonoscopy before CRC diagnosis. The two recent case-controlled studies also showed that men and women diagnosed with CRC were less likely to have ever had colonoscopy before CRC diagnosis, but this result was not statistically significant in one study [25] and the results of the other study [24] are of limited use, as the specific impact of colonoscopy could not be separated from that of flexible sigmoidoscopy. In the cohort study, a negative screening colonoscopy was significantly associated with a reduced incidence of CRC over at least 10 years [26].

There is also indirect evidence from FOBT trials that FOBT followed by colonoscopy if the test is positive reduces CRC mortality[29 – 31]. Some authors have also suggested that evidence from flexible sigmoidoscopy studies, for which case-controlled studies showed a reduction in CRC mortality, can be extrapolated to colonoscopy as it provides a more complete examination of the colon [32]. In addition, recent evidence on the prevalence of advanced proximal neoplasia occurring in the absence of polyps in the distal colon [17, 33, 34] also favors the use of colonoscopy rather than sigmoidoscopy as the primary method of CRC screening. Finally, colonoscopy with polypectomy has been shown in several studies [35 – 39] to significantly reduce the incidence of CRC and mortality from CRC.

The projected impact of screening colonoscopy on CRC incidence and mortality has also been estimated in cost-effectiveness studies, using various transition models in hypothetical average-risk individuals aged 50 years. In the model of Frazier et al. [40], screening colonoscopy every 10 years was estimated to reduce CRC incidence by 58% and CRC mortality by 64%. In Sonnenberg & Delcò's model [41], a single colonoscopy at age 65 was estimated to prevent 23% of CRCs, while colonoscopy every 10 years starting at age 50 was estimated to prevent 75% of CRCs. In the model of Vijan et al. [42], the estimated reduction in CRC mortality varied from a high 64% with the assumption of 100% patient compliance to a low 21% with 25% patient compliance.

Guidelines on the use of colonoscopy for CRC screening in asymptomatic individuals at average risk

Since 1997, many guidelines have been published on CRC screening. Guidelines on CRC screening in average-risk individuals, published since 2000 and that are of moderate and good quality [32, 43 – 52], are reported in **Table e3**. While these guidelines agree that CRC screening is effective in reducing CRC mortality in average-risk individuals, there is no consensus on the best screening strategy. Indeed, while some guidelines recommend screening colonoscopy every 10 years starting at age 50 in average-risk individuals, others argue that they cannot recommend for or against colonoscopy due to the lack of evidence.

The recommendation to begin CRC screening in average-risk patients at age 50 is supported by several studies confirming that CRC is infrequent in individuals aged 40–49 years [14,16,19]. The 10-year interval for screening colonoscopy is based on evidence that it takes an average of 10 years for the transformation of an adenomatous polyp into an invasive cancer, and is supported by results from case-controlled and cohort studies showing very low rates of advanced neoplasia or cancer at 5-year follow-up [26,53,54].

Primary studies on the use of other tests for CRC screening in asymptomatic individuals at average risk

Published evidence on the effectiveness of FOBT and flexible sigmoidoscopy is briefly reviewed, due to the lack of consensus in guidelines on the appropriateness of colonoscopy and to the absence of randomized controlled trials on its effectiveness. In addition, a short overview of newer techniques, i.e. virtual colonoscopy and fecal DNA testing, is provided.

FOBT is a widely used noninvasive screening test for CRC, followed by colonoscopy in the event of a positive result. Its sensitivity for CRC detection is lower than that of colonoscopy, ranging from 37% to 80% [55–57], meaning that many cases of CRC are not detected by the initial FOBT screening. Authors therefore suggest repeating the test every year (annual) or every 2 years (biennial) if the test is negative. In contrast to screening colonoscopy, evidence on the effectiveness of screening FOBT comes from four large RCTs, with long follow-up periods (12–18 years) [29–31,58–64] (**Table e4**). In the systematic review published by the Cochrane Collaboration in 2007 [65], results including the four abovementioned trials showed a statistically significant 16% reduction in CRC mortality with FOBT screening. No difference was found, however, in all-cause mortality. Some authors have argued that lesions found through screening programs with FOBT were likely to have been detected because of the high prevalence of colorectal lesions and the frequency of colonoscopy rather than because of the ability of FOBT to detect colorectal lesions [66,67]. Nevertheless, all guidelines include FOBT as a screening option for CRC.

