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

APPENDICES
Part 1

Appendix 1 – Scope

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Part 2 Appendix 7 and 8 – Health economic evaluation
Appendix 1 – Scope

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Colonoscopic surveillance for prevention of colorectal cancer in people with ulcerative colitis, Crohn’s disease or adenomas.

1.1 Short title

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

2 The remit

The Department of Health has asked NICE: ‘To produce a short clinical guideline on colonoscopic surveillance for patients with ulcerative colitis, Crohn’s disease and polyps to prevent colorectal cancer.’

3 Clinical need for the guideline

3.1 Epidemiology

a) 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 people diagnosed with colorectal cancer survive for at least 5 years after diagnosis.

b) Adults with inflammatory bowel disease (IBD: ulcerative colitis or Crohn’s disease) or with polyps have a higher risk of developing colorectal cancer than the general population. Colonoscopic surveillance can be used for people in these high-risk groups to detect any problems early and potentially prevent progression to colorectal cancer.
c) Polyps can be either precancerous (neoplastic adenomas) or non-precancerous (non-neoplastic, including hyperplastic polyps). Strong evidence suggests that detecting and removing adenomas reduces the risk of cancer. Small polyps are rarely malignant and are unlikely to progress to invasive cancers.

d) The prevalence of ulcerative colitis is approximately 100 to 200 per 100,000 and the annual incidence is 10 to 20 per 100,000 respectively. The risk of 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.

e) The prevalence of Crohn's disease is 50 to 100 per 100,000 and the annual incidence is 5 to 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 for the same extent of colonic involvement.

3.2 Current practice

a) In 2002, the British Society of Gastroenterology (BSG) issued guidelines for surveillance after removal of adenomatous polyps. These recommend that the frequency of post-operative surveillance should depend on the size and number of adenomas removed.

b) The 2002 BSG guidance recommended colonoscopic surveillance for IBD should start 8 to 10 years after onset of extensive colitis. They recommended surveillance every 3 years during the 2nd decade of disease, every 2 years for the 3rd decade and annually from the 4th decade onwards. For left-sided disease they recommended colonoscopy should be started after 15 to 20 years of disease and repeated every 5 years, with flexible sigmoidoscopy in the interim years. The guidance recommended annual surveillance in patients with primary sclerosing cholangitis (PSC) because of their higher risk for colorectal neoplasia.
c) Guidelines from the BSG in 2004 suggested that people with IBD should discuss with their clinical team whether colonoscopic surveillance is appropriate for them but should comply with the 2002 guidelines.

d) Updated BSG Guidelines for polyps and IBD are being developed at the moment but due to variations in current practice, there is a need for an evidence-based national clinical guideline on colonoscopic surveillance in these high-risk groups.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, ‘Further information’).

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

a) Adults (18 years and older) with IBD (defined as ulcerative colitis or Crohn's disease involving the large bowel).

b) Adults with polyps (including adenomas) in the colon or rectum.

4.1.2 Groups that will not be covered

a) Children (younger than 18 years).

b) Adults with newly diagnosed or relapsed adenocarcinoma of the colon or rectum.

c) Adults with polyps that have previously been treated for colorectal cancer.
d) Adults with a genetic familial history of colorectal cancer: hereditary non-polyposis colorectal cancer.

e) Adults with a familial history of polyposis syndromes: familial adenomatous polyposis.

4.2 **Healthcare setting**

a) Primary care.

b) Secondary care.

4.3 **Clinical management**

4.3.1 **Key clinical issues that will be covered**

a) Colonoscopic surveillance (using conventional colonoscopy or chromoscopy) for prevention and early detection of colorectal cancer compared with:

- no surveillance
- surveillance using other methods, such as flexible sigmoidoscopy, double-contrast barium enema, computed tomographic colonography, and tri-modal imaging (high resolution white light endoscopy, narrow-band imaging and auto-fluorescence imaging).

b) Initiation of surveillance and the frequency of ongoing surveillance (considering factors including duration and extent of condition, number, size and location of polyps).

c) Information and support needs of people undergoing or considering undergoing colonoscopic surveillance.

4.3.2 **Clinical issues that will not be covered**

a) Diagnosis and assessment of IBD or polyps.

b) Diagnosis and management of colorectal cancer.
4.4 **Main outcomes**

a) Progression to colorectal cancer

b) Stage at presentation.

c) Progression or regression of dysplasia at most recent follow-up of IBD.

d) Overall mortality or survival.

e) Reported adverse effects of colonoscopic surveillance techniques.

f) Health-related quality of life (related to colonoscopic surveillance).

g) Resource use and costs.

4.5 **Economic aspects**

Developers will take into account both clinical and cost-effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see 'Further information').

4.6 **Status**

4.6.1 **Scope**

This is the consultation draft of the scope. The consultation dates are 28 October to 25 November 2009.

4.6.2 **Timing**

The development of the guideline recommendations will begin in January 2010.
5 Related NICE guidance

5.1 Published guidance

5.1.1 NICE guidance to be updated

None.

5.1.2 NICE guidance to be incorporated

This guideline will incorporate the following NICE guidance:


5.1.3 Other related NICE guidance


5.2 Guidance under development

NICE is currently developing the following related guidance (details available from the NICE website):

- Diagnosis and management of colorectal cancer. NICE clinical guideline. Publication expected October 2011.

6 Further information

Information on the guideline development process is provided in:

- ‘How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS’
• ‘The guidelines manual’.

These are available from the NICE website (www.nice.org.uk/guidelinesmanual). Information on the progress of the guideline will also be available from the NICE website (www.nice.org.uk/guidelinesmanual).
Appendix 2 – Review questions and review protocol

KEY CLINICAL QUESTIONS

Review question 1:
• Is colonoscopic surveillance for prevention and/or early detection of colorectal cancer in adults with inflammatory bowel disease (IBD) or polyps clinically effective compared with no surveillance?

Review question 2:
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])?

Review question 3:
• When should colonoscopic surveillance be started and what should be the frequency of surveillance?

Review question 4:
• What are the information and support needs of people, or carers of people undergoing or considering undergoing colonoscopic surveillance?
Review protocol for colonoscopic surveillance for patients with ulcerative colitis, Crohn’s colitis or polyps in the prevention colorectal cancer.

**KEY CLINICAL QUESTION 1**

<table>
<thead>
<tr>
<th>Details</th>
<th>Notes and status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review question 1</td>
<td></td>
</tr>
<tr>
<td>Is colonoscopic surveillance for prevention and/or early detection of colorectal cancer in adults with inflammatory bowel disease or polyps clinically effective compared with no surveillance?</td>
<td></td>
</tr>
<tr>
<td>Objective(s)</td>
<td>To determine the safety and effectiveness of colonoscopic surveillance in the prevention of colorectal cancer in high risk groups.</td>
</tr>
<tr>
<td>Criteria for considering studies</td>
<td>PICO</td>
</tr>
<tr>
<td>Population</td>
<td>Adults with ulcerative colitis, Crohn’s colitis/disease and polyps (including adenomas) in the colon or rectum.</td>
</tr>
<tr>
<td>Intervention(s)</td>
<td>Colonoscopic surveillance using:</td>
</tr>
<tr>
<td></td>
<td>• conventional colonoscopy or</td>
</tr>
<tr>
<td></td>
<td>• chromoscopy.</td>
</tr>
<tr>
<td>Comparator(s)</td>
<td>No surveillance</td>
</tr>
<tr>
<td>Outcome(s)</td>
<td>h) Progression to colorectal cancer and stage at presentation.</td>
</tr>
<tr>
<td></td>
<td>i) Progression or regression of dysplasia/polyps at most recent follow-up in IBD</td>
</tr>
<tr>
<td></td>
<td>j) Overall mortality and survival</td>
</tr>
<tr>
<td></td>
<td>k) Reported adverse effects of colonoscopic surveillance techniques.</td>
</tr>
<tr>
<td></td>
<td>l) Health related quality of life.</td>
</tr>
<tr>
<td></td>
<td>m) Resource use and costs.</td>
</tr>
</tbody>
</table>
**KEY CLINICAL QUESTION 2A**

<table>
<thead>
<tr>
<th>Details</th>
<th>Notes and status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review question 2</td>
<td>Which colonoscopic surveillance technique (using conventional colonoscopy) for prevention and/or early detection of colorectal cancer in adults with IBD or polyps is more clinically effective compared with other methods of surveillance (flexible sigmoidoscopy [FSIG], double-contrast barium enema [DCBE], computed tomographic colonography [CTC], tri-modal imaging [high-resolution white light endoscopy, narrow-band imaging [NBI] and auto-fluorescence imaging)?</td>
</tr>
<tr>
<td>Objective(s)</td>
<td>To determine the safety and effectiveness of colonoscopic surveillance compared with other surveillance techniques in the prevention of colorectal cancer in high-risk groups.</td>
</tr>
<tr>
<td>Criteria for considering studies</td>
<td>PICO</td>
</tr>
<tr>
<td>Population</td>
<td>Adults with ulcerative colitis, Crohn’s colitis/disease and polyps (including adenomas) in the colon or rectum.</td>
</tr>
<tr>
<td>Intervention(s)</td>
<td>Colonoscopic surveillance using conventional colonoscopy</td>
</tr>
<tr>
<td>Comparator(s)</td>
<td>Surveillance using other methods (flexible sigmoidoscopy [FSIG], double-contrast barium enema [DCBE], computed tomographic colonography [CTC], tri-modal imaging: narrow-band imaging, high-resolution white light endoscopy and auto-fluorescence imaging</td>
</tr>
<tr>
<td>Outcome(s)</td>
<td>n) Progression to colorectal cancer and stage at presentation.</td>
</tr>
<tr>
<td></td>
<td>o) Progression or regression of dysplasia/polyps at most recent follow up in IBD.</td>
</tr>
<tr>
<td></td>
<td>p) Overall mortality and survival.</td>
</tr>
<tr>
<td></td>
<td>q) Reported adverse effects of colonoscopic</td>
</tr>
</tbody>
</table>
surveillance techniques.

r) Health-related quality of life.
s) Resource use and costs.

How to be searched
As per the Guidelines Manual. No additional databases are required.
Date restriction: none.
Language restriction: English language.
Study design: systematic reviews, RCTs and back-to-back clinical trials.

Review strategy GRADE profiles

KEY CLINICAL QUESTION 2B

Details
Review question 2 Is colonoscopic surveillance with a dye (chromoscopy) for prevention and/or early detection of colorectal cancer clinically effective compared with conventional colonoscopy?

Objective(s) To determine the safety and effectiveness of colonoscopic surveillance compared with other surveillance techniques in the prevention of colorectal cancer in high-risk groups.

Criteria for considering studies PICO

Population Adults with ulcerative colitis, Crohn’s colitis/disease or polyps (including adenomas) in the colon or rectum.

Intervention(s) Colonoscopic surveillance using chromoscopy

Comparator(s) Conventional colonoscopy

Outcome(s) t) Progression to colorectal cancer and stage at presentation.
   u) Progression or regression of dysplasia/polyps at most recent follow-up in IBD.
   v) Overall mortality and survival.
   w) Reported adverse effects of colonoscopic surveillance techniques.
   x) Health-related quality of life.
   y) Resource use and costs.
How to be searched

As per the Guidelines Manual. No additional databases are required.
Date restriction: none.
Language restriction: English language.
Study design: systematic reviews, RCTs and back-to-back clinical trials.

Review strategy
GRADE profiles

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**KEY CLINICAL QUESTION 3**

<table>
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<tr>
<th>Details</th>
<th>Notes and status</th>
</tr>
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<tbody>
<tr>
<td><strong>Review question 3</strong></td>
<td>When should colonoscopic surveillance be started and what should be the frequency of surveillance?</td>
</tr>
<tr>
<td><strong>Objective(s)</strong></td>
<td>To determine when surveillance should be started and how frequently should it be done for the techniques.</td>
</tr>
<tr>
<td><strong>Criteria for considering studies</strong></td>
<td>PICO</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>Adults with ulcerative colitis, Crohn’s colitis/disease and polyps (including adenomas) in the colon or rectum.</td>
</tr>
</tbody>
</table>
| **Intervention(s)** | Colonoscopic surveillance using:  
- conventional colonoscopy or  
- chromoscopy |
| **Comparator(s)** | • No surveillance  
• Surveillance using other methods (flexible sigmoidoscopy [FSIG], double-contrast barium enema [DCBE], computed tomographic colonography [CTC], tri-modal imaging [high-resolution white-light endoscopy, narrow-band imaging, and auto-fluorescence imaging]) |
| **Outcome(s)** | z) Factors including: extent and duration of disease, size, number, site and type of polyps/lesions.  
aa) Progression to colorectal cancer and stage at presentation.  
bb) Overall mortality and survival. |
**KEY CLINICAL QUESTION 4**

<table>
<thead>
<tr>
<th>Details</th>
<th>Notes and status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review question 4</td>
<td>What are the information and support needs of people or the carers of people undergoing or considering undergoing colonoscopic surveillance?</td>
</tr>
<tr>
<td>Objective(s)</td>
<td>To determine information and support needs for patients and carers.</td>
</tr>
<tr>
<td>Criteria for considering studies</td>
<td>PICO</td>
</tr>
<tr>
<td>Population</td>
<td>Adults with ulcerative colitis, Crohn's colitis/disease and polyps (including adenomas) in the colon or rectum.</td>
</tr>
</tbody>
</table>
| Intervention(s) | Colonoscopic surveillance using:  
• conventional colonoscopy or  
• chromoscopy  
Comparator(s) | • No surveillance  
• Surveillance using other methods (flexible sigmoidoscopy [FSIG], double-contrast barium enema [DCBE], computed tomographic colonography [CTC], tri-modal imaging [high-resolution white light endoscopy, narrow band imaging and auto-fluorescence imaging])  
Outcome(s) | • Patient satisfaction  
• Patient experience  
• Reported adverse effects of colonoscopic surveillance techniques  
How to be searched | As per the Guidelines Manual. No additional databases are required.  
Date restriction: none.  
Language restriction: English language.  
Study design: all study types; especially qualitative studies.  
Review strategy | Meta-thematic analysis |
Appendix 3 – Results of GDG short questionnaires

Short Questionnaire for GDG

Name: 

Position: 

Affiliation: 

SECTION A: CLINICAL MANAGEMENT

**Question A1a:** Is it appropriate to group ulcerative colitis and Crohn’s disease together as inflammatory bowel disease and consider one pathway for colonoscopic surveillance for them?

**Question A1b:** In addition to the specified subgroups, are there any additional subgroups that should be considered separately (if evidence is available)?

**Question A2:** Is it appropriate to consider all people with polyps and produce guidance for all sub-groups instead of just focusing on adenomas?

**Question A3:** The comparators that will be considered are flexible sigmoidoscopy (FSIG), double-contrast barium enema (DCBE), computed tomographic colonography (CTC), tri-modal imaging (high resolution white light endoscopy, narrow-band imaging and auto-fluorescence imaging). Are there any surveillance...
techniques that are commonly used for these high-risk groups that have not been covered as comparators?

END OF QUESTIONNAIRE
THANK YOU FOR YOUR TIME

Results

<table>
<thead>
<tr>
<th>Question A1a: Is it appropriate to group ulcerative colitis and Crohn’s disease together as inflammatory bowel disease and consider one pathway for colonoscopic surveillance for them?</th>
<th>Question A1b: In addition to the specified subgroups, are there any additional subgroups that should be considered separately (if evidence is available)?</th>
</tr>
</thead>
<tbody>
<tr>
<td>GDG1</td>
<td>Yes</td>
</tr>
<tr>
<td>GDG2</td>
<td>The diseases behave differently but are both associated with an increased risk of cancer. Emphasis needs to be placed on Crohn’s colitis not Crohn’s elsewhere.</td>
</tr>
<tr>
<td>GDG3</td>
<td>At the moment Crohn’s and colitis are put together and the treatment is similar i.e. same drugs used. Although some drugs help Crohn’s and not colitis at all. They could follow the same pathway to some extent but the Colonoscopic surveillance must be tailored to the severity not just the condition.</td>
</tr>
<tr>
<td>GDG4</td>
<td>Yes</td>
</tr>
<tr>
<td>GDG5</td>
<td>Yes, particularly as some cases remain IBD unclassified. Initially it will probably be best to consider IBD as a whole, but that does not mean that there may not be differences in the final recommendations for each disease.</td>
</tr>
<tr>
<td>GDG6</td>
<td>Yes (note that it’s only Crohn’s patients with Crohn’s colitis who are at risk though)</td>
</tr>
<tr>
<td>GDG7</td>
<td>My view would be that if the evidence suggests different outcomes for each condition then there ought to be separate pathways otherwise one pathway would be easier to follow.</td>
</tr>
<tr>
<td>GDG8</td>
<td>We should consider one pathway for colonoscopic surveillance for them. However, depending on the severity of Crohn’s disease it might be more appropriate for those with ulcerative colitis to have more frequent or intensive surveillance but still working towards the same pathway. People on immuno-suppression with a strong family history of cancer or those with large colorectal adenomas should also be dealt with centrally.</td>
</tr>
<tr>
<td>GDG9</td>
<td>Probably not.</td>
</tr>
</tbody>
</table>

SUMMARY: Most members are happy with considering one pathway for inflammatory bowel disease (IBD) combining ulcerative colitis and Crohn’s colitis. If evidence is available for post surgery (partial resection) for IBD, or for immunosuppressed individuals or those with a family history separately, the sub-group will be considered.
**Question A2: Is it appropriate to consider all people with polyps and produce guidance for all sub-groups instead of just focusing on adenomas?**

| GDG1 | This is the area of concern, there is great confusion between the different types of polyps and the individual follow-up requirements. As often the person receiving information will be frequently unaware of the difference between certain kinds of polyps the advice needs to be clear i.e. many of the polyps identified will be hyperplastic and usually require no further surveillance. The number, size and differentiation of the adenomas will determine the follow-up protocol. This is well described in the BSG guidelines. |
| GDG2 | There is published guidance from BSG on polyp surveillance including familial risks and metaplastic polyps. It is my opinion that NICE should read this guidance then accept it as it stands and not reinvent the wheel. |
| GDG3 | No – Some polyps which are very common in the bowel are not connected to IBD. Focusing on Adenomas and persons with multiple polyps should have definite guidelines of care. I.e. Colonoscopic surveillance every so many years etc. |
| GDG4 | Yes |
| GDG5 | Yes. I think that would clarify the situation and prepare for changes in the long term as more data becomes available (e.g. hyperplastic/serrated polyps remain an important grey area at the moment and really need some management guidelines. Solitary Peutz-Jeghers polyposis may also be worth considering). |
| GDG6 | Within polyps cohort, focus will be on adenomas, but comments on other polyp types would be worthwhile. Consider covering other surveillance cohorts too – post colorectal cancer surgery (easy); family history of cancer/ polyposis (complex) |
| GDG7 | - |
| GDG8 | We should look at people with all polyps as adenomas or only a small fraction of polyps. |
| GDG9 | I think guidance should be produced for all groups, but there is still very little data on the subject. |

**SUMMARY:** Most members feel that the different sub-groups for polyps should be considered separately if possible and guidance given accordingly. We will consider all sub-groups but data may not be available for all.

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**Question A3: The comparators that will be considered are flexible sigmoidoscopy (FSIG), double-contrast barium enema (DCBE), computed tomographic colonography (CTC), tri-modal imaging (high resolution white light endoscopy, narrow-band imaging and auto-fluorescence imaging). Are there any surveillance techniques that are commonly used for these high-risk groups that have not been covered as comparators?**

| GDG1 | Not within imaging. |
| GDG2 | Rigid sigmoidoscopy may be appropriate for a select group. |
| GDG3 | Colonoscopy |
| GDG4 | Colonoscopy |
| GDG5 | - |
| GDG6 | Presumably the above are being compared against colonoscopy. Chromoendoscopy (pan-colonic dye-spraying) needs to be considered too. Other option is "no surveillance" |
| GDG7 | - |
| GDG8 | Flexible sigmoidoscopy, double contrast enema, colonoscopy, tri-modal imaging, narrow-band imaging, auto-fluorescence imaging, standard CT scan of abdomen should all be used |
| GDG9 | No. |

**SUMMARY:** As per the scope we will be considering colonoscopy and chromoendoscopy as interventions and comparing them to the above listed comparators. Rigid sigmoidoscopy has not been included in this guideline, but as the searches were wide enough to catch any relevant studies for this population using rigid sigmoidoscopy.
Appendix 4 – Lists of excluded studies

Databases covered for systematic searches

- MEDLINE/MEDLINE In-Process
- EMBASE
- CINAHL (Cumulative Index to Nursing and Allied Health Literature)
- Cochrane Database of Systematic Reviews – CDSR (Cochrane reviews)
- Database of Abstracts of Reviews of Effects – DARE (other reviews)
- Cochrane Central Register of Controlled Trials – CENTRAL (clinical trials)
- Health Technology Assessment (HTA) database (technology assessments)

Review question 1

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

Eligibility criteria

Inclusion criteria

- Population
  - Adults (18 years and older) with IBD (defined as ulcerative colitis or Crohn’s disease involving the large bowel).
  - Adults with polyps (including adenomas) in the colon or rectum.
- Intervention
  - Colonoscopic surveillance for prevention and early detection of colorectal cancer.
- Comparators
  - No surveillance.
- Study design
  - Systematic reviews, RCTs, observational studies.

