

## Clinical practice guidelines for surveillance colonoscopy

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## Guideline launch notification

Please note that the draft *Clinical Practice Guidelines for Surveillance Colonoscopy* were released for public consultation for the period of **2 April 2018 to 2 May 2018**. All feedback on the draft received during the consultation period has been considered by the Working Party.

The draft *Clinical Practice Guidelines for Surveillance Colonoscopy* have been submitted to NHMRC for consideration.

If you would like to be notified via email when the final guidelines are launched please contact [guidelines\(at\)cancer.org.au](mailto:guidelines(at)cancer.org.au).

## 1 Foreword

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The polyp-cancer sequence means that appropriately timed colonoscopy could dramatically reduce both colorectal cancer (CRC) incidence and mortality by detecting and completely removing conventional and serrated adenomas, from which the majority of CRC arises. To maximise this potential benefit, colonoscopy must be performed to a very high standard at appropriate intervals.

The number of colonoscopies performed annually in Australia is fast approaching one million; if these procedures were all directed towards 50 to 80 year olds, each Australian in that age group could already have a colonoscopy performed every 8 years. However, data also show that there is enormous geographic disparity among annual rates of colonoscopy per head of population. Despite incidence and mortality statistics trending towards improvement, even greater favourable trends might be expected, given the high volume of colonoscopy in Australia. These findings suggest that we could be doing better when it comes to technical performance of colonoscopy, and compliance with national guidelines on indications for the procedure, including timing of surveillance procedures.

As was the case when these guidelines were last updated in 2011, the current update has had to rely on evidence from studies that included colonoscopies performed more than a decade ago. In the interim, the technical quality of colonoscopes has increased dramatically and the care with which these instruments need to be used has attracted more and more attention. Thus, extrapolating from the available literature to generate reasonable recommendations remains as difficult now as it was in 2011.

Over the same time period, it has become even clearer that colonoscopy is far from perfect; that it is less protective against post-colonoscopy cancers in the proximal (right) colon than in the distal (left) colon and that, even on the left side, colonoscopy is nowhere near completely protective against subsequent CRC development. It is now established that fewer interval CRCs develop among the patients of proceduralists with higher adenoma detection rates. Given that colonoscopy currently provides limited protection against CRC in the right colon, attention needs to be given to the sessile serrated adenoma detection rate, which is an emerging indicator of colonoscopy quality. Of course, detection alone is not enough. Whether detected lesions are conventional adenomas or sessile serrated adenomas, colonoscopy is only protective if polypectomy is complete.

Colonoscopy is only protective if polypectomy is complete. It is therefore incumbent upon every colonoscopist not only to maintain, but to improve their diagnostic and therapeutic skills, to be able to practise 'modern' high-quality colonoscopy.

As guidelines, the recommendations regarding surveillance intervals outlined in this document cannot be applied rigidly to each and every patient. Bowel preparation, for instance, may be suboptimal, interval symptoms may develop, or repeat procedure intervals based on a strong family history of CRC may take precedence over a surveillance interval dictated by a person's latest colonoscopy findings. Nevertheless, the guidance based on this up-to-date, evidence-based literature review will allow clinicians to better manage not only individual patients, but also colonoscopy waiting lists, and help balance the greater urgency of colonoscopy for symptomatic patients and those with positive immunochemical faecal occult blood test at screening (including National Bowel Cancer Screening Program participants) against the urgency of surveillance colonoscopy procedures.

Dr Cameron Bell

Chair, Surveillance Colonoscopy Guidelines Working Party

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## 2 Introduction

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## 2.1 Introduction

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Colorectal cancer (CRC) is the second most common internal malignancy affecting Australians.<sup>[1]</sup> Age-standardised incidence and mortality rates are falling, yet CRC still kills more Australians than any other cancer except for lung cancer despite the fact that CRC biology offers a window of opportunity for prevention and cure.

The adenoma-cancer sequence means that appropriately timed colonoscopy could dramatically reduce both CRC incidence and mortality by detecting and completely removing conventional and serrated adenomas, from which the majority of CRC arises. To maximise this potential benefit, colonoscopy must be performed to a very high standard at appropriate intervals.

## 2.2 Purpose and scope

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These guidelines update the 2011 edition by reviewing literature published in the interim. They focus on the appropriate use of colonoscopy in CRC prevention and address three main questions:

- when to repeat colonoscopy after removal of adenomatous polyps?
- when to repeat colonoscopy after curative resection of CRC?
- when to perform colonoscopy in those patients with inflammatory bowel disease (IBD) who have an increased risk of developing CRC?

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## 2.3 Intended users

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These guidelines are intended for use by health professionals advising patients who are at increased risk of CRC (due to a personal past history of precancerous polyps, CRC or IBD) about the need for and timing of future colonoscopy. They may also be of interest to policy makers and educators providing training in medicine or other health sciences.

They are not intended as health information for the general public.

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## 2.4 Target populations

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These guidelines cover a range of Australian populations, including:

- people with precancerous lesions detected on colonoscopy
- people with a diagnosis of CRC
- some people with a diagnosis of IBD (ulcerative colitis or Crohn's disease).

These guidelines are not intended to apply to people for whom colonoscopy is indicated for screening or investigation of symptoms rather than for the purpose of surveillance:

- people with a family history of CRC or known familial syndromes
- people with symptoms and signs that may suggest CRC
- people with a positive faecal occult blood test.

Clinicians should consider the specific needs of patients with CRC from culturally diverse groups, including younger people, Aboriginal and Torres Strait Islander peoples and culturally and linguistically diverse communities.

It is worth noting that for each systematic review, the search strategies specifically included terms designed to identify data relevant to Aboriginal and Torres Strait Islander peoples. However, the literature searches did not identify any studies specifically relevant to Aboriginal and Torres Strait Islander populations that met the inclusion criteria.

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## 2.5 Healthcare settings in which the guideline will be applied

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These guidelines apply to the range of public and private healthcare settings in which services are provided for the target populations. These include:

- general practice;
- hospitals;
- specialist clinics;
- imaging services;
- pathology services;
- allied health care services.

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## 2.6 Funding

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The Australian Government Department of Health commissioned and funded Cancer Council Australia to undertake the current revision and update of this guideline.

## 2.7 NHMRC approved recommendation types and definitions

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This guideline includes evidence-based recommendations, consensus-based recommendations and practice points as defined by the Level and Grades for Recommendations for Guidelines Developers<sup>[2]</sup> (see NHMRC approved recommendation types and definitions in the *Summary of recommendations* section).

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## 2.8 Methodology

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The methodology adopted for this guideline revision has been recorded in the Technical Report, which outlines the development process, lists the clinical questions and detailed technical documentation.

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## 2.9 Scheduled review of these guidelines

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It is inevitable that parts of this guideline will become out of date as further literature is published. Newly published evidence relevant to each systematic review question will be monitored. If strong evidence supporting a change in the guideline is published, the working party will consider if an update is required for a specific section. We recommend that the guideline as a whole should be reviewed and updated every 5 years.

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## 2.10 Acknowledgement

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The update of the guidelines was overseen by a multidisciplinary working party with input by subcommittees. We thank the members of the working party, subcommittees, systematic reviewers and all others who contributed to the development of these guidelines.

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## 2.11 References

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1. ↑ Australian Institute of Health and Welfare (AIHW). *Reports and data: Health conditions, disability & deaths (Cancer)*. [homepage on the internet] Australian Government; 2019 [cited 2019 Aug 16; updated 2019 Jan 9]. Available from: <https://www.aihw.gov.au/reports-data/health-conditions-disability-deaths/cancer/overview>.
2. ↑ National Health and Medical Research Council. *NHMRC levels of evidence and grades for recommendations for guideline developers*. Canberra: National Health and Medical Research Council; 2009 Available from: [https://www.nhmrc.gov.au/\\_files\\_nhmrc/file/guidelines/developers/nhmrc\\_levels\\_grades\\_evidence\\_120423.pdf](https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf).

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## 3 Summary of recommendations

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The guideline recommendations were approved by the Chief Executive Officer of the National Health and Medical Research Council (NHMRC) on 7 December 2018 under section 14A of the *National Health and Medical Research Council Act 1992*.

### 3.1 Summary of recommendations

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This is a summary of the recommendations in these guidelines, please note that some sections do not have associated recommendations.

For explanation of recommendations types, levels of evidence and grades for recommendations, see #NHMRC approved recommendation types and definitions and #Levels of evidence and grades for recommendations below.

### 3.2 Summary of recommendations

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#### 3.2.1 Advances in colonoscopy, CT colonography and other methods

#### 3.2.2 Bowel preparation

##### Practice point

High-quality bowel preparation is a crucial pre-requisite for successful colonoscopy. Optimal preparation is achieved with split-dose or same-day preparation timing.

**Practice point**

PEG-based bowel preparations are safer for those with co-morbidities and the elderly.

**Practice point**

A low-residue diet can be used on the days prior to colonoscopy with appropriate preparation timing.

**Practice point**

Factors associated with poor preparation should be assessed and patients at high risk of poor preparation should be offered additional preparation volume and split-dose timing.

**Practice point**

Preparation quality should be documented on the colonoscopy report using a validated preparation scale.

**Practice point**

Where the preparation is inadequate, repeat colonoscopy should normally be offered within 12 months.

**Practice point**

Successful bowel preparation should be achieved in  $\geq 90\%$  of all colonoscopies.

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### 3.2.3 Advances in technique

#### Practice point

Fundamental colonoscopic inspection technique should ensure systematic exposure of the proximal sides of folds and flexures, intensive intraprocedural cleansing and adequate distension of the colon.

#### Practice point

Colonoscopists should undergo training in the fundamentals of mucosal exposure and inspection techniques, and in the endoscopic appearance of adenomas and serrated lesions to increase detection rates and improve clinical outcomes of colonoscopy.

#### Practice point

Water exchange should be considered to improve adenoma detection through an effect on mucosal cleansing and higher rates of adequate bowel preparation.

#### Practice point

A second examination of the proximal colon in either the forward view or in retroflexion is recommended to improve lesion detection, particularly in patients with an expected higher prevalence of neoplasia.

#### Practice point

Sessile polyps under 10mm in size should be removed using cold snare polypectomy. This is preferred over hot snare, which is unnecessary in most situations. Hot biopsy forceps should not be used because they are associated with unacceptably high rates of incomplete resection and deep mural injury.

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### 3.2.4 Technological advances

#### Practice point

High-definition colonoscopes should be used routinely, as the mainstay of colonoscopy is a careful white-light examination of the well prepared colon.

#### Practice point

Electronic chromoendoscopy should be used for lesion characterisation, but has limited value in lesion detection.

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### 3.2.5 Adjunct technologies

#### Practice point

Chromoendoscopy should be considered for routine colonoscopy to improve the detection and characterisation of colorectal polyps.

#### Practice point

Chromoendoscopy should be considered for patients undergoing surveillance for inflammatory bowel disease, although a recent study has shown equivalence with high resolution white-light endoscopy.

#### Practice point

CO<sub>2</sub> insufflation should be used routinely to improve patient tolerability of colonoscopy.

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### 3.2.6 Quality of colonoscopy

#### Practice point

Accurate and sufficient information about the procedure (and optimally consent) should be provided to patients prior to the commencement of bowel preparation for colonoscopy.

#### Practice point

Colonoscopy should be performed only for accepted indications, which should be clearly documented.

#### Practice point

Less than 10% of patients should require a repeat procedure due to poor bowel preparation, this should be offered within 12 months.

#### Practice point

Unadjusted rates for caecal intubation should be  $\geq 90\%$ .

#### Practice point

Photo-documentation, that terminal ileum or the base of the caecum (appendix orifice and ileocaecal valve) has been reached, should be performed to confirm completeness of the examination.

#### Practice point

Withdrawal times of  $>6$  minutes for examinations without polypectomy are a surrogate marker for adenoma detection rates, but cannot be relied on as an independent quality indicator.

**Practice point**

Individual proceduralists should routinely document and maintain their adenoma detection rate at >25% in patients over the age of 50-years and without a diagnosis of inflammatory bowel disease.

**Practice point**

Serrated polyp detection rates are likely to be an equally valid marker of quality as adenoma detection rate, and increasing evidence suggests that maintaining a rate of >10% in patients over age 50 years without a diagnosis of inflammatory bowel disease may prove to be an additional, useful quality indicator in the future.

**Practice point**

Perforation rates post colonoscopy should be <1/1000. This is more relevant for population programs and large endoscopy units rather than individual colonoscopists.

**Practice point**

All colonoscopists should have their training certified by the Conjoint Committee for the Recognition of Training in Gastrointestinal Endoscopy and undergo regular recertification through an endorsed program.

**Practice point**

Comprehensive computer-generated colonoscopy reports with embedded photo-documentation should be generated at the time of the procedure, and provided to patients and relevant clinicians.

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### 3.2.7 CT colonography

#### Practice point

Due to its excellent safety profile and high accuracy for detecting colonic carcinoma, CT colonography is an alternative for patients unable to have colonoscopy. Bowel preparation is still required prior to the examination.

#### Practice point

In patients at risk of colorectal carcinoma who have had an incomplete colonoscopy, CT colonography should be performed to allow assessment of the entire colonic mucosa.

#### Practice point

It is safe to perform same-day CT colonography following incomplete colonoscopy, including in patients who have had a biopsy or simple polypectomy. However, CT colonography should be delayed in patients with complex endoscopic intervention and in patients at high risk of perforation such as active colitis or high-grade stricture.

#### Practice point

CT colonography should only be interpreted by radiologists who have undergone specialist training and are accredited by RANZCR.

#### Practice point

Patients with a CT colonography detected polyp over 10mm should be referred for polypectomy. Patients with polyps 6–9mm can be offered either polypectomy or repeat colonic examination at 3 years.

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### 3.2.8

### 3.2.9 Colonoscopic surveillance after polypectomy

#### Practice point

Endoscopists and pathologists need to be aware of serrated polyps and be able to recognise and endoscopically manage them.

#### Practice point

Hyperplastic polyps should be clearly distinguished from sessile serrated adenomas and traditional serrated adenomas. Although hyperplastic polyps are classified amongst serrated polyps, they do not have malignant potential when they are diminutive, confined to the rectosigmoid colon and not associated with proximal serrated polyps.

#### Practice point

Consistently high quality colonoscopy is imperative for optimal cost-effectiveness and for implementation of uniform surveillance guidelines.

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### 3.2.10 First surveillance intervals following removal of low-risk conventional adenomas only

Evidence-based recommendation	Grade
<p><i>Low-risk individuals - conventional adenomas only</i></p> <p>First surveillance intervals should be no sooner than 5 years following the complete removal of low-risk conventional adenomas only (1-2 small [<math>&lt;10\text{mm}</math>] tubular adenomas without high-grade dysplasia).</p>	<p><b>D</b></p>

#### Consensus-based recommendation

*Low-risk individuals - conventional adenomas only*

**Consensus-based recommendation**

First surveillance interval of 10 years is appropriate for most individuals following complete removal of low-risk conventional adenomas only (1-2 small [ $<10\text{mm}$ ] tubular adenomas without high-grade dysplasia).

**Practice point**

Consistently high-quality colonoscopy is imperative for optimal cost effectiveness and for implementation of uniform surveillance guidelines.

**Practice point**

Polyp/adenoma size as per the endoscopist documentation should be used for determining surveillance intervals. All endoscopists should ensure size measurements are accurate using a reference standard (eg an open biopsy forceps or snare).

