Colonoscopic surveillance for prevention of colorectal cancer in patients with ulcerative colitis, Crohn's disease or adenomas

Full guideline

Draft, September 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.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

This clinical guideline will incorporate the following NICE guidance:

- Computed tomographic colonography (virtual colonoscopy). NICE interventional procedure guidance 129 (2005).

Introduction

Adults with inflammatory bowel disease (IBD, which covers ulcerative colitis and Crohn's disease) or with adenomas have a higher risk of developing colorectal cancer than the general population. Colorectal cancer is the third most common cancer in the UK, with approximately 32,300 new cases diagnosed and 14,000 deaths in England and Wales each year. Around half of the people diagnosed with colorectal cancer survive for at least 5 years after diagnosis.

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

The prevalence of Crohn's disease is approximately 50–100 per 100,000 and the annual incidence is 5–10 per 100,000. The risk of developing colorectal cancer for people with Crohn's disease is considered to be similar to that for people with ulcerative colitis with the same extent of colonic involvement.

Colonoscopic surveillance in people with IBD or adenomas can detect any problems early and potentially prevent progression to colorectal cancer. For people who are not in these high-risk groups, the NHS Bowel Cancer Screening Programme (www.cancerscreening.nhs.uk/bowel/publications/nhsbcsp-guidance-note-01.html) offers screening using faecal occult blood testing every 2 years to all men and women aged 60–74 years. People undergoing colonoscopic surveillance are not generally offered screening as part of the Bowel Cancer Screening programme.

The British Society of Gastroenterology (BSG) issued guidelines for colonoscopic surveillance for people who have had adenomas removed and for people with IBD (Atkin and Saunders 2002; Eaden and Mayberry 2002; updated by Cairns et al. 2010). NICE has developed this short clinical guideline on the use of colonoscopic surveillance because of variations in clinical practice. The evidence-based recommendations and algorithms developed in the NICE guideline are broadly consistent with those in the 2010 BSG guidelines. Both guidelines used a similar evidence base, with the exception of health economics evidence, which was not considered for the BSG guidelines. Some members of the NICE guideline development group were also members of the group that developed the BSG guidelines. However, there are some differences between the two guidelines because the processes and methods used to develop each guideline were different.

Throughout this guideline, the term ‘adenomas’ is used. However, other terms have been used in the clinical studies included in the evidence review, for example ‘polyps’ or ‘adenomatous polyps’.

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 adenomas.

Treatment and care should take into account patients' needs and preferences. People with IBD or adenomas 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 inflammatory bowel disease

1.1.1 Offer colonoscopic surveillance to people with inflammatory bowel disease (IBD) whose symptoms started 10 years ago and who have:

- extensive or left-sided ulcerative colitis (but not proctitis alone) **or**
- extensive or left-sided Crohn's colitis.

1.1.2 Offer a baseline colonoscopy with chromoscopy to people with IBD who are being considered for colonoscopic surveillance 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 (but not proctitis alone) or left-sided Crohn's colitis. **Intermediate risk:** • extensive ulcerative or Crohn's colitis with mild active inflammation that has been confirmed histologically **or** • post-inflammatory adenomas **or** • family history of colorectal cancer in a first-degree relative aged 50 years or over. **High risk:** • extensive ulcerative or Crohn's colitis with moderate or severe active inflammation that has been confirmed histologically **or** • primary sclerosing cholangitis (including after liver transplant) **or** • colonic stricture in the past 5 years **or** • any grade of dysplasia in the past 5 years **or** • family history of colorectal cancer in a first degree relative aged under 50 years.

1.1.3 Offer colonoscopic surveillance to people with IBD as defined in 1.1.1 based on their risk of developing colorectal cancer (see table 1), determined at the last complete colonoscopy:

- Low risk: offer at 5 years.
- Intermediate risk: offer at 3 years.
- High risk: offer within 1 year.

1.1.4 For people with IBD who have been offered colonoscopic surveillance, use colonoscopy with chromoscopy as the method of surveillance.

1.1.5 Offer a repeat colonoscopy with chromoscopy if any colonoscopy is incomplete. Consider whether a more experienced colonoscopist is needed.

People with adenomas

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

1.1.7 Use the findings at adenoma removal to determine people's risk of developing colorectal cancer (see table 2).

Table 2 Risk of developing colorectal cancer in people with adenomas

Low risk: • one or two adenomas smaller than 10 mm. **Intermediate risk:** • three or four adenomas smaller than 10 mm **or** • one or two adenomas if one is 10 mm or larger. **High risk:** • five or more adenomas smaller than 10 mm **or** • three or more adenomas if one is 10 mm or larger.

1.1.8 Offer the appropriate colonoscopic surveillance strategy to people with adenomas based on their risk of developing colorectal cancer (see table 2):

- Low risk: do not offer colonoscopic surveillance.
- Intermediate risk: offer colonoscopic surveillance at 3 years:
  - if low- or intermediate-risk adenomas are found, offer surveillance at 3 years
  - if high-risk adenomas are found, offer surveillance within 1 year
  - if there is one negative colonoscopy (that is, no adenomas are found) offer surveillance at 3 years
  - if there are two consecutive negative colonoscopies, stop surveillance (see recommendation 1.1.14)
- High risk: offer colonoscopic surveillance within 1 year:
  - if the colonoscopy is negative, or low- or intermediate-risk adenomas are found, offer surveillance at 3 years (with follow-up surveillance as for the intermediate-risk group)
  - if high-risk adenomas are found, offer surveillance within 1 year.

1.1.9 Offer a repeat colonoscopy if any colonoscopy is incomplete. Consider whether a more experienced colonoscopist is needed.

1.1.10 If colonoscopy is not clinically appropriate (for example, because of comorbidity or because colonoscopy cannot be tolerated), consider computed tomographic colonography[1] (CTC) or double contrast barium enema as a single examination for people who have had adenomas removed and are at high or intermediate risk of developing colorectal cancer (see table 2).

1.1.11 When colonoscopy remains clinically inappropriate, consider CTC or barium enema for ongoing surveillance but discuss the risks and benefits with the person and their family or carers.

Providing information and support

1.1.12 Discuss the potential benefits, limitations and risks with people who are considering colonoscopic surveillance including:

- early detection and prevention of colorectal cancer **and**
- quality of life and psychological outcomes.

1.1.13 Inform people who have been offered colonoscopy, CTC, or barium enema about the procedure, including:

- bowel preparation
- impact on everyday activities
- sedation
- potential discomfort
- risk of perforation and bleeding.

1.1.14 At each surveillance, discuss the potential benefits, limitations and risks of ongoing surveillance. Base a decision to stop surveillance on potential benefits for the person, their preferences and any

[1] Computed tomographic colonography (virtual colonoscopy). NICE interventional procedure guidance 129 (2005).

comorbidities. Make the decision jointly with the person and if appropriate their family or carers.

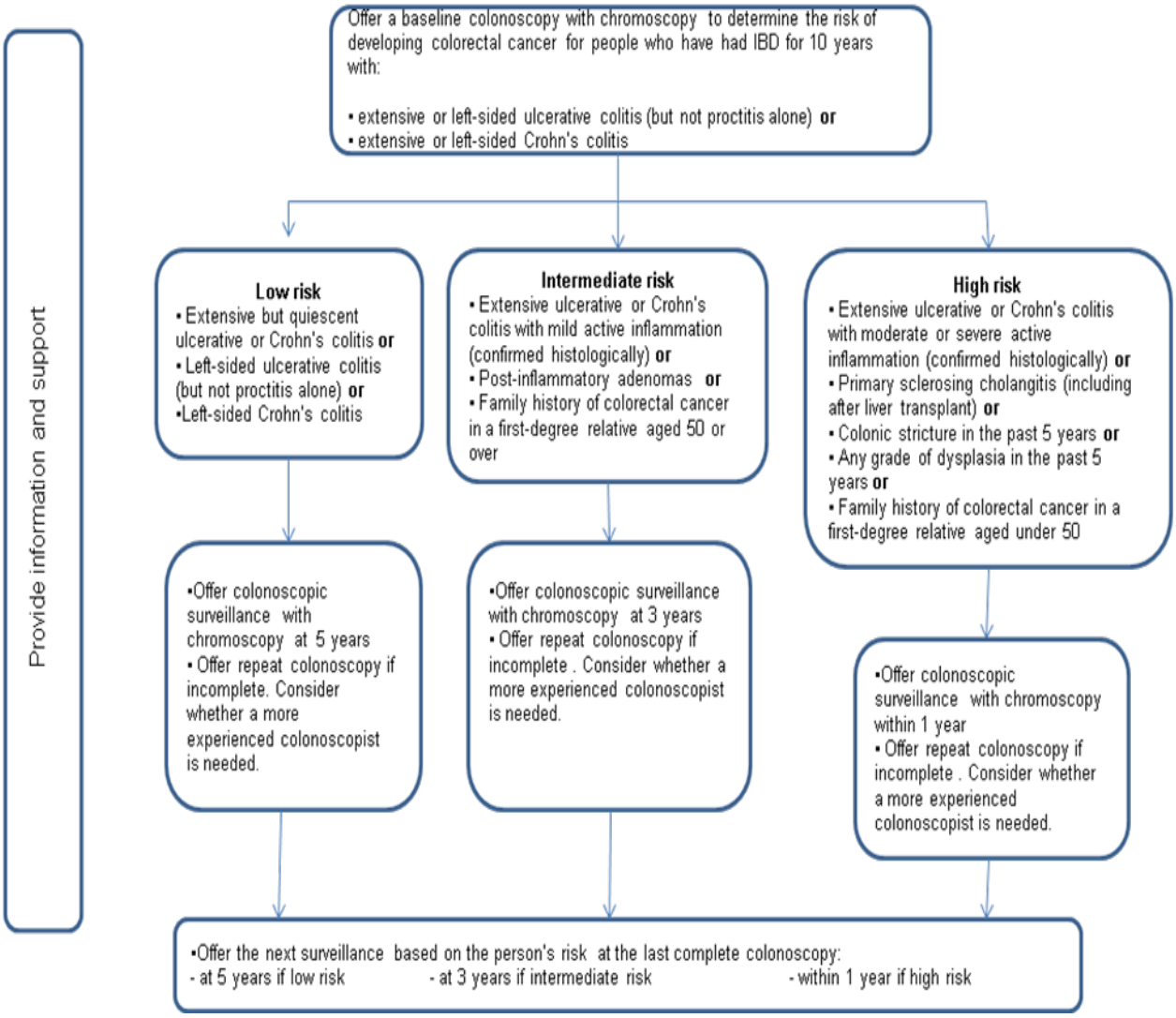
1.1.15 If there are any findings at surveillance that need treatment or referral, discuss the options with the person and if appropriate their family or carers.

1.1.16 Throughout the surveillance programme, give the person and their family 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 should include illustrations.

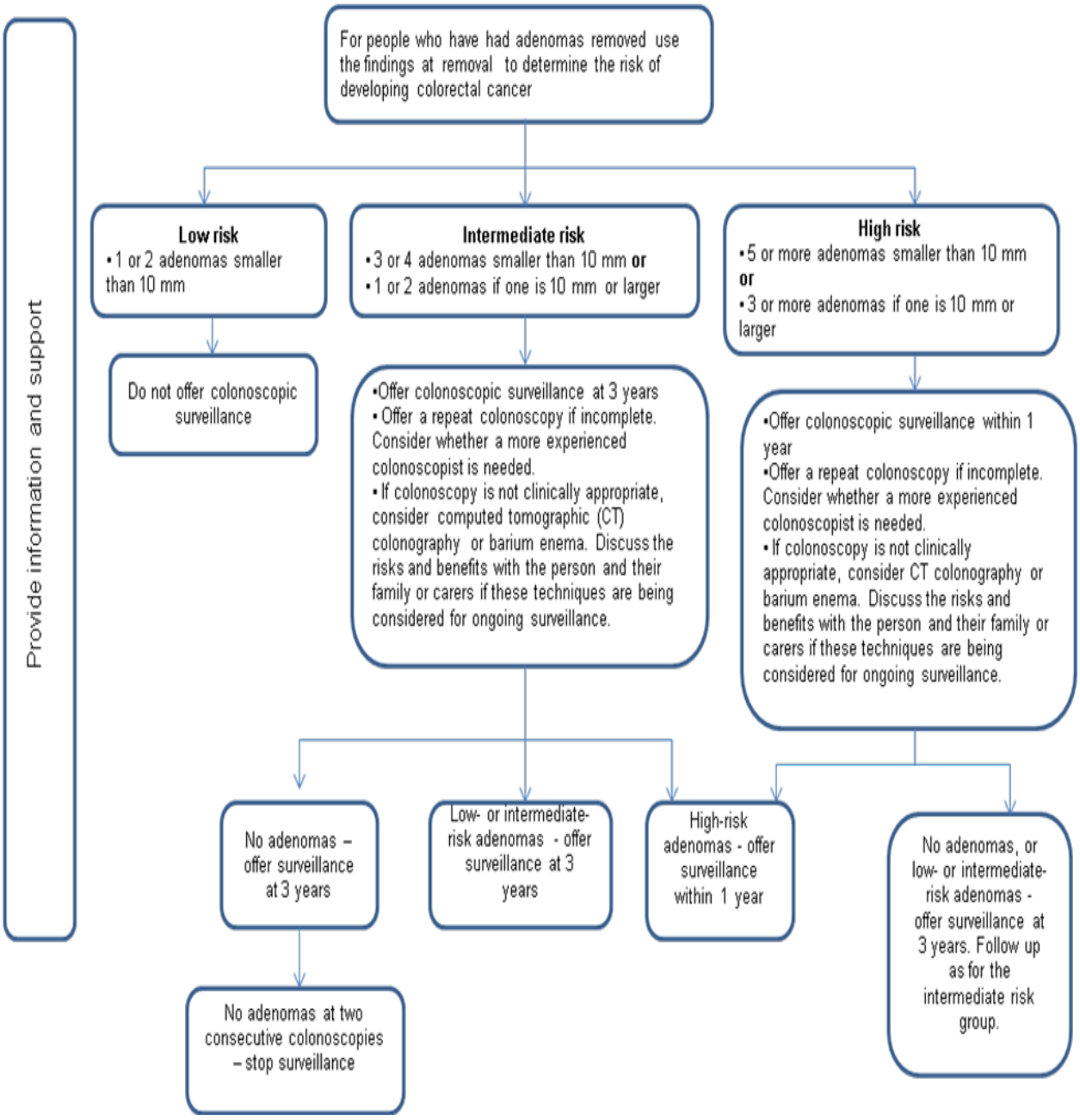
1.2 Care pathways

The care pathways are reproduced from the quick reference guide for the guideline, which is available at www.nice.org.uk/guidance/CGXXXQuickRefGuide (these details will apply when the final version of the guideline is published).

