

Post-polypectomy colonoscopy surveillance: European Society of Gastrointestinal Endoscopy (ESGE) Guideline



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This Guideline is an official statement of the European Society of Gastrointestinal Endoscopy (ESGE). The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system was adopted to define the strength of recommendations and the quality of evidence.

Main recommendations: The following recommendations for post-polypectomy endoscopic surveillance should be applied only after a high quality baseline colonoscopy with complete removal of all detected neoplastic lesions.

1 In the low risk group (patients with 1–2 tubular adenomas <10 mm with low grade dysplasia), the ESGE recommends participation in existing national screening programmes 10 years after the index colonoscopy. If no screening programme is available, repetition of colonoscopy 10 years after the index colonoscopy is recommended (strong recommendation, moderate quality evidence).

2 In the high risk group (patients with adenomas with villous histology or high grade dysplasia or ≥10 mm in size, or ≥3 adenomas), the ESGE recommends surveillance colonoscopy 3 years after the index colonoscopy (strong recommendation, moderate quality evidence). Patients with 10 or more adenomas should be referred for genetic counselling (strong recommendation, moderate quality evidence).

3 In the high risk group, if no high risk adenomas are detected at the first surveillance examination, the ESGE suggests a 5-year interval before a second surveillance colonoscopy (weak recommendation, low quality evidence). If high risk adenomas are detected at first or subsequent surveillance examinations, a 3-year repetition of surveillance colonoscopy is recommended (strong recommendation, low quality evidence).

4 The ESGE recommends that patients with serrated polyps <10 mm in size with no dysplasia should be classified as low risk (weak recommendation, low quality evidence). The ESGE suggests that patients with large serrated polyps (≥10 mm) or those with dysplasia should be classified as high risk (weak recommendation, low quality evidence).

5 The ESGE recommends that the endoscopist is responsible for providing a written recommendation for the post-polypectomy surveillance schedule (strong recommendation, low quality evidence).

Abbreviations

CRC	colorectal cancer
ESGE	European Society of Gastrointestinal Endoscopy
g-FOBT/FIT	guaiac-based faecal occult blood test/ faecal immunochemical test
HGD	high grade dysplasia

Introduction

Colorectal cancer (CRC) represents a major cause of morbidity and mortality in Western countries [1–3]. CRC screening has been shown to be effective in reducing CRC incidence and/or mortality [4–7], and population-based screening is widely recommended in Europe [8]. The effect of endoscopic screening is conveyed via two mechanisms. First, removal of precancerous adenomatous polyps at the time of the index examination and the detection of CRC at an early stage reduce CRC incidence and/or mortality [4,9–11]. Secondly, stratification based on the endoscopic

findings allows patients at greater risk to benefit from endoscopic surveillance [12–14]. Patients with adenomatous polyps are at greater risk of future development of advanced neoplasia (adenomas ≥ 10 mm or with unfavourable histology or cancer) [15–18]. This may be because serious lesions were missed or not radically removed at the initial examination, or because an inherent imbalance of cell proliferation in an individual leads to accelerated carcinogenesis in apparently normal mucosa [16, 19–23].

It is assumed that if patients in whom precancerous polyps have been found are entered into a surveillance programme, then metachronous or recurrent adenomatous lesions and cancer will be detected at an earlier stage. However, no randomized study has directly assessed how much benefit is contributed by the efficacy of post-polypectomy surveillance. The efficacy of endoscopic surveillance has been addressed only in epidemiological series. Such studies have indicated that patients who are not entered into a surveillance programme have a three- to fourfold greater risk of CRC [18, 23].

Screening series have reported an adenoma prevalence of 15%–30% [12, 13, 24, 25]. With the use of high definition colonoscopy equipment, adenomas are found in up to 50% of the population [26, 27]. Thus, an indiscriminate use of post-polypectomy surveillance would represent a substantial burden on endoscopy resources, also resulting in unnecessary costs and longer waiting times for other indications. Currently, close to 20% of endoscopic capacity is occupied by surveillance colonoscopies, approximately the same proportion as primary screening examinations [28–30]. With several European countries initiating population-based screening programmes, the burden of surveillance can be expected to increase in the near future. Although colonoscopy is generally regarded as a safe procedure, a risk of major complications remains [31]. In patients at increased risk of developing cancer, the balance of benefit and risk is generally regarded as favourable. However, the risks, albeit small, may become relevant if the gain associated with surveillance colonoscopies is substantially reduced.

When considering the lack of strong evidence to support post-polypectomy surveillance, and the substantial workload involved, a conservative approach would appear reasonable. It should be remembered that the aim of population-based CRC screening is to reduce the incidence and mortality of CRC, and to do so with a sustainable expenditure of medical and economic resources. For the best balance between the benefits and drawbacks of post-polypectomy surveillance, it should only be offered to patients with a substantial residual risk of CRC. Epidemiological and clinical studies have shown that it is possible to stratify the risk of CRC and to identify a small subgroup of patients with a greater incidence of CRC that persists after baseline polypectomy [21, 32].

The aim of this evidence-based and consensus-based Guideline, commissioned by the European Society of Gastrointestinal Endoscopy (ESGE), is to provide caregivers with a comprehensive review of risk stratification following removal of precancerous neoplastic lesions and with practical recommendations for scheduling endoscopic surveillance. This Guideline does not address surveillance after endoscopic or surgical resection of a malignant polyp, or surveillance in patients affected by hereditary colorectal syndromes.

Methods



The ESGE commissioned this Guideline. The guideline development process included meetings, telephone conferences, and on-line discussions among members of the guideline committee during February 2012 and February 2013. Subgroups were formed, each in charge of a series of clearly defined key questions (Appendix 1, available online). The committee chairs (C.H., J.M.D.) worked with the subgroup leaders (J.M.D., E.Q., J.R.) to identify pertinent search terms that always included, as a minimum, “post-polypectomy endoscopic surveillance” as well as terms pertinent to specific key questions. Searches were performed in Medline. Articles were first selected by title; their relevance was then confirmed by review of the corresponding manuscripts, and articles with content that was considered irrelevant, including that relating to hereditary colorectal syndromes, were excluded. A repository of selected literature was made available to all members of the guideline development group. Evidence tables were generated for each key question, summarizing the evidence of the available studies. For important outcomes, articles were individually assessed by means of the Grades of Recommendation Assessment, Development, and Evaluation (GRADE) system for grading evidence levels and recommendation strengths (Appendix 2, available online) [33].

Each subgroup developed draft proposals that were presented to the entire group for general discussion during a meeting held in February 2013 (Düsseldorf, Germany). Further details on the methodology of ESGE guidelines have been reported elsewhere [33].

In March 2013, a draft prepared by C.H. was sent to all group members. After agreement on a final version, the manuscript was submitted to *Endoscopy* for publication. The journal subjected the manuscript to peer review, and the manuscript was amended to take into account the reviewers' comments. All authors agreed on the final revised manuscript.

This Guideline was issued in 2013 and will be considered for review in 2018, or sooner if new and relevant evidence becomes available. Any updates to the guideline in the interim will be no-

Box 1 Main definitions adopted for this Guideline.

Term	Definition
High quality colonoscopy	Complete colonoscopy with a meticulous inspection of adequately cleaned colorectal mucosa. Neoplastic lesions have also been completely removed and retrieved for histological examination.
Index colonoscopy	First high quality colonoscopy on which surveillance strategy is based
Metachronous lesion	Any lesion that is detected at surveillance colonoscopies
Low risk group	1–2 tubular adenomas < 10 mm with low-grade dysplasia; serrated polyps < 10 mm and no dysplasia
High risk group	Adenoma with villous histology or high grade dysplasia or ≥ 10 mm in size, or ≥ 3 adenomas; serrated polyps ≥ 10 mm or with dysplasia
Advanced adenoma	Adenoma with villous histology or high grade dysplasia or ≥ 10 mm in size
Advanced neoplasia	Adenoma with villous histology or high grade dysplasia or ≥ 10 mm in size, or colorectal cancer
Serrated polyp	Hyperplastic polyps, sessile serrated polyp, traditional serrated adenomas, and mixed lesions

ted on the ESGE website: <http://www.esge.com/esge-guidelines.html>.

Recommendations and statements

Evidence statements and recommendations are stated in italics, key evidence statements and recommendations are in bold. See **Box 1** for main definitions for this Guideline.

The following recommendations for post-polypectomy endoscopic surveillance should only be applied after a high quality baseline colonoscopy with complete removal of all detected neoplastic lesions.

Colonoscopy that is performed in quality-controlled settings has been associated with a substantial reduction in subsequent CRC incidence and mortality and with a very low risk of metachronous advanced neoplasia [4, 34, 35]. However, large observational studies have recently shown that the protective effect of colonoscopy, whether or not it includes polypectomy, is reduced when it is done in suboptimal conditions [5, 36]. Moreover, studies involving head-to-head colonoscopy and computed tomography (CT) colonography and tandem colonoscopy have demonstrated that colonoscopy misses some polyps [37, 38]. In a systematic review of tandem colonoscopy studies, colonoscopy miss rates for polyps ≥ 10 mm, 6–9 mm, and < 5 mm were found to be 2%, 13%, and 26%, respectively [37]. Endoscopist- and centre-related quality factors have been shown to predict a higher risk of interval CRC [39–41]. Endoscopists and endoscopic centres performing low quality examinations, as measured by adenoma/polyp detection rate and cecal intubation rate, have consistently been associated with a higher risk of post-colonoscopy interval CRC [39, 40, 42]. In addition, the incomplete removal of lesions has consistently been shown to increase the subsequent risk of CRC [16, 23, 43].

For these reasons, widespread implementation of quality assurance programmes is necessary for adequate efficacy of post-polypectomy surveillance. Factors associated with the quality of colonoscopy and of bowel cleansing have been reviewed in specific ESGE Guidelines [44, 45]. There is no evidence that overutilization of endoscopic surveillance can compensate for an initially suboptimal colonoscopy. Moreover, to duplicate an invasive and costly procedure, rather than to address, for example, the quality of bowel cleansing and improved endoscopist training, seems unacceptable from the point of view of cost-effectiveness and patient acceptability. Briefly, high quality colonoscopies should be complete up to the caecum with a meticulous inspection of adequately cleaned colorectal mucosa. Neoplastic lesions should be completely removed (en bloc when feasible) and retrieved for histological examination. This does not contradict early repetition of the colonoscopy if the quality of the initial procedure was suboptimal because of inadequate bowel cleansing or other factors (see below in the specific scenarios, and **Table e1**, available online).

Appropriate scheduling of surveillance

The ESGE recommends that the endoscopist is responsible for providing a written recommendation for the post-polypectomy surveillance schedule (strong recommendation, low quality evidence), and that this should be audited (weak recommendation, low quality evidence).

Surveillance colonoscopies represent a major part of all colonoscopies performed, being nearly 30% in a recent survey [46]. This proportion may increase with the widespread adoption of CRC screening programmes and with improved adenoma detection

related to the use of high resolution colonoscopy and dye-spraying techniques [3, 47, 48]. For these reasons, the required capacity of colonoscopy services is heavily dependent on correct indications and timings for post-polypectomy surveillance [49–51]. Studies have shown that a large proportion of surveillance procedures are inappropriate in both selection of cases and timing of surveillance, representing both over- and underuse of surveillance [46, 51–58]. In a recent survey, 69% of post-polypectomy surveillance procedures were inappropriate regarding either timing or indication [46]. In another study, over 40% of patients with small adenomas had an inappropriately early surveillance examination [52]. Moreover, surveillance is still recommended to patients with clinically irrelevant hyperplastic lesions who do not need any endoscopic surveillance [46, 52–58]. (See also **Table e2**, available online).

Appropriateness of surveillance not only depends on the characteristics and number of completely removed polyps, but also on factors such as the quality of endoscopy, and the patient's age and life-expectancy. For these reasons, the endoscopist should be the professional who advises the patient on the appropriate surveillance interval. Since histology reports become available some time after the polypectomy, we recommend that the endoscopist updates and/or finalizes the endoscopy report after receiving the histology report; the updated colonoscopy report should include a written recommendation on the appropriate surveillance, taking into account all endoscopic, histological, and patient-related factors. Adherence to published surveillance guidelines should be monitored as part of a quality assurance programme [59–61].

Low risk group

In the low risk group (patients with 1–2 tubular adenomas < 10 mm with low grade dysplasia), the ESGE recommends participation in existing national screening programmes 10 years after the index colonoscopy. If no screening programme is available, repetition of colonoscopy 10 years after the index colonoscopy is recommended (strong recommendation, moderate quality evidence).

Long-term CRC risk in low risk group (see **Table 3a**)

Epidemiological studies have assessed long-term CRC incidence/mortality risk in patients with 1–2 tubular adenomas < 10 mm with low grade dysplasia. In a retrospective study [62], including 1618 patients with adenomas resected by rigid sigmoidoscopy who did not undergo endoscopic surveillance, patients stratified to this low risk group had a similar risk of developing CRC compared with the general population (standardized incidence ratio [SIR] 0.5, 95% confidence interval [CI] 0.1–1.3). The same finding was reported in a registry-based study that included 5779 post-polypectomy patients: the low risk group did not have an increased risk of cancer despite the lack of surveillance (SIR 0.68, 95%CI 0.44–0.99) [18]. Furthermore, case-control studies have also confirmed a low long-term risk of CRC in these patients, with a more profound effect during the 5 years immediately following the index polypectomy [22, 23, 63]. A conservative policy of post-polypectomy endoscopic surveillance was recently tested and found to be adequate in two prospective screening sigmoidoscopy trials [9, 11].

Incidence of metachronous advanced neoplasia in the low risk group

Several cohort studies have compared the incidence of metachronous advanced adenomas between a low risk group and a control

Table 3 Long-term colorectal cancer risk. **a** Studies reporting standardized incidence ratio (SIR) with 95 % confidence intervals (CI) in low and high risk groups as compared with the general population.

First author	Variable	Low risk	High risk
Atkin [62]	SIR (95 %CI)	0.5 (0.1 – 1.3)	3.6 (2.4 – 5.0)
Cottet [18]	SIR (95 %CI)	0.8 (0.4 – 1.5)	4.3 (2.9 – 6.0)

Table 3 Long-term colorectal cancer risk. **b** Studies comparing incidence (hazard ratio [HR] or risk ratio [RR]) of metachronous advanced neoplasia between low risk and high risk groups, and patients without neoplasia at baseline examination.

First author	Variable	Low risk	High risk
Yamaji [15]	HR (95 %CI)	Nonadvanced: 2.6 (1.6 – 4.2)	Advanced: 6.6 (3.7 – 12)
Lieberman [35]	RR (95 %CI)	Tubular < 10 mm: 2.6 (0.2 – 5.7)	Tubular > 10 mm: 6.4 (2.7 – 14.9) Villous pattern: 6.1 (2.5 – 14.7) High grade dysplasia: 6.9 (2.6 – 18.1)
Miller [66]	RR (95 %CI)	< 5 mm: 1.1 (0.4 – 3.3) 5 – 9 mm: 1.5 (0.6 – 3.9) Tubular: 0.9 (0.4 – 2.3)	≥ 10 mm: 2.1 (1.3 – 2.7) Villous pattern: 4.2 (1.5 – 11.5)
Chung [64]	HR (95 %CI)	Nonadvanced: 1.1 (0.6 – 2.2)	Advanced: 6.0 (3.7 – 9.7)

CI, confidence interval

group without adenoma at index colonoscopy [15,35,64–66] (Table 3b; see also Table e4, available online). One study found a higher incidence of advanced neoplasia (hazard ratio [HR] 2.6; 95%CI 1.6–4.2) in the low risk group compared with controls [15]. None of the other studies detected a statistically significant difference, either at 5 years [35, 64–66] or at 6–10 years of follow-up [65, 66]. Two randomized controlled trials (RCTs) [35, 67], as well as three cohort studies [64, 66,68], compared the prevalence of advanced neoplasia at different intervals between the index examination and the first surveillance colonoscopy in the low risk group. No statistically significant difference was found when comparing intervals of 2 vs 4 years, 3 vs 5 years, and 3–5 vs 6–10 years [35,64,66,67,69].

Timing of surveillance/return to screening in low risk group

For individuals without increased risk of CRC (i.e., risk similar to that in the general population) a 10-year interval before undergoing surveillance colonoscopy or returning to a screening programme appears to be justified by the long-term efficacy of lower gastrointestinal endoscopy (i.e., sigmoidoscopy or colonoscopy) as demonstrated in RCTs and case–control studies [7, 11, 70]

High risk group

In the high risk group (patients with adenomas with villous histology or high grade dysplasia or ≥ 10 mm in size, or ≥ 3 adenomas), the ESGE recommends surveillance colonoscopy 3 years after the index colonoscopy (strong recommendation, moderate quality evidence). Patients with 10 or more adenomas should be referred for genetic counselling (strong recommendation, moderate quality evidence).

Long-term CRC risk in the high risk group (see Table 3a)

Epidemiological studies have indicated that the high risk group is at increased risk of CRC compared with the general population. Patients stratified into the high risk group who were followed for 14 years (without endoscopic surveillance) had a 3.6– to 6.6-fold increase in CRC risk, compared with the general population [62]. Another study found that patients with advanced adenomas who did not undergo endoscopic surveillance had a 4.26 (95%CI 2.89–6.04) times greater risk for CRC [18]. Epidemiological series

also showed a high efficacy of endoscopic surveillance in reducing the CRC risk in the high risk group [22, 23, 63].

Incidence of metachronous advanced neoplasia in the high risk group

In prospective cohort studies, the incidence of metachronous advanced neoplasia was 5–7 times higher in the high risk group compared with individuals without adenomas at the index colonoscopy [15,35,64]. A pooled analysis included individual data on 9167 participants from 8 prospective post-polypectomy trials with a mean follow-up of 47 months. The crude risk of advanced neoplasia during follow-up was 15.5% in the high risk group and 6.9% in the low risk group [32]. In a multivariate analysis, size, multiplicity, and presence of villous component of the baseline lesions appeared to be independent risk factors for metachronous advanced neoplasia, whilst high grade dysplasia was not [32]. These results were largely confirmed by two meta-analyses [71,72]. The risk of metachronous advanced lesions seems to be higher in the high risk groups, but the contribution of each individual unfavourable adenoma feature (size, multiplicity, villous component) was less consistent [32, 71, 72]. Further data on these individual factors in the high risk group are provided in Table e4 and Table e5 (available online).

It has been suggested that individuals with 5 small adenomas, or 3 or more adenomas where at least one was ≥ 10 mm, could benefit from endoscopic surveillance 1 year after the last endoscopy [73]. In a pooled analysis of 4 surveillance studies, including 3226 patients, these individuals had a doubled risk of metachronous advanced lesions compared with those in the high risk group who did not have these characteristics [73]. However, these individuals did not have higher risk of CRC, and there is considerable uncertainty about how this higher risk of advanced neoplasia may translate into CRC risk.

Timing of surveillance in the high risk group

In the US National Polyp Study, following adenoma resection 1418 patients were randomly allocated to either a 1-year followed by a 3-year surveillance colonoscopy or to a single 3-year surveillance colonoscopy. The incidence of advanced lesions was 3.3% in both groups [74]. In a retrospective observational study,

the cumulative incidence of metachronous advanced neoplasia in the high risk group increased with increasing surveillance interval; after intervals of 1–3, 3–5, 5–10 and 10–20 years, the incidences of metachronous advanced neoplasia were 3.8%, 13.1%, 34.7% and 52%, respectively [68]. In contrast, another observational study found no association between the duration of the surveillance interval (from 0.5 to 10 years) and the risk of metachronous advanced neoplasia in the high risk group (the risk varied between 9.9% and 11.4%) [65]. This finding was confirmed in a case–control study where the risk of CRC was unchanged if the surveillance interval was prolonged from 3 years to 5 years [75]. In line with current recommendations [76], we propose that individuals with 10 or more adenomas be referred for genetic counselling because of the risk of familial adenomatous polyposis (FAP) or other genetic diseases, such as *MYH*-associated polyposis. Tailored surveillance programmes for patients with hereditary colorectal cancer syndromes are outside the scope of this guideline.

In the high risk group, if no high risk adenomas are detected at the first surveillance examination, the ESGE suggests a 5-year interval before a second surveillance colonoscopy (weak recommendation, low quality evidence). If high risk adenomas are detected at first or subsequent surveillance examinations, a 3-year repetition of surveillance colonoscopy is recommended (strong recommendation, low quality evidence). The ESGE found insufficient evidence to give recommendations in the case where no high risk adenomas are detected during 2 consecutive surveillance colonoscopies. However, intervals longer than 5 years appear reasonable (very low quality evidence).

Three recent cohort studies have investigated the risk of metachronous advanced lesions at second surveillance colonoscopy, according to the findings at the baseline and first surveillance colonoscopy [65,77,78] (Table e6, available online). The study designs were prone to selection bias because of nonadherence, which might affect generalizability. However, despite heterogeneity in the study populations, results were reassuringly consistent across the studies. In individuals with high risk adenomas at the index colonoscopy and no high risk adenomas at the first surveillance endoscopy, the risk of metachronous advanced neoplasia at the second surveillance colonoscopy was higher than among individuals without high risk adenomas detected at the index colonoscopy [65,77,78]. The absolute risk of metachronous advanced neoplasia at the second surveillance colonoscopy was 5.9%–6.7% among individuals with high risk adenomas at the index colonoscopy, and 3.1%–5.7% among individuals without high risk adenomas [65,77,78]. This supports the recommendation of a second surveillance colonoscopy after 5 years. For individuals with high risk adenomas detected at endoscopic surveillance, the risk of metachronous advanced neoplasia was higher than for individuals without high risk adenomas, regardless of the findings at previous examinations. The absolute risk for metachronous advanced neoplasia at second surveillance endoscopy ranged from 11.5% to 19.3% for individuals with high risk adenomas at first surveillance colonoscopy [65,77,78]. In comparison, the risk varied from 3.1% to 6.7% for individuals without advanced neoplasia at first surveillance [65,77,78]. No study addressed the risk of metachronous advanced neoplasia after two surveillance colonoscopies without high risk adenomas. When considering the progressive decrease in the incidence of such lesions at the first two surveillance colonoscopies, intervals longer than 5 years may appear reasonable.

Serrated polyps (see also Table e7, available online)

The ESGE recommends that patients with serrated polyps <10 mm in size with no dysplasia should be classified as low risk (weak recommendation, low quality evidence). The ESGE suggests that patients with large serrated polyps (≥10 mm) or those with dysplasia should be classified as high risk (weak recommendation, low quality evidence).

Patients with 5 or more serrated polyps proximal to the sigmoid, of which 2 or more are sized ≥10 mm, or with 20 or more serrated polyps of any size but distributed throughout the colon, meet the World Health Organization criteria for serrated polyposis and should be referred for genetic counselling (strong recommendation, low quality evidence).

Serrated polyps are classified into different subgroups: (i) hyperplastic polyps, (ii) sessile serrated polyps, (iii) mixed polyps, and (iv) traditional serrated adenomas. No prospective study has yet assessed the long-term risk of CRC in patients with neoplastic and non-neoplastic serrated lesions, leading to uncertainty on the usefulness of endoscopic surveillance.

Hyperplastic polyps

Observational studies found that in the absence of any neoplasia, hyperplastic polyps are not associated with advanced adenomas [79,80], although a slightly increased risk of adenomas was found [81,82]. The coexistence of hyperplastic polyps with adenomas at index colonoscopy does not increase the risk of adenomas and advanced adenomas at surveillance compared with adenomas alone [81–83]. Indirect evidence of the indolent behavior of hyperplastic polyps is also found in sigmoidoscopy and colonoscopy studies [13,79].

Sessile serrated polyps (also defined as sessile serrated adenomas/lesions)

One retrospective pathology-based study showed that 15% of patients with sessile serrated polyps at index examination developed advanced neoplasia (CRC/HGD) within approximately 8 years of follow-up, compared with 5.5% of patients with baseline adenomas within 3 years of follow-up [80]. However, the difference in follow-up durations generates some uncertainty about such a comparison [80]. Another study demonstrated that in 50% of patients with sessile serrated polyps at baseline, subsequent sessile serrated polyps were detected within approximately 3 years of follow-up [84]. However, patients with nondysplastic sessile serrated polyps did not present an increased risk of metachronous advanced neoplasia, although size ≥10 mm or proximal location were predictors of synchronous advanced neoplasia [85,86]. In particular, large serrated polyps were associated with a higher risk of proximal CRC [86]. Three studies have found an association between type of lesion detected during follow-up and type of lesions found at baseline colonoscopy [84,87,88]. Patients with sessile serrated lesions are more likely to develop further sessile serrated lesions. However, there is no evidence of an increased risk of metachronous CRC [84,87,88]. We recommend that some patients, who fulfil the WHO criteria for serrated polyposis syndrome, should be considered for genetic counselling [89]. This includes: (i) individuals with 5 or more serrated polyps proximal to the sigmoid with 2 or more of those being ≥10 mm in diameter, and (ii) individuals with 20 or more serrated polyps of any size distributed throughout the colon (both right- and left-sided).

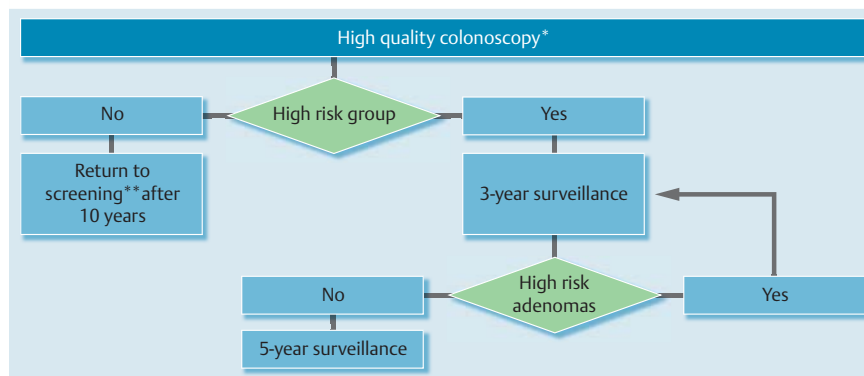


Fig. 1 Dichotomization of patients following a high quality colonoscopy in which high risk lesions have or have not been detected. High risk group: patients with an adenoma ≥ 10 mm; or with high grade dysplasia; or a villous component or ≥ 3 adenomas; serrated polyp ≥ 10 mm or with dysplasia. * Excluding those in whom cancer has already developed. ** To a screening programme if available, otherwise to repetition of colonoscopy.

Mixed polyps and traditional serrated adenomas

Sessile serrated lesions that harbour an adenomatous component are called mixed polyps [90]. These lesions present with a dysplastic component, analogously to the traditional serrated adenomas. No data exist regarding the incidence of metachronous advanced lesions.

Since most pathologists do not yet correctly classify serrated lesions into the several subtypes, we have preferred not to subclassify such lesions for the purposes of our statement [91].

Specific scenarios

In the case of piecemeal resection of adenomas larger than 10 mm, endoscopic follow-up within 6 months is recommended before the patient is entered into a surveillance programme (strong recommendation, moderate quality evidence).

Incomplete removal of larger neoplastic lesions must be ruled out before an endoscopic surveillance schedule is recommended (Table e1c and d, available online). Recently, inadequate polypectomy has been reported in up to 17% of lesions ≥ 10 mm, especially if piecemeal polypectomy had been performed [92]. Incomplete excision of neoplastic lesions has been consistently shown to increase the risk of post-colonoscopy interval CRC [43]. For this reason, an early follow-up of these lesions is recommended within 6 months (Table e1b, available online), even if the resection was apparently complete on the basis of endoscopic and histologic criteria [92, 93]. Normal macroscopic appearance of the polypectomy site and negative scar biopsy specimens at the first follow-up have been shown to be predictive of long-term eradication [93].

The ESGE found insufficient evidence to provide recommendations on post-polypectomy surveillance based on other potential risk factors, such as age, or family history of CRC (very low quality evidence). However, it seems reasonable to stop endoscopic surveillance at 80 years, or earlier depending on life expectancy (in the case of co-morbidities).

A pooled analysis showed that age was a strong risk factor for metachronous advanced neoplasia. The risk was almost three times higher among individuals older than 80 years compared with those between 50 and 59 years (OR 2.7; 95%CI 1.3–5.6) [94]. Conversely, there was no significant difference between individuals aged 50 to 59 and those aged 60 to 69 [64]. Older people could be more prone to complications of colonoscopy, and the potential benefit of endoscopic surveillance may be limited by reduced life expectancy, especially when the estimated 10–20-year duration of the traditional adenoma–carcinoma sequence is taken into account. No studies have assessed the optimal age for stopping surveillance. Although statistical simulations indi-

cate that surveillance should be stopped between 75 and 85 years, this needs to be confirmed by future trials [95]. Therefore, individualized recommendations should be based on general health status, comorbidity and the findings at previous colonoscopies [96]. It is likely that individuals with limited life expectancy (i.e., shorter than 10 years) will not benefit from post-polypectomy endoscopic surveillance [95, 96].

A recent meta-analysis reviewed the influence of family history on the incidence of metachronous advanced neoplasia [97]. In all studies, including 21 595 participants, a positive family history was defined as having at least one first-degree relative with CRC (parents, siblings, or children) [64, 94, 98, 99]. None of the studies assessed the influence of family history stratified by age at diagnosis and the number of relatives with CRC. The proportion of participants with a positive family history of CRC ranged between 4.9% and 27.5% [64, 99]. No association was found between first-degree family history of CRC and metachronous advanced neoplasia (OR 1.20, 95%CI 0.96–1.50). Similarly, race/ethnicity did not appear to predict rate of metachronous advanced adenoma at endoscopic surveillance [100].

The ESGE recommends an early repetition of colonoscopy or a shorter surveillance interval in patients in whom an optimal inspection of colorectal mucosa has been hampered by an inadequate preparation, especially if neoplastic lesions have been detected in the initial examination.

An inadequate level of bowel preparation has been associated with a reduced detection of neoplastic lesions and, therefore, with a higher risk of missed lesions (Table e1a, available online) [101–103]. It has also been shown to be a strong risk factor for metachronous advanced adenoma at surveillance [104]. Thus, early repetition of colonoscopy seems advisable. For instance, if no high risk lesions have been detected and a sufficient level of mucosal inspection has been achieved (i.e., allowing reasonable exclusion of the presence of lesions ≥ 5 mm), rather than 10 years before the subsequent screening colonoscopy, a 5-year interval has been suggested [60]. When repeating colonoscopy or shortening the surveillance interval, all the recommendations for an adequate bowel preparation, including split regimen, must be followed [45].

The ESGE recommends against the use of interval faecal occult blood tests (FOBTs) for post-polypectomy surveillance (strong recommendation, low quality evidence). In the case of an unplanned positive FOBT, the decision to repeat colonoscopy should be based on clinical judgment (weak recommendation, low quality evidence).

The risk of metachronous CRC in patients following polypectomy is stratified by the findings at the index colonoscopy. For this reason, the attempt to re-stratify risk of CRC by applying a guaiac-faecal occult blood test/faecal immunochemical test (g-FOBT/FIT) would appear to be mere duplication. Although interval CRC may be detected by g-FOBT/FIT, the expected low prevalence of disease would result in a high false-positive rate and a substantial burden on personal, endoscopic, and economic resources. In two nonrandomized studies including high risk individuals, a total of 1856 participants underwent at least one interval FIT during a colonoscopy-based CRC screening programme [105,106]. Colonoscopy was performed in 454 FIT-positive individuals; it led to detection of 18 CRCs, giving a positive predictive value of 4% which is dramatically lower than in a primary FIT screening setting [107]. Unplanned FOBT, although recommended against, may turn out to be positive. The decision whether or not to repeat a colonoscopy should depend on careful clinical evaluation, including the quality of the latest colonoscopy, and the time interval between the latest colonoscopy and FOBT.

The ESGE suggests that individuals with symptoms in the surveillance interval should be managed as clinically indicated (weak recommendation, low quality evidence).

Patients under appropriate surveillance are at low risk of CRC but interval CRC may develop, whether polypectomy has been done or not [5,16]. Thus, repetition of colonoscopy should be considered if there is clinical suspicion of interval CRC.

Discussion

Following a high quality colonoscopy with no detection of CRC, patients may be simply dichotomized according to the presence or absence of high risk adenomatous and serrated colorectal lesions (● Fig. 1). Endoscopic surveillance is recommended for individuals in the high risk group (● Box 1). Surveillance is not indicated for individuals in the low risk group, as with individuals with normal colonoscopy findings, for whom return to screening after 10 years is recommended. This simple approach eliminates confusion about the timing of surveillance colonoscopy, and optimizes the utilization of endoscopic resources. Nevertheless, it offers intensive surveillance, i.e., 3 colonoscopies over 10 years, to individuals who are the most likely to benefit from this.

The main difference between the ESGE and the recent US Multi-Society Task Force (MSTF) post-polypectomy Guidelines is the American recommendation for 5–10-year endoscopic surveillance in the low risk group [60]. The main reason for the 5-year US-MSTF recommendation is the possibility of inadequate preparation or poor quality endoscopic examination. We excluded low quality colonoscopy from the scope of our main recommendations. However, in the specific scenarios, we also allowed the possibility of shortening the interval to the next screening colonoscopy in the case of inadequate bowel preparation. There is insufficient evidence regarding the appropriate surveillance interval after a suboptimal colonoscopy, and we want to emphasize the need to repeat colonoscopy as soon as is practicable in the case of a suboptimal examination. In contrast to the ESGE recommendations, the European quality assurance guidelines propose that the first surveillance in patients with 5 polyps or more or with adenoma ≥ 20 mm should be after 1 year rather than 3 years. However, the evidence to underpin this advice does not appear firm [61]. In particular, these patients do not show a high-

er risk of incident CRC, whilst it is unlikely that the moderate increase in the risk of advanced adenoma may represent a significant cause of morbidity/mortality in the subsequent 2 years of follow-up [32,61]. Moreover, our Guideline already recommends that patients with an adenoma ≥ 10 mm that was removed piecemeal should have a 6-month surveillance, according to our guideline.

Overall, discrepancies among the main recommendations of different societies seem to be related to the quality of the supporting studies. It should be remembered that most of these studies were carried out before the advent of high resolution colonoscopy and before quality assurance had been incorporated into clinical practice [32].

There is little consistency in the surveillance recommendations for patients with serrated polyps [60,61], because of the lack of firm data on the risk of subsequent polyps and CRC in these patients. However, because of the consistently higher risk of synchronous advanced neoplasia in patients with large serrated polyps, we preferred to recommend a prudent approach until more definitive evidence becomes available.

The ESGE Guideline provides an evidence-based risk-stratification strategy for post-polypectomy surveillance, limiting surveillance to patients with a greater CRC risk. This approach husbands resources whilst maximizing benefits. Such an approach seems of critical importance when the progressive implementation of CRC screening programs throughout Europe is considered. Further studies in this field, especially dealing with serrated lesions, are needed (● Table e8, available online).

ESGE guidelines represent a consensus of best practice based on the available evidence at the time of preparation. They may not apply in all situations and should be interpreted in the light of specific clinical situations and resource availability. Further controlled clinical studies may be needed to clarify aspects of these statements, and revision may be necessary as new data appear. Clinical consideration may justify a course of action at variance to these recommendations. ESGE guidelines are intended to be an educational device to provide information that may assist endoscopists in providing care to patients. They are not rules and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment.

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Appendix e1 and e2, Table e1–e8,

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Appendix e1

	Task forces (leader in bold)
Task force 1 <i>Efficacy, safety, cost of post-polypectomy surveillance in general</i>	
1. What are the benefits of endoscopic surveillance after colorectal polypectomy?	Rembacken, Hassan
2. What are the risks and burden (including costs) of endoscopic surveillance after colorectal polypectomy? What is the impact of inappropriately performed surveillance colonoscopy?	Rembacken
3. How should the timing of the next endoscopy be communicated to the referring physician or patient? (Integrated in the endoscopy report? Letter to the patient?)	Hassan
4. Do patients comply with scheduled timing of surveillance colonoscopy? Do endoscopists follow recommendations about the timing of surveillance colonoscopy? How can this be improved ?	Hassan
5. What if a patient has an interval faecal occult blood test (FOBT) before the time recommended for surveillance?	Dumonceau
6. What if a patient develops new symptoms such as diarrhea, constipation or minor rectal bleeding?	Dumonceau
7. What if the baseline bowel preparation was poor or inadequate?	Dumonceau
Task force 2 <i>Definition of categories of risks for advanced neoplasia/colorectal cancer (CRC) following polypectomy; definition of intervals for surveillance colonoscopy</i>	
1. Define categories of risk for AN/CRC following polypectomy. Consider for the definition the following main risk factors (including their reliability):	
a. Main risk factors	
(i) Number of adenomas	Hassan
(ii) Adenoma size	Ferlitsch
(iii) High grade dysplasia/villous component/serrated, etc	Jover, Hazewinkel
b. Other risk factors	
(i) Family history of CRC	Quintero, Gimeno-García
(ii) Age	
(iii) Pathological findings: resection margins (nonevaluable, lateral margin involvement, deep margin involvement, complete pathological resection), villous component; in addition to this, in case of carcinoma discuss invasion depth, vascular or lymphatic invasion, differentiation	Pox, Hazewinkel
(iv) What to do in case of no or incomplete polyp retrieval	Chaussade
2. After having classified patients into the categories listed above, define the post-polypectomy risk of advanced neoplasia/CRC patients in each of the categories? Is it increased as compared with those without adenomatous polyps?	Quintero, Gimeno-García
3. For each category of risk, If surveillance colonoscopy is effective, what is the evidence regarding the timing of the first surveillance colonoscopy? What is the influence of other parameters (i. e. patient age or comorbidities)?	Hassan, Ferlitsch
4. For each category of risk, if the first surveillance colonoscopy finds polyps, what should be the timing of the second post-polypectomy colonoscopy?	Kalager
5. For each category of risk, in the case of a first surveillance colonoscopy that is negative for polyps:	Løberg
a. Is there evidence of the efficacy of a second post-polypectomy colonoscopy? If yes, what is the evidence regarding its timing? What timing do we recommend?	Kalager
b. If the first and second surveillance colonoscopies are negative, is there evidence of the efficacy of a third post-polypectomy colonoscopy? If yes, what is the evidence regarding its timing? What timing do we recommend ?	Løberg
Task force 3 <i>Particular cases</i>	
1. What is our recommendation for patients with large adenoma and piecemeal resection? Include patient age, pathological findings (complete, indeterminate or incomplete resection etc) and preparation quality in the recommendation	Regula, Ribeiro, Dumonceau, Rembacken

Appendix e2 a Levels of evidence according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.¹

Evidence level	
High quality	One or more well-designed and well-executed randomized controlled trials (RCTs) that yield consistent and directly applicable results. This also means that further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality	RCTs with important limitations (i. e. biased assessment of the treatment effect, large loss to follow-up, lack of blinding, unexplained heterogeneity), indirect evidence originating from similar (but not identical) populations of interest, and RCTs with a very small number of participants or observed events. In addition, evidence from well-designed controlled trials without randomization, well-designed cohort or case – control analytic studies, and multiple time series with or without intervention are in this category. It also means that further research will probably have an important effect on our confidence in the estimate of effect and may change the estimate.
Low quality	Observational studies would typically be rated as low quality because of the risk for bias. ² It also means that further research is very likely to have an important effect on our confidence in the estimate of effect and will probably change the estimate.
Very low quality ³	Evidence is conflicting, of poor quality, or lacking, and hence the balance of benefits and harms cannot be determined. Any estimate of effect that is very uncertain as evidence is either unavailable or does not permit a conclusion.

¹ Atkins D, Best D, Briss PA et al. Grading quality of evidence and strength of recommendations. *BMJ* 2004; 328: 1490

² Quality of evidence based on observational studies may be rated as moderate or even high, depending on circumstances under which evidence is obtained from observational studies. Factors that may contribute to upgrading the quality of evidence include a large magnitude of the observed effect, a dose – response association, or the presence of an observed effect when all plausible confounders would decrease the observed effect.

³ Insufficient evidence to determine for or against routinely providing a service.

Appendix e2 b Strength of recommendations according to the Grading of Assessment, Development and Evaluation (GRADE) system.¹

Strength of recommendation	
Strong	Benefits clearly outweigh risks and burden or vice-versa. Usually stated as “we recommend”.
Weak	Benefits closely balanced with risks and burden. Usually stated as “we suggest”.

¹ Atkins D, Best D, Briss PA et al. Grading quality of evidence and strength of recommendations. *BMJ* 2004; 328: 1490

Table 1 Association between quality of the index colonoscopy and subsequent risk of colorectal neoplasia. **a** Endoscopic findings, quality of colon cleansing, quality of bowel preparation.

First author, year	Study design	Description	Participants/Data collected	Outcomes	Results	Level of evidence
Harewood, 2003 [101]	Observational retrospective	Data from an US national endoscopic database. Relationship between bowel preparation and finding of colonic polyps	93 004 colonoscopies Preparation adequate in 76.9%	Relationship between preparation adequacy and polyp detection	Preparation adequacy was associated with colonic lesion detection: OR 1.2 (95%CI 1.2–1.3) Adequate preparation demonstrated a closer association with identification of “nonsignificant” lesions (polyps ≤ 9 mm); OR 1.2 (95%CI 1.2–1.3), compared with “significant” lesion detection (mass lesion, polyps > 9 mm): OR 1.1 (95%CI 1.0–1.1)	Low
Froehlich, 2005 [102]	Observational prospective	Multicentre prospective study. Relationship between quality of bowel preparation and colonoscopy findings. Assessment of colonic cleansing on a 5-point scale and categorized in 3 levels	5832 patients Demographics, clinical indication for colonoscopy, diagnosis, and technical parameters were recorded	Relationship between preparation adequacy and polyp detection	Detection of polyps of any size depended on cleansing quality: OR 1.7; (95%CI 1.3–2.4), for intermediate quality compared with low quality preparation OR 1.5 (95%CI 1.1–1.9) for high quality compared with low quality preparation For polyps > 10 mm in size, corresponding ORs were: 1.0 for low quality cleansing; OR 1.8 (95%CI 1.1–3.1) for intermediate quality cleansing; and OR 1.7 (95%CI 1.1–2.7) for high-quality cleansing. Cancers were not detected less frequently in the case of poor preparation.	Moderate
Rex, 2002 [103]	Observational prospective	Characteristics of colonic cleansing and proportion of colonoscopies where surveillance colonoscopy had to be repeated sooner than recommended because of bad bowel preparation	200 patients Colonoscopies prospectively asked to designate examinations that should be repeated at an interval sooner than would otherwise be recommended because of imperfect preparation. The data were used to perform a cost analysis of the economic effect of bowel preparation on direct costs of colonoscopy.	Relationship between bowel cleansing and colonoscopy scheduled sooner than recommended	Colonoscopies brought back earlier than suggested or required by current practice standards because of imperfect bowel preparation (20% vs 12.5%, <i>P</i> = 0.04)	Low
Lebwohl, 2011 [108]	Observational retrospective	Characteristics of repeated colonoscopy in cases where the test was repeated because of poor preparation	12 787 patients from a hospital-based endoscopy unit; 3047 (24%) with bad preparation, 216 with repeated colonoscopy and optimal preparation for analysis of missed polyps	Factors associated with early repeat colonoscopy and findings in the repeated colonoscopy	Factors associated with early repeat colonoscopy: lack of rectal intubation, OR 3.6; (95%CI 2.5–5.2); and finding a polyp, OR 1.6 (95%CI 1.2–2.1) Adenoma miss rate of 42% (95%CI 35%–49%) Advanced adenoma miss rate was 27% (95%CI 17%–41%).	Low
Chokshi, 2012 [109]	Observational retrospective	Screening colonoscopies with poor preparation in the Aronchik scale. Adenoma detection rate in the repeated colonoscopy	133 patients with poor preparation who returned for a repeated colonoscopy	Adenoma miss rate	33.8% of patients had missed adenomas. Per-adenoma miss rate: 47.9% Adenomas more frequently missed in proximal colon	Low
Hillyer, 2013 [110]	Observational prospective	Survey between endoscopists about practice characteristics regarding bowel preparation and recommended follow-up colonoscopy intervals	288 US endoscopists completed the survey. Questions were grouped into four sections: demographic, practice characteristics, bowel preparation regimens used, and recommended follow-up colonoscopy interval based on clinical findings and bowel preparation quality. Proportion of suboptimal bowel preparation per week.	Interval recommendations related to quality of bowel preparation	Differences between interval recommendations at each level of bowel preparation quality (< 10% vs. ≥ 10%) were statistically significant for a small adenoma < 10 mm (<i>P</i> < 0.0001), and for a large adenoma ≥ 10 mm (<i>P</i> < 0.0001). Those reporting a higher proportion of suboptimal preparations more often recommended shorter intervals for each clinical scenario.	Low
Kim, 2012 [111]	Observational prospective	Survey between endoscopists about factors related to concerns for missed polyps	296 endoscopists. After each procedure, the endoscopists responded to a questionnaire that elicited information on the degree of concern for missed polyps, colonoscopic technical factors, and surveillance intervals	Factors associated with nonadherence to the recommended surveillance interval	Based on multivariate analysis, only the endoscopist’s concern was an independent factor associated with adherence to guidelines (<i>P</i> = 0.008). Poor bowel preparation, loop formation, and colonoscopy experience were independent factors associated with a high concern for missed polyps	Low

OR, odds ratio; CI, confidence interval.

Table e1 Association between quality of the index colonoscopy and subsequent risk of colorectal neoplasia. **b** Type of endoscopic resection.

First author, year	Study design, study objective	Intervention	Participants	Outcomes	Results	Level of evidence
Toyonaga, 2010 [112]	Retrospective study n = 268 Japan	Endoscopic submucosal dissection (ESD) of laterally spreading tumour (LST) > 20 mm	n = 268 Single operator Single institution	Local recurrence of adenoma at 1 and 3 years	Local recurrence, 0%	Low
Tanaka, 2001 [113]	Retrospective study Japan	Endoscopic mucosal resection (EMR) of LST > 20 mm	n = 120	En bloc resection rate: En bloc R0 resection rate was 22%	Recurrent tumour occurred in 7.7% of patients who had no subsequent surgical treatment and who followed up for 60.8 months.	Low
Cao, 2009 [114]	Meta-analysis	EMR ESD	n = 2,103 ESD = 853 EMR = 1250	En bloc resection, curative resection	Higher en bloc and curative resection rates irrespective of lesion size, for ESD compared with EMR	High
Moss, 2012 [115]	Prospective multicentre study (7 centres) Australian ICE study	Wide field EMR EMR > 20 mm or LST	n = 903	Colonoscopy at 4 and 12 months Systematic biopsies of the scar	Recurrence at 4 months: 19% Abstract 2012 In case of normal colonoscopy at 4 months and normal biopsies, the recurrence rate at 12 months was 0.6%	Moderate
Park, 2011 [116]	Retrospective study Korea 3 experiences endoscopists	Early colorectal carcinoma (T1 tumour)	n = 231 Tumour size 17.7 mm (5 – 55 mm)	Colonoscopy at 3, 6, 12 months, 3 and 5 years Biopsies of the scar Follow up lost 17%	Right side location of tumour, piecemeal resection, and submucosal carcinoma were associated with R1 resection	Low
Khashab, 2009 [93]	Retrospective study in a tertiary centre		n = 136	Recurrence at 4 – 6 months and 1 year	Absence of visible polyp associated with negative biopsy specimen at first follow-up was associated with a very low level (2%) of late recurrence at 1 year. Recurrence rate at 1 year was high (27%).	Low
Repici, 2012 [117]	Systematic review		22 studies 2841 patients	R0 en bloc resection	Follow-up of patients with R0 en bloc resection showed that recurrence rate was close to 0%.	High
Moss, 2011 [118]	Prospective multicentre study	Endoscopic piecemeal mucosal resection Polyp > 20 mm or greater	n = 479	Colonoscopy at 4 and 12 months Recurrence rate 19%	Late recurrence rate at 1 year is low in patients with normal colonoscopy and normal histology of the scars.	Moderate

OR, odds ratio; CI, confidence interval.

Table e1 Association between quality of the index colonoscopy and subsequent risk of colorectal neoplasia. **c** Pathological findings: resection margins (nonevaluable, lateral margin involvement, deep margin involvement, complete pathological resection).

First author, year	Study design, study objective	Intervention	Participants	Outcomes	Results	Level of evidence
Brenner, 2012 [23]	Population based case-control study To assess the role of colonoscopy-related factors and polyp characteristics on the colorectal cancer (CRC) risk after polyp detection.	Comparison of cases and controls in regard to colonoscopy-related factors and polyp characteristics.	155 cases with CRC and 260 controls, each with polyp detection in the last 10 years	Polyps	Not all polyps removed (29.0% in cases vs. 9.6% in controls) OR 3.7 (95%CI 2.1 – 6.6)	Moderate
Huang, 2012 [69]	Retrospective observational study Cause and risk of interval CRC after polypectomy	Surveillance colonoscopy	1794 patients undergoing surveillance colonoscopy within 5 years after colonoscopic polypectomy.	Interval cancers	14 interval cancers detected: 50% in patients with incompletely removed adenomas, 36% missed cancers, 14% new cancers.	Low
Pabby, 2005 [43]	Retrospective analysis of a randomized trial To analyze cause of interval cancers	Surveillance colonoscopy at 1 and 4 years	2079 patients with one or more adenomas removed at index colonoscopy taking part in the dietary Polyp Prevention Trial	Interval cancers	13 interval cancers detected: 4/13 of these cancers due to incomplete removal of adenomas, 3/13 were missed cancers.	Low

OR, odds ratio; CI, confidence interval

Table e1 Association between quality of the index colonoscopy and subsequent risk of colorectal neoplasia. **d** Incomplete resection.

First author, year	Study design, study objective	Intervention	Participants	Outcomes	Results	Level of evidence
Moss, 2011 [118]	Prospective multi-centre study	Endoscopic mucosal resection (EMR) Polyp > 20 mm or greater	n = 479	Colonoscopy at 4 and 12 months Recurrence rate 19%	EMR was attempted in 96.9%. Resection was technically unsuitable in 9/15 cases and a submucosal carcinoma was found in 6/15 cases. Surgery was done in 40/479 patients (8.3%). In 35% of cases, surgery was indicated for a submucosal invasive carcinoma, and in 26/40 (65%) for unsuitable lesions for EMR at the 1st or 2nd attempt. After incomplete resection, patients underwent a 2nd attempt which was successful in 64%.	Moderate

Table e2 Appropriateness of post-polypectomy colonoscopy indications.

First author, year	Study design, Study objective	Intervention	Participants	Outcomes	Results	Level of evidence
Radaelli, 2012 [28]	Prospective cohort study Inappropriate rate of post-polypectomy surveillance	Surveillance colonoscopy	902 patients with initial finding of adenomas	Appropriateness	54% inappropriate	High
Ransohoff, 2011 [56]	Retrospective study Inappropriate rate of post-polypectomy surveillance	Surveillance colonoscopy	10 089 optical colonoscopies	Appropriateness	24% hyperplastic 35% low risk	Moderate
Mysliewic, 2004 [53]	Survey study Inappropriate rate of post-polypectomy surveillance	Survey	665 endoscopists	Appropriateness	24% – 35% hyperplastic 50% low risk	Low
Petruzzello, 2012 [46]	Prospective cohort study Inappropriate rate of post-polypectomy surveillance	Surveillance colonoscopy	1489 optical colonoscopies	Appropriateness	Post-polypectomy or post-colorectal cancer surveillance accounted for 77% of the inappropriate control procedures	High

Table e4 Studies addressing the incidence of metachronous advanced neoplasia at different time intervals in years after the index colonoscopy.

First author, year	Study design	Participants (n)	First follow-up	Incidence of recurrent advanced neoplasm	Other results ¹	Level of evidence
Jorgensen, 1995 [67]	RCT	n = 673 with small sessile or pedunculated adenomas (<5 mm)	2 years, n = 332 4 years, n = 341	Risk of advanced neoplasia: 2 years: ≥ 1 cm 10.4%, high grade dysplasia (HGD) 1.1%, villous 6.5% 4 years: ≥ 1 cm 9.6%, HGD 0%, villous 8.9%	Advanced neoplasia: 2 years: 3.4% 4 years: 5.6%	High
Noshirwani, 2000 [119]	Adenoma registry	n = 697	3 years	Risk of advanced neoplasia: Patients with low risk adenomas: 3.8% had advanced adenomas at follow-up 2.5% had multiple adenomas Patients had multiple adenomas ≥ 1 cm: 8.3% had advanced adenomas 2.8% had multiple adenomas Patients with multiple adenomas: 15.3% had advanced adenomas 13.9% had multiple adenomas	Only number and size of baseline adenomas were associated with either multiple recurrent adenomas or high risk adenomas	Low
Bonithon-Kopp, 2004 [120]	RCT	n = 640	3 years	Risk of advanced neoplasia: Patients with multiple adenomas at index colonoscopy: at follow-up 16.9% had advanced neoplasia and 18.1% had multiple adenomas Patients with 2 adenomas at index colonoscopy: at follow-up 12.8% had advanced neoplasia and 7.3% had multiple adenomas Patients with 1 adenoma at index colonoscopy: at follow-up 3.9% had advanced neoplasia and 5% had multiple adenomas Patients with villous pattern at index colonoscopy: at follow-up 10.3% had advanced neoplasia and 10.3% had multiple adenomas	Proximal location and the number of adenomas at index colonoscopy were the main predictors of recurrence	High
Matsuda, 2009 [121]	Observational Retrospective	n = 5309 (including 2006 without adenoma)	5 years	Risk of advanced neoplasia: 2.6% in patients without adenomas on the index colonoscopy; 6.7% with adenoma <6 mm; 13.4% with adenoma ≥6 mm; 12.6% with intramucosal cancer.	Cumulative incidence of advanced neoplasia at 5 years higher in patients with adenoma ≥6 mm or intramucosal cancer	Low
Yamaji, 2004 [15]	Observational Prospective	n = 6225 (including 4084 without adenoma)	~3.5 years	Risk of advanced neoplasia: 0.74% in patients without adenomas; 2.2% with nonadvanced adenoma; 6.2% with advanced adenoma	Incidence rate of metachronous advanced adenoma was higher in those with advanced adenomas	Low
Lieberman, 2007 [35]	RCT	n = 724 with adenoma on the initial colonoscopy, and n = 298 without adenomas	Advanced adenoma, 3 years Nonadvanced adenoma: randomized <3 years and 5 years	Risk of advanced neoplasia: 12.4% in patients with advanced adenoma 4.5% at <3 years and 5.8% at 5 years in patients with nonadvanced adenoma 2.4% in patients without adenoma	Lack of association between recurrence rates and time to surveillance	High
Pinsky, 2009 [65]	Retrospective	n = 2607 with and without adenomas on the index colonoscopy	3.4 years to 4.7 years	Risk of advanced neoplasia: 10.5% in patients with advanced adenoma 6.8% with nonadvanced adenoma 4.9% with nonadenomatous polyps and 3.1% with no polyps	Lack of association between recurrence rates and time to surveillance	Low

Table e4 (Continuation)

First author, year	Study design	Participants (n)	First follow-up	Incidence of recurrent advanced neoplasm	Other results ¹	Level of evidence
Martinez, 2009 [32]	Pooled analysis from 8 prospective studies	n = 9167 with adenomas at baseline colonoscopy	4 (most studies clearing colonoscopy 1 year after index colonoscopy) ²	Risk of advanced neoplasia: 16.3% in patients with advanced adenomas 7.4% with nonadvanced	Age Male Large adenomas Villous pattern High grade dysplasia	High
Huang, 2010 [68]	Retrospective	n = 1356 with adenomas at basal colonoscopy	1–3 years 3–5 years 5–10 years 10–20 years	Risk of advanced neoplasia: Patients with advanced adenoma had 3.8%, 13.1%, 34.7%, 52% at the corresponding surveillance intervals. Patients with non-advanced adenomas had 0.9%, 3.9%, 5.8%, 29.2% respectively	Age Male Large adenomas Villous pattern High grade dysplasia Number of adenomas	Low
Miller, 2010 [66]	Retrospective	n = 202 with adenomas at baseline colonoscopy and n = 197 without adenomas	5 years vs 6–10 years	Risk of advanced neoplasia: 26% in patients with advanced adenomas, 5% with nonadvanced adenomas and 7% with normal colonoscopy at 5 years In participants without adenomas or with nonadvanced adenomas there was no difference	Proximal location	Low
Chung, 2011 [64]	Prospective, single-centre	n = 1210 with adenomas at baseline colonoscopy, and n = 1242 without adenomas	Normal group: 5 years Nonadvanced adenoma: randomized <3 and 5 years, or 5 years Advanced adenoma group: 3 years and 5 years	Risk of advanced neoplasia: Patients without adenomas: 2% Patients with non-advanced adenomas 2.4% Patients with advanced adenomas 10.1%	Multiple adenomas (3 or more) Large adenoma (≥ 1 cm)	Low
Cottet, 2012 [18]	Prospective, single-centre Risk of CRC in patients with past history of adenoma resection compared with the general population	n = 5779 with adenomas on the index colonoscopy	Median follow-up 7.7 years	Risk of advanced neoplasia: SIR 2.2, 95%CI [1.7–2.9] for advanced adenoma (2.8%) SIR 0.7, 95%CI [0.4–0.99] for non-advanced adenoma (0.8%)	Multiple adenomas (3 or more) Advanced adenoma	Moderate
Brenner, 2012 [23]	Retrospective case-control study assessing the risk of CRC after adenoma resection	n = 2582 with CRC 1798 controls	3 years, 5 years, 6–10 years	Risk of CRC: Risk reduction in patients with high risk adenomas: at 3 years, 60%; 5 years, 50%; 6–10 years, no reduction Risk reduction patients with low risk adenomas at 3 years, 80%; 5 years, 60%, 6–10 years, 20% (not significant)	Overall, post-polypectomy risk reduction of CRC is lost in individuals with advanced and nonadvanced adenomas after 6 years	Moderate
Martinez, 2012 [73]	Pooled analysis of 4 RCTs comparing 1 year recurrent advanced neoplasia according to US and UK guidelines	n = 3226 with adenomas at baseline colonoscopy	1 year	Risk of advanced neoplasia: Patients with low risk adenomas 3.8% (US) to 4.4% (UK) Patients with high risk adenoma 11.2% (US) to 9.9% (UK) ³ Patients with highest risk 18.7%		High

RCT, randomized controlled trial; CI, confidence interval; SIR, standardized incidence rate.

¹ Risk factors associated with recurrent advanced neoplasms in the multivariate analysis.

² With each additional adenoma there was a linear increase in risk of advanced neoplasia.

³ The UK guideline classifies the risk of metachronous advanced neoplasia at three levels based on the number of adenomas and size: low (2 or fewer adenomas < 10 mm), intermediate (3 to 4 adenomas < 10 mm, or at least 1 adenoma ≥ 10 mm) and high (5 or more adenomas or 3 adenomas, at least one ≥ 10 mm). In the present ESGE Guideline, intermediate risk is included in the high risk category.

Table e5 Association between polyp characteristics and incidence of metachronous lesions. **a** Risk of advanced neoplasia by number of adenomas.

First author, year	Study design	Partici-pants	Number of adenomas at index colonoscopy					Level of evidence
			1	2	3 and more	4	5 and more	
Liebermann, 2007 [35]	Prospective study	n = 3121 50–75 years	Advanced neoplasia 6.5%	Advanced neoplasia 6.5%	Advanced neoplasia 15.9%	Advanced neoplasia 15.9%	Advanced neoplasia: 5–9 mm, 17.2% ≥10 mm, 12.5%	High
Bertario, 2003 [98]	Prospective study	n = 1086		HR 2 (95%CI 0.7–5.8)				High
Laiyemo, 2008 [99]	Prospective study	n = 1905		RR 1.4 (95%CI 0.9–2.1)	RR 1.8 (95%CI 1.2–2.81)			High
Martinez, 2009 [32]	Pooled data from 8 prospective studies	n = 9167	OR 1	OR 1.4 (95%CI 1.2–1.7)	OR 1.9 (95%CI 1.5–2.3)	OR 2.4 (95%CI 1.7–3.4)	OR 3.9 (95%CI 2.8–5.4)	High
Saini, 2006 [71]	Systematic review Pooled RR from 4 studies 4-year follow-up	n = 3254			RR 2.5 (95%CI 1.1–6.0)			High

HR, hazard ratio; CI, confidence interval; RR, relative risk; OR, odds ratio.

Table e5 Association between polyp characteristics and incidence of metachronous lesions. **b** Risk of colorectal cancer (CRC) by number of adenomas at index colonoscopy.

First author, year	Study design	Partici-pants	Number of adenomas at index colonoscopy					Level of evidence
			1	2	3 and more	4	5 and more	
Bertario, 2003 [98]	Prospective study	n = 1086		And more: HR 2.8 (95%CI 0.8– 10.1)				High
Martinez, 2009 [32]	Pooled data from 8 prospective studies	n = 9167	0.5% (95%CI 0.4–0.7)	0.5% (95%CI 0.2–0.9)	1.1% (95%CI 0.4–1.8)	1.2 (95%CI 0.0–1.7)	0.8 (95%CI 0.0–1.7)	High

HR, hazard ratio; CI, confidence interval.

Table 5 Association between polyp characteristics and incidence of metachronous lesions. **c** Risk of advanced neoplasia (both advanced adenomas and colorectal cancer [CRC]) by size of adenoma at index colonoscopy.

First author, year	Study design	Participants	Risk of advanced neoplasia		Risk of CRC		Level of evidence
			Index adenoma <10 mm and tubular	Index adenoma 10–20 mm	Index adenoma >20 mm	Index adenoma >10 mm	
Liebermann, 2007 [35]	Prospective study	n = 3121 50–75 years	RR 2.6 (95%CI 1.2–5.7), irrespective of count vs no neoplasia RR 1.9, <i>P</i> = 0.13, by 1 or 2 RR 5.0, <i>P</i> < 0.001, by 3 or more	RR 6.4 (95%CI 2.7–14.9)			High
Bertario, 2003 [98]	Prospective study	n = 1086		HR 1.9 (95%CI 0.5–6.6)	HR 4 (95%CI 1.1–14.4)	HR 1.1 (95%CI 0.2–0.62)	Moderate
Laiyemo, 2008 [99]	Prospective study	n = 1905		RR 1.5 (95%CI 1.0–2.1)			Moderate
Martinez, 2009 [32]	Pooled data from 8 prospective studies	n = 9167	For 5–10 mm OR 1.17 (95%CI 0.95–1.42),	OR 2.27 (95%CI 1.84–2.78)	OR 3.0 (95%CI 2.2–4), <i>P</i> < 0.0001		High
Saini, 2006 [71]	Systematic review Pooled RR from 4 studies: Adenoma size > 10 mm vs smaller adenomas Follow-up 3 years (3 studies) and 4 years (1 study)	n = 3254		>10 mm RR 1.4 (95%CI 0.9–2.3)			High

RR, relative risk; CI, confidence interval; HR, hazard ratio; OR, odds ratio.

Table e6 a Timing of the second post-polypectomy colonoscopy.

First author, year	Study design, study objective	Intervention	Participants	Outcomes	Results	Level of evidence,
Blumberg, 2000 [122]	Retrospective assessment of 204 patients with adenomas at initial endoscopy who underwent a second and third colonoscopy	Second surveillance colonoscopy	204 patients with initial finding of adenomas	Neoplasia	15% at second surveillance colonoscopy in those with a negative first surveillance endoscopy vs 40% in those with adenomas at first surveillance procedure	Low
Pinsky, 2009 [65]	Retrospective assessment of Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial	Second surveillance colonoscopy	1350 patients with/without adenomas who underwent two surveillance colonoscopies	Advanced neoplasia	Advanced neoplasia finding at 1st surveillance colonoscopy increases risk of advanced neoplasia at 2nd surveillance, regardless of baseline findings. Advanced neoplasia finding at baseline without advanced neoplasia at 1st surveillance colonoscopy only slightly increases the risk of finding advanced neoplasia at 2nd surveillance colonoscopy 2°	Low
Robertson, 2009 [78]	Chemoprevention trial (acetylsalicylic acid (ASA)/folate); observational study	Second surveillance colonoscopy	564 patients	High risk finding at 2nd surveillance colonoscopy	High risk finding at 1st surveillance procedure substantially increases the risk of high risk finding at 2nd. Nonadvanced neoplasia finding at 1st moderately increases the risk of high risk finding at 2nd colonoscopy. If 1st surveillance is negative, high risk finding at baseline substantially increases the risk of high risk finding at 2nd surveillance. If low risk finding at 1st, the risk of HRF at 2nd is moderately increased, regardless of baseline finding.	Moderate
Laiyemo, 2009 [77]	Observational follow-up study Polyp Prevention Trial (PPT)	Second surveillance colonoscopy	774	High risk finding at 2nd surveillance optical colonoscopy	High risk finding at 1st surveillance is highly predictive of high risk finding at 2nd surveillance. Baseline high risk finding does not predict result at 2nd surveillance. Low risk finding at 1st slightly increases the risk of high risk finding at 2nd surveillance.	Moderate

Table e6 b Timing of the second post-polypectomy colonoscopy; if no polyps are found at the first surveillance colonoscopy.

First author, year	Study design	Participants	Low risk adenoma at baseline, and normal findings at 1st surveillance, % with advanced neoplasia at 2nd surveillance	High risk adenoma at baseline, and normal findings at 1st surveillance, % with advanced neoplasia at 2nd surveillance	Level of evidence
Pinsky[65]	Retrospective study	n = 2607	3.9%	5.9%	Low
Laiyemo [77]	Prospective cohort study	n = 1297	2.8%	4.8%	Moderate
Robertson [78]	Prospective cohort study	n = 564	4.9%	12.3%	Moderate

Table e7 Serrated polyps.

First author, year	Study design	Method	Subjects	Outcomes	Results	Level of evidence	
Salaria, 2012 [88]	Case – control	Patients with SSA/Ps identified between 2002 – 2004 compared with patients with tubular adenomas	93 SSA/P patients (63 years, 54% male). 43 patients underwent follow-up colonoscopy 92 tubular adenoma patients (67 years, 57% male). 66 patients underwent follow-up colonoscopy	Detected lesions during follow-up colonoscopy	SSA group n = 43 Mean follow-up interval 2.7 years Any lesion 97%, CRC 2.3%, HGD 2.3% SSA/Ps 51% Tubular adenoma 37% Hyperplastic polyps 42%	Tubular adenoma group n = 66 Mean follow-up interval 3.1 years Any lesion 96% CRC 0% HGD 0% SSA/Ps 3% Tubular adenoma 80% Hyperplastic polyps 18%	Low
Teriaky, 2012 [84]	Retrospective observational	Patients with SSA/Ps diagnosed in 2005 were identified. Charts were analysed to gather data over a 5-year follow up period	23 SSA/P patients (66 years, 58% male). 22 patients underwent follow-up colonoscopy	Detected lesions during follow-up colonoscopy	5 year follow-up period n = 22 Mean number of colonoscopies 2.2 Mean interval between colonoscopies 17 months CRC in 1 patient (5%) 20 adenomas, including 2 HGDs identified in unknown number of patients 21 SSA/Ps, including 2 with LGD and 1 with HGD identified in 11 patients (50%) 2 TSAs/TVA, including 1 HGD identified in unknown number of patients 17 hyperplastic polyps identified in unknown number of patients	Very low	
Schreiner, 2010 [85]	Prospective observational	Follow-up data of patients who underwent screening colonoscopy between 1994 and 1997 were analysed. Hyperplastic polyps and SSA/Ps were defined as nondysplastic serrated polyps (NDSPPs)	3121 asymptomatic patients (50 – 75 years, 97% male.) 1371 patients underwent follow-up colonoscopy	Any neoplasia during follow-up colonoscopy	Surveillance within 5.5 years after baseline colonoscopy In the absence of any neoplasia at baseline colonoscopy, the presence of a proximal NDSP on index colonoscopy is associated with an increased risk of any adenoma during surveillance (OR 3.1, 95%CI 1.6 – 6.2), but not of advanced neoplasia (OR 2.1, 95%CI 0.4 – 9.9). In patients with baseline tubular adenomas, there was no difference in risk for adenomas (OR 0.96 95%CI 0.6 – 1.6) or advanced neoplasia (OR 1.2 95%CI 0.5 – 3.3) during surveillance in patients with and without baseline proximal NDSPPs.	Low	
Lu, 2010 [80]	Case – control	Patients with polyps diagnosed between 1980 and 2001 as hyperplastic polyps were reviewed. Follow-up data was obtained for each SSA/P patient and matched with control hyperplastic polyps and adenoma patients	55 SSA/P patients (63 years, 56% male). 40 patients underwent follow-up colonoscopy 55 patients with hyperplastic polyps and 55 patients with adenomatous polyps matched for age and gender	Detected high-grade lesions (HGD or CRC) during follow-up	SSA/P group: 15% developed high-grade lesions; follow-up 8.3 years. Hyperplastic polyp group: 3.6% developed high-grade lesions; follow-up 2.8 years. Adenomatous polyp group: 5.5% developed high-grade lesions; follow-up 3.2 years.	Very low	
Laiyemo, 2009 [83]	Retrospective observational	Qualifying and baseline colonoscopy (within 1 year) were defined as baseline colonoscopy. Subsequently patients were followed-up for 4 years and underwent follow-up colonoscopy	1637 patients: all diagnosed with adenomas 6 months before baseline colonoscopy (61 years, male 64.4%)	Adenoma and advanced adenoma recurrence during follow-up	Follow up within 3 years No association between the presence of baseline hyperplastic polyps and recurrence of adenoma (OR 1.2, 95%CI 0.9 – 1.2) or advanced adenoma (OR 1.3 95%CI 0.8 – 2.0). No association between proximal (OR 1.0 95%CI 0.7 – 1.5) or distal hyperplastic polyps (OR 1.3 95%CI 0.96 – 1.7) location and adenoma recurrence	Low	

Table e7 (Continuation)

First author, year	Study design	Method	Subjects	Outcomes	Results	Level of evidence
Imperiale, 2008 [81]	Observational	Follow-up colonoscopy data of patients who underwent screening colonoscopy between 1995 and 2000 were analysed.	199 patients with hyperplastic polyps at baseline colonoscopy (57 years, 64% male) 1057 patients with no polyps at baseline colonoscopy (57 years, 55% male)	Adenoma and advanced adenoma recurrence during follow-up	Hyperplastic polyps group Mean follow-up 4.7 years Any adenoma 24% Advanced adenoma 2% No polyps group Mean follow-up 5.4 years Any adenoma 15% Advanced adenoma 1% OR 1.98, 95%CI 1.45–2.71 OR 1.80, 95%CI 0.56–5.74	Low
Lazarus, 2005 [87]	Retrospective observational	Polyps diagnosed between 1978 and 1982 were reviewed. Subsequently follow-up data was obtained from pathology reports and patient records	239 patients: 56 with hyperplastic polyps (51 years, 55% male) 38 serrated adenoma patients (56 years, 61% male) 7 mixed hyperplastic polyps patients (60 years, 57% male) 119 tubular adenoma patients (57 years, 63% male) 19 TVA patients (62 years, 53% male)	Relationship between index and follow-up polyp types	Mean follow-up 94 months Hyperplastic polyps group: 93% of subsequent polyps were hyperplastic polyps Serrated adenoma group: 70% of subsequent polyps were serrated adenomas Tubular adenoma group: 70% of subsequent polyps were adenomas	Low
Huang, 2001 [124]	Retrospective observational	Patients with hyperplastic polyps diagnosed between 1972 and 1994 and patients with no polyps (controls) at index colonoscopy were identified. Groups were compared for subsequent diagnosis of adenomas during follow-up colonoscopy	43 hyperplastic polyps patients (age?, 69% male) 362 control patients (age?, 48% male)	Adenoma recurrence during follow-up	Median follow-up 4.3 years In 43% of patients with hyperplastic polyps subsequent adenomas were detected, compared with 21% of patients with no polyps at index colonoscopy (RR 2.0, 95%CI 1.2–3.4)	Low

SSA/P, sessile serrated adenoma/polyp; CRC, colorectal cancer; HGD, high grade dysplasia; LGD, low-grade dysplasia; NDSPP, nondysplastic serrated polyps; TSAs/TVA, traditional serrated adenomas/tubulovillous adenoma; OR, odds ratio; 95%CI, 95% confidence interval; RR, relative risk.

Table e8 Topics to be addressed by future research.

What are the main reasons for inappropriate use of surveillance colonoscopies? How can we improve the use of surveillance colonoscopy?
What is the rate of colonoscopies for which inadequate bowel preparation results in a shorter interval to the next screening/surveillance colonoscopy?
What is the correct surveillance interval for the first surveillance colonoscopy in the high risk group?
What is the correct surveillance interval for the second surveillance colonoscopy in the high risk group?
What is the residual risk in the high risk group following two negative surveillance colonoscopies?
In patients with serrated polyps, what is the risk of metachronous CRC, high risk adenomas, and serrated polyps?
How accurately do pathologists differentiate among the different types of serrated polyps?
Is age useful in stratifying surveillance intervals in the high risk group? What are the risks of terminating surveillance at age 80 years?
At what rate is interval g-FOBT/FIT performed during surveillance? What are the main reasons for these tests?
How many patients require an unplanned colonoscopy for symptoms during surveillance?
Do high quality colonoscopies facilitate longer surveillance intervals (e.g., for the high risk group)?

CRC, colorectal cancer; g-FOBT/FIT, guaiac- faecal occult blood test/faecal immunochemical test.