**Practice point**

Surveillance intervals should be determined after the colon has been cleared of all significant neoplasia, once histology is known and in the context of individualised assessment of benefit to the patient.

**Practice point**

A shorter surveillance interval of 5 years could be considered for men who fit the criteria for the metabolic syndrome, because they may have increased risk of metachronous advanced neoplasia following removal of low-risk adenomas.

**Practice point**

Return to the National Bowel Cancer Screening Program with a faecal occult blood test after 4 years, is an appropriate option and should be discussed with the patient.

**Practice point**

Patients with 1–2 diminutive (<6mm) low-risk adenomas have a very low risk of metachronous neoplasia and should be returned to the NBCSP after 4 years unless there are significant extenuating factors.

**Practice point**

Individuals with a significant family history of colorectal cancer should be assessed according to current Australian clinical practice guidelines for the prevention, early detection and management of colorectal cancer (see Risk and screening based on family history) in addition to these recommendations, and the shorter interval used.

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### 3.2.11 First surveillance intervals following removal of high-risk conventional adenomas only

Evidence-based recommendation	Grade
<p><i>High-risk individuals – conventional adenomas only</i></p> <p>First surveillance intervals should be within 5 years following removal of high-risk conventional adenomas only, i.e. those with one or more of the following features:</p> <ul style="list-style-type: none"> <li>■ size ≥10mm</li> <li>■ high-grade dysplasia</li> <li>■ villosity</li> <li>■ 3–4 adenomas.</li> </ul>	<b>D</b>

**Consensus-based recommendation**

*High-risk individuals – conventional adenomas only*

First surveillance intervals following removal of high-risk conventional adenomas only should be stratified according to the type and number of high-risk features (size ≥10mm, high-grade dysplasia (HGD), villosity, 3–4 adenomas):



### Consensus-based recommendation

A surveillance interval of 5 years is recommended for patients with either of the following:

- \* 1-2 tubular adenomas with HGD or tubulovillous or villous adenomas (with or without HGD), all of which are <10mm
- \* 3-4 tubular adenomas without HGD, all of which are <10mm

A surveillance interval of 3 years is recommended for patients with any of the following:

- \* 1-2 tubular adenomas with HGD or tubulovillous or villous adenomas (with or without HGD), where the size of one or both is  $\geq 10$ mm
- \* 3-4 tubular adenomas, where the size of one or more is  $\geq 10$ mm
- \* 3-4 tubulovillous and/or villous adenomas and/or HGD, all <10mm

### Practice point

Surveillance intervals should be determined after the colon has been cleared of all significant neoplasia, once histology is known, and in the context of individualised assessment of benefit to the patient.

### Practice point

Consistently high-quality colonoscopy is imperative for optimal cost effectiveness and for implementation of uniform surveillance guidelines.

### Practice point

Polyp/adenoma size as per the endoscopist documentation should be used for determining surveillance intervals. All endoscopists should ensure size measurements are accurate using a reference standard (eg an open biopsy forceps or snare).

### Practice point

Polyps removed at colonoscopy should be sent separately for histology to guide surveillance recommendations.

**Practice point**

Clinicians should accurately include features relevant to surveillance intervals in their procedure reports so that individualised surveillance recommendations can be made.

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### 3.2.12 First surveillance intervals following removal of $\geq 5$ conventional adenomas only

Evidence-based recommendation	Grade
<p><i><math>\geq 5</math> conventional adenomas only</i></p> <p>First surveillance intervals following complete removal of <math>\geq 5</math> conventional adenomas only, should be no longer than 3 years.</p>	<b>D</b>

**Consensus-based recommendation**

*$\geq 5$  conventional adenomas only*

First surveillance intervals should be within 3 years and stratified based on the number, size and histology following complete removal of  $\geq 5$  adenomas only.

For those with 5–9 adenomas, recommended surveillance intervals are:

- \* 3 years if all tubular adenomas  $< 10$ mm without high grade dysplasia (HGD)
- \* 1 year if any adenoma  $\geq 10$ mm or with HGD and/or villosity

For those with  $\geq 10$  adenomas, the recommended surveillance interval is 1 year, regardless of size or histology.

**Practice point**

Surveillance intervals should be determined after the colon has been cleared of all significant neoplasia, once histology is known, and in the context of individualised assessment of benefit to the patient.

**Practice point**

Consistently high-quality colonoscopy is imperative for optimal cost effectiveness and for implementation of uniform surveillance guidelines.

**Practice point**

Polyp/adenoma size as per the endoscopist documentation should be used for determining surveillance intervals. All endoscopists should ensure size measurements are accurate using a reference standard (eg an open biopsy forceps or snare).

**Practice point**

Polyps removed at colonoscopy should be sent separately for histology to guide surveillance recommendations.

**Practice point**

Clinicians should accurately record adenoma features relevant to surveillance intervals so that individualised surveillance recommendations can be made.

**Practice point**

An underlying familial predisposition to colorectal cancer should be considered in all individuals with  $\geq 10$  polyps removed. Referral to a familial cancer clinic should be considered, along with appropriate psychological support.

Separate screening and surveillance recommendations apply to patients with diagnosed or likely familial syndromes (see Should family history affect surveillance intervals?).

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**Table 3. Summary of recommendations for first surveillance intervals following removal of conventional adenomas only**

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### 3.2.13 First surveillance intervals following removal of serrated polyps (with or without conventional adenoma)

Evidence-based recommendation	Grade
<p><i>Sessile and traditional serrated adenomas (with or without conventional adenomas)</i></p> <p>First surveillance intervals should be no greater than 5 years and should be based on features of synchronous conventional adenomas (if present) following complete removal of sessile and traditional serrated adenomas.</p>	<b>D</b>

Consensus-based recommendation
<p><i>Sessile and traditional serrated adenomas (with or without conventional adenomas)</i></p> <p>First surveillance intervals should be based on the number, size and presence of dysplasia in the serrated polyps and synchronous conventional adenomas (if present) following complete removal of sessile and traditional serrated adenomas.</p> <p><b>Clinically significant serrated polyps only</b></p> <p>5 years for:</p> <ul style="list-style-type: none"> <li>‡ 1-2 sessile serrated adenomas all &lt;10mm without dysplasia.</li> </ul> <p>3 years for:</p> <ul style="list-style-type: none"> <li>‡ 3-4 sessile serrated adenomas, all &lt;10mm without dysplasia</li> <li>‡ 1-2 sessile serrated adenomas ≥10mm or with dysplasia, or hyperplastic polyp ≥10mm</li> <li>‡ 1-2 traditional serrated adenomas, any size.</li> </ul> <p>1 year for:</p> <ul style="list-style-type: none"> <li>‡ ≥5 sessile serrated adenomas &lt;10mm without dysplasia</li> <li>‡ 3-4 sessile serrated adenomas, one or more ≥10mm or with dysplasia</li> <li>‡ 3-4 traditional serrated adenomas, any size.</li> </ul> <p><b>Clinically significant serrated polyps and synchronous conventional adenomas</b></p> <p>5 years for:</p> <ul style="list-style-type: none"> <li>‡ 2 in total, sessile serrated adenoma &lt;10mm without dysplasia.</li> </ul>

### Consensus-based recommendation

3 years for:

- \* 3-9 in total, all sessile serrated adenomas <10mm without dysplasia
- \* 2-4 in total, any serrated polyp  $\geq$ 10mm and/or dysplasia
- \* 2-4 in total, any traditional serrated adenoma.

1 year for:

- \*  $\geq$ 10 in total, all sessile serrated adenomas <10mm without dysplasia
- \*  $\geq$ 5 in total, any serrated polyp  $\geq$ 10mm and/or dysplasia
- \*  $\geq$ 5 in total, any traditional serrated adenoma.

### **Synchronous high-risk conventional adenoma (tubulovillous or villous adenoma, with or without HGD and with or without size $\geq$ 10mm)**

3 years for:

- \* 2 in total, sessile serrated adenoma <10mm, without dysplasia
- \* 2 in total, serrated polyp  $\geq$ 10mm and/or dysplasia
- \* 2 in total, any traditional serrated adenoma.

1 year for:

- \*  $\geq$ 3 total adenomas, sessile serrated adenoma any size with or without dysplasia
- \*  $\geq$ 3 total adenomas, one or more traditional serrated adenoma.

### Practice point

Surveillance is recommended for 'clinically significant' serrated polyps:

- \* sessile serrated adenomas
- \* traditional serrated adenomas
- \* hyperplastic polyps  $\geq$ 10mm.

### Practice point

High-quality endoscopy is imperative to identify accurately and to completely remove sessile and traditional serrated adenomas and synchronous conventional adenomas.

**Practice point**

Polyp/adenoma size as per the endoscopist documentation should be used for determining surveillance intervals. All endoscopists should ensure size measurements are accurate using a reference standard (eg an open biopsy forceps or snare).

**Practice point**

Polyps removed should be submitted separately for histologic assessment to inform surveillance recommendations.

**Practice point**

High-quality pathology interpretation is critical to correctly diagnose sessile and traditional serrated lesions and advanced serrated polyps.

**Practice point**

High-quality reporting from endoscopists and pathologists is required to allow accurate risk stratification for surveillance interval recommendations.

**Practice point**

Surveillance intervals should be determined after the colon has been cleared of all significant neoplasia, once histology is known and in the context of individualised assessment of benefit to the patient.

**Practice point**

Small, particularly distal, true hyperplastic polyps do not require surveillance.

#### Practice point

Clinicians should be aware of the cumulative serrated polyp count and diagnostic criteria for serrated polyposis syndrome and recommend surveillance. See *Clinical practice guidelines for the prevention, early detection and management of colorectal cancer*, Serrated polyposis syndrome for diagnostic criteria and recommended surveillance.

### Table 9. Summary of recommendations for first surveillance intervals following removal of clinically significant serrated polyps ( $\pm$ conventional adenomas)

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#### 3.2.14 First surveillance intervals following removal of large sessile or laterally spreading adenomas

##### Consensus-based recommendation

*Large sessile and laterally spreading lesions*

First surveillance interval should be approximately 12 months in individuals who have undergone **en-bloc** excision of large sessile and laterally spreading lesions.

##### Consensus-based recommendation

*Large sessile and laterally spreading lesions*

First surveillance interval should be approximately 6 months in individuals who have undergone **piecemeal** excision of large sessile and laterally spreading lesions.

#### Practice point

Consideration should be given to referring large sessile and laterally spreading lesions to experienced clinicians trained in and regularly undertaking high quality EMR to reduce the risk of recurrence.

**Practice point**

Patients with large sessile and laterally spreading lesions should be informed of the requirement for scheduled surveillance before proceeding to EMR.

**Practice point**

At surveillance following piecemeal or en-bloc excision of large sessile and laterally spreading lesions, the EMR scar should be identified, photodocumented and systematically evaluated for recurrence, including biopsies. These individuals are at high risk for synchronous and/or metachronous lesions and require very careful evaluation of the remaining colon at the same time.

**Practice point**

Endoscopic mucosal resection (EMR) of large sessile and laterally spreading lesions (>20mm) is usually piecemeal and all lesions that undergo piecemeal excision are at higher risk of recurrence and require scheduled surveillance. Risk factors for recurrence after EMR are piecemeal excision, larger lesion size (>40mm) and the presence of high-grade dysplasia in the resected specimen.

**Practice point**

In patients who have undergone piecemeal excision of large sessile and laterally spreading lesions (in whom the first surveillance colonoscopy at 6 months is clear), the next surveillance colonoscopy should be considered around 12-18 months, especially in those who had large lesions (>40mm) or high-grade dysplasia at index EMR.

**Practice point**

Consideration should be given to tattooing all lesions which may need to be identified subsequently. Those that may need surgical resection should be tattooed distal to the lesion in three locations around the circumference of the bowel to facilitate recognition.



**Practice point**

Consistently high-quality colonoscopy is imperative for optimal cost effectiveness and for implementation of uniform surveillance guidelines.

**Practice point**

Polyp/adenoma size as per the endoscopist documentation should be used for determining surveillance intervals. All endoscopists should ensure size measurements are accurate using a reference standard (eg an open biopsy forceps or snare).

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### 3.2.15 Should family history affect surveillance intervals?

Evidence-based recommendation	Grade
<p><i>Family history of CRC</i></p> <p>First surveillance intervals following adenoma removal in those with a family history of colorectal cancer should be based on patient factors and the adenoma history, unless a genetic syndrome is known or suspected.</p>	<p><b>D</b></p>

**Practice point**

To identify those who may have an increased familial risk of colorectal cancer, a family history of colorectal cancer and associated malignancies including number of affected relatives, relatedness and age of onset should be taken and updated every 5 to 10 years.

**Practice point**

In individuals who are undergoing screening colonoscopy for colorectal cancer based on family history, adenoma surveillance and screening recommendations should be compared and the shorter interval used. Refer to Clinical practice guidelines for the prevention, early detection and management of colorectal cancer (2017) (see Recommendations for risk and screening based on family history of colorectal cancer).

**Practice point**

To address individual's concerns, clinicians should take adequate time to explain the relationship of family history to recommended surveillance intervals and refer for counselling where appropriate.

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### 3.2.16 Subsequent surveillance intervals

**Practice point**

The findings of the previous two colonoscopies predict high-risk findings on the subsequent colonoscopy and should be considered when recommending subsequent surveillance intervals.

**Practice point**

For individuals who have undergone two or more colonoscopies, the surveillance interval for the next (3rd) colonoscopy should be based on the reports and histology from the two most recent procedures (1st and 2nd colonoscopies) as per Tables 14–16 (see Table 13 as a quick reference guide).

(Table 13 is provided at the end of this section as a reference guide to Tables 14-16)

**Table 14. Recommended surveillance intervals for 3rd colonoscopy - conventional adenomas only at 1st and 2nd colonoscopy**

**Table 15. Recommended surveillance intervals for 3rd colonoscopy.** a. (top) clinically significant serrated polyps only at 2nd colonoscopy. b. (bottom) clinically significant serrated polyps with synchronous conventional adenomas at 2nd colonoscopy.

**Table 16. Recommended surveillance intervals for 3rd colonoscopy - clinically significant serrated polyps at 1st colonoscopy, no adenomas or conventional adenomas only at 2nd colonoscopy**

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### 3.2.17 The elderly and stopping rules

#### Practice point

Careful assessment and shared decision-making should be utilised when considering surveillance colonoscopy in the elderly, most of whom will have no significant findings and will not benefit.

#### Practice point

Surveillance colonoscopy in those  $\geq 75$  years should be considered based on age, co-morbidity and the preferences of the patient. The reproducible and validated Charlson score is useful to assess life expectancy and could be implemented to assist decision-making (see Tables 17 and 18 below).

#### Practice point

In obtaining consent for colonoscopy for an elderly patient, complication rates should reflect the individual risk based on age and comorbidity rather than 'standard' figures.

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### 3.2.18 Malignant polyps

#### Practice point

Endoscopists should be familiar with endoscopic appearances suggestive of a malignant polyp.

#### Practice point

Removal of polyps likely to be malignant should be en-bloc or patients should be referred to a centre specialising in endoscopic excision of large and flat polyps.

**Practice point**

Tattoos should be applied 2-3cm distal to the polypectomy site if future site localisation or surgery is necessary.

**Practice point**

Malignant polyps should be reviewed by a second pathologist with a specialist gastrointestinal interest where histological diagnosis is unclear or difficult. Multidisciplinary review and management (endoscopist, pathologist and surgeon as a minimum) is appropriate in public and private settings although the nature may differ.