People with IBD



People with adenomas



1.3 Overview

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

Colonoscopic surveillance in people at high risk of developing colorectal cancer can detect precancerous changes early on and potentially prevent progression to colorectal cancer. It can also identify invasive cancer early. However, in clinical practice there is variation in when colonoscopic surveillance starts and how frequently it is offered to people at high risk. This NICE short clinical guideline aims to improve the care of people with IBD or adenomas at high risk of developing colorectal cancer by making evidence-based recommendations on the use of colonoscopic surveillance.

1.3.2 Who this guideline is for

This guideline is for healthcare professionals who provide care for people 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 adenomas in the colon or rectum.

2 How this guideline was developed

2.1 Introduction

'Colonoscopic surveillance for prevention of colorectal cancer in patients with ulcerative colitis, Crohn's disease and adenomas (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'

The eligibility criteria for including studies were developed with the help of the Guideline Development Group (GDG) using a questionnaire (see appendix 3). For this guideline, colonoscopic surveillance was considered as an intervention. The results from the included studies are presented in 'Grading of recommendations, assessment, development and evaluation' (GRADE) profiles and evidence statements. GRADE profiles were modified to allow for

evidence from both randomised controlled trials (RCTs) and observational studies to be presented together for the same outcomes.

For each review question, the evidence sections are split. The evidence for people with IBD is presented first, followed by the evidence for people with adenomas.

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 adenomas clinically effective compared with no surveillance?

Clinical effectiveness of colonoscopic surveillance compared with no surveillance in 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 GDG. Overall, limited evidence was available; only four studies met the eligibility criteria (for the review protocol and inclusion and exclusion criteria, see appendices 2 and 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 aim of the Cochrane review was to assess the effectiveness of cancer surveillance programmes in reducing the mortality rate from colorectal cancer in patients with ulcerative colitis and colonic Crohn's disease. 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 colonoscopic surveillance with no

surveillance in people who had one, two or more surveillance colonoscopies and is considered in this guideline in section 2.5. Another study (Velayos et al. 2006) also examined the effect of the number of surveillance colonoscopies on progression to colorectal cancer and is considered in this guideline in section 2.5. The review assessed the three studies using a validated scale developed by Downs and Black (1998)[2] 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 reported 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.

The other primary study identified (Lutgens et al. 2009) showed a significant difference in the 5-year cancer-related mortality rate in people undergoing surveillance compared with those not having surveillance.

The characteristics of the three primary studies are summarised in table 1 and the evidence is reviewed in GRADE profile 1. The GRADE assessment of quality, which is by outcome and not by study, is different to the quality assessments in the Cochrane review because different methods have been used.

The GDG agreed that a 10% improvement in the long-term clinical outcomes would be significant and this percentage was used for the imprecision calculation. Detailed evidence tables for the included studies are given in appendix 6.

[2] 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.

1 **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			

2

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 considerations	Quality
Outcome 1: detected carcinoma at early stage (Duke's stage A or B; AJCC stage 0 or 1)										
1 (C)	Case–control study	**Dukes' 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 carcinoma at advanced stage (Duke's stage C or D; AJCC stage 3B–C and 4)										
1 (C)	Case–control study	**Dukes' 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%)							

GRADE profile 1: Colonoscopic surveillance compared with no surveillance for IBD contd										
Outcome 3: 5-year overall survival										
1 (C)	Case–control study	76.2 ± 12.1%[b]	36.3 ± 12.7%	[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 no 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 study	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]						

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

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; CRC: colorectal cancer; IBD: inflammatory bowel disease; (L): Lashner et al. (1990); (Lu): Lutgens et al. (2009); N: not serious; NNTB/H: number needed to treat to benefit/harm; **NS**: not significant; OR: odds ratio; RR: relative risk; S: serious; VS: very serious; U: upgrade

All evidence found was for people with extensive colitis (ulcerative or Crohn's colitis) at least 8–10 years after onset of symptoms.

[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 study.
[e] Lutgens et al. (2009): when the 11 people with simultaneous IBD and CRC diagnosis 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).

2.2.3 Evidence statements (see GRADE profile 1)

2.2.3.1 *Low quality evidence showed that colonoscopic surveillance statistically significantly increased the probability of detecting cancer at an earlier stage. There was a corresponding statistically 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 no surveillance group compared with the surveillance group, but the difference was not significant.*

2.2.3.5 *Very low quality evidence showed that dysplasia was a more frequent indication for colectomy in the surveillance group compared with the no surveillance group. This difference was statistically significant.*

2.2.3.6 *Very low quality evidence found a statistically significantly increased cancer detection rate in the surveillance group compared with the no surveillance group after adjustment for covariates by the Cox proportional hazards model.*

2.2.3.7 *Low quality evidence showed a tendency for a higher overall mortality rate for the no surveillance group compared with the surveillance group.*

2.2.3.8 *Low quality evidence found the 5-year colorectal cancer related mortality rate to be statistically significantly higher for the no 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 such as decision tree versus Markov models, and when applicable, informed 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.

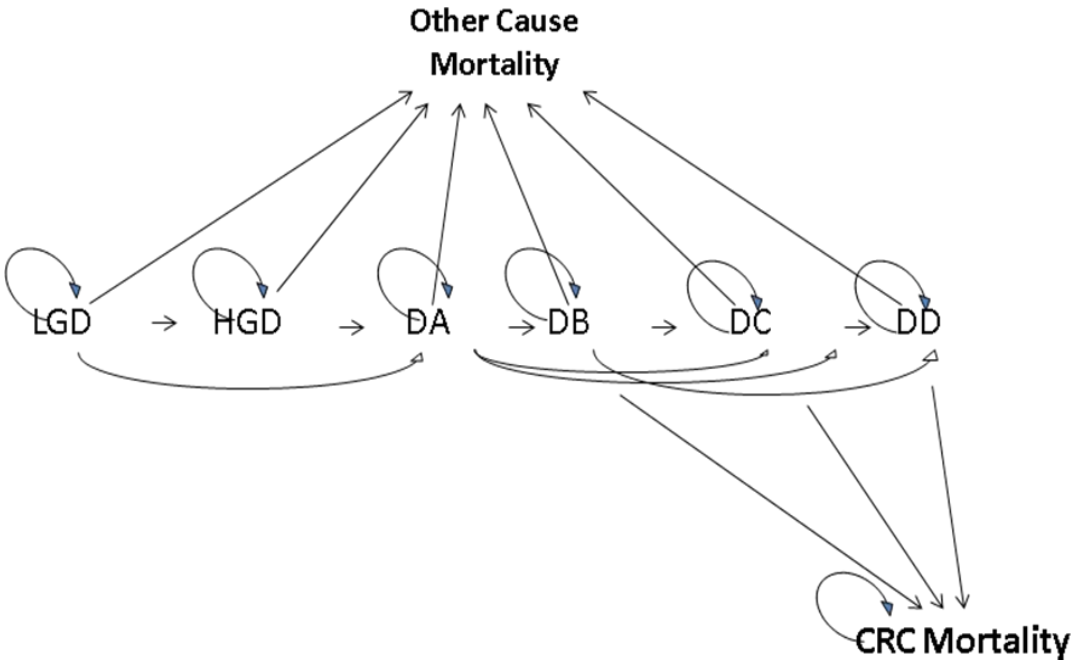
A major component of the model is the natural history of dysplasia, because dysplasia is a precancerous marker for colorectal cancer. During the evidence review, the presence of any grade of dysplasia in the past 5 years was found to be one of the risk factors for the high-risk group (please see the evidence to recommendations section 2.2.5). Therefore, the model could only determine the cost effectiveness of surveillance for the high-risk group because dysplasia was only included as a risk factor in this group (please see the care pathway, people with IBD). Furthermore, it was not possible to construct an additional cost-effectiveness model or carry out an economic evaluation for the low- and intermediate-risk groups because of the lack of natural history data.

The model included men and women aged 30–85 who had flat dysplastic lesions (that is, non-resectable low- or high-grade dysplasia) who had 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 split the single state of dysplasia into two mutually exclusive states of low-grade and high-grade dysplasia. Similarly, the single colorectal cancer state was broken down into four mutually exclusive states of Dukes' A, Dukes'

B, Dukes' C and Dukes' D colorectal cancer. Any other cause of mortality was considered in all states in the model (see figure 1).

Figure 1: Colonoscopic surveillance model for people with IBD in the high-risk group



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 (every fourth cycle in the model) and it was assumed that colonoscopy was carried out at the beginning of the scheduled cycle. In the model, the development of colorectal cancer could be sequential, that is, progress 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. People with high-grade dysplasia could also progress directly to colorectal cancer and were assumed not to regress to low-grade dysplasia. Progression to colorectal cancer could occur either asymptomatically or symptomatically between the scheduled surveillance colonoscopies. Over time, if people in the three risk groups 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 from a published cost-effectiveness study by Tappenden et al. (2004). The transition probabilities from both studies were calculated using a Bayesian dirichlet method. Details are presented in appendix 7. 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 (quality of life benefits) 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 method; 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 a person in 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 people with 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 uplifted to incorporate the relevant NICE guidance published since 2004 (personal communication with Paul Tappenden and Hazel Pilgrim, 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 sensitivity 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

	QALYs	Cost (£)	Incremental QALYs	Incremental cost (£)	ICER (£)
No surveillance	16.42	2320.44			
Surveillance – high-risk group only	17.19	15,785.13	0.77	13,464.69	17,557.32
QALY: quality-adjusted life year; ICER: incremental cost-effectiveness ratio					

The analysis suggested that surveillance for 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

	QALYs	Costs (£)	Incremental QALYs	Incremental costs (£)	ICER (£)	Probabili of being cost effective at £20,000 per QALY gained (%
No surveillance	13.04	7368.92	–	–	–	
Surveillance – high-risk group only	14.64	16,316.82	1.61	8947.90	5571.44	9
QALY: quality-adjusted life year; ICER: incremental cost-effectiveness ratio						

The incremental cost-effectiveness ratio (ICER) from the probabilistic sensitivity analysis was lower than the ICER from the deterministic sensitivity analysis. This suggests that there may be a high degree of uncertainty associated with some model parameters, which resulted in a large change in the ICER. However, in spite of the uncertainty the probabilistic sensitivity analysis suggests that there is a 99% probability that colonoscopic surveillance for the high-risk group (among the three risk groups) with IBD is cost effective at the usual threshold of £20,000 per QALY gained.

2.2.5 Evidence to recommendations

The GDG considered that although the quality of the evidence was very low to low, there was still 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 because it would be unethical to randomise people with IBD to have no colonoscopic surveillance. The GDG also considered that the evidence obtained was sufficient to make recommendations in favour of colonoscopic surveillance, and 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 for 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. This would improve 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.

The health economic modelling indicated that colonoscopic surveillance is a cost-effective use of resources for people with any grade of dysplasia in the past 5 years. Because people with any grade of dysplasia share a similar risk of developing colorectal cancer as people in the ‘high-risk’ group, specifically those who have extensive ulcerative or Crohn’s colitis with moderate or severe active inflammation that has been confirmed histologically, or primary sclerosing cholangitis (including after liver transplant), or colonic stricture in the past 5 years, or a family history of colorectal cancer in a first-degree relative aged under 50 years, the cost-effectiveness results could be extrapolated to the high-risk group. The GDG acknowledged that, given the quality of the data and the number of simplifying assumptions in the model, the results were exploratory. The assumptions covering compliance and complications would increase uncertainty in the ICERs and could potentially increase them. The GDG also felt that because all the studies included for this review question looked at people who had IBD for at least 10 years, it would

be appropriate only to offer surveillance to people 10 years after symptom onset.

2.2.6 Recommendations

Recommendation 1.1.1

Offer colonoscopic surveillance to people with IBD whose symptoms started 10 years ago and who have:

- extensive or left-sided ulcerative colitis (but not proctitis alone) **or**
- extensive or left-sided Crohn's colitis.

Clinical effectiveness of colonoscopic surveillance compared with no surveillance in people with adenomas

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 the review protocol and inclusion and exclusion criteria, see appendices 2 and 4) and examined the effectiveness of colonoscopic surveillance compared with no surveillance. The two studies were initially considered to be relevant, but were later considered by the GDG not to provide relevant evidence of the benefits of colonoscopic surveillance. In Thiis-Evensen (1999a) people had flexible sigmoidoscopy, and on discovering polyps, they were offered colonoscopic polypectomy. In Jorgensen (1993) an indirect comparison was made. Mortality rates were compared in people offered colonoscopic surveillance and in people who had died from colorectal cancer 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 was 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 related analysis (Tappenden et al. 2004).

There was no direct evidence demonstrating the clinical effectiveness of colonoscopic surveillance after adenoma removal in reducing colorectal cancer mortality. However, one observational study reported a 70–90% lower than expected incidence of colorectal cancer in people undergoing colonoscopic surveillance compared with the reference populations (Winawer et al. 1993a). A full systematic review of the literature was not possible because of time constraints. Existing economic models, including screening and surveillance, were examined. 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 from Tappenden et al. (2004). Tappenden et al. obtained estimates from two sources: the National Polyp Study (Winawer et al. 1993a) and calibrating their model against published incidence and mortality data. Because these data were based on the model constructed by Tappenden et al (2004) and not directly on clinical evidence, they were highly dependent on the structure of the model. This means that transferring these estimates to another model may have resulted in inconsistencies and uncertainty.

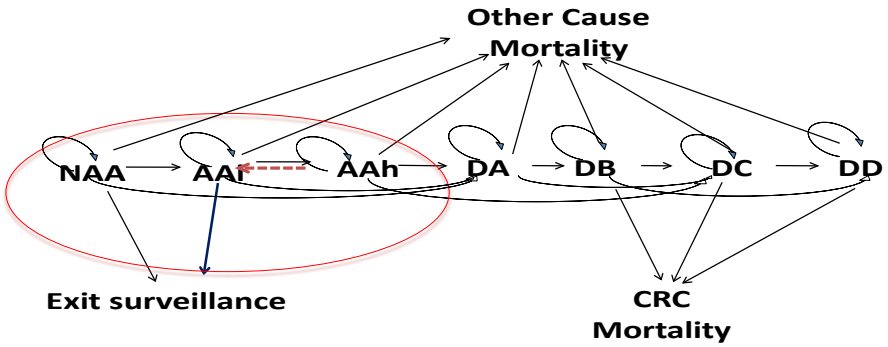
A Markov model was developed based on Tappenden et al. (2004) and is presented in figure 2. It included 50-year old men and women who had adenomas removed at baseline colonoscopy. The analysis was run over a 50-year time horizon. In the model, three strategies were examined: no surveillance, surveillance in all risk groups (low-, intermediate- and high-risk groups), and surveillance in intermediate- and high-risk groups only. 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.

In the model, colonoscopic surveillance after adenoma removal is consistent with the current BSG guidelines (Cairns et al. 2010). The person's risk state is determined after the baseline colonoscopy and is based on the number and size of adenomas removed. People are offered colonoscopic surveillance based on their risk state, as follows:

- Low risk: no surveillance is recommended. However surveillance at 5 years, then no surveillance if subsequent colonoscopy results are negative can be considered and will be explored in the analysis.
- Intermediate risk: surveillance is offered every 3 years until there are two consecutive negative colonoscopies, then surveillance is stopped.
- High risk: a colonoscopy is offered at or within 1 year to detect missed lesions:
  - if high-risk adenomas are detected, the person remains high risk.
  - if results are negative, or low- or intermediate-risk adenomas are detected, the surveillance programme for people at intermediate risk is followed.

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 were 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. Estimated transition probabilities were assumed to be constant with the exception of age-related adenoma incidence (Tappenden et al. 2004) and age-specific mortality rates, which were taken from published government sources. The effectiveness of colonoscopic surveillance was modelled as an intervention under near-perfect conditions to determine whether colonoscopic surveillance using colonoscopy for the early detection of adenomas and colorectal cancer is clinically and cost effective compared with no surveillance.

The three diagnostic states in the model, low, intermediate and high risk, differ only in terms of the surveillance offered. Movement between diagnostic states is only possible through surveillance using tunnel states or symptomatic presentation of colorectal cancer. According to surveillance criteria people can drop out of surveillance and can be assumed to return to UK population norms. Any newly developed adenomas will be removed during surveillance. If any lesions are confirmed 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 adenomas are more likely to develop them in the future than people who have never had adenomas (Winawer et al. 1993a). It was assumed in the model that all colorectal cancers arise from pre-existing adenomas, and the GDG considered this assumption to be appropriate. For the purpose of the guideline, when comparing a surveillance programme with no surveillance, the sensitivity and specificity of colonoscopy were assumed to be 100% for adenoma detection. This was agreed with the GDG. Utility values 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 the stage of cancer and treatment (Ness et al. 1999, 2000). The GDG agreed with the assumption that the utility values for people who are cancer free or have undiagnosed (asymptomatic) cancer would be the same as those for the general population. Surveillance costs were obtained from NHS reference costs.

Costs for the stage-specific lifetime treatment of colorectal cancer were based on Tappenden et al. (2004) (personal communication with Paul Tappenden and Hazel Pilgrim, 8 April 2010). Full details of the utility values and costs are presented in appendix 8.

The overall deterministic results are presented in table 4 and more detailed results are given in appendix 8. These results indicate that the most cost-effective surveillance strategy is to include surveillance for low-, intermediate- and high-risk groups with an ICER below the usual threshold (£20,000 per QALY gained). Surveillance of only the intermediate- and high-risk groups was associated with an ICER below £20,000 per QALY gained and the incremental costs were lower than the strategy that includes the low-risk group, but the potential gain in QALYs was also lower. However, these results are highly sensitive to the natural history data, which were extrapolated from another model and are highly uncertain. Therefore, the results should be interpreted with caution.

Table 4: Deterministic analysis over a 50-year period

	QALYs	Costs (£)	Incremental QALYs	Incremental costs (£)	ICER (£)
No surveillance	16.11	641.06	–	–	–
Colonoscopic surveillance in intermediate- and high-risk groups	16.16	841.54	0.05	200.49	4235.75
Colonoscopic surveillance in all risk groups	16.26	1177.03	0.15	535.97	3669.70

QALY: quality-adjusted life year; ICER: incremental cost-effectiveness ratio; all risk groups: low-, intermediate, and high-risk groups.

The overall probabilistic sensitivity analysis results are presented in table 5 and more detailed results are given in appendix 8. The analysis shows that the results are consistent with the deterministic analysis.

Table 5: Probabilistic sensitivity analysis over a 50-year period

	QALYs	Costs (£)	Incremental QALYs	Incremental costs (£)	ICER (£)	Probability of being cost effective at £20,000 per QALY gained
No surveillance	16.12	562.91	–	–	–	–
Colonoscopic surveillance in intermediate- and high-risk groups	16.17	786.25	0.04	223.33	5298.03	78
Colonoscopic surveillance in all risk groups	16.25	1167.77	0.13	604.85	4626.57	81
QALY: quality-adjusted life year; ICER: incremental cost-effectiveness ratio; all risk groups: low-, intermediate, and high-risk groups.						

The probabilistic sensitivity analysis suggests that the probability of colonoscopic surveillance being cost effective at £20,000 per QALY gained is 78% in the intermediate- and high-risk groups only and 81% in all risk groups (including the low-risk group).

The GDG acknowledged that, given the quality of the data and the number of simplifying assumptions in the model, the results were exploratory. The assumptions covering compliance and complications would result in an increase in uncertainty in the ICERs and could potentially increase them. Details of the cost-effectiveness analysis are discussed in appendix 8.

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 (1999a) and Jorgensen (1993). These articles showed that the risk of colorectal cancer in people with adenomas in the low-risk group is similar to that of the general population.

The GDG noted that carrying out colonoscopic surveillance in all risk groups was the most cost-effective strategy according to the deterministic and probabilistic sensitivity analysis results. The GDG noted that the modelling did

not consider issues around compliance, colonoscopy-related complications or the sensitivity or specificity of colonoscopy. However, the GDG did not consider that these factors would increase the results beyond the thresholds that are considered cost effective. The GDG discussed the uncertainty around the clinical benefits of surveillance in the low-risk group. The GDG considered that the potential risks of perforation and bleeding associated with colonoscopy and removal of adenomas outweighed the potential benefits of surveillance in low-risk groups (Ransohoff et al. 1991). In the absence of evidence confirming that an increased detection rate of adenomas and colorectal cancer leads to reduced mortality from colorectal cancer in the low-risk group, the GDG decided that surveillance in this group should not be recommended as routine practice in the NHS. However the GDG highlighted that clinical judgement should be used when considering people's comorbidities and the potential risks of bleeding and perforation for each colonoscopy.

2.2.11 Recommendations

Recommendation 1.1.6

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

Table 2 Risk of developing colorectal cancer in people with adenomas

Low risk:

- one or two adenomas smaller than 10 mm.

Intermediate risk:

- three or four adenomas smaller than 10 mm **or**
- one or two adenomas if one is10 mm or larger.

High risk:

- five or more adenomas smaller than 10 mm **or**
- three or more adenomas if one is 10 mm or larger.

2.3 Colonoscopic surveillance techniques

2.3.1 Review question

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

Colonoscopic surveillance techniques in 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 (Dekker et al. 2007) met the eligibility criteria (for the review protocol and inclusion and exclusion criteria, see appendices 2 and 4).

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 (mean duration 21 ± 8.6 years). 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 (that is, the 42 patients in the study received both procedures)	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 (the 42 patients in the study received both procedures)	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 (see GRADE profile 2)

2.3.3.1 Moderate quality evidence comparing narrow-band imaging with conventional colonoscopy in people with ulcerative colitis of long duration showed no significant difference in the number of neoplastic lesions detected 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 et al. (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 for people with IBD.

2.3.6 Recommendations

No recommendations were made on the use of other surveillance methods for people with IBD (see Evidence to recommendations for details).

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 (Rex et al. 1995, Winawer et al. 2000) and two systematic reviews (Van den Broek et al. 2009, Mulhall et al. 2005) 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 adenomas met the inclusion and exclusion criteria (for the review protocol and inclusion and exclusion criteria, see appendices 2 and 4).

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.

1 **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	Diagnostic efficacy of CTC in detecting adenomas, 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; CTC: CT colonography; 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 adenomas										
Primary outcome: detection and removal of adenomas										
1 (V)	Systematic review/meta-analysis	236/537 (44%)	219/536 (41%)	OR = 1.19 (95% CI 0.86 to 1.64) **NS**	N	N	N	N	N	High
FSIG plus DCBE versus conventional colonoscopy for adenomas										
Primary outcome: adenoma detection										
1 (R)	RCT	23/75 (31%)	13/74 (18%)	OR = 2.07 (95% CI 0.90 to 4.92) **NS**	N	N	N	N	S	Moderate[b]
CTC versus conventional colonoscopy for adenomas										
Primary outcome: adenoma detection										
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). Sensitivity and specificity increased as polyp size increased.	N	N	N	N	S	Moderate[c]

GRADE profile 3 contd.

DCBE versus conventional colonoscopy for adenomas

Primary outcome: adenoma detection								
1 (W)	Controlled trial	Polyps were detected in 392 of the 862 colonoscopic examinations (45%); adenomas were detected in 242 colonoscopic examinations (28%). Findings on barium enema were positive in 222 of the 862 paired examinations (26%) and in 139 (35%) of the 392 colonoscopic examinations in which one or more polyps were detected.	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; **NS**: not significant; 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 (see GRADE profile 3)

2.3.8.1 High quality evidence comparing narrow-band imaging with colonoscopy (white light endoscopy) to detect adenomas showed that narrow-band imaging did 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 Moderate quality evidence showed that computed tomographic (CT) colonography was highly specific for polyps larger than 9 mm. This evidence also showed that sensitivity for CT colonography increased with polyp size.

2.3.8.4 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.

2.3.9 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 adenomas.

The GDG agreed that conventional colonoscopy (high-resolution white-light endoscopy) should be used for routine colonoscopic surveillance in people with adenomas because of its increased detection rate of adenomas compared with other techniques.

The GDG noted that there was ongoing research comparing CT colonography with conventional colonoscopy. It considered that when conventional

colonoscopy was contraindicated (for example if it was inappropriate because of comorbidity or could be tolerated) or incomplete, CT colonography or double-contrast barium enema should be considered for risk assessment. This was because of the high level of specificity of CT colonography for large polyps (larger than 9 mm).

The GDG noted that there was no evidence to support the safety and efficacy of CT colonography as a routine surveillance technique. Because CT colonography and double-contrast barium enema were not evaluated in the reviewed evidence, the GDG considered that any decision about using these methods as alternative surveillance techniques should be made on a case-by-case basis.

The GDG also recognised the significant inter-operator variability of colonoscopy. It recommended that if a colonoscopy is incomplete, a repeat colonoscopy should be undertaken, with a more experienced colonoscopist if appropriate.

2.3.11 Recommendations

Recommendation 1.1.9

Offer a repeat colonoscopy if any colonoscopy is incomplete. Consider whether a more experienced colonoscopist is needed.

Recommendation 1.1.10

If colonoscopy is not clinically appropriate (for example, because of comorbidity or because colonoscopy cannot be tolerated) consider computed tomographic colonography[3] (CTC) or double contrast barium enema as a single examination for people who have had adenomas removed and are at high or intermediate risk of developing colorectal cancer (see table 2). '

Recommendation 1.1.11

When colonoscopy remains clinically inappropriate, consider CTC or barium enema for ongoing surveillance but discuss the risks and benefits with the person and their families or carers.

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)?

[3] Computed tomographic colonography (virtual colonoscopy) NICE interventional procedure guidance 129 (2005).

Conventional colonoscopy compared with chromoscopy in 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 colonoscopy for IBD and met the eligibility criteria (for the review protocol and inclusion and exclusion criteria, see appendices 2 and 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. For this review question the histopathology of the adenomas at presentation could not be determined by the surveillance technique, so the numbers and types of lesions were used because of their relevance to the long-term clinical outcomes. The GDG agreed that any statistically significant improvement in detection would be used for the imprecision calculation.

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 colonoscopy, 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; 8 people 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 colonoscopy, 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)	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration	Quality
Outcome 1: Total number of people with intra-epithelial neoplasia detected										
4[a]	RCT/CT	48/366 (13.11%)	23/356 (6.46%)	OR = 2.21 (1.31 to 3.74)	N	N	N	N	N	High

CI: confidence interval; CT: controlled trial; M-H fixed: Mantel-Haenszel fixed-effects model; N: not serious; OR: odds ratio;

[a] Kiesslich et al. (2003, 2007), Marion et al. (2008) and Rutter et al. (2004a)

2.4.3 Evidence statements (see GRADE profile 4)

2.4.3.1 High quality evidence showed that chromoscopy detected statistically significantly more intra-epithelial dysplastic lesions in people with extensive colitis (at least 8 years' duration) 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 supported the use of chromoscopy compared with conventional colonoscopy. The GDG discussed that using chromoscopy instead of colonoscopy would increase the procedure time, and in practice, four mapping biopsies (to determine the extent of inflammation) and on average one targeted biopsy would be taken when using chromoscopy. The GDG noted that no health economic analysis was conducted for this question and there may be additional costs from the use of dye and the extra time needed for the procedure. However, the GDG also acknowledged that fewer biopsies would be needed, which could lead to reduced pathology cost and time. Therefore, the costs could potentially equalise. In addition, it noted that currently the NHS uses the same health resource group (HRG) code 'FZ26A Endoscopic or Intermediate Large Intestine Procedure 19 years and over' for both procedures (Department of Health 2010). The GDG considered that the significantly increased detection rate made chromoscopy the favoured method for colonoscopic surveillance in people with IBD. It also recognised the significant inter-operator variability in colonoscopy, and recommended that if any colonoscopy was incomplete, a repeat colonoscopy should be undertaken with a more experienced colonoscopist if appropriate.

2.4.6 Recommendation

Recommendation 1.1.2

Offer a baseline colonoscopy with chromoscopy to people with IBD who are being considered for colonoscopic surveillance 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 (but not proctitis alone) or left-sided Crohn's colitis.

Intermediate risk:

- extensive ulcerative or Crohn's colitis with mild active inflammation that has been confirmed histologically **or**
- post-inflammatory adenomas **or**
- family history of colorectal cancer in a first-degree relative aged 50 years or over.

High risk:

- extensive ulcerative or Crohn's colitis with moderate or severe active inflammation that has been confirmed histologically **or**
- primary sclerosing cholangitis (including after liver transplant) **or**
- colonic stricture in the past 5 years **or**
- any grade of dysplasia in the past 5 years **or**
- family history of colorectal cancer in a first degree relative aged under 50 years.

Recommendation 1.1.4

For people with IBD who have been offered colonoscopic surveillance, use colonoscopy with chromoscopy as the method of surveillance.

Recommendation 1.1.5

Offer a repeat colonoscopy with chromoscopy if any colonoscopy is incomplete. Consider whether a more experienced colonoscopist is needed.

Conventional colonoscopy compared with chromoscopy in people with adenomas

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 the review protocol and inclusion and exclusion criteria, see appendices 2 and 4).

The Cochrane review (Brown et al. 2007) 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. For this review question the stage at presentation could not be determined by the surveillance technique, so the number and size of adenomas were used because of their relevance to the long-term clinical outcomes. The GDG agreed that any statistically significant improvement in detection would be used for the imprecision calculation.

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 before 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 before 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 history on screening programme; older than 60 years with symptoms, N = 203	Chromoscopy using 0.4% indigo carmine, with high-resolution imaging, n = 103	Conventional colonoscopy, n = 100	

GRADE profile 5: Chromoscopy compared with conventional colonoscopy for adenomas

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: total number of polyps detected in proximal colon – IV random										
2[b]	RCT	270	281	WMD = 0.55 (0.07 to 1.03)	N	N	N	N	N	High
Outcome 3: total number of polyps detected in distal colon – IV fixed										
2[c]	RCT	270	281	WMD = 0.37 (0.20 to 0.54)	N	N	N	N	N	High
Outcome 4: total number of neoplastic lesions detected – IV random										
3[d]	RCT/CT	369	380	WMD = 0.33 (–0.04 to 0.71) **NS**	N	N	N	S[h]	N	Moderate
Outcome 5: total number of neoplastic lesions detected in proximal colon – IV random										
2[e]	RCT/CT	270	281	WMD = 0.33 (–0.05 to 0.71) **NS**	N	N	N	S[h]	N	Moderate
Outcome 6: total number of neoplastic lesions detected in distal colon – IV fixed										
2[f]	RCT/CT	270	281	WMD = 0.09 (–0.08 to 0.26) **NS**	N	N	N	S[h]	N	Moderate
Outcome 7: total number of diminutive neoplastic lesions detected – IV random										
3[g]	RCT/CT	369	380	WMD = 0.28 (0.08 to 0.47)	N	N	N	N	N	High

CI: confidence interval; CT: controlled trial; IV: inverse variance 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) and Lapalus et al. (2006)
[c] Brooker et al. (2002) and Lapalus et al. (2006)

[d] Brooker et al. (2002), Lapalus et al. (2006) and Le Rhun et al. (2004)
[e] Brooker et al. (2002) and Lapalus et al. (2006)
[f] Brooker et al. (2002) and Lapalus et al. (2006)
[g] Brooker et al. (2002), Lapalus et al. (2006) and Le Rhun et al. (2004)
[h] The outcomes were downgraded for imprecision as there no significant difference between the two arms.

2.4.8 Evidence statements (see GRADE profile 5)

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 detected statistically significantly more polyps in the proximal colon than conventional colonoscopy.

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

2.4.8.4 Moderate quality evidence showed that there was no statistically significant difference in the number of neoplastic lesions detected by chromoscopy compared with conventional colonoscopy.

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

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

2.4.8.7 High quality evidence showed that chromoscopy detected statistically significantly more 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 adenomas and neoplastic lesions using chromoscopy compared with conventional colonoscopy. However, the GDG felt that there may be additional costs from the use of the dye and the additional time needed for the procedure. While the GDG understood that the total cost difference was likely to be small, it considered that the limited clinical benefit did not justify a change in practice. It therefore recommended that chromoscopy should not be used for colonoscopic surveillance in people with adenomas. 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.

2.4.11 Recommendations

No recommendations were made on the use of chromoscopy for people with adenomas (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?

Initiation and frequency of surveillance in 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 the review protocol, inclusion and exclusion criteria, see appendices 2 and 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, four were primary studies (Karlén et al. 1998; Manning et al. 1987; Odze et al. 2004[4]; Rutter et

[4] Manning et al. 1987 and Odze et al. 2004 were subsequently excluded.

al. 2006) and two were reviews: one meta-analysis of 116 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 search. The technical team therefore decided to broaden the search criteria to try and identify other similar relevant prognostic studies that may have been missed.

Additional searches found 1781 articles (including some duplicates and non-English language papers). Of these, 130 were assessed as relevant based on the title and abstract alone. Including the 11 papers already assessed as relevant, 140 articles in total (1 duplicate) were considered for this question. Studies that were included in any of the meta-analyses were re-examined to see if any other relevant outcomes were reported (based on the abstract alone). This resulted in a total of 173 papers considered as relevant based on the title and abstract. Details of the included studies and a list of excluded studies are given in appendix 4. The main reasons for exclusion based on the title and abstract were papers evaluating the use of DNA techniques (including gene staining), methylation or microsatellite instability for risk assessment, or when direct comparisons were not reported.

No direct evidence was identified comparing different surveillance programmes, including when surveillance is started or its frequency. To provide evidence on whether such recommendations could be made, the review question was interpreted as follows: is there any evidence that there are subgroups of adults with IBD who are at higher risk of developing colorectal cancer? This makes the underlying assumption that if people are shown to be at high risk, they would benefit from more intensive surveillance.

The included studies compared the risk of colorectal cancer in adults with IBD. The characteristics of the studies are summarised in table 10. The evidence reviewed related to the timing of surveillance and prognostic factors. A GRADE profile has not yet been developed for prognostic studies, so modified

full GRADE profiles were not completed. Many factors were not consistent among the studies (for example the clinical and prognostic factors, summary estimates and quality) and so it was not appropriate to pool any results, or to present overall estimates, such as means or medians. Therefore the results of each included study are presented separately and the principles of GRADE (limitations, inconsistencies, directness) were applied when generating the evidence statements. Imprecision was not assessed because of the lack of a summary estimate and there were no agreed methods. Prospective cohort studies were considered high quality but could move to moderate, low or very low depending on other factors (Schünemann et al. 2008). Evidence tables for the included studies are available in appendix 6.

Table 10: Summary of study characteristics

Study	Study design	Population
Eaden et al. (2001)	Meta-analysis of 116 studies	24,478 people with ulcerative colitis 1698 with CRC
Jess et al. (2005)	Meta-analysis of 6 studies	6538 people with Crohn's disease 55 with CRC
Soetikno et al. (2002)	Meta-analysis of 11 studies	16,844 people with ulcerative colitis 564 with ulcerative colitis and PSC 560 with CRC, including 60 with ulcerative colitis and PSC
Thomas et al. (2007)	Meta-analysis of 20 studies	Over 2677 people with ulcerative colitis 508 with LGD 31 with CRC
Askling et al. (2001)	Retrospective (assumed) cohort, with nested case–control	19,876 people with ulcerative colitis or Crohn's disease 143 with CRC
Brentnall et al. (1996)	Prospective cohort	45 people with ulcerative colitis 20 with PSC 13 with dysplasia
Broome et al. (1992)	Retrospective (assumed) cohort	72 people with ulcerative colitis 5 with PSC 17 with dysplasia, carcinoma, and/or DNA aneuploidy
Broome et al. (1995)	Retrospective (assumed) cohort	120 people with ulcerative colitis 40 with PSC and ulcerative colitis 7 with CRC
D'Haens et al. (1993)	Retrospective case–control	58 people with ulcerative colitis 29 with PSC 9 with CRC
Ekbom et al. (1990)	Retrospective (assumed) cohort	1655 people with Crohn's disease 12 with CRC
Florin et al. (2004)	Retrospective case–control	384 people with ulcerative colitis 90 with PSC 8 with CRC
Friedman et al. (2001)	Retrospective (assumed) cohort	259 people with Crohn's disease 5 with CRC
Gilat et al. (1988)	Prospective (assumed) cohort	1035 people with ulcerative colitis Number with CRC not reported
Gupta et al. (2007)	Retrospective cohort	418 people with ulcerative colitis 65 with any neoplasia 15 progressed to advanced neoplasia
Gyde et al. (1988)	Retrospective cohort	823 people with ulcerative colitis 38 with CRC
Hendriksen et al. (1985)	Retrospective (assumed) cohort	783 people with ulcerative colitis 7 with colonic cancer

Study	Study design	Population
Jess et al. (2006)	Retrospective (assumed) cohort	692 people with IBD 29 with colorectal dysplasia
Jess et al. (2007)	Retrospective (assumed) cohort, with nested case–control	145 people with IBD 43 with neoplasia
Karlén et al. (1998)	Retrospective cohort, with nested case–control	142 people with ulcerative colitis 40 with CRC (deaths)
Kvist et al. (1989)	Retrospective (assumed) cohort	759 people with ulcerative colitis 17 with CRC
Langholz et al. (1992)	Retrospective (assumed) cohort	161 people with ulcerative colitis 6 with CRC
Lennard-Jones et al. (1990)	Prospective cohort	401 people with extensive ulcerative colitis 22 with CRC
Loftus et al. (2005)	Prospective cohort (with matched controls)	213 people with IBD/ulcerative colitis 71 with PSC-IBD 11 with CRC
Nuako et al. (1998) FH	Retrospective (assumed) case–control	297 people with ulcerative colitis 31 with CRC
Nuako et al. (1998) PSC	Prospective (assumed) case–control	342 people with ulcerative colitis 171 with CRC
Rutter et al. (2004b, 2004c)	Retrospective case–control	204 people with ulcerative colitis 68 with colorectal neoplasia
Rutter et al. (2006)	Retrospective (assumed) cohort	354 people with ulcerative colitis 215 with dysplasia or CRC
Stewenius et al. (1995)	Retrospective (assumed) cohort	471 people with ulcerative colitis 9 with CRC
Velayos et al. (2006)	Retrospective case–control	356 people with ulcerative colitis 188 with CRC
CRC: colorectal cancer; FH: family history; IBD: inflammatory bowel disease; LGD: low-grade dysplasia; PSC: primary sclerosing cholangitis		

Table 11: Summary of frequency of surveillance

	Gupta et al. (2007)	Jess et al. (2007)	Karlen et al. (1998)	Velayos et al. (2006)	Overall quality
Study design	Retrospective cohort	Retrospective (assumed) cohort, with nested case–control	Retrospective cohort, with nested case–control	Retrospective case–control	Very low (retrospective and consistency could not be assessed)
Frequency of colonoscopy	HR 1.7 (95% CI 0.9 to 3.0) for association of frequency of colonoscopy (1 or more per year) with any neoplasia HR 3.9 (95% CI 1.3 to 11.4) for advanced neoplasia (univariate only)	Adjusted OR 5.3 (95% CI 1.4 to 20) for colorectal neoplasia if one or more colonoscopic surveillances during the disease course compared with no surveillance	RR 0.29 (95% CI 0.06 to 1.31) for risk of CRC mortality if colonoscopic surveillance ever compared with never. RR 0.43 (95% CI 0.05 to 3.76) for risk of CRC mortality if one colonoscopic surveillance compared with never. RR 0.22 (95% CI 0.03 to 1.74) for risk of CRC mortality if two or more colonoscopic surveillances compared with never.	Adjusted OR 0.4 (95% CI 0.2 to 0.7) for risk of CRC with one or two colonoscopies compared with none Adjusted OR 0.3 (95% CI 0.1 to 0.8) for risk of CRC with two colonoscopies compared with none	

HR: hazard ratio; CI: confidence interval; OR: odds ratio; RR: relative risk; CRC: colorectal cancer

Risk of CRC mortality: assessed as very low quality because of limitations in studies (retrospective and consistency could not be assessed).
Risk of CRC: assessed as very low quality because of limitations in study (retrospective and consistency could not be assessed).
Risk of advanced neoplasia: assessed as very low quality because of limitations in studies (retrospective, concerns over detection bias).

Table 12: Summary of prognostic factors

Type of IBD

	Jess et al. (2006)	Overall quality
Study design	Retrospective (assumed) cohort	Very low (retrospective and consistency could not be assessed)
Disease - IBD	HR 0.7 (95% CI 0.2 to 3.0) for risk of recurrence and progression of dysplasia in Crohn's disease compared with ulcerative colitis	
IBD: inflammatory bowel disease; HR: hazard ratio		

Gender

	Ekbom et al. (1990)	Gupta et al. (2007)	Gyde et al. (1988)	Jess et al. (2006)	Overall quality
Study design	Retrospective (assumed) cohort	Retrospective cohort	Retrospective cohort	Retrospective (assumed) cohort	Low (retrospective and no significant inconsistency)
Gender	SIR for CRC 2.8 (95% CI 1.1 to 5.8) in men; 2.1 (0.7 to 4.8) in women. Not direct comparison	HR 1.5 (95% CI 0.9 to 2.4) for association of gender (male) with any neoplasia HR 2.5 (95% CI 0.8 to 7.8) for advanced neoplasia (univariate only)	No difference between RR of CRC in men and women (**NS**.)	HR 2.8 (95% CI 0.3 to 23) for risk of recurrence and progression of dysplasia in men compared with women	
SIR: standardised incidence ratio; CRC: colorectal cancer; HR: hazard ratio; **NS**: not significant; RR: relative risk;					

Age

	Friedman et al. (2001)	Overall quality
Study design	Retrospective (assumed) cohort	Very low quality (retrospective, consistency could not be assessed)
Age	Risk of neoplasia (LGD, HGD, CRC) identified on surveillance was higher in people aged over 45 years (p = 0.048) compared with people aged 45 years and younger This remained significant when adjusted for duration of disease	
LGD: low-grade dysplasia; HGD: high-grade dysplasia; CRC: colorectal cancer		

Age at diagnosis

	Brentnall et al. (1996)	Broome et al. (1992)	D'Haens et al. (1993)	Ekbom et al. (1990)	Gupta et al. (2007)	Gyde et al. (1988)	Jess et al. (2006)	Overall quality
Study design	Prospective cohort	Retrospective (assumed) cohort	Retrospective case–control	Retrospective (assumed) cohort	Retrospective cohort	Retrospective cohort	Retrospective (assumed) cohort	
Age at diagnosis or onset	No significant association of age at onset of UC with development of dysplasia (indefinite, LGD, HGD) (logistic coefficient – 0.03; p = 0.58)	No significant association of age at onset of UC with development of dysplasia and/or DNA aneuploidy (logistic coefficient – 0.041; p = 0.153)	OR 1.04 (95% CI 1.00 to 1.08) for association of risk of dysplasia or CRC with age at onset of symptoms in years (conditional logistic regression)	SIR 9.5 (95% CI 3.1 to 23.2) for CRC if aged < 30 years at diagnosis; 1.6 (0.6 to 3.3) if aged 30 years or over. Not direct comparison – compared with the general population.	HR 0.7 (95% CI 0.4 to 1.2) for association of age (< 25 years) with any neoplasia HR 1.6 (95% CI 0.6 to 4.5) for advanced neoplasia (univariate only)	RR 107.1 (observed/expected; 95% CI 55.3 to 187.2) for extensive colitis with age of onset 15–24 years compared with the general population RR 27.9 (observed/expected; 95% CI 15.2 to 46.8) for extensive colitis with age of onset 25–39 years compared with the general population RR 3.3 (observed/expected; 95% CI 0.7 to 9.8) for extensive colitis with age of onset aged 40 and over compared with the general population	HR 0.7 (95% CI 0.2 to 2.9) for risk of recurrence and progression of dysplasia for age of IBD diagnosis at over 40 years compared with 40 years and younger HR 0.7 (95% CI 0.2 to 3.3) for risk of recurrence and progression of dysplasia for age of dysplasia diagnosis at over 50 years compared with 50 years and younger	Low quality (significant inconsistency, and confounding with age, duration of disease)

UC: ulcerative colitis; LGD: low-grade dysplasia; HGD: high-grade dysplasia; OR: odds ratio; CRC: colorectal cancer; SIR: standardised incidence ratio; HR: hazard ratio; CI: confidence interval; RR relative risk; IBD: inflammatory bowel disease

Duration of disease

	Brentnall et al. (1996)	Broome et al. (1992)	Gilat et al. (1988)	Gupta et al. (2007)	Gyde et al. (1988)	Kvist et al. (1989)	Langholz et al. (1992)	Lennard-Jones et al. (1990)	Stewenius et al. (1995)	Overall quality
Study design	Prospective cohort	Retrospective (assumed) cohort	Prospective (assumed) cohort	Retrospective cohort	Retrospective cohort	Retrospective (assumed) cohort	Retrospective (assumed) cohort	Prospective cohort	Retrospective (assumed) cohort	
Duration of disease	No significant association of duration of disease with development of dysplasia (indefinite, LGD, HGD) (logistic coefficient 0.07; p = 0.35)	Significant association of duration of disease with development of dysplasia and/or DNA aneuploidy (logistic coefficient 0.051; p = 0.038)	Association of duration with risk of CRC included in Eaden et al. (2001) analysis Cumulative incidence of CRC with total colitis 0% at 10 years; 9.3% at 15 years; 13.8% at 20 years	HR 1.6 (95% CI 0.9 to 2.8) for association of duration of disease (> 15 years) with any neoplasia HR 2.0 (95% CI 0.6 to 6.3) for advanced neoplasia (univariate only)	Association of duration with risk of CRC included in Eaden et al. (2001) analysis	Association of duration of disease with CRC risk included in Eaden et al. (2001) analysis	Association of duration with risk of CRC included in Eaden et al. (2001) analysis Cumulative incidence of CRC with extensive disease 1.8% at 25 years	Association of duration of disease with CRC risk included in Eaden et al. (2001) analysis	Association of duration with risk of CRC included in Eaden et al. (2001) analysis Cumulative incidence of CRC with total colitis at diagnosis 5% at 15 years; 8% at 20 years; 8% at 25 years Cumulative incidence of CRC with initial or later total colitis 6% at 15 years; 8% at 20 years; 10% at 25 years	Moderate quality (some inconsistency)

LGD: low-grade dysplasia; HGD: high-grade dysplasia; CRC: colorectal cancer; HR: hazard ratio; CI: confidence interval

Duration of disease contd

	Eaden et al. (2001)	Ekbom et al. (1990)	Hendriksen et al. (1985)	Lennard-Jones et al. (1990)	Loftus et al. (2005)	Rutter et al. (2006)	Overall quality
Study design	Meta-analysis of 116 studies	Retrospective (assumed) cohort	Retrospective (assumed) cohort	Prospective cohort	Prospective cohort (with matched controls)	Retrospective (assumed) cohort	Moderate quality (some inconsistency)
Duration of disease 0–10 years (all ulcerative colitis)	Cumulative probability of CRC 1.6% (95% CI 1.2 to 2) by 10 years	SIR for CRC 2.5 (95% CI 1.0 to 5.1) for duration of follow-up < 10 years. Not direct comparison – as compared with general population	Cumulative risk of CRC 0.8% (no CI reported) by 10 years		Cumulative risk of dysplasia or CRC at 5 years 33% (95% CI 17 to 46) for PSC-IBD compared with 13% (2 to 21) for ulceratve colitis (p = 0.054) Cumulative risk of CRC at 5 years 14% (95% CI 3 to 25) for PSC-IBD compared with 4% (0 to 10) for ulcerative colitis (p = 0.13)	Cumulative incidence of neoplasia at 10 years 1.5%; 0% for CRC	
Duration of disease 11–20 years (all ulcerative colitis)	Cumulative probability of CRC 8.3% (95% CI 4.8 to 11.7) by 20 years	SIR for CRC 2.0 (95% CI 0.4 to 6.0) for duration of follow-up 10–19 years. Not direct comparison – as compared with general population	Cumulative risk of CRC 1.1% (no CI reported) by 15 years, and 1.4% (95% CI 0.7 to 2.8) by 18 years	Cumulative risk of HGD or CRC at 15 years 4%. Cumulative risk of HGD or CRC at 20 years 7%		Cumulative incidence of neoplasia at 20 years 7.7%; 2.5% for CRC	
Duration of disease 21–30 years (all ulcerative colitis)	Cumulative probability of CRC 18.4% (95% CI 15.3 to 21.5) by 30 years	SIR for CRC 3.2 (95% CI 0.4 to 11.4) for duration of follow-up of 19 years or more. Not direct comparison – as compared with general population		Cumulative risk of HGD or CRC at 25 years 13%		Cumulative incidence of neoplasia at 30 years 15.8%; 7.6% for CRC	
Duration of disease over 30 years (all ulcerative colitis)						Cumulative incidence of neoplasia at 40 years 22.7%; 10.8% for CRC Cumulative incidence of neoplasia at 45 years 27.5%; 13.5% for CRC	

CRC: colorectal cancer; CI: confidence interval; SIR: standardised incidence ratio; HGD: high-grade dysplasia; PSC: primary sclerosing cholangitis; IBD: inflammatory bowel disease

Extent of disease

	Eaden et al. (2001)	Jess et al. (2005)	Askling et al. (2001)	Ekbom et al. (1990)	Gupta et al. (2007)	Gyde et al. (1988)	Hendriksen et al. (1985)	Jess et al. (2006)	Kvist et al. (1989)	Overall quality
Study design	Meta-analysis of 116 studies	Meta-analysis of 6 studies	Retrospective (assumed) cohort, with nested case–control	Retrospective (assumed) cohort	Retrospective cohort	Retrospective cohort	Retrospective (assumed) cohort	Retrospective (assumed) cohort	Retrospective (assumed) cohort	Moderate (some inconsistency)
Extent of disease	Total ulcerative colitis only: Cumulative probability of CRC 2.1% (95% CI 1.0 to 3.2) by 10 years, 8.5% (3.8 to 13.3) by 20 years, 17.8% (8.3 to 27.4) by 30 years	Meta-regression of 4 studies showed no significant influence of disease extent on SIR for CRC. Noted however, that the prevalence was similar across the included studies	RR 3.5 (95% CI 1.2 to 20) of CRC if pancolitis or colorectal Crohn's disease compared with ulcerative colitis or Crohn's disease. This did not significantly modify the association with FH of CRC (p = 0.51 interaction)	SIR 1.0 (95% CI 0.1 to 3.4) for risk of CRC if disease confined to the terminal ileum; 3.2 (0.7 to 9.2) for terminal ileum and part of the colon; 5.6 (2.1 to 12.2) for the colon alone; 1.2 (0.0 to 5.9) for other; 4.4 (2.0 to 8.4) for any colonic involvement. Not direct comparison – as compared with the general population	HR 1.1 (95% CI 0.4 to 3.5) for association of extent of disease with any neoplasia. No extensive disease in advanced neoplasia group (univariate only)	RR 19.2 (observed/expected; no CI reported, p = 0.001) of CRC in extensive colitis compared with the general population RR 3.6 (observed/expected; no CI reported, p = 0.01) of CRC in left sided colitis and proctitis compared with the general population	Cumulative risk of CRC not influenced by initial extent of the colon. Cumulative risk after 18 years was 1.3%	HR 0.9 (95% CI 0.2 to 4.6) for risk of recurrence and progression of dysplasia in pancolitis or pure colonic Crohn's disease compared with other extent	Crude CRC rates for 'left-sided' (proctosigmoiditis and left-sided disease) and universal disease were 'virtually the same' at 3% Time courses for duration of disease in the two groups were 'indistiguishable'	

CRC: colorectal cancer; CI: confidence interval; SIR: standardised incidence ratio; HR: hazard ratio; RR: relative risk

Primary sclerosing cholangitis

	Soetikno et al. (2002)	Brentnall et al. (1996)	Broome et al. (1992)	Broome et al. (1995)	D'Haens et al. (1993)	Florin et al. (2004)	Gupta et al. (2007)	Jess et al. (2006)	Jess et al. (2007)	Loftus et al. (2005)	Nuako et al. (1998) PSC	Velayos et al. (2006)	Overall quality
Study design	Meta-analysis of 11 studies	Prospective cohort	Retrospective (assumed) cohort	Retrospective (assumed) cohort	Retrospective case–control	Retrospective case–control	Retrospective cohort	Retrospective (assumed) cohort	Retrospective (assumed) cohort, with nested case–control	Prospective cohort (with matched controls)	Prospective (assumed) case–control	Retrospective case–control	
PSC	OR 4.79 (95% CI 3.58 to 6.41) of colorectal neoplasia (dysplasia or carcinoma) if UC and PSC compared with UC alone OR 4.09 (95% CI 2.89 to 5.76) of CRC if UC and PSC compared with UC alone Results for fixed effect model presented. Similar results found for random effects model	Risk of CRC associated with PSC and UC included in Soetikno et al. (2002) analysis	Risk of CRC associated with PSC and UC included in Soetikno et al. (2002) analysis	Risk of CRC associated with PSC and UC included in Soetikno et al. (2002) analysis Cumulative risk of dysplasia or CRC with PSC and UC of 9% after 10 years; 31% after 20 years; 50% after 25 years compared with 2%, 5% and 10% for UC alone (comparison of life table curves [p < 0.001])	OR 9.00 (95% CI 1.14 to 71.04) for association of risk of dysplasia or CRC with pericholangitis or PSC (conditional logistic regression)	OR 3.6 (95% CI 1.3 to 10.2) for risk of HGD or CRC in PSC-IBD compared with UC	HR 1.1 (95% CI 0.2 to 8.0) for association of PSC with any neoplasia No PSC in advanced neoplasia group (univariate only)	HR 5.0 (95% CI 1.1 to 23) for risk of recurrence and progression of dysplasia in PSC compared with no PSC	Adjusted OR 6.9 (95% 1.2 to 40) for colorectal neoplasia if PSC compared with no PSC (includes cases from Jess et al. 2006)	HR 1.7 (95% CI 0.6 to 4.9) for dysplasia or CRC in PSC-IBD compared with UC HR 1.9 (95% CI 0.3 to 11.9) for CRC in PSC-IBD compared with UC Both adjusted for age, duration of IBD, date of IBD diagnosis	Adjusted OR 1.23 (95% CI 0.62 to 2.42) for risk of CRC in PSC compared with no PSC	OR 1.1 (95% CI 0.5 to 2.3) for risk of CRC in PSC compared with no PSC	Moderate (some inconsistency)

PSC: primary sclerosing cholangitis; OR: odds ratio; CI: confidence interval; UC: ulcerative colitis; CRC: colorectal cancer; HGD: high-grade dysplasia; IBD: inflammatory bowel disease

Family history

	Askling et al. (2001)	Jess et al. (2007)	Nuako et al. (1998 FH)	Velayos et al. (2006)	Overall quality
Study design	Retrospective (assumed) cohort, with nested case–control	Retrospective (assumed) cohort, with nested case–control	Retrospective (assumed) case–control	Retrospective case–control	Low quality (retrospective and some inconsistency)
At least one first-degree relative with CRC	RR 2.5 (95% CI 1.4 to 4.4) for CRC if family history of CRC compared with no family history of CRC	Adjusted OR 1.4 (95% CI 0.3 to 5.9) for colorectal neoplasia if first-degree relative with CRC compared with no relative with CRC	Adjusted OR 2.31 (95% CI 1.03 to 5.18) for CRC in family history compared with no family history. Adjusted for sex, age, and year of ulcerative colitis diagnosis	Adjusted OR 3.7 (95% CI 1.0 to 13.2) for risk of CRC in family history compared with no family history	
Relative aged < 50 at diagnosis of CRC	RR 9.2 (95% CI 3.7 to 23) for CRC if relative aged < 50 at diagnosis of CRC compared with no family history of CRC				
Relative aged ≥ 50 at diagnosis of CRC	RR 1.7 (95% CI 0.8 to 3.4) for CRC if relative aged ≥ 50 at diagnosis of CRC compared with no family history of CRC				

CRC: colorectal cancer; RR: relative risk; CI: confidence interval; OR: odds ratio

Severity of inflammation

	Gupta et al. (2007)	Jess et al. (2007)	Rutter et al. (2004 b and c)	Overall quality
Study design	Retrospective cohort	Retrospective (assumed) cohort, with nested case–control	Retrospective case–control	Low quality (retrospective, some inconsistency)
inflammation score (mean)	HR 1.4 (95% CI 0.9 to 2.3) for association of inflammation with any neoplasia HR 3.0 (95% CI 1.4 to 6.3) for advanced neoplasia Remained significant for advanced neoplasia when adjusted for frequency of colonoscopy	Adjusted OR 1.3 (95% CI 0.6 to 2.9) for association of mean macroscopic inflammation score with colorectal neoplasia Adjusted OR 0.7 (95% CI 0.3 to 1.5) for association of mean microscopic inflammation score with colorectal neoplasia	Adjusted OR 4.69 (95% CI 2.10 to 10.48) for association between histological inflammation score and colorectal neoplasia	
Inflammation score (cumulative mean)	HR 1.7 (95% CI 0.9 to 3.1) for association of inflammation with any neoplasia HR 3.4 (95% CI 1.1 to 10.4) for advanced neoplasia Similar results when adjusted for frequency of colonoscopy			
Inflammation score (maximum)	HR 1.0 (95% CI 0.7 to 1.5) for association of inflammation with any neoplasia HR 2.2 (95% CI 1.2 to 4.2) for advanced neoplasia Similar results when adjusted for frequency of colonoscopy			

Location of dysplasia

	Jess et al. (2006)	Overall quality
Study design	Retrospective (assumed) cohort	Very low quality (retrospective and consistency could not be assessed)
Location of dysplasia	HR 5.4 (95% CI 1.0 to 28) for risk of recurrence and progression of dysplasia in dysplasia distal to splenic flexure compared with proximal	

HR: hazard ratio; CI: confidence interval; OR: odds ratio

Dysplasia at diagnosis

	Thomas et al. (2007)	Overall quality
Study design	Meta-analysis of 20 studies	Moderate quality
Progression of LGD to CRC	OR 9.0 (95% CI 4.0 to 20.5) of CRC if LGD diagnosis compared with no dysplasia. Meta-regression showed no significant effect of duration of disease on CRC risk (p = 0.57)	
Progression of LGD to HGD or CRC	OR 11.9 (95% CI 5.2 to 27) of HGD or CRC if LGD diagnosis compared with no dysplasia	

Colonic appearance

	Rutter et al. (2004 b and c)	Overall quality
Study design	Retrospective case–control	Very low quality (retrospective and consistency could not be assessed)
Colonoscopic appearance	OR 0.38 (95% CI 0.19 to 0.73) for risk of CRC of normal appearance compared with abnormal appearance	

Post-inflammatory polyps

	Rutter et al. (2004 b and c)	Velayos et al. (2006)	Overall quality
Study design	Retrospective case–control	Retrospective case–control	Very low quality (retrospective)
Post-inflammatory polyps	OR 2.29 (95% CI 1.28 to 4.11) for risk of CRC with post-inflammatory polyps compared with no polyps	Adjusted OR 2.5 (95% CI 1.4 to 4.6) for risk of CRC with pseudopolyps compared with none	

Colonic stricture

	Rutter et al. (2004 b and c)	Overall quality
Study design	Retrospective case–control	Very low quality (retrospective and consistency could not be assessed)
Colonic stricture	OR 4.62 (95% CI 1.03 to 20.8) for risk of CRC with colonic stricture compared with no stricture	

CI: confidence interval; CRC: colorectal cancer; FH: family history; HR: hazard ratio; HGD: high-grade dysplasia; LGD: low-grade dysplasia; NS: non-significant; PSC: primary sclerosing cholangitis; RR: relative risk; SIR: standardised incidence ratio

2.5.3 Evidence statements

Frequency of surveillance (see table 11)

2.5.3.1 Very low quality evidence (one study) showed that an increased number of surveillance colonoscopies was associated with a lower risk of colorectal cancer mortality (although this was not significant).

2.5.3.2 Very low quality evidence (one study) showed a decreased risk for colorectal cancer with an increased number of surveillance colonoscopies.

2.5.3.3 Very low quality evidence (two studies) showed an increased risk for advanced neoplasia with an increased number of surveillance colonoscopies (possible detection bias).

Prognostic factors (see table 12)

2.5.3.4 Very low quality evidence (one study) showed that the risk of recurrence or progression of dysplasia was no different for people with Crohn's disease or ulcerative colitis.

2.5.3.5 Low quality evidence (four studies) showed that the risk of neoplasia (incidence, recurrence, progression) was no different for men or women.

2.5.3.6 Very low quality evidence (one study) showed that the risk of identifying neoplasia was higher in people aged over 45 years, even when adjusted for duration of IBD.

2.5.3.7 Low quality evidence (seven studies) showed that the risk of dysplasia or colorectal cancer increased with a lower age at diagnosis.

2.5.3.8 Moderate quality evidence (14 studies) showed that the risk of dysplasia or colorectal cancer increased with duration of inflammatory bowel disease.

2.5.3.9 Moderate quality evidence (nine studies) showed that people with extensive or total colitis had a higher risk of dysplasia than those without extensive or total colitis; this increased for people with a younger age at diagnosis.

2.5.3.10 Moderate quality evidence (nine studies) showed that people with primary sclerosing cholangitis had a higher risk of neoplasia than those without primary sclerosing cholangitis.

2.5.3.11 Low quality evidence (four studies) showed that a family history of colorectal cancer was associated with an increased risk of colorectal cancer (which increased if the relative was younger than 50 years).

2.5.3.12 Low quality evidence (three studies) showed that increased inflammation was a predictor of neoplasia.

2.5.3.13 Very low quality evidence (one study) showed that the risk of recurrence and progression of dysplasia was higher if located distally compared with proximally.

2.5.3.14 Moderate quality evidence (one meta-analysis) showed that low-grade dysplasia was associated with progression to high-grade dysplasia and colorectal cancer compared with no dysplasia.

2.5.3.15 Very low quality evidence (one study) showed that a normal appearance at colonoscopy was associated with a lower risk of colorectal cancer.

2.5.3.16 Very low quality evidence (two studies) showed that post-inflammatory polyps were associated with a higher risk of colorectal cancer.

2.5.3.17 Very low quality evidence (one study) showed that colonic stricture was associated with a higher risk of colorectal cancer.

2.5.4 Health economic modelling

No health economic modelling was undertaken for this review question.

2.5.5 Evidence to recommendations

Because there was no direct evidence for surveillance schemes for different subgroups of the IBD population, the GDG made recommendations based on the risk of people with IBD developing colorectal cancer, taking into account the significant risk factors from the available evidence. Although the evidence showed that the risk of colorectal cancer increased with a lower age at diagnosis of IBD, this could be confounded by duration of disease or overall age, so recommendations were based on the duration of disease. This was consistent with the recommendation to start surveillance 10 years after onset of symptoms. The GDG felt that there were differences in the incidence of colorectal cancer by disease duration between the Eaden et al. (2001) meta-analysis and the Rutter et al. (2006) study. However, people taking part in the latter study were on surveillance and therefore the Eaden et al. (2001) figures were considered to be more realistic. The GDG also felt that a detailed look at severity of inflammation was necessary because it is a precursor to dysplasia. It felt that using a validated score for describing inflammation would be useful, as used in the Gupta et al. (2007) study. The GDG also considered 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 presence of dysplasia at diagnosis was a significant factor for progression to high-grade dysplasia and colorectal cancer and was therefore included as a risk factor in the high-risk group. Although the evidence for colonic stricture was very low quality, the GDG considered that strictures are an indication of malignancy or severe inflammation, so further surveillance and investigation would be warranted.

Although there was a reasonable amount of evidence evaluating different risk factors, no one study compared all of the factors directly. The GDG therefore stratified the risk groups in the recommendations based on their knowledge and expertise.

Because there was no direct evidence for timings of surveillance for the different risk groups, these were determined by GDG consensus. The GDG felt strongly that before entering the surveillance programme 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 these people should remain on surveillance in the high-risk group. However, management of dysplasia was outside the scope of this guideline, so a recommendation was made that people should be referred for further investigations or treatment if there are any findings at surveillance. The GDG also made a recommendation about stopping surveillance. This was based on its expertise and knowledge.

2.5.6 Recommendations

Recommendation 1.1.2

Offer a baseline colonoscopy with chromoscopy to people with IBD who are being considered for colonoscopic surveillance 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 (but not proctitis alone) or left-sided Crohn's colitis.

Intermediate risk:

- extensive ulcerative or Crohn's colitis with mild active inflammation that has been confirmed histologically **or**
- post-inflammatory adenomas **or**
- family history of colorectal cancer in a first-degree relative aged 50 years or over.

High risk:

- extensive ulcerative or Crohn's colitis with moderate or severe active inflammation that has been confirmed histologically **or**
- primary sclerosing cholangitis (including after liver transplant) **or**
- colonic stricture in the past 5 years **or**
- any grade of dysplasia in the past 5 years **or**
- family history of colorectal cancer in a first degree relative aged under 50 years.

Recommendation 1.1.3

Offer colonoscopic surveillance to people with IBD as defined in 1.1.1 based on their risk of developing colorectal cancer (see table 1), determined at the last complete colonoscopy:

- Low risk: offer at 5 years.
- Intermediate risk: offer at 3 years.
- High risk: offer within 1 year.

Recommendation 1.1.14

At each surveillance, discuss the potential benefits, limitations and risks of ongoing surveillance. Base a decision to stop surveillance on potential benefits for the person, their preferences, and any comorbidities. Make the

decision jointly with the person and if appropriate their family or carers.

Recommendation 1.1.15

If there are any findings at surveillance that need treatment or referral, discuss the options with the person and if appropriate their family or carers.

Initiation and frequency of surveillance in people with adenomas

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 a further four articles were identified through manual reference searching. Only six articles met the eligibility criteria (for the review protocol, inclusion and exclusion criteria, see appendices 2 and 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 included in the meta-analyses or the outcomes of interest were not reported (Kronborg et al. 2006; Lieberman et al. 2007, 2008; Nusko et al. 2002). The Martinez et al. (2009) meta-analysis included the data from the Lieberman et al. (2000) study and additional data up to June 2005. The updated data from Lieberman et al. (2007) and the prevalence study of advanced histology in smaller adenomas (Lieberman et al. 2008) were not included in the meta-analysis, but were 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. Nusko et al. (2002) 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, or with high-grade dysplasia or with invasive cancer).

The characteristics of the included studies are summarised in table 13 and the evidence reviewed in GRADE profiles 6 and 7. Detailed evidence tables for the included studies are available in appendix 6.

Table 13: Summary of study characteristics

Study	Aim	Study type	Population	Prognostic factors or surveillance programmes	Outcomes used for GRADE profile
Kronborg et al. (2006)	To 'measure the outcome resulting from extension of intervals between colonoscopies as measured by risk of new neoplasia as well as complications in two patient groups believed to carry different risks of new neoplasia'	Three randomised long-term surveillance trials	20 years of surveillance of people with previously diagnosed adenomas, N = 671, 73, and 200	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)	To 'determine the 5.5-year cumulative incidence rate of advanced neoplasia in patients with and without neoplasia at the baseline screening colonoscopy' and 'whether there is an association between baseline endoscopic findings and subsequent risk of advanced neoplasia'	Observational cohort, with nested randomised comparison	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 adenomas >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)	To compare 'proportions of advanced histologic features' and to 'determine whether there were	Observational cohort	People undergoing colonoscopic surveillance with	1. Histopathology of the index polyp 2. Location of the index	Prevalence of advanced histology and its association

Study	Aim	Study type	Population	Prognostic factors or surveillance programmes	Outcomes used for GRADE profile
	any risk factors for advanced histology in each patient group'		largest index polyp being less than 10 mm, in 2005, N = 5977	polyp	with the distal colon
Martinez et al. (2009)	To 'estimate absolute risks of metachronous advanced adenoma, colorectal cancer, and their combination (advanced colorectal neoplasia) and to identify patient characteristics and adenoma features that are associated independently with risk of these outcomes'	Meta-analysis from selected studies (not systematically identified)	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)	To 'identify predictive variables' and whether 'these risk factors of advanced pathology could also be used to predict the likely time interval to the development of metachronous adenomas of advanced pathology'	Observational cohort	People undergoing surveillance after 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.	To evaluate the incidence of	Systematic	Criterion for inclusion	14 studies, reported a	Risk factors for

Study	Aim	Study type	Population	Prognostic factors or surveillance programmes	Outcomes used for GRADE profile
(2006)	advanced adenomas at 3-year surveillance colonoscopy in high- and low-risk groups. Also to determine associated risk factors	review and meta-analysis	was people with a personal history of adenomas, N = 10,009 (but differs by analysis because of study inclusion)	total of 6 risk factors: 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	recurrent advanced adenomas

Two studies included in the meta-analyses were RCTs comparing different surveillance frequencies (Lund et al. 2001; Winawer et al. 1993b). Lund et al. compared six surveillance strategies for people with colonic adenomas: colonoscopy every 2 years or every 5 years, or flexible sigmoidoscopy every year, every 2 years, or every 5 years. The authors concluded that 'a surveillance interval of 5 years was as effective as shorter intervals in terms of cancer prevention'. However, it should be noted that the trial was stopped early because of lower rates of adenoma recurrence than expected, and therefore the trial was not powered to detect differences among the surveillance strategies. Winawer et al. compared two surveillance strategies in people with adenomatous polyps: two colonoscopies 1 and 3 years after adenoma removal and one colonoscopy 3 years after adenoma removal. The results showed that the relative risk of detecting any adenomas with two colonoscopies compared with one was 1.3 (95% confidence interval [CI] 1.1 to 1.6). However, the detection rate of advanced adenomas was the same for both strategies (3.3%; relative risk 1.0; 95% CI 0.5 to 2.2).

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

Quality assessment							Summary of findings			
Study	**Design**	**Limitations**	**Inconsistency**	**Directness**	**Imprecision**	**Other considerations**	**RR (95% CI)**			**Quality**
							Surveillance groups			
Detection of new adenomas by surveillance group										
Kronborg et al. (2006)	RCT	S*	N	N	S[†]	None	**B: 48 months (n = 340) vs A: 24 months (n = 331)**	**D: 12 months (n = 32) vs C: 6 months (n = 42)**	**F: 24 months (n = 103) vs E: 12 months (n = 97)**	Low
							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**	
Winawer et al. (1993b)	RCT	N	N	S[¥]	N	None	**2-exam: 1 and 3 years (n = 338) vs 1-exam: 3 years (n = 428)**			Moderate
							RR = 1.3 (1.1 to 1.6) p = 0.006			
Detection of new advanced[a] adenomas by surveillance group										
Kronborg et al. (2006)	RCT	S*	N	N	S[†]	None	**B: 48 months (n = 340) vs A: 24 months (n = 331)**	**D: 12 months (n = 32) vs C: 6 months (n = 42)**	**F: 24 months (n = 103) vs E: 12 months (n = 97)**	Low
							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**	
Winawer et al. (1993b)	RCT	N	N	S[¥]	N	None	**2-exam: 1 and 3 years (n = 338) vs 1-exam: 3 years (n = 428)**			Moderate
							RR =1.0 (0.5 to 2.2) **NS**			
Detection of colorectal cancer by surveillance group										
Kronborg et al. (2006)	RCT	S*	N	N	S[†]	None	**B: 48 months (n = 340) vs A: 24 months (n = 331)**	**D: 12 months (n = 32) vs C: 6 months (n = 42)**	**F: 24 months (n = 103) vs E: 12 months (n = 97)**	Low
							RR = 6.22 (1.06 to 117)[c]	RR = 0.82 (0.43 to 1.52) **NS**	RR = 0.88 (0.57 to 1.34) **NS**	
Lund et al. (2001)	RCT	S[b]	N	N	N/A	Underpowered for difference	Authors concluded that 'a surveillance interval of five years was as effective as shorter intervals in terms of cancer prevention'. No comparisons reported because of the lack of power.			Very low

						between strategies				
Adverse events										
Kronborg et al. (2006)	RCT	S*	N	N	N	None	**B: 48 months (n = 340) vs A: 24 months (n = 331)**	**D: 12 months (n = 32) vs C: 6 months (n = 42)**	**F: 24 months (n = 103) vs E: 12 months (n = 97)**	Moderate
							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	

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 population under surveillance was not stratified by risk for different strategies.
[†] 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.
[b] The trial was stopped early because of the low rate of adenoma recurrence.
[c] Therefore there is an increased risk for cancer progression (RR = 6.22) if surveillance is done after 48 months instead of 24 months.

GRADE profile 7: When and at what frequency should colonoscopic surveillance be offered to people with adenomas? 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 et al. (2008)	Multi-centre registry	S*	N	N	N	Sensitivity analysis done for misclassification[a] for prevalence	1–5 mm group: 1.7% (1.2 to 2.0)	Very low
							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)	Very low
							>10 mm group (p = 0.002)	
Risk factors for advanced metachronous neoplasia (advanced adenomas[b] and invasive cancer)								
Martinez et al. (2009)	Meta-analysis of 8 studies (6	S[c]	N	N	N	Patient level data used and confounders adjusted	Older age (p < 0.0001 for trend)	Low
							Male sex: OR = 1.40 (1.19 to 1.65)	
							Number and size of previous adenomas (p < 0.0001 for trend)	

Quality assessment							Summary of findings			
Study	**Design**	**Limitations**	**Inconsistency**	**Directness**	**Imprecision**	**Other considerations**	**R; RR; OR (95% CI)**			**Quality**
	RCTs)					by multivariate logistic regression	Presence of villous features: OR = 1.28 (1.07 to 1.52)			
							Proximal location: OR = 1.68 (1.43 to 1.98)			
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)			Moderate
							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			
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 multivariate logistic regression	Prp	Low risk[f]		High risk[g]
							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)
							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	N	N	N	N	None	RF	RR	RD	H
							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
							Dysplasi	HGD vs no HGD		

Quality assessment							Summary of findings				
Study	Design	Limitations	Inconsistency	Directness	Imprecision	Other considerations	R; RR; OR (95% CI)				Quality
							a	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 (see GRADE profiles 6 and 7)

2.5.8.1 Low to moderate quality evidence showed that the detection of new adenomas was higher at 1 and 3 years compared with 3 years alone.