Flexible sigmoidoscopy, usually followed by colonoscopy if an adenoma is found in the distal colon, was reported as identifying 70% to 80% of patients with advanced neoplasia[23,68,69]. However, recent studies have demonstrated that a significant number of advanced proximal neoplasms occur in the absence of distal neoplasia in average-risk patients [17,33,34], especially in women [20] and older patients [33,70]. There is also a lack of consensus about which flexible sigmoidoscopy findings necessitate subsequent colonoscopy. Some authors advocate performing colonoscopy when any polyp is detected, while others recommend colonoscopy only after detection of large, multiple, or high-risk adenomas. The effectiveness of flexible sigmoidoscopy screening with colonoscopic follow-up was evaluated in a small RCT [23,71,72], which showed a significantly lower incidence of CRC in individuals undergoing flexible sigmoidoscopy screening. Mortality results from six ongoing trials involving flexible sigmoidoscopy screening should soon be available [73–80]. Three case-controlled studies have been published since 1997 [25,81,82] (**Table e5**) showing that sigmoidoscopy screening reduces mortality from cancer of the distal colon and rectum (odds ratio [OR] range 0.24–0.56). However, in a case-controlled study published in 1995, sigmoidoscopy alone did not reduce mortality from CRC [27].

Computed tomography colonography (CTC), also called virtual colonoscopy, is a recent technique consisting of CT-scan images of the colon, which are then reconstructed by computer into virtual fly-through pictures of the colonic lumen. CTC is not yet endorsed by most guidelines as a screening option. In a meta-analysis of the accuracy of CTC [83], results showed that sensitivity was very heterogeneous (between 21% and 96%). Improvements in technology, training, and standardization of the technique are required before CTC can be recommended for widespread screening [54].

Fecal DNA testing, which detects genetic mutations characteristic of CRC in cells found in stools, is also still under development. Its sensitivity was reported to be four times that of FOBT for detecting invasive cancer [84]. It has only recently been recommended for CRC screening by the US Multi-Society Task Force on CRC [52].

Primary studies on the use of colonoscopy for CRC screening in individuals with a family history of CRC or adenomatous polyps

Individuals with a family history of CRC or adenomatous polyps, but without any currently known genetic susceptibility (HNPCC or FAP), have an increased risk of developing CRC compared with those without a family history. In a meta-analysis of cohort and case-controlled studies, the pooled relative risk of developing CRC if at least one first-degree relative had been diagnosed with CRC was estimated at 2.24 (95%CI 2.06–2.43), and increased to 3.97 (95%CI 2.60–6.06) if at least two first-degree relatives were affected [85]. The pooled relative risk of CRC also increased to 3.87 (95%CI 2.40–6.22) with a relative diagnosed with CRC before age 45 and was found to be 1.99 (95%CI 1.55–2.55) with a first-degree relative with adenomatous polyps [86]. Yield of screening colonoscopy in persons with a positive family history of CRC or adenomas is indeed higher than in persons without a family history[87–90]. However, in individuals aged <50 years, the yield appears to be quite low, and some authors question the need for screening colonoscopy before the age of 50 years [89,91].

No randomized study was found examining the effectiveness of screening colonoscopy in patients with a family history of CRC or adenoma, with regard to reducing CRC incidence and mortality. In a small case-controlled study of asymptomatic individuals participating in a screening colonoscopy program for first-degree relatives of CRC patients [92], screening colonoscopy had been performed previously in 2.5% of individuals diagnosed with CRC, compared with 48.7% of individuals without CRC (*P* < .0001).

Guidelines on the use of colonoscopy for CRC screening in individuals with a family history of CRC or adenomatous polyps

Despite the absence of published studies on the effectiveness of screening colonoscopy in individuals with a family history of CRC or adenomas in reducing CRC incidence and mortality, published guidelines agree that it is appropriate to offer screening colonoscopy to individuals at slight or moderate risk of developing CRC on the basis of a positive family history [32,43,45,46,48, 49,51,93,94–96] (**Table e6**). They recommend starting screening at a lower age than for individuals at average risk. However, the definition of level of risk, the age at which to start screening colonoscopy, and the frequency of screening colonoscopy vary between guidelines.

Table 9 2008 European Panel on the Appropriateness of Gastrointestinal Endoscopy (EPAGE II): definitions related to screening colonoscopy for colorectal cancer (CRC).