**Practice point**

Standardised synoptic reporting should be used to assist clinical decision making (structured reporting protocols are available at the Royal College of Pathologists of Australasia website).

**Practice point**

Low-risk malignant polyps have all of the following features: superficial submucosal invasion (<1000 microns), moderate or well differentiated histology, no lymphovascular invasion, clear margins and no other risk features. In these cases, where the endoscopist is certain that the lesion has been completely removed, then the neoplasm should be considered cured by endoscopic polypectomy.

**Practice point**

Polyps that do not satisfy low risk criteria or have other histological risk features (often not routinely reported) including: malignant invasion depth >2mm, invasion width >3mm, tumour budding and cribriform architecture, should be considered at risk of harbouring residual bowel wall cancer or lymph node metastases. A magnitude of the risk should be estimated and the need for formal surgical resection considered.

**Practice point**

Cases considered for surgery must have an assessment of surgical risk using validated surgical risk scoring systems, e.g. Risk Prediction in Surgery.

**Practice point**

A discussion of risk of residual cancer balanced against risk of surgery must occur with the patient to determine ultimate management choice.

**Practice point**

Multi-disciplinary management and audit are important.

**Practice point**

Surveillance recommendations for a T1 adenocarcinoma as per 2017 Australian Clinical practice guidelines for the prevention, early detection and management of colorectal cancer should be followed for completely resected malignant polyps.

**Practice point**

A patient who has had potential incomplete endoscopic resection of a malignant polyp not undergoing surgery should undergo repeat colonoscopy to assess recurrence at an interval of 3 months.

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### 3.2.19 Role of surveillance colonoscopy after curative resection for colorectal cancer

### 3.2.20 Pre and perioperative colonoscopy in patients with colorectal cancer undergoing resection

Evidence-based recommendation	Grade
A preoperative colonoscopy should be attempted in all patients with a newly diagnosed colorectal cancer.	<b>C</b>

Evidence-based recommendation	Grade
Colonoscopy should be performed 3–6 months after resection for patients with obstructive colorectal cancer in whom a complete perioperative colonoscopy could not be performed and in whom there is residual colon proximal to the location of the pre-operatively obstructing cancer.	<b>C</b>

Practice point
In cases of a colorectal cancer that may be difficult to identify at surgery, particularly using the laparoscopic approach, submucosal tattoo should be placed in three places approximately 2 cm distal to the lesion at the time of colonoscopy. This should be clearly documented in the colonoscopy report.

Practice point
If the index colorectal cancer (CRC) obstructs the lumen and prevents passage of a colonoscope, consideration should be given to specific pre-operative assessment of the proximal colon by alternative means. CT colonography (CTC) can be considered. However, its role in this clinical scenario requires further analysis. It is safe to perform same-day CTC following an incomplete colonoscopy, including in patients who have had a biopsy or simple polypectomy. CTC should be delayed in patients with complex endoscopic intervention and in patients at high risk of perforation, such as those with active colitis or high-grade stricture.

**Practice point**

Proximal visualisation is unnecessary if the colon proximal to the cancer is to be included in the resection specimen. In patients with residual un-visualised colon, colonoscopy should be performed 3–6 months after surgery, providing no non-resectable distant metastases are found.

**Practice point**

In patients with a defunctioning loop ileostomy, it is preferable to undertake colonoscopy after this is reversed to enable adequate bowel preparation.

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### 3.2.21 Follow-up colonoscopy after colorectal cancer resection

Evidence-based recommendation	Grade
<p>Colonoscopy should be performed 1 year after the resection of a sporadic cancer, unless a complete postoperative colonoscopy has been performed sooner.</p> <p><b>Recommendation unchanged from 2011 edition of clinical practice guidelines for surveillance colonoscopy.</b></p>	<b>C</b>

Evidence-based recommendation	Grade
<p>If the perioperative colonoscopy or the colonoscopy performed at 1 year reveals advanced adenoma, then the interval before the next colonoscopy should be guided by recommended surveillance intervals according to polyp features.</p> <p><b>Recommendation unchanged from 2011 edition of clinical practice guidelines for surveillance colonoscopy.</b></p>	<b>C</b>

Evidence-based recommendation	Grade
<p>If the colonoscopy performed at 1 year is normal or identifies no advanced adenomas, then the interval before the next colonoscopy should be five 5 years (i.e. colonoscopies at 1, 6, and 11 years after resection).</p>	<b>C</b>

Evidence-based recommendation	Grade
<p><b>Recommendation unchanged from 2011 edition of clinical practice guidelines for surveillance colonoscopy.</b></p>	

Consensus-based recommendation
<p>If surveillance colonoscopy reveals adenoma, then the interval before the next colonoscopy should be guided by polyp features (evidence-based recommendation, Grade C). However, if subsequent colonoscopy is normal, then surveillance should revert back to the intervals recommended for initial cancer surveillance (colonoscopy at 6 and 11 years post resection).</p> <p><b>Recommendation unchanged from 2011 edition of clinical practice guidelines for surveillance colonoscopy.</b></p>

Consensus-based recommendation
<p>If all colonoscopies performed at 1, 6 and 11 years post resection are normal, follow-up can be with either of the following options:</p> <ul style="list-style-type: none"> <li>* faecal occult blood test every 2 years</li> <li>* colonoscopy at 10 years (i.e. 21 years post resection)</li> </ul> <p><b>Recommendation unchanged from 2011 edition of clinical practice guidelines for surveillance colonoscopy.</b></p>

Practice point
<p>Patients undergoing either local excision (including transanal endoscopic microsurgery) of rectal cancer or advanced adenomas or ultra-low anterior resection for rectal cancer should be considered for periodic examination of the rectum at 6-monthly intervals for 2 or 3 years using either digital rectal examination, rigid proctoscopy, flexible proctoscopy, and/or rectal endoscopic ultrasound. These examinations are considered to be independent of the colonoscopic examination schedule described above</p>

Practice point
<p>Patients with incomplete colonoscopy pre-operatively (e.g. impassable distal lesion) should have a semi-urgent elective post-operative colonoscopy when feasible, independent of surveillance intervals.</p>



### Practice point

Surveillance colonoscopy in those age  $\geq 75$  years should be based on age and comorbidity as assessed by the reproducible and validated Charlson score. Charlson score is useful to assess life expectancy and could be implemented to stratify benefits of surveillance colonoscopy in the elderly (see Table 18. Charlson score for colonoscopy benefit).

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## 3.2.22 Patient selection for surveillance colonoscopy following resection

### Practice point

Patients with hereditary colorectal cancer syndromes should have surveillance colonoscopy performed post-operatively as per the Clinical practice guidelines for the prevention, early detection and management of colorectal cancer.

### Practice point

Other clinically high-risk patients should be considered for more frequent surveillance colonoscopy after surgery than would otherwise be recommended (e.g. initial post-operative colonoscopy at 1 year and then 1–3 yearly depending on personalised estimate of risk). These include patients:

- ✦ whose initial diagnosis was made younger than age 40 years
- ✦ with suspected but un-identified hereditary colorectal cancer syndromes
- ✦ with multiple synchronous cancers or advanced adenomas at initial diagnosis.

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### 3.2.23 Colonoscopic surveillance and management of dysplasia in inflammatory bowel disease (IBD)

#### 3.2.24 Initiation of surveillance in IBD

Evidence-based recommendation	Grade
Surveillance colonoscopy should commence after 8 years of onset of inflammatory bowel disease symptoms in those with at least distal (left-sided) ulcerative colitis or Crohn's colitis with involvement of at least one third of the colon.	<b>C</b>

Evidence-based recommendation	Grade
In the presence of primary sclerosing cholangitis (PSC), surveillance colonoscopy should commence upon the diagnosis of PSC.	<b>B</b>

Practice point
A family history of colorectal cancer in a first degree relative represents an intermediate risk factor. Surveillance colonoscopy may begin after 8 years of the onset of symptoms of inflammatory bowel disease, or 10 years before the age of the youngest relative with colorectal cancer, whichever is earliest.

Practice point
Those with isolated proctitis or small bowel Crohn's disease do not require surveillance colonoscopy.

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### 3.2.25 Surveillance interval for IBD patients

Consensus-based recommendation
<b>Patients with IBD at high risk of CRC</b> (those with PSC, ongoing chronic active inflammation, prior colorectal dysplasia, evidence of intestinal damage with colonic stricture, pseudopolyps or foreshortened tubular colon or family history of CRC at age $\leq 50$ years) should undergo yearly surveillance colonoscopy.

**Consensus-based recommendation**

**Patients with IBD at intermediate risk of CRC** (those with quiescent disease, no high risk features or family history of CRC in a first-degree relative) should undergo surveillance colonoscopy every 3 years.

**Consensus-based recommendation**

**Patients with IBD at low risk of CRC** (those with quiescent disease and no other risk factors, and with inactive disease on consecutive surveillance colonoscopies) may undergo surveillance colonoscopy every 5 years.

**Practice point**

Consider increased frequency of surveillance (intervals less than 3 years) in patients with a family history of CRC in a first-degree relative <50 years of age because this may be an additional risk factor for CRC.

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### 3.2.26 Recommended surveillance techniques in IBD patients

Evidence-based recommendation	Grade
Chromoendoscopy should be incorporated into surveillance procedures, especially in high-risk patients.	<b>A</b>

Evidence-based recommendation	Grade
Taking targeted, rather than random, biopsies is the recommended method of identifying dysplasia in patients with inflammatory bowel disease.	<b>B</b>

Evidence-based recommendation	Grade
Random biopsies are recommended in IBD patients with PSC, prior dysplasia, and intestinal damage (colonic stricture or foreshortening).	<b>C</b>

Evidence-based recommendation	Grade
Standard-definition colonoscopy is not recommended for surveillance procedures, especially in the absence of chromoendoscopy	<b>B</b>

Consensus-based recommendation
Proceduralists performing surveillance colonoscopy in patients with IBD should be familiar with and adhere to surveillance guidelines.

Practice point
<p>IBD surveillance requires high-quality colonoscopy:</p> <ul style="list-style-type: none"> <li>✦ performing the colonoscopy when the patient is in clinical and endoscopic remission</li> <li>✦ excellent bowel preparation</li> <li>✦ the use of high-definition colonoscopes</li> <li>✦ ensuring optimal and full visualisation of the mucosal surface during slow withdrawal.</li> </ul>

Practice point
Dye spray chromoendoscopy can be applied with a spray catheter or by incorporating dye in the reservoir of the water pump.

Practice point
Either methylene blue or indigo carmine is an appropriate dye for chromoendoscopy.

Practice point
Upon identification of invisible dysplasia on random biopsies, confirmation of diagnosis and grade is required by at least two GI pathologists. Chromoendoscopy is then recommended to determine if there is multifocal dysplasia.

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### 3.2.27 Management of elevated dysplastic lesions in patients with IBD

Evidence-based recommendation	Grade
Raised lesions containing dysplasia may be treated endoscopically provided that the entire lesion is removed and there is no dysplasia in flat mucosa elsewhere in the colon.	<b>C</b>

Evidence-based recommendation	Grade
If a raised dysplastic lesion cannot be completely removed, surgical intervention is strongly recommended.	<b>D</b>

Consensus-based recommendation
<p>In the presence of multifocal low-grade dysplasia that cannot be removed endoscopically, at least frequent surveillance colonoscopy is required. Surgical management is an alternative based on case-by-case discussion.</p> <p>Surveillance colonoscopy with chromoendoscopy within 3–12 months should be carried out after endoscopic resection of an elevated dysplastic lesion in inflammatory bowel disease.</p>

Practice point
The important objective for the endoscopist performing surveillance procedures is to identify lesions that are safely and completely resectable endoscopically. This is based on endoscopic features of the identified lesion and elsewhere in the colon.

Practice point
Nomenclature should reflect the SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease. The term 'dysplasia associated lesion or mass (DALM)' should not be used.

**Practice point**

Consider referral to an experienced endoscopist to perform surveillance for inflammatory bowel disease using chromoendoscopy to exclude multi-focal dysplasia followed by endoscopic resection of the dysplastic lesion.

**Practice point**

Close colonoscopic surveillance is required following endoscopic resection of dysplasia given the risk of multifocal dysplasia and metachronous dysplasia.

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### 3.2.28 High-grade dysplasia in IBD

Evidence-based recommendation	Grade
Patients with endoscopically non-resectable high-grade dysplasia should undergo colectomy.	<b>C</b>

Evidence-based recommendation	Grade
For patients with endoscopically resectable high grade dysplasia, whether polypoid or non-polypoid, continued colonoscopic surveillance after complete resection of the lesion is recommended rather than referral for colectomy.	<b>C</b>

**Consensus-based recommendation**

Patients with resected high-grade dysplasia should undergo further surveillance in 3–12 months. Subsequent surveillance intervals depend on the findings of each subsequent surveillance colonoscopy.

**Consensus-based recommendation**

Patients with invisible high-grade dysplasia (HGD) should undergo more intensive colonoscopic surveillance than patients with visible HGD.

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### 3.2.29 Low-grade dysplasia in IBD

Evidence-based recommendation	Grade
Unifocal low-grade dysplasia should be followed by ongoing surveillance using high-definition white-light endoscopy and chromoendoscopy at 6 months. If 6-month surveillance colonoscopy is normal, surveillance should be repeated annually.	<b>C</b>

Evidence-based recommendation	Grade
Low-grade dysplasia in flat mucosa should be evaluated for multifocal dysplasia by an endoscopist with expertise in inflammatory bowel disease surveillance using high-definition white-light endoscopy and/or chromoendoscopy.	<b>C</b>

Consensus-based recommendation
Visible dysplasia should be resected endoscopically and then followed up with surveillance colonoscopy with high-definition white-light endoscopy and chromoendoscopy within 3-12 months.

Consensus-based recommendation
Consider shorter surveillance intervals for flat dysplasia located in the distal colon, as this is associated with higher risk of progression.

Practice point
When determining an individual's appropriate surveillance frequency, the risk factors for progression of low-grade dysplasia (LGD) towards high-grade dysplasia (HGD) or colorectal cancer are: older age at diagnosis of LGD (age >55 years), male sex and inflammatory bowel disease duration of >8 years at diagnosis of LGD.

**Practice point**

Multifocal low-grade dysplasia is associated with a sufficiently high risk of future cancer that colectomy is usually recommended. Patients who elect to avoid surgery require follow-up surveillance at 3 months, preferably with chromoendoscopy and high-definition white-light endoscopy. If 3-month surveillance colonoscopy is normal, surveillance should be repeated annually.

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### 3.2.30 Indefinite dysplasia in IBD

Evidence-based recommendation	Grade
Indefinite dysplasia in flat mucosa does not require surgery, but follow-up colonoscopic surveillance is recommended, preferably with chromoendoscopy, at more frequent intervals.	<b>D</b>

**Consensus-based recommendation**

Indefinite dysplasia should be reviewed by a second gastro-intestinal pathologist.

**Consensus-based recommendation**

After detecting indefinite dysplasia, inflammation (if present) should be treated and colonoscopy should be repeated.

**Practice point**

If indefinite dysplasia is detected at random biopsy, repeat colonoscopy with enhanced imaging techniques may assist in defining an endoscopically resectable lesion, or a lesion amenable to further targeted biopsies.



**Practice point**

If there are features of active inflammation, repeat colonoscopy following escalation of therapy may assist in further defining indefinite dysplasia.