Exclusion criteria

- Population
  - Children (younger than 18 years).
– Adults with newly diagnosed or relapsed adenocarcinoma of the colon or rectum.
– Adults with polyps that have previously been treated for colorectal cancer.
– Adults with a genetic familial history of colorectal cancer: hereditary non-polyposis colorectal cancer.
– Adults with a familial history of polyposis syndromes: familial adenomatous polyposis.

• Intervention
  – Diagnosis and assessment of IBD or polyps.
  – Diagnosis and management of colorectal cancer.

• Comparators
  – Comparators other than no surveillance.

• Study design
  – Case series and any single arm uncontrolled studies.

Evidence review results
• Initial 9688 hits including duplicates
• Total of 6533 unique articles
• Additional articles found via daisy chaining: 2
• Excluded on the basis of title and abstract: 6198
• Articles ordered full text: 335

Articles selected for review based on the inclusion and exclusion criteria were 2 primary studies for IBD and 2 primary studies for adenomas. The Guideline Development Group (GDG) felt that the two primary studies for adenomas were incorrectly selected and these were removed from the review by the technical team. The Group also referred to a new article (Lutgens et al. 2009) that was published in December 2009, which met the inclusion criteria for IBD and was added to the analysis. As the literature searches were done in October 2009, this paper was not identified by the technical team.
Included studies for people with IBD


Included studies for people with adenomas

Two papers were included for this review but were excluded by the GDG.
Excluded studies


NICE clinical guideline 118 – Colonoscopic surveillance


Cafferty FH, Wong JM, Yen AM et al. (2007) Findings at follow-up endoscopies in subjects with suspected colorectal abnormalities: effects of baseline findings and time to follow-up. Cancer Journal 13 (4): 263–70. MEDLINE. Excluded – findings at follow-up endoscopies


Huang CS, Lal SK, Farraye FA (2005) Colorectal cancer screening in average risk individuals. Cancer Causes and Control 16 (2): 171–88. Excluded – narrative review on different screening techniques for CRC, but reported studies are on general population


NICE clinical guideline 118 – Colonoscopic surveillance


Mak T, Senevrayar K, Laloo F et al. (2007) The impact of new screening protocol on individuals at increased risk of colorectal cancer. Colorectal Disease 9 (7): 635–40. MEDLINE. Excluded – impact of new screening protocol on individuals at increased risk of CRC

Maltz BE, Schwartz DA (2008) To lap or not to lap, that is the question...no longer? Inflammatory Bowel Diseases 14 (8): 1161–2. MEDLINE. Excluded – on title


NICE clinical guideline 118 – Colonoscopic surveillance 33


Nozaki R, Takagi K, Takano M et al. Clinical investigation of colorectal cancer detected by follow-up colonoscopy after endoscopic polypectomy. Diseases of the Colon & Rectum 40 (10 Suppl.). MEDLINE. Excluded – single arm of 6715 patients undergoing surveillance


NICE clinical guideline 118 – Colonoscopic surveillance 34


Pickard M, Dewar EP, Kapadia RC et al. (2007) Follow up of patients with colorectal polyps: are the BSG guidelines being adhered to? Colorectal Disease 9 (3): 203–6. MEDLINE. Excluded – adhering to BSG guidelines


NICE clinical guideline 118 – Colonoscopic surveillance 35


Seow CH, Ee HC, Willson AB et al. (2006) Repeat colonoscopy has a low yield even in symptomatic patients. Gastrointestinal Endoscopy 64 (6): 941–7. Excluded – to be used for RQ3


**Review question 2A**

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

**Eligibility criteria**

*Inclusion criteria*

- **Population**
  - Adults (18 years and older) with IBD (defined as ulcerative colitis or Crohn's disease involving the large bowel).
  - Adults with polyps (including adenomas) in the colon or rectum.
- **Intervention**
  - Other methods of surveillance (flexible sigmoidoscopy, double-contrast barium enema, computed tomographic colonography, tri-modal imaging, high-resolution white light endoscopy, narrow-band imaging and auto-fluorescence imaging)
- **Comparators**
  - Conventional colonoscopy
- **Study design**
  - Systematic review, RCTs, controlled back to back clinical trials

*Exclusion criteria*

- **Population**
  - Children (younger than 18 years).
  - Adults with newly diagnosed or relapsed adenocarcinoma of the colon or rectum.
  - Adults with polyps that have previously been treated for colorectal cancer.
  - Adults with a genetic familial history of colorectal cancer: hereditary non-polyposis colorectal cancer.
  - Adults with a familial history of polyposis syndromes: familial adenomatous polyposis.
• Intervention
  – Interventions other than those listed above.

• Comparators
  – Comparators other than conventional colonoscopy.

• Study design
  – Systematic review, RCTs, controlled back-to-back clinical trials.

Evidence review results
• Initial 14,701 hits including duplicates
• Total of 9544 unique articles
• Excluded on the basis of title and abstract: 9436
• Articles ordered full text: 108

Articles selected for review based on the inclusion and exclusion criteria were 5 studies, 1 primary study for people with IBD and 4 (2 primary studies, 2 systematic reviews) for people with adenomas.
Review flow chart

Total Hits 14701

Unique articles 9544

Ordered full text 108

Included articles 5

5157 excluded

9436 excluded

103 excluded

Included studies for people with IBD


Included studies for people with adenomas


Excluded studies


Adler A, Papanikolaou I, Setka E et al. (2006) [A prospective, randomised study comparing Narrow Band Imaging (NBI) and conventional wide angle colonoscopy for identification of colorectal adenomas]. Zeitschrift fur Gastroenterologie 44 (8): 842. Excluded: used systematic review


Blue Cross Blue Shield Association (2004) CT colonography (‘virtual colonoscopy’) for colon cancer screening. Chicago IL: Blue Cross Blue Shield Association (BCBS). Excluded: discussion on CTC


Ebell M (2000) Which is better at detecting polyps and adenomas in patients with a history of polyps: colonoscopy or double-contrast barium enema (DCBE)? Evidence-Based Practice 3 (9): 11-2, 2p. Excluded: narrative review


Lin OR, Praveen K, Schembre DB et al. (2005) Screening sigmoidoscopy and colonoscopy for reducing colorectal cancer mortality in asymptomatic persons. Cochrane Database of Systematic Reviews issue 2. Excluded: protocol for a review


Pedersen BG, Christiansen TEM, Bjerregaard NC et al. Colonoscopy and multidetector-array computed-tomographic colonography: detection rates and feasibility. Endoscopy 35 (9): 736–42. Excluded: discussion on detection rates and feasibility


Ransohoff DF (2005) Computed tomographic colonography without cathartic preparation performed well in detecting colorectal polyps. ACP Journal Club 142 (2); 49. Excluded: not looking at the review question


Virtual colonoscopy. Medical Letter on Drugs & Therapeutics (2005); 47 (1202): 15–16. MEDLINE. Excluded: discussion on CTC. No comparative arm


**Review question 2B**

Is colonoscopic surveillance with a dye (chromoscopy) for prevention and/or early detection of colorectal cancer clinically effective compared with colonoscopic surveillance with conventional colonoscopy?

**Eligibility criteria**

*Inclusion criteria*

- **Population**
  - Adults (18 years and older) with IBD (defined as ulcerative colitis or Crohn’s disease involving the large bowel).
  - Adults with polyps (including adenomas) in the colon or rectum.
- **Intervention**
  - Chromoscopy.
- **Comparators**
  - Conventional colonoscopy.
- **Study design**
  - Systematic review, RCTs, controlled back-to-back clinical trials.

*Exclusion criteria*

- **Population**
  - Children (younger than 18 years).
  - Adults with newly diagnosed or relapsed adenocarcinoma of the colon or rectum.
  - Adults with polyps that have previously been treated for colorectal cancer.
  - Adults with a genetic familial history of colorectal cancer: hereditary non-polyposis colorectal cancer.
  - Adults with a familial history of polyposis syndromes: familial adenomatous polyposis.
- **Intervention**
  - Interventions other than chromoscopy.
- **Comparators**
  - Comparators other than conventional colonoscopy.
- **Study design**
  - Systematic review, RCTs, controlled back-to-back clinical trials.
Evidence review results

- Initial 14,701 hits including duplicates
- Total of 9544 unique articles
- Excluded on the basis of title and abstract: 9521
- Articles ordered full text: 23

Articles selected for review based on the inclusion and exclusion criteria were 10 studies; 5 for people with IBD and 5 for people with adenomas. Two studies, one for each population (Hurlstone et al. 2004 and Hurlstone et al. 2005) met the inclusion criteria but were excluded from the review after discussion with the GDG and advice from the editors of the journal because there was some uncertainty about the methods used. Therefore the relevant evidence was 4 primary studies for people with IBD and 1 Cochrane systematic review and 3 primary studies for people with adenomas.
Included studies for people with IBD


Included studies for people with adenomas


Excluded studies


Brooker J, Shah S, Suzuki N et al. (2000). Pan-colonic dye spray to aid adenoma detection during colonoscopy: a randomized controlled trial. Gut 46 (Suppl. 2): A77. Excluded: used the later study with more recent results


Review question 3

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

Eligibility criteria

Inclusion criteria

- Population
  - Adults (18 years and older) with IBD (defined as ulcerative colitis or Crohn's disease involving the large bowel).
  - Adults with polyps (including adenomas) in the colon or rectum.
- Intervention
  - Chromoscopy or conventional colonoscopy.
- Factors
  - Looking at any prognostic factors or surveillance schemes for colorectal cancer.
- Study design
  - No study design filter.

Exclusion criteria

- Population
  - Children (younger than 18 years).
- Adults with newly diagnosed or relapsed adenocarcinoma of the colon or rectum.
- Adults with polyps that have previously been treated for colorectal cancer.
- Adults with a genetic familial - history of colorectal cancer: hereditary non-polyposis colorectal cancer.
- Adults with a familial history of polyposis syndromes: familial adenomatous polyposis.

**Intervention**
- Interventions other than chromoscopy or conventional colonoscopy.

**Evidence review results**
- initial 14,701 hits including duplicates
- Total of 9544 unique articles
- Excluded on the basis of title and abstract: 9478
- Articles ordered full text: 62
- Additional articles found via daisy chaining: 4 (for people with adenomas).

Articles selected for review based on the inclusion and exclusion criteria were 6 for people with IBD and 6 for people with adenomas. Additionally 5 primary articles for people with IBD were provided by the GDG that were not identified by the technical team. The technical team decided to broaden the search criteria to try and identify other similar relevant prognostic studies that might have been missed because of strict search strategies and/or strict inclusion or exclusion criteria.

- Additional searches found 1781 articles (including some duplicates and non-English language papers).
- Based on the title and abstract alone 130 were assessed as relevant.
- Including the 11 papers already assessed as relevant, 140 articles in total (1 duplicate) were considered for this question.
- Where appropriate, reference lists of studies were checked to identify any further studies for inclusion. Studies identified as relevant from the searches and included in any of the meta-analyses were re-examined to see if any other relevant outcomes were reported (based on abstract alone).
- A total of 173 papers were considered as relevant based on title and abstract.
- Based on full text 28 studies were included.
The additional studies identified from the updated search resulted in a total of 28 studies reviewed for this question.

**Included studies for people with IBD**


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


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

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Included studies for people with adenomas


Excluded studies


Ahsgren L, Jonsson B, Stenling R et al. (1993) Prognosis after early onset of ulcerative colitis. A study from an unselected patient population. Hepato-Gastroenterology 40: 467–70. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD)


Ataseven H, Parlak E, Yuksel I et al. (2009) Primary sclerosing cholangitis in Turkish patients: characteristic features and prognosis. Hepatobiliary & Pancreatic Diseases International 8: 312–5. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD)

Atkin WS, Morson BC, Cuzick J (1992) Long-term risk of colorectal cancer after excision of rectosigmoid adenomas [see comment]. New England Journal of Medicine 326: 658–62. Excluded – intervention was rigid sigmoidoscopy and one of the exclusion criteria was colonoscopy


Baxter NN, Goldwasser MA, Paszat LF et al. (2009) Association of colonoscopy and death from colorectal cancer. Annals of Internal Medicine 150: 1–8. Excluded – case control study but the controls were not true controls (not individuals that had polypectomy without surveillance)


Binder V, Hendriksen C, Kreiner S (1985) Prognosis in Crohn's disease – based on results from a regional patient group from the county of Copenhagen. Gut 26: 146–50. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD)


Branco BC, Harpaz N, Sachar DB et al. (2009) Colorectal carcinoma in indeterminate colitis. Inflammatory Bowel Diseases 15: 1076–81. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD)


Chawla LS, Chinna JS, Dilawari JB et al. (1990) Course and prognosis of ulcerative colitis. Journal of the Indian Medical Association 88: 159–60. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD)


Cooke WT, Mallas E, Prior P et al. (1980) Crohn's disease: course, treatment and long term prognosis. Quarterly Journal of Medicine 49: 363–84. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD)


de Silva MV, Fernando MS, Fernando D (2000) Comparison of some clinical and histological features of colorectal carcinoma occurring in patients below and above 40 years. Ceylon Medical Journal 45: 166–8. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD)


Ebell M (2002) Which patients with colorectal polyps are at greater risk of early recurrence? Evidence-Based Practice 5: 8–9, 2p. Excluded – conference abstract


Engelsgjerd M, Farraye FA, Odze RD (1999) Polypectomy may be adequate treatment for adenoma-like dysplastic lesions in chronic ulcerative colitis. Gastroenterology 117: 1286–94. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD)


Jess T (2008) Prognosis of inflammatory bowel disease across time and countries. An epidemiological study of population-based patient cohorts. Danish Medical Bulletin 55: 103–20. Excluded – although systematic review with meta-analysis, summary estimates as reported were not relevant to this question as did not compare subgroups of people with IBD. Checked reference list [review; 81 refs]

Inflammatory Bowel Diseases 12: 669–76. Excluded – not all the patients were undergoing colonoscopic surveillance

Jess T, Riis L, Vind L et al. (2007) Changes in clinical characteristics, course, and prognosis of inflammatory bowel disease during the last 5 decades: a population-based study from Copenhagen, Denmark. Inflammatory Bowel Diseases 13: 481–9. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD).


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Lee PY, Fletcher WS, Sullivan ES et al. (1994) Colorectal cancer in young patients: characteristics and outcome. American Surgeon 60: 607–12. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD)


MacDougall IP (1964) The cancer risk in ulcerative colitis. Lancet 2: 655–8. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD)

Manning AP, Bulgim OR, Dixon MF et al. (1987) Screening by colonoscopy for colonic epithelial dysplasia in inflammatory bowel disease. Gut 28: 1489–94. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD)


Moore PA, Dilawari RA, Fidler WJ (1984) Adenocarcinoma of the colon and rectum in patients less than 40 years of age. American Surgeon 50: 10–4. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD)


Palascak-Juif V, Bouvier AM, Cosnes J et al. (2005) Small bowel adenocarcinoma in patients with Crohn's disease compared with small bowel adenocarcinoma de novo. Inflammatory Bowel Diseases 11: 828–32. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD)


Park SH, Kim YM, Yang SK et al. (2007) Clinical features and natural history of ulcerative colitis in Korea. Inflammatory Bowel Diseases 13: 278–83. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD)


Rodriguez-Bigas MA, Mahoney MC, Weber TK et al. (1996) Colorectal cancer in patients aged 30 years or younger. Surgical Oncology 5: 189–94. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD)


Schoen RE, Pinsky PF, Weissfeld JL et al. (2003) Results of repeat sigmoidoscopy 3 years after a negative examination [see comment]. JAMA 290: 41–8. Excluded – sigmoidscopy results


Shaughnessy A (1998) Is it necessary to perform a colonoscopy in patients found to have small adenomas on screening sigmoidoscopy? Evidence-Based Practice 1: –7, insert. Excluded – not available at British Library


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Weterman IT, Biemond I, Pena AS (1990) Mortality and causes of death in Crohn's disease. Review of 50 years' experience in Leiden University Hospital. Gut 31: 1387–90. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD)


Wolters FL, Russel MG, Stockbrugger RW (2004) Systematic review: has disease outcome in Crohn's disease changed during the last four decades? Alimentary Pharmacology & Therapeutics 20: 483–96. Excluded – no direct comparison of risk of colorectal cancer by subgroup (as identified at index colonoscopy or related to IBD) [review; 200 refs]


**Review question 4**

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

**Eligibility criteria**

*Inclusion criteria*

- **Population**
  - Adults (18 years and older) with IBD (defined as ulcerative colitis or Crohn's disease involving the large bowel) considering colonscopy.
  - Adults with polyps (including adenomas) in the colon or rectum considering colonscopy.
- **Intervention**
  - Any discussion of patient preference or views on the procedure or the process of surveillance.
- **Study design**
  - No study design filter.

*Exclusion criteria*

- **Population**
  - Children (younger than 18 years).
  - Adults with newly diagnosed or relapsed adenocarcinoma of the colon or rectum.
  - Adults with polyps that have previously been treated for colorectal cancer.
  - Adults with a genetic familial history of colorectal cancer: hereditary non-polyposis colorectal cancer.
  - Adults with a familial history of polyposis syndromes: familial adenomatous polyposis.
- **Intervention**
  - Views or preferences on interventions other than chromoscopy or conventional colonoscopy or surveillance.
Evidence review results

- Initial 1910 hits including duplicates
- Excluded on the basis of title and abstract: 1882
- Articles ordered full text: 28

Articles selected for review based on the inclusion and exclusion criteria were seven primary studies. It was agreed not to split by the evidence by groups for this question.

Review flow chart

Included studies (both groups)


Excluded studies


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### Appendix 5 – Search strategies and literature search

**Scoping searches**

Scoping searches were undertaken in September 2009 using the following websites and databases (listed in alphabetical order); browsing or simple search strategies were employed. The search results were used to provide information for scope development and project planning.

<table>
<thead>
<tr>
<th>Guidance/guidelines</th>
<th>Systematic reviews/economic evaluations</th>
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<tr>
<td>Age Concern England</td>
<td>Clinical Evidence</td>
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<tr>
<td>American Gastroenterological Association</td>
<td>Cochrane Database of Systematic Reviews (CDSR)</td>
</tr>
<tr>
<td>American Society of Colon &amp; Rectal Surgeons</td>
<td>Database of Abstracts of Reviews of Effects (DARE)</td>
</tr>
<tr>
<td>Association of Coloproctology of Great Britain and Ireland</td>
<td>Health Economics Evaluations Database (HEED)</td>
</tr>
<tr>
<td>Beating Bowel Cancer</td>
<td>Health Technology Assessment Database (HTA)</td>
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<tr>
<td>British Geriatric Society</td>
<td>NHS Economic Evaluation Database (NHS EED)</td>
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<tr>
<td>British Society of Gastroenterology</td>
<td>NHS R&amp;D Service Delivery and Organisation (NHS SDO) Programme</td>
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<tr>
<td>Canadian Medical Association Infobase</td>
<td>National Institute for Health Research (NIHR) Health Technology Assessment Programme</td>
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<tr>
<td>Clinical Knowledge Summaries</td>
<td>TRIP Database</td>
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<td>Department of Health</td>
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<td>Guidelines International Network (GIN)</td>
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<td>Lynn’s Bowel Cancer Campaign</td>
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<td>National Association for Crohn’s and Colitis (NACC)</td>
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<td>National Health and Medical Research Council (Australia)</td>
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<td>National Institute for Health and</td>
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</table>
Main searches

The following sources were searched for the topics presented in the sections below.

- Cochrane Database of Systematic Reviews – CDSR (Wiley)
- Cochrane Central Register of Controlled Trials – CENTRAL (Wiley)
- Database of Abstracts of Reviews of Effects – DARE (CRD Databases)
- Health Technology Assessment Database HTA (CRD Databases)
- CINAHL (EBSCO and NHS Evidence – Search 2.0)
- EMBASE (Ovid)
- MEDLINE (Ovid)
The searches were conducted in November 2009. The aim of the searches was to provide evidence on colonoscopic surveillance (using conventional colonoscopy or chromoscopy) for prevention and early detection of colorectal cancer compared with no surveillance. Search filters for systematic reviews, randomised controlled trials, and observational studies were appended to the search strategies to retrieve high quality papers (see Identification of systematic reviews, randomised controlled trials, and observational studies).