2.5.8.2 Low to moderate quality evidence showed that the detection of new advanced adenomas tended to be the same at different surveillance frequencies.

2.5.8.3 Very low to low quality evidence showed that the detection of colorectal cancer was higher at 4 years compared with 2 years.

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

2.5.8.5 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 baseline colonoscopy were significant predictors for risk of new neoplasia.

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

2.5.8.7 Very low quality evidence that studied the risk associated with small adenomas and distal location showed that the prevalence of advanced histology[5] increased with the size of the polyp.

2.5.8.8 Very low quality evidence on 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 statistically significant in the 6–9 mm and >10 mm groups.

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

2.5.8.9 Low quality evidence showed that being older, being male, an increase in the number and size of previous adenomas, the presence of villous features and proximal location at baseline colonoscopy were significant predictors for advanced metachronous neoplasia (advanced adenomas and invasive cancer).

2.5.8.10 Moderate quality evidence showed that 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[6]. Men with large adenomas had a significantly higher risk than other people.

2.5.8.11 Moderate quality evidence showed that the time taken for advanced metachronous adenomas to develop in 5% of people at low risk[7] was10.4 years, in 10% it was12.2 years and in 20% it was 16.2 years.

2.5.8.12 Moderate quality evidence showed that the time taken for advanced metachronous adenomas to develop in 5% of people at high risk[8] was 0.5 years, in 10% it was 6.1 years and in 20% it was 15.6 years.

2.5.8.13 Moderate quality evidence showed that the risk for recurrent advanced adenomas[9] increased with increasing number and size of adenomas at baseline colonoscopy.

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

2.5.9 Evidence to recommendations

Because there was no direct evidence for surveillance strategies for the different subgroups of the population who had adenomas removed previously, the GDG made recommendations based on their risk of developing colorectal cancer, taking into account the significant risk factors from the available evidence. The GDG felt that there was enough evidence to stratify people who had previously had adenomas removed according to their risk of developing advanced neoplasia (advanced adenoma and colorectal cancer). It felt that the frequency of surveillance should be based on the risk assessment. The GDG felt that the evidence showed that only the number and size of the adenomas removed at baseline colonoscopy were consistent significant predictors for neoplasia and therefore should determine the risk state. Villous histology was also a significant predictor for advanced neoplasia, although the confidence intervals were wide (odds ratio 1.28, 95% CI 1.07 to 1.52) (Martinez et al. 2009). However, the GDG considered that because pathologists' classification of villous histology tends to vary, particularly for small biopsies, including this predictor 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.

Because there was very limited direct evidence on frequency of surveillance for different risk groups (Lund et al. 2001), the timing of surveillance was based on evidence relating to the incidence of advanced adenomas and colorectal cancer and risk for the disease as described above, and also RCTs with different surveillance frequencies without risk stratification (Kronborg et al. 2006; Winawer et al. 1993b).

Results from ongoing research on the long-term safety of people at low risk not having surveillance are expected to be reported in the next 2 years (Cairns et al. 2010). This will give valuable evidence for the future.

The GDG also made a recommendation about stopping surveillance. This was based on its expertise and knowledge.

2.5.10 Recommendations

Recommendation 1.1.7

Use the findings at adenoma removal to determine people's risk of developing colorectal cancer (see table 2).

Table 2 Risk of developing colorectal cancer in people with adenomas

Low risk:

- one or two adenomas smaller than 10 mm.

Intermediate risk:

- three or four adenomas smaller than 10 mm **or**
- one or two adenomas if one is10 mm or larger.

High risk:

- five or more adenomas smaller than 10 mm **or**
- three or more adenomas if one is 10 mm or larger.

Recommendation 1.1.8

Offer the appropriate colonoscopic surveillance strategy to people with adenomas, based on their risk of developing colorectal cancer (see table 2).

- Low risk: do not offer colonoscopic surveillance.
- Intermediate risk: offer colonoscopic surveillance at 3 years:
  - if low- or intermediate-risk adenomas are found, offer surveillance at 3 years
  - if high-risk adenomas are found, offer surveillance within 1 year
  - if there is one negative colonoscopy (that is, no adenomas are found) offer surveillance at 3 years
  - if there are two consecutive negative colonoscopies, stop surveillance (see recommendation 1.1.14).
- High risk: offer colonoscopic surveillance within 1 year:
  - if the colonoscopy is negative, or low- or intermediate-risk adenomas are found, offer surveillance at 3 years (with follow-up surveillance as for the intermediate-risk group)
  - if high-risk adenomas are found, offer surveillance within 1 year.

Recommendation 1.1.14

At each surveillance, discuss the potential benefits, limitations and risks of ongoing surveillance. Base a decision to stop surveillance on potential benefits for the person, their preferences and any comorbidities. Make the decision jointly with the person and if appropriate their family or carers.

2.6 Providing information and support

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 the review protocol, inclusion and exclusion criteria, see appendices 2 and 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 14 and detailed evidence tables are available in appendix 6.

The seven studies are:

- Rutter et al. (2006): a 58-question self-administered postal questionnaire with an 85.4% response rate.
- Thiis-Evensen et al. (1999b): a postal questionnaire studying the psychological 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): a study examining the effectiveness of visual illustrations in improving people's understanding of the preventative aim of flexible sigmoidoscopy screening.
- Makoul et al. (2009): a pretest–post-test study assessing a multimedia patient education programme that provides information about colorectal cancer and screening.
- Sequist et al. (2009): a RCT promoting colorectal cancer screening. The screening options in this study also looked at faecal occult blood testing.

- Miles et al. (2009): a postal survey examining the psychological impact of being assigned to colonoscopic surveillance after detection of adenomatous polyps.

Table 14 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. (1999b)	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 after 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 after previous colonoscopies
People's preference	
Sheikh et al. (2004)	Of people who had had a previous colonoscopy, 55% preferred this method for repeat screening, compared with only 30% of people who had never had a colonoscopy (p = 0.017) Of people who had had a previous sigmoidoscopy, 53% preferred this method for repeat screening, compared with only 33% of people who had never had a sigmoidoscopy, although the differences were not statistically significant
Thiis-Evensen et al. (1999b)	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. (2009)	A pretest–post-test multimedia patient education programme on colorectal cancer screening, which used graphics and audio, led to a significant increase in the 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)	A 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 mailings about 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% vs 5.2%; p = 0.10)
Psychological impact of surveillance	
Thiis-Evensen et al. (1999b)	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 polyps (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 (see table 14)

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

- *39% found bowel preparation difficult to take.*
- *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 this method for repeat screening, compared with only 30% of those who had never had a colonoscopy*
- *53% of those who had had a previous sigmoidoscopy preferred this method for repeat screening, 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 7.6% 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 a good understanding.*
- *The addition of the illustrations resulted in significantly better understanding, even after controlling for age, sex and socioeconomic status.*
- *A pretest–post-test 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 about 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 people attending the screening examination than in the control group.*

- *People offered surveillance reported lower psychological distress and anxiety than people with either no polyps 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 normal day-to-day 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 on 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 may not be generalisable to all people with IBD and/or adenomas and this should be considered when reading the evidence. Recognising the limitations of the evidence and using the experience of the GDG members, recommendations were made on information provision for people considering colonoscopic surveillance.

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

2.6.6 Recommendations

Recommendation 1.1.12

Discuss the potential benefits, limitations and risks with people who are considering colonoscopic surveillance including:

- early detection and prevention of colorectal cancer **and**
- quality of life and psychological outcomes.

Recommendation 1.1.13

Inform people who have been offered colonoscopy, CTC, or barium enema about the procedure, including:

- bowel preparation
- impact on everyday activities
- sedation
- potential discomfort
- risk of perforation and bleeding.

Recommendation 1.1.14

At each surveillance, discuss the potential benefits, limitations and risks of ongoing surveillance. Base a decision to stop surveillance on potential benefits for the person, their preferences, and any comorbidities. Make the decision jointly with the person and if appropriate their family or carers.

Recommendation 1.1.15

If there are any findings at surveillance that need treatment or referral, discuss the options with the person and if appropriate their family or carers.

Recommendation 1.1.16

Throughout the surveillance programme, give people and their family 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 should include illustrations.

3 Research recommendations

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

3.1 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 evidence from RCTs 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 after adenoma removal. RCTs should be undertaken to determine the comparative effect of different surveillance programmes on survival (preferably with a follow-up of 5 years and longer) and quality of life in people at increased risk of colorectal cancer because of IBD or adenomas. Such trials should also assess any differential effects associated with risk category (as defined in this guideline).

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

What is the natural history of progression to colorectal cancer in people with IBD or adenomas?

Why this is important

There is very limited evidence on the natural history of progression to colorectal cancer, and how factors such as extent of disease, grade of dysplasia and adenoma-related factors affect progression. Long-term studies (ideally with a follow-up of 20 years or longer) should be conducted to

determine the natural history of colorectal cancer in people with IBD or adenomas.

3.3 Effectiveness of biomarkers for determining level of risk of colorectal cancer

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

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 people with IBD or adenomas. Research should be undertaken to identify the biomarkers that are predictive of colorectal cancer, if any can improve levels of early detection, and how they can be used to improve risk stratification.

3.4 Adenoma types and risk of colorectal cancer

Does the risk of colorectal cancer depend on the type of adenoma?

Why this is important

There is no high quality evidence on the association between risk of colorectal cancer and some adenoma types (sessile, hyperplastic non-adenomatous). Research should be undertaken to determine if the level of risk of colorectal cancer depends on the adenoma type.

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 in people with IBD and adenomas.

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 October 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

Askling J, Dickman PW, Karlén P et al. (2001) Family history as a risk factor for colorectal cancer in inflammatory bowel disease. Gastroenterology 120 (6): 1356–62

Atkin WS, Saunders BP (2002) Surveillance guidelines after removal of colorectal adenomatous polyps. Gut 51(Suppl. V): v6–v9

Brentnall TA, Haggitt RC, Rabinovitch PS et al. (1996) Risk and natural history of colonic neoplasia in patients with primary sclerosing cholangitis and ulcerative colitis. Gastroenterology 110: 331–8

Brooker JC, Saunders BP, Shah SG et al. (2002) Total colonic dye-spray increases the detection of diminutive adenomas during routine colonoscopy: a randomized controlled trial. Gastrointestinal Endoscopy 56: 333–8

Broome U, Lindberg G, Lofberg R (1992) Primary sclerosing cholangitis in ulcerative colitis – a risk factor for the development of dysplasia and DNA aneuploidy? Gastroenterology 102: 1877–80

Broome U, Lofberg R, Veress B et al. (1995) Primary sclerosing cholangitis and ulcerative colitis: evidence for increased neoplastic potential. Hepatology 22: 1404–8

Brotherstone H, Miles A, Robb KA et al. (2006) The impact of illustrations on public understanding of the aim of cancer screening. Patient Education and Counseling 63: 328–35

Brown SR, Baraza W, Hurlstone P (2007) Chromoscopy versus conventional endoscopy for the detection of polyps in the colon and rectum [review; 36 refs]. Cochrane Database of Systematic Reviews CD006439

Cairns SR, Scholefield JH, Steele RJ et al. and the British Society of Gastroenterology and the Association of Coloproctology for Great Britain and Ireland (2010) Guideline for colorectal cancer screening and surveillance in moderate and high risk groups (update from 2002). Gut 59: 666–90

Choi PM, Nugent FW, Schoetz DJ et al. (1993) Colonoscopic surveillance reduces mortality from colorectal cancer in ulcerative colitis. Gastroenterology 105: 418–24

Choi PM, Zelig MP (1994) Similarity of colorectal cancer in Crohn's disease and ulcerative colitis: implications for carcinogenesis and prevention. Gut 35: 950–4

Collins PD, Mpofu C, Watson AJ et al. (2006) Strategies for detecting colon cancer and/or dysplasia in patients with inflammatory bowel disease [update of Cochrane Database of Systematic Reviews 2004 issue 2: CD000279; PMID: 15106148] [review; 90 refs]. Cochrane Database of Systematic Reviews CD000279

Dekker E, van den Broek FJC, Reitsma JB et al. (2007) Narrow-band imaging compared with conventional colonoscopy for the detection of dysplasia in patients with longstanding ulcerative colitis. Endoscopy 39: 216–21

Department of Health (2010) National Schedule of Reference Costs 2008–09 for NHS Trusts and PCTs combined. Available from: www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_111591

Downs SH, Black N (1998) The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. Journal of Epidemiology and Community Health 52: 377–84

Eaden JA, Abrams KR, Mayberry JF (2001) The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut 48: 526–35

Florin TH, Pandeya N, Radford-Smith GL (2004) Epidemiology of appendicectomy in primary sclerosing cholangitis and ulcerative colitis: its influence on the clinical behaviour of these diseases. Gut 53: 973–9

Friedman S, Rubin PH, Bodian C et al. (2001) Screening and surveillance colonoscopy in chronic Crohn's colitis. Gastroenterology 120: 820–6

Gilat T, Fireman Z, Grossman A et al. (1988) Colorectal cancer in patients with ulcerative colitis. A population study in central Israel. Gastroenterology 94: 870–7

Gupta RB, Harpaz N, Itzkowitz S et al. (2007) Histologic inflammation is a risk factor for progression to colorectal neoplasia in ulcerative colitis: a cohort study. Gastroenterology 133: 1099–105

Gyde SN, Prior P, Allan RN et al. (1988) Colorectal cancer in ulcerative colitis: a cohort study of primary referrals from three centres. Gut 29: 206–17

Hendriksen C, Kreiner S, Binder V (1985) Long term prognosis in ulcerative colitis – based on results from a regional patient group from the county of Copenhagen. Gut 26: 158–63

Jess T, Gamborg M, Matzen P et al. (2005) Increased risk of intestinal cancer in Crohn's disease: a meta-analysis of population-based cohort studies. American Journal of Gastroenterology 100: 2724–9

Jess T, Loftus EV Jr, Velayos FS et al. (2006) Incidence and prognosis of colorectal dysplasia in inflammatory bowel disease: a population-based study from Olmsted County, Minnesota. Inflammatory Bowel Diseases 12: 669–76

Jess T, Loftus EV Jr, Velayos FS et al. (2007) Risk factors for colorectal neoplasia in inflammatory bowel disease: a nested case–control study from Copenhagen county, Denmark and Olmsted county, Minnesota. American Journal of Gastroenterology 102: 829–36

Jørgensen OD, Kronborg O, Fenger C. (1993) The Funen Adenoma Follow-up Study. Incidence and death from colorectal carcinoma in an adenoma surveillance program. Scandinavian Journal of Gastroenterology 28: 869–74

Jørgensen OD, Kronborg O, Fenger C et al. (2007) Influence of long-term colonoscopic surveillance on incidence of colorectal cancer and death from the disease in patients with precursors (adenomas). Acta Oncologica 46: 355–60

Karlén P, Kornfeld D, Brostrom O et al. (1998) Is colonoscopic surveillance reducing colorectal cancer mortality in ulcerative colitis? A population based case control study. Gut 42: 711–4

Kiesslich R, Fritsch J, Holtmann M et al. (2003) Methylene blue-aided chromoendoscopy for the detection of intraepithelial neoplasia and colon cancer in ulcerative colitis. Gastroenterology 124: 880–8

Kiesslich R, Goetz M, Lammersdorf K et al. (2007) Chromoscopy-guided endomicroscopy increases the diagnostic yield of intraepithelial neoplasia in ulcerative colitis. Gastroenterology 132: 874–82

Kronborg O, Jorgensen OD, Fenger C et al. (2006) Three randomized long-term surveillance trials in patients with sporadic colorectal adenomas. Scandinavian Journal of Gastroenterology 41: 737–43

Kvist N, Jacobsen O, Kvist HK et al. (1989) Malignancy in ulcerative colitis. Scandinavian Journal of Gastroenterology 24: 497–506

Langholz E, Munkholm P, Davidsen M et al. (1992) Colorectal cancer risk and mortality in patients with ulcerative colitis. Gastroenterology 103: 1444–51

Lapalus M-G, Helbert T, Napoleon B et al. (2006) Does chromoendoscopy with structure enhancement improve the colonoscopic adenoma detection rate? Endoscopy 38: 444–8

Lashner BA, Kane SV, Hanauer SB (1990) Colon cancer surveillance in chronic ulcerative colitis: historical cohort study. American Journal of Gastroenterology 85: 1083–7

Le RM, Coron E, Parlier D et al. (2006) High resolution colonoscopy with chromoscopy versus standard colonoscopy for the detection of colonic neoplasia: a randomized study. Clinical Gastroenterology and Hepatology 4: 349–54

Lennard-Jones JE, Melville DM, Morson BC et al. (1990) Precancer and cancer in extensive ulcerative colitis: findings among 401 patients over 22 years. Gut 31: 800–6

Lieberman DA, Moravec M, Holub J et al. (2008) Polyp size and advanced histology in patients undergoing colonoscopy screening: implications for CT colonography [abstract]. Gastroenterology 135 (4): 1100–5

Lieberman DA, Weiss DG, Harford WV et al. (2007) Five-year colon surveillance after screening colonoscopy [see comment]. Gastroenterology 133: 1077–85

Loftus EV Jr, Harewood GC, Loftus CG et al. (2005) PSC-IBD: a unique form of inflammatory bowel disease associated with primary sclerosing cholangitis. Gut 54: 91–6

Lund JN, Scholefield JH, Grainge MJ et al. (2001) Risks, costs, and compliance limit colorectal adenoma surveillance: lessons from a randomised trial. Gut 49: 91–96

Makoul G, Cameron KA, Baker DW et al. (2009) A multimedia patient education program on colorectal cancer screening increases knowledge and willingness to consider screening among Hispanic/Latino patients. Patient Education and Counseling 76: 220–6

Manning AP, Bulgim OR, Dixon MF et al. (1987) Screening by colonoscopy for colonic epithelial dysplasia in inflammatory bowel disease. Gut 28: 1489–94

Marion JF, Waye JD, Present DH et al. (2008) Chromoendoscopy-targeted biopsies are superior to standard colonoscopic surveillance for detecting dysplasia in inflammatory bowel disease patients: a prospective endoscopic trial. American Journal of Gastroenterology 103: 2342–9

Martinez ME, Baron JA, Lieberman DA et al. (2009) A pooled analysis of advanced colorectal neoplasia diagnoses after colonoscopic polypectomy. Gastroenterology 136 (3):832–41

Miles A, Atkin WS, Kralj-Hans I et al. (2009) The psychological impact of being offered surveillance colonoscopy following attendance at colorectal screening using flexible sigmoidoscopy. Journal of Medical Screening 16: 124–30

Mulhall BP, Veerappan GR, Jackson JL (2005) Meta-analysis: computed tomographic colonography. Annals of Internal Medicine 142: 635–50

Nuako KW, Ahlquist DA, Mahoney DW et al. (1998) Familial predisposition for colorectal cancer in chronic ulcerative colitis: a case–control study. Gastroenterology 115: 1079–83

Nuako KW, Ahlquist DA, Sandborn WJ et al. (1998) Primary sclerosing cholangitis and colorectal carcinoma in patients with chronic ulcerative colitis: a case–control study. Cancer 82: 822–6

Nusko G, Mansmann U, Kirchner T et al. (2002) Risk related surveillance following colorectal polypectomy Gut 51: 424–8

Odze RD, Farraye FA, Hecht JL et al. (2004) Long-term follow-up after polypectomy treatment for adenoma-like dysplastic lesions in ulcerative colitis [abstract]. Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association 2 (7): 534–41

Ransohoff DF, Lang CA, Kuo HS (1991) Colonoscopic surveillance after polypectomy: considerations of cost effectiveness. Annals of Internal Medicine 114 (3): 177–82

Rex DK, Helbig CC (2007) High yields of small and flat adenomas with high-definition colonoscopes using either white light or narrow band imaging. Gastroenterology 133: 42–7

Rutter MD, Saunders BP, Schofield G et al. (2004a) Pancolonic indigo carmine dye spraying for the detection of dysplasia in ulcerative colitis [see comment]. Gut 53: 256–60

Rutter M, Saunders B, Wilkinson K et al. (2004b) Severity of inflammation is a risk factor for colorectal neoplasia in ulcerative colitis. Gastroenterology 126: 451–9

Rutter MD, Saunders BP, Wilkinson KH et al. (2004c) Cancer surveillance in longstandinq ulcerative colitis: endoscopic appearances help predict cancer risk. Gut 53: 1813–6

Rutter MD, Saunders BP, Wilkinson KH et al. (2006a) Intangible costs and benefits of ulcerative colitis surveillance: a patient survey. Diseases of the Colon and Rectum 49: 1177–83

Rutter MD, Saunders BP, Wilkinson KH et al. (2006b) Thirty-year analysis of a colonoscopic surveillance program for neoplasia in ulcerative colitis. Gastroenterology 130: 1030–8

Saini SD, Kim HM, Schoenfeld P (2006) Incidence of advanced adenomas at surveillance colonoscopy in patients with a personal history of colon adenomas: a meta-analysis and systematic review. Gastrointestinal Endoscopy 64: 614–26

Schunemann HJ, Oxman AD, Brozek J et al. (2008) Grading quality of evidence and strength of recommendations for diagnostic tests and strategies. BMJ 336: 1106–10

Sequist TD, Zaslavsky AM, Marshall R et al. (2009) Patient and physician reminders to promote colorectal cancer screening: a randomized controlled trial. Archives of Internal Medicine 169: 364–71

Sheikh RA, Kapre S, Calof OM et al. (2004) Screening preferences for colorectal cancer: a patient demographic study. Southern Medical Journal 97: 224–30

Soetikno RM, Lin OS, Heidenreich PA et al. (2002) Increased risk of colorectal neoplasia in patients with primary sclerosing cholangitis and ulcerative colitis: a meta-analysis. Gastrointestinal Endoscopy 56: 48–54

Stewenius J, Adnerhill I, Anderson H et al. (1995) Incidence of colorectal cancer and all cause mortality in non-selected patients with ulcerative colitis and indeterminate colitis in Malmo, Sweden. International Journal of Colorectal Disease 10: 117–22

Tappenden P, Eggington S, Nixon R et al. (2004) Colorectal cancer screening options appraisal: cost-effectiveness, cost-utility and resource impact of alternative screening options for colorectal cancer. Report to the English Bowel Cancer Screening Work Group.

Thiis-Evensen E, Hoff GS, Sauar J et al. (1999a) Population-based surveillance by colonoscopy: effect on the incidence of colorectal cancer: Telemark Polyp Study I. Scandinavian Journal of Gastroenterology 34: 414–20

Thiis-Evensen E, Wilhelmsen I, Hoff GS et al. (1999b) The psychologic effect of attending a screening program for colorectal polyps. Scandinavian Journal of Gastroenterology 34: 103–9

Thomas T, Abrams KA, Robinson RJ et al. (2007) Meta-analysis: cancer risk of low-grade dysplasia in chronic ulcerative colitis. Alimentary Pharmacology and Therapeutics 25: 657–68

van den Broek FJ, Reitsma JB, Curvers WL et al. (2009) Systematic review of narrow-band imaging for the detection and differentiation of neoplastic and nonneoplastic lesions in the colon. Gastrointestinal Endoscopy 69(1): 124–35

Velayos FS, Loftus J, Jess T et al. (2006) Predictive and protective factors associated with colorectal cancer in ulcerative colitis: a case–control study. Gastroenterology 130: 1941–9

Winawer SJ, Zauber AG, Ho MN et al. (1993a) Prevention of colorectal cancer by colonoscopic polypectomy. The New England Journal of Medicine 329: 1977–1981

Winawer SJ, Zauber AG, O'Brien MJ et al. (1993b) Randomized comparison of surveillance intervals after colonoscopic removal of newly diagnosed adenomatous polyps. New England Journal of Medicine 328: 901–6

Winawer SJ, Stewart ET, Zauber AG et al. (2000) A comparison of colonoscopy and double-contrast barium enema for surveillance after polypectomy. New England Journal of Medicine 342: 1766–72

7.2 Glossary

Adenoma

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

Baseline colonoscopy

A colonoscopic examination in which measurements are taken (after a run-in period where applicable). The results of subsequent colonoscopies can be compared with the baseline colonoscopy.

Bowel preparation

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

Chromoscopy

Diagnosis of gastric or renal function by the administration of dyes and subsequent examination of the stomach contents or the urine.

Colitis

Inflammation of the part of the large intestine (colon) that extends from the caecum to the rectum.

Colonoscopy

The endoscopic examination of the large intestine (colon) and the distal part of the small bowel.

Computed tomographic colonography

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

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.

Crohn's disease

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

Diminutive lesion

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

Drop out (of surveillance)

Stopping surveillance after meeting the exit criteria.

Dysplasia

Abnormal development or growth of tissues, organs or cells. Dysplasia can be low grade or high grade. High-grade dysplasia increases the chances of cancer developing and spreading.

Follow-up

Observation over a period of time of a person, group or initially defined population, to observe changes in health status or health-related variables.

Incremental analysis

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

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.

Index colonoscopy

A ratio or other number derived from a series of colonoscopies and used as an indicator or measure.

Inflammation

A local response to cellular injury that is marked by capillary dilation, leukocytic infiltration, redness, heat, pain, swelling, and often loss of function. Inflammation helps to eliminate toxic substances and damaged tissue.

Inflammatory bowel disease

A group of inflammatory conditions of the colon and small intestine. In this guideline, inflammatory bowel disease refers to Crohn's disease and ulcerative colitis.

Life-years gained

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

Malignant

A growth that tends to spread into nearby normal tissue and travel to other parts of the body..

Mucosa

The thin layer (mucous membrane) that 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.

Narrow band imaging

The use of blue and green light at certain wavelengths to examine capillaries, veins and other tissues. It allows these to be seen more easily in and below the mucosa, or lining, of the gastrointestinal tract.

Number needed to treat to benefit (NNTB)

NNTB is an epidemiological measure used in assessing the effectiveness of a healthcare 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 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.

Proctitis

Inflammation of the anus and rectum.

Sedation

Inducing a relaxed state, usually by using sedatives.

Sensitivity

In diagnostic testing, sensitivity refers to the chance of having a positive test result in a person who has a certain 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 negative’) – 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 way 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. For a 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. For a multiway simple sensitivity analysis (scenario analysis) two or more parameters are varied at the same time and the overall effect on the results is evaluated. For a threshold sensitivity analysis the critical value of parameters above or below which the conclusions of the study will change are identified. For a 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

A minimally invasive medical examination of the large intestine from the rectum through to 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, specificity refers to the chance of having a negative test result given that a person does not have a certain 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 positive’) – 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.

7.3 Abbreviations

Abbreviation	Meaning
AA	Advanced adenoma
AJCC	American Joint Committee on Cancer
ARR	Absolute risk reduction
CEAC	Cost effectiveness acceptability curve
CI	Confidence interval
CRC	Colorectal cancer
CT	Computed tomography
CTC	Computed tomographic colonography
DA	Dukes' A
DB	Dukes' B
DC	Dukes' C
DCBE	Double-contrast barium enema
DD	Dukes' D
FH	Family history
FSIG	Flexible sigmoidoscopy
GDG	Guideline development group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HGD	High-grade dysplasia
HR	Hazard ratio
IBD	Inflammatory bowel disease
ICER	Incremental cost-effectiveness ratio
LGD	Low-grade dysplasia
NAA	Non-advanced adenoma
NBI	Narrow band imaging
NNTB	Number needed to treat to benefit
NNTH	Number needed to treat to harm
NS	Not significant
OR	Odds ratio
PSC	Primary sclerosing cholangitis
QALY	Quality-adjusted life year
RCT	Randomised clinical trial
RD	Risk difference
RF	Risk factor
RR	Relative risk
SD	Standard deviation
SIR	Standardised incidence ratio
UC	Ulcerative colitis
WMD	Weighted mean difference

8 Contributors

8.1 The Guideline Development Group

Peter Howdle

Emeritus Professor and Chair of the Guideline Development Group

Wendy Atkin

Professor of Epidemiology, Imperial College London

Matthew Rutter

Consultant Gastroenterologist, University Hospital of North Tees

Janusz Jankowski

Professor of Gastroenterology, University Hospitals of Leicester NHS Trust

Bruce Fox

Consultant Gastrointestinal Radiologist, Derriford Hospital, Devon

Carol Makin

Consultant General and Colorectal Surgeon, Wirral University Teaching Hospital

Julie D'Silva

Consultant Endoscopist, Clinical Lead for Quality and Assurance Endoscopy Services, Rotherham General Hospital NHS Trust

Marco Novelli

Professor of Histopathology, University College Hospital NHS Foundation Trust London

Tracey Cole

Patient member

Elaine Trump

Patient member

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.

Beth Shaw

Technical Adviser

Prashanth Kandaswamy

Technical Adviser (Health Economics)

Tarang Sharma

Technical Analyst, 2009–2010

Jonathan Nyong

Assistant Technical Analyst, 2009–2010

Kim Jeong

Technical Analyst (Health Economics)

Yaminah Rajput

Assistant Technical Analyst (Health Economics)

Victoria Kelly

Project Manager

Michael Heath

Programme Manager

Louise Foster

Information Specialist

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.

Professor Mike Drummond - Chair

Director, Centre for Health Economics, University of York

Dr Graham Archard

General Practitioner, Dorset

Ms Catherine Arkley

Lay member

Dr David Gillen

Medical Director, Wyeth Pharmaceutical

Dr Ruth Stephenson

Consultant in Anaesthetics Clinical Ethics Lead, NHS Grampian

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:

National Institute for Health and Clinical Excellence (2010) Colonoscopic surveillance for prevention of colorectal cancer in patients with ulcerative colits, Crohn's disease or adenomas. London: National Institute for Health and Clinical Excellence. Available from: www.nice.org.uk/guidance/CG[XX]