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### 3.2.31 Anxiety in colonoscopy: approaches to minimise anxiety and its adverse effects

### 3.2.32 Anxiety and colonoscopy: approaches to minimise anxiety and its adverse effects

**Practice point**

Providing pre-colonoscopy advice to patients by means of educational material, video and clinical explanation can assist in improving the patient experience with the procedure, and in reducing decreasing anxiety and abdominal pain during the procedure.

**Practice point**

Endoscopists should aim to control pain and discomfort during a colonoscopy procedure in order to reduce patient anxiety.

**Practice point**

Physicians should be able to provide accurate and relevant information about colonoscopy for patients who are undergoing open access colonoscopy (without prior consultation with an endoscopist).

**Practice point**

Gastroenterology clinics are recommended to evaluate shifting towards a biopsychosocial approach to healthcare and encouraging patients to participate in decision-making in order to provide them with a greater sense of control, thus reducing anxiety.

**Practice point**

The use of neutral language around colonoscopy may be useful in order to break down the stigma and taboo surrounding the procedure and bowel health issues.

**Practice point**

Clinicians should ensure that patients understand the standard practice and convey information about the procedure as clearly as possible (e.g., whether they will be conscious, whether they will experience pain, etc.).

Note: Clinicians should also follow the Clinical Care Standards that apply to the preparation of patients for procedures, including informed consent (see Australian Commission on Safety and Quality in Health Care Colonoscopy Clinical Care Standards).

**Practice point**

Patients who receive the amount of information consistent with their preferences (information seekers versus avoiders) report lower anxiety and more satisfaction with the intervention, and experience less pain and shorter time in recovery. Colonoscopists can assess patients' desire for information by asking the patient directly, for example "how much information would you like about XX (this procedure)? Are you someone who prefers to get a lot of information or just the basics?"

**Practice point**

Music provided to patients prior to and during colonoscopy may reduce their discomfort.

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### 3.2.33 Socio-economic factors

#### 3.2.34 Impact of socioeconomic factors on surveillance colonoscopy

##### Practice point

Clinicians should advise patients that modification of lifestyle factors can reduce their risk of polyp recurrence and colorectal cancer.

##### Practice point

Information and instructions for bowel preparation and colonoscopy need to be tailored to meet the needs of most Australians who have inadequate or poor health literacy.

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#### 3.2.35 Impact made by socioeconomic factors in treatment groups undergoing surveillance colonoscopy

##### Practice point

After curative resection for colorectal cancer, survival outcomes in disadvantaged patients may be improved by clinicians and health systems by addressing the barriers and access to optimal clinical care.

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**Table 13 Colonoscopy findings and surveillance intervals: reference guide to Tables 14-16**

1 <sup>st</sup> colonoscopy findings	2 <sup>nd</sup> colonoscopy findings	3 <sup>rd</sup> colonoscopy surveillance interval
	Normal colonoscopy or	

1 <sup>st</sup> colonoscopy findings	2 <sup>nd</sup> colonoscopy findings	3 <sup>rd</sup> colonoscopy surveillance interval
Conventional adenomas only	conventional adenomas only	Table 14
	Clinically significant serrated polyps <i>without</i> synchronous conventional adenomas	Table 15a
	Clinically significant serrated polyps <i>with</i> synchronous conventional adenomas	Table 15b
	Normal colonoscopy or conventional adenomas only	Table 16
Clinically significant serrated polyps <i>with or without</i> synchronous conventional adenomas	Clinically significant serrated polyps <i>without</i> synchronous conventional adenomas	Table 15a
	Clinically significant serrated polyps <i>with</i> synchronous conventional adenomas	Table 15b
	Normal colonoscopy or conventional adenomas only	Table 16

**Table 17. Surveillance recommendations for individuals age  $\geq 75$  years**

Age (years)	Charlson score <sup>a</sup>	
	$\leq 4$	$> 4$
75–80	Surveillance colonoscopy to be considered <sup>b,c</sup>	Surveillance colonoscopy not recommended
$> 80$	Surveillance colonoscopy not recommended	

<sup>a</sup>Charlson for colonoscopy benefit can be simplified as per Table 18; <sup>b</sup>colonoscopy should be considered an option dependent on a clear conversation about the low risk of significant colorectal pathology, taking the

patient's wishes into consideration; <sup>c</sup>consent for colonoscopy should include age appropriate statistics on risk.

**Table 18. Charlson score for colonoscopy benefit**

Age	Medical conditions	
75–79 years (3 points for age)	<p><b>May</b> have <i>one</i> of these conditions only (1 point each):</p> <ul style="list-style-type: none"> <li>Mild liver disease</li> <li>Diabetes without end-organ damage</li> <li>Cerebrovascular disease</li> <li>Ulcer disease</li> <li>Connective tissue disease</li> <li>Chronic pulmonary disease</li> <li>Dementia</li> <li>Peripheral vascular disease</li> <li>Congestive heart failure</li> <li>Myocardial infarction</li> </ul>	<p><b>May not</b> have <i>any</i> of these medical conditions (<math>\geq 1</math> point each):</p> <ul style="list-style-type: none"> <li>Moderate/severe liver disease</li> <li>Diabetes with end-organ damage</li> <li>Hemiplegia</li> <li>Moderate or severe renal disease</li> <li>AIDS</li> <li>Metastatic or non-metastatic solid organ or haematopoietic malignancy</li> </ul>
80 years (4 points for age)	May not have any of the above medical conditions	

### 3.3 NHMRC approved recommendation types and definitions

This guideline includes evidence-based recommendations (EBR), consensus-based recommendations (CBR) and practice points (PP) as defined in the table below. Recommendations and practice points were developed by working party members and sub-committee members.

Each EBR was assigned a grade by the expert working group, taking into account the volume, consistency, generalisability, applicability and clinical impact of the body of evidence according to NHMRC Level and Grades for Recommendations for Guidelines Developers.<sup>[1]</sup>

Type of recommendation	Definition
<b>Evidence-based recommendation</b>	A recommendation formulated after a systematic review of the evidence, indicating supporting references
<b>Consensus-based recommendation</b>	A recommendation formulated in the absence of quality evidence, after a systematic review of the evidence was conducted and failed to identify admissible evidence on the clinical question
<b>Practice point</b>	A recommendation on a subject that is outside the scope of the search strategy for the systematic review, based on expert opinion and formulated by a consensus process

*Source: National Health and Medical Research Council. Procedures and requirements for meeting the NHMRC standard for clinical practice guidelines. Melbourne: National Health and Medical Research Council, 2011*

### 3.4 Levels of evidence and grades for recommendations

These guidelines are intended for use by all practitioners and health workers who require information about surveillance colonoscopy - in adenoma follow-up, following curative resection of colorectal cancer, and for cancer surveillance in inflammatory bowel disease. They are specifically revising the colonoscopic surveillance sections of the Clinical Practice Guidelines for the prevention, early detection and management of colorectal cancer 2005 chapters 8, 9, 17, and introduce a new chapter on cancer surveillance in inflammatory bowel disease. They also cover psychosocial care (chapter 18 in the 2005 Guidelines), socio economic factors and cost effectiveness (chapters 23 and 22 in the 2005 Guidelines). The guidelines have been produced by a process of systematic literature review; critical appraisal and consultation encompassing all interested parties in Australia (see Appendices).

The following table provides a list of the evidence-based recommendations detailed in the text of each chapter. The table below provides details on the highest level of evidence identified to support each recommendation (I-IV). The Summary of Recommendations table includes the grade for each recommendation (A-D). The key references that underpin the recommendation are provided in the last column. Individual levels of evidence can be found in the Evidence Summaries for each recommendation in each chapter.

Each recommendation was assigned a grade by the expert working group taking into account the volume, consistency, generalisability, applicability and clinical impact of the body of evidence supporting each recommendation.

When no Level I or II evidence was available and in some areas, in particular where there was insufficient evidence in the literature to make a specific evidence-based recommendation, but also strong and unanimous expert opinion amongst the working group members about both the advisability of making a clinically relevant statement and its content, recommended best practice points were generated. Thus, the practice points relate to the evidence in each chapter, but are more expert opinion-based than evidence-based. These can be identified throughout the guidelines with the following: Practice point (PP).

<b>Grade of Recommendation</b>	<b>Description</b>
A	Body of evidence can be trusted to guide practice
B	Body of evidence can be trusted to guide practice in most situations
C	Body of evidence provides some support for recommendations but care should be taken in its application.
D	Body of evidence is weak and recommendation must be applied with caution

Source: National Health and Medical Research Council. NHMRC levels of evidence and grades for recommendations for developers of guidelines. Canberra: NHMRC; 2009. ([https://www.nhmrc.gov.au/\\_files\\_nhmrc/file/guidelines/developers/nhmrc\\_levels\\_grades\\_evidence\\_120423.pdf](https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf))

## Levels of Evidence

### Designations of levels of evidence for intervention research questions (NHMRC, 2009)<sup>[2]</sup>

<b>Level</b>	<b>Intervention</b>
I	A systematic review of level II studies
II	A randomised controlled trial
III-1	A pseudo-randomised controlled trial (ie alternate allocation or some other method)
III-2	A comparative study with concurrent controls: <ul style="list-style-type: none"> <li>• non-randomised, experimental trial</li> <li>• cohort study</li> <li>• case-control study</li> <li>• interrupted time series with a control group</li> </ul>
III-3	A comparative study without concurrent controls: <ul style="list-style-type: none"> <li>• historical control study</li> <li>• two or more single-arm studies</li> <li>• interrupted time series without a parallel control group</li> </ul>
IV	Case series with either post-test or pre-test/post-test outcomes

Source: National Health and Medical Research Council. NHMRC levels of evidence and grades for recommendations for developers of guidelines. Canberra: NHMRC; 2009. ([https://www.nhmrc.gov.au/\\_files\\_nhmrc/file/guidelines/developers/nhmrc\\_levels\\_grades\\_evidence\\_120423.pdf](https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf))

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## 3.5 References

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1. ↑ National Health and Medical Research Council. *NHMRC levels of evidence and grades for recommendations for guideline developers*. Canberra: National Health and Medical Research Council; 2009 Available from: [https://www.nhmrc.gov.au/\\_files\\_nhmrc/file/guidelines/developers/nhmrc\\_levels\\_grades\\_evidence\\_120423.pdf](https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf).
2. ↑ National Health and Medical Research Council. *NHMRC levels of evidence and grades for recommendations for guideline developers*. Canberra: National Health and Medical Research Council; 2009 Available from: [https://www.nhmrc.gov.au/\\_files\\_nhmrc/file/guidelines/developers/nhmrc\\_levels\\_grades\\_evidence\\_120423.pdf](https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf).

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## 4 Plain language summary

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Colonoscopy is a test to examine the inside of the bowel using a long thin tube with a camera at its tip. Colonoscopy is done by specialist doctors called endoscopists.

The main purpose of colonoscopy is to look for cancer or polyps, which are abnormal growths that could become cancer. Adenomas are the most common types of polyps.

Doctors will arrange for someone to have a colonoscopy (also called 'a scope') if they have symptoms of possible bowel cancer, if they have had a previous bowel problem, if bowel cancer runs in their family, or if they have had an abnormal result on a test ('faecal occult blood test') done as part of the National Bowel Cancer Screening Program or via their general practitioner or pharmacist.

Regular colonoscopy repeated every few years is recommended for some people. These include people who have previously had cancer, people who have had pre-cancerous polyps removed, some people who have inflammatory bowel diseases (IBD) and people with a strong family history of bowel cancer.

These guidelines contain information for doctors about how to do colonoscopy, how often to do it and repeat it, and how to care for people when cancer or other bowel disease is found. These guidelines are an update of the 2011 guidelines for surveillance colonoscopy, and follow on from the current national bowel (colorectal) cancer guidelines, which were updated in 2017.<sup>[1]</sup>

### 4.1 Improvements in colonoscopy

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All medical tests sometimes miss the medical condition they are designed to detect. Colonoscopy picks up the vast majority (approximately 95%) of cancers and adenomas. Some endoscopists are better at finding growths than others - it takes training and practice.



Doctors and medical technicians are continually improving techniques and methods to make colonoscopy safer and more efficient. Areas of improvement include:

- how the bowel is emptied and cleaned out before a colonoscopy, including what the person is allowed to eat before the procedure and the timing of the preparation doses
- the medical instruments (colonoscopes) used, including the type of camera, electronics, attachments that improve the doctor's ability to find abnormal growths
- the use of different dyes to help abnormal growths show up on the camera
- the way the endoscopist performs the colonoscopy
- how findings are recorded
- training methods for endoscopists.

Other methods, such as computed tomography (CT) colonography, do not use a camera inside the bowel. CT colonography is a type of scan done from the outside of the body.

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## 4.2 Colonoscopy in people who have previously had polyps removed

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How often a person needs a colonoscopy depends on what was found on their last colonoscopy and on other tests. These help doctors judge their risk of bowel cancer during the next few years. There are several different types of polyps. A person's risk of developing cancer depends on the type.

When a polyp is removed, the pathologist tests it to work out exactly which type it is. This involves examining it under a microscope to look at the types of cells.

The recommended time to a person's next colonoscopy could range from 1 year to 10 years, depending on the pathology report. Some patients may not need any further colonoscopies.

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## 4.3 Colonoscopy for people with bowel cancer

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Bowel cancer is often found during colonoscopy, before having a surgical operation to remove the cancer. If a bowel cancer is found in another way, colonoscopy is usually then recommended to check the remainder of the bowel. Sometimes, if the cancer blocks the inside of the bowel and prevents the camera passing through, another type of scan, such as a CT colonography, may be used.

In most people after surgery for bowel cancer, colonoscopy should be repeated 1 year later. In some cases (if it was not completed before the cancer operation), colonoscopy might need to be performed 3 to 6 months after surgery.

After bowel cancer surgery and the repeated colonoscopy 1 year later, most people need regular follow-up colonoscopies long term. This may be continued for as long as the person is expected to benefit from repeatedly having their bowel checked, while taking into account their estimated life expectancy. How often these follow-up colonoscopies are needed depends on how many and what type of polyps are found at the first colonoscopy after surgery. The timing recommended is then according to polyp follow-up guidelines.

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## 4.4 Colonoscopy for people with inflammatory bowel disease (IBD)

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Inflammatory bowel disease (IBD) is a long-term medical condition that involves continual or recurring attacks of painful inflammation in areas of the bowel. There are two types of IBD: ulcerative colitis and Crohn's disease.

Regular colonoscopy is recommended for many people with IBD, if their type of IBD increases their risk of bowel cancer.

When signs of IBD are discovered during colonoscopy, samples (biopsies) of abnormal bowel lining are removed to be examined under a microscope by a pathologist. The pathologist's report and the findings of the colonoscopy help doctors work out the best treatment for the person, including whether they have a higher risk of bowel cancer.

For people with IBD, when and how often to have colonoscopy depends on their individual circumstances. For some people with IBD, colonoscopy should start as soon as they get the diagnosis. For others, the first surveillance colonoscopy is recommended 8 years after the symptoms began. Colonoscopy should be repeated at intervals (often every 1, 3 or 5 years) depending on the individual's risk of bowel cancer. At each colonoscopy, the lining of the bowel is carefully inspected and small pieces of bowel lining (biopsies) are often removed for testing by a pathologist. Some people with IBD do not have an increased risk of bowel cancer and don't require colonoscopy for the purpose of preventing bowel cancer.

Any suspicious-looking growths are removed during the colonoscopy, if possible. If growths cannot be removed during colonoscopy, the person may need to have bowel surgery. Colonoscopy is repeated more frequently after growths have been removed.

The person's doctors will continually reassess whether to remove abnormal growths or just keep checking them from time to time.

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## 4.5 Coping with colonoscopy

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Having a colonoscopy can be stressful. It is common for someone to be a little anxious when they are about to have a colonoscopy. Most people do not experience severe anxiety.

A colonoscopy is usually done while the person has been given a strong sedative or a light anaesthetic. This helps people feel calm and relaxed during the procedure.

Doctors and nurses should carefully explain what will happen and what to expect. Written information or a video before the day of the colonoscopy can help people know what to expect and might help people cope better. Some people prefer to get more detailed information than others.

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## 4.6 Improving bowel health for people living in poorer and more remote areas

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On average, poorer people and people living in rural and remote places are more likely to die from bowel cancer. This may be because they are missing out on the best quality care. Aboriginal and Torres Strait Islander people, people living in remote and regional areas, and people living in poorer areas are less likely than other Australian to have colonoscopies recommended for them after they have an abnormal result on the screening test.

Hospitals, specialists and GPs should make extra efforts to promote access for these people to get the follow-up they need, including access to clear information and colonoscopy.

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## 4.1 Advances in colonoscopy, CT colonography and other methods - Introduction

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## 4.1.1 Introduction

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Colonoscopy remains the primary method for investigating symptoms and pathologies of the colon (and rectum) and terminal ileum. Computed tomography (CT) colonography also has a role under certain circumstances, but other modalities such as magnetic resonance colonography and capsule colonography are not yet in routine use and are not covered in this section. Accepted indications for colonoscopy include a positive faecal occult blood test, new and persistent lower gastrointestinal symptoms (particularly bleeding or change in bowel habit), or significant family history of bowel cancer. However, like any test, colonoscopy and CT colonography have limitations in terms of accuracy and risk that must be considered before an individual is subjected to them.

As with other diagnostic tests, colonoscopy has a false negative rate for detection of colorectal cancer and adenomas. This needs to be taken into consideration when decisions are made about the choice and timing of surveillance procedures. While the overall sensitivity for colorectal cancer is 95%,<sup>[1]</sup> the available literature suggests that cancer miss rates are higher for the proximal colon than elsewhere in the large bowel.<sup>[2]</sup> In a systematic review of polyp miss rates as determined by tandem colonoscopy, Van Rijn et al (2006)<sup>[3]</sup> identified studies in which patients had undergone two same-day colonoscopies with polypectomy. The research yielded six studies, involving a total of 465 patients. The pooled miss rate for polyps of any size was 22%. Adenoma miss rate by size was 2.1% for adenomas  $\geq 10$ mm, 13% for adenomas 5–10mm, and 26% for adenomas 1–5mm, respectively. Analysis of the data suggests that, in expert hands, colonoscopy rarely misses polyps  $\geq 10$ mm, but the miss rate increases significantly with smaller sized polyps.

In a large multicentre study, Heresbach et al (2008)<sup>[4]</sup> examined adenoma miss rate by performing a large multicentre study, with same-day back-to-back video colonoscopy performed by two different colonoscopists in randomised order and blinded to results of the other examination. The miss rates for all polyps, all adenomas, polyps  $\geq 5$ mm, adenomas  $\geq 5$ mm, and advanced adenomas were 28%, 20%, 12%, 9% and 11%, respectively, which are not trivial. Greater diameter (1mm increments) and number of polyps ( $\geq 3$ ) were independently associated with a lower polyp miss rate, whereas sessile or flat shape was significantly associated with a higher miss rate.<sup>[4]</sup>

The miss rate of colonoscopy, however, is operator-dependent, with rates of polyp and cancer detection varying between colonoscopists. This translates into variable colorectal cancer protection following colonoscopy such that, unlike other screening tests, the performance characteristics of colonoscopy are not fixed, and vary with operator, patient, technical, and system factors.<sup>[5]</sup> Improvements in colonoscopy have therefore focused on these factors to reduce the variation in performance.

No systematic review was performed for this section. The guidance is based on current international guidelines and consensus statements considered to be relevant to Australian practice.

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### 4.1.1.1 Chapter subsections

Please see:

- Bowel preparation

- Advances in technique
- Technological advances
- Adjunct technologies
- Quality of colonoscopy
- CT colonography

## 4.1.2 References

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## 4.2 Bowel preparation

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- 1 Background
- 2 Overview of evidence (non-systematic literature review)
  - 2.1 Available bowel preparation types
  - 2.2 Preparation timing
  - 2.3 Dietary preparation
  - 2.4 Factors associated with poor preparation
  - 2.5 Documentation of bowel preparation
- 3 References

## 4.2.1 Background

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High-quality bowel preparation is a crucial pre-requisite for successful colonoscopy. Inadequate bowel preparation is associated with lower polyp and adenoma detection rates, longer procedure time, increased need for repeat procedures, higher cost and a higher rate of patient drop out from screening programs.<sup>[1][2][3][4][5][6]</sup>

With these considerations, overseas guidelines have recommended acceptable rates of bowel preparation adequacy, ranging from 85% (American Society for Gastrointestinal Endoscopy<sup>[7]</sup>) to 90% (European Society for Gastroenterology<sup>[8]</sup>).

The ideal bowel preparation should be safe, effective and well tolerated but a single preparation type and dosing regimen will not suit all patients. Safe bowel preparation requires an understanding of preparation types and their potential adverse outcomes. Preparation timing is important for efficacy and dietary preparation has implications for satisfaction and tolerance. Understanding the risk factors for poor preparation helps individualise regimens for optimal outcome.

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## 4.2.2 Overview of evidence (non-systematic literature review)

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No systematic reviews were undertaken for this topic. Practice points were based on selected evidence and guidelines (see Guideline development process).

### 4.2.2.1 Available bowel preparation types

Most bowel preparations are based on an osmotic mechanism of action and work by retaining or drawing fluid into the bowel lumen (Table 1). Some also contain a stimulant. Polyethylene glycol (PEG)-based preparations generally have a good safety profile and should be considered the first choice for patients of older age or with organ dysfunction including renal failure, heart failure or cirrhosis.

Combination preparations with sodium picosulfate, magnesium oxide and citric acid both contain osmotic and stimulant effects. They are lower in volume than PEG-based preparations, which may enhance compliance but may also increase the risk of dehydration if adequate additional fluids are not consumed. They should be used with caution in the elderly, those with renal impairment and those at risk of dehydration.

Sodium phosphate is a potent hyperosmotic preparation. It has been associated with cases of acute kidney injury and phosphate nephropathy causing irreversible renal failure. This preparation should be avoided in those of older age, those with kidney, heart or liver disease, inflammatory bowel disease (IBD), and those on medications that alter renal blood flow/electrolytes.<sup>[9][10]</sup>

There is limited evidence from head to head efficacy studies on which to recommend one specific type of bowel preparation over another. However, lower volume PEG-based preparations appear to be as effective as high volume PEG-based preparations.<sup>[11][12]</sup>

**Table 1. Main types of bowel preparation currently used in Australia**

Main ingredient	Action	Main types	Volume (without clear fluids)	Pro	Con
<b>PEG</b>	Osmotic	PEG PEG + ascorbate components PEG + ascorbate components	1000mL x 3 1000mL x 2*# 500mL x 2*#	Safe and effective Modest fluid /electrolyte shift when consumed as per recommendations First choice for patients with: renal failure, heart failure, cirrhosis, IBD, older age	Larger volumes may be less well tolerated
<b>Sodium picosulfate, magnesium oxide, citric acid</b>	Stimulant and osmotic	Sodium picosulfate + magnesium oxide and citric acid	250mL x 2*‡	Lower volume	Generally well tolerated Beware in renal impairment (transient hypermagnesemia) Beware dehydration (consider PEG-based preparation in elderly /comorbidities)
					Risk of dehydration and acute kidney injury Risk of phosphate nephropathy and irreversible renal failure

<b>Sodium phosphate</b>	Hyperosmotic	Sodium phosphate liquid <sup>§</sup>  Sodium phosphate tablets <sup>§</sup>	45mL x 2 32 tablets	Low volume or tablet form	Avoid in: <ul style="list-style-type: none"> <li>■ elderly</li> <li>■ heart failure</li> <li>■ renal impairment</li> <li>■ cirrhosis</li> <li>■ IBD</li> <li>■ patients on medications that alter renal blood flow /electrolytes</li> </ul>
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Abbreviations: PEG: Polyethylene glycol; IBD: inflammatory bowel disease; \*recommended additional minimum of 500mL clear fluids per dose; <sup>§</sup>750mL minimum additional clear fluid recommended per dose; #recommend avoiding in G6PG deficiency; † recommend avoiding in phenylketonuria.

**Note:** This table does not list all commercially available bowel preparations. Some companies create combination kits containing more than one form of bowel preparation.

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#### 4.2.2.2 Preparation timing

The timing of bowel preparation is one of the most important factors associated with optimal bowel preparation. Split-dose bowel preparation is associated with a significantly increased chance of successful bowel preparation when compared with traditional ‘day-prior’ preparation. In a meta-analysis, success with spit-dose preparation compared with day-prior preparation was 85% versus 63% (absolute difference 22%; confidence interval [CI] 16–27%).<sup>[13]</sup>

The runway time or timing of the last dose prior to the procedure is also important.<sup>[13][14]</sup> In the meta-analysis by Bucci et al, there was a significantly greater chance of preparation success when the last dose was taken ≤3 hours or 4–5 hours prior to the colonoscopy as compared with >5 hours prior to the colonoscopy.<sup>[13]</sup> Taking bowel preparation within 3–5 hours of the procedure is also likely to be safe from an anaesthetic viewpoint. A meta-analysis of six separate randomised control trials found no significant difference in the gastric residual volume of patients having a split-dosed procedure as compared to a day-prior preparation or no preparation.<sup>[15]</sup>



'Same-day' bowel preparation is when the entire preparation is taken on the same day as the colonoscopy. In a meta-analysis, same-day preparation had a similar efficacy and patient tolerance to a split-dose preparation.<sup>[16]</sup>

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#### 4.2.2.3 Dietary preparation

Several low residue diets are as effective as a clear fluid restriction prior to colonoscopy with significantly increased patient satisfaction and tolerability.<sup>[17][18][19]</sup> Low residue diets such as the 'white diet' (Table 2) can be used on the day(s) prior to colonoscopy in a split-dose preparation regimen without impairing the quality of the preparation, while achieving significant improvements in patient satisfaction and tolerability.<sup>[17]</sup> This is also likely to be effective with same-day preparation.

**Table 2. Food and fluids permitted in the white diet and those not allowed**

Foods & fluids permitted	Milk (regular, low fat, skim), water, lemonade, soda or mineral water, clear (not coloured) sports drinks  White-coloured yoghurt (no added fruit or insulin), mayonnaise, cream, sour cream, butter and margarine, oil for cooking  Regular white bread/toast, popped rice cereal (e.g. Rice Bubbles), eggs  White rice, regular pasta, potatoes (peeled), rice noodles  Plain rice crackers, white flour, sugar  Chicken breast (no skin), white fish fillet (no skin)  Plain cream cheese, cheddar cheese, ricotta, fetta, cottage, parmesan or mozzarella cheese, white sauce, white chocolate, vanilla ice cream, lemonade ice-block (e.g. 'Icy-pole'), clear jelly, custard, 'milk bottles' (white confectionery)
Foods not allowed	Anything not listed above  Other white-coloured foods such as pears, parsnip, cauliflower, onion, high fibre white bread, tofu, coconut, porridge, banana, mushrooms, semolina, couscous, popcorn
Source: Butt et al (2016).	

#### 4.2.2.4 Factors associated with poor preparation

Factors associated with an increased risk of poor bowel preparation include reduced health literacy, older age, constipation, chronic diseases, diabetes, cirrhosis, neurological conditions such as stroke and dementia, immobility, spinal injury, prior gastrointestinal surgery, opioids and antidepressant medication.<sup>[20][21][22]</sup>

Providing larger volumes of bowel preparation in a split dose should be considered for patients at significant risk of poor preparation or those with a history of inadequate bowel preparation. In a study of patients with a prior poor bowel preparation, success rate was higher among those randomised to 4L split-dosed PEG than those randomised to 2L split-dosed PEG: 81.1% versus 67.4% odds ratio [OR] 2.07; CI: 1.163–3.689).<sup>[23]</sup> Validated scoring systems such as the one by Gimeno-Garcia et al<sup>[22]</sup> may help in identifying those at risk of poor preparation, but a corresponding management algorithm is awaited.

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#### 4.2.2.5 Documentation of bowel preparation

The quality of bowel preparation should be documented on every colonoscopy report using a validated score, ideally after cleaning has been performed. The Boston Bowel Preparation Scale (BPPS) is the most validated score and is recommended.<sup>[24]</sup> The Ottawa scale<sup>[25]</sup> requires documentation of stool volume so may be less clinically applicable, and Harefield cleansing scale is detailed and thus probably better suited to research.<sup>[26]</sup> The Aronchick scale<sup>[27]</sup> is an insertion scale with simple categories, which is often used in electronic endoscopy reporting systems. The following scores indicate successful bowel preparation:

BPPS	≥6
Ottawa scale	≤7
Harefield cleansing scale	Total score A or B
Aronchick scale	Excellent, good, or fair

Whichever scale is used, inadequate preparation should be clearly documented and those with inadequate preparation should be offered repeat colonoscopy within 12 months.<sup>[7]</sup>

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#### Practice point

High-quality bowel preparation is a crucial pre-requisite for successful colonoscopy. Optimal preparation is achieved with split-dose or same-day preparation timing.

**Practice point**

PEG-based bowel preparations are safer for those with co-morbidities and the elderly.

**Practice point**

A low-residue diet can be used on the days prior to colonoscopy with appropriate preparation timing.

**Practice point**

Factors associated with poor preparation should be assessed and patients at high risk of poor preparation should be offered additional preparation volume and split-dose timing.

**Practice point**

Preparation quality should be documented on the colonoscopy report using a validated preparation scale.

**Practice point**

Where the preparation is inadequate, repeat colonoscopy should normally be offered within 12 months.

**Practice point**

Successful bowel preparation should be achieved in  $\geq 90\%$  of all colonoscopies.

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## 4.3 Advances in technique

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- 3 Practice Points
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### 4.3.1 Background

In addition to technological improvements in colonoscope design and adjunctive technologies, various techniques have been evaluated to improve the performance of colonoscopy for the detection of colorectal neoplasia and reduce the operator dependence of colonoscopy. These techniques are intended to assist in exposing hidden mucosa, and complement those technologies that can assist in highlighting and improving the recognition of mucosal lesions.

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### 4.3.2 Overview of evidence (non-systematic literature review)

No systematic reviews were undertaken for this topic. Practice points were based on selected evidence and guidelines (see Guideline development process).

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### 4.3.2.1 Instrument insertion

#### 4.3.2.1.1 Water exchange/immersion

Water exchange is the technique of filling the colon with clean water during instrument insertion, while simultaneously removing dirty water. Several studies have shown that the improvement in quality of bowel preparation achieved through this technique is associated with improved adenoma detection rates. An infusion volume of at least 500mL appears necessary.<sup>[1]</sup> Water exchange does, however, increase procedure time by prolonging the insertion time to caecum.<sup>[1]</sup>

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### 4.3.2.2 Instrument withdrawal

#### 4.3.2.2.1 Mucosal inspection technique

Colonoscopy is a highly operator-dependent procedure. The magnitude of the difference in adenoma detection between high- and low-detector endoscopists in the same practice context far exceeds the improvements seen from technological adjuncts or advances in colonoscopy.

Colonoscopy fundamentally requires deliberate and systematic interrogation of the colorectal mucosa. The technique for mucosal inspection that has been shown to be associated with improved detection involves:

- systematic deflection of the instrument tip during withdrawal to scrutinise the proximal surfaces of colonic folds, flexures and valves
- intensive washing and suctioning of residual debris and pools and fluid
- adequate luminal distension.<sup>[2]</sup>

Intraprocedural cleansing of the colon is essential to achieve high rates of adequate preparation, with reported mean washing times of over 4 minutes.<sup>[3]</sup>

Both external review of technique (by videorecording<sup>[4]</sup>) or audit of detection performance<sup>[5]</sup> are known to motivate improvements in detection. Training in mucosal inspection behaviours and in lesion recognition improves adenoma detection.<sup>[6][7][8]</sup>

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#### **4.3.2.2.2 Withdrawal time**

The importance of withdrawal time for high quality colonoscopy has been over-emphasised after the initial landmark study demonstrating an association between longer withdrawal time and adenoma detection rates.<sup>[9]</sup> While effective inspection of the colorectal mucosa takes time merely increasing the time taken is not the required behaviour. Rather, effective detection requires meticulous mucosal exposure technique together with recognition of neoplastic lesions. Institutional policies of forced withdrawal time targets have not been successful,<sup>[10]</sup> unless combined with education and timed segmental inspection targets.<sup>[11]</sup> Withdrawal time remains only a surrogate indicator of those mucosal inspection behaviours required for neoplasia detection.

#### **4.3.2.2.3 Proximal colon examination**

Observational studies from the USA and Germany have consistently shown lower levels of protection against cancer in the right colon/proximal colon (ie proximal to the splenic flexure).<sup>[12][13][14][15]</sup> Studies have examined the benefit of instrument retroflexion in the proximal colon, performed after an initial inspection from the caecum to the hepatic flexure in the forward view. Retroflexion is possible in the right colon in over 90% of patients,<sup>[16]</sup> although randomised controlled trials have shown that a second forward-view examination of the proximal colon is as effective for additional polyp detection as a second examination in retroflexion.<sup>[17][18]</sup> The yield of a second right colon examination is higher when polyps have been found on the forward view, and in patients who are older, male or have bleeding indications.<sup>[16]</sup>

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#### **4.3.2.3 Polyp size estimation**

Once detected, polyps should be assessed prior to resection. Assessment should include documentation of the location, size and morphology of the lesion. Accurate measurement of polyp size is important for the determination of appropriate surveillance intervals.

Endoscopic measurement of polyp size is limited by human and technology bias. Endoscopists are known to be influenced by terminal digit preference for 'pleasing' numbers.<sup>[ref]</sup> The fish-eye lens of colonoscopes causes distortion in which objects in the centre of the display appear magnified, while objects at the periphery appear smaller and warped.<sup>[19][20]</sup> Furthermore, the two-dimensional display creates a lack of depth awareness.

Accuracy of polyp measurement can be improved by the use of reference cues, such as comparison of the lesion with a device of known dimensions (e.g. the tip of a snare catheter or an open snare wire).<sup>[20]</sup> To mitigate against technology bias and minimise visual size illusions, the lesion should be touching the measurement device and kept in the centre of the display.

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#### 4.3.2.4 Routine polypectomy

The protective effect of colonoscopy on colorectal cancer incidence derives from the detection and removal of precancerous lesions.<sup>[21]</sup> Polypectomy is therefore central to the practice of colonoscopy. However, like other aspects of colonoscopy practice, is highly operator dependent. Up to 27% of interval cancers may be due to incomplete endoscopic resection,<sup>[21]</sup> and rates of incomplete hot snare resection of nonpedunculated neoplastic polyps vary significantly between endoscopists within a reported range of 6.5% to 22.7%.<sup>[22]</sup>

Cold snare polypectomy has become the standard of care for diminutive (1–5mm) colorectal polyps and is the recommended technique in international guidelines for sessile polyps  $\leq 9\text{mm}$ .<sup>[23]</sup> Cold snaring is more effective and efficient than cold forceps resection and is virtually without risk. Cold biopsy forceps should be avoided because of high rates of incomplete resection.<sup>[23]</sup>

The major benefit of cold snare techniques is safety, by avoiding the risk of thermal mural injury that is associated with post-polypectomy syndrome, perforation and delayed bleeding. Hot biopsy forceps are associated with unacceptably high rates of deep thermal injury but also incomplete resection, and should not be used.<sup>[23]</sup> Because immediate bleeding can be visualised and treated, cold techniques can even be used safely in patients taking antiplatelet agents and anticoagulants.<sup>[24]</sup>

Large ( $\geq 20\text{mm}$ ) sessile and laterally-spreading polyps can increasingly be removed endoscopically, rather than with surgical resection. Patients with these lesions should be referred to centres with expertise in advanced colonoscopic resection techniques.<sup>[23]</sup> [Back to top](#)

#### 4.3.3 Practice Points

##### Practice point

Fundamental colonoscopic inspection technique should ensure systematic exposure of the proximal sides of folds and flexures, intensive intraprocedural cleansing and adequate distension of the colon.

##### Practice point

Colonoscopists should undergo training in the fundamentals of mucosal exposure and inspection techniques, and in the endoscopic appearance of adenomas and serrated lesions to increase detection rates and improve clinical outcomes of colonoscopy.

#### Practice point

Water exchange should be considered to improve adenoma detection through an effect on mucosal cleansing and higher rates of adequate bowel preparation.

#### Practice point

A second examination of the proximal colon in either the forward view or in retroflexion is recommended to improve lesion detection, particularly in patients with an expected higher prevalence of neoplasia.

#### Practice point

Sessile polyps under 10mm in size should be removed using cold snare polypectomy. This is preferred over hot snare, which is unnecessary in most situations. Hot biopsy forceps should not be used because they are associated with unacceptably high rates of incomplete resection and deep mural injury.

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## 4.4 Technological advances

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### 4.4.1 Background

Since these guidelines were last updated in 2011, there has been ongoing research and development in endoscope design, aimed at improved detection of colonic neoplasia, reducing miss rates, and enhancing lesion characterisation for diagnosis.<sup>[1][2]</sup> These new features include technologies aimed at increased mucosal views through wider angle visualisation and ultra-magnification endoscopic systems allowing *in vivo* histological assessment. Many of these technologies are now commercially available. However, there is still a need for

further studies, including cost-benefit analysis, before they can be adopted as mainstream practice. Established technologies include high-definition colonoscopy, wide-angle colonoscopy and electronic chromoendoscopy, such as narrow band imaging (NBI; Olympus), flexible spectral imaging colour enhancement such as Fujinon intelligent chromoendoscopy (FICE) and i-SCAN (Pentax). These technologies are now incorporated into all of the latest generation colonoscopes, with high-definition white-light endoscopy (WLE) now the standard of care in routine colonoscopy.

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## 4.4.2 Overview of evidence (non-systematic literature review)

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No systematic reviews were undertaken for this topic. Practice points were based on selected evidence and guidelines (see Guideline development process).

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### 4.4.2.1 Extra-Wide-Angle-View colonoscopy

Wide angle colonoscopy with vision of 170° has become standard in the latest generation colonoscopes. Despite the aim of improving the detection of lesions hidden behind colonic folds, all studies in the available literature, with one exception<sup>[3]</sup>, suggest that wide angle colonoscopes do not significantly reduce polyp miss rates, which have been estimated to be as high as 31% in systematic reviews.<sup>[2][4][5][6]</sup>

Given these high rates of missed lesions, there has been an emergence of new technologies aimed at reducing miss rates through wider mucosal visualisation up to 330°. These include Third Eye Retroscope and Third Eye Panoramic (Avantis Medical Systems). Fuse Full Spectrum Endoscopy colonoscopy platform (Endo-Choice Inc); and the Extra-Wide-Angle-View colonoscope (Olympus).<sup>[2]</sup> While many of these technologies have shown promise through increased detection rates over standard forward viewing colonoscopy, none have shown an absolute superiority to standard colonoscopy and therefore cannot be recommended as standard of care. Continued emphasis has been placed on excellent bowel preparation, completed procedures to caecum and methodical, attentive and slow withdrawal as the keys to polyp detection.<sup>[7]</sup>

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### 4.4.2.2 Ultra-magnifying technologies

In recent years there has been increasing interest in a 'predict-resect-and-discard' policy for management of diminutive polyps.<sup>[8][9][10]</sup> Ultra-magnifying technologies such as confocal light endomicroscopy and endocytoscopy have advanced considerably and are now commercially available. These emerging technologies may offer most in correct histological classification of polyps prior to resection and discard or in surveillance in patients with inflammatory bowel disease (IBD). However, due to cost, time and the expertise required, they are still not part of mainstream practice<sup>[11]</sup> (see also Recommended techniques for surveillance in IBD patients).

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#### 4.4.2.3 Electronic chromoendoscopy

In the era of push-button technologies, electronic chromoendoscopy refers to imaging technologies that result in detailed contrast enhancement of blood vessels, which aids in lesion detection and characterisation.<sup>[12]</sup> There is now a wide range of available technologies including NBI, FICE and i-scan.<sup>[13][14]</sup>

Narrow-band imaging technology is the most commonly used and researched optical digital method of performing image-enhanced endoscopy. First-generation NBI had poor brightness and contrast enhancement, which limited its usefulness. The second-generation NBI, released in 2012, was able to deliver more than one-and-a-half times higher brightness, and twice the viewable distance in the lumen, than the first-generation NBI.<sup>[15]</sup>

The utility of electronic chromoendoscopy over WLE has been evaluated in four broad areas:

- adenoma detection in individuals at average risk for colorectal cancer
- adenoma detection in hereditary syndromes
- dysplasia detection in IBD
- lesion characterisation.

With respect to adenoma detection in average risk individuals, most studies have compared NBI with WLE. Numerous studies, including multiple meta-analyses, have not demonstrated an advantage for NBI over WLE.<sup>[16]</sup><sup>[17][18][19]</sup> Given these poor results, additional studies are required to determine the final application of these modalities in routine endoscopy practice.

In contrast to average-risk populations, in high-risk settings electronic chromoendoscopy has been demonstrated to result in improved detection rates over high-definition WLE.<sup>[20][21]</sup> The European Society for Gastroenterology currently endorses the routine use of high-definition panchromoendoscopy in patients with known or suspected Lynch syndrome or serrated polyposis syndrome – acknowledging, however, that overall evidence remains low.<sup>[22]</sup>

Narrow-band imaging is the only modality studied in dysplasia detection in IBD and has not been demonstrated to improve detection rates over WLE<sup>[23]</sup> (see also Recommended techniques for surveillance in IBD patients).

Lastly, lesion characterisation remains an area of promise for electronic chromoendoscopy technologies, with several studies showing high accuracy with negative predictive value >90%.<sup>[24][25][26][27]</sup> However, these results have not been replicated outside of expert centres.

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#### Practice point

High-definition colonoscopes should be used routinely, as the mainstay of colonoscopy is a careful white-light examination of the well prepared colon.

#### Practice point

Electronic chromoendoscopy should be used for lesion characterisation, but has limited value in lesion detection.

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## 4.5 Adjunct technologies

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### 4.5.1 Colonoscopy

### 4.5.2 Overview of evidence (non-systematic literature review)

No systematic reviews were undertaken for this topic. Practice points were based on selected evidence and guidelines (see Guideline development process).

#### 4.5.2.1 'Add-on' devices

Inspection on withdrawal could contribute to polyps being missed, as visualisation of the proximal surface of haustral folds may be limited. Several back-to-back colonoscopy trials have reported adenoma miss rates of up to 25%.<sup>[1][2]</sup> Sessile serrated adenomas or non-polypoid lesions have limited contrast in relation to the surrounding mucosa and can be overlooked.<sup>[3]</sup> This may contribute to the relatively high risk of interval cancers in the proximal colon.<sup>[3][4]</sup> As a result, 'add-on' technologies have been developed to improve visualisation, especially in areas behind haustral folds. These include:

- Transparent Cap (TC)
- EndoRing
- Endocuff
- G-EYE endoscope
- Third Eye Panoramic device
- Third Eye Retroscope.

The TC is the most studied add-on device. The cap is attached to the tip of a colonoscope prior to the examination. Although adding to the cost of colonoscopy, it has been proposed as a method for shortening withdrawal time in addition to improving adenoma detection rates (ADR).<sup>[5]</sup> When used by more experienced colonoscopists, the TC does not improve either the caecal intubation rate or the ADR, but does shorten the caecal intubation time. It may have utility for difficult cases, especially when initial caecal intubation fails.<sup>[6]</sup> A meta-analysis of 16 studies examining the role of the TC revealed a marginal benefit for polyp detection rate (relative risk 1.08) and no difference in ADR.<sup>[7]</sup> However, the TC has been shown to improve detection of serrated lesions (12.8% vs 6.6%).<sup>[8]</sup>

Brand et al recently published the results of a pooled analysis of three technologies (the Third Eye Retroscope, the Full Spectrum Endoscope, and the EndoRing), concluding that these adjunct technologies may enhance detection of small (<10mm) adenomas.<sup>[9]</sup>

In a multicentre back-to-back study involving 116 patients comparing colonoscopy with and without the EndoRing reported, adenoma miss rates of 10% versus 48% and polyp miss rates of 9% versus 53%.<sup>[10]</sup>

The Endocuff is a similar device, which appears to increase the detection of diminutive polyps and improve ADR.<sup>[11]</sup> However, a larger randomised control trial involving 1063 patients showed no change in the ADR.<sup>[12]</sup>

Shirin et al recently conducted a study over >1000 patients using a balloon based device, the G-EYE colonoscope.<sup>[13]</sup> Significantly more adenomas were detected when this technology was used compared with conventional colonoscopy.

With all of these devices the additional cost is a factor that must be considered before incorporation into practice, considering the modest gains reported.

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#### 4.5.2.2 Chromoendoscopy

Chromoendoscopy (dye spray) has been introduced to enhance the detection of polyps, particularly diminutive flat lesions that may be otherwise difficult to detect.<sup>[14]</sup> When combined with high magnification, chromoendoscopy was found to be highly efficient in differentiating adenomatous from non-adenomatous polyps.<sup>[15][16][17]</sup> It has also been strongly advocated in patients undergoing surveillance for IBD inflammatory bowel disease (IBD).<sup>[18][19][20]</sup> However, in a more recent non inferiority trial, high-definition white-light endoscopy was as effective as chromoendoscopy<sup>[21]</sup> (see also Colonoscopic surveillance and management of dysplasia in inflammatory bowel disease (IBD)).

Based on results from their studies, Lapalus<sup>[22]</sup> and Le Rhun<sup>[23]</sup> could not recommend the systematic use of chromoendoscopy for overall adenoma detection, although there was improvement seen in detecting small adenomas in the proximal colon. Other studies reported that chromoendoscopy detected more polyps compared with standard colonoscopy,<sup>[24][25]</sup> particularly in patients with Lynch syndrome.<sup>[26][27]</sup>

Despite being advocated for close to two decades, chromoendoscopy struggles to be accepted in mainstream clinical practice and as a result appears to have been superseded by electronic image enhanced technologies for characterisation of colorectal polyps.

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#### 4.5.2.3 Carbon dioxide (CO<sub>2</sub>) insufflation

A recent meta-analysis has confirmed that, when compared to air insufflation, CO<sub>2</sub> insufflation clearly reduces post-colonoscopy pain and distension and allows more rapid caecal intubation, but does not improve completion rates or adenoma detection.<sup>[28]</sup> It appears to be safe even in patients with airway disease.<sup>[29]</sup>

Barriers to implementation include the lack of incorporation of CO<sub>2</sub> insufflation into standard endoscopy systems, the resulting cost of retrofitting CO<sub>2</sub> insufflation, and the ongoing cost of the gas itself, estimated at US\$3 per procedure.<sup>[30]</sup>

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#### Practice point

Chromoendoscopy should be considered for routine colonoscopy to improve the detection and characterisation of colorectal polyps.

#### Practice point

Chromoendoscopy should be considered for patients undergoing surveillance for inflammatory bowel disease, although a recent study has shown equivalence with high resolution white-light endoscopy.

#### Practice point

CO<sub>2</sub> insufflation should be used routinely to improve patient tolerability of colonoscopy.

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## 4.6 Quality of colonoscopy

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### 4.6.1 Background

High-quality colonoscopy is dependent on patient-related factors, operator-related factors, system-related factors and equipment.<sup>[1]</sup>

Operator factors, which are arguably the most significant, include appropriate training and experience of the colonoscopist, proper risk assessment of the patient, complete examination to the caecum with adequate mucosal visualisation and bowel preparation, the ability to detect and remove polyps safely, adequate documentation, timely and appropriate management of adverse events, follow-up of histopathology, and appropriate screening and surveillance intervals based on published guidelines.<sup>[2]</sup> In Australia the Conjoint Committee for Recognition of Training in Gastrointestinal Endoscopy provides a framework to certify training of endoscopists. Recently recertification of colonoscopists has been introduced by the Gastroenterological Society of Australia (GESA). Requirements for recertification every 3 years include at least 150 logged procedures over the 3 years with a 95% completion rate, at least 25% adenoma detection rate (ADR) in eligible patients (intact colons, over age 50 years and without a diagnosis of inflammatory bowel disease) and completion of a cognitive review. The aim of recertification is to maintain colonoscopy expertise, continue to develop skills and to increase the safety standards and quality of care delivered to patients.

Quality assurance key performance indicators for the colonoscopy procedure include consent, indication, preparation, caecal intubation rates, polyp detection and removal, withdrawal time and complication rates.<sup>[3]</sup> Adequate documentation, through a comprehensive computer-generated report incorporating relevant images, is also critical.<sup>[4]</sup>

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## 4.6.2 Overview of evidence (non-systematic literature review)

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No systematic reviews were undertaken for this topic. Practice points were based on selected evidence and guidelines (see Guideline development process).

### 4.6.2.1 Consent

Patients must provide informed consent to undergo any endoscopic procedure. The requirements for an adequate bowel preparation form part of the consent, along with a full explanation of the procedure, including any risks and potential complications, the indication and any alternative investigation options. Patients must be given the opportunity to ask questions and receive advice.<sup>[5]</sup>

Clinicians should also follow the Clinical Care Standards that apply to the preparation of patients for procedures, including informed consent (see Australian Commission on Safety and Quality in Health Care Colonoscopy Clinical Care Standards).

### 4.6.2.2 Indication

The National Bowel Cancer Screening Program Quality Working Group<sup>[5]</sup> recommends that, prior to colonoscopy, the colonoscopist should ensure that the indication for performing the colonoscopy is appropriate and documented. The indications for asymptomatic patients should conform to the national clinical practice guidelines<sup>[6]</sup> for the prevention, early detection and management of colorectal cancer (CRC) and include a significant family history of CRC, personal history of CRC or polyps, colitis surveillance or a positive faecal occult blood test. The use of colonoscopy for screening other asymptomatic patients is not supported by the Australian Government, unlike in other countries including the USA. Symptomatic patients should have relevant symptoms documented on the colonoscopy report.

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### 4.6.2.3 Preparation

Effective bowel preparation is obligatory for high quality colonoscopy. See Bowel preparation.

Several societies suggest that poor preparation should be present in less than 10–15% of studies.<sup>[7][8]</sup> Several validated preparation scores exist but poor preparation is probably best defined clinically by the requirement to repeat the examination (i.e. 'adequate' versus 'inadequate'), and should routinely be documented in the colonoscopy report.

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#### 4.6.2.4 Caecal intubation rate

Caecal intubation is defined as deep intubation into the caecum with the tip of the colonoscope being able to touch the appendiceal orifice.<sup>[7]</sup> Caecal intubation demonstrates a complete examination of the colon, and is fundamental for colorectal cancer screening.<sup>[7]</sup> The intubation of the caecum should ideally be documented by an image of the appendiceal orifice and/or terminal ileum, if intubated.<sup>[7]</sup>

Lower caecal intubation rates correlate with higher rates of interval cancer and lower case volume, with experienced operators achieving 95% or higher.<sup>[9]</sup> Performance indicators set by the National Bowel Cancer Screening Program Quality Working Group<sup>[5]</sup> include caecal intubation rates of 90% for general patients and 95% for patients undergoing screening colonoscopy (unadjusted rates including studies with poor preparation and obstructing cancer). Other societies suggest appropriate caecal intubation rates of between 90% and 95%.<sup>[10]</sup> The GESA recertification guideline suggests a caecal intubation rate of at least 95%.

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#### 4.6.2.5 Withdrawal time

Longer withdrawal times are associated with increased adenoma detection.<sup>[11][12]</sup> The National Bowel Cancer Screening Program Quality Working Group<sup>[5]</sup> recommends that the mean colonoscopy withdrawal time from the caecum for each proceduralist should be 6 minutes or greater for procedures where no polypectomy is performed. This recommendation is similar to those in European Society for Gastroenterology (ESGE) guideline<sup>[7]</sup> and American Society for Gastrointestinal Endoscopy/American College of Gastroenterology<sup>[13]</sup> guidelines. However, as noted above, withdrawal time is likely to be a surrogate marker for ADR and, as such, should not be relied upon as an independent marker of quality.<sup>[14]</sup>

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#### 4.6.2.6 Polyp detection, removal and retrieval

The UK NHS Bowel Cancer Screening Programme defines ADR as the number of colonoscopies at which one or more histologically confirmed adenomas is removed, divided by the total number of colonoscopies performed.<sup>[7]</sup> It is the best validated key performance indicator for colonoscopy, with the total number of adenomas per colonoscopy a less well studied alternative.<sup>[15]</sup> Studies of ADR variability between endoscopists report a three- to six-fold difference in ADR.<sup>[11][16][17][18]</sup> Adenoma detection rate does not address detection of serrated polyps, which do not count toward ADR. Similarly, the detection of serrated polyps also differs between endoscopists.<sup>[19][20]</sup>

Adenoma detection rate correlates inversely with the incidence of interval colorectal cancer. Kaminski et al<sup>[21]</sup> demonstrated a significant increase in interval cancers in individual colonoscopists with an ADR below 20%. Corley et al demonstrated increasing benefit from higher ADRs.<sup>[22]</sup> The ESGE guidelines recognise that there is a difference between populations in whom screening colonoscopy is performed (e.g. the USA, where suggested

ADRs are 15% for women and 25% for men) and for colonoscopy populations enriched with patients with positive faecal occult blood testing, in whom the ADR should be nearer to 35%.<sup>[7]</sup> The GESA recertification rate is for 25% in all patients over the age of 50 years, excluding those with IBD. Missed serrated polyps in the proximal colon do confer an increased risk of CRC and serrated detection targets have been suggested for screening colonoscopy (e.g. 5%). Australian colonoscopy cohorts have now regularly demonstrated serrated polyp detection rates above 10%.<sup>[23]</sup> European guidelines<sup>[7]</sup> recommend that a minimum of 90% of resected polyps should be retrieved.

Measurement of ADR often requires manual calculation and is time consuming to generate in endoscopy units without electronic linking between endoscopy reporting systems and histopathology reports. To overcome difficulties measuring ADR, a recent suggestion of using polypectomy rates as a surrogate for ADR has been studied and validated.<sup>[24][25]</sup> However, a study by Boroff et al warns that while the correlation with ADR is reliable in the right colon, it is not in the left colon.<sup>[26]</sup> Therefore, while measurement of polypectomy rate cannot be recommended as an alternative to measurement of ADR, for endoscopy units that have difficulty in measuring ADR, measurement of polypectomy rate is a reasonable first step.

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#### 4.6.2.7 Complications

There is some evidence to suggest that an increased volume of colonoscopy performed by individual colonoscopists results in fewer complications.<sup>[27][28][29]</sup> As a result, the UK NHS Bowel Screening Program suggests a lifetime experience of 1000 colonoscopies and an annual number of 150 colonoscopies before becoming certified to perform bowel cancer screening program colonoscopy.<sup>[30]</sup>

The traditional complications of colonoscopy include pain, aspiration, perforation and bleeding (usually post polypectomy). However, this risk is offset by the fact that a missed cancer or advanced polyp is a bad outcome, which is mitigated by a high ADR. Perforation in screening colonoscopy approximates 1/1000<sup>[31]</sup> and could be used as a useful indicator of colonoscopy safety in large colonoscopy units or in national screening programs. This increases to around 1/500 post polypectomy.<sup>[31]</sup> The rates are higher when resecting larger polyps.<sup>[32]</sup> For screening populations enriched with those with positive faecal blood tests, the likelihood of adenomas and advanced adenomas is increased<sup>[7]</sup> and the overall colonoscopy complication rate is likely to be increased unless the quality of colonoscopy consistently high across colonoscopy services.

The British Joint Advisory Committee and the Australian Quality Working Group guidelines state colonoscopy perforation rates should be <1:1000,<sup>[5][33]</sup> while Rex et al<sup>[13]</sup> suggest perforation rates >1 in 500 for all colonoscopies or 1 in 1000 for screening colonoscopies require evaluation of practice.

Post polypectomy bleeding is defined as rectal blood loss that requires a blood transfusion and occurs up to 2 weeks post polypectomy.<sup>[7]</sup> Bleeding risk is affected by many factors including the definition of bleeding, use of antiplatelet and anti-thrombotic medication, lesion characteristics, colonoscopist volume and different diathermy settings.<sup>[32][34][35][36]</sup> Due to this wide range of variables that impact on post polypectomy bleeding, there is a large range of reported incidence in the literature, with rates ranging from 1:10 to 1:300 colonoscopies.<sup>[37][38]</sup>

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#### 4.6.2.8 Documentation

A clear and comprehensive report is an essential part of quality endoscopy.<sup>[4]</sup> The key elements of a colonoscopy report include:<sup>[39]</sup>

- patient demographics and history
- assessment of patient risk and comorbidity
- indication(s)
- a technical description of the procedure (including bowel preparation quality and depth of insertion)
- findings (abnormalities, including site, size)
- interventions
- unplanned events and complications
- assessment
- follow-up plan (including surveillance recommendations)
- pathology samples sent.

Computer-generated reports enhance compliance, enable audit, and facilitate photo-documentation, particularly of landmarks of completion (e.g. ileal mucosa) and any pathology.<sup>[40]</sup> The report should be given to the patient, and routinely reach the relevant clinicians, including referring doctors and reporting pathologists.

However, compliance with quality colonoscopy reporting is poor, impairing communication, follow-up, audit and even remuneration.<sup>[41][42]</sup>

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#### 4.6.3 Practice Points

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##### Practice point

Accurate and sufficient information about the procedure (and optimally consent) should be provided to patients prior to the commencement of bowel preparation for colonoscopy.

**Practice point**

Colonoscopy should be performed only for accepted indications, which should be clearly documented.

**Practice point**

Less than 10% of patients should require a repeat procedure due to poor bowel preparation, this should be offered within 12 months.

**Practice point**

Unadjusted rates for caecal intubation should be  $\geq 90\%$ .

**Practice point**

Photo-documentation, that terminal ileum or the base of the caecum (appendix orifice and ileocaecal valve) has been reached, should be performed to confirm completeness of the examination.

**Practice point**

Withdrawal times of  $>6$  minutes for examinations without polypectomy are a surrogate marker for adenoma detection rates, but cannot be relied on as an independent quality indicator.

**Practice point**

Individual proceduralists should routinely document and maintain their adenoma detection rate at >25% in patients over the age of 50-years and without a diagnosis of inflammatory bowel disease.

**Practice point**

Serrated polyp detection rates are likely to be an equally valid marker of quality as adenoma detection rate, and increasing evidence suggests that maintaining a rate of >10% in patients over age 50 years without a diagnosis of inflammatory bowel disease may prove to be an additional, useful quality indicator in the future.

**Practice point**

Perforation rates post colonoscopy should be <1/1000. This is more relevant for population programs and large endoscopy units rather than individual colonoscopists.

**Practice point**

All colonoscopists should have their training certified by the Conjoint Committee for the Recognition of Training in Gastrointestinal Endoscopy and undergo regular recertification through an endorsed program.

**Practice point**

Comprehensive computer-generated colonoscopy reports with embedded photo-documentation should be generated at the time of the procedure, and provided to patients and relevant clinicians.

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## 4.7 CT colonography

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### 4.7.1 Background

Computed tomography colonography (CTC) is a minimally invasive method of examining the colon and rectum. It requires bowel preparation and the oral administration of faecal tagging agents prior to the insertion of a rectal tube, which is used to inflate the colon with carbon dioxide. A low-dose CT scan is then performed in two positions, comprising a supine scan and then either a prone or lateral decubitus study. Advanced post-processing techniques and dedicated imaging software enable the colon to be examined in both a multi-planar two-dimensional and a three-dimensional 'virtual colonoscopy' mode which simulates traditional endoscopic views. The procedure is well tolerated, does not require sedation and is extremely safe, with a perforation rate of 0.04%, the vast majority of which are asymptomatic and managed conservatively.<sup>[1]</sup> CT colonography can be performed immediately following a simple polypectomy but should be delayed in patients who have undergone complex endoscopic intervention as this increases the risk of perforation. Likewise, CTC should be avoided in patients with active colitis or obstructing strictures.

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### 4.7.2 Overview of evidence (non-systematic literature review)

No systematic reviews were undertaken for this topic. Practice points were based on selected evidence and guidelines (see Guideline development process).

#### 4.7.2.1 Polyp detection rates

In a study with over 1200 patients comparing same-day CTC with segmentally unblinded optical colonoscopy (OC), CTC had a sensitivity of 94% for the detection of polyps over 10mm, performing as well as OC.<sup>[2]</sup> The high sensitivity of CTC for the detection of colorectal cancer (CRC) has been confirmed in a subsequent meta-analysis involving 49 studies and 11,151 patients.<sup>[3]</sup>

The sensitivity of CTC for the detection of polyps 6-9 mm is variable, with one meta-analysis reporting a sensitivity of 59% for these diminutive lesions.<sup>[4]</sup> A limitation of this analysis is that many of the included studies were published in 2005 or before, with some dating back to 1997, and therefore the data do not take account of technological advances in hardware and software, improved reader training, and faecal tagging which are routinely used today.

The natural history of polyps measuring 6–9mm is yet to be fully defined. Radiologists do not report polyps that are less than 6mm, as the overwhelming majority of these do not harbour advanced histology.<sup>[5]</sup>

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#### 4.7.2.2 Interval cancer rates

The interval cancer rates following a negative CTC are low and in one study involving 1050 patients with a negative CTC and follow-up average of 4.7 years found one interval cancer<sup>[6]</sup> while another study with 1429 patients with negative CTC and mean follow-up of 5.7 years found two interval cancers, one occurring 5 years post CTC and the other 10 years post initial CTC.<sup>[5]</sup> Reader training and experience is vital to maintain the high accuracy of CTC and the low interval cancer rate, so CTC should only be reported by radiologists who are accredited for CTC interpretation by the Royal Australian and New Zealand College of Radiologists (RANZCR).

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#### 4.7.2.3 Radiation dose and cancer risk

CTC requires the use of ionising radiation which carries a risk of producing radiation induced malignancy. The inherently high contrast between the gas containing gut lumen and soft tissue colonic wall allows for a low dose CT to be performed without reducing the sensitivity of the examination. Typical radiation doses for CTC are 5mSv or less,<sup>[7]</sup> while the use of modern iterative reconstructive methods is allowing the dose to fall as low as 1 mSv which is less than half of the annual natural background radiation dose. Modelling of CTC every 5 years between the ages of 50 and 80 years, and using a relatively high dose of 7-8 mSv would prevent between 24 and 35 CRCs for every radiation-induced malignancy.<sup>[8]</sup> The radiation dose of CTC is significantly lower than the dose acquired during inferior tests such as barium enema.

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#### 4.7.2.4 Extracolonic findings

CTC examines not only the colonic mucosa but also the contents of the abdominal and pelvic cavities, the spine and lung bases. Hence extracolonic findings are frequently encountered, the vast majority of which can be accurately characterised as benign and of no clinical significance. The rates of potentially important findings, such as extracolonic malignancy and vascular aneurysms, varies and is up to 16% depending upon the definition used, the CTC technique and the population being studied.<sup>[9][10]</sup> The diagnosis of these conditions has potential benefit to patients, but may require further investigations.

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**Practice point**

Due to its excellent safety profile and high accuracy for detecting colonic carcinoma, CT colonography is an alternative for patients unable to have colonoscopy. Bowel preparation is still required prior to the examination.

**Practice point**

In patients at risk of colorectal carcinoma who have had an incomplete colonoscopy, CT colonography should be performed to allow assessment of the entire colonic mucosa.

**Practice point**

It is safe to perform same-day CT colonography following incomplete colonoscopy, including in patients who have had a biopsy or simple polypectomy. However, CT colonography should be delayed in patients with complex endoscopic intervention and in patients at high risk of perforation such as active colitis or high-grade stricture.

**Practice point**

CT colonography should only be interpreted by radiologists who have undergone specialist training and are accredited by RANZCR.

### Practice point

Patients with a CT colonography detected polyp over 10mm should be referred for polypectomy. Patients with polyps 6–9mm can be offered either polypectomy or repeat colonic examination at 3 years.

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## 4.8 Colonoscopic surveillance after polypectomy - Introduction

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### 4.8.1 Introduction

Compared with individuals in whom no adenomas are found at colonoscopy, those in whom adenomas have been found and removed are at an increased risk of developing subsequent adenomas. This is the basis for surveillance, with the ultimate goal of reducing colorectal cancer (CRC)-related mortality.

An overall increase in colonoscopy numbers and quality has resulted in substantially more adenomas being detected and more individuals requiring subsequent surveillance. In the 10 years between 2000–2001 and 2009–2010, the utilisation of Medicare Benefits Schedule items for colonoscopy increased in all Australian states and territories. In per capita terms, there was an 84% increase, from 13.4 per 1000 to 24.6 per 1000 population, between the two periods.<sup>[1]</sup> The expansion of the National Bowel Cancer Screening Program (NBCSP) will further add to the demand for colonoscopies and the associated financial burden.

The cost is not only financial. Although colonoscopy is generally safe,<sup>[2]</sup> cumulative procedures add risks, and surveillance is increasingly used in the elderly, for whom risks are higher.<sup>[3]</sup> The ‘burden’ of surveillance colonoscopy on colonoscopy services is also increasingly recognised; there is a major concern that it diverts resources away from others needing colonoscopy (e.g. diagnostic and screening procedures).

To rationalise resource utilisation, surveillance colonoscopy should be directed to those who will benefit most; procedures which are of little, if any, clinical benefit – such as colonoscopies for patients in whom surveillance procedures are less likely to detect significant pathology – should be minimised. In systematic reviews of the overuse of medical care, colonoscopy is consistently featured.<sup>[4][5]</sup> The screening and surveillance colonoscopy literature also highlights poor compliance with guidelines, with procedures often recommended too frequently overall but with those at high risk often having procedures less frequently than recommended by guidelines.<sup>[6][7][8][9]</sup>

Given the high quality of contemporary colonoscopy, with a lower risk of missing significant polyps and higher adenoma detection rates at index colonoscopy, recommendations based on data from previous eras of lower quality colonoscopy would result in inappropriately frequent surveillance colonoscopy.<sup>[10]</sup> New understandings must also be incorporated. In generating the current guidelines, all of these issues have been considered as well as initiatives to ensure Australia's colonoscopy services are of high quality.<sup>[11]</sup>

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## 4.8.2 Colorectal cancer precursors

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Two main pathways are recognised in the development of CRC:

- the classic adenoma-carcinoma pathway, with conventional tubular, tubulovillous and villous adenoma precursors
- the serrated pathway, with sessile serrated adenoma (SSA) and traditional serrated adenoma (TSA) precursors).

The pathway by which CRC develops in patients with longstanding inflammatory bowel disease (IBD) is different (see Colonoscopic surveillance and management of dysplasia in IBD)

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### 4.8.2.1 Conventional (tubular, tubulovillous and villous) adenomas

Sixty-five to 70% of CRCs originate from adenomas, which are clonal proliferations of colonic epithelial cells with intraepithelial dysplasia or neoplasia.<sup>[12]</sup> Observational and autopsy studies first suggested adenomas were precursor lesions,<sup>[13][14]</sup> with a prevalence of 20–53% in adults over 50 years of age and 30% over 35 years of age.<sup>[15]</sup> The lifetime risk of CRC is much lower, at 5–6%.<sup>[16][17]</sup> This means that only a minority of adenomas develop into cancer, highlighting the variable natural history of adenomas, with phases of growth, stability and regression.<sup>[18][19]</sup> The 10-year cumulative progression from adenoma to carcinoma is less than 10%<sup>[20]</sup> or 0.25% transition rate per year.<sup>[15]</sup> Variability in growth and malignant potential are determined by genetic or epigenetic cumulative mutations as well as environmental (diet and lifestyle) interventions.

The main pathways in CRC carcinogenesis are

- the chromosomal instability pathway affecting APC, KRAS and TP53, characteristic of adenomas in familial adenomatous polyposis
- the microsatellite instability pathway, which involves mutation of tandem repeats (also known as microsatellites) due to inactivation of the DNA mismatch repair (MMR) genes, characteristic of adenomas occurring in Lynch syndrome.

Conventional adenomas may appear macroscopically as elevated, flat or depressed. Elevated lesions may be sessile or pedunculated.<sup>[21][22]</sup> Classifications of endoscopic appearance of polyps, such as the Paris classification (Figure 1),<sup>[23]</sup> are useful for standardised polyp description in endoscopy reports.<sup>[24][25]</sup>

Accumulation of mutations over time leads to a small tubular adenoma increasing in size, the dysplasia becoming high grade and an increasing proportion of villous features. An advanced adenoma (AA) is an adenoma with any one of three features: size  $\geq 10$ mm, high-grade dysplasia (HGD) or villosity. The ability to develop angiogenesis and local spread to the lymphatics (found in the submucosal layer in the colon) is associated with progression to a malignant polyp or frank adenocarcinoma. The chance of any single adenoma harbouring a malignant focus is related to size: <1% if <1cm, 5% if 1–2cm and 10–20% if >2cm.<sup>[22]</sup>

Advanced adenoma features and adenoma multiplicity ( $\geq 3$  adenomas) are also related to the risk of an individual developing future (metachronous) adenomas.

**Figure 1. Paris classification of superficial (Type 0) colonic neoplasia<sup>[23]</sup>**

Adapted with permission from *Clinical Gastroenterology and Hepatology*, Vol 10(9), Holt BA, Bourke MJ, Wide field endoscopic resection for advanced colonic mucosal neoplasia: current status and future directions, 969–979, © 2012 AGA Institute. Published by Elsevier Ltd.

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#### 4.8.2.2 Serrated polyps

Over the last 20–25 years, lesions previously labelled as hyperplastic polyps (HPs) have been renamed serrated polyps (SPs), and are characterised by serrated architecture. There are three main sub-groups: true hyperplastic polyps, SSA and TSAs. Whilst the true diminutive distal HP has no significant malignant potential, the malignant potential of the SSA and TSA has been clearly established and they are thought to be responsible for around 20% of CRCs. Although the natural history of the SSA and TSA continue to be studied, it is clear some SPs have an indolent course, often remaining benign for many years, but with the potential to then progress rapidly. Factors associated with this malignant transformation are not clear at this stage.

The initiating event for SPs is up-regulation of the MAPK pathway, usually by mutation of the BRAF oncogene. BRAF mutation is the initiating event in the vast majority of SSAs and two-thirds of TSAs, but is extremely rare in conventional adenomas (which are instead initiated by dysregulation of the Wnt pathway, usually by mutation of the APC tumour suppressor gene). The serrated pathway is thought to progress via DNA methylation, which may lead to silencing of MLH1 (and thus microsatellite instability) and other genes, including up-regulation of the Wnt pathway. These additional changes are associated with the development of dysplasia and rapid progression to malignancy.<sup>[17][26]</sup>

Histologically, SPs are characterised by exaggerated, saw-toothed, luminal serrations. Subtypes, specifically SSAs, show dilation and distortion in the bases of the colonic crypts.<sup>[22]</sup> SPs from all locations must be assessed by the same reproducible histologic criteria to ensure diagnostic accuracy and consistency, although this may be challenging. Endoscopically, SSAs are often subtle, with indistinct edges and a cloud-like surface. They are more often located in the right colon and covered by a mucous cap. They are characteristically inconspicuous and are easily missed. TSAs are often located more distally and more closely resemble conventional adenomas. The NBI International Colorectal Endoscopic<sup>[27]</sup> and Workgroup serrated polypS and Polyposis (WASP)<sup>[28]</sup> classifications offer guidance about characterisation of polyps at endoscopy.

Endoscopic and histologic features of higher-risk SPs continue to be described; limitations in this area include the relatively recent recognition and classification of SPs, their relatively low prevalence and variable pathologic definition, particularly the distinction between HPs and SSAs. Size  $\geq 10\text{mm}$ , proximal location and the co-existence of conventional dysplasia have been suggested as important features of higher risk (see First surveillance intervals following removal of high risk conventional adenomas only).

In light of increased understanding of SPs, surveillance recommendations for individuals following the removal of SPs with or without synchronous conventional (tubular, tubulovillous or villous) adenomas are separated from those with conventional adenomas alone.

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## 4.8.3 Surveillance considerations

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### 4.8.3.1 Quality of care

Surveillance guidelines are based on the expectation of high-quality care from both endoscopists and pathologists. Endoscopy quality is discussed further in Quality of colonoscopy. Standards for pathology can be found in the section on Pathologic considerations).

### 4.8.3.2 Quantifying risk

The exact risk for an individual of developing metachronous neoplasia (MN) and CRC-specific mortality must be balanced against the risks of surveillance, taking into consideration the patient's situation and wishes. Surveillance recommendations require full knowledge of the procedure performed, the findings, pathology results and previous history, since the risk of MN is variable, with increasing recognition that some post-polypectomy sub-groups are at very low risk of metachronous advanced neoplasia (MAN).

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## 4.8.4 Limitations of evidence on which to recommend surveillance intervals

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### 4.8.4.1 Methodological limitations

There are no contemporary high-quality studies comparing outcomes from different surveillance intervals. The main studies on which we have based surveillance intervals to date, have recruited from the late 1980s and 1990s and therefore likely underestimate the efficacy of index colonoscopy as performed today. No randomised controlled trials with a control arm of no colonoscopy/polypectomy or including longer surveillance intervals have been performed. Highly controlled trials<sup>[29][30][31][32]</sup> which compare surveillance intervals with good surveillance participation and compliance with interval recommendations do not reflect the norm. The generalisability of the results of these studies is questionable, as are those from single centres, from countries not reflective of the Australian population's demographics and risk factors or even from 'community' studies from more westernised countries<sup>[33]</sup> with other methodologic limitations.

The literature is replete with retrospective cohort studies where surveillance has been performed on a variable proportion, usually less than half, with little information about the reasons for non-participation in surveillance, leading to selection bias. Additionally, there is considerable variation around the recommended surveillance intervals, which often seem to have been determined by default rather than being predetermined. The proportion of patients who are symptomatic varies, as do the background risk factors including personal adenoma history and family history.

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### 4.8.4.2 Outcomes

Outcomes reported also vary between studies. Commonly reported outcomes include MN, metachronous adenoma (MA), metachronous advanced adenoma (MAA), metachronous advanced neoplasia (MAN) and metachronous CRC. Specific and varying terms such as metachronous low-risk adenomas or high-risk adenomas also make comparison of outcomes difficult.

### 4.8.4.3 Quality of colonoscopy and pathology

The greatest difficulty in using the available literature to formulate recommendations about surveillance colonoscopy is the difference in quality between 'historical' and 'modern' colonoscopy. Major technical advances in colonoscopy and greater attention to procedural quality in the past 15 years make it difficult to extrapolate from earlier studies, which failed to mention important quality parameters, such as the quality of bowel preparation, complications, caecal intubation rates and withdrawal times, as well as endoscopist experience and their adenoma detection rates. Additional challenges are variation in pathology, particularly in terms of diagnosis of advanced histologic features and classification of SPs.

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#### Practice point

Endoscopists and pathologists need to be aware of serrated polyps and be able to recognise and endoscopically manage them.

#### Practice point

Hyperplastic polyps should be clearly distinguished from sessile serrated adenomas and traditional serrated adenomas. Although hyperplastic polyps are classified amongst serrated polyps, they do not have malignant potential when they are diminutive, confined to the rectosigmoid colon and not associated with proximal serrated polyps.

#### Practice point

Consistently high quality colonoscopy is imperative for optimal cost-effectiveness and for implementation of uniform surveillance guidelines.

### 4.8.5 Colonoscopic surveillance after polypectomy subsections and recommendations

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- First surveillance intervals following removal of low risk conventional adenomas only (SAD1)
- First surveillance intervals following removal of high risk conventional adenomas only (SAD2)
- First surveillance intervals following removal of  $\geq 5$  conventional adenomas only (SAD5)
- First surveillance intervals following removal of serrated polyps (with or without conventional adenoma) (SAD4)
- First surveillance intervals following removal of large sessile or laterally spreading adenomas (SAD3)
- Should family history affect surveillance intervals?(SFH1)
- Subsequent surveillance colonoscopies
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- Colonoscopic surveillance after polypectomy: Discussion

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## 4.9 First surveillance intervals following removal of low-risk conventional adenoma

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## 4.9.1 Definition

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The low risk category refers to 1-2 small (<10mm) tubular adenