Colorectal cancer: colonoscopic surveillance for prevention of colorectal cancer in patients with ulcerative colitis, Crohn's disease and polyps

Full guideline

Draft for consultation, May 2010

This guideline was developed following the NICE short clinical guideline process. This document includes all the recommendations, details of how they were developed and summaries of the evidence they were based on.

Contents

Disclaimer

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions in the NHS in England and Wales.

This guidance represents the view of NICE, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

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Introduction

Patient-centred care

This guideline offers best practice advice on the use of colonoscopic surveillance in adults with inflammatory bowel disease (IBD, which covers ulcerative colitis and Crohn's disease) or polyps.

Treatment and care should take into account patients' needs and preferences. People with IBD or polyps should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health's advice on consent (available from www.dh.gov.uk/consent) and the code of practice that accompanies the Mental Capacity Act (summary available from www.publicguardian.gov.uk). In Wales, healthcare professionals should follow advice on consent from the Welsh Assembly Government (available from www.wales.nhs.uk/consent).

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the patient's needs. Treatment and care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Families and carers should also be given the information and support they need.

1 Summary

1.1 List of all recommendations

People with IBD

1.1.1 Offer colonoscopic surveillance to people with left-sided or extensive ulcerative colitis (except proctitis alone) or Crohn's colitis of a similar extent from 10 years after onset of symptoms

1.1.2 Offer colonoscopic surveillance using chromoscopy to people with IBD.

1.1.3 Offer people with IBD who are being considered for colonoscopic surveillance a baseline colonoscopy to determine their risk of developing colorectal cancer (see table 1).

Table 1 Risk of developing colorectal cancer in people with IBD

Low risk: -extensive but quiescent ulcerative colitis or Crohn's colitis **or** -left-sided ulcerative colitis or similar extent of Crohn's colitis. **Intermediate risk:** -extensive colitis with mild active histological inflammation **or** -presence of post-inflammatory polyps **or** -family history of colorectal cancer in a first degree relative aged 50 years or over. **High risk:** -extensive colitis with moderate or severe active histological inflammation **or** -primary sclerosing cholangitis (including post-transplant) **or** -presence of colonic stricture in the past 5 years **or** -dysplasia (any grade) in the past 5 years **or** -family history of colorectal cancer in a first degree relative aged under 50 years.

1.1.4 Offer colonoscopic surveillance to people with IBD based on their risk of developing colorectal cancer (see table 1), determined at each colonoscopy.

- Low risk: offer every 5 years.
- Intermediate risk: offer every 3 years.
- High risk: offer every year.

People with polyps

1.1.5 Offer colonoscopic surveillance only to people who have had adenomas removed and are at high or intermediate risk (see table 2) of developing colorectal cancer.

1.1.6 Offer white-light endoscopy for colonoscopic surveillance to people who have had adenomas removed and are at high or intermediate risk (see table 2) of developing colorectal cancer.

1.1.7 If colonoscopy is not clinically appropriate or is incomplete consider offering colonoscopic surveillance using computed tomographic colonography (CTC) to people who have had adenomas removed and are at high or intermediate risk (see table 2) of developing colorectal cancer.

1.1.8 Offer people with adenomatous polyps who are being considered for colonoscopic surveillance a baseline colonoscopy to determine their risk of developing colorectal cancer (see table 2).

Table 2 Risk of developing colorectal cancer in people with polyps

Low risk: -one or two adenomas smaller than 1 cm. **Intermediate risk:** -three or four adenomas smaller than 1 cm **or** -one or two adenomas if one is larger than 1 cm. **High risk:** -five or more adenomas smaller than 1 cm **or** -three or more adenomas if one is 1 cm or larger.

1.1.9 Offer colonoscopic surveillance to people with adenomatous polyps based on their risk of developing colorectal cancer (see table 2), determined at each colonoscopy.

- Low risk: do not offer colonoscopic surveillance.
- Intermediate risk: offer colonoscopic surveillance every 3 years until there are two consecutive negative colonoscopies, then stop surveillance.
- High risk: offer one colonoscopy at one year after diagnosis. If no adenomas are found, or low-risk or intermediate-risk adenomas are found, follow the advice above for intermediate risk. If high-risk adenomas are found, continue colonoscopic surveillance every year.

All adults

1.1.10 Discuss the benefits and risks with people considering colonoscopic surveillance including:

- early detection and prevention of colorectal cancer **and**
- effects on mortality, morbidity, quality of life and psychological outcomes.

1.1.11 Before offering colonoscopic surveillance, inform people about the procedure they are having, including:

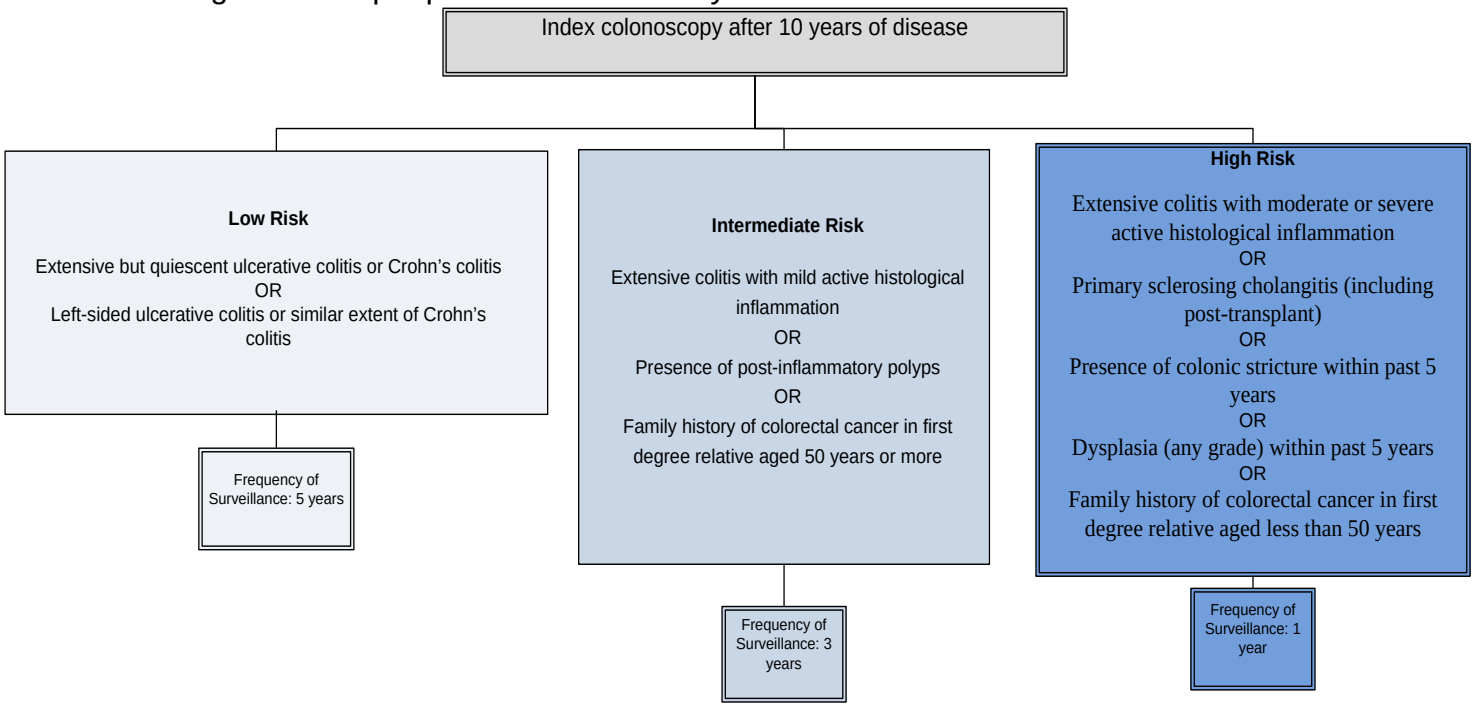
- bowel preparation
- sedation
- potential discomfort
- impact on everyday activities.

1.1.12 Throughout the surveillance programme, give people and their families or carers the opportunity to discuss any issues with a

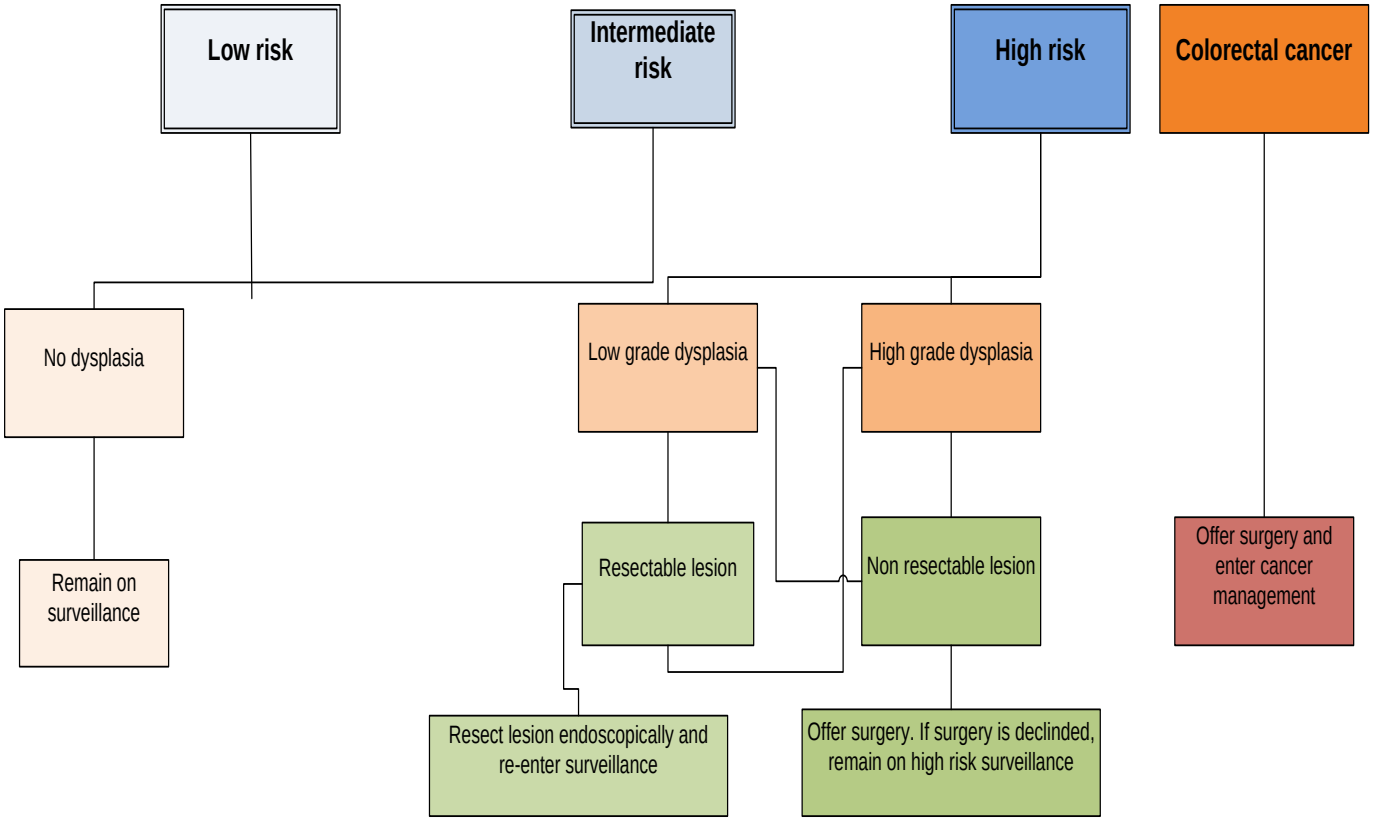
healthcare professional. Information should be provided in a variety of formats tailored to the person's needs, and if appropriate, could include illustrations.

1.2 Care pathway

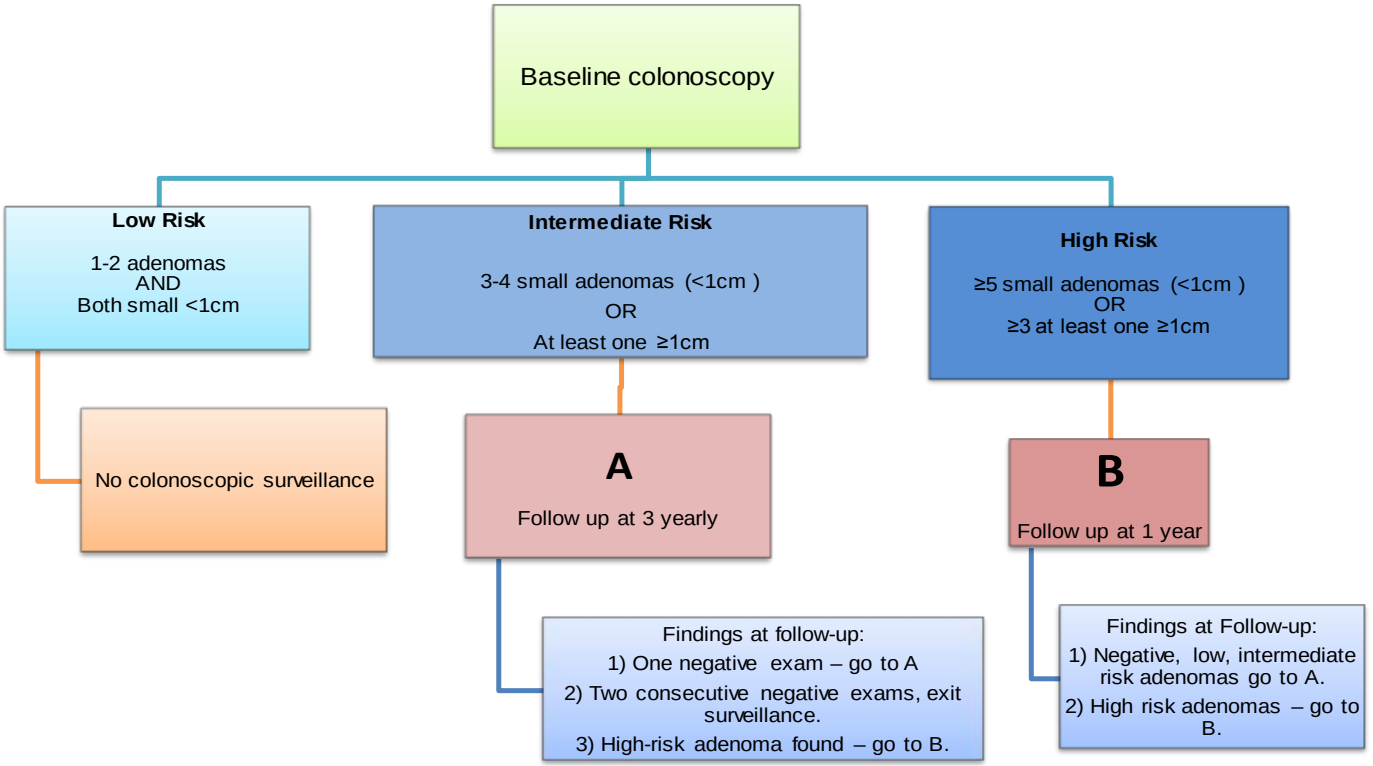
Surveillance algorithm for people with inflammatory bowel disease



Surveillance algorithm for people with dysplasia



Surveillance algorithm for people after adenoma removal



1.3 Overview

1.3.1 Colonoscopic surveillance for colorectal cancer in high-risk groups: inflammatory bowel disease and polyps

Colorectal cancer is the third most common cancer in the UK. There are approximately 32,300 new cases diagnosed and around 14,000 deaths in England and Wales each year. Around half of people diagnosed with colorectal cancer survive for at least 5 years after diagnosis.

Some adults with IBD (ulcerative colitis or Crohn's disease) or with adenomatous polyps have a higher risk of developing colorectal cancer than the general population. Polyps can be either precancerous (neoplastic adenomas) or non-precancerous (non-neoplastic, including hyperplastic polyps). Strong evidence suggests that detecting and removing adenomas reduces the risk of developing colorectal cancer. Larger polyps (>1 cm) have a higher potential to be malignant and are more likely to progress to invasive cancers.

The prevalence of ulcerative colitis is approximately 100–200 cases per 100,000 and the annual incidence is 10–20 cases per 100,000. The risk of developing colorectal cancer in people with ulcerative colitis is estimated to be 2% after 10 years of having the disease, 8% after 20 years and 18% after 30 years.

The prevalence of Crohn's disease is 50–100 cases per 100,000 and the annual incidence is 5–10 cases per 100,000. The risk of developing colorectal cancer in people with Crohn's disease affecting the colon is considered to be similar to that for people with ulcerative colitis.

Colonoscopic surveillance can detect problems early on and potentially prevent progression to colorectal cancer. However, there is variation in current practice in the timing (initiation and frequency) of colonoscopic surveillance in people at increased risk. This short clinical guideline aims to improve the care of people with IBD or polyps at high risk of developing colorectal cancer by

making evidence-based recommendations on the use of colonoscopic surveillance.

1.4 Who this guideline is for

This document is intended to be relevant to healthcare professionals who provide care to people who are at high risk of developing colorectal cancer in primary and secondary care settings. The target population is adults with IBD (ulcerative colitis or Crohn's colitis) or with adenomatous polyps in the colon or rectum.

2 How this guideline was developed

2.1 Introduction

Results from the included studies are presented in GRADE profiles and evidence statements. The GRADE profiles were modified to allow for evidence from both randomised controlled trials (RCTs) and observational studies for the same outcomes.

'Colonoscopic surveillance for colorectal cancer in high-risk groups: inflammatory bowel disease and polyps' (NICE clinical guideline XX) is a NICE short clinical guideline. For a full explanation of how this type of guideline is developed, see 'The guidelines manual' (2009) at www.nice.org.uk/GuidelinesManual'

2.2 Clinical effectiveness of colonoscopic surveillance compared with no surveillance

2.2.1 Review question

Is colonoscopic surveillance for prevention and/or early detection of colorectal cancer in adults with IBD or polyps clinically effective compared with no surveillance?