Term	Definition
Average risk	Any patient without slightly increased, moderately increased or high risk
Slightly increased risk	Any of the following: Colorectal cancer in one first-degree relative Colorectal cancer in two second-degree relatives Adenomatous polyp in one first-degree relative Personal history of ovarian or endometrial cancer History of ovarian or endometrial cancer in one first-degree relative First-degree relatives
Moderately increased risk	Any of the following: Colorectal cancer in two first-degree relatives Colorectal cancer in one first-degree relative with onset before age of 50 First-degree relatives
High risk	Any of the following: Family history of FAP Family history of HNPCC First-degree relatives
Positive screening fecal occult blood test (FOBT)	At least one stool test for occult blood shows a positive reaction
Sigmoidoscopy	Flexible tube (60 cm)
Positive findings at screening sigmoidoscopy	Low-risk adenoma High-risk adenoma
Low-risk adenomas	All of the following: No more than 2 adenomas Size < 1 cm Tubular histology No high-grade dysplasia First-degree familial anamnesis negative
High-risk adenomas	Any of the following: Villous or tubulovillous histology or serrated adenoma (any size, number or grade of dysplasia) Size ≥ 1 cm Multiple adenomas (≥ 3) Large sessile adenomas High-grade dysplasia

HNPCC, hereditary nonpolyposis colorectal cancer; FAP, familial adenomatous polyposis

Primary studies and guidelines on the use of colonoscopy for CRC screening in individuals with a family history of hereditary nonpolyposis colorectal cancer (HNPCC)

HNPCC is an autosomal-dominant inherited condition characterized by the development of CRC at a mean age of 45 years and a 80 % lifetime risk of CRC [97,98] and it is the most common hereditary form of CRC (5 % – 6 % of all CRC cases). An accelerated adenoma–carcinoma progression is described owing to the presence of larger adenomas with more dysplasia than in nonfamilial cases [99]. Two-thirds of cancers occur in the right colon [99], thus necessitating an examination of the entire colon.

Only one prospective controlled study [100,101] of screening colonoscopy for CRC in HNPCC families was found in the literature. Järvinen and colleagues found that a 3-year interval colonoscopy (or double-contrast barium enema and flexible sigmoidoscopy) screening in families with HNPCC significantly reduced the CRC rate of 62 % within a 15-year follow-up period [100].

Despite the lack of evidence, guidelines agree that it is appropriate to offer screening colonoscopy to individuals with a family history of HNPCC [32,43,46–49,51,93–96,98] (**Table e7**). They recommend colonoscopy starting at the age of 20–25 years or 10 years prior to the earliest age at diagnosis in the family. The recommended interval for colonoscopy is every 1 or 2 years until age 40, then annually.

Primary studies and guidelines on the use of colonoscopy for CRC screening in individuals with a family history of familial adenomatous polyposis (FAP)

FAP is an autosomal-dominant syndrome caused by mutations in the adenomatous polyposis coli (APC) gene, characterized by the presence of more than 100 adenomas in the colon. The average age for first adenomas in FAP is 16 years, and the average age for colon cancer is 39 years. Affected persons have a 100 % risk of developing colorectal cancer [5]. A variant of FAP, called attenuated APC (AAPC), is associated with a variable number of adenomas (usually 20–100), a proximal colonic distribution of adenomas, and a relatively delayed onset of CRC that is approximately 10 years later than for FAP.

No controlled study was found on screening colonoscopy for CRC in patients with a family history of FAP or attenuated FAP. Most of the available evidence stems from observational studies in registries. In a study of patients in a registry, CRC mortality was significantly lower in patients who underwent endoscopy screening compared with those who presented with symptoms [102].

Current guidelines on endoscopic procedures for individuals with a family history of FAP are presented in **Table e8** [32, 43,46–48,51,93–96]. If the genetic test result is positive, annual flexible sigmoidoscopy is recommended, starting at the age of 10–15 years. According to one guideline[46], colonoscopy is an alternative to flexible sigmoidoscopy and the Scottish guidelines [96] recommend colonoscopy every 2–3 years in addition to flexible sigmoidoscopy. If the genetic test result is negative, most
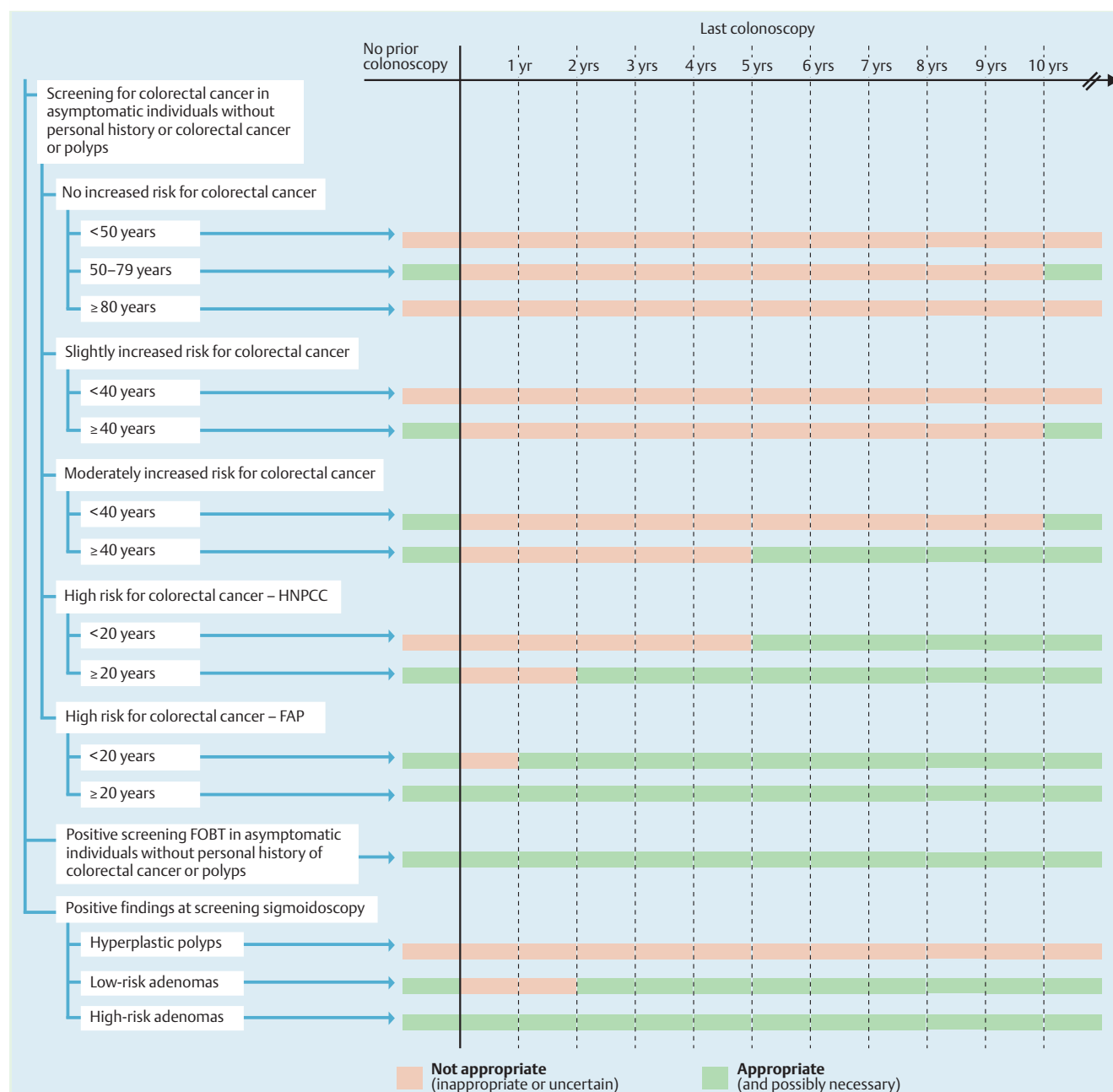
Fig. 1 a Appropriateness of ratings of clinical indications for performing colonoscopy in patients for colorectal cancer (CRC) screening (simplified decision tree). HNPCC, hereditary nonpolyposis colorectal cancer; FAP, familial adenomatous polyposis; FOBT, fecal occult blood test. Copyright © 2008 IUMSP/CHUV, Lausanne, Switzerland – EPAGE II.

guidelines suggest screening as for average-risk individuals. In cases of attenuated FAP, guidelines recommend colonoscopy every 2–3 years, beginning in the late teens, because of the preponderance of proximal colonic adenomas.

Results: EPAGE II appropriateness criteria
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Out of 463 indications, 97 scenarios pertained to screening for colorectal cancer (CRC). Indications related to screening were considered appropriate, uncertain, and inappropriate, in 51%, 20% and 29% of scenarios, respectively. Disagreement between panelists occurred in only 7% of scenarios. Screening was considered mandatory in 33 scenarios ("necessary indications") by the

panel. ● **Table 9** shows the definitions used by panelists for the assessment of appropriateness of screening colonoscopy.

● **Fig. 1 a** shows the overall color-coded panel results as a simplified, clustered dichotomy, of "Not appropriate" ("inappropriate" or "uncertain" grouped together) versus "Appropriate" ("appropriate" and "appropriate and necessary" grouped together). In this simplified view, screening colonoscopy is considered appropriate and possibly necessary in average-risk patients aged over 50 years without prior colonoscopy, patients with slightly or moderately increased risk aged over 40 years, high-risk patients aged over 20 years, patients with a positive FOBT test result, and patients who are found to have adenomas at sigmoidoscopy.

Fig. e1b depicts appropriateness criteria in more detail, with the full range of categories (inappropriate, uncertain, appropriate,

appropriate and necessary). In average-risk individuals, panelists consider colonoscopy appropriate above 50 years of age. Subsequent screening colonoscopy is then considered appropriate at 10-year intervals up to the age of 80. As familial or personal risk of CRC increases, the age at which a first colonoscopy is recommended decreases, to 40 years for slightly and moderately increased risk, and to 20 years of age for high-risk individuals. Similarly, with increasing risk, subsequent surveillance intervals become shorter. A positive FOBT in an asymptomatic individual without personal history of polyps or CRC and without prior colonoscopy is considered an appropriate and even necessary (mandating) indication for performing colonoscopy. While it is deemed appropriate to repeat colonoscopy when FOBT remains positive, even if the first examination is normal, it is even considered necessary to do so after 2 years or more. Colonoscopy is considered appropriate in a patient with low-risk adenomas at sigmoidoscopy, and necessary if sigmoidoscopy reveals high-risk adenomas. Figure **e1b** also shows for which indications colonoscopy is mandatory (necessary). Failure to carry out the procedure in these situations would represent underuse. For the definition of necessity, refer to the companion article regarding methods in this journal [7].

Conclusions
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Colonoscopy is widely recommended as a screening procedure with a high diagnostic and therapeutic yield. In individuals at high risk for CRC, the place of colonoscopy appears to be undisputed. However, debate continues on whether colonoscopy screening should be adopted for average-risk individuals, given the current lack of high-quality evidence based on randomized controlled trials. General screening for CRC in the population has also become a subject of debate in recent years: although it is widely accepted and practiced in many countries, some authors doubt its benefits and therefore advise against widespread screening in the general population.

In spite of the relatively high yield of screening colonoscopy for adenomas and CRC and the results of simulation models, the evidence from small case-controlled studies, and indirect evidence from RCTs and cohort studies on polypectomy, RCTs of FOBT, and case-controlled studies on flexible sigmoidoscopy, does not permit measurement of the real effectiveness of screening colonoscopy for CRC prevention, when considered in terms of CRC and overall mortality reduction. Nevertheless, there is a shift favoring colonoscopy over the other tests in the United States and in some European countries. Compared with the other tests, colonoscopy is more sensitive and allows the removal of polyps, precursors of most CRCs, during the procedure. On the other hand, colonoscopy is associated with complications, and has imperfect sensitivity. Furthermore, the technical quality of colonoscopy may be a matter of concern (e.g., cecal intubation rate, missed lesions, withdrawal time).

The EPAGE II panel considered screening colonoscopy appropriate in average-risk individuals above 50 years, at 40 years in case of slight or moderate risk, and at 20 years in those with high risk for CRC. The appropriate interval for subsequent screening colonoscopy shortens in proportion to the increased risk of CRC. A positive FOBT is always considered an appropriate indication for colonoscopy. If the procedure was not done for necessary (mandating) indications this would represent underuse of colonoscopy.

The results from the EPAGE II panel are available online (http://www.epage.ch) and may contribute to the optimal use of available resources and to improved patient care regarding colonoscopy.

Appendix: The EPAGE II Study Group
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The following figure and tables are available online:
www.thieme-connect.com/media/endoscopy/200903/supmat/endo844.pdf

Fig. e1b Appropriateness ratings of clinical indications for performing colonoscopy in patients for colorectal cancer (CRC) screening: (full decision tree). HNPCC, hereditary nonpolyposis colorectal cancer; FAP, familial adenomatous polyposis; FOBT, fecal occult blood test.
Table e1 Diagnostic yield of colonoscopy screening for colorectal cancer (CRC).
Table e2 Case-controlled and cohort studies of colonoscopy screening for colorectal cancer (CRC).
Table e3 Guidelines for colorectal cancer (CRC) screening.
Table e4 Randomized controlled trials of fecal occult blood test (FOBT) screening versus no screening for colorectal cancer (CRC).
Table e5 Case-controlled and cohort studies involving sigmoidoscopy screening for colorectal cancer (CRC).
Table e6 Guidelines for colorectal cancer (CRC) screening in individuals with a family history of CRC or adenomatous polyps.
Table e7 Guidelines for colorectal cancer (CRC) screening in individuals with a family history of hereditary nonpolyposis colorectal cancer (HNPCC).
Table e8 Guidelines for colorectal cancer (CRC) screening in individuals with a family history of familial adenomatous polyposis (FAP).