The MEDLINE search strategy is presented below. It was translated for use in all of the other databases.

Database: Ovid MEDLINE(R)<1950 to October Week 5 2009>

Date searched: 11th November 2009

Search strategy:

-------------------------------------------------------------------------------------------
1. ulcerative colitis/
2. (ulcer$ adj4 colitis).tw.
3. (rectocolitis or colitide$).tw.
4. crohn disease/
5. crohn$.tw.
6. ((terminal or regional or granulomatous) adj3 (ileitis or colitis)).tw.
7. (ileocolitis or enteritis).tw.
8. inflammatory bowel disease/
9. (inflam$ adj3 bowel$ adj3 (disease$ or disorder$)).tw.
10. polyps/
11. intestinal polyps/
12. colonic polyps/
13. exp adenomatous polyps/
15. ((adenomatous or famili$ or hereditary or inherit$) adj3 polyposis).tw.
17. or/1-16
18. exp colonoscopy/
19. (colonoscop$ or coloscop$ or sigmoidoscop$ or chromoscop$).tw.
20. mass screening/
21. population surveillance/
22. or/18-21
The searches were conducted in November 2009. The aim of the searches was to provide evidence on colonoscopic surveillance (using conventional colonoscopy or chromoscopy) for prevention and early detection of colorectal cancer compared with surveillance using other methods, such as flexible sigmoidoscopy, double-contrast barium enema, computed tomographic colonography, and tri-modal imaging (high resolution white light endoscopy, narrow-band imaging and auto-fluorescence imaging).

The MEDLINE search strategy is presented below. It was translated for use in all of the other databases.

Database: MEDLINE(R) <1950 to November Week 2 2009>
Date searched: 23rd November 2009
Search strategy:

1. ulcerative colitis/ use mesz
2. (ulcer$ adj4 colitis).tw. use mesz
3. (colitide$ or rectocolitis).tw. use mesz
4. crohn disease/ use mesz
5. crohn$.tw. use mesz
6. ((terminal or regional or granulomatous) adj3 (ileitis or colitis)).tw. use mesz
7. (ileocolitis or enteritis).tw. use mesz
8. inflammatory bowel disease/ use mesz
9. (inflam$ adj3 bowel$ adj3 (disease$ or disorder$)).tw. use mesz
10. polyps/ use mesz
11. intestinal polyps/ use mesz
12. colonic polyps/ use mesz
13. exp adenomatous polyps/ use mesz
14. (polyp? or adenoma$).tw. use mesz
15. ((adenomatous or famil$ or hereditary or inherit$) adj3 polyposis).tw. use mesz
16. (gardner adj syndrom$).tw. use mesz
17. or/1-16
18. sigmoidoscopy/ use mesz
19. proctoscopy/ use mesz
Identification of evidence on the information and support needs of people undergoing or considering undergoing colonoscopic surveillance.

The searches were conducted in December 2009. The aim of the searches was to provide evidence on the information and support needs of people undergoing or considering undergoing colonoscopic surveillance.

The MEDLINE search strategy is presented below. It was translated for use in all of the other databases.
Database: Ovid MEDLINE(R) <1950 to November Week 3 2009>
Date searched: 10th December 2009
Search strategy:

1. Colitis, Ulcerative/
2. (ulcer$ adj4 colitis).tw.
3. (rectocolitis or colitide$).tw.
4. crohn disease/
5. crohn$.tw.
6. ((terminal or regional or granulomatous) adj3 (ileitis or colitis)).tw.
7. (ileocolitis or enteritis).tw.
8. inflammatory bowel disease/
9. (inflam$ adj3 bowel$ adj3 (disease$ or disorder$)).tw
10. polyps/
11. intestinal polyps/
12. colonic polyps/
13. exp adenomatous polyps/
15. ((adenomatous or famil$ or hereditary or inherit$) adj3 polyposis).tw.
17. or/1-16
18. exp colonoscopy/
19. proctoscopy/
20. (colonoscop$ or coloscop$ or colonograp$ or chromoscop$ or sigmoid?oscop$ or proctosigmoid?scop$ or proctoscop$ or rectoscop$).tw.
21. fsig.tw.
22. barium sulfate/
23. enema/
24. 22 and 23
25. (barium adj3 (enema$ or exam$)).tw.
26. (double adj2 contrast$ adj2 (enema$ or exam$)).tw
27. (contrast$ adj2 enema$).tw.
28. (clyasma$ or clyster$ or enteroclysis$).tw.
29. dcbe.tw.
30. or/24-29
31. colonography, computed tomographic/
32. (comput$ adj2 tomograp$ adj2 (colonograp$ or pneumocolon$)).tw.
33. (ct adj2 (colonograp$ or pneumocolon$)).tw.
34. (virtual adj2 (colonoscop$ or pneumocolon$)).tw.
35. (trimodal$ adj2 imag$).tw.
36. (tri adj2 modal$ adj2 imag$).tw.
37. (high adj2 resolution adj2 endoscop$).tw.
38. (white adj2 light adj2 endoscop$).tw.
39. wle.tw.
40. (narrow adj2 band adj2 imag$).tw.
41. (narrowband adj2 imag$).tw.
42. nbi.tw.
43. fluorescence/
44. microscopy, fluorescence/
45. (auto$ fluorescence adj2 (imag$ or endoscop$)).tw.
46. (auto$ adj$ fluorescence adj2 (imag$ or endoscop$)).tw.
47. population surveillance/
48. mass screening/
49. or/18-21,30-48
50. 17 and 49
51. Qualitative research/
52. Nursing Methodology Research/
53. Interview/
54. Questionnaires/
55. Narration/
56. Health Care Surveys/
57. (qualitative$ or interview$ or focus group$ or questionnaire$ or narrative$ or narrati$ or sur$).tw.
58. (ethno$ or emic or etic or phenomenolog$ or grounded theory or constant compar$ or (thematic$ adj3 analys$) or theoretical sampl$ or purposive sampl$).tw.
59. (hermeneutic$ or heidegger$ or husser$ or colaizzi$ or van kaam$ or van manen$ or giorgi$ or glasser$ or strauss$ or ricoeur$ or spiegelberg$ or merleau$).tw.
60. (metasynthes$ or meta-synthes$ or metasummar$ or meta-summar$ or meta-stud$ or meta-stud$).tw.
61. or/51-60
62. 50 and 61
63. Patients/
64. Family/
65. Spouses/
66. Caregivers/
67. or/63-66
68. Pamphlets/
69. Needs Assessment/
70. Information Centers/
71. Information Services/
72. Health Education/
73. Information Dissemination/
74. Counseling/
75. Social Support/
76. Self-Help Groups/
77. Self Care/
78. or/68-77
79. 67 and 78
80. Patient Education as Topic/
82. Consumer Health Information/
83. ((patient$ or famil$ or relative$ or carer$ or caregiver$ or care-giver$ or spous$ or husband$ or wife$ or wive$ or partner$) adj5 (educat$ or informat$ or communicat$ or pamphlet$ or handout$ or hand-out$ or hand out$ or booklet$ or leaflet$ or support$ or need$ or advice$ or advis$)).ti.
84. ((patient$ or famil$ or relative$ or carer$ or caregiver$ or care-giver$ or spous$ or husband$ or wife$ or wive$ or partner$) adj5 (counsel$ or selfhelp$ or self-help$ or self help$ or selfcar$ or self-car$ or self car$)).ti.
85. or/80-84
86. 79 or 85
87. 50 and 86
88. exp patients/px
89. exp parents/px
90. exp family/px
91. caregivers/px
92. stress, psychological/
93. Emotions/
94. Anxiety/
95. Fear/
96. exp consumer satisfaction/
97. ((patient$ or parent$ or famil$ or carer$ or caregiver$ or care-giver$ or inpatient$ or in-patient$) adj2 (experience$ or belief$ or stress$ or emotion$ or anx$ or fear$ or
Identification of systematic reviews, randomised controlled trials, and observational studies

Search filters for systematic reviews, randomised controlled trials, and observational studies were appended to the search strategy on Identification of evidence on colonoscopic surveillance (and evidence on surveillance using other methods) above to retrieve high quality evidence.

The MEDLINE search filters are presented below. They were translated for use in the MEDLINE and EMBASE searches.

Systematic Reviews

2. Meta-Analysis as Topic/
4. exp Review Literature as Topic/
5. (metaanaly$ or metanaly$ or (meta adj2 analy$)).tw.
6. (review$ or overview$).tw.
7. (systematic$ adj4 (review$ or overview$)).tw.
8. ((quantitative$ or qualitative$) adj4 (review$ or overview$)).tw.
9. ((studies or trial$) adj1 (review$ or overview$)).tw.
10. (integrat$ adj2 (research or review$ or literature)).tw.
11. (pool$ adj1 (analy$ or data)).tw.
12. (handsearch$ or (hand adj2 search$)).tw.
14. or/1-13
Randomised Controlled Trials

1. Randomized Controlled Trial.pt.
2. Controlled Clinical Trial.pt.
3. Clinical Trial.pt.
4. exp Clinical Trials as Topic/
5. placebos/
6. Random Allocation/
7. Double-blind Method/
8. Single-Blind Method/
9. Cross-Over Studies/
10. ((random$ or control$ or clinical$) adj2 (trial$ or stud$)).tw.
12. placebo$.tw.
13. ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).tw.
14. (crossover$ or (cross adj over$)).tw.
15. or/1-14

Observational Studies

1. Epidemiological studies/
2. exp case-control studies/
3. exp cohort studies/
4. Cross-Sectional Studies/
5. Comparative Study.pt.
6. case control$.tw.
7. case series.tw.
8. (cohort adj (study or studies)).tw.
9. cohort ana$y.tw
10. (follow up adj (study or studies)).tw.
11. (observational adj (study or studies)).tw.
12. longitudinal.tw.
13. prospective.tw.
14. retrospective.tw.
15. cross sectional.tw.
16. or/1-15
Health economics

Sources

The following sources were searched to identify economic evaluations and quality of life data relating to colonoscopic surveillance (using conventional colonoscopy or chromoscopy) for prevention and early detection of colorectal cancer compared with no surveillance

- Health Economic Evaluations Database – HEED (Wiley)
- NHS Economic Evaluation Database – NHS EED (Wiley and CRD website)
- EMBASE (Ovid)
- MEDLINE (Ovid)
- MEDLINE In-Process (Ovid)

Strategies

The searches were undertaken in November 2009. The MEDLINE search strategy presented in the sections RQ1 and RQ2 were used and translated for use in NHS EED and HEED. Filters to retrieve economic evaluations and quality of life papers were appended to the MEDLINE search strategy to identify relevant evidence.

The MEDLINE economic evaluations and quality of life search filters are presented below. They were translated for use in the MEDLINE In-Process and EMBASE databases.

Economics evaluations

1. Economics/
2. exp "Costs and Cost Analysis"/
3. Economics, Dental/
4. exp Economics, Hospital/
5. exp Economics, Medical/
6. Economics, Nursing/
7. Economics, Pharmaceutical/
8. Budgets/
9. exp Models, Economic/
10. Markov Chains/
11. Monte Carlo Method/
12. Decision Trees/
13. econom$.tw.
14. cba.tw.
15. cee.tw.
16. cua.tw.
17. markov$.tw.
18. (monte adj carlo).tw.
19. (decision adj2 (tree$ or analys$)).tw.
20. (cost or costs or costing$ or costly or costed).tw.
21. (price$ or pricing$).tw.
22. budget$.tw.
23. expenditure$.tw.
24. (value adj2 (money or monetary)).tw.
25. (pharmacoeconomic$ or (pharmaco adj economic$)).tw.
26. or/1-25

Quality of life
1. "Quality of Life"/
2. quality of life.tw.
3. "Value of Life"/
4. Quality-Adjusted Life Years/
5. quality adjusted life.tw.
6. (qaly$ or qald$ or qale$ or qtime$).tw.
7. disability adjusted life.tw.
8. daly$.tw.
9. Health Status Indicators/
10. (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shortform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
11. (sf6 or sf 6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
12. (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
13. (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortform sixteen or short form sixteen).tw.
14. (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
15. (euroqol or euro qol or eq5d or eq 5d).tw.
16. (qol or hqol or hqol or hrqol).tw.
17. (hye or hyes).tw.
18. health$ year$ equivalent$.tw.
19. utilit$.tw.
20. (hui or hui1 or hui2 or hui3).tw.
21. disutili$.tw.
22. rosser.tw.
23. quality of wellbeing.tw.
24. quality of well-being.tw.
25. qwb.tw.
26. willingness to pay.tw.
27. standard gamble$.tw.
28. time trade off.tw.
29. time tradeoff.tw.
30. tto.tw.
31. or/1-30
## Appendix 6 – Evidence tables

### Review question 1: People with inflammatory bowel disease

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Study design</th>
<th>Follow-up</th>
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</thead>
<tbody>
<tr>
<td>Choi et al. (1993)</td>
<td>Prospective case–control study. The authors compared the groups for: a) age at diagnosis of ulcerative colitis (UC); b) age at diagnosis of cancer; c) duration of UC before cancer. No statistically significant difference was found by the Mann-Whitney test (P &gt; 0.05)</td>
<td>The median follow-up after diagnosis of cancer until death or last visit was 4.9 years (range 0.4–11.4 years) for the surveillance group and 1.4 years (range 0.1–12.1 years) for the no surveillance group. Patients with duration of disease of 8 years or more and extension of disease proximal to the sigmoid colon were included. CRC incidence: 41 had colorectal carcinoma out of 2050 patients; 19 of those had surveillance and 22 did not have surveillance.</td>
<td>Patients with ulcerative colitis from the Lahey Clinic Medical Center in Seattle, USA (N = 500).</td>
<td>The patients on surveillance had biopsies every 2 years (every 3 years in the early years of the programme) after negative results on two consecutive annual examinations. Any specimens with suspicion of dysplasia were reviewed by two pathologists. In patients with biopsies indefinite dysplasia were included.</td>
<td>No surveillance</td>
<td>Survival analysis was done using the Kaplan-Meier product limit method. The statistical significance of differences was analysed by the Tarone-Ware method. <strong>Duke’s stage of carcinoma when detected:</strong> 15/19 were detected at Duke’s stage A or B for the surveillance group versus 9/22 for the no surveillance group (P = 0.039). The removal of two patients whose colorectal carcinoma was detected without surveillance still showed a statistically significant difference (P = 0.036). <strong>5-year survival:</strong> 5-year overall survival rate was 77.2%±10.1% for the surveillance group versus 36.3%±12.7% for the no surveillance group (P = 0.026). Removing the patients whose colorectal carcinoma was detected without surveillance still showed a statistically significant difference (P = 0.037) and 5-year overall survival in the surveillance arm changed to 76.2%±12.1%. The 5-year survival of the two groups by Dukes’ stage did not show a statistically significant difference (P &gt; 0.05). <strong>Overall mortality:</strong> 4 deaths occurred in the surveillance group versus 11 in the no surveillance group.</td>
<td>The authors state that the big difference in the follow-up time between the two groups was the high early mortality rate for the no surveillance group. The study compared the two groups for three different criteria and found no statistical significance.</td>
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### Evidence table for review question 1: Is colonoscopic surveillance for prevention and/or early detection of colorectal cancer in adults with inflammatory bowel disease clinically effective compared with no surveillance?

<table>
<thead>
<tr>
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<tr>
<td>Lashner et al. (1990)</td>
<td>Historical cohort study</td>
<td>Eligible patients entered the registry on June 15 1984, until death or the end of the study on November 15 1986.</td>
<td>Patients (N = 186) were taken from the Chicago inflammatory bowel disease registry. Eligible patients had extensive ulcerative colitis (defined as continued disease from any point proximal to the splenic flexure to the distal rectum) with at least 9 years of disease duration. Cohort 1: n = 91 had surveillance at least once during the study period. Cohort 2: n = 95 had no surveillance within the study (but could have it outside).</td>
<td>Colonoscopic surveillance at least once during the study period. Patients had 4.2± 3.0 (range 1–16) colonoscopies during the study period at a mean of 17 years after symptom onset. Patients who were found to have cancer on referral or their first colonoscopy were excluded.</td>
<td>No surveillance within the programme</td>
<td>No statistically significant difference was seen between the two groups in sample size, sex, age at symptom onset and family history for colon cancer. There was no morbidity or mortality directly from colonoscopy. A total of 92% of people from the surveillance group and 94% from the control group had complete vital status information at the end of the study. Duration of disease at colectomy: 19±2.7 years in the surveillance group versus 14.3±11.8 years in the control group. Colectomy: 33 people in the surveillance group versus 51 in the control group. Colectomy was performed 4 years later in the surveillance group. Indication for colectomy: cancer – 3 people in the surveillance group versus 6 in the control group; dysplasia – 10 people in the surveillance group versus 3 in the control group; active disease – 20 people in the surveillance group versus 42 in the control group. Mortality: 6 people in the surveillance group versus 14 in the control group. However, deaths caused by cancer were more frequent in the surveillance group than in the control group, where deaths were more frequent because of exacerbation. The survival curves showed a significant reduction in mortality in the surveillance group (p &lt; 0.05).</td>
<td>The authors mention potential sources of bias for misclassification for both surveillance and cancer. As some patients had their dysplasia discovered in programmes outside the study surveillance and some patients not receiving surveillance could have had surveillance outside the surveillance programme within the study, further error could have been introduced. The sample size of the study was also small and this could potentially favour the null hypothesis. The study had an overall follow up of 93% of patients giving it a high validity. The authors also performed a Cox proportional hazards model to adjust for prognostic factors.</td>
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Evidence table for review question 1: Is colonoscopic surveillance for prevention and/or early detection of colorectal cancer in adults with inflammatory bowel disease clinically effective compared with no surveillance?

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<tr>
<td>Lutgens et al. (2009)</td>
<td>Retrospective case–control study.</td>
<td>Data were taken from 1971 to 1 July 2006 (primary end point of the study) or the date of death. When a patient was lost to follow-up, the last visit to the hospital was recorded as end of follow-up. 21% (31 patients) were lost to follow-up.</td>
<td>Patients with IBD (N = 149; 89 with ulcerative colitis, 59 with Crohn’s disease and 1 with indeterminate colitis) with CRC were taken from a nationwide pathology database (PALGA) in the Netherlands. Overall 42 deaths occurred from 145 (29%) people and metastasised CRC was the direct cause of death for 30 of those (six patients died from metastasis of a Colonoscopic surveillance (n = 23) For the surveillance group patients had to have at least one or more surveillance colonoscopies at regular intervals (every 1–3 years). Surveillance was intended to detect neoplasia by taking four random biopsies every 10 cm in addition to targeted biopsies of suspicious areas. Surveillance started after a median of 14.3 (standard 8) years after diagnosis of IBD. CRC developed after a</td>
<td>No surveillance (n = 126)</td>
<td>Survival analyses were calculated by Kaplan-Meier curves and Cox regression analyses were used for calculations and the Tarone-Ware method was used to compare the differences between the survival curves. <strong>Overall survival</strong> The overall 5-year survival rates were 100% in the surveillance group and 65% in the non-surveillance group (P = 0.029). <strong>Overall mortality</strong> One patient from the surveillance group died compared with 29 in the non-surveillance group (P = 0.047). The CRC-related 5-year mortalities were 0% in the surveillance group and 26% in the non-surveillance group (P = 0.042). Cox regression analysis showed that</td>
<td>The study has the results of ulcerative colitis and Crohn’s disease patients in the analysis. There were no statistically significant differences seen between the two groups in patient characteristics. Cox regression analysis was used to examine the effect of type of IBD, age at CRC diagnosis, comorbidity, presence of primary sclerosing cholangitis and surveillance on CRC-related mortality. The authors tried to minimise selection bias by excluding patients</td>
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Using the Cox proportional hazards model the surveillance group had 61% reduction in mortality compared with the control group. The relative risk for death was 0.39 (95% CI 0.15 to 1.00).

**Cancer detection rate:** the surveillance group had 67% increased cancer detection rate compared with the control group. The relative risk for cancer detection was 1.67 (95% CI 0.30 to 9.33).

**Colectomy:** the surveillance group had 47% reduction in colectomy rate compared with the control group. The relative risk for colectomy was 0.53 (95% CI 0.34 to 0.83).
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<td>presence of primary sclerosing cholangitis, median interval between onset of IBD symptoms and diagnosis of CRC and mean follow-up time after CRC. No statistically significant difference was found between the groups.</td>
<td>follow-up. Four of these were immediately after diagnosis of CRC and were excluded from survival analysis.</td>
<td>different cancer, and another six died from complications of colectomy.</td>
<td>median of 6.4 years (range 1–21) after initiation of surveillance.</td>
<td>colonoscopic surveillance improved survival and CRC-related mortality but this did not reach statistical significance (P = 0.10, and 0.08 when 11 patients that had simultaneous IBD and CRC diagnosis were excluded). When the 11 patients were excluded, the 5-year overall mortality changed to 0% in the surveillance group and 36% in the non-surveillance group (P = 0.02). The CRC-related mortality changed to 0% and 29% (P = 0.03).</td>
<td>Tumour stage&lt;br&gt;Tumour classification was not available for 11 patients (93%). There were 12 (52.2%) patients in the surveillance group in whom tumours were detected at stage 0 or 1 (AJCC – American Joint Committee on Cancer, which is equivalent to T in situ and T1, T2, NO, MO) compared with 28 (24.3%) in the no surveillance group (P = 0.004). There were fewer people with advanced stage tumours, stage 3B–C and 4 tumours (AJCC, which is equivalent to T3, T4, N1, N2, MO, M1), in the surveillance group compared with 48 (41.7%) in the non-surveillance group (P = 0.049).&lt;br&gt;&lt;br&gt;5-Aminosalicylic acid prescription&lt;br&gt;Ten patients (7%) did not have any information regarding the use of 5-ASA prescription, so were excluded from the analysis. Out of the included 139 people, 119 (86%) had used 5-ASA during the course of their disease and 64 (54%) of those had 5-ASA medication for more who were diagnosed with IBD and CRC simultaneously. The authors stated that lack of randomisation may have led to volunteer bias, but felt that because the mean duration of disease was longer (22.7 years versus 19.3 years) this was not a major issue. Four cancers in the surveillance group were found to be interval cancers, but it was hard to determine if these were not detected during a previous colonoscopy.</td>
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Evidence table for review question 1: Is colonoscopic surveillance for prevention and/or early detection of colorectal cancer in adults with inflammatory bowel disease clinically effective compared with no surveillance?

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<td>than three-quarters of their disease duration and all developed CRC. In the surveillance group 20 (100%) and 96 (77%) in the no surveillance group had used 5-ASA preparations (P = 0.08). Using Cox regression, the effect of 5-ASA on survival and surveillance is not significant (P = 0.96 and P = 0.098 respectively).</td>
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</tbody>
</table>
### Evidence table for review question 1: Is colonoscopic surveillance for prevention and/or early detection of colorectal cancer in adults with adenomas clinically effective compared with no surveillance?

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<tr>
<th>Study ID</th>
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<tr>
<td>Thiis-Evensen (1999a)</td>
<td>Prospective cohort study. Population randomised into a screening (intervention) group and a control group.</td>
<td>1983–1996</td>
<td>Screening (intervention group): 400 men and women in Oslo, Norway. Control group: 399. 324 (81%) out of the 400 enrolled attended the screening because of the presence of polyps in 1983, 277 (85%) were still alive in 1996. In the control group of 399, 358 (89%) were still alive in 1996. 210 (76%) from the screening group and 241 (68%) in the control group, 451 (71%) people in total attended in 1996. Mean age of people attending was 67.4 years in the screening group and 67 years in the control group. Range: 63–72 years for both groups.</td>
<td>Screening intervention with FSIG and colonoscopy.</td>
<td>No screening.</td>
<td>Forty-eight of the controls (12% of the original group of 399) had a colonoscopic examination between 1983 and 1996. Ten of these people had a total of 18 adenomas removed, 8 of which measured 5–10 mm in diameter and the largest 10 mm; none showed more than moderate dysplasia. In the screening group 27 (7% of the original group of 400) had a colonoscopy other than the study colonoscopies in 1983, 1985 and 1989. Three of these people (1%) each had one adenoma removed, the largest measuring 5 mm in diameter and showing moderate dysplasia. <strong>Incidence of CRC:</strong> 12 people had CRC diagnosed during 13 years of observation. Two people in the screening group had CRC compared with 10 in the control group (relative risk 0.2; 95% CI 0.03 to 0.95, P = 0.02). <strong>Overall mortality:</strong> overall accumulated death rate, from January 1983 to December 1994, showed 55 (14%) deaths in the screening group, compared with 35 (9%) in the control group (relative risk 1.57; 95% CI 1.03 to 2.4, P = 0.02). The higher mortality in the screening group 324 (81%) people accepted FSIG screening at the initial stage (mean age 54.4 years). People in whom polyps were detected had a full colonoscopy with polypectomy and were offered follow-up by colonoscopy with polypectomy. People in the control group were not informed about their status as enrolled control. The people in both groups matched for age, sex and body mass index.</td>
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<td>Jorgensen (1993)</td>
<td>Prospective randomised study of patients with colorectal adenomas subject to different surveillance follow-up. The group was compared with controls from the normal Danish population, Eide (1986) and Stryker (1987), matched for age and sex.</td>
<td>Long term (1–24 years) colonoscopic surveillance.</td>
<td>Population of patients with all types of adenomas regardless of size and method of removal. 2041 patients were included from 1978 to 2002. Their ages were between 24 and 76 years old (average 60.8 years for men and 60.1 years for women). 497 men and 362 women had advanced adenoma that is, adenomas &gt; 10 mm. A clean colon was achieved before patients were included in the study. No patient had a history of familial adenomatous polyposis (FAP), hereditary nonpolyposis colorectal cancer (HNCC) or IBD. Patients participating in a chemoprevention trial were excluded.</td>
<td>Surveillance intervention with colonoscopy was supplemented with double-contrast barium enema (DCBE). Colonoscopy was performed in all patients and complete in 1871; incomplete colonoscopy was supplemented by DCBE in 148 leaving 22 who had documentation of a clean colonoscopy before patients were included in the study.</td>
<td>No surveillance.</td>
<td>115 of 2041 patients had reached 24 years of colonoscopic surveillance after inclusion at November 2002. Colonoscopy had been performed 6289 times and DCBE 998 times during 13,993 patient years of surveillance. Compliance: 72.9% in men and 76.3% in women. Colonoscopy was complete in 95% of the examinations for men and 92% for women. Incidence of CRC: CRC was found in 27 (23.48%) of the 115 that had 24 years of colonoscopic surveillance (relative risk 0.65; 95% CI, 0.43 to 0.95) of which 14 were men (relative risk 0.54; 95% CI 0.29 to 0.90) and 13 were women (relative risk 0.86; 95% CI 0.46 to 1.46). At the end of the study, three patients died from CRC (relative risk 0.12; 95% CI, 0.03 to 0.36). Risk of CRC relative to various reference populations: RR (95% CI) Large (≥ 10 mm) adenomas – 0.16 (0.08 to 0.30) Severe dysplastic adenomas – 0.09 (0.04 to 0.21) The relative risk of CRC and death from CRC in the total study population (2041 patients) was calculated from 1978 to 2002 by dividing the observed number by the number expected in a standard Danish population with the same age and sex distribution. The estimates of RR were adjusted for differences in the age, sex and calendar specific incidence and death rates.</td>
<td>Comments</td>
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could be explained by a collectively higher frequency of deaths caused by coronary heart disease, cerebrovascular accidents, sudden death, chronic obstructive lung disease and alcohol abuse (P = 0.03).

**Adverse effects**

There were no complications from the endoscopic examinations and polypectomies.
**Evidence table for review question 1: Is colonoscopic surveillance for prevention and/or early detection of colorectal cancer in adults with adenomas clinically effective compared with no surveillance?**

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<td>colon without neoplasia.</td>
<td>0.17) Villous adenomas – 0.96 (0.46 to 1.76) All with adenomas – 0.89 (0.43 to 1.64) Large (≥ 10 mm) adenomas – 0.57 (0.27 to 1.04)</td>
<td></td>
<td>Adverse effects: severe complications from surveillance examinations were seen in 20 patients and two died from these complications. One death was from diagnostic colonic perforation and the other from coronary occlusion after colonoscopy with polypectomy.</td>
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## Review question 2A: People with adenomas

### Evidence table for review question 2A (a, b): Is colonoscopic surveillance for prevention and/or early detection of colorectal cancer in adults with inflammatory bowel disease or polyps clinically effective compared with comparators?

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<th>Study ID</th>
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<tr>
<td>Van den Broek (2009)</td>
<td>Systematic review of three randomised control trials (RCTs): Narrow band imaging (NBI) versus white light endoscopy (WLE)</td>
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<td>Rex and Helbig (2007)</td>
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<td>Alder (2007)</td>
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<td>Inoue (2008)</td>
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<td>Pooled results</td>
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<tr>
<td>Author (RCT): NBI vs WLE</td>
<td>No. of NBI</td>
<td>No. of WLE</td>
<td>Patients with adenoma detected by NBI (%)</td>
<td>Patients with adenoma detected by WLE (%)</td>
<td>Odds ratio (95% CI) of NBI vs WLE</td>
<td>No. of adenomas detected by NBI (mean per patient)</td>
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<td>Rex and Helbig (2007)</td>
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*Includes two invasive cancers

**Rex and Helbig (2007):** 434 patients were included aged 50 years or older with an intact colon. There was no difference in the percentage of patients with adenoma for the entire cohort for WLE (67%) vs NBI (65%) (p = 0.61). One highly experienced endoscopist performed all examinations. No complications occurred.

**Alder (2007):** 401 patients were included (mean age 59.4 years, 52.6% men). Adenomas were detected more frequently in the NBI group (23%) than in the control group (17%) with 17 colonoscopies needed to find one additional adenoma patient; however the difference was not statistically significant (p = 0.129).

**Inoue (2008)** demonstrated a significantly improved adenoma detection rate by NBI vs WLE (mean number of adenomas per evaluated patient, 0.84 vs 0.55; p = 0.046). No advantage for NBI could be demonstrated when the proportion of patients with at least one adenoma was compared between NBI and WLE. An insufficient allocation method caused inadequate distribution of NBI procedures among all participating endoscopists. Rex and Helbig (2007) and Alder (2007) could not demonstrate an increased adenoma detection rate (both per lesion and per patient) by NBI in two large randomised studies.

Some differences existed among the three randomised studies:
- Rex and Helbig used high-definition monitors,
Evidence table for review question 2A (a, b): Is colonoscopic surveillance for prevention and/or early detection of colorectal cancer in adults with inflammatory bowel disease or polyps clinically effective compared with comparators?

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Seven endoscopists without previous experience of NBI performed the examinations.

**Inoue (2008):** 205 polyps were removed from 109 (44.86%) patients out of a total of 243 patients randomised; 127 of these polyps (67%) were assigned to the NBI group and 78 (38%) to the control group (WLE). Of the 205 polyps detected, 169 (82.4%) were neoplastic, with 66 (39.1%) detected in the control group and 103 (60.1%) detected in the NBI group.

Six endoscopists with unknown experience performed the examinations; one performed more than 60% of the examinations.

There were no immediate complications. All patients were contacted within 2 weeks of the procedure, and none of them reported any significant adverse effects from colonoscopy or polyp resection.

- There were differences in NBI-systems, inclusion criteria, and endoscopist experience. The pooled results of the three randomised studies revealed a non-significant increase in the number of patients with at least one adenoma (odds ratio [OR] 1.19; 95% CI, 0.86 to 1.64) or the total number of adenomas (OR 1.23; 95% CI, 0.93 to 1.61) when NBI was used for detection.

Dekker (2007)  Prospective RCT: cross-over study design

Forty-two patients with longstanding ulcerative colitis. The study group comprised 31 men and 11 women with a mean age (±SD) of 50 ± 11.2 years. The mean duration (±SD) of their ulcerative colitis was 21 ± 8.6 years.

Narrow-band imaging (NBI) Conventional colonoscopy

The number of patients with true positive findings (8 for NBI vs. 7 for WLE) and false-positive findings (9 for NBI vs. 6 for WLE) for the endoscopic procedures was not significantly different (p = 0.705 and p = 0.581, respectively).

All participants underwent NBI and conventional colonoscopy with at least 3 weeks between the two procedures to allow healing of any biopsy sites. All colonoscopies were performed by one of three experienced endoscopists, who were blinded with respect to the
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<tr>
<td>Rex (1995)</td>
<td>RCT</td>
<td>One hundred and forty-nine patients aged 40 years or more with symptoms suggestive of colonic disease were randomised. Mean age was 63 years.</td>
<td>Flexible sigmoidoscopy (FSIG) plus air-contrast barium enema (ACBE).</td>
<td>Colonoscopy</td>
<td>More of the patients undergoing colonoscopy first had at least one adenoma, and this difference approached significance (OR 2.07; 95% CI 0.90 to 4.92). More large adenomas (≥ 5 mm and ≥ 1 cm) were detected in patients undergoing colonoscopy first, but these differences did not reach significance. Patients initially undergoing FSIG plus ACBE were more likely to require the alternative procedure (colonoscopy) than were patients initially undergoing colonoscopy to require ACBE (OR 4.46; 95% CI 1.47 to 16.4).</td>
<td>There was no significant difference in the number of detected neoplastic lesions between the 2 techniques (9 for NBI vs. 12 for WLE, p = 0.672). Only the number of false-positive lesions was significantly higher for NBI than is was for WLE (43 vs. 16, p = 0.015). endoscopic and histopathological findings of the first procedure. The NBI system used in this study was a first generation prototype, which might explain the low yield of NBI.</td>
<td>Patient with incomplete initial colonoscopy and patients with polyps seen on FSIG plus barium enema underwent alternative procedure (barium enema or colonoscopy). No significant differences were noted in demographic, historical, clinical, or biochemical variables between the two groups. The strategy of initial FSIG plus ACBE detected more patient with diverticulosis than did initial colonoscopy, whereas the strategy of initial colonoscopy detected more patients with adenomas (p = 0.06)</td>
</tr>
<tr>
<td>Mulhall</td>
<td>Systematic review</td>
<td>Prospective studies of adults undergoing CT colonography after full bowel preparation, with colonoscopy as</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Characteristics of the CT</td>
</tr>
</tbody>
</table>
**Evidence table for review question 2A (a, b): Is colonoscopic surveillance for prevention and/or early detection of colorectal cancer in adults with inflammatory bowel disease or polyps clinically effective compared with comparators?**

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Study design</th>
<th>Follow-up</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcomes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>(2005)</td>
<td>and meta-Analysis on CT colonography</td>
<td>the gold standard were selected. Data on sensitivity and specificity overall and for detection of polyps less than 6 mm, 6 to 9 mm, and greater than 9 mm in size were reported. Thirty three studies provided data on 6393 patients. <strong>Overall pooled per patient sensitivity:</strong> for CT colonography was 70% (95% CI 53% to 87%). Sensitivity increased progressively as polyp size increased: It was 48% (95% CI 25% to 70%) (range 14–86%) for detection of polyps smaller than 6 mm, 70% (95% CI 55% to 84%) (range 30–95%) for polyps 6 to 9 mm, and 85% (95% CI 79% to 91%) (range 48–100%) for polyps larger than 9 mm. Each of these analyses was statistically heterogeneous. <strong>Overall pooled per patient specificity:</strong> Specificity was more consistent across polyp sizes. Overall, CT colonography was 86% specific (95% CI 84% to 88%) on the basis of data from 14 studies. Specificity improved as polyp size increased, and the results were homogeneous within each stratum. Four studies reported specificity for detection of polyps smaller than 6 mm, and the pooled specificity from these studies was 91% (95% CI 89% to 95%). For polyps 6 to 9 mm in size (6 studies), specificity was 93% (95% CI 91% to 95%) and to 97% (95% CI 96% to 97%) for polyps larger than 9 mm (15 studies).</td>
<td></td>
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<tr>
<td>Winawer (2000)</td>
<td>Controlled trial comparing colonoscopy and double-contrast barium enema (DCBE)</td>
<td>Nine hundred and seventy three patients underwent one or more colonoscopic examinations for surveillance. In 580 of these patients, 862 paired colonoscopic examinations and barium enema was performed. Colonscopic and barium enema examination. Colonoscopic examination without barium enema. Polyps were detected in 392 of 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 of the 392 colonoscopic examinations in which one or more polyps were detected (rate of detection of polyps, 35%; 95% CI 31% to 40%). Half of these</td>
<td>Colonography scanner, including width of collimation, type of detector, and mode of imaging, explained some of the heterogeneity. Limitations: the studies differed widely, and the extractable variables explained only a small amount of the heterogeneity. Only a few studies examined the newest CT colonography.</td>
<td></td>
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</tbody>
</table>

Winawer (2000) | Controlled trial comparing colonoscopy and double-contrast barium enema (DCBE) | Nine hundred and seventy three patients underwent one or more colonoscopic examinations for surveillance. In 580 of these patients, 862 paired colonoscopic examinations and barium enema was performed. Colonscopic and barium enema examination. Colonoscopic examination without barium enema. Polyps were detected in 392 of 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 of the 392 colonoscopic examinations in which one or more polyps were detected (rate of detection of polyps, 35%; 95% CI 31% to 40%). Half of these | Colonoscopy was used as the reference measure with the knowledge that it is not perfect and does miss polyps. In this study, the rate of missed adenomas was 20% for colonoscopic examination, and all missed polyps were ≤ 1.0 cm. | The study design permitted a direct blinded comparison of colonoscopic examination with barium enema without interfering with complete colonoscopy in each patient. |
<table>
<thead>
<tr>
<th>Study ID</th>
<th>Study design</th>
<th>Follow-up</th>
<th>Population</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>

polyps were adenomas, and the remainder were primarily normal mucosal tags, with some hyperplastic polyps.
**Review question 2B: People with inflammatory bowel disease**

**Evidence table for review question 2B: Is colonoscopic surveillance with a dye (chromoscopy) for prevention and/or early detection of colorectal cancer in adults with inflammatory bowel disease clinically effective compared with colonoscopic surveillance without dye (conventional colonoscopy)?**

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Study design</th>
<th>Follow up</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kiesslich et al. (2003)</td>
<td>Prospective randomised trial. Randomised 1:1 into two groups A or B – for chromo-endoscopy (with the use of a dye) or for conventional endoscopy respectively. The randomisation was done using a computer-aided system and the results were kept in a sealed envelope and opened only before the colonoscopy by an</td>
<td>None</td>
<td>Total (N = 165): group A (chromo-endoscopy; n = 84) and group B (conventional endoscopy; n = 81). 263 consecutive patients with clinically inactive, long standing ulcerative colitis (≥ 8 years) were recruited from an outpatient clinic in the University of Mainz, Germany. The sample size was calculated to be 170 patients (85 in each group) using alpha as 0.05 and a</td>
<td>Chromoscopy using 0.1% methylene blue (A; n = 84). For group A the colon was stained in a segmented fashion, 30 cm at a time using a spraying catheter (Olympus PW-IL, Hamburg, Germany). After 1-minute excess dye was removed by suction and staining was considered complete when the tiny glandular duct openings of the mucosa (pits) were clearly visible. Magnification</td>
<td>Conventional colonoscopy (B; n = 81). In group B colonoscopy was performed using conventional video colonoscopy. The average duration for the procedure was 35±9.3 minutes (range 19–59 minutes).</td>
<td>RCT with well reported blinding, concealment, inclusion and exclusion criteria with a consort chart explaining the same. Sample size calculated to be 85 required in each arm, 87 recruited but because of insufficient bowel preparation each arm had less participants than required. The two arms were compared for age, duration of UC, body mass index, stool frequency, rectal bleeding, temperature, haemoglobin, prevalence of primary</td>
</tr>
</tbody>
</table>

**Targeted biopsies**
An average of 40.8 biopsies was taken per patient: 42.2 biopsies per patient in group A and 38.2 in group B.

For A, 14.4/42.2 biopsies were targeted compared with 4.3/38.2 biopsies in group B (P = 0.044).

**Colorectal neoplasia**
A total of 46 neoplastic lesions were seen in 19 patients. 42 of these lesions were intraepithelial neoplasia (32 LGD, 10 HGD and 4 invasive cancers).

More dysplasia was detected in group A compared with group B (32 versus 10; P = 0.003).

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Group A</th>
<th>Group B</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td></td>
<td>84</td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>Patients with IN</td>
<td>13</td>
<td>6</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Total number IN lesions</td>
<td>32</td>
<td>10</td>
<td>0.00315</td>
<td></td>
</tr>
<tr>
<td>LGD lesions</td>
<td>24</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HGD lesions</td>
<td>8</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Invasive cancers</td>
<td>3</td>
<td>1</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Polypoid lesions</td>
<td>8</td>
<td>6</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>IN in flat mucosa (Fisher exact test)</td>
<td>24</td>
<td>4</td>
<td>0.0007</td>
<td></td>
</tr>
</tbody>
</table>

NS: not significant; IN: intraepithelial neoplasia
Adapted from table 5 in Kiesslich (2003)

**Extent of disease/inflammation - not relevant for guideline**
There was a significantly better correlation between the
### Evidence table for review question 2B: Is colonoscopic surveillance with a dye (chromoscopy) for prevention and/or early detection of colorectal cancer in adults with inflammatory bowel disease clinically effective compared with colonoscopic surveillance without dye (conventional colonoscopy)?

<table>
<thead>
<tr>
<th>Study ID</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Kiesslich et al. (2007)</td>
<td>Prospective randomised trial. Randomised 1:1 into two groups A or B – for chromoendoscopy with endomicroscopy (with the use of a dye) or with</td>
<td>None</td>
<td>Total (N = 161): group A (chromoendoscopy; n = 80) and group B (conventional endoscopy; n = 73). 192 consecutive patients with long standing ulcerative colitis</td>
<td>Chromoscopy using 0.1% methylene blue with endomicroscopy (A; n = 80). The confocal laser endoscope was advanced into the ileum or caecum and 5 ml of fluorescein</td>
<td>Conventional colonoscopy (B; n = 73). Colonoscopy was performed using conventional video endoscopes (Pentax EC 3830FK). Four biopsy</td>
<td>Biopsy specimens About 50% less biopsies were needed per patient in group A versus group B, 21.2 compared with 42.2 respectively (P = 0.008). Significantly less number of biopsies were needed for group A: 1888 compared to 3081 (P = 0.008). The total number of biopsy specimens containing intraepithelial neoplasia was 57 in group A compared to 7 in group B (P &lt; 0.0001).</td>
<td>RCT with well reported blinding, concealment, inclusion and exclusion criteria with a consort chart available from a supplement. Sample size calculated to be 54 required in each arm, and 80</td>
</tr>
</tbody>
</table>
### Evidence table for review question 2B: Is colonoscopic surveillance with a dye (chromoscopy) for prevention and/or early detection of colorectal cancer in adults with inflammatory bowel disease clinically effective compared with colonoscopic surveillance without dye (conventional colonoscopy)?

<table>
<thead>
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<th>Comparison</th>
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<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marion</td>
<td>Prospective</td>
<td>People with inflammatory bowel disease</td>
<td>Chromoscopy</td>
<td>1) Random</td>
<td>The number of positive findings of LGD and HGD was compared</td>
<td>The different...</td>
<td></td>
</tr>
</tbody>
</table>

#### Study details:
- **Confocal laser endoscopy** respectively.
- The randomisation was done using a computer-aided system and the results were kept in a sealed envelope and opened only before the colonoscopy by an independent person who was blinded to the study question.
- The sample size was calculated to be 114 patients (57 in each group) using alpha as 0.05 and a power of 90% and a 3.5-fold increase in the yield of neoplasia detection for chromoendoscopy.
- 161 patients were recruited but 8 had insufficient bowel preparation and were excluded and 153 completed the study protocol.

#### Study design details:
- **Study ID**: Marion
- **Study design**: Prospective
- **Follow up**: People with inflammatory bowel disease
- **Population**: Chromoscopy
- **Intervention**: 1) Random
- **Comparison**: The number of positive findings of LGD and HGD was compared

#### Outcomes:
- The total number of targeted biopsy specimens containing intraepithelial neoplasia was 57 in group A compared with 13 in group B (P < 0.0001).
- **Colorectal neoplasia**
  - A total of 23 neoplastic lesions were seen in 15 patients. All of these lesions were intraepithelial neoplasia (15 LGD, 8 HGD).
  - Group A detected 4.75-fold more neoplasia compared with group B (19 versus 4; P = 0.005).
  - Group A detected significantly more flat neoplasia compared with B (16 versus 2; P = 0.002).

#### Diagnostic accuracy:
- The presence of neoplastic changes could be predicted by endomicroscopy with a sensitivity of 94.7%, specificity of 98.3%, accuracy 97.8%.
Evidence table for review question 2B: Is colonoscopic surveillance with a dye (chromoscopy) for prevention and/or early detection of colorectal cancer in adults with inflammatory bowel disease clinically effective compared with colonoscopic surveillance without dye (conventional colonoscopy)?

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<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>et al. (2008)</td>
<td>Single blind trial with three methods within the same patient population.</td>
<td>None</td>
<td>Ulcerative or Crohn's colitis (N = 102, 64 male and 34 female) were included in the study at Mount Sinai Medical Centre, New York, USA. People more than 18 years of age with a confirmed diagnosis of extensive ulcerative colitis defined as at least left sided (n = 79) or Crohn's colitis involving at least one-third of the colon (n = 23). The median age of onset was 27 years (range 3–65) and the median duration of disease was 21.5 years (range 5–75) and all had enrolled in a surveillance programme at</td>
<td>With 0.1% methylene blue dye. A dye sprayer was used to spray 0.1% methylene blue dye during reintubation to the caecum. After reinsertion of the caecum, the scope was withdrawn slowly and the mucosa examined after dye spray and any visible lesions were biopsied or removed by endoscopic resection. The method took 15 minutes and 12 seconds (range 5:09–28:35).</td>
<td>Non-targeted conventional colonoscopy – the colon was examined and four quadrant random biopsies were taken from segments defined by the endoscopist using multibite forceps.</td>
<td>Chromoscopy showed a higher yield of dysplasia than targeted conventional colonoscopy, 17 people with dysplasia were found compared with 3 after random biopsy (P &lt; 0.001). Chromoscopy showed a significantly more effective than random biopsy, 20 people with dysplasia were found compared with 3 after random biopsy (P &lt; 0.0002), but 2 patients were found to have dysplasia only by random biopsy and not by any of the two targeted methods.</td>
<td>Techniques were performed on patients back-to-back and the pathology specimens were analysed by an expert gastrointestinal pathologist who was blinded to the method of collection. There was no long-term follow up and the authors stated that methylene blue may cause DNA damage with white light exposure and therefore the long-term implications of single stranded DNA breaks and oxidative changes in patients with colitis are unknown.</td>
</tr>
</tbody>
</table>

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### Evidence table for review question 2B: Is colonoscopic surveillance with a dye (chromoscopy) for prevention and/or early detection of colorectal cancer in adults with inflammatory bowel disease clinically effective compared with colonoscopic surveillance without dye (conventional colonoscopy)?

<table>
<thead>
<tr>
<th>Study ID</th>
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<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Rutter et al. (2004a)</td>
<td>Prospective single blind trial with three methods within the same patient population.</td>
<td>None</td>
<td>Patients (N = 100) with longstanding extensive ulcerative colitis [UC] attending routine colonoscopic</td>
<td>Chromoscopy with 0.1% indigo carmine</td>
<td>1) Non-targeted quadrantic – on initial intubation, inspection of the entire colonic</td>
<td>Dysplasia yield by method (per biopsy)</td>
<td>The different techniques were performed on the patients back-to-back and all biopsy specimens were analysed by one</td>
</tr>
</tbody>
</table>

#### Dysplasia yield by method per patient

<table>
<thead>
<tr>
<th></th>
<th>Random non-targeted</th>
<th>Targeted with and without dye</th>
<th>Chromoscopy</th>
<th>Random non-targeted</th>
<th>Targeted conventional colonscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysplasia (D)</td>
<td>1</td>
<td>19</td>
<td>6</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td>No dysplasia (ND)</td>
<td>2</td>
<td>83</td>
<td>3</td>
<td>82</td>
<td>85</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>99</td>
<td>9</td>
<td>93</td>
<td>93</td>
</tr>
</tbody>
</table>

Adapted from tables 2 and 3 from Marion 2008

Agreement between chromoscopy findings and colectomy for the 4 patients that had colectomy: 3 with dysplasia and 1 without (though 1/3 was HGD, not all LGD as detected by chromoscopy.

- All patients received standard bowel preparation (Fleets Phosphoda, MiraLax, or Citrate of Magnesia-based preps) and each patient acted as his or her own control.
- The only significant equipment expense was the dye spray catheter ($185) which can be sterilised and used up to 20 times, and the study used the cheaper methylene blue dye over the indigo carmine dye.
- 39% had previous documented dysplasia (38 LGD, 2 HGD, 10 indefinite for dysplasia). Four had polypoid lesions, others had uncharacterised or not visible lesions (detected using random biopsy).

**Rutter et al.**

Prospective single blind trial with three methods within the same patient population.
<table>
<thead>
<tr>
<th>Study ID</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Each patient underwent back-to-back colonoscopic examination: first with random colonoscopic surveillance, followed by targeted colonoscopic surveillance and then using pancolonic indigo carmine dye spray.</td>
<td>surveillance for ulcerative colitis at St Mark’s Hospital, UK. There were 61 male and 39 female patients. Median age was 53 years (range 33–79); median age at onset of UC was 27 years (range 7–67); and the median duration of colitis was 24 years (range 8–52). For 11 patients this was their index screening and 89 patients had undergone surveillance previously. The documented proximal extent of macroscopic inflammation was the transverse colon in 12 patients, hepatic flexure in 4 patients, ascending colon in 1 patient, and pancolonic in 83 patients.</td>
<td>designed dye spray catheter (Olympus PW-5V1). After allowing a few seconds for the dye to settle onto the mucosal surface excess pools of indigo carmine were suctioned. The mucosa was then scrutinised, and any abnormalities not identified on initial examination were biopsied or removed. The median time for the procedure was 10 minutes (range 4–22).</td>
<td>mucosa was done on withdrawal. At 10 cm intervals, the mucosa was photographed and quadrantic non-targeted colonic biopsies taken as per the American Society of Gastroenterology Endoscopy (ASGE) guidelines (about 2–40 per colon). 2) Pre-dye spray targeted biopsies – in addition, any suspicious areas of mucosa was photographed and biopsied or removed, as clinically indicated. Suspicious areas were defined as any mucosal irregularity that was not felt to Overall, 157 suspicious mucosal areas were detected in 61 patients. 43 abnormalities (from 20 patients) were detected during the pre-dye spray colonoscopy, and following indigo carmine dye spraying 114 additional abnormalities (in 55 patients) were detected. Median size was 4 mm (range 1–40). Six of the abnormalities were pedunculated, 69 were sessile, 75 were flat topped elevated abnormalities, and 7 abnormalities were described as irregular appearing mucosa.</td>
<td>Pre-dye spray targeted biopsies</td>
<td>Of the 43 abnormalities detected during the pre-dye spray colonoscopy, 9 lesions were hyperplastic polyps and 32 were inflammatory or post-inflammatory polyps. Two patients had dysplastic lesions (a 20 mm sessile lesion on quiescent mucosa at the hepatic flexure in a 71 year old male with no previous dysplasia and a 15 mm sessile lesion on mildly inflamed mucosa in the sigmoid colon in an 80 year old female with previous dysplasia, who has repeatedly declined surgery unless cancer was detected). Targeted biopsies showed low-grade dysplasia, confirming the endoscopist's impression that these were dysplasia-associated lesions/masses [DALMs].</td>
<td>Dye spray targeted biopsies</td>
<td>Both DALM lesions were visible after indigo carmine dye spraying. Of the 114 additional abnormalities detected following dye spraying, seven were dysplastic (from 5 patients). Five of these abnormalities were tubular adenomas with LGD, and two were serrated adenomas with LGD. Three of the lesions were described as flat lesions and four were sessile. The size of these well circumscribed adenomas ranged from 2 to 6 mm. Two adenomas were found in the caecum, two at the hepatic flexure, two in the transverse colon, and one in the descending colon. Two of the adenomas occurred proximal to the extent of colitis and five were within the UC extent (four in well healed disease, one in an area of mild inflammation). Of the other 107 abnormalities detected following dye spraying, 41 were hyperplastic polyps, 65 post-inflammatory and inflammatory polyps, and one was described as villiform mucosa but without of two experienced gastrointestinal histopathologists, who were blinded to the protocol used. Any specimen showing dysplasia was independently reported by both, and in the event of inter-observer variation a consensus opinion was reached. According to the authors, despite being back-to-back colonoscopies, the lesions detected by the dye were not missed lesions as that would give a missed rate of 350% and felt they minimised this by doing a meticulous examination.</td>
</tr>
<tr>
<td>Study ID</td>
<td>Study design</td>
<td>Follow up</td>
<td>Population</td>
<td>Intervention</td>
<td>Comparison</td>
<td>Outcomes</td>
<td>Comments</td>
</tr>
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<td>----------</td>
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</tbody>
</table>
|          |              |           | The study size was calculated to be 100 based on a pre-dye spray dysplasia detection rate of 8% and an assumption of using dye doubling the rate (power of 90% and alpha of 0.05). 108 consecutive people were invited and 101 consented but one test was abandoned at the patient's request. | be entirely consistent with chronic or active ulcerative colitis, regardless of whether or not it was felt to be dysplastic. The median time for the procedure was 11 minutes (range 4–18). | dysplasia. | Dysplasia detection summary
With regard to dysplasia detection, the non-targeted biopsy protocol (2904 biopsies) detected no dysplasia from 100 patients, the pre-dye spray targeted biopsy protocol (43 biopsies) detected two dysplastic lesions in two of the 100 patients, and the dye spray targeted biopsy protocol (114 biopsies) detected these two dysplastic lesions plus seven additional dysplastic lesions in five more of the 100 patients. Thus overall, dysplasia was detected in 7% of patients. There was a strong statistical trend towards an increase in dysplasia detection with dye spraying (7/100 patients v 2/100 patients; p = 0.06, paired exact test). Compared with the non-targeted biopsy protocol, the targeted biopsies detected dysplasia in significantly more patients (7/100 patients v 0/100 patients; p = 0.02, paired exact test). |
Forest plots: people with inflammatory bowel disease

Outcome 1: Total number of patients with intraepithelial neoplasia detected

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Chromoscopy</th>
<th>Conventional colonoscopy</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>3.1.1 Randomised studies</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kiesslich 2003</td>
<td>13</td>
<td>84</td>
<td>6</td>
<td>81</td>
</tr>
<tr>
<td>Kiesslich 2007</td>
<td>11</td>
<td>80</td>
<td>4</td>
<td>73</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>164</td>
<td>154</td>
<td>10</td>
<td>24</td>
</tr>
<tr>
<td>Total events</td>
<td>24</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Chi² = 0.05, df = 1 (P = 0.82); I² = 0%</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 2.30 (P = 0.02)</td>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>

3.1.2 Back to back studies

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Chromoscopy</th>
<th>Conventional colonoscopy</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
<th>Odds Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
</tr>
<tr>
<td>Marion 2008</td>
<td>17</td>
<td>102</td>
<td>11</td>
<td>102</td>
</tr>
<tr>
<td>Rutter 2004</td>
<td>7</td>
<td>100</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>202</td>
<td>202</td>
<td>13</td>
<td>202</td>
</tr>
<tr>
<td>Total events</td>
<td>24</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Chi² = 0.77, df = 1 (P = 0.38); I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.89 (P = 0.06)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) 366 356 100.0% 2.21 [1.31, 3.74]

Total events 48 23

Heterogeneity: Chi² = 1.01, df = 3 (P = 0.80); I² = 0%
Test for overall effect: Z = 2.96 (P = 0.003)
Test for subgroup differences: Not applicable
Review question 2B: People with adenomas

Evidence table for review question 2B (b): Is colonoscopic surveillance with a dye (chromoscopy) for prevention and/or early detection of colorectal cancer in adults with adenomas clinically effective compared with colonoscopic surveillance without dye (conventional colonoscopy)?

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Study design</th>
<th>Follow up</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcomes</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brown et al. (2007)</td>
<td>Systematic review of RCTs. Cochrane review – included four RCTs: Brooker et al. (2002); Hurlstone et al. (2004); Lapalus et al. (2006); Le Rhun et al. (2004) (total of 1009 participants)</td>
<td>Databases searched from 1966-October 2006</td>
<td>Included: participants undergoing chromoscopic or conventional colonoscopy for investigation of gastrointestinal symptoms or as apart of a screening programme. Excluded: patients undergoing surveillance for IBD or patients undergoing surveillance for known polyposis syndromes; familial adenomatous polyposis (FAP) or hereditary non polyposis colorectal cancer (HNPCC).</td>
<td>Chromoscopy</td>
<td>Conventional colonoscopy</td>
<td>Detection outcomes based on number of polyps and neoplastic lesions detected. All significantly in favour of chromoscopy. <strong>Primary outcomes</strong> The number of polyps (neoplastic and non-neoplastic) detected was statistically significantly greater for all studies and highly significant when the studies were combined (WMD fixed 0.77; 95% CI 0.52 to 1.01). This enhanced yield was maintained even if neoplastic lesions only were considered (WMD fixed 0.35; 95% CI 0.23 to 0.47). However, tests for heterogeneity were significant in this analysis group. This may be indicative of the yield of neoplastic lesions, which varied significantly between studies. Almost all patients had either no polyps or 1 polyp. It was therefore estimated that over 95% of patients would have 0, 1 or 2 polyps and that a standard deviation of 2.00 for polyps and 1.00 for neoplastic lesions was reasonable and in agreement with the data from the one study that gave that data. Again there was a significant difference in favour of the chromoscopy group (OR [fixed] 2.13: 95% CI 1.47 to 3.10) which was maintained when considering neoplastic lesions only (OR [fixed] 1.61: 95% CI 1.24 to 2.09). <strong>Secondary outcomes</strong> With regard to secondary outcomes the number of diminutive neoplastic lesions and the number of patients with at least 1 diminutive neoplastic lesion were all increased in favour of chromoscopy compared with conventional colonoscopy (WMD fixed 0.27; 95% CI 0.14 to 0.40) and OR [fixed] 1.71; 95% CI 1.23 to 2.37) respectively. In addition, the number of Good Cochrane review – The two UK studies were single pass chromoscopy and the two French studies were 'back-to-back', which is known to increase polyp yield (Hixson 1990; Rex 1997). After the removal of these two studies (due to heterogeneity) - chromoscopy was still favoured. Heterogeneity was not seen when the results were pooled for patients with at least 1 polyp or 1 neoplastic lesion. Chromoscopy was favoured in all outcomes studied, with more than twice as much detection for patients with 3 or more polyps. This</td>
<td></td>
</tr>
<tr>
<td>Study ID</td>
<td>Study design</td>
<td>Follow up</td>
<td>Population</td>
<td>Intervention</td>
<td>Comparison</td>
<td>Outcomes</td>
<td>Comments</td>
</tr>
<tr>
<td>---------</td>
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<td>-----------</td>
<td>------------</td>
<td>--------------</td>
<td>------------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>patients with 3 or more neoplastic lesions was more than twice as likely to be detected using chromoscopy (OR [fixed] 2.55; 95% CI 1.49 to 4.36). The trend of enhanced detection of polyps (neoplastic and nonneoplastic) with chromoscopy was maintained even if outcome measures were considered for the proximal and distal colon separately. Although also showing this trend, two outcome variables failed to show a significant difference: total number of neoplastic lesions and diminutive neoplastic lesions detected in the distal colon.</td>
<td></td>
<td></td>
<td>was maintained for both distal and proximal colon. The authors conclude that chromoscopy should be the gold standard test for polyp detection until further research is done on the newer techniques. Data from the Hurlstone et al. (2004) study was not included for this guideline.</td>
<td></td>
</tr>
</tbody>
</table>
**Forest Plots: People with adenomatous polyps (revised from Brown 2007 Cochrane Review)**

Removed Hurlstone 2004 as noted above. Also applied random effects model if heterogeneity 50% or greater.

**Outcome 1: Total number of polyps detected**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Chromoscopy Mean</th>
<th>SD</th>
<th>Total</th>
<th>Conventional colonoscopy Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brooker 2002</td>
<td>2.06</td>
<td>2</td>
<td>124</td>
<td>0.81</td>
<td>2</td>
<td>135</td>
<td>33.5%</td>
<td>1.25</td>
<td>[0.76, 1.74]</td>
</tr>
<tr>
<td>Lapalus 2006</td>
<td>1.54</td>
<td>2</td>
<td>146</td>
<td>1.05</td>
<td>2</td>
<td>146</td>
<td>35.1%</td>
<td>0.49</td>
<td>[0.03, 0.95]</td>
</tr>
<tr>
<td>Le Rhun 2004</td>
<td>1.74</td>
<td>2</td>
<td>99</td>
<td>1.05</td>
<td>1.8</td>
<td>99</td>
<td>31.4%</td>
<td>0.69</td>
<td>[0.16, 1.22]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>369</td>
<td></td>
<td></td>
<td>380</td>
<td>100.0%</td>
<td>0.81</td>
<td>[0.35, 1.26]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.10; Chi² = 5.19, df = 2 (P = 0.07); I² = 61%
Test for overall effect: Z = 3.46 (P = 0.0005)

**Outcome 2: Total number of polyps detected in the proximal colon**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Chromoscopy Mean</th>
<th>SD</th>
<th>Total</th>
<th>Conventional colonoscopy Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brooker 2002</td>
<td>1.21</td>
<td>1</td>
<td>124</td>
<td>0.41</td>
<td>1</td>
<td>135</td>
<td>49.6%</td>
<td>0.80</td>
<td>[0.56, 1.04]</td>
</tr>
<tr>
<td>Lapalus 2006</td>
<td>0.58</td>
<td>1</td>
<td>146</td>
<td>0.27</td>
<td>1</td>
<td>146</td>
<td>50.4%</td>
<td>0.31</td>
<td>[0.08, 0.54]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>270</td>
<td></td>
<td></td>
<td>281</td>
<td>100.0%</td>
<td>0.55</td>
<td>[0.07, 1.03]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.11; Chi² = 8.23, df = 1 (P = 0.004); I² = 88%
Test for overall effect: Z = 2.26 (P = 0.02)
Outcome 3: Total number of polyps detected in the distal colon

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Chromoscopy Mean</th>
<th>SD</th>
<th>Total</th>
<th>Conventional colonoscopy Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean Difference</th>
<th>IV, Fixed, 95% CI</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brooker 2002</td>
<td>0.85</td>
<td>1</td>
<td>124</td>
<td>0.39</td>
<td>1</td>
<td>135</td>
<td>0.46</td>
<td>(0.22, 0.70)</td>
<td></td>
</tr>
<tr>
<td>Lepailus 2006</td>
<td>0.96</td>
<td>1</td>
<td>146</td>
<td>0.67</td>
<td>1</td>
<td>146</td>
<td>0.29</td>
<td>(0.06, 0.52)</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>270</td>
<td></td>
<td></td>
<td>281</td>
<td></td>
<td>100.0%</td>
<td>0.37</td>
<td>(0.20, 0.54)</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 0.99, \text{df} = 1 (P = 0.32); \text{I}^2 = 0\%$
Test for overall effect: $Z = 4.34 (P < 0.0001)$

Outcome 4: Total number of neoplastic lesions detected

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Chromoscopy Mean</th>
<th>SD</th>
<th>Total</th>
<th>Conventional colonoscopy Mean</th>
<th>SD</th>
<th>Total</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brooker 2002</td>
<td>1.01</td>
<td>1</td>
<td>124</td>
<td>0.3</td>
<td>1</td>
<td>135</td>
<td>0.71</td>
<td>(0.47, 0.95)</td>
<td></td>
</tr>
<tr>
<td>Lepailus 2006</td>
<td>0.79</td>
<td>1</td>
<td>146</td>
<td>0.6</td>
<td>1</td>
<td>146</td>
<td>0.19</td>
<td>[-0.04, 0.42]</td>
<td></td>
</tr>
<tr>
<td>Le Rhun 2004</td>
<td>0.6</td>
<td>1</td>
<td>99</td>
<td>0.5</td>
<td>0.9</td>
<td>99</td>
<td>0.10</td>
<td>[-0.17, 0.37]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>369</td>
<td></td>
<td></td>
<td>380</td>
<td></td>
<td>100.0%</td>
<td>0.33</td>
<td>[-0.04, 0.71]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 0.09, \text{df} = 2 (P = 0.85); \text{I}^2 = 85\%$
Test for overall effect: $Z = 1.77 (P = 0.08)$
Outcome 5: Total number of neoplastic lesions detected in the proximal colon

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Chromoscopy Mean</th>
<th>Conventional colonoscopy Mean</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brooker 2002</td>
<td>0.79</td>
<td>0.26</td>
<td>0.53 (0.28, 0.77)</td>
<td></td>
</tr>
<tr>
<td>Lapalus 2006</td>
<td>0.43</td>
<td>0.29</td>
<td>0.14 [-0.09, 0.37]</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI): 270
Heterogeneity: $\tau^2 = 0.06, \chi^2 = 5.21, df = 1 (p = 0.02); I^2 = 81$
Test for overall effect: $Z = 1.71 (p = 0.09)$

Outcome 6: Total number of neoplastic lesions detected in the distal colon

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Chromoscopy Mean</th>
<th>Conventional colonoscopy Mean</th>
<th>Mean Difference</th>
<th>IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brooker 2002</td>
<td>0.22</td>
<td>0.1</td>
<td>0.12 [-0.12, 0.36]</td>
<td></td>
</tr>
<tr>
<td>Lapalus 2006</td>
<td>0.36</td>
<td>0.3</td>
<td>0.06 [-0.17, 0.29]</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI): 270
Heterogeneity: $\chi^2 = 0.12, df = 1 (p = 0.73); I^2 = 0$
Test for overall effect: $Z = 1.03 (p = 0.30)$

Outcome 7: Total number of diminutive adenomas detected

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Chromoscopy Mean</th>
<th>Conventional colonoscopy Mean</th>
<th>Mean Difference</th>
<th>IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brooker 2002</td>
<td>0.72</td>
<td>0.27</td>
<td>0.45 (0.21, 0.69)</td>
<td></td>
</tr>
<tr>
<td>Lapalus 2006</td>
<td>0.61</td>
<td>0.32</td>
<td>0.29 (0.06, 0.52)</td>
<td></td>
</tr>
<tr>
<td>Le Rhun 2004</td>
<td>0.4</td>
<td>0.3</td>
<td>0.10 [-0.12, 0.32]</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI): 369
Heterogeneity: $\tau^2 = 0.02, \chi^2 = 4.36, df = 2 (p = 0.11); I^2 = 54$
Test for overall effect: $Z = 2.73 (p = 0.006)$
**Review question 3: People with Inflammatory bowel disease**

**Evidence table for review question 3: When should colonoscopic surveillance be started and what should be the frequency of surveillance?**

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Study design</th>
<th>Follow-up</th>
<th>Population</th>
<th>Prognostic factors or surveillance</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eaden et al. (2001)</td>
<td>Meta-analysis of 116 studies</td>
<td>...</td>
<td>24,478 people with UC 1698 cases of CRC</td>
<td><strong>Duration of disease</strong>&lt;br&gt;0 to 10 years (all UC)&lt;br&gt;Cumulative probability of CRC 1.6% (1.2 to 2) by 10 years</td>
<td>...</td>
</tr>
<tr>
<td>Jess et al. (2005)</td>
<td>Meta-analysis of 6 studies</td>
<td>...</td>
<td>6538 people with CD 55 cases of CRC</td>
<td><strong>Extent of disease</strong>&lt;br&gt;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.</td>
<td>...</td>
</tr>
<tr>
<td>Soetikno et al. (2002)</td>
<td>Meta-analysis of 11 studies</td>
<td>...</td>
<td>16,844 people with UC 564 with UC and PSC 560 cases of CRC, including 60 in people with UC and PSC</td>
<td><strong>PSC</strong>&lt;br&gt;OR 4.79 (3.58 to 6.41) of colorectal neoplasia (dysplasia or carcinoma) if UC and PSC compared with UC alone&lt;br&gt;OR 4.09 (2.89 to 5.76) of CRC if UC and PSC compared with UC alone&lt;br&gt;Results for fixed effect model presented. Similar results were found for the random effects model.</td>
<td>...</td>
</tr>
<tr>
<td>Thomas et al. (2007)</td>
<td>Meta-analysis of 20 studies</td>
<td>...</td>
<td>Over 2,677 people with UC 508 cases of LGD 31 cases of CRC</td>
<td><strong>Progression of LGD to CRC</strong>&lt;br&gt;OR 9.0 (4.0 to 20.5) of CRC if LGD diagnosis compared with no dysplasia&lt;br&gt;Meta-regression showed no significant effect of duration of disease on CRC risk (p = 0.57)</td>
<td>...</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Progression of LGD to HGD or CRC</strong>&lt;br&gt;OR 11.9 (5.2 to 27) of HGD or CRC if LGD diagnosis compared with no dysplasia</td>
<td>...</td>
</tr>
</tbody>
</table>
### Evidence table for review question 3: When should colonoscopic surveillance be started and what should be the frequency of surveillance?

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Study design</th>
<th>Follow-up</th>
<th>Population</th>
<th>Prognostic factors or surveillance</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Askling et al. (2001)</td>
<td>Retrospective (assumed) cohort, with nested case control</td>
<td>169,333 person years</td>
<td>19,876 people with UC or CD 143 cases of CRC</td>
<td>RR 3.5 (1.2 to 20) of CRC if pancolitis or colorectal CD compared with UC or CD. This did not significantly modify the association with FH of CRC (p = 0.51 interaction)</td>
<td>…</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>RR 2.5 (1.4 to 4.4) of CRC if FH with CRC compared with no FH with CRC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>RR 9.2 (3.7 to 23) of CRC if relative aged &lt;50 at diagnosis of CRC compared with no FH with CRC</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>RR 1.7 (0.8 to 3.4) of CRC if relative aged ≥50 at diagnosis of CRC compared with no FH with CRC</td>
<td></td>
</tr>
<tr>
<td>Brentnall et al. (1996)</td>
<td>Prospective cohort</td>
<td>79 years</td>
<td>45 people with UC 20 with PSC 13 cases of dysplasia</td>
<td>Duration of disease No significant association of duration of disease with development of dysplasia (indefinite, LGD, HGD) (logistic coefficient 0.07; p = 0.35)</td>
<td>…</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>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)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PSC Risk of CRC associated with PSC and UC included in Soetikno (2002) analysis</td>
<td></td>
</tr>
<tr>
<td>Broome et al. (1992)</td>
<td>Retrospective (assumed) cohort</td>
<td>≥15 years</td>
<td>72 people with UC 5 with PSC 17 cases of dysplasia, carcinoma, and/or DNA aneuploidy</td>
<td>Duration of disease Significant association of duration of disease with development of dysplasia and/or DNA aneuploidy (logistic coefficient 0.051; p = 0.038)</td>
<td>…</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Age at diagnosis or onset No significant association of age at onset of UC with development of dysplasia and/or DNA aneuploidy (logistic coefficient—0.041; p = 0.153)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PSC Risk of CRC associated with PSC and UC included in Soetikno (2002) analysis</td>
<td></td>
</tr>
<tr>
<td>Broome et al. (1995)</td>
<td>Retrospective (assumed) cohort</td>
<td>Mean observation time 9 years</td>
<td>120 people with UC 40 with PSC and UC 7 cases of CRC</td>
<td>Risk of CRC associated with PSC and UC included in Soetikno (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 &lt; 0.001])</td>
<td>…</td>
</tr>
</tbody>
</table>
### Evidence table for review question 3: When should colonoscopic surveillance be started and what should be the frequency of surveillance?

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Study design</th>
<th>Follow-up</th>
<th>Population</th>
<th>Prognostic factors or surveillance</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>D'Haens et al. (1993)</td>
<td>Retrospective case control</td>
<td>Not clear</td>
<td>58 people with UC 29 with PSC 9 cases of CRC</td>
<td>OR 1.04 (1.00 to 1.08) for association of risk of dysplasia or CRC with age at onset of symptoms in years (conditional logistic regression) PSC OR 9.00 (1.14 to 71.04) for association of risk of dysplasia or CRC with pericholangitis or PSC (conditional logistic regression)</td>
<td>...</td>
</tr>
<tr>
<td>Ekbom et al. (1990)</td>
<td>Retrospective (assumed) cohort</td>
<td>Over 20 years (max)</td>
<td>1655 people with CD 12 cases of CRC</td>
<td>Gender SIR for CRC 2.8 (1.1 to 5.8) in men; 2.1 (0.7 to 4.8) in women. Not direct comparison. Duration of disease 0 to 10 years (all UC) SIR for CRC 2.5 (1.0 to 5.1) for duration of follow-up &lt;10 years. Not direct comparison – compared with the general population Duration of disease 11 to 20 years (all UC) SIR for CRC 2.0 (0.4 to 6.0) for duration of follow-up 10 to 19 years. Not direct comparison – compared with the general population Duration of disease 21 to 30 years (all UC) SIR for CRC 3.2 (0.4 to 11.4) for duration of follow-up of 19 years or more. Not direct comparison – compared with the general population Age at diagnosis or onset SIR 9.5 (3.1 to 23.2) for CRC if aged &lt;30 years at diagnosis; 1.6 (0.6 to 3.3) if aged 30 years or more. Not direct comparison – compared with the general population Extent of disease SIR 1.0 (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 – compared with the general population.</td>
<td>...</td>
</tr>
<tr>
<td>Florin et al. (2004)</td>
<td>Retrospective case control</td>
<td>Not clear</td>
<td>384 people with UC 90 with PSC 8 cases of CRC</td>
<td>PSC OR 3.6 (1.3 to 10.2) for risk of HGD or CRC in PSC-IBD compared with UC</td>
<td>...</td>
</tr>
</tbody>
</table>
### Evidence table for review question 3: When should colonoscopic surveillance be started and what should be the frequency of surveillance?

<table>
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</thead>
<tbody>
<tr>
<td>Friedman et al. (2001)</td>
<td>Retrospective (assumed) cohort</td>
<td>Not clear</td>
<td>259 people with CD 5 cases of CRC</td>
<td>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.</td>
<td>...</td>
</tr>
<tr>
<td>Gilat et al. (1988)</td>
<td>Prospective (assumed) cohort</td>
<td>Mean 11.5 years (SD 8.3)</td>
<td>1035 people with UC Number of cases of CRC not reported</td>
<td>Duration of disease Association of duration with risk of CRC included in Eaden (2001) analysis Cumulative incidence of CRC with total colitis 0% at 10 years; 9.3% at 15 years; 13.8% at 20 years</td>
<td>...</td>
</tr>
<tr>
<td>Gupta et al. (2007)</td>
<td>Retrospective cohort</td>
<td>Median 6.7 years</td>
<td>418 people with UC 65 cases of any neoplasia 15 progressed to advanced neoplasia</td>
<td>Gender HR 1.5 (0.9 to 2.4) for association of gender (male) with any neoplasia HR 2.5 (0.8 to 7.8) for advanced neoplasia (univariate only)</td>
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<td>Duration of disease HR 1.6 (0.9 to 2.8) for association of duration of disease (&gt;15 years) with any neoplasia HR 2.0 (0.6 to 6.3) for advanced neoplasia (univariate only)</td>
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<td>Age at diagnosis or onset HR 0.7 (0.4 to 1.2) for association of age (&lt;25 years) with any neoplasia HR 1.6 (0.6 to 4.5) for advanced neoplasia (univariate only)</td>
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<td>Extent of disease HR 1.1 (0.4 to 3.5) for association of extent of disease with any neoplasia No extensive disease in advanced neoplasia group (univariate only)</td>
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<td></td>
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<td></td>
<td>PSC HR 1.1 (0.2 to 8.0) for association of PSC with any neoplasia No PSC in advanced neoplasia group (univariate only)</td>
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<td>Severity of inflammation Inflammation score (mean) HR 1.4 (0.9 to 2.3) for association of inflammation with any neoplasia HR 3.0 (1.4 to 6.3) for advanced neoplasia Remained significant for advanced neoplasia when adjusted for frequency of colonoscopy</td>
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<td>Severity of inflammation Inflammation score (cumulative mean) HR 1.7 (0.9 to 3.1) for association of inflammation with any neoplasia HR 3.4 (1.1 to 10.4) for advanced neoplasia Similar results when adjusted for frequency</td>
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## Evidence table for review question 3: When should colonoscopic surveillance be started and what should be the frequency of surveillance?

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</table>
| Gyde et al. (1988) | Retrospective cohort | 16,928 patient years at risk | 823 people with UC 38 cases of CRC | **Severity of inflammation**  
Inflammation score (maximum)  
HR 1.0 (0.7 to 1.5) for association of inflammation with any neoplasia  
HR 2.2 (1.2 to 4.2) for advanced neoplasia  
Similar results when adjusted for frequency of colonoscopy | |
| | | | | **Frequency of colonoscopy**  
HR 1.7 (0.9 to 3.0) for association of frequency of colonoscopy (1 or more per year) with any neoplasia  
HR 3.9 (1.3 to 11.4) for advanced neoplasia (univariate only) | |
| Gender | No difference between RR of CRC in men and women (p = NS) | |
| Duration of disease | Association of duration with risk of CRC included in Eaden et al. (2001) analysis | |
| Age at diagnosis or onset | RR 1071 (observed/expected; 55.3 to 187.2) for extensive colitis with age of onset 15 to 24 years compared to the general population  
RR 27.9 (observed/expected; 15.2 to 46.8) for extensive colitis with age of onset 25 to 39 years compared to the general population  
RR 3.3 (observed/expected; 0.7 to 9.8) for extensive colitis with age of onset aged 40 and over compared to the general population | |
| Extent of disease | 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 | |
<table>
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<tbody>
<tr>
<td>Hendriksen et al. (1985)</td>
<td>Retrospective (assumed) cohort</td>
<td>Mean 6.7 years</td>
<td>783 people with UC 7 cases of colonic cancer</td>
<td>Duration of disease 0 to 10 years (all UC) Cumulative risk of CRC 0.8% (no CI reported) by 10 years</td>
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<td></td>
<td>Duration of disease 11 to 20 years (all UC) Cumulative risk of CRC 1.1% (no CI reported) by 15 years, and 1.4% (0.7 to 2.8) by 18 years</td>
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<td>Extent of disease Cumulative risk of CRC not influenced by initial extent of the colon. Cumulative risk after 18 years was 1.3%</td>
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<tr>
<td>Jess et al. (2006)</td>
<td>Retrospective (assumed) cohort</td>
<td>Median 14 years</td>
<td>692 people with IBD 29 cases of CR dysplasia</td>
<td>Disease – IBD HR 0.7 (0.2 to 3.0) for risk of recurrence and progression of dysplasia in CD compared with UC</td>
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<td>Gender HR 2.8 (0.3 to 23) for risk of recurrence and progression of dysplasia in men compared with women</td>
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<td>Age at diagnosis or onset HR 0.7 (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 (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</td>
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<td>Extent of disease HR 0.9 (0.2 to 4.6) for risk of recurrence and progression of dysplasia in pancolitis or pure colonic CD compared with other extent</td>
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<td>PSC HR 5.0 (1.1 to 23) for risk of recurrence and progression of dysplasia in PSC compared with no PSC</td>
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<td>Location of dysplasia HR 5.4 (1.0 to 28) for risk of recurrence and progression of dysplasia in dysplasia distal to splenic flexure compared with proximal</td>
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</table>
### Evidence table for review question 3: When should colonoscopic surveillance be started and what should be the frequency of surveillance?

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<tbody>
<tr>
<td>Jess et al.</td>
<td>Retrospective (assumed) cohort, with nested case control</td>
<td>Not clear</td>
<td>145 people with IBD 43 cases of neoplasia</td>
<td>PPSC Adjusted OR 6.9 (1.2 to 40) for colorectal neoplasia if PSC compared with no PSC (includes cases from Jess 2006)</td>
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<td>Family history Adjusted OR 1.4 (0.3 to 5.9) for colorectal neoplasia if first degree relative with CRC compared with no relative with CRC</td>
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<td>Severity of inflammation Adjusted OR 1.3 (0.6 to 2.9) for association of mean macroscopic inflammation score with colorectal neoplasia</td>
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<td>Frequency of colonoscopy Adjusted OR 5.3 (1.4 to 20) for colorectal neoplasia if 1 or more colonoscopic surveillances during the disease course compared with no surveillance</td>
</tr>
<tr>
<td>Karlén et al.</td>
<td>Retrospective cohort, with nested case control</td>
<td>Not clear</td>
<td>142 people with UC 40 cases of CRC (deaths)</td>
<td>Frequency of colonoscopy RR 0.29 (0.06 to 1.31) for risk of CRC mortality if colonoscopic surveillance ever compared with never</td>
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<td>RR 0.43 (0.05 to 3.76) for risk of CRC mortality if 1 colonoscopic surveillance compared with never</td>
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<td>RR 0.22 (0.03 to 1.74) for risk of CRC mortality if 2 or more colonoscopic surveillances compared with never</td>
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<tr>
<td>Kvist et al.</td>
<td>Retrospective (assumed) cohort</td>
<td>Median 11 years</td>
<td>759 people with UC 17 cases of CRC</td>
<td>Duration of disease Association of duration of disease with CRC risk included in Eaden et al. (2001) analysis</td>
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<td>Extent of disease Crude CRC rates for &quot;left-sided&quot; (proctosigmoiditis and left-sided disease) and universal disease were 'virtually the same' at 3%</td>
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<td>Time courses for duration of disease in the two groups were 'indistinguishable'</td>
</tr>
<tr>
<td>Langholz et al.</td>
<td>Retrospective (assumed) cohort</td>
<td>Median 11.7 years</td>
<td>1161 people with UC 6 cases of CRC</td>
<td>Duration of disease Association of duration with risk of CRC included in Eaden et al. (2001) analysis</td>
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<tr>
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<td>Cumulative incidence of CRC with extensive disease 1.8% at 25 years</td>
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</tbody>
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### Evidence table for review question 3: When should colonoscopic surveillance be started and what should be the frequency of surveillance?

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</table>
| Lennard-Jones et al. (1990) | Prospective cohort | 3,706 patient years | 401 people with extensive UC 22 cases of CRC | **Duration of disease**
- Association of duration of disease with CRC risk included in Eaden et al. (2001) analysis
- **Cumulative risk of HGD or CRC at 15 years 4%**
- **Cumulative risk of HGD or CRC at 20 years 7%**
- **Cumulative risk of HGD or CRC at 25 years 13%** | ... |
| Loftus et al. (2005) | Prospective cohort (with matched controls) | Not clear | 213 people with IBD/UC 71 with PSC-IBD 11 cases of CRC | **Duration of disease**
- 0 to 10 years (all UC) Cumulative risk of dysplasia or CRC at 5 years 33% (17 to 46) for PSC-IBD compared with 13% (2 to 21) for UC (p = 0.054)
- 11 to 20 years (all UC) Cumulative risk of CRC at 15 years 14% (3 to 25) for PSC-IBD compared with 4% (0 to 10) for UC (p = 0.13)
- **PSC**
- HR 1.7 (0.6 to 4.9) for dysplasia or CRC in PSC-IBD compared with UC
- HR 1.9 (0.3 to 11.9) for CRC in PSC-IBD compared with UC
- Both adjusted for age, duration of IBD, date of IBD diagnosis | ... |
| Nuako et al. (1998) FH | Retrospective (assumed) case control | Not clear | 297 people with UC 31 cases of CRC | Family history
- At least one first-degree relative with CRC
- **Adjusted OR 2.31 (1.03 to 5.18) for CRC in FH compared with no FH**
- Adjusted for sex, age, and year of UC diagnosis | ... |
| Nuako et al. (1998) PSC | Prospective (assumed) case control | Not clear | 342 people with UC 171 with CRC | **PSC**
- Adjusted OR 1.23 (0.62 to 2.42) for risk of CRC in PSC compared with no PSC | ... |
| Rutter et al. (2004b, 2004c) | Retrospective case control | Not clear | 204 people with UC 68 cases of CRC neoplasia | Severity of inflammation
- Inflammation score (mean) Adjusted OR 4.69 (2.10 to 10.48) for association between histological inflammation score and colorectal neoplasia
- Colonoscopic appearance
- OR 0.38 (0.19 to 0.73) for risk of CRC on a normal appearance compared with not normal
- Post-inflammatory polyps
- OR 2.29 (1.28 to 4.11) for risk of CRC with post-inflammatory polyps compared with no polyps
- Colonic stricture
- OR 4.62 (1.03 to 20.8) for risk of CRC with colonic stricture compared with no stricture | ... |
## Evidence table for review question 3: When should colonoscopic surveillance be started and what should be the frequency of surveillance?

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<tbody>
<tr>
<td>Rutter et al. (2006)</td>
<td>Retrospective (assumed) cohort</td>
<td>Mean 8.5 years</td>
<td>354 people with UC 215 cases of dysplasia or CRC</td>
<td>Duration of disease 0 to 10 years (all UC): Cumulative incidence of neoplasia at 10 years 1.5%; 0% for CRC; Duration of disease 11 to 20 years (all UC): Cumulative incidence of neoplasia at 20 years 7.7%; 2.5% for CRC; Duration of disease 21 to 30 years (all UC): Cumulative incidence of neoplasia at 30 years 15.8%; 7.6% for CRC; Duration of disease over 30 years (all UC): 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</td>
<td>...</td>
</tr>
<tr>
<td>St envoyis et al. (1995)</td>
<td>Retrospective (assumed) cohort</td>
<td>Mean follow-up 14.8 years; 14.5 years cancer incidence</td>
<td>471 people with UC 9 cases of CRC</td>
<td>Duration of disease: 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</td>
<td>...</td>
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<tr>
<td>Velayos et al. (2006)</td>
<td>Retrospective case control</td>
<td>Not clear</td>
<td>356 people with UC 188 cases of CRC</td>
<td>PSC: OR 1.1 (0.5 to 2.3) for risk of CRC in PSC compared with no PSC; Family history: At least one first-degree relative with CRC: Adjusted OR 3.7 (1.0 to 13.2) for risk of CRC in FH compared with no FH; Post-inflammatory polyps: Adjusted OR 2.5 (1.4 to 4.6) for risk of CRC with pseudopolyps compared with none; Frequency of colonoscopy: Adjusted OR 0.4 (0.2 to 0.7) for risk of CRC with 1 or 2 colonoscopies compared with none; Adjusted OR 0.3 (0.1 to 0.8) for risk of CRC with 2 colonoscopies compared with none</td>
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</table>
Review question 3: People with adenomas

Evidence table for review question 3: When should colonoscopic surveillance be started and what should be the frequency of surveillance?

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<th>Outcomes</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Kronborg et al. (2006)</td>
<td>Randomised surveillance study.</td>
<td>10 years</td>
<td>Between 1981 and 1991 a total of 673 patients (382 men, 291 women; age, 28-77 years) with newly diagnosed adenomas were allocated at random to either 24 months (group A) or 48 months years (group B) between surveillance examinations.</td>
<td>Colonoscopic surveillance: group A = 2 years, group B = 4 years, group C = 6 months, group D = 12 months, E = 12 months and F = 24 months, between surveillance examinations.</td>
<td>Colorectal neoplasia and adenoma detection B versus A After the first follow-up period (24 months in A and 48 months in B) fewer patients had adenomas detected in group A than in group B but it was not statistically significant (58 of 292 versus 64 of 232; RR = 0.7, 95% CI 0.5 to 1.0), and the number of patients with significant neoplasia did not differ (10 of 292 versus 13 of 232; RR = –0.6, 95% CI 0.3 to 1.4). Overall, adenomas were detected in a smaller proportion of surveillance examinations in group A than in group B (123 of 684 versus 83 of 300; RR = 0.7, 95% CI 0.5 to 0.8). The same was true of significant new neoplasia (18 of 684 versus 17 of 300; RR = 0.5, 95% CI 0.2 to -0.9). In group A the total number of patients having new adenomas and new significant neoplasia was 95 and 16, respectively. In group B the figures were 77 and 17, respectively. New adenomas tended to be detected more often in group A, but advanced new adenomas appeared equally as frequently in groups A and B. Overall, larger size contributed mainly to the advanced state (19 and 21 patients), whereas severe dysplasia and villousness was seen in 3 patients in both arms. However, CRC was diagnosed significantly more often in group B. D versus C The number of patients was limited, but the cumulative number of surveillance years was 10 years on average in both groups. Advanced new adenomas tended to be more frequent in the D group (p = 0.08), but the one case of cancer was detected in group C at a planned examination 6 months after a ‘clean colon’. The cancer was at an early stage and the patient developed another early CRC more than 5 years later. Nearly all new adenomas were at an advanced stage because of large size alone. F versus E The two groups were similar initially and the average time of...</td>
<td>The age, sex, and polyp characteristics of the patients were distributed evenly in the two groups. The study was randomised by random numbers but no details of concealment or blinding of pathologists is mentioned. Advanced adenomas were defined as those with severe dysplasia or being at least 10 mm in diameter or villous.</td>
</tr>
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<td>compared as relative risks (RR) with 95% confidence intervals. RR was calculated as the risk in the group with the longest interval of surveillance.</td>
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<td>D) between examinations during the first 5 years and then every year in all.</td>
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<td>Finally, 200 patients with similar adenomas to those in groups C and D were randomised to intervals of 12 months (group E) or 24 months (group F), the intake being from 1988 to 2000.</td>
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<td>Patients without complete colonoscopy and less than optimal compliance were kept in the study surveillance was 5 years. The number of colonoscopies was nearly twice as high in group E, but the number of new adenomas regardless of state was similar. There was no significant difference in risk of CRC but the two cancers in group E were both early stage, one being detected 12 months after a 'clean colon' (a mucinous tumour), the other, 57 months after a 'clean colon' and the patient's refusal to undergo further examinations. In group F the cancers were more advanced. Three of the four patients had a 'clean colon' 24 months before the CRC was detected during a planned examination, but one had many recurrences at the site of the original large sessile adenoma in the rectum, before the cancer was detected (Dukes' B).</td>
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<td>by colonoscopy, but DCBE was used if the patient refused colonoscopy. If a surveillance examination was done more than 3 months after the date planned, the examination was considered 'in between'.</td>
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<td>Relative risks of new adenomas and carcinomas during surveillance with 95% CI</td>
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<td>B versus A</td>
<td>D versus C</td>
<td>F versus E</td>
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<td></td>
<td>0.88 (0.69 to 1.12)</td>
<td>0.82 (0.43 to 1.52)</td>
<td>0.88 (0.57 to 1.34)</td>
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<td>Advanced new adenomas</td>
<td>1.15 (0.61 to 2.15)</td>
<td>3.12 (0.87 to 14.50)*</td>
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<td>Colorectal carcinomas</td>
<td>6.22 (1.06 to 117, 48)**</td>
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<td>*p = 0.08; **p = 0.04</td>
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<td>Adapted from table V in Kronborg (2006)</td>
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<td>Absolute events</td>
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<td>B versus A</td>
<td>D versus C</td>
<td>F versus E</td>
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<td>A: two diagnostic perforations and two therapeutic perforations and B: one diagnostic perforation and one polypectomy syndrome.</td>
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<td>Adverse events</td>
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<td>77 complications to colonoscopy were minor and treated without surgery, six during surveillance. The perforations occurred during surveillance in each of the two groups and were treated successfully with suture alone. A perforation during initial colonoscopy in group A proved fatal, the patient dying of septicemia after inadequate closure of a temporary colostomy. A: two diagnostic perforations and two therapeutic perforations and B: one diagnostic perforation and one polypectomy syndrome.</td>
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<td>D versus C</td>
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<td>Two severe complications (1 diagnostic perforation and 1 polypectomy syndrome)</td>
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### Evidence table for review question 3: When should colonoscopic surveillance be started and what should be the frequency of surveillance?

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| Lieberman et al. (2007) | Patients with cancer or adenomas with high-grade dysplasia had follow-up based on clinician decisions. 
501 participants with no neoplasia at baseline were matched to patients with adenomas ≥10 mm and assigned to surveillance at 5 years. | 5.5 years | Patients were enrolled in 13 Veterans Affairs Medical Centres between February 1994 and January 1997. 24 centres were selected to achieve geographic and racial diversity. 
Among patients who met the eligibility criteria, 1463 (31.4%) declined to participate, 3196 eligible patients were enrolled, and 3121 had complete colonoscopy examinations to | Surveillance intervals of 2 or 5 years and adenoma detection in groups based on index colonoscopy results: according to the following hierarchy: no neoplasia, hyperplastic polyp, 1 or 2 tubular adenomas <10 mm, 3 or more tubular adenomas <10 mm, tubular adenoma ≥10 mm, adenoma with villous histology (25% or more), adenoma with high-grade dysplasia, invasive cancer. | 1171 patients with neoplasia and 501 with no neoplasia at baseline were scheduled to have at least 1 follow-up colonoscopy within 5.5 years. 
**Neoplasia detection** 
The relative risk in patients with baseline neoplasia was 1.92 (95% CI 0.83 to 4.42) with 1 or 2 tubular adenomas <10 mm, 5.01 (95% CI 2.10 to 11.96) with 3 or more tubular adenomas <10 mm, 6.40 (95% CI 2.74 to 14.94) with tubular adenomas >10 mm, 6.05 (95% CI 2.48 to 14.71) for villous adenomas, and 6.87 (95% CI 2.61 to 18.07) for adenomas with high-grade dysplasia. 
The most serious outcome was the finding of invasive cancer or high-grade dysplasia. The rates of interval high-grade dysplasia or cancer per 1000 person-years of follow-up. The risk of high-grade dysplasia or cancer per 1000 person-years of follow-up was 0.7 with no neoplasia at baseline, 1.5 with tubular adenomas <10 mm, 6.4 with large tubular adenomas (>10 mm), 6.2 with villous adenomas, 26.0 with high-grade dysplasia. | All pathology was reviewed locally and sent for blinded central pathology review. When there was a discrepancy, a third referee pathologist reviewed the material. 
The authors compared demographic factors (age, race) and possible risk factors for advanced neoplasia (family history, smoking, use of non-steroidal anti-inflammatory drugs) to determine whether the surveillance cohort was similar to patients who did not receive surveillance. In the neoplasia group, the rate of active smoking was higher in patients |
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<td>Lieberman et al. (2008)</td>
<td>During the study period, the Clinical Outcomes Research Initiative repository (CORI) consortium included 65 practice sites in 25 states. Ten sites contributed more than 500 reports, 6 sites contributed 100–500 reports, and 1 site contributed less than 100 reports.</td>
<td>Retrospective, registry</td>
<td>Patients were asymptomatic adults receiving colonoscopy for screening during 2005 from 17 practice sites, which provide both colonoscopy and pathology reports to the Clinical Outcomes Research Initiative repository. Patients were included in this analysis if they were over age 20 years undergoing screening with no symptoms of lower gastrointestinal tract.</td>
<td>Colonoscopic surveillance for polyps less than 10 mm. Size of polyp and location of polyp’s association with advanced histology.</td>
<td>Three asymptomatic groups were included: average risk, family history of CRC or adenoma, and patients receiving colonoscopy for a positive faecal occult blood test or polyp found at screening sigmoidoscopy. Patients were stratified by indication group. Among 13,992 asymptomatic patients who had screening colonoscopy, 6360 patients (45%) had polyps, with complete histology available in 5977 (94%) patients. <strong>Advanced histology</strong> The proportion with advanced histology (defined as an adenoma with villous or serrated histology, high-grade dysplasia, or an invasive cancer) was 1.7% in the 1 to 5 mm group, 6.6% in the 6 to 9 mm group, 30.6% in the greater than 10 mm group. <strong>Distal location</strong> Distal location was associated with advanced histology in the 6 to 9 mm group (p = 0.04) and in the greater than 10-mm group (p = 0.002).</td>
<td>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). Advanced histology was defined as an adenoma with villous or serrated histology, high-grade dysplasia, or an invasive cancer. The risk factors compared were age, sex, and the presence of symptoms.</td>
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<td>Lund et al. (2001)</td>
<td>RCT to investigate whether regular endoscopic surveillance and polypectomy would decrease the incidence of colorectal cancer and to determine if identification of low- and high-risk groups would allow less frequent surveillance in the low-risk group.</td>
<td>Total person years follow up was 5148 years</td>
<td>Included if undergoing colonoscopy: (i) colorectal symptoms, including rectal bleeding; (ii) possible polyp or other incidental findings on barium enema; or (iii) investigation of positive faecal occult bloods.</td>
<td>Those found to have colonic adenomas between June 1984 and January 1995 were considered for recruitment to one of six surveillance strategies involving either colonoscopy every 2 or five years or flexible sigmoidoscopy every year, every 2 years, or every 5 years.</td>
<td>NOTE: reported only those outcomes related to interval of surveillance for colonoscopy (other outcomes either included in the Saini 2006 review or not relevant for this question). Early termination because of low rates of adenoma recurrence meant that the trial was underpowered to detect differences in the effect of the various surveillance intervals. However, the authors reported that ‘follow up endoscopy for colonic adenomas can be reduced safely to five yearly intervals for the vast majority of patients (excluding patients with hereditary non-polyposis colorectal cancer and familial adenomatous polyposis)’.</td>
<td>sex, race, indication for colonoscopy (that were similar) and location of largest polyp. Significant limitations because of early termination and lack of power.</td>
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<tr>
<td>Martinez et al. (2009)</td>
<td>Pooled analysis of eight North American studies (six were randomised controlled trials).</td>
<td>Median follow-up period of 47.2 months</td>
<td>Individual patients: included people at average with a first-time diagnosis of adenomatous polyps. Study inclusion</td>
<td>Determining the actual risk of developing advanced adenomas and cancer after polypectomy or the factors that determine risk.</td>
<td>Advanced colorectal neoplasia was diagnosed in 1082 (11.8%) of the patients, 58 of whom (0.6%) had invasive cancer. <strong>Definitions</strong> Definitions for adenomas were as follows: tubular ≤25% villous component), tubulovillous (26–75% villous component), or villous (&gt;75% villous component). They considered advanced adenomas to be 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)</td>
<td>Patient level data was used from the included studies. Of the 10,021 men and women who were enrolled in the individual studies, we excluded patients who had a colorectal cancer present at...</td>
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<td>Schatzkin et al. (2000); Baron et al. (1999, 2003); Winawer et al. (1993b); Alberts et al. (2000, 2005); Greenberg et al. (1994); Lieberman et al. (2000)</td>
<td>studies: (1) 800 or more study participants; (2) complete baseline colonoscopy with removal of one or more adenomas and removal of all visualised lesions; (3) a specified schedule of surveillance follow-up; (4) end point data regarding the number, size, and histopathology of adenomas and colorectal cancers detected.</td>
<td>histology). They then combined advanced adenomas and invasive cancer into an end point of advanced colorectal neoplasia or metachronous advanced neoplasia. <strong>Risk factors for advanced metachronous adenomas</strong> Risk of a metachronous advanced adenoma was higher among patients with 5 or more baseline adenomas (24.1%; standard error, 2.2) and those with an adenoma 20 mm in size or greater (19.3%; standard error, 1.5). Risk factor patterns were similar for advanced adenomas and invasive cancer. <strong>Risk factors for metachronous advanced neoplasia</strong> Multivariate analyses: older age (p &lt; 0.0001 for trend) and male sex (odds ratio [OR], 1.40; 95% confidence interval [CI], 1.19 to 1.65) were significantly associated with an increased risk for metachronous advanced neoplasia, as were the number and size of previous adenomas (p &lt; .0001 for trend), the presence of villous features (OR, 1.28; 95% CI, 1.07 to 1.52), and proximal location (OR, 1.68; 95% CI, 1.43 to 1.98). High-grade dysplasia was not associated independently with metachronous advanced neoplasia after adjustment for other adenoma characteristics. baseline (n = 27) and those who did not have a follow-up colonoscopy performed after the first 6 months of the study (n = 827) because these were likely people who were not under typical postpolypectomy surveillance. Thus, data for 9167 (91.5%) patients remained for inclusion in our pooled analyses.</td>
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<td>Nusko et al. (2002)</td>
<td>Follow-up records of 1159 patients undergoing surveillance examination. The following statistical procedures were performed: (1) multiple</td>
<td>A total of 3134 patients undergoing endoscopic removal of colorectal adenomas were prospectively recorded on the Erlangen Registry of Colorectal Identifying risk factors determining surveillance intervals for patients with metachronous adenomas of advanced pathology</td>
<td>A total of 3134 patients undergoing endoscopic removal of colorectal adenomas between 1978 and 1996. Single adenomas were found in 1052 patients (53.6%) and 797 (46.4%) had multiple initial lesions. Mean age at the initial clearing examination for patients who were followed up was 57.08 years (SD 11.25) compared with 59.74 (SD 11.61) for those who were not followed up. A total of 1159 patients underwent regular follow-up examinations: 747 (64%) of these patients were males and 412 (36%) were females. 100 patients (8.6%) had a parental history of colorectal carcinoma while in 24 patients (2.1%) the relevant data were not available. <strong>Risk factors for advanced metachronous adenomas</strong> Large registry data, studying risk factors. All patients were offered a chance to participate in a scheduled follow-up programme, however 1849 patients either refused follow-up or underwent examinations at other endoscopy.</td>
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<td>regression analysis; (2) likelihood ratio tests; (3) calculation of the times t0.05, t0.10, and t0.20 for the relevant risk groups based on their hazard functions; (4) 1000 bootstrap samples</td>
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<td>Polyps between 1978 and 1996. The patients had no previous history of colorectal adenomas or carcinomas. Patients with a familial history of adenomatous polyposis or hereditary non-polyposis colon cancer syndrome, or inflammatory bowel disease were excluded.</td>
<td>Considering only patients with tubular adenomas at the initial clearing procedure, a multivariate model for related observations revealed that adenoma size (p &lt; 0.0001), multiplicity (p = 0.021), parental history of colorectal carcinoma (p = 0.0168), and an interactive effect between size and sex (p = 0.00392) were significant predictive variables. Male patients with large adenomas had a significantly higher risk of developing advanced metachronous adenomas than other patients. <strong>Stratification</strong> Low-risk group containing patients with no parental history of colorectal carcinoma and with only small (&lt;10 mm) tubular adenomas at the initial clearing examination: 12.2 (95% CI 10.1 to 15.2) years were needed for advanced adenomas to develop in more than 10% of patients. The estimate for 5% was 10.4 years (95% CI 4.1 to 13.2) and for 20% was 15.6 years (95% CI 11.5 to 18.2). High-risk group containing all other patients: those with multiple or large adenomas, tubulovillous or villous adenomas, or a parental history of colorectal carcinoma: 6.1 (95% CI 3.2 to 11.5) years were needed for advanced adenomas to develop in more than 10% of patients. The estimate for 5% was 0.5 years (95% CI 0.1 to 1.6) and for 20% was 15.6 years (95% CI 11.5 to 18.2).</td>
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<td>Saini et al. (2006)</td>
<td>Systematic review and meta analysis</td>
<td>Three electronic databases (MEDLIN, PREMEDLINE, and EMBASE) were searched</td>
<td>Study population was patients with a personal history of adenomas. Studies enrolling Nine hundred seventy-one references were identified but fifteen primary studies were included.</td>
<td>Bonithon-Kopp et al. (2000) showed that the only RR that was statistically significant was for number of adenomas only: RR 3.26 (95% CI 1.81 to 5.89). Martinez et al. (2001) showed that the only RR that was statistically significant was for size only: RR 1.77 (95% CI 1.30 to 2.41) Van Stolk et al. (1998) did not find any statistically significant RR for</td>
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<td>Considering only patients with tubular adenomas at the initial clearing procedure, a multivariate model for related observations revealed that adenoma size (p &lt; 0.0001), multiplicity (p = 0.021), parental history of colorectal carcinoma (p = 0.0168), and an interactive effect between size and sex (p = 0.00392) were significant predictive variables. Male patients with large adenomas had a significantly higher risk of developing advanced metachronous adenomas than other patients. <strong>Stratification</strong> Low-risk group containing patients with no parental history of colorectal carcinoma and with only small (&lt;10 mm) tubular adenomas at the initial clearing examination: 12.2 (95% CI 10.1 to 15.2) years were needed for advanced adenomas to develop in more than 10% of patients. The estimate for 5% was 10.4 years (95% CI 4.1 to 13.2) and for 20% was 15.6 years (95% CI 11.5 to 18.2). High-risk group containing all other patients: those with multiple or large adenomas, tubulovillous or villous adenomas, or a parental history of colorectal carcinoma: 6.1 (95% CI 3.2 to 11.5) years were needed for advanced adenomas to develop in more than 10% of patients. The estimate for 5% was 0.5 years (95% CI 0.1 to 1.6) and for 20% was 15.6 years (95% CI 11.5 to 18.2).</td>
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Saini et al. (2006) as the outcomes used in their study did not include the ones extracted from this primary paper.

Kept despite Saini et al. (2006) as the outcomes used in their study did not include the ones extracted from this primary paper.

All Mesh and free key words used for the searches were given in the paper. The PRISMA chart was available.
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<td>Winawer et al. (1993) found the incidence of advanced adenomas at 3-year surveillance colonoscopy was 1.4% in the low-risk patients versus 5–4% in the high-risk patients: RR 3.87 (95% CI 1.09 to 13.66). Advanced adenomas defined as adenomas ≥1 cm, villous histological features, or with cancer.</td>
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**Number and size**
Four trials: Bonithon-Kopp et al. (2000), Martinez et al. (2001), Van Stolk et al. (1998), Winawer et al. (1993): provided adequate data to determine the incidence of recurrent advanced adenomas at surveillance colonoscopy on the basis of: (1) the number of adenomas at index colonoscopy (>3 vs 1 or 2) the pooled RR was 2.52 (95% CI 1.07 to 5.97), and the pooled absolute risk difference was 5% (95% CI 1% to 10%); and (2) the size of the largest adenoma at index colonoscopy (≥1 cm [large] vs <1 cm [small]) the pooled RR was 1.39 (95% CI 0.86 to 2.26), and the pooled absolute risk difference was 2% (95% CI –2% to 6%)

The heterogeneity was significant for both cases, p < 0.001 and p < 0.05.

**Histological diagnosis**
Three trials: Bonithon-Kopp et al. (2000), Martinez et al. (2001), Van Stolk et al. (1998): provided adequate data to determine the incidence of recurrent advanced adenomas at surveillance colonoscopy on the basis of adenoma histologic features (tubulovillous/villous vs tubular). The pooled RR was 1.26 (95% CI 0.95 to 1.66), and the pooled absolute risk difference was 2% (95% CI –1% to 4%). The test of heterogeneity for the pooled RR was not significant (p > 0.2), indicating that the individual studies did not demonstrate significant differences in the RR of recurrent advanced adenomas.

**Dysplasia**
Two studies: Bonithon-Kopp et al. (2000) and Van Stolk et al. (1998) provided adequate data to determine the incidence of recurrent advanced adenomas on the basis of the degree of dysplasia at index...
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<td>colonoscopy (high grade vs no high-grade dysplasia). The pooled RR was 1.84 (95% CI 1.06 to 3.19), and the pooled absolute risk difference was 4% (95%CI 0 to 8%). The test of heterogeneity for the pooled RR was not significant (p &gt; 0.2)</td>
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<tr>
<td>Risk factors for advanced adenomas at surveillance</td>
<td>Nine studies identified a total of 5 risk factors that were associated with advanced adenomas at surveillance colonoscopy: (1) number of adenomas, (2) size of largest adenoma, (3) incomplete index colonoscopy, (4) concurrent proximal and distal adenomas, and (5) parental history of CRC.</td>
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<tr>
<td>Risk factors for recurrence of adenomas</td>
<td>14 studies reported a 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, and (6) adenoma in the proximal colon.</td>
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### Risk factors for advanced adenomas at surveillance

#### Nine studies identified a total of 5 risk factors that were associated with advanced adenomas at surveillance colonoscopy:

- **Number of adenomas**
- **Size of largest adenoma**
- **Incomplete index colonoscopy**
- **Concurrent proximal and distal adenomas**
- **Parental history of CRC**

### Risk factors for recurrence of adenomas

#### 14 studies reported a total of 6 risk factors:

- **Number of adenomas**
- **Size of largest adenoma**
- **Patient age**
- **Tubulovillous/villous features or severe dysplasia**
- **Advanced adenoma**
- **Adenoma in the proximal colon**

---

**Winawer et al. (1993b)**

RCT to compare follow-up colonoscopy at 3 years and follow-up colonoscopy at both 1 and 3 years in people with newly diagnosed adenomatous polyps.

- **RCT to compare follow-up colonoscopy at 3 years and follow-up colonoscopy at both 1 and 3 years in people with newly diagnosed adenomatous polyps.**
- **Study design:** RCT to compare follow-up colonoscopy at 3 years and follow-up colonoscopy at both 1 and 3 years in people with newly diagnosed adenomatous polyps.
- **Follow up:** Median interval between enrollment and initial follow-up examination was 1.15 years in the two-examination group; 3.15 years in the one-examination group. Follow-up clinical status was determined for 97.2% (1379/1418).
- **Population:** 9112 patients referred for colonoscopy who had no history of polypectomy, IBD, familial polyposis, or colorectal cancer identified at 7 clinical centres. Of 3778 patients in whom polyps were detected, 2632 (69%) had adenomas and were eligible for randomisation; Participants were randomly assigned to a follow-up examination either 1 and 3 years after colonoscopy (the two-examination group) or 3 years after colonoscopy (the one-examination group). Follow-up colonoscopy 6 years after the examination at entry was also offered to both groups.
- **Prognostic factors or surveillance programmes:**
- **Outcomes:**

<table>
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<th>2-exam group (N=338)</th>
<th>1-exam group (N=428)</th>
<th>RR (95% CI)</th>
<th>p = 0.006</th>
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<tr>
<td>Any adenomas</td>
<td>141 (41.7%)</td>
<td>137 (32.0%)</td>
<td>1.3 (1.1 to 1.6)</td>
<td>p = 0.006</td>
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<tr>
<td>Adenoma with advanced pathological feature (&lt;1.0 cm, HGD, or invasive cancer)</td>
<td>11 (3.3%)</td>
<td>14 (3.3%)</td>
<td>1.0 (0.5 to 2.2)</td>
<td>p = 0.99</td>
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**NOTE:** reported only those outcomes related to interval of surveillance for colonoscopy (other outcomes either included in the Saini 2006 review or not relevant for this question)
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<td>1418 (53.9%) of eligible patients with adenomas consented to participate.</td>
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### Review question 4: People with Inflammatory bowel disease or adenomas

**Evidence table for review question 4: What are the information and support needs of people, or the carers of people, undergoing or considering undergoing colonoscopic surveillance?**

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<td>Sequist et al. (2009)</td>
<td>A randomised controlled trial (RCT) to promote colorectal cancer (CRC) screening</td>
<td>Participants included 21,860 patients aged 50 to 80 years who were overdue for CRC screening. Allocated to patient intervention group: 10,930 patients (all received allocation intervention). Allocated to patient control group: 10,930.</td>
<td>Patients overdue for CRC screening received a mailing, which included the following: (1) an educational pamphlet detailing screening options, (2) a dedicated telephone number to schedule FSIG or colonoscopy. The initial mailing occurred during the first month of the intervention and a second mailing was sent to patients still overdue for screening 6 months later.</td>
<td>The primary study outcome was completion of one of the following three options during the 15-month study period: FOBT, FSIG, or colonoscopy. The secondary outcome was detection of colorectal adenomas. <strong>Screening rates</strong> Patients who received the mailing were significantly more likely to complete colorectal cancer screening than those who did not (44.0% versus 38.1%; p &lt; 0.001). The impact of the mailing did not differ between women and men. <strong>Detection of adenomas</strong> Detection of adenomas tended to be greater among patients who received mailings compared with the control group (5.7% vs 5.2%; p = 0.10).</td>
<td>All data were collected from the electronic record, and study outcomes were assessed 15 months after the start of the intervention for all randomised patients.</td>
</tr>
<tr>
<td>Rutter et al. (2006)</td>
<td>A 58-question self-administered postal questionnaire design looking at: • The quality of life of patients on surveillance. • Colonoscopy • Kranz health opinion survey • surveillance</td>
<td>281 of 329 patients (85.4%) responded. Median age was 55 (range 26–84) years. 167 patients were male and 114 female (no significant difference from nonrespondents: p = 0.88). Median duration of colitis was 25 (range 10–53) years. Patients had undergone a median of six surveillance colonoscopies (range 1–15; total number Colonoscopy: • Convenience. 39% respondents found the bowel preparation difficult to take. • Experience of colonoscopy. 60.2% respondents found their last colonoscopy comfortable or very comfortable, 30.1% found it uncomfortable, and 9.7% found it very uncomfortable. Patients 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) • Complications: 16.4% respondents experienced abdominal pain (attributed to the procedure) in the week following their last...</td>
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Evidence table for review question 4: What are the information and support needs of people, or the carers of people, undergoing or considering undergoing colonoscopic surveillance?

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| 1777     |              |            | 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 (HADS) anxiety score (p < 0.0001) but not with the drug doses used during the procedure. Five patients (1.7%) reported complications after previous colonoscopies. | Surveillance:  
- Information: when asked about the level of involvement in the treatment decision-making, 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. 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 patient thought they had received too much. 35.8% had sought other sources of information. 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.  
- The surveillance program: 97.8% of the patients felt that the surveillance was important for them.  
- Cancer concern: 96.4% of respondents thought that the surveillance program 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, 1.8% of patients 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. |
| Study ID          | Study design                                                                                                                                                                                                 | Population                                                                                      | Intervention                                                                                                                                                                                                                                                                                  | Outcomes                                                                 | Comments                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|                                                                                                                                                                                                                                                                                                                                                              |                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| Makoul et al. (2009) | A pretest–posttest design to assess a multimedia patient Education Program (PEP) that provides information about CRC and CRC screening, and encourages people to talk with their physicians about getting screened. | A total of 270 adults, age 50–80 years, participated in Spanish for all phases of the pretest–posttest design. | Patients were randomly assigned to a version of the multimedia program that opened with either a positive or a negative introductory appeal. Structured interviews assessed screening behaviour, willingness to consider screening options, intention to discuss CRC screening with the doctor. Two versions of a 5-minute PEP in both Spanish and English (using information gained through a series of structured interviews and focus groups in a primarily Spanish-speaking community) were developed. |                                                                                                                                                                                                                                                                                                                                                              | The paper refers to patient/community education. The program involved the patients/community on how to make screening information and options easier. Information was tailored to the community/patient needs. Overall, there was no difference in participant response to both positive and negative appeals. Limitations: focus was on Spanish-speaking adults in a Hispanic/latino community which precludes generalisation to a broader audience. |

**Screening relevant knowledge**

<table>
<thead>
<tr>
<th>Screening options</th>
<th>Pretest (%)</th>
<th>Posttest (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSIG</td>
<td>11.5</td>
<td>53</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>23.3</td>
<td>57</td>
<td></td>
</tr>
</tbody>
</table>

**Willingness to consider CRC screening**

<table>
<thead>
<tr>
<th>Screening options</th>
<th>Pretest (%)</th>
<th>Posttest (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSIG</td>
<td>54.1</td>
<td>78.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>64.8</td>
<td>84.4</td>
<td></td>
</tr>
</tbody>
</table>

The tables above show increases in the participants’ knowledge of the primary screening options and willingness to consider CRC screening after exposure to the patient education program. The program made more than 90% of patients want to discuss CRC with their doctors. There was no significant difference between response to the positive and negative introductory appeals in terms of this intention (90.4% and 94.5% respectively).
<table>
<thead>
<tr>
<th>Study ID</th>
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<th>Outcomes</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Sheikh et al. (2004)</td>
<td>A questionnaire design study to determine patients' screening preferences.</td>
<td>Adult patients attending the internal medicine and family practice clinics were chosen on the basis of availability and ease of collecting data. 193 patients responded to the questionnaire.</td>
<td>A description of screening procedures given in a packet.</td>
<td>154 (79.8%) of the 193 patients preferred some sort of screening. Of those who had had a previous colonoscopy, 55% preferred a repeat screening compared with only 30% of those who had never had a colonoscopy (p = 0.017). Of those who had had a previous sigmoidoscopy, 53% preferred a repeat screening compared with only 33% of those who had never had a sigmoidoscopy, although the differences were not statistically significant.</td>
<td>The study demonstrates diversity in patient choices for CRC screening.</td>
</tr>
<tr>
<td>Brotherstone et al. (2006)</td>
<td>Randomly allocating people to study the effectiveness of visual illustrations in improving people’s understanding of the preventive aim of flexible sigmoidoscopy (FSIG) screening</td>
<td>318 people aged 60–64 were sent a timed, dated appointment to attend FSIG screening. 318 people aged 60–64 were sent a timed, dated appointment to attend FSIG screening.</td>
<td>They were randomised either to be sent a written leaflet alone (n = 151) or a written leaflet along with a set of illustrations showing the development of cancer from polyps and removal of polyps during FSIG (n = 167). A sample of 123 (39%) of the 318 people to whom the information was sent were selected at random for a telephone interview within 2 to 4 weeks of the information materials being sent out. The interviews were recorded and transcribed, and coded by two</td>
<td>The primary outcome was awareness of the preventive aim of FSIG screening. Of the 123 randomly selected for interview, 25 could not be contacted, 16 telephone numbers were incorrect, 2 respondents had communication difficulties, 4 were on holiday during the interview period, and 3 of the interviews were terminated prematurely. 8 people declined to be interviewed. 65 (53%) interviews were completed and recorded, 35 (54%) with participants who were sent the written information only and 30 (46%) with those who had been sent illustrations as well. There was no significant difference in age, gender or socioeconomic status between people who were interviewed (n = 65) and those who were not (n = 58).</td>
<td>The leaflet was based on materials that had been piloted and were used in the UK FSIG Trial. The leaflet contained comprehensive information about FSIG screening, risk factors for colorectal cancer, how screening works, what the test involves, what happens if precancers are found, whether there are risks associated with having the test, and the reliability of the...</td>
</tr>
<tr>
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<tr>
<td></td>
<td>Postal questionnaire design aimed to study the psychologic effect of attending a screening program.</td>
<td>451 people were invited for a colonoscopic examination to detect and remove colorectal polyps. Mean age was 67.2 years (range 63–72 years), and 48% were women. As controls for those subjected to endoscopy, a group of 447 matched for age and sex were randomly drawn from the population registry.</td>
<td>Fourteen days and 3 and 17 months after the examination, the attendees received a questionnaire by mail composed of Goldberg’s General Health Questionnaire (GHQ-28), the Hospital Anxiety and Depression Scale (HADS) and questions designed to evaluate how the attendees had experienced the colonoscopic screening examination and to register whether polyps had been detected. Questionnaires were sent to a total of 429 individuals. The same questionnaire was also mailed to the control group (matched for age and sex) who did not enrol in the endoscopic screening.</td>
<td>In the written information group, 57% had s good understanding of the aims of the test, while in the group who were sent written information and illustrations, 84% had s 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).</td>
<td>There was a wide CI that was not accounted for in the study.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Questions</th>
<th>Replies (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Were polyps found at the examination?</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>294 (72)</td>
</tr>
<tr>
<td>No</td>
<td>96 (24)</td>
</tr>
<tr>
<td>Do not remember</td>
<td>16 (4)</td>
</tr>
<tr>
<td>Did you find the examination uncomfortable?</td>
<td></td>
</tr>
<tr>
<td>Yes, very</td>
<td>21 (5)</td>
</tr>
<tr>
<td>Moderately</td>
<td>184 (45)</td>
</tr>
<tr>
<td>No</td>
<td>204 (50)</td>
</tr>
<tr>
<td>Would you attend a repeat examination in 5 years’ time?</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>368 (90)</td>
</tr>
<tr>
<td>No</td>
<td>9 (2)</td>
</tr>
<tr>
<td>I am not sure</td>
<td>31 (7.6)</td>
</tr>
<tr>
<td>Are you content to have attended this endoscopic examination?</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>405 (99.3)</td>
</tr>
<tr>
<td>No</td>
<td>2 (0.5)</td>
</tr>
<tr>
<td>I am not sure</td>
<td>1 (0.2)</td>
</tr>
</tbody>
</table>

The lower and more favourable scores for GHQ-28 and HADS in the screened group compared with controls may be due to a sense of relief lasting for several months after successful participation with no serious findings.
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<tr>
<td>Miles et al. (2009)</td>
<td>Postal survey examining the psychological impact of being assigned to colonoscopic surveillance following detection of adenomatous polyps at FSIG screening.</td>
<td>Participants were men and women aged 55–64 years, at average risk of getting CRC. People with no polyp = 26,573, lower risk polyps removed at flexible sigmoidoscopy = 7401 and higher risk polyps who underwent colonoscopy and were either assigned to CS = 1543 or discharged = 183 (n = 35,700). A sub-sample (n = 6389) had also completed a detailed questionnaire prior to screening attendance making it possible to compare pre- and postscreening results in this group.</td>
<td>Participants were sent a detailed questionnaire 3–6 months after screening, by which time they had been told whether or not they needed colonoscopic surveillance. The response rate to the questionnaire was 90%.</td>
<td>The scores for both GHQ-28 and HADS were lower, indicating a lower level of psychiatric morbidity among those attending the examination than the controls. There was a trend towards higher scores with increasing time after the examination in the screened group.</td>
<td></td>
</tr>
</tbody>
</table>

Primary outcome variables

Bowel cancer worry was assessed before and after screening with the question: ‘How worried are you about getting bowel cancer’ (response options on a 4-point Likert scale: ‘not worried at all, a bit worried, quite worried, very worried’)

Psychological distress was measured after screening using the 12-item version of the General Health Questionnaire (GHQ-12)

Positive psychological consequences of screening were assessed after screening using three items from the positive emotional subscale of the Psychological Consequences of screening Questionnaire (PCQ)

Secondary outcome variables

Reassurance was assessed after screening using a single item on reassurance from the PCQ.

Bowel symptoms were assessed before and after screening with questions related to bowel movement.

GP attendance was measured before and after screening using one question: ‘About how many times have you seen your GP in the last 3 months. It was scored so that high scores
<table>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>indicated more visits.</td>
<td></td>
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**Results**

People offered surveillance reported lower psychological distress and anxiety than those with either no polyp (p < 0.05) or lower risk polyps (p < 0.01). The surveillance group also reported more positive emotional benefits of screening than the other outcome groups. Post screening bowel cancer worry and bowel symptoms were higher in people assigned to surveillance, but both declined over time, reaching levels observed in either one or both of the other two groups found to have polyps, suggesting these results were a consequence of polyp detection rather than surveillance.

---

\textsuperscript{a} The screening options in this study also looked at FOBT and the results reported included FOBT screening.

\textsuperscript{b} The screening options in this study also looked at FOBT.

\textsuperscript{c} The results report the percentage of participants at pretest and posttest who provided correct answers. Pretest–posttest differences were evaluated with McNemar's test.

\textsuperscript{d} The results report the percentage of participants at pretest and posttest indicating willingness to consider primary screening options. Pretest–posttest differences were evaluated with McNemar's test.