People with IBD

2.2.2 Evidence review

A total of 9688 articles were found by systematic searches, of which 6533 were unique articles. An additional two articles were identified from references in reviews and one article was found by the Guideline Development Group (GDG). Overall limited evidence was available, only four studies met the eligibility criteria (for review protocol and inclusion and exclusion criteria, see appendix 4) and examined the effectiveness of colonoscopic surveillance compared with no surveillance. There were three primary studies (Choi et al. 1993; Lashner et al. 1990; Lutgens et al. 2009) and one Cochrane systematic review (Collins et al. 2006).

The Cochrane review included three primary studies: two studies (Choi et al. 1993; Lashner et al. 1990) compared colonoscopic surveillance with no surveillance; the other study (Karlén et al. 1998) compared surveillance colonoscopy with no surveillance, one or two or more surveillance colonoscopies and is considered in this guideline in section 2.5. Another study (Velayos et al. 2006) also studied the effect of the number of surveillance colonoscopies on progression to colorectal cancer and also has been considered in this guideline in section 2.5. The review assessed the three studies using a validated scale developed by Downs and Black (1998)[1] and all studies were scored as 'high quality'. The authors of the Cochrane review concluded that there was no clear evidence that colonoscopic surveillance prolonged survival in people with extensive colitis (ulcerative colitis or Crohn's colitis). They felt the evidence suggested that colorectal cancer tends to be detected at an earlier stage in people who are undergoing surveillance and these people therefore have a better prognosis. But lead-time bias (the period between early detection of disease and the time of its usual clinical presentation) could contribute substantially to this apparent benefit.

[1] Downs and Black's (1998) checklist can be used for both randomised and non-randomised studies. The criteria for assessment include an overall score for study quality and a profile of scores for the quality of reporting, internal validity (bias and confounding), power and external validity

The other primary study identified (Lutgens et al. 2009) showed a significant difference in the 5-year cancer-related mortality rates in people undergoing surveillance compared with no surveillance

The characteristics of the three primary studies are summarised in table 1 and the evidence is reviewed in GRADE profile 1. The detailed evidence tables for the included studies are given in appendix 6.

Table 1: Summary of study characteristics for the three primary studies

	Study		
Parameters	**Choi et al. (1993)**	**Lashner et al. (1990)**	**Lutgens et al. (2009)**
Population	People with ulcerative colitis of at least 8 years' duration and extension of disease proximal to the sigmoid colon	People with extensive ulcerative colitis (defined as continued disease from any point proximal to the splenic flexure to the distal rectum) of at least 9 years' duration	People with IBD; 89 with ulcerative colitis, 59 with Crohn's disease and 1 with indeterminate colitis. For the surveillance group, surveillance started after a median of 14.3 (standard 8) years after diagnosis of IBD
Intervention	Surveillance with biopsies every 2 years (every 3 years in the early years of the programme) after negative results on two consecutive annual examinations	People had 4.2 ± 3.0 (range 1–16) colonoscopies during the study period at a mean of 17.0 years after symptom onset	At least one or more surveillance colonoscopies at regular intervals (every 1–3 years) to detect neoplasia; four random biopsies taken every 10 cm in addition to targeted biopsies of suspicious areas
Comparator	No surveillance	No surveillance	No surveillance
Outcomes used for GRADE profile	Stage of carcinoma (early and advanced) detected, 5-year overall survival and overall mortality	Number of colectomies, indication for colectomy, cancer detection rate and overall mortality	Stage of carcinoma (early and advanced) detected, 5-year overall survival, overall mortality and 5-year colorectal cancer-related mortality
IBD: inflammatory bowel disease			

GRADE profile 1: Colonoscopic surveillance compared with no surveillance for IBD

No. of studies	Design	Colonoscopic surveillance	No colonoscopic surveillance	OR/RR (95% CI) [ARR] NNTB (95% CI)	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration	Quality
Outcome 1: detected at early stage of carcinoma (Duke's stage A or B; AJCC stage 0 or 1)										
1 (C)	Case control study	**Duke's stage A or B**		OR = 5.42 (1.14 to 28.95); RR = 1.93 (1.15 to 3.51) [ARR = 0.38]; NNTB = 2.63 (1.62 to 13.11)	N	N	N	N	N	⊕⊕ Low
		15/19 (79.0%)	9/22 (40.9%)							
1 (Lu)	Case control study	**AJCC stage 0 or 1**		OR = 3.39 (1.21 to 9.45) RR = 2.14 (1.24 to 3.43) [ARR = 0.28]; NNTB = 3.60 (2.08 to 14.90)						
		12/23 (52.2%)	28/115[a] (24.3%)							
Outcome 2: detected at advanced stage of carcinoma (Duke's stage C or D; AJCC stage 3B–C and 4)										
1 (C)	Case control study	**Duke's stage C or D**		OR = 0.18 (0.03 to 0.88) RR = 0.36 (0.14 to 0.83) [ARR = 0.38]; NNTB = 2.63 (1.62 to 13.11)	N	N	N	N	N	⊕⊕ Low
		4/19 (21.1%)	13/22 (59.1%)							
1 (Lu)	Case control study	**AJCC stage 3B–C and 4**		OR = 0.29 (0.07 to 0.97) RR = 0.42 (0.16 to 0.92) [ARR = 0.243]; NNTB = 4.12 (2.56 to 35.39)						
		4/23 (17.4%)	48/115 (41.7%)							
Outcome 3: 5-year overall survival										

1 (C)	Case control study	76.2 ± 12.1%[b]	36.3 ± 12.7%	OR = 5.62 (3.0 to 11.27) RR = 2.1 (1.60 to 2.82) [ARR = 0.399]; NNTB=2.51 (1.93 to 3.74)	N	N	N	N	N	⊕⊕ Low
1 (Lu)	Case control study	100%	65%	RR = 1.54 (1.35 to 1.80) [ARR = 0.35]; NNTB=2.86 (2.23 to 3.80)						
Outcome 4: colectomy										
1 (L)	Cohort study	33/91 (36.3%)	51/95 (53.7%)	RR = 0.68 (0.48 to 0.93) [ARR = 0.174]; NNTB = 5.74 (3.22 to 32.42)[c]	S[d]	N	N	N	N	⊕ Very low
Outcome 5: indication for colectomy										
1 (L)	Cohort study	**Cancer**			S[d]	N	N	N	N	⊕ Very low
		3/91 (3.3%)	6/95 (6.3%)	RR = 0.52 (0.15 to 1.85) **NS**						
		Dysplasia								
		10/91 (11.0%)	3/95 (3.2%)	RR = 3.48 (1.07 to 11.48) [ARR = –0.078]; NNTB = 12.77 (6.12 to 184.82)						
Outcome 6: cancer detection rate										
1 (L)	Cohort study	Using the Cox proportional hazards adjustment the surveillance group had a 67% increased cancer detection rate compared with the non surveillance group; RR = 1.67 (0.30 to 9.33)			S[d]	N	N	N	N	⊕ Very low
Outcome 7: overall mortality										
1 (C)	Case control	4/19 (21.1%)	11/22 (50%)	OR = 0.26 (0.05 to 1.25) **NS** RR = 0.42 (0.16 to 1.02) **NS**	N	N	N	N	N	⊕⊕ Low
1 (Lu)	Case control study	1/23 (4.35%)	29/115 (25.22%)	OR = 0.13 (0.003 to 0.92) RR = 0.17 (0.03 to 0.86) [ARR = 0.208]; NNTB = 4.79 (3.23 to 2.03) [e]						
1 (L)	Cohort study	6/91(6.6%)	14/95 (14.7%)	RR = 0.45 (0.18 to 1.07) **NS**[f]	S[d]	N	N	N	N	⊕ Very low
Outcome 8: 5-year CRC related mortality										
1 (Lu)	Case control study	0%	26%	[ARR = 0.26 (0.18 to 0.35)] NNTB = 3.85 (2.83 to 5.44)	N	N	N	N	N	⊕⊕ Low

AJCC: American Joint Committee on Cancer; ARR: absolute risk reduction; (C): Choi et al. (1993); CI: confidence interval; IBD: inflammatory bowel disease; (L): Lashner et al. (1990); (Lu): Lutgens et al. (2009); N: not serious; NNTB/H: number needed to treat/harm; **NS**: not significant; OR: odds ratio; RR: relative risk; S: serious; VS: very serious; U: upgrade

[a] Lutgens et al. (2009): the tumour stages could not be found for 11 people and so 115 instead of 126 people were studied.
[b] Choi et al. (1993): the 5-year overall survival rate was 77.2 ± 10.1% for the surveillance group but changed to 76.2 ± 12.1% after adjusting for (removing) the people in whom colorectal cancer was detected without the surveillance programme.
[c] Lashner et al. (1990): using the Cox proportional hazards model for adjustment, the surveillance group had 47% reduction in colectomy rate compared with the no surveillance group; RR = 0.53 (0.34 to 0.83).
[d] Downgraded to serious because some people not receiving surveillance could have had surveillance outside the surveillance programme within the study.
[e] Lutgens et al. (2009): when the 11 people were excluded,
[f] Lashner et al. (1990): using the Cox proportional hazards model for adjustment, the surveillance group had 61% reduction in mortality compared with the no surveillance group; RR = 0.39 (0.15 to 1.00), remaining non-significant.

2.2.3 Evidence statements

2.2.3.1 *Low quality evidence showed that colonoscopic surveillance statistically significantly increased the probability of detecting cancer at an earlier stage, with a corresponding significant decrease in the probability of detecting cancer at a later stage.*

2.2.3.2 *Low quality evidence found the 5-year overall survival rate to be statistically significantly higher for the surveillance group.*

2.2.3.3 *Very low quality evidence showed a statistically significantly lower rate of colectomy in the surveillance group.*

2.2.3.4 *Very low quality evidence showed that cancer was a more frequent indication for colectomy in the non-surveillance group compared with the surveillance group, but the difference was not statistically significant.*

2.2.3.5 *Very low quality evidence showed that dysplasia was statistically significantly a more frequent indication for colectomy in the surveillance group compared with the non-surveillance group.*

2.2.3.6 *Very low quality evidence found a statistically significantly increased cancer detection rate in the surveillance group compared with the non-surveillance group after adjustment for covariates by the Cox proportional hazards model.*

2.2.3.7 *Low quality evidence showed a statistically significantly higher overall mortality rate for the non-surveillance group compared with the non-surveillance group..*

2.2.3.8 *Low quality evidence found the 5-year colorectal cancer related mortality rate to be significantly higher for the non-surveillance group compared with the surveillance group.*

2.2.4 Health economic modelling

No cost-effectiveness studies were found that specifically examined colonoscopic surveillance for the prevention of colorectal cancer in people with IBD. However, three studies were found that examined colonoscopic surveillance in people with ulcerative colitis (Nguyen et al. 2009, Provenzale et al. 1995; Delco et al. 2000). All three studies explored approaches to modelling strategies, and when applicable, to inform the model structure. Given the absence of any appropriate analysis that addressed the decision problem directly, a new cost-effectiveness model was developed based on the views of the GDG and clinical data available at the time of guideline development.

The model was initially developed assuming that the colonoscopic surveillance programme would be dependent on the degree of dysplasia (because dysplasia is a premalignant marker for colorectal cancer). However, at a later stage the GDG decided that the programme should be based on the risk of a person developing colorectal cancer, as follows:

- low risk: offer colonoscopic surveillance every 5 years
- intermediate risk – offer colonoscopic surveillance every 3 years
- high risk – offer colonoscopic surveillance every year.

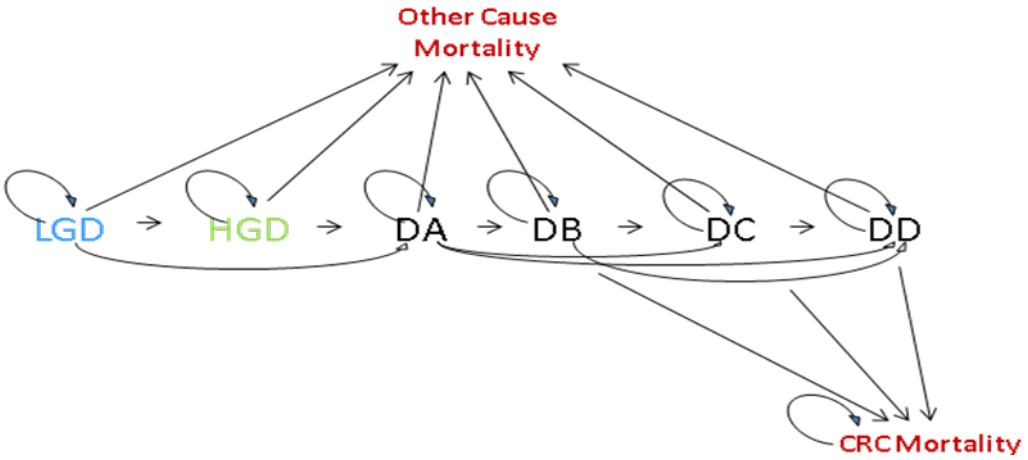
Because of time constraints, therefore, the initial model that was based on dysplasia could only determine the cost effectiveness of surveillance for the high-risk group, that is, ‘dysplasia (any grade) in the past five years’. See the surveillance algorithm for people with inflammatory bowel disease, section 1.2.

The model included men and women aged 30–85 who had non-resectable low- or high-grade dysplasia, and declined surgery. The analysis was run over a 55-year time horizon (cycle length 3 months) and examined the use of colonoscopic surveillance compared with no surveillance. Evidence that

colonoscopic surveillance was effective required a reduction in colorectal cancer related mortality.

The model used the following health states: low-grade dysplasia, high-grade dysplasia, asymptomatic cancer (Dukes' A, B, C, D), symptomatic cancer (Dukes' A, B, C, D), other cause mortality and colorectal cancer related mortality (see figure 1).

Figure 1: Markov state diagram for the 'high-risk' group in the IBD colonoscopic surveillance programme



LGD: low-grade dysplasia; HGD: high-grade dysplasia; DA: Dukes' A; DB: Dukes' B; DC: Dukes' C; DD: Dukes' D; CRC: colorectal cancer

Colonoscopic surveillance is recommended every year in the high-risk group and it was assumed that colonoscopy was undertaken at the beginning of the scheduled cycle. The development of colorectal cancer could be sequential, that is, progression from low-grade to high-grade dysplasia to cancer, or from low-grade dysplasia directly to colorectal cancer because some people do not progress through a detectable phase of high-grade dysplasia. Those with high-grade dysplasia could also progress directly to colorectal cancer and were assumed not to regress to low-grade dysplasia. Progress to colorectal cancer could occur either asymptomatically or symptomatically between the scheduled surveillance colonoscopies. Over time, if people had no evidence of progression they would remain in the same health state.

The natural history of the progression of IBD to colorectal cancer is unknown. Therefore, the probabilities of moving from one health state to another were based on a published clinical study that examined colonoscopic surveillance for colorectal cancer in UK patients with ulcerative colitis (Rutter et al. 2006) and were calculated using a Bayesian dirichlet method. The probabilities of progressing symptomatically or asymptomatically to colorectal cancer were obtained from a published cost-effectiveness study by Tappenden et al. (2004). The model assumed there were no complications from colonoscopy – although perforation and bleeding are serious risks they occur infrequently and were assumed to be negligible.

Utility values were not available for all the health states. Several studies reported utility values obtained from a disease-specific questionnaire (the Inflammatory Bowel Disease Questionnaire). However these values could not be used for calculating quality-adjusted life years (QALYs) because they did not report the values on a 0–1 scale, which is the format for generic questionnaires. Therefore, the utility values for people with low- and high-grade dysplasia were taken from a study of people with Crohn's disease (based on disease severity using a time trade off methodology; Gregor et al. 1997). The GDG confirmed that this approach was acceptable; a person with low-grade dysplasia has a lower quality of life than the general population and a person with high-grade dysplasia has a lower quality of life than a person with low-grade dysplasia. Stage-specific utility values for colorectal cancer were obtained from Ness et al. (1999).

Colonoscopic surveillance costs were obtained from NHS reference costs and the GDG. The costs for the lifetime stage-specific treatment of colorectal cancer were obtained from Paul Tappenden and Hazel Pilgrim (personal communication, 8 April 2010). Full details of utility values and costs are presented in appendix 7.

Both deterministic (base case using only point estimates) and probabilistic analyses (using a range of values and simulations to take into account uncertainty) were conducted to examine cost effectiveness.

The overall deterministic results are presented in table 2 and more detailed results are given in appendix 7.

Table 2: Deterministic analysis over a 55-year period

Intervention	QALYs	Cost (£)	Incremental QALYs	Incremental cost (£)	ICER (£)
No surveillance	16.42	2,320.44			
Surveillance – high-risk group only	17.19	15,785.13	0.77	13,464.69	17,557.32
ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life year					

The base-case analysis suggests that surveillance in the high-risk group is cost effective.

The overall probabilistic sensitivity analysis results are presented in table 3 and more detailed results are given in appendix 7.

Table 3: Probabilistic sensitivity analysis over a 55-year period

Intervention	QALYs	Cost (£)	Incremental QALYs	Incremental cost (£)	ICER (£)
No surveillance	13.04	7,368.92			
Surveillance – high-risk group only	14.64	16,316.82	1.61	8,947.90	5,571.44
ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life year					

The probabilistic sensitivity analysis incremental cost-effectiveness ratio (ICER) was lower than the deterministic ICER. This suggests that there may be a high degree of uncertainty associated with some model parameters resulting in a large change in the ICER.

The current analysis indicates that colonoscopic surveillance is a cost-effective programme for people considered at high risk of developing colorectal cancer among the three risk groups for IBD surveillance, with an ICER below £20,000 per QALY gained when deterministic and probabilistic analyses are considered.

2.2.5 Evidence to recommendations

The GDG considered that although the quality of the evidence was very low to low, there was still clear evidence in favour of colonoscopic surveillance compared with no surveillance for people with IBD. The GDG also felt that it would not be possible to find RCT evidence for this review question and the evidence obtained was sufficient to make recommendations in favour of colonoscopic surveillance. The GDG also considered that because of the similar colorectal cancer risk in ulcerative colitis and Crohn's colitis (Choi and Zelig 1994) recommendations could be made for Crohn's colitis despite most of the evidence being in people with ulcerative colitis. There was also some discussion about the evidence potentially showing lead-time bias, with early detection achieved because of colonoscopic surveillance, therefore improving 5-year survival but not overall survival. However, Lutgens et al. (2009) showed a significant difference in the 5-year cancer-related mortality rates in people undergoing surveillance compared with no surveillance, which does not support the effect of lead-time bias.

Finally, the health economic modelling indicated that colonoscopic surveillance is a cost-effective use of resources for people at high risk of developing colorectal cancer. The population in the economic model comprised one subcategory of the high-risk group (defined in care pathway section 1.2). The GDG considered that this population’s risk of cancer development was similar for the entire category and therefore, the results could be extrapolated to the entire high-risk group. The GDG also felt that because all the studies included for this review question looked at people who had disease of at least 10 years’ duration, it would be appropriate to only offer surveillance after 10 years of disease duration.

2.2.6 Recommendations

Recommendation 1.1.1

Offer colonoscopic surveillance to people with left-sided or extensive ulcerative colitis (except proctitis alone) or Crohn's colitis of a similar extent from 10 years after onset of symptoms.

People with polyps

2.2.7 Evidence review

A total of 9688 articles were found by systematic searches, of which 6533 were unique articles. Overall, two studies met the eligibility criteria (for review protocol and inclusion and exclusion criteria, see appendix 4) and examined the effectiveness of colonoscopic surveillance compared with no surveillance. Although two studies were initially considered to be relevant, they were excluded by the GDG as being not relevant. In Thiis-Evensen (1999) people had incomplete flexible sigmoidoscopy, and on discovering polyps, they were offered colonoscopic polypectomy.

In Jorgensen (2003) an indirect comparison was made. Mortality rates were compared in people offered colonoscopic surveillance and people who died from colorectal cancer (controls) in Denmark, with data taken from the cancer registry.

Therefore, no evidence meeting the eligibility criteria was identified for this group.

2.2.8 Evidence statement

2.2.8.1 There is no evidence for or against colonoscopic surveillance for the prevention and early detection of colorectal cancer after adenoma removal.

2.2.9 Health economic modelling

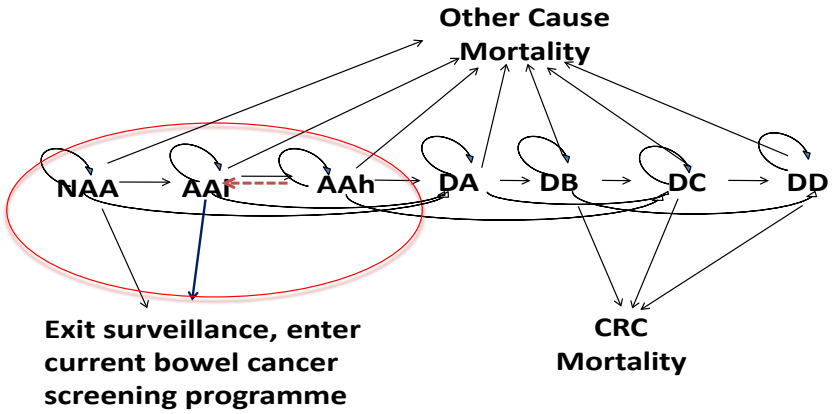
A search for cost-effectiveness studies found no directly relevant studies for colonoscopic surveillance and one possible analysis (Tappenden et al. 2004).

Given the absence of an appropriate analysis, a Markov model was developed. The model included 50-year old men and women who had polyps removed at baseline colonoscopy. The analysis was run over a 50-year time horizon. Based on the clinical effectiveness and recommendations made by the GDG, the model compared clinical and cost effectiveness of a periodic colonoscopic surveillance programme using conventional colonoscopy compared with no surveillance for the early detection of adenomas and colorectal cancer.

There was limited evidence on the natural history of polyps or adenomas leading to colorectal cancer (Winawer et al. 1993; Tappenden et al. 2004). A full systematic review of the literature was not possible because of time constraints. Examination of existing economic models, including screening and surveillance, was carried out. Information about the natural history of undetected colorectal cancer, the related probabilities of progressing through undiagnosed cancer states and the probabilities of clinical presentation by cancer stage were obtained by calibrating against published incidence and mortality data (Tappenden et al. 2004).

The model is based on Tappenden et al. (2004) and is presented in figure 2. The effectiveness of colonoscopic surveillance was considered using the early detection of polyps or adenomas and neoplastic changes compared with no surveillance. Detection rates of early cancer (Dukes' A and Dukes' B colorectal cancer) leading to mortality from the disease were considered using lifetime treatment costs for colorectal cancer in each strategy.

Figure 2: Colonoscopic surveillance model for people with adenomas



NAA: non-advanced adenoma, low risk, AAi: advanced adenoma, intermediate risk; AAh: advanced adenoma, high risk; DA: Dukes' A; DB: Dukes' B; DC: Dukes' C; DD: Dukes' D; CRC: colorectal cancer

In the model people are grouped into a finite number of Markov states, and all events or progression are represented as transitions from one state to another with a certain probability. Transition probabilities estimated in the model are assumed to be constant, with the exception of age-related adenoma incidence (Tappenden et al. 2004) and age-specific mortality rate (Office of National Statistics 2008). The effectiveness of colonoscopic surveillance is modelled as an intervention under near-perfect conditions to determine whether colonoscopic surveillance using colonoscopy for the early detection of adenomas and colorectal cancer was clinically and cost effective compared with no surveillance. The effectiveness of colonoscopic surveillance in removing adenomas for prevention of colorectal cancer is measured from the QALY gains in people who exit the surveillance programme according to the surveillance strategies. Subsequent analyses are considered if appropriate.

In the model the surveillance schedule broadly follows the British Society of Gastroenterology guidelines (Atkin and Saunders 2002; Cairns et al. 2010). The person's risk state is defined during the baseline colonoscopy in terms of the index lesion, which is the adenoma or most advanced adenoma present with the greatest potential for malignancy.

Currently, colonoscopic surveillance for people who have had polyps removed are determined by their risk state at baseline colonoscopy, and are as follows:

- Low risk: surveillance at 5 years, then no surveillance if colonoscopy results are negative, that is there are no newly developed adenomas and no colorectal cancer is detected.
- Intermediate risk: offer colonoscopic surveillance every 3 years until there are two consecutive negative colonoscopies, then stop surveillance..
- High risk surveillance at 12 months:
  - if high-risk adenomas are detected, surveillance every year.
  - if results are negative, or low- or intermediate-risk adenomas are detected, follow the programme for people at intermediate risk.

In the model, three strategies were examined; no surveillance, surveillance in low, intermediate and high-risk groups, and surveillance in intermediate and high-risk groups. The model includes the person's risk state after the removal of adenomas focused on the number and size of adenomas. Any newly developed adenomas will be removed during surveillance. If any lesions are found during surveillance that are suspected to be malignant, the surveillance programme will be stopped and the person referred for appropriate diagnosis and treatment. Empirical evidence strongly suggests that people with a history of polyps are more likely to develop polyps in the future than people who have never had polyps (Winawer 1993). The GDG agreed that in the model all colorectal cancers arise from pre-existing adenomas.

Utility values (health benefits) for health states and treatment were obtained from published studies. Data on stage-specific utility values for colorectal cancer were limited and no EQ-5D values were available. Utility values were assessed in relation to stage of cancer and treatment (Ness et al. 1999, 2000). The GDG agreed that the utility values for people who are cancer free or have undiagnosed (asymptomatic) cancer were similar to those of the general population. Surveillance costs were obtained from NHS reference costs. Costs for the stage-specific lifetime treatment of colorectal cancer were obtained from Paul Tappenden and Hazel Pilgrim (personal communication, 8

April 2010). Full details of the utility values and costs are presented in appendix 7.

A base-case estimate of the incremental cost effectiveness ratio (ICER) for colonoscopic surveillance in intermediate and high-risk groups only in comparison with no surveillance was –£2749.48 per QALY gained. A negative ICER is interpreted as dominating compared with no surveillance, indicating surveillance in intermediate and high-risk groups is less expensive and more effective. The overall deterministic results are presented in table 4 and more detailed results are given in appendix 7.

Table 4: Deterministic analysis over a 45-year period

Intervention	QALY	Cost (£)	Incremental QALY	Incremental cost (£)	ICER (£)
No surveillance	15.48	664.72	–	–	–
Colonoscopic surveillance following BSG guideline (low, intermediate and high-risk groups)	15.63	11,120.88	0.152	10,456.17	68,771.48
Colonoscopic surveillance in intermediate and high-risk groups only	15.55	444.52	0.074	-220.19	Dominating
BSG: British Society of Gastroenterology; ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life year					

The overall probabilistic sensitivity analysis results are presented in table 5 and more detailed results are given in appendix 7. The analysis shows that colonoscopic surveillance in the intermediate and high-risk groups is cost effective compared with the current British Society of Gastroenterology guideline or no surveillance.

Table 5: Probabilistic sensitivity analysis over a 45-year period

Intervention	QALY	Costs	Incremental QALY	Incremental cost (£)	ICER (£)
No surveillance	14.87	938.10	–	–	–
Colonoscopic surveillance following BSG guideline (low, intermediate and high-risk groups)	15.04	11,120.88	0.165	10,182.79	61,666.51
Colonoscopic surveillance in intermediate and high-risk groups only	15.00	627.81	0.125	–2,482.07	Dominating

BSG: British Society of Gastroenterology; ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life year

The probabilistic sensitivity analysis suggests that colonoscopic surveillance in intermediate and high-risk groups has a probability of being cost effective of 52.9%. The additional QALYs gained were mainly from preventing colorectal cancer by detecting and removing adenomas during surveillance.

The GDG acknowledged the necessary assumptions used in the model and the limitations of the model. Therefore, the results of the cost-effectiveness analysis were approached with caution. The details of the cost-effectiveness analysis are discussed in appendix 7.

2.2.10 Evidence to recommendations

Because of the lack of evidence, the GDG made recommendations based on experience, and the colorectal cancer incidence and overall mortality reported in Thiis-Evensen (1999) and Jorgensen (2003). These articles showed that the risk of cancer in people with polyps in the low-risk group is similar to that of the general population. Therefore, no surveillance is recommended for the low-risk group. The GDG noted that there is a national bowel screening programme in the UK for adults aged 60–69 years. This was also supported by the health economic modelling, which showed that surveillance in intermediate and high-risk groups is cost effective compared with no surveillance.

2.2.11 Recommendations

Recommendation 1.1.5

Offer colonoscopic surveillance only to people who have had adenomas removed and are at high or intermediate risk of developing colorectal cancer.

2.3 Colonoscopic surveillance techniques

2.3.1 Review question

Which colonoscopic surveillance technique (using conventional colonoscopy or chromoscopy) for prevention and/or early detection of colorectal cancer in adults with IBD or polyps is more clinically effective compared with other methods of surveillance (flexible sigmoidoscopy, double-contrast barium enema, computed tomographic colonography, tri-modal imaging [high-resolution white light endoscopy, narrow-band imaging. and auto-fluorescence imaging])?

People with IBD

2.3.2 Evidence review

A total of 14,701 articles were found by systematic searches, of which 9544 were unique articles. The full text was ordered for 108 articles. One study met the eligibility criteria (for review protocol and inclusion and exclusion criteria, see appendix 2).

The characteristics of the primary study are summarised in table 6 and the evidence is reviewed in GRADE profile 2.

Table 6: Summary of study characteristics

Study	Population	Study characteristics	Outcomes used for GRADE profile
Dekker et al. (2007)	Forty-two patients with ulcerative colitis of long duration. The study group comprised 31 men and 11 women with a mean age (±SD) of 50 ± 11.2 years	Prospective RCT: Cross-over study design	Detection of neoplastic lesion with narrow-band imaging compared with conventional colonoscopy
RCT: randomised controlled trial; SD: standard deviation			

GRADE profile 2: Conventional colonoscopy compared with narrow-band imaging

No. of studies	Design	Conventional Colonoscopy	Other technique	SN	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
NBI versus conventional colonoscopy for inflammatory bowel disease										
Primary outcome:										
1 (D)	RCT	8/42 (19%)	7/42 (17%)	SN for NBI = 67%	N	N	N	N	S	Moderate[a]

(D): Dekker et al. (2007); N: not serious; NBI: narrow-band imaging; RCT: randomised controlled trial; S: serious; SN: sensitivity

[a] The study did not contain a predefined sample size and therefore included only 42 people. A first-generation prototype NBI system with an experimental light source was used.

2.3.3 Evidence statements

2.3.1 Moderate quality evidence comparing narrow-band imaging with conventional colonoscopy showed no significant difference in the number of detected neoplastic lesions (in people with ulcerative colitis of long duration) between the two techniques.

2.3.4 Health economic modelling

No health economic modelling was undertaken for this review question.

2.3.5 Evidence to recommendations

The GDG agreed that the Dekker (2007) study was underpowered, that is, the sample size was small and not a true representation of people with IBD. In addition, narrow-band imaging is not routinely used for colonoscopic surveillance in the UK. Therefore the GDG considered that it was not possible to recommend narrow-band imaging in this population.

2.3.6 Recommendations

No recommendations were made for this population (see Evidence to recommendations for details).

People with polyps

2.3.7 Evidence review

A total of 14,701 articles were found by systematic searches, of which 9544 were unique articles. The full text was ordered for 108 articles. Two primary studies and two systematic reviews that looked at the effectiveness of conventional colonoscopy compared with narrow-band imaging, double-contrast barium enema, CT colonography and flexible sigmoidoscopy for surveillance for polyps met the inclusion and exclusion criteria (for review protocol and inclusion and exclusion criteria, see appendix 2).

The characteristics of the included studies are summarised in table 7 and the evidence is reviewed in GRADE profile 3. The forest plots for the meta-

analysis of outcomes and a detailed evidence table for the two systematic reviews are given in appendix 6.

Table 7: Summary of study characteristics

Study	Population	Study characteristics	Outcomes used for GRADE profile
Van den Broek et al. (2009)	A pooled result of 537 people undergoing NBI compared with 536 people having conventional colonoscopy	Systematic review of three RCTs: NBI compared with conventional colonoscopy (white light endoscopy)	Detection and removal of adenomas with NBI compared with conventional colonoscopy
Rex et al. (1995)	149 people aged at least 40 years (mean age 63) with symptoms suggestive of colonic disease	RCT comparing flexible sigmoidoscopy plus double contrast barium enema	Adenoma detection
Mulhall et al. (2005)	Prospective studies of adults undergoing CT colonography after full bowel preparation, with colonoscopy as the gold standard. 33 studies provided data on 6393 people	Systematic review and meta-analysis of CT colonography	Pooled sensitivity and specificity for polyp detection
Winawer et al. (2000)	973 people underwent one or more surveillance colonoscopies. In 580 of these people, 862 paired surveillance colonoscopies and double-contrast barium enema were performed	Controlled trial comparing colonoscopy and double-contrast barium enema	Adenoma detection
CT: computed tomography; NBI: narrow-band imaging; RCT: randomised controlled trial			

GRADE profile 3: Conventional colonoscopy compared with double-contrast barium enema, flexible sigmoidoscopy, narrow-band imaging and CT colonography

No. of studies	Design	Conventional colonoscopy	Other technique	OR (95% CI) SN SP p value	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Quality
NBI versus conventional colonoscopy for polyps										
Primary outcome:										
1 (V)	Systematic review/meta analysis	236/537 (44%)	219/536 (41%)	OR = 1.19 (95% CI 0.86 to 1.64)	N	N	N	N	N	High
FSIG plus DBCE versus conventional colonoscopy for polyps										
Primary outcome:										
1 (R)	RCT	13/74 (18%)	23/75 (31%)	OR = 2.07 (95% CI 0.90 to 4.92)	N	N	N	N	S	Moderate[b]
CTC versus conventional colonoscopy for polyps										
Primary outcome:										
1 (M)	Systematic review/meta analysis	33 studies providing data on 6393 people		Pooled SN for CTC = 70% (95% CI 53% to 87%). Pooled SP for CTC = 86% (95% CI 84% to 88%; p = 0.001)	N	N	N	N	S	Moderate[c]
DCBE versus conventional colonoscopy for polyps										
Primary outcome:										
1 (W)	Controlled trial	558/580 (96%)	380/393 (97%)	Adenomatous polyps detected by DCBE were significantly related to the size of the adenomas (p = 0.009). The SN and SP for DCBE were 38% and 86% respectively	N	N	N	N	S	Low

CI: confidence interval; CTC: computed tomographic colonography; DCBE: double-contrast barium enema; FSIG: flexible sigmoidoscopy; IBD: inflammatory bowel disease; (M): Mulhall et al. (2005); N: not serious; NBI: narrow-band imaging; OR: odds ratio; (R): Rex et al. (1995); RCT: randomised controlled trial; S: serious; SN: sensitivity; SP: specificity; (V): Van den Broek et al. (2009); (W): Winawer et al. (2000)

[a] The study did not contain a predefined sample size and therefore included only 42 people. A first-generation prototype NBI system with an experimental light source was used.
[b] Downgraded based on small sample size.
[c] Eighteen of the studies used colonoscopy as the gold standard. Eleven studies used segmental unblinded colonoscopy or optimised colonoscopy.

2.3.8 Evidence statements

2.3.8.1 High quality evidence comparing narrow-band imaging with colonoscopy (white light endoscopy) to detect adenomas showed that narrow-band imaging does not significantly improve the detection of adenomas .

2.3.8.2 Moderate quality evidence showed a non significant two-fold increase in adenoma detection rate with conventional colonoscopy compared with flexible sigmoidoscopy plus double-contrast barium enema.

2.3.8.3 Low quality evidence showed that colonoscopic examination detected more polyps than double-contrast barium enema. Half of these polyps were adenomas, and the remainder were primarily normal mucosal tags, with some hyperplastic polyps.

2.3.8.4 Moderate quality evidence showed that computed tomographic (CT) colonography is highly specific, particularly for polyps larger than 9 mm. This evidence also showed that sensitivity for CT colonography increases with polyp size.

2.3.9 Health economic modelling

No health economic modelling was undertaken for this review question.

2.3.10 Evidence to recommendations

The GDG agreed that the Rex (1995) study was underpowered, that is, the sample size was small and not a true representation of people with polyps. The GDG noted that there was ongoing research comparing CT colonography with conventional colonoscopy.

The GDG recommended using conventional colonoscopy (high-resolution white-light endoscopy) for routine colonoscopic surveillance in people with

polyps because of its increased adenoma detection rate compared with other techniques.

2.3.11 Recommendations

Recommendation 1.1.6

Offer white-light endoscopy for colonoscopic surveillance to people who have had adenomas removed and are at high or intermediate risk (see table 2) of developing colorectal cancer.

Recommendation 1.1.7

If colonoscopy is not clinically appropriate or is incomplete consider offering colonoscopic surveillance using computed tomographic colonography (CTC) to people who have had adenomas removed and are at high or intermediate risk (see table 2) of developing colorectal cancer.

2.4 Conventional colonoscopy compared with chromoscopy

2.4.1 Review question

Is colonoscopic surveillance with a dye (chromoscopy) for prevention and/or early detection of colorectal cancer clinically effective compared with colonoscopic surveillance without a dye (conventional colonoscopy)?

People with IBD

2.4.2 Evidence review

A total of 14,701 articles were found by systematic searches, of which 9544 were unique articles. The full text was ordered for 23 articles. Only four studies examined the effectiveness of chromoscopy compared with conventional colonoscopic surveillance for IBD and met the eligibility criteria (for review protocol and inclusion and exclusion criteria, see appendix 4). The four primary studies were Kiesslich et al. (2003, 2007), Marion et al. (2008) and Rutter et al. (2004a).

The characteristics of the included primary studies are summarised in table 8 and the evidence reviewed in GRADE profile 4. The forest plots for the meta-analysis of outcomes and the detailed evidence tables for the included studies are given in appendix 6. The meta-analysis of the dichotomous outcomes used the pooled odds ratio calculated by the Mantel-Haenszel fixed-effects model because the heterogeneity was less than 50%. Subgroup analysis was performed when appropriate.

Table 8: Summary of study characteristics

Study	Population	Intervention	Comparator	Outcomes used for GRADE profile
Kiesslich et al. (2003) RCT	People with clinically inactive, ulcerative colitis (of at least 8 years duration), N = 165	Chromoscopy using 0.1% methylene blue, n = 84	Conventional colonoscopy, using conventional video colonoscopies, n = 81	Total number of neoplastic lesions, number of LGD, HGD and flat neoplastic lesions detected, and number of people with neoplastic lesions
Kiesslich et al. (2007) RCT	People with clinically inactive, ulcerative colitis (of at least 8 years duration), N = 161; Eight patients were excluded because of insufficient bowel preparation; therefore N=153.	Chromoscopy using 0.1% methylene blue with endomicroscopy, n = 80	Conventional colonoscopy, using conventional video colonoscopies, n = 73	Total number of neoplastic lesions, number of LGD, HGD and flat neoplastic lesions detected and number of people with neoplastic lesions
Marion et al. (2008) Back-to-back controlled trial	People with extensive ulcerative colitis (at least left sided, n = 79) or Crohn's colitis (at least one third of the colon, n = 23), N = 102	Chromoscopy using 0.1% methylene blue, n = 102	Conventional colonoscopy, n = 102, targeted and random	Total number of neoplastic lesions, number of LGD, HGD and flat neoplastic lesions detected and number of people with neoplastic lesions
Rutter et al. (2004a) Back-to-back controlled trial	People with extensive ulcerative colitis of long duration, N = 100	Chromoscopy with 0.1% indigo carmine, n = 100	Conventional colonoscopy, n = 100, targeted and random	Total number of neoplastic lesions, number of LGD lesions detected and number of people with neoplastic lesions
RCT: randomised controlled trial; HGD: high-grade dysplasia; LGD: low-grade dysplasia				

GRADE profile 4: Chromoscopy compared with conventional colonoscopy for IBD

No. of studies	Design	Chromoscopy	Conventional colonoscopy	OR M-H, fixed (95%CI) RR (95%CI) ARR, NNTB (95%CI)	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration	Quality
Outcome 1: mean number of people with intra-epithelial neoplasia										
4[a]	RCT/CT	48/366 (13.11%)	23/356 (6.46%)	OR = 2.21 (1.31 to 3.7)	N	N	N	N	N	High
Outcome 2: mean number of intra-epithelial neoplastic lesions detected per biopsy										
2[b]	RCT/CT	**Targeted chromoscopy**			N	N	N	N	N	High
		31/196 (15.82%)	18/6261 (0.29%)	OR = 85.47(45.31 to 161.21)						
1[c]		**Random and targeted chromoscopy**								
		19/1688 (1.13%)	4/3041 (0.13%)	OR = 8.76 (2.97 to 25.78)						
Outcome 3: mean number of intra-epithelial neoplastic lesions detected per person										
4[d]	RCT/CT	82/366 (22.40%)	32/356 (8.99%)	OR = 3.02 (1.93 to 4.72)	N	N	N	N	N	High
Outcome 4: mean number of LGD lesions per person										
2[e]	CT	**Targeted chromoscopy**			N	N	N	N	N	High
		30/196 (15.31%)	17/6261 (0.27%)	OR = 85.96 (45.00 to 164.21)						
1[f]	RCT	**Random and targeted chromoscopy**								
		12/1688 (0.71%)	3/3081 (0.10%)	OR = 7.35 (2.07 to 26.07)						
Outcome 5: mean number of LGD lesions per person										
4[g]	RCT/CT	66/366 (18.03%)	28/356 (7.86%)	OR = 2.65 (1.65 to 4.27)	N	N	N	N	N	High
Outcome 6: mean number of HGD lesions per biopsy										
1[h]	CT	**Targeted chromoscopy**			N	N	N	N	N	High
		1/82 (1.22%)	1/3314 (0.03%)	OR = 40.90 (2.54 to 104.33)						

1[i]	RCT	**Random and targeted chromoscopy**								
		7/1688 (0.41%)	1/3081 (0.03%)	OR = 12.83 (1.58 to 659.66)						
Outcome 7: mean number of HGD lesions per person										
3[j]	RCT/CT	16/266 (6.02%)	4/256 (1.56%)	OR = 4.02 (1.32 to 12.24)	N	N	N	N	N	High

ARR: absolute risk reduction; CI: confidence interval; CT: controlled trial; HGD: high-grade dysplasia; IBD: inflammatory bowel disease; LGD: low-grade dysplasia; M-H fixed: Mantel-Haenszel fixed-effects model; N: not serious; NNTB: number needed to treat; OR: odds ratio; RR: relative risk; S: serious

[a] Kiesslich et al. (2003, 2007), Marion et al. (2008) and Rutter et al. (2004a)
[b] Marion et al. (2008) and Rutter et al. (2004a)
[c] Kiesslich et al. (2007)
[d] Kiesslich et al. (2003, 2007), Marion et al. (2008) and Rutter et al. (2004a)
[e] Marion et al. (2008) and Rutter et al. (2004a)
[f] Kiesslich et al. (2007)
[g] Kiesslich et al. (2003, 2007), Marion et al. (2008) and Rutter et al. (2004a)
[h] Marion et al. (2008)
[i] Kiesslich et al. (2007)
[j] Kiesslich et al. (2003, 2007) and Marion et al. (2008)

2.4.3 Evidence statements

2.4.3.1 High quality evidence showed that chromoscopy detects statistically significantly more intra-epithelial neoplastic lesions in people with extensive colitis (at least 8 years duration) compared with conventional colonoscopy.

2.4.3.2 High quality evidence showed that chromoscopy detects statistically significantly more intra-epithelial neoplastic lesions compared with conventional colonoscopy.

2.4.3.3 High quality evidence showed that chromoscopy detects statistically significantly more intra-epithelial neoplastic lesions compared with conventional colonoscopy.

2.4.3.4 High quality evidence showed that chromoscopy detects statistically significantly more low-grade dysplastic lesions per biopsy compared with conventional colonoscopy.

2.4.3.5 High quality evidence showed that chromoscopy detects statistically significantly more low-grade dysplastic lesions compared with conventional colonoscopy.

2.4.3.6 High quality evidence showed that chromoscopy detects statistically significantly more high-grade dysplastic lesions per biopsy compared with conventional colonoscopy.

2.4.3.7 High quality evidence shows that chromoscopy detects statistically significantly more high-grade dysplastic lesions compared with conventional colonoscopy.

2.4.4 Health economic modelling

No health economic modelling was undertaken for this review question.

2.4.5 Evidence to recommendations

The GDG felt that the high quality evidence was clearly in favour of chromoscopy compared with conventional colonoscopy. Chromoscopy should therefore become the standard technique for colonoscopic surveillance in people with IBD. The GDG discussed that using chromoscopy instead of colonoscopy would increase the procedure time. The Group also stated that, in practice, four mapping biopsies (used to map the extent of inflammation) and on average one targeted biopsy would be taken when using chromoscopy. However, the GDG felt that the significantly increased detection rate made chromoscopy the favoured method for colonoscopic surveillance in people with IBD.

2.4.6 Recommendation

Recommendation 1.1.2

Offer colonoscopic surveillance using chromoscopy to people with IBD.

People with polyps

2.4.7 Evidence review

A total of 14,701 articles were found by systematic searches, of which 9544 were unique articles. The full text was ordered for 23 articles. One Cochrane systematic review that looked at the effectiveness of chromoscopy compared with conventional colonoscopic surveillance for polyps met the eligibility criteria (for review protocol and inclusion and exclusion criteria, see appendix 4).

The Cochrane review (Brown et al. 2007) was updated in 2009 but no additional studies were found. The review included four studies (Brooker et al. 2002; Hurlstone et al. 2004; Lapalus et al. 2006; Le Rhun et al. 2006). The aim of the review was to determine whether chromoscopy increased the detection rate of polyps and neoplastic lesions during endoscopic examination of the colon and rectum. The Hurlstone et al. (2004) study was not included in the analysis by the technical team after discussion with the GDG and advice

from the editors of the journal because there was some uncertainty about the methods used.

The characteristics of the included studies are summarised in table 9 and the evidence is reviewed in GRADE profile 5. The forest plots for the meta-analysis of outcomes and a detailed evidence table for the systematic review are given in appendix 6. The meta-analysis of the dichotomous outcomes used the pooled odds ratio calculated by the Mantel-Haenszel method and the meta-analysis of the continuous outcomes used the inverse variance method. The fixed-effects model was used when the heterogeneity was less than 50% and the random-effects model was used when the heterogeneity was greater than 50%.

Table 9: Summary of study characteristics

Study		Population	Intervention	Comparator	Outcomes used for GRADE profile
Brown et al. (2007) included Brooker et al. (2002), Hurlstone et al. (2004), Lapalus et al. (2006), and Le Rhun et al. (2006)	Brooker et al. (2002)	People enrolled at consultation prior to colonoscopy who had an indication for colonoscopy and who were at high risk for colorectal cancer (personal history of adenoma, with or without first-degree family history) N = 259	Chromoscopy with 0.1% indigo carmine, n = 124	Conventional colonoscopy, n = 135	Total number of polyps detected by location, total number of neoplastic lesions detected by location, number of diminutive neoplastic lesions detected
	Lapalus et al. (2006)	People enrolled at consultation prior to colonoscopy who had an indication for colonoscopy and who were at high risk for colorectal cancer (personal history of adenoma, with or without first-degree family history), N = 292	Conventional colonoscopy followed by pan-colonic chromoscopy using indigo carmine with high-resolution imaging, n = 146	Conventional colonoscopy, two passes, n = 146	
	Le Rhun et al. (2006)	People referred to four centres over 18-month period with: known polyps on surveillance programme; family	Chromoscopy using 0.4% indigo carmine, with high-resolution imaging,	Conventional colonoscopy, n = 100	

		history on screening programme; older than 60 years with symptoms, N = 203	n = 103		

GRADE profile 5: Chromoscopy compared with conventional colonoscopy for polyps

No. of studies	Design	Chromoscopy N: total pooled study population in this arm	Conventional colonoscopy N: total pooled study population in this arm	WMD (95%CI) IV fixed/ random OR (95%CI) M-H fixed/ random	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration	Quality
Outcome1: total number of polyps detected – IV random										
3[a]	RCT	369	380	WMD = 0.81 (0.35 to 1.26)	N	N	N	N	N	High
Outcome 2: mean number of polyps detected by each method per total polyps detected – M-H random										
3[b]	RCT	1026	1026	OR = 3.20 (1.83 to 5.61)	N	N	N	N	N	High
Outcome 3: total number of polyps detected in proximal colon – M-H random										
2[c]	RCT	270	281	WMD = 0.55 (0.07 to 1.03)	N	N	N	N	N	High
Outcome 4: total number of polyps detected in distal colon – IV fixed										
2[d]	RCT	270	281	WMD = 0.37 (0.20 to 0.54)	N	N	N	N	N	High
Outcome 5: total number of neoplastic lesions detected – IV random										
3[e]	RCT/CT	369	380	WMD = 0.33 (–0.04 to 0.71) **NS**	N	N	N	S	N	Moderate
Outcome 6: mean number of neoplastic lesions detected by each method per total number of lesions – M-H Random										
2[f]	RCT/CT	750	750	OR = 2.20 (0.97 to 4.99) **NS**	N	N	N	S	N	Moderate
Outcome 7: total number of neoplastic lesions detected in proximal colon – IV random										
2[g]	RCT/CT	270	281	WMD = 0.33 (–0.05 to 0.71) **NS**	N	N	N	S	N	Moderate
Outcome 8: total number of neoplastic lesions detected in distal colon – IV fixed										
2[h]	RCT/CT	270	281	WMD = 0.09 (–0.08 to 0.26) **NS**	N	N	N	S	N	Moderate
Outcome 9: total number of diminutive neoplastic lesions detected – IV random										
3[i]	RCT/CT	369	380	WMD = 0.28 (0.08 to 0.47)	N	N	N	N	N	High
Outcome 10: mean number of diminutive adenomas detected by each method per total number of lesions – M-H fixed										
2[j]	RCT/CT	750	750	OR = 2.47 (1.86 to 3.27)	N	N	N	N	N	High
CI: confidence interval; CT: controlled trial; IV: inverse variance method; M-H: Mantel-Haenszel method; N: not serious; **NS:** not statistically										

significant; OR: odds ratio; RCT: randomised controlled trial; S: serious; VS: very serious; WMD: weighed mean difference

[a] Brooker et al. (2002), Lapalus et al. (2006) and Le Rhun et al. (2004)
[b] Brooker et al. (2002), Lapalus et al. (2006) and Le Rhun et al. (2004)
[c] Brooker et al. (2002) and Lapalus et al. (2006)
[d] Brooker et al. (2002) and Lapalus et al. (2006)
[e] Brooker et al. (2002), Lapalus et al. (2006) and Le Rhun et al. (2004)
[f] Brooker et al. (2002) and Lapalus et al. (2006)
[g] Brooker et al. (2002) and Lapalus et al. (2006)
[h] Brooker et al. (2002) and Lapalus et al. (2006)
[I] Brooker et al. (2002), Lapalus et al. (2006) and Le Rhun et al. (2004)
[j] Brooker et al. (2002) and Lapalus et al. (2006)

2.4.8 Evidence statements

2.4.8.1 *High quality evidence showed that chromoscopy detected statistically significantly more polyps than conventional colonoscopy.*

2.4.8.2 *High quality evidence showed that chromoscopy had a statistically significantly higher probability of detecting polyps than conventional colonoscopy.*

2.4.8.3 *High quality evidence showed that chromoscopy detected statistically significantly more polyps in the proximal colon than conventional colonoscopy.*

2.4.8.4 *High quality evidence showed that chromoscopy detected statistically significantly more polyps in the distal colon than conventional colonoscopy.*

2.4.8.5 *Moderate quality evidence showed that there was no statistical difference in the number of neoplastic lesions detected by chromoscopy compared with conventional colonoscopy.*

2.4.8.6 *Moderate quality evidence showed that there was no statistical difference in the probability of detecting neoplastic lesions by chromoscopy compared with conventional colonoscopy.*

2.4.8.7 *Moderate quality evidence showed that there was no statistical difference in the number of neoplastic lesions detected in the proximal colon by chromoscopy compared with conventional colonoscopy.*

2.4.8.8 *Moderate quality evidence showed that there was no statistical difference in the number of neoplastic lesions detected in the distal colon by chromoscopy compared with conventional colonoscopy.*

2.4.8.9 High quality evidence showed that chromoscopy detected statistically significantly more diminutive neoplastic lesions than conventional colonoscopy.

2.4.8.10 High quality evidence showed that chromoscopy had a statistically significantly higher probability of detecting diminutive neoplastic lesions than conventional colonoscopy.

2.4.9 Health economic modelling

No health economic modelling was undertaken for this review question.

2.4.10 Evidence to recommendations

The GDG agreed that there was increased detection of polyps and neoplastic lesions using chromoscopy compared with conventional colonoscopy. However, the GDG felt that because of the additional time and costs involved with limited benefit, chromoscopy should not be used for colonoscopic surveillance in people with polyps. The number of people undergoing surveillance after adenoma removal is much larger than the number of people with IBD on surveillance programmes, therefore the benefit needed to be significant to be clinically important.

A cost-effectiveness analysis showed that surveillance in intermediate-risk group (every 3 years) and high-risk group (within 1 year) was a cost-effective strategy compared with no surveillance in the low-risk (every 5 years) ,intermediate-risk and high-risk groups.

2.4.11 Recommendations

No recommendations were made for this population (see Evidence to recommendations for details).

2.5 Initiation and frequency of surveillance

2.5.1 Review question

When should colonoscopic surveillance be started and what should be the frequency of surveillance?

People with IBD

2.5.2 Evidence review

A total of 14,701 articles were found by systematic searches, of which 9544 were unique articles. The full text was ordered for 62 articles and only six met the eligibility criteria (for review protocol, inclusion and exclusion criteria, see appendix 4). Only limited evidence was available and there was no direct evidence for specific surveillance schemes for the different subgroups for people with IBD. Of the included studies by the technical team, four were primary studies (Karlén et al. 1998; Manning et al. 1987; Odze et al. 2004; Rutter et al. 2006) and two were reviews: one meta-analysis of 116 pooled primary studies (Eaden et al. 2001) and one meta-analysis of 11 studies, comparing the risk of colorectal neoplasia in people with ulcerative colitis with and without primary sclerosing cholangitis (Soetikno et al. 2002). Additionally five primary studies were suggested by the GDG (Askling et al. 2001; Gupta et al. 2007; Rutter et al. 2004b, 2004c; Velayos et al. 2006) that were not identified by the systematic review. The technical team therefore decided to broaden the search criteria and identify other similar relevant prognostic studies that may have been missed. This work is ongoing and the results will be available for the final version.

The characteristics of the included studies are summarised in table 10 and the evidence is reviewed in GRADE profiles 6 and 7 for the intervention of surveillance and prognostic factors respectively. A GRADE profile has not yet been developed for prognostic studies, so the profile for diagnostic studies was modified. Prospective cohort studies were considered as high quality but could move to moderate, low or very low depending on other factors (Schünemann et al. 2008). Detailed evidence tables for the included studies are available in appendix 6.

1 **Table 10: Summary of study characteristics**

Study	Population	Prognostic factors or surveillance programmes	Outcomes used for GRADE profile
Askling et al. (2001)	People with ulcerative colitis or Crohn's disease born between 1941 and 1995, N = 19,876	Family history of colorectal cancer. Regression models were adjusted for age, sex, extent of inflammation (ulcerative colitis: proctitis, left-sided colitis, pancolitis, or unspecified; Crohns's disease: ileal, ileocolonic, colorectal, or unspecified), cohort of origin (regional vs inpatient cohort), family history of colorectal cancer or IBD, and type of IBD	Risk of colorectal cancer
Eaden et al. (2001)	People with ulcerative colitis. Meta-analysis of 116 studies	Risk of colorectal cancer: • in people with ulcerative colitis or total colitis • based on duration of colitis • based on geographical location • depending on colectomy • based on 10-year intervals • in children (not relevant for this guideline)	Cumulative incidence of colorectal cancer by disease duration (10-year intervals)
Gupta et al. (2007)	People with ulcerative colitis with no dysplasia at index colonoscopy, N=418	Degree of inflammation. Potential confounders (including disease extent, duration, age at diagnosis, or presence of primary sclerosing cholangitis, or the use of aminosalicylates, purine analogue immunomodulators, corticosteroids, or folic acid) were studied	Risk of any neoplasia and advanced neoplasia
Karlén et al. (1998)	People with ulcerative colitis of at least 5 years' duration; cases: 40, controls: 102	Differences in the number of surveillance colonoscopies between the cases and controls	Colorectal cancer by number of surveillance colonoscopies
Manning et al. (1987)	189 people with colitis who had undergone colonoscopic surveillance	DET group: 112 had disease duration of at least 8 years, with extensive or total disease (98 with ulcerative colitis, 5 with Crohn's disease and 9 with indeterminate idiopathic colitis). Non-DET group: 77 had colitis of less than 8 years' duration and/or disease that was not extensive or total (50 with ulcerative colitis, 12 with Crohn's disease and 15 with indeterminate idiopathic colitis)	Risk of dysplasia by severity of colitis and incidence of dysplasia by disease duration (decade of disease: 8–10 years intervals)
Odze et al. (2004)	People with ulcerative colitis compared with people without	People with ulcerative colitis with adenoma-like lesions or masses compared with people with ulcerative colitis with sporadic	People with high-grade dysplasia and progression to colorectal

Study	Population	Prognostic factors or surveillance programmes	Outcomes used for GRADE profile
	ulcerative colitis with sporadic adenomas. These people were divided into two subgroups: one consisted of 24 people who had adenoma-like lesions or masses, and the other contained 10 people with sporadic adenomas	adenomas and people without ulcerative colitis with adenomas as controls to determine the recurrence rate, risk of dysplasia and cancer	cancer for adenoma-like lesions or masses and sporadic adenomas
Rutter et al. (2004b)	People with extensive ulcerative colitis of long duration; cases: 68, controls: 136	Prognostic factors: backwash ileitis, shortened colon, tubular colon, featureless colon, scarring, segment of severe inflammation, normal colonic appearance, post-inflammatory polyps and colonic stricture	Risk for colorectal neoplasia
Rutter et al. (2004c)	People with extensive ucerative colitis of long duration; cases: 68, controls: 136	Segmental colonoscopic and histological inflammation. Other data included history of primary sclerosing cholangitis, family history of colorectal cancer, and smoking and drug history (mesalamine 5-aminosalicylic acid, azathioprine and folate)	Risk for colorectal neoplasia
Rutter et al. (2006)	People with histologically proven ulcerative colitis and macroscopic inflammation proximal to the splenic flexure	Colonoscopic surveillance once or twice a year from 8 years after symptom onset. The incidence of neoplasia and/or cancer by disease duration. Progression to cancer by stage of dysplasia.	Cumulative incidence of colorectal cancer by disease duration (10-year intervals). Progression to colorectal cancer for DALMs and sporadic adenomas and by dysplasia
Soetikno et al. (2002)	People with ulcerative colitis with and without primary sclerosing cholangitis	Risk for colorectal dysplasia and colorectal cancer in people with primary sclerosing cholangitis and ulcertiave colitis	Risk of dysplasia and colorectal cancer in people with primary sclerosing cholangitis and ulcerative colitis
Velayos et al. (2006)	People with chronic ulcerative colitis	Patient, clinical, endoscopic and therapeutic factors identified in the literature as associated or potentially associated with colorectal cancer risk.	Risk of colorectal cancer

Study	Population	Prognostic factors or surveillance programmes	Outcomes used for GRADE profile
DALM: dysplasia associated lesions or mass; DET: colitis for 8 years or longer, which was extensive or total by at least one of the following: barium enema; colonoscopic appearances; colonic histology; IBD: inflammatory bowel disease			

1

GRADE profile 6: When and at what frequency should colonoscopic surveillance be offered to people with IBD? Intervention of surveillance

Quality assessment									Summary of findings		
Study	**Design**	**Limitations**	**Inconsistency**	**Directness**	**Imprecision**	**Other considerations**	**Cases**	**Controls**	**RR, OR, HR (95% CI)**	**Risk difference (95% CI)**	**Quality**
Colorectal cancer risk by number of surveillance colonoscopies											
Karlén et al. (1998)	Nested case control	S[a]	N	N	S[b]	None	Ever	2/40	18/102	RR = 0.29 (0.06 to1.31) **NS**	0.13 (0.00 to 0.22)	Very low
							1	1	6	RR = 0.43 (0.05 to 3.76) **NS**	0.03 (–0.07 to 0.10)	
							2+	1	12	RR = 0.22 (0.03 to 1.74) **NS**	0.09 (–0.02 to 0.18)	
Velayos et al. (2006)	Case control	S[c]	N	N	N	Multivariate conditional logistic analysis of all variables	Surveillance colonoscopies <1			OR = 1.0		Very low
							Surveillance colonoscopies 1 or 2			OR = 0.4 (0.2 to 0.7)		
							Surveillance colonoscopies >2			OR = 0.3 (0.1 to 0.8)		
Advanced neoplasia (defined as low- or high-grade dysplasia or colorectal cancer) risk by number of surveillance colonoscopies											
Gupta et al. (2007)	Single retrospective cohort	VS[d]	N	N	N	None	One or more colonoscopies per year			HR = 5.4 (1.7 to 17.0)		Very low

cases: people that died from colorectal cancer; CI: confidence interval; controls: people that did not die from colorectal cancer; ever: one or more surveillance colonoscopies; HR: hazard ratio; IBD: inflammatory bowel disease; N: not serious; **NS**: not statistically significant; OR: odds ratio; RR: relative risk; S: serious; VS: very serious;

[a] The study did not adjust for confounders.
[b] The 95% confidence intervals did not give statistically nor clinically significant results.
[c] The study was a retrospective study.
[d] The study was a retrospective and only single arm.

GRADE profile 7: When and at what frequency should colonoscopic surveillance be offered to people with IBD? Determining significant predictors

Quality assessment							Summary of findings		
Study	**Design**	**Limitations**	**Inconsistency**	**Directness**	**Imprecision**	**Other considerations**	**Cumulative probabilities; RR; OR (95% CI); HR; RD (95% CI)**		**Quality**
Cumulative incidence of colorectal cancer by disease duration (10-year intervals)									
Eaden et al. (2002)	Meta-analysis of 116 studies	S[a]	N	S[b]	N	None	2% by 10 years, 8% by 20 years, and 18% by 30 years		Low
Rutter et al. (2006)	Prospective case series	S*	N	N	N	None	0% at 10 years, 2.5% at 20 years, 7.6% at 30 years, 10.8% at 40 years and 13.5% at 45 years		Very low
Incidence of neoplasia by disease duration (decade of disease: 8–10-year intervals or 10-year intervals)									
Manning et al. (1987)	Prospective cohort	S[c]*	N	N	N	None	10.3 % by 1st decade, 17.5% by 2nd decade, 19.6% by 3rd decade, 33.3% by 4th decade, and 25.0% by 5th decade		Moderate
Rutter et al. (2006)	Prospective case series	S*	N	N	N	None	The actuarial cumulative incidence of neoplasia by disease duration was 1.5% at 10 years, 7.7% at 20 years, 15.8% at 30 years, 22.7% at 40 years and 27.5% at 45 years		Very low
Risk of dysplasia by severity of colitis									
Manning et al. (1987)	Prospective cohort	S[d]*	N	N	N	None	DET group[e]: 36/112 (32.14%)	Non-DET group[f]: 6/77 (7.80%)	Moderate
							RR = 4.13 (1.91 to 9.24); RD = 0.24 (0.13 to 0.34)		
Patients with new adenoma-like masses and sporadic adenomas									
Odze et al. (2004)	Retrospective comparative registry study	S[g]*	N	N	N	S[†]	Adenoma-like masses 15/24 (62.50%)	Sporadic adenomas 5/10 (50%)	Very low
							RR = 1.25 (0.69 to 2.77); RD = –0.13 (–0.46 to 0.22) **NS**		

Quality assessment							Summary of findings			
Study	**Design**	**Limitations**	**Inconsistency**	**Directness**	**Imprecision**	**Other considerations**	**Cumulative probabilities; RR; OR (95% CI); HR; RD (95% CI)**			**Quality**
Patients with HGD for adenoma-like masses and sporadic adenomas										
Odze et al. (2004)	Retrospective comparative registry study	S*	N	N	N	S[†]	Adenoma-like masses 3/24 (12.50%)	Sporadic adenomas 2/10 (20%)		Very low
							RR=0.63 (0.15 to 2.90); RD= 0.08 (–0.17 to 0.41) **NS**			
Progression to colorectal cancer for resectable lesions										
Odze et al. (2004)	Retrospective comparative registry study	S*	N	N	N	S*	Adenoma-like masses 1/24 (4.17%)	Sporadic adenomas 0/10 (0%)		Very low
							RD = –0.04 (–0.21 to 0.25) **NS**			
Rutter et al. (2006)	Prospective case series	S*	N	N	No serious	S[†]	Adenoma-like DALM 20 people 28 lesions		Sporadic adenomas32 patients	Very low
							LG DALM 15 people 19 lesions; 21.4% (S)+ 30% (C)	HG DALM 7 people 9 lesions; 28.6% (S)+ 33.3% (C)	2/32 (6.2%) developed CRC. This risk was not significantly higher than the whole study population (p = 0.67)	
Risk of dysplasia for people with PSC and ulcertiave colitis										
Soetikno et al. (2002)	Meta-analysis of 11 studies[h]	S*	N	N	N	None	People with ulcerative colitis and PSC are at increased risk compared with those with ulcerative colitis alone; OR = 4.79 (3.58 to 6.41) with the Mantel-Haenszel method and OR = 5.11, 95% CI (3.15 to 8.29) with the Der Simonian and Laird method			Moderate

Quality assessment							Summary of findings			
Study	**Design**	**Limitations**	**Inconsistency**	**Directness**	**Imprecision**	**Other considerations**	**Cumulative probabilities; RR; OR (95% CI); HR; RD (95% CI)**			**Quality**
Risk of colorectal cancer for people with PSC and ulcertiave colitis										
Soetikno et al. (2002)	Meta-analysis of 11 studies[i]	S*	N	N	None	None	Patients with ulcerative colitis and PSC are at increased risk compared with those with ulcerative colitis alone; OR = 4.09 (2.89 to 5.76) with the Mantel-Haenszel method and OR = 4.26 (2.80 to 6.48) with the Der Simonian and Laird method			Moderate
Progression to colorectal cancer by dysplasia										
Rutter et al. (2006)	Prospective case series	S*	N	N	None	S[†]	Indefinite for dysplasia 1/32 (3.13%)	LGD 9/46 (19.56%)	HGD 7/19 (36.84%)	Very low
							HGD vs LGD RR = 1.88 (0.81 to 4.160; RD = –0.13 (–0.42 to 0.05) **NS**			
Predictive and protective factors for colorectal neoplasia										
Rutter (2004b)	Case control	S[j]	N	N	N	None	Normal colonic appearance	OR = 0.38 (0.19 to 0.73)	p = 0.003	Low
							Post inflammatory polyps	OR = 2.29 (1.28 to 4.11)	p = 0.005	
							Colonic stricture	OR = 4.62 (1.03 to 20.8)	p = 0.05	
Rutter et al. (2004c)	Case control	S[k]	N	N	N	None	Histological inflammation score	OR = 5.13 (2.36 to 11.14)	p < 0.001	Low
Risk factors for advanced neoplasia (defined as low grade or high grade dysplasia or colorectal cancer)										
Gupta et al. (2007)	Single retrospective cohort	VS[l]	N	N	N	None	Inflammation score mean	HR = 3.8 (1.7 to 8.6)		Low
Predictive and protective factors associated with colorectal cancer										
Askling et al. (2001)	Single Cohort,	S[m]	N	S[n]	N	None	Family history of CRC	RR = 2.5 (1.4 to 4.4)		Very low

Quality assessment							Summary of findings		
Study	**Design**	**Limitations**	**Inconsistency**	**Directness**	**Imprecision**	**Other considerations**	**Cumulative probabilities; RR; OR (95% CI); HR; RD (95% CI)**		**Quality**
	registry follow-up						Family history of CRC relative <50	RR = 9.2 (3.7 to 23)	
							Family history of CRC relative ≥50	RR = 1.7 (0.8 to 3.4) **NS**	
Velayos et al. (2006)	Case control	S[o]	N	N	N	None	Family history of CRC	OR = 3.7 (1.0 to 13.2)	Low
							Smoking	OR = 0.5 (0.2 to 0.9)	
							PSC	OR = 1.1 (0.5 to 2.3) **NS**	
							Post-inflammatory pseudopolyps	OR = 2.5 (1.4 to 4.6)	

(C): patients undergoing immediate colectomy; CI: confidence interval; CRC: colorectal cancer; DALM: dysplasia associated lesions or mass; HGD: high grade dysplasia; HR: hazard ratio; LGD: low grade dysplasia; N: not serious; **NS**: not significant; OR: odds ratio; PSC: primary sclerosing cholangitis; RCT: randomised controlled trial; RD: risk difference; RR: relative risk; (S): patients on surveillance; S: serious; VS: very serious.

* The study did not adjust for confounders.
† The 95% CIs did not give statistically or clinically significant results.
[a] The study pooled results from individual studies weighted by sample size. No adjustment for confounders.
[b] The study included five primary studies looking at children, which is outside the scope of this guideline.
[c] Only a single pathologist confirmed the diagnosis of dysplasia.
[d] Only a single pathologist confirmed the diagnosis of dysplasia.
[e] DET group: colitis for 8 years or longer in duration, which was extensive or total by at least one of the following: barium enema; colonoscopic appearances; colonic histology.
[f] Non-DET group: colitis of less than 8 years' duration and/or disease that was not extensive or total by any criterion.
[g] The study was uncontrolled.
[h] The study had three independent reviewers.
[i] The study had three independent reviewers.
[j] The study was a retrospective case control study.
changes in inflammation over the course of the disease and there was no validation of the scoring system used to distinguish the

Quality assessment							Summary of findings	
Study	Design	Limitations	Inconsistency	Directness	Imprecision	Other considerations	Cumulative probabilities; RR; OR (95% CI); HR; RD (95% CI)	Quality
degree of inflammation. [l] The study was a retrospective and only single arm. [m] The statistical analyses were done by comparing the risk of colorectal cancer with the general population. [n] The study assessed the relative risk for CRC compared with that of the general population using standardised incidence ratios. [o] The study was a retrospective study.								

2.5.3 Evidence statements

2.5.3.1 Very low quality evidence showed a statistically significant trend towards an increased number of surveillance colonoscopies reducing the risk of colorectal cancer death.

2.5.3.2 Very low quality evidence also showed increased risk for advanced neoplasia with increased surveillance colonoscopies but the authors suggested that it could be because of detection bias.

2.5.3.3 Moderate quality evidence showed that people with colitis with duration of 8 years or longer, which was extensive or total, had a significantly higher risk of dysplasia than those without extensive or total colitis.

2.5.3.4 Very low quality evidence showed there was no significant difference in risk to cancer progression in people with ulcerative colitis with resectable lesions compared with the general population with resectable lesions.

2.5.3.5 Moderate quality evidence showed that people with primary sclerosing cholangitis had a significantly higher probability of - developing dysplasia than those with ulcerative colitis.

2.5.3.6 Moderate quality evidence showed that people with primary sclerosing cholangitis had s significantly higher probability of developing colorectal cancer than those with ulcerative colitis.

2.5.3.7 Very low quality evidence showed that the effect of dysplasia on progression to colorectal cancer was not statistically significant but people with high-grade dysplasia had a higher risk than those with low-grade dysplasia.

2.5.3.8 Low quality evidence showed that having post-inflammatory polyps or colonic stricture and increased histological inflammation were

significant predictors of colorectal neoplasia with a normal colonic appearance being a significant protective factor.

2.5.3.9 Low quality evidence showed that increased mean inflammation score was a significant predictor of advanced neoplasia.

2.5.3.10 Low to very low quality evidence showed that having a family history of colorectal cancer (which increased if the relative was younger than 50 years) or the presence of post-inflammatory polyps were significant predictors of colorectal cancer with smoking being a significant protective factor.

2.5.4 Health economic modelling

No health economic modelling was undertaken for this review question.

2.5.5 Evidence to recommendations

As there was no direct evidence for surveillance schemes for the different subgroups within the IBD population, the GDG made recommendations based on the assessment of their risk of developing colorectal cancer, based on the significant risk factors from the evidence that was available. The GDG felt that there were differences in the incidence of colorectal cancer by disease duration between the Eaden et al. (2001) and Rutter et al. (2006) studies. However, people taking part in the latter study were on surveillance and therefore the Eaden et al. (2001) figures are closer to reality. The GDG also felt that a detailed look at disease severity in terms of inflammation was necessary because it is a precursor to dysplasia. It felt that using a validated score for describing inflammation would be a useful tool, as used in the Gupta et al. (2007) study. The GDG also felt that there is sufficient agreement internationally that proctitis does not increase colorectal cancer risk and therefore people with proctitis do not need surveillance. Apart from the duration, extent and severity of the disease, having a family history of colorectal cancer was an important prognostic factor for neoplasia. The GDG stated that even though smoking was a significant predictor for colorectal cancer in one study, other studies did not

show this effect and so therefore this result should be considered with caution. The GDG felt these were the key factors for determining risk of developing colorectal cancer for surveillance in people with IBD. The GDG felt strongly that before entering the surveillance algorithm a confirmed histological diagnosis was essential. The GDG also stated that any resectable lesion found should be removed endoscopically. For people with flat dysplastic lesions, surgery should be offered but if declined they should remain on surveillance within the high-risk group.

2.5.6 Recommendations

Recommendation 1.1.3

Offer people with IBD who are being considered for colonoscopic surveillance a baseline colonoscopy to determine their risk of developing colorectal cancer (see table 1).

Table 1 Risk of developing colorectal cancer in people with IBD

Low risk: -extensive but quiescent ulcerative colitis or Crohn's colitis **or** -left-sided ulcerative colitis or similar extent of Crohn's colitis. **Intermediate risk:** -extensive colitis with mild active histological inflammation **or** -presence of post-inflammatory polyps **or** -family history of colorectal cancer in a first degree relative aged 50 years or over. **High risk:** -extensive colitis with moderate or severe active histological inflammation **or** -primary sclerosing cholangitis (including post-transplant) **or** -presence of colonic stricture in the past 5 years **or** -dysplasia (any grade) in the past 5 years **or** -family history of colorectal cancer in a first degree relative aged under 50 years.

Recommendation 1.1.4

Offer colonoscopic surveillance to people with IBD based on their risk of developing colorectal cancer (see table 1), determined at each colonoscopy.

-Low risk: offer every 5 years.

-Intermediate risk: offer every 3 years.

-High risk: offer every year.

People with polyps

2.5.7 Evidence review

A total of 14,701 articles were found by systematic searches, of which 9544 were unique articles. The full text was ordered for 62 articles and then a further four articles were identified through manual reference searching. Only limited evidence was available and six articles met the eligibility criteria (for review protocol, inclusion and exclusion criteria, see appendix 4). Of these two were meta-analyses of primary studies (Martinez et al. 2009; Saini et al. 2006) and four were primary studies that were not covered at all or the outcomes of interest were not covered by the reviews (Kronborg et al. 2006; Lieberman et al. 2007, 2008; Martinez et al, 2009; Nusko et al, 2002). The Martinez et al. (2009) review had included the data from the Lieberman et al. (2000) study but because it collected data only until June 2005, the updated data available from Lieberman et al. (2007) and the prevalence study of advanced histology in smaller adenomas of Lieberman et al. (2008) were not included in the meta-analysis and were therefore included in our analysis. The Saini et al. (2006) systematic review included the Nusko et al. (2002) study, but only for the outcome of risk factors for recurrent adenomas, so it was included in our analysis for two additional outcomes, risk factors and time taken for the development of advanced metachronous adenomas (defined as larger than 10 mm in size, or with high-grade dysplasia or with invasive cancer).

1 The characteristics of the included studies are summarised in table 11 and
2 their evidence reviewed in GRADE profiles 8 and 9. Detailed evidence tables
3 for the included studies are available in appendix 6.

4 **Table 11: Summary of study characteristics**

Study	Population	Prognostic factors or surveillance programmes	Outcomes used for GRADE profile
Kronborg et al. (2006)	10 years of surveillance of people with previously diagnosed adenomas, N = 946	1. Surveillance group A: 24 months 2. Surveillance group B: 48 months 3. Surveillance group C: 6 months 4. Surveillance group D: 12 months 5. Surveillance group E: 12 months 6. Surveillance group F: 24 months	Recurrence risk of new adenomas, advanced adenomas and progression to colorectal cancer
Lieberman et al. (2007)	5 years of surveillance of people with previously diagnosed polyps, N = 3121	Histopathology of the index polyp: 1. with 1 or 2 tubular adenomas <10 mm 2. with 3 or more tubular adenomas <10 mm 3. with tubular adenoma >10 mm 4. with villous adenomas 5. with adenomas with high-grade dysplasia	Risk of new neoplasia, high-grade dysplasia and colorectal cancer by histopathology of index
Lieberman et al. (2008)	People undergoing colonoscopic surveillance with largest index polyp being less than 10 mm, in 2005, N = 5977	1. Histopathology of the index polyp 2. Location of the index polyp	Prevalence of advanced histology its association with the distal colon
Martinez et al. (2009)	Meta-analysis of 8 studies (6 RCTs) for people undergoing surveillance after polypectomy. Median follow-up period of 47.2 months and N = 10,021	Risk factors considered: 1. age 2. sex 3. race 4. family history of colorectal cancer 5. smoking status 6. body mass index 7. previous polyps 8. number of adenomas 9. location of polyps 10. size of largest adenoma 11. adenomas histology 12. high-grade dysplasia	Risk factors for advanced metachronous neoplasia
Nusko et al. (2002)	People undergoing surveillance post polypectomy, N = 1159	Risk factors considered: 1. size of largest adenoma 2. parental history of colorectal cancer 3. histological type 4. dysplasia 5. location of adenomas 6. multiplicity	Risk factors and time taken for progression to advanced metachronous adenomas
Saini et al. (2006)	Criterion for inclusion was	14 studies, reported a total of 6 risk factors:	Risk factors for recurrent

Study	Population	Prognostic factors or surveillance programmes	Outcomes used for GRADE profile
	people with a personal history of adenomas	1. number of adenomas 2. size of largest adenoma 3. patient age 4. tubulovillous/villous features or severe dysplasia 5. advanced adenoma 6. adenoma in the proximal colon	advanced adenomas

GRADE profile 8: When and at what frequency should colonoscopic surveillance be offered to people with polyps?
Frequency of surveillance

Quality assessment							Summary of findings			
Study ID	Design	Limitations	Inconsistency	Directness	Imprecision	Other considerations	RR (95% CI)			Quality
							Surveillance groups			
							B (n = 340) vs A (n = 331)	D (n = 32) vs C (n = 42)	F (n = 103) vs E (n = 97)	
Recurrence risk of new adenomas by surveillance group										
Kronborg et al. (2006)	RCT	S*	N	N	S†	None	RR = 0.88 (0.69 to 1.12) **NS**	RR = 0.82 (0.43 to 1.52) **NS**	RR = 0.88 (0.57 to 1.34) **NS**	Low
Recurrence risk of new advanced[a] adenomas by surveillance group										
Kronborg et al. (2006)	RCT	S*	N	N	S†	None	RR = 1.15 (0.61 to 2.15) **NS**	RR = 3.12 (0.87 to 14.50) **NS**	RR = 0.97 (0.40 to 2.35) **NS**	Low
Progression to colorectal cancer by surveillance group										
Kronborg et al. (2006)	RCT	S*	N	N	S†	None	RR = 6.22 (1.06 to 117)	RR = 0.82 (0.43 to 1.52) **NS**	RR = 0.88 (0.57 to 1.34) **NS**	Low
Adverse events										
Kronborg et al. (2006)	RCT	S*	N	N	N	None	7 total, 6 during surveillance. Perforation at initial colonoscopy seen in group A was fatal (septicemia). A: 2 diagnostic perforations and 2 therapeutic perforations; B: 1 diagnostic perforation and 1 polypectomy syndrome	2 total (1 diagnostic perforation and 1 polypectomy syndrome) both in group C. None seen in D	2 total, one diagnostic perforation seen in each group	Moderate

CI: confidence interval; N: not serious; **NS**: not significant; RCT: randomised controlled trial; RR: relative risk; S: serious
Surveillance group A: 24 months, surveillance group B: 48 months, surveillance group C: 6 months, surveillance group D: 12 months, surveillance group E: 12 months, surveillance group F: 24 months

* The study was randomised by random numbers but no details of concealment or blinding of pathologists is mentioned.
† The 95% confidence intervals did not give statistically nor clinically significant results.
[a] The advanced adenomas were defined as those with severe dysplasia or being at least 10 mm in diameter or villous.

GRADE profile 9: When and at what frequency should colonoscopic surveillance be offered to people with polyps? Determining significant predictors

Quality assessment							Summary of findings	
Study	**Design**	**Limitations**	**Inconsistency**	**Directness**	**Imprecision**	**Other considerations**	**R; RR; OR (95% CI)**	**Quality**
Risk of new neoplasia by histopathology of the polyps at index colonoscopy								
Lieberman et al. (2007)	Multi-centre registry	S*	N	N	N	None	Compared with no neoplasia at baseline: 1 or 2 tubular adenomas <10 mm: RR = 1.92 (0.83 to 4.42) **NS**	Very low
							≥3 tubular adenomas <10 mm: RR = 5.01 (2.10 to 11.96)	
							Tubular adenoma >10 mm: RR = 6.40 (2.74 to14.94)	
							Villous adenoma: RR = 6.05 (2.48 to 14.71)	
							High-grade dysplasia: RR = 6.87 (2.61 to18.07)	
Risk of high-grade dysplasia or cancer by histopathology of the polyps at index colonoscopy								
Lieberman et al. (2007)	Multi-centre registry	S*	N	N	N	None	Rates per 1000 person-years of follow-up no neoplasia at baseline: R = 0.7 (0 to 2.0) **NS**	Very low
							1.5 with tubular adenomas <10 mm (0 to 2.9) **NS**	
							>10 mm tubular: R = 6.4 (0 to 13.5) **NS**	
							Villous adenomas: R = 6.2 (0 to 14.7) **NS**	
							HGD: R = 26.0 (3.2 to 48.8) vs no neoplasia at baseline: RR = 7.23 (2.81 to 18.17)	
Prevalence of advanced histology (defined as an adenoma with villous or serrated histology, HGD, or an invasive cancer) in 2005								
Lieberman	Multi-centre	S*	N	N	N	Sensitivity analysis	1–5 mm group: 1.7% (1.2 to 2.0)	Very low

Quality assessment							Summary of findings			
Study	**Design**	**Limitations**	**Inconsistency**	**Directness**	**Imprecision**	**Other considerations**	**R; RR; OR (95% CI)**			**Quality**
et al. (2008)	registry					done for misclassification[a] for prevalence	6–9 mm group: 6.6% (4.6 to 11.7) >10 mm group: 30.6% (29.2 to 40.0)			
Distal location's associated with advanced histology in 2005										
Lieberman et al. (2008)	Multi-centre registry	S*	N	N	N	None	6–9 mm group (p = 0.04) >10 mm group (p = 0.002)			Very low
Risk factors for advanced metachronous neoplasia (advanced adenomas[b] and invasive cancer)										
Martinez et al. (2009)	Meta-analysis of 8 studies (6 RCTs)	S[c]	N	N	N	Patient level data used and confounders adjusted by multivariate logistic regression	Older age (p < 0.0001 for trend) Male sex: OR = 1.40 (1.19 to 1.65) Number and size of previous adenomas (p < 0.0001 for trend) Presence of villous features: OR = 1.28 (1.07 to 1.52) Proximal location: OR = 1.68 (1.43 to 1.98)			Low
Risk factors for advanced metachronous adenomas (defined as defined as larger than 10 mm or with HGD or invasive carcinoma)										
Nusko et al. (2002)	Single centre registry, prospective single cohort	S[d]	N	N	N	Adjusted by multivariate logistic regression	Considering only patients with tubular adenomas at index: adenoma size (p < 0.0001) Multiplicity of adenomas at index (p = 0.021) Parental history of colorectal carcinoma (p = 0.017) An interactive effect between size and sex (p = 0.00392): male patients with large adenomas had a significantly higher risk than others			Moderate
Time taken for advanced metachronous adenomas (defined as larger than 10 mm or with HGD or invasive carcinoma) to develop over time										
Nusko et al. (2002)	Single centre registry, prospective single cohort	S[e]	N	N	N	1000 Bootstrap samples done for sensitivity analyses and confounders adjusted by	Prp	Low-risk[f]	High risk[g]	Moderate
							5%	10.4 years (4.1 to 13.2)	0.5 years (0.1 to 1.6)	
							10 %	12.2 years (10.1 to 15.2)	6.1 years (3.2 to 11.5)	

Quality assessment							Summary of findings				
Study	**Design**	**Limitations**	**Inconsistency**	**Directness**	**Imprecision**	**Other considerations**	**R; RR; OR (95% CI)**				**Quality**
						multivariate logistic regression	20 %	16.2 years (10.5 to 19.2)	15.6 years (11.5 to 18.2)		
Risk factors for recurrent advanced adenomas (defined as adenomas ≥1 cm, villous histological features, or with cancer) based on adenomas at index colonoscopy											
Saini et al. (2006)	Systematic review	S	N	N	N	None	RF	RR	RD	H	Moderate
							Number and size of adenomas	>3 vs 1 or 2			
								2.52 (1.07 to 5.97)	5% (1% to 10%)	p < 0.001	
							Histological diagnosis	tubulovillous/villous vs tubular			
								1.26 (0.95 to 1.66) **NS**	2% (–1% to 4%) **NS**	p > 0.2	
							Dysplasia	HGD vs no HGD			
								1.84 (1.06 to 3.19)	4% (0 to 8%)	p > 0.2 **NS**	

CI: confidence interval; H: heterogeneity; HGD: high-grade dysplasia; N: not serious; **NS**: not significant; OR: odds ratio; Prp: proportion of patients expected to develop advanced metachronous adenomas; R: risk; RD: risk difference; RF: risk factor; RR: relative risk; S: serious

* The study did not adjust for confounders.
[a] The sensitivity analysis was done to determine how misclassification of polyp size would impact the outcome. The analysis assumed that polyps were either overestimated in size by 1 mm (for example, a 10-mm polyp is reclassified as 9 mm) or underestimated (a 9-mm polyp is reclassified as 10 mm).
[b] The advanced adenomas were defined as those that had one or more of the following features: 10 mm in diameter or larger, presence of high-grade dysplasia, or greater than 25% villous features (also classified as tubulovillous or villous histology).
[c] The study combined randomised and non-randomised studies together.
[d] The study only had a single arm cohort.
[e] The study only had a single arm cohort.
[f] People at low risk were defined as: no parental history of colorectal carcinoma and with only small (<10 mm) tubular adenomas at index.
[g] People at high risk were defined as: those with multiple or large adenomas, tubulovillous or villous adenomas, or a parental history of colorectal cancer.

2.5.8 Evidence statements

2.5.8.1 Low quality evidence showed a statistically significant higher risk for cancer progression after 48 months of surveillance compared with 24 months.

2.5.8.2 Moderate quality evidence showed adverse events of perforations and polypectomy syndrome during follow-up at 6–48 months.

2.5.8.3 Very low quality evidence showed that having at least three tubular adenomas smaller than 10 mm, or tubular adenomas larger than 10 mm, or villous adenomas or high-grade dysplasia at index colonoscopy were significant predictors for risk of new neoplasia.

2.5.8.4 Very low quality evidence showed that having high-grade dysplasia compared with no neoplasia at index colonoscopy was a significant predictor for high-grade dysplasia or colorectal cancer in the future.

2.5.8.5 Very low quality evidence that studied the risk associated with small adenomas and distal location, showed that the prevalence of advanced histology[2] increased with the size of the polyp: 1.7% in the 1–5 mm group, 6.6% in the 6–9 mm group and 30.6% in the >10–mm group.

2.5.8.6 Very low quality evidence that studied the risk associated with small adenomas and distal location showed that the prevalence of advanced histology in the distal colon increased with polyp size and was a statistically significant in the 6–9 mm group and in the >10 mm group.

2.5.8.7 Low quality evidence showed that being older, being male, increasing number and size of prior adenomas, presence of villous

[2] Advanced histology was defined as an adenoma with villous or serrated histology, high-grade dysplasia, or an invasive cancer.

features and proximal location at index colonoscopy were significant predictors for advanced metachronous neoplasia (advanced adenomas[3] and invasive caner).

2.5.8.8 Moderate quality evidence showed that having an increased adenoma size, multiplicity of adenomas, parental history of colorectal cancer and an interactive effect between adenoma size and sex (male) were significant predictors for advanced metachronous adenomas[4]. Men with large adenomas had a significantly higher risk than others.

2.5.8.9 Moderate quality evidence showed that the time taken for advanced metachronous adenomas to develop in 5% of people at low risk[5] was10.4 years, in 10% it was12.2 years and in 20% it was 16.2 years.

2.5.8.10 Moderate quality evidence showed that time taken for advanced metachronous adenomas to develop in 5% of high risk people[6] was 0.5 years, in 10% was 6.1 years and in 20% was 15.6 years.

2.5.8.11 Moderate quality evidence showed that the risk for recurrent advanced adenomas[7] increased with increasing number and size of adenomas at index colonoscopy.

2.5.9 Evidence to recommendations

As there was no direct evidence for surveillance schemes for the different subgroups within the population who had adenomatous polyps removed

[4] Advanced metachronous adenomas were defined as larger than 10 mm or with high-grade dysplasia or invasive carcinoma.
[4] Advanced metachronous adenomas were defined as larger than 10 mm or with high-grade dysplasia or invasive carcinoma.
[5] People at low risk were defined as: no parental history of colorectal carcinoma and with only small (<10 mm) tubular adenomas at index colonoscopy.
[6] People at high risk were defined as: those with multiple or large adenomas, tubulovillous or villous adenomas, or a parental history of colorectal carcinoma.
[7] Advanced adenomas were defined as adenomas ≥1 cm, villous histological features, or with cancer.

previously, the GDG made recommendations based on the assessment of their risk of developing colorectal cancer, based on the significant risk factors from the evidence that was available. The GDG felt that there was enough evidence to stratify people who had previously had adenomas according to their risk of developing neoplasia. It felt that the frequency of surveillance should be based on the risk assessment. The GDG felt that the evidence showed that the number and size of the adenomas at index colonoscopy were consistent significant predictors for neoplasia and therefore should determine the risk state for surveillance. Villous histology was also a significant predictor for advanced neoplasia, though the confidence intervals around the odds were wide (odds ratio 1.28, 95% CI 1.07 to 1.52). The GDG considered that because villous histology is subject to wide variation in classification by pathologists, particularly in small biopsies, inclusion of this variable could lead to wide variation in referral rates for colonoscopy. The GDG also stated that all adenomas detected during colonoscopic surveillance should be removed endoscopically.

Ongoing research on the long-term safety of people at low risk having no surveillance is expected to report outcomes in the next 2 years (Cairns et al. 2010). This will give valuable evidence on future guidance development in this area.

2.5.10 Recommendations

Recommendation 1.1.8

Offer people with adenomatous polyps who are being considered for colonoscopic surveillance a baseline colonoscopy to determine their risk of developing colorectal cancer (see table 2).

Table 2 Risk of developing colorectal cancer in people with polyps

Low risk: -one or two adenomas smaller than 1 cm**.** **Intermediate risk:** -three or four adenomas smaller than 1 cm **or** -one or two adenomas if one is larger than 1 cm. **High risk:** -five or more adenomas smaller than 1 cm **or** -three or more adenomas if one is 1 cm or larger.

Recommendation 1.1.9

Offer colonoscopic surveillance to people with adenomatous polyps based on their risk of developing colorectal cancer (see table 2), determined at each colonoscopy.

- Low risk: do not offer colonoscopic surveillance.
- Intermediate risk: offer colonoscopic surveillance every 3 years until there are two consecutive negative colonoscopies, then stop surveillance.
- High risk: offer one colonoscopy at one year after diagnosis. If no adenomas are found, or low-risk or intermediate risk adenomas are found, follow the advice above for intermediate risk. If high-risk adenomas are found, continue colonoscopic surveillance every year.

2.6 Information and support needs for patients

2.6.1 Review question

What are the information and support needs of people, or the carers of people, undergoing or considering undergoing colonoscopic surveillance?

2.6.2 Evidence review

A total of 1910 articles were found by systematic searches, of which 28 were unique articles. Full text was ordered for these articles and only seven met the eligibility criteria (for review protocol, inclusion and exclusion criteria, see appendix 4). Thematic analysis was used to analyse these seven studies to adequately answer the review question.

The characteristics of the included studies are summarised in Table 12 and detailed evidence tables are available in appendix 5.

The seven studies are:

- Rutter et al. (2006): a 58-question self-administered postal questionnaire design with an 85.4% response rate.
- Thiis-Evensen et al. (1999): a postal questionnaire design aimed to study the psychologic effect of attending a screening programme to detect and remove colorectal polyps.
- Sheikh et al. (2004): a questionnaire design study to determine people's screening preferences.
- Brotherstone et al. (2006): effectiveness of visual illustrations in improving people's understanding of the preventive aim of flexible sigmoidoscopy screening.
- Makoul et al. (2009): a pretest–posttest design to assess a multimedia patient education programme that provides information about colorectal cancer and screening.

- Sequist et al. (2009): a randomised control trial to promote colorectal cancer screening. The screening options in this study also looked at faecal occult blood test (FOBT) and the results reported included FOBT screening.
- Miles et al. (2009): postal survey examining the psychological impact of being assigned to colonoscopic surveillance after detection of adenomatous polyps.

Table 12 Thematic analysis

People's experience of the procedure	
Rutter et al. (2006)	39% of the respondents found bowel preparation difficult to take 60.2% of the respondents found their last colonoscopy comfortable or very comfortable People expressed less discomfort with more experienced colonoscopists (r = 0.20, p = 0.0007) There was a correlation between comfort and pethidine dose (r = 0.16, p = 0.007, i.e. those with more discomfort were given more pethidine)
Thiis-Evensen et al. (1999)	When asked if they found the colonoscopic examination uncomfortable, 50% said no, 45% found it moderately uncomfortable and 5% found it very uncomfortable
Rutter et al. (2006)	16.4% of the respondents experienced abdominal pain (attributed to the procedure) in the week following their last colonoscopy, of which 3.7% stated that the pain interfered with everyday activities. Post-procedural pain was strongly related to the Hospital Anxiety and Depression Scale anxiety score (p< 0.0001) but not with the drug doses used during the procedure. Five patients (1.7%) reported complications following previous colonoscopies
People's preference	
Sheikh et al. (2004)	Of those who had had a previous colonoscopy, 55% preferred a repeat, compared with only 30% of those who had never had a colonoscopy (p = 0.017) Of those who had had a previous sigmoidoscopy, 53% preferred a repeat, compared with only 33% of those who had never had a sigmoidoscopy, although the differences were not statistically significant
Thiis-Evensen et al. (1999)	When asked if they would attend a repeat examination in 5 years' time, 90% said yes, 2% said no and 7.6% were not sure
Information given	
Rutter et al. (2006)	91.4% described the information given as easy to understand, 2.6% thought it was difficult and 6.1% could not remember being given information
Rutter et al. (2006)	When asked about the amount of information they had received about the surveillance programme, 83.8% thought they had received the right amount of information, 16.2% thought they had received too little, and no one thought they had received too much 65.5% reported being content with their current involvement, whereas 34.2% preferred to be more involved and only 0.4% wished to be less involved
Brotherstone et al. (2006)	In the written information group, 57% had a good understanding of the aims of the test, while in the group who were sent written information and illustrations, 84% had a good understanding The addition of the illustrations resulted in significantly better understanding (OR = 3.75; CI: 1.16 to 12.09; p= 0.027) which remained significant after controlling for age, gender and socioeconomic status (OR = 10.85; CI: 1.72 to 68.43; p = 0.011).
Makoul et al.	A pretest–posttest multimedia patient education programme on colorectal cancer screening led to a significant increase in the

(2009)	knowledge of flexible sigmoidoscopy (from 11.5% to 53.0%; p < 0.001) and colonoscopy (from 23.3% to 57.0%; p < 0.001) More than 90% of people wanted to discuss colorectal cancer with their doctors after the education programme
Surveillance programme	
Rutter et al. (2006)	97.8% of people felt that surveillance was important for them 96.4% thought that the surveillance programme gave them reassurance, while 3.6% stated that the programme made them more anxious When asked about the effect of the surveillance programme on reducing risk of colorectal cancer, 1.8% believed it completely removed the risk, 67.9% believed it greatly reduced the risk, 24.4% believed it moderately reduced the risk, and 5.9% believed it slightly reduced the risk
Makoul et al. (2009)	Multimedia pretest–posttest patient education programme led to a significant increase in the number of people willing to undergo colorectal cancer screening with flexible sigmoidoscopy (from 54.1% to 78.1%; p < 0.001) and colonoscopy (from 64.8% to 84.4%; p < 0.001)
Sequist et al. (2009)	People who received the mailings of colorectal cancer screening were significantly more likely to complete screening than those who did not (44.0% vs 38.1%; p < 0.001) Detection of adenomas tended to be greater among people who received mailings compared with the control group (5.7% versus 5.2%; p = 0.10)
Psychological impact of surveillance	
Thiis-Evensen et al. (1999)	The scores for both Goldberg's General Health Questionnaire (GHQ-28) and the Hospital Anxiety and Depression Scale were lower, indicating a lower level of psychiatric morbidity among those attending the examination than the controls
Miles et al. (2009)	People offered surveillance reported lower psychological distress and anxiety than those with either no polyp (p < 0.05) or lower risk polyps (p < 0.01). The surveillance group also reported more positive emotional benefits of screening than the other outcome groups. Post-screening bowel cancer worry and bowel symptoms were higher in people assigned to surveillance, but both declined over time, reaching levels observed in either one or both of the other two groups found to have polyps, suggesting these results were a consequence of polyp detection rather than surveillance
CI: confidence interval; OR: odds ratio	

2.6.3 Evidence statements

2.6.3.1 There is limited evidence describing people's experience of colonoscopy.

- *39% found bowel preparation unpleasant.*
- *50% did not find the examination uncomfortable, 45% found it moderately uncomfortable and 5% found it very uncomfortable.*
- *People expressed less discomfort with a more experienced colonoscopist and with sedation.*

2.6.3.2 There is limited evidence describing people's preference.

- *55% of those who had had a previous colonoscopy preferred a repeat, compared with only 30% of those who had never had a colonoscopy*
- *53% of those who had had a previous sigmoidoscopy preferred a repeat, compared with only 33% of those who had never had a sigmoidoscopy, although the differences were not statistically significant*
- *When asked if they would attend a repeat examination in 5 years' time, 90% said yes, 2% said no and 8% were not sure.*

2.6.3.3 There is limited evidence describing the amount of information given and how the information improved people's understanding.

- *57% in the written information group had a good understanding of the aims of the screening test, while in the group who were sent written information and illustrations, 84% had good understanding.*
- *The addition of the illustrations resulted in significantly better understanding, even after controlling for age, sex and socioeconomic status.*

- *A pretest–posttest multimedia patient education programme on colorectal cancer screening using graphics and audio led to a significant increase in the knowledge of flexible sigmoidoscopy and colonoscopy.*
- *More than 90% of people wanted to discuss colorectal cancer with their doctors after the education programme.*
- *When asked about the amount of information they had received about the surveillance programme, 83.8% thought they had received the right amount of information.*
- *91.4% described the information given as easy to understand and 2.6% thought it was difficult.*

2.6.3.4 There is limited evidence describing the benefits, risks and uptake of a surveillance programme.

- *People who received mailings of colorectal cancer screening were significantly more likely to undergo screening than those who did not.*
- *Detection of adenomas tended to be greater among people who received mailings compared with the control group.*
- *The multimedia pretest–post-test patient education programme led to a significant increase in the number of people willing to undergo colorectal cancer screening with flexible sigmoidoscopy and colonoscopy.*
- *97.8% of people felt that surveillance was important for them.*
- *96.4% thought that the surveillance programme gave them reassurance, while 3.6% stated that the programme made them more anxious.*
- *When asked about the effect of the surveillance programme on reducing the risk of colorectal cancer, 67.9% believed it greatly reduced the risk.*

2.6.3.5 Two papers described the psychological impact of surveillance.

- *A lower level of psychiatric morbidity was noticed among those attending the screening examination than in the control group.*
- *People offered surveillance reported lower psychological distress and anxiety than those with either no polyp or lower risk polyps. The surveillance group also reported more positive emotional benefits of screening than the other outcome groups.*

2.6.4 Health economic modelling

No health economic modelling was undertaken for this review question.

2.6.5 Evidence to recommendations

The patient experts on the GDG drew on their personal experience and that of patient groups to inform the evidence to recommendations. They considered that the figure '39% finding bowel preparation difficult to take' was low and would have expected a higher number of people to have reported discomfort during bowel preparation. They suggested that the phrase 'difficult to take' could be more accurately described as 'unpleasant' because people describe discomfort felt before, during and after the procedure. This includes bloating and abdominal cramps.

The patient experts advised that people should be told to expect discomfort during the procedures (which include bowel preparation, colonoscopy, flexible sigmoidoscopy) and that they may not be able to undertake day-to-day (normal) activities after bowel preparation. They also noted that sedation and an experienced colonoscopist help to reduce discomfort.

The patient experts agreed with the evidence (Sequist et al. 2009; Makoul et al. 2009; Rutter et al. 2006) that giving adequate information in a way that people understand improves the uptake, knowledge and understanding of colonoscopic surveillance. People should also be given the opportunity to speak to a consultant.

The patient experts also pointed out that being in a surveillance programme does not have a negative psychological impact. However, the benefits as well as the risks should be properly explained to people considering colonoscopic surveillance.

The GDG advised that some of the evidence provided is not true for some groups and this should be considered when reading the evidence statements. It advised that the evidence statements should be seen as an extract from the evidence provided. However, based on the experience of the GDG members, recommendations were made on information provision for people considering colonoscopic surveillance.

The GDG also advised that the information and support needs for people considering colonoscopic surveillance should be offered before surveillance and should continue during the surveillance programme.

2.6.6 Recommendations

Recommendation 1.1.10

Discuss the benefits and risks with people considering colonoscopic surveillance including:

- -early detection and prevention of colorectal cancer **and**
- -effects on mortality, morbidity, quality of life and psychological outcomes.

Recommendation 1.1.11

Before offering colonoscopic surveillance, inform people about the procedure they are having, including:

- -bowel preparation
- -sedation
- -potential discomfort
- -impact on everyday activities.

Recommendation 1.1.12

Throughout the surveillance programme, give people and their families or carers the opportunity to discuss any issues with a healthcare professional. Information should be provided in a variety of formats tailored to the person's needs, and if appropriate, could include illustrations.

3 Research recommendations

We have made the following recommendations for research, based on our review of evidence, to improve NICE guidance and patient care in the future.

Although outside the Scope of this guideline, the GDG wished to highlight the importance of colorectal cancer prevention strategies. Specifically, they considered that chemoprevention (aspirin, folic acid) should be evaluated in people at increased risk (that is, with IBD or polyps). There is evidence from studies carried out in other clinical areas (for example, ischaemic heart disease) that has demonstrated a reduced risk of colorectal cancer in people taking aspirin, multivitamins, or folic acid over a long period of time, but this effect has not been evaluated in the population covered by this guideline.

Surveillance programmes for people at increased risk of colorectal cancer

How effective are colonoscopic surveillance programmes in improving overall survival and cancer-related survival in people at increased risk of colorectal cancer?

Why this is important

There is no randomised controlled trial evidence on the effectiveness of colonoscopic surveillance programmes in improving survival in people at increased risk of colorectal cancer. Although there is some observational evidence in people with IBD, there is no evidence in people post polypectomy. Randomised controlled trials should be undertaken to determine the effect of surveillance programmes on survival (preferably, 5 years and longer follow-up) and quality of life in people at increased risk of colorectal cancer because of IBD or polyps.

Natural history of progression to colorectal cancer in people at increased risk

What is the natural history of colorectal cancer in people at increased risk of colorectal cancer (people with IBD or polyps)?

Why this is important

There is very limited evidence on the natural history of progression to colorectal cancer, and how progression differs with various factors, such as extent of disease, grade of dysplasia, or polyp-related factors. Long-term studies (ideally including a facility for 20 years follow-up or more) should be conducted to determine the natural history of colorectal cancer in people with IBD or polyps, and to identify those factors which impact on the progression of disease.

Lack of randomised controlled trial evidence on the effectiveness of biomarkers for risk stratification

Which biomarkers, including epigenic and genetic markers, are predictors of colorectal cancer? How should these be used to improve the stratification of the risk of colorectal cancer?

Why this is important

There is no high quality evidence on the predictive value of biomarkers, including epigenic and genetic markers, for colorectal cancer in adults at increased risk (inflammatory bowel disease or polyps). Research should be undertaken to identify those biomarkers which are predictive of colorectal cancer, if any can improve levels of early detection, and how they can be used to improve risk stratification.

Polyp types and risk of colorectal cancer

Does the risk of colorectal cancer differ by type of polyp?

Why this is important

There is no high quality evidence on the association between risk of colorectal cancer and some polyp types (sessile, hyperplastic non-adenomatous). Research should be undertaken to determine the level of risk of colorectal cancer associated with polyp type in adults with these polyps.

4 Other versions of this guideline

This is the full guideline. It contains details of the methods and evidence used to develop the guideline. It is available from our website (www.nice.org.uk/guidance/CG[XX]Guidance). **[Note: these details will apply to the published full guideline.]**

Quick reference guide

A quick reference guide for healthcare professionals is available from www.nice.org.uk/guidance/CG[XX]QuickRefGuide

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N1[XXX]). **[Note: these details will apply when the guideline is published.]**

'Understanding NICE guidance'

A summary for patients and carers ('Understanding NICE guidance') is available from www.nice.org.uk/guidance/CG[XX]PublicInfo

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N1[XXX]). **[Note: these details will apply when the guideline is published.]**

We encourage NHS and voluntary sector organisations to use text from this booklet in their own information about colonoscopic surveillance.

5 Related NICE guidance

Published

- Improving outcomes in colorectal cancer. NICE cancer service guidance (2004). Available from www.nice.org.uk/guidance/CSGCC
- Wireless capsule endoscopy for investigation of the small bowel. NICE interventional procedure guidance 101 (2004). Available from www.nice.org.uk/guidance/IPG101

Under development

NICE is developing the following guidance (details available from www.nice.org.uk):

- Diagnosis and management of colorectal cancer. NICE clinical guideline. Publication expected July 2011.
- The management of Crohn's disease. NICE clinical guideline. Publication date to be confirmed.

6 Updating the guideline

NICE clinical guidelines are updated so that recommendations take into account important new information. New evidence is checked 3 years after publication, and healthcare professionals and patients are asked for their views; we use this information to decide whether all or part of a guideline needs updating. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations.

7 References, glossary and abbreviations

7.1 References

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7.2 Glossary

Absolute risk reduction (risk difference)

The difference in event rates between two groups (one subtracted from the other) in a comparative study.

Absolute risk

Measures the probability of an event or outcome occurring (for example an adverse reaction to the drug being tested) in the group of people under study. Studies that compare two or more groups of patients may report results in terms of the absolute risk reduction**.**

Adenoma

A benign tumour of a glandular structure or of glandular origin.

Baseline

The initial set of measurements at the beginning of a study (after A run-in period where applicable), with which subsequent results are compared.

Bias

Systematic (as opposed to random) deviation of the results of a study from the 'true' results that is caused by the way the study is designed or conducted.

Blinding (masking)

Keeping the study participants, caregivers, researchers and outcome assessors unaware about the interventions to which the participants have been allocated in a study.

Bowel preparation

The use of various laxatives to clear out the bowel in preparation for lower gastrointestinal surgery or other bowel investigation, for example colonoscopy or barium enema.

Case report (or case study)

Detailed report on one patient (or case), usually covering the course of that person's disease and their response to treatment.

Case series

Report of a number of cases of a given disease, usually covering the course of the disease and the response to treatment. There is no comparison (control) group of patients.

Case-control study

Comparative observational study in which the investigator selects individuals who have experienced an event (for example, developed a disease) and others who have not (controls), and then collects data to determine previous exposure to a possible cause.

Cohort

A group of people sharing some common characteristic (for example patients with the same disease), followed up in a research study for a specified period of time.

Cohort study

A retrospective or prospective follow-up study. Groups of individuals to be followed up are defined on the basis of presence or absence of exposure to a suspected risk factor or intervention. A cohort study can be comparative, in

which case two or more groups are selected on the basis of differences in their exposure to the agent of interest.

Colonoscopy

The endoscopic examination of the colon and the distal part of the small bowel.

Comorbidity

Two or more diseases or conditions occurring at the same time, such as depression and anxiety.

Comparability

Similarity of the groups in characteristics likely to affect the study results (such as health status or age).

Computed tomographic colonography

A medical imaging procedure which uses X-rays and computers to produce two- and three-dimensional images of the colon (large intestine) from the lowest part, the rectum, all the way to the lower end of the small intestine and display them on a screen. The procedure is used to diagnose colon and bowel disease, including polyps, diverticulosis and cancer.

Confidence intervals

A way of expressing certainty about the findings from a study or group of studies, using statistical techniques. A confidence interval describes a range of possible effects (of a treatment or intervention) that are consistent with the results of a study or group of studies. A wide confidence interval indicates a lack of certainty or precision about the true size of the clinical effect and is seen in studies with too few patients. Where confidence intervals are narrow they indicate more precise estimates of effects and a larger sample of patients

studied. It is usual to interpret a '95%' confidence interval as the range of effects within which we are 95% confident that the true effect lies.

Confounding

In a study, confounding occurs when the effect of an intervention on an outcome is distorted as a result of an association between the population or intervention or outcome and another factor (the ‘confounding variable’) that can influence the outcome independently of the intervention under study.

Consensus methods

Techniques that aim to reach an agreement on a particular issue. Formal consensus methods include Delphi and nominal group techniques, and consensus development conferences. In the development of clinical guidelines, consensus methods may be used where there is a lack of strong research evidence on a particular topic. Expert consensus methods will aim to reach agreement between experts in a particular field.

Consistency

The extent to which the conclusions of a collection of studies used to support a guideline recommendation are in agreement with each other. See also Homogeneity.

Control group

A group of patients recruited into a study that receives no treatment, a treatment of known effect, or a placebo (dummy treatment) – in order to provide a comparison for a group receiving an experimental treatment, such as a new drug.

Cost benefit analysis

A type of economic evaluation where both costs and benefits of healthcare treatment are measured in the same monetary units. If benefits exceed costs, the evaluation would recommend providing the treatment.

Cost-consequences analysis (CCA)

A type of economic evaluation where various health outcomes are reported in addition to cost for each intervention, but there is no overall measure of health gain.

Cost-effectiveness analysis (CEA)

An economic study design in which consequences of different interventions are measured using a single outcome, usually in 'natural' units (for example, life-years gained, deaths avoided, heart attacks avoided, cases detected). Alternative interventions are then compared in terms of cost per unit of effectiveness.

Cost-effectiveness model

An explicit mathematical framework, which is used to represent clinical decision problems and incorporate evidence from a variety of sources in order to estimate the costs and health outcomes.

Cost-utility analysis (CUA)

A form of cost-effectiveness analysis in which the units of effectiveness are quality-adjusted life-years (QALYs).

Critical appraisal

The process of appraising a piece of research or a systematic review for the quality of its method and content, generally used in order to make judgements about the quality of the research or review, and the effectiveness of the intervention under study.

Crohn's disease

Chronic ileitis that typically involves the distal portion of the ileum, often spreads to the colon, and is characterised by diarrhoea, cramping, and loss of appetite and weight with local abscesses and scarring.

Cross-sectional study

The observation of a defined set of people at a single point in time or time period – a snapshot. (This type of study contrasts with a longitudinal study which follows a set of people over a period of time.)

Diagnostic study

A study to assess the effectiveness of a test or measurement in terms of its ability to accurately detect or exclude a specific disease.

Diminutive lesion

A very small abnormal change in structure of an organ or part due to injury or disease.

Dominance

A term used in health economics describing when an option for treatment is both less clinically effective and more costly than an alternative option. The less effective and more costly option is said to be 'dominated'.

Double blind/masked study

A study in which neither the subject (patient) nor the observer (investigator/clinician) is aware of which treatment or intervention the subject is receiving. The purpose of blinding is to protect against bias.

Drop-out

A participant who withdraws from a clinical trial before the end.

Drowsiness

A state of near-sleep, a strong desire for sleep, or sleeping for unusually long periods.

Dysplasia

Abnormal development or growth of tissues, organs, or cells. Dysplasia can be low grade or high grade. High-grade dysplasia represents a more advanced progression towards malignant transformation.

Economic evaluation

Comparative analysis of alternative health strategies (interventions or programmes) in terms of both their costs and consequences.

Effect (as in effect measure, treatment effect, estimate of effect, effect size)

The observed association between interventions and outcomes or a statistic to summarise the strength of the observed association.

Epidemiological study

The study of a disease within a population, defining its incidence and prevalence and examining the roles of external influences (for example, infection, diet) and interventions.

Equity

Fair distribution of resources or benefits.

Exclusion criteria (clinical study)

Criteria that define who is not eligible to participate in a clinical study.

Exclusion criteria (literature review)

Explicit standards used to decide which studies should be excluded from consideration as potential sources of evidence.

External validity

The degree to which the results of a study hold true in non-study situations, for example in routine clinical practice. May also be referred to as the generalisability of study results to non-study patients or populations.

Extrapolation

The application of research evidence based on studies of a specific population to another population with similar characteristics.

False negative

A negative result in a diagnostic test when the person being tested **does** possess the attribute for which the test is conducted.

False positive

A positive result in a diagnostic result when the person being tested **does not** possess the attribute for which the test is conducted.

Follow up

Observation over a period of time of an individual, group or initially defined population whose appropriate characteristics have been assessed in order to observe changes in health status or health related variables.

Generalisability

The degree to which the results of a study or systematic review can be extrapolated to other circumstances, particularly routine healthcare situations in the NHS in England and Wales.

Heterogeneity

A term used to illustrate the variability or differences between studies in the estimates of effects.

Homogeneity

This means that the results of studies included in a systematic review or meta-analysis are similar and there is no evidence of heterogeneity. Results are usually regarded as homogeneous when differences between studies could reasonably be expected to occur by chance.

Inflammatory bowel disease

A group of inflammatory conditions of the colon and small intestine. The major types of inflammatory bowel disease are Crohn's disease and ulcerative colitis.

Inclusion criteria (literature review)

Explicit criteria used to decide which studies should be considered as potential sources of evidence.

Incremental analysis

The analysis of additional costs and additional clinical outcomes with different interventions.

Incremental cost

The mean cost per patient associated with an intervention minus the mean cost per patient associated with a comparator intervention.

Incremental cost effectiveness ratio (ICER)

The difference in the mean costs in the population of interest divided by the differences in the mean outcomes in the population of interest.

Incremental net benefit (INB)

The value (usually in monetary terms) of an intervention net of its cost compared with a comparator intervention. The INB can be calculated for a given cost-effectiveness (willingness to pay) threshold. If the threshold is £20,000 per QALY gained then the INB is calculated as: (£20,000 x QALYs gained) – Incremental cost.

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In epidemiology and related sciences, this word usually means a rating scale, for example, a set of numbers derived from a series of observations of specified variables. Examples include the various health status indices, and scoring systems for severity or stage of cancer.

Inflammation

A local response to cellular injury that is marked by capillary dilatation, leukocytic infiltration, redness, heat, pain, swelling, and often loss of function and that serves as a mechanism initiating the elimination of noxious agents and of damaged tissue.

Intention-to-treat analysis (ITT analysis)

An analysis of the results of a clinical study in which the data are analysed for all study participants as if they had remained in the group to which they were randomised, regardless of whether or not they remained in the study until the end, crossed over to another treatment or received an alternative intervention.

Internal validity

The degree to which the results of a study are likely to approximate the ‘truth’ for the participants recruited in a study (that is, are the results free of bias?). It refers to the integrity of the design and is a prerequisite for applicability (external validity) of a study’s findings.

Intervention

Healthcare action intended to benefit the patient, for example, drug treatment, surgical procedure, psychological therapy.

Life-years gained

Average years of life gained per person as a result of the intervention.

Longitudinal study

A study of the same group of people at more than one point in time. (This type of study contrasts with a cross sectional study which observes a defined set of people at a single point in time).

Malignant

Literally means growing worse and resisting treatment.

Morbidity rates

Morbidity rates are the number of cases of an illness, injury or condition within a given time, usually one year. It is also the ratio of sick persons to well persons in a defined population.

Mortality rates

The proportion of deaths in a defined population.

Mucosa

The mucous membrane, or the thin layer which lines body cavities and passages.

Multivariate model

A statistical model for analysis of the relationship between two or more predictor (independent) variables and the outcome (dependent) variable.

Narrative summary

Summary of findings given as a written description.

Narrow band imaging

Characterised by light with wavelengths of narrow bands that improves the visibility of capillaries, veins and other subtle tissue structures by optimising the absorbance and scattering characteristics of light. It enhances vasculature within and beneath the mucosa, or lining, of the gastrointestinal (GI) tract.

Negative predictive value

The proportion of people with negative test results who do not have the disease.

Number needed to treat to benefit (NNTB)

NNTB is an epidemiological measure used in assessing the effectiveness of a health-care intervention, typically a treatment with medication. The NNTB is the number of patients who need to be treated in order to prevent one additional bad outcome (that is, the number of patients that need to be treated for one to benefit compared with a control in a clinical trial). It is defined as the inverse of the absolute risk reduction. The ideal NNTB is 1, where everyone improves with treatment and no-one improves with control. The higher the NNTB, the less effective is the treatment

Number needed to treat to harm (NNTH)

NNTH is an epidemiological measure that indicates how many patients need to be exposed to a risk factor to cause harm in one patient that would not otherwise have been harmed. It is defined as the inverse of the attributable risk. Intuitively, the lower the number needed to harm, the worse the risk factor.

Observational study

Retrospective or prospective study in which the investigator observes the natural course of events with or without control groups; for example, cohort studies and case–control studies.

Odds ratio (OR)

A measure of treatment effectiveness. The odds of an event happening in the treatment group, expressed as a proportion of the odds of it happening in the control group. The ‘odds’ is the ratio of events to non-events.

Outcome

Measure of the possible results that may stem from exposure to a preventive or therapeutic intervention. Outcome measures may be intermediate endpoints or they can be final endpoints.

P value

If a study is done to compare two treatments then the P value is the probability of obtaining the results of that study, or something more extreme, if there really was no difference between treatments. (The assumption that there really is no difference between treatments is called the 'null hypothesis'.) Suppose the P-value was P=0.03. What this means is that if there really was no difference between treatments then there would only be a 3% chance of getting the kind of results obtained. Since this chance seems quite low we should question the validity of the assumption that there really is no difference between treatments. We would conclude that there probably is a difference between treatments. By convention, where the value of P is below 0.05 (that is, less than 5%) the result is seen as statistically significant. Where the value of P is 0.001 or less, the result is seen as highly significant. P values just tell us whether an effect can be regarded as statistically significant or not. In no way do they relate to how big the effect might be, for which we need the confidence interval.

Polyps

A projecting mass of swollen and hypertrophied or tumorous membrane (as in the nasal cavity or the intestine) -- called also polypus.

Prognostic factor

Patient or disease characteristics, for example. age or co-morbidity, which influence the course of the disease under study. In a randomised trial to compare two treatments, chance imbalances in variables (prognostic factors) that influence patient outcome are possible, especially if the size of the study is fairly small. In terms of analysis these prognostic factors become confounding factors. See also Prognostic marker.

Prospective study

A study in which people are entered into the research and then followed up over a period of time with future events recorded as they happen. This contrasts with studies that are retrospective.

Qualitative research

Research concerned with subjective outcomes relating to social, emotional and experiential phenomena in health and social care.

Quality-adjusted life year (QALY)

A statistical measure, representing 1 year of life, with full quality of life.

Quantitative research

Research that generates numerical data or data that can be converted into numbers, for example clinical trials or the national census which counts people and households.

Randomisation

Allocation of participants in a research study to two or more alternative groups using a chance procedure, such as computer generated random numbers. This approach is used in an attempt to ensure there is an even distribution of participants with different characteristics between groups and thus reduce sources of bias.

Randomised controlled trial

A form of clinical trial to assess the effectiveness of medicines or procedures. Considered reliable because it tends not to be biased.

Reference case

When estimating clinical and cost effectiveness in a technology appraisal, the reference case specifies the methods that are considered by NICE to be the most appropriate for the Appraisal Committee's purpose and are also consistent with an NHS objective of maximising health gain from limited resources.

Relative risk

Also known as risk ratio; the ratio of risk in the intervention group to the risk in the control group. The risk (proportion, probability or rate) is the ratio of people with an event in a group to the total in the group. A relative risk (RR) of 1 indicates no difference between comparison groups. For undesirable outcomes, an RR that is less than 1 indicates that the intervention was effective in reducing the risk of that outcome.

Retrospective study

A retrospective study deals with the present/ past and does not involve studying future events. This contrasts with studies that are prospective.

Sedation

The inducing of a relaxed easy state especially by the use of sedatives.

Selection bias (also allocation bias)

A systematic bias in selecting participants for study groups, so that the groups have differences in prognosis and/or therapeutic sensitivities at baseline. Randomisation (with concealed allocation) of patients protects against this bias.

Semi-structured interview

Structured interviews involve asking people pre-set questions. A semi-structured interview allows more flexibility than a structured interview. The interviewer asks a number of open-ended questions, following up areas of interest in response to the information given by the respondent.

Sensitivity

In diagnostic testing, it refers to the chance of having a positive test result given that you have the disease. 100% sensitivity means that all those with the disease will test positive, but this is not the same the other way around. A patient could have a positive test result but not have the disease - this is called a 'false positive'. The sensitivity of a test is also related to its 'negative predictive value' (true negatives) - a test with a sensitivity of 100% means that all those who get a negative test result do not have the disease. To fully judge the accuracy of a test, its Specificity must also be considered.

Sensitivity analysis

A means of representing uncertainty in the results of economic evaluations. Uncertainty may arise from missing data, imprecise estimates or methodological controversy. Sensitivity analysis also allows for exploring the generalisability of results to other settings. The analysis is repeated using different assumptions to examine the effect on the results. One-way simple sensitivity analysis (univariate analysis): each parameter is varied individually

in order to isolate the consequences of each parameter on the results of the study. Multi-way simple sensitivity analysis (scenario analysis): two or more parameters are varied at the same time and the overall effect on the results is evaluated. Threshold sensitivity analysis: the critical value of parameters above or below which the conclusions of the study will change are identified. Probabilistic sensitivity analysis: probability distributions are assigned to the uncertain parameters and are incorporated into evaluation models based on decision analytical techniques (For example, Monte Carlo simulation).

Sigmoidoscopy

Is the minimally invasive medical examination of the large intestine from the rectum through the last part of the colon. There are two types of sigmoidoscopy, flexible sigmoidoscopy, which uses a flexible endoscope, and rigid sigmoidoscopy, which uses a rigid device. Flexible sigmoidoscopy is generally the preferred procedure.

Specificity

In diagnostic testing, it refers to the chance of having a negative test result given that you do not have the disease. 100% specificity means that all those without the disease will test negative, but this is not the same the other way around. A patient could have a negative test result yet still have the disease - this is called a 'false negative'. The specificity of a test is also related to its 'positive predictive value' (true positives) - a test with a specificity of 100% means that all those who get a positive test result definitely have the disease. To fully judge the accuracy of a test, its Sensitivity must also be considered.

Standard deviation

A measure of the spread, scatter or variability of a set of measurements. Usually used with the mean (average) to describe numerical data.

Statistical power

The ability of a study to demonstrate an association or causal relationship between two variables, given that an association exists. For example, 80% power in a clinical trial means that the study has a 80% chance of ending up with a P value of less than 5% in a statistical test (that is, a statistically significant treatment effect) if there really was an important difference (for example 10% versus 5% mortality) between treatments. If the statistical power of a study is low, the study results will be questionable (the study might have been too small to detect any differences). By convention, 80% is an acceptable level of power. See also P value.

Structured interview

A research technique where the interviewer controls the interview by adhering strictly to a questionnaire or interview schedule with pre-set questions.

Symptom

A departure from normal function or feeling which is noticed by a patient, indicating the presence of disease or abnormality.

Synthesis of evidence

A generic term to describe methods used for summarising (comparing and contrasting) evidence into a clinically meaningful conclusion in order to answer a defined clinical question. This can include systematic review (with or without meta-analysis), qualitative and narrative summaries.

Systematic error

Refers to the various errors or biases inherent in a study. See also Bias.

7.3 Abbreviations

Abbreviation	Meaning
ARR	Absolute risk reduction
CEAC	Cost effectiveness acceptability curve
CEAF	Cost effectiveness acceptability frontier
CI	Confidence interval
CTC	Computed tomographic colonography
ER	Endoscopic resection
FSIG	Flexible sigmoidoscopy
GDG	Guideline development group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HR	Hazard ratio
IBD	Inflammatory bowel disease
ICER	Incremental cost-effectiveness ratio
MD	Mean difference
NBI	Narrow band imaging
NNTB	Number needed to treat to benefit
NNTH	Number needed to treat to harm
NPV	Negative predictive value
OR	Odds ratio
PPV	Positive predictive value
QALY	Quality-adjusted life year
RCT	Randomised clinical trial
RR	Relative risk
RS	Reference standard
SC	Standard care
SD	Standard deviation
SE	Standard error
SF-36	Short form-36
WMD	Weighted mean difference

8 Contributors

8.1 The Guideline Development Group

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8.2 The short clinical guidelines technical team

A short clinical guidelines technical team was responsible for this guideline throughout its development. It prepared information for the Guideline Development Group, drafted the guideline and responded to consultation comments. The following NICE employees made up the technical team for this guideline.

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8.3 The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring adherence to NICE guideline development processes. In particular, the panel ensures that stakeholder comments have been adequately considered and responded to. The panel includes members from the following perspectives: primary care, secondary care, lay, public health and industry.

To be added

[Name; style = Unnumbered bold heading]

[job title, including name of hospital/university or other organisation, and city/county if relevant; style = NICE normal]

[Name; style = Unnumbered bold heading]

[job title, including name of hospital/university or other organisation, and city/county if relevant; style = NICE normal]

8.4 Declarations of interest

A full list of all declarations of interest made by this Guideline Development Group is available on the NICE website (www.nice.org.uk).

8.5 Authorship and citation

Authorship of this document is attributed to the NICE Short Clinical Guidelines Technical Team and members of the Guideline Development Group under group authorship.

The guideline should be cited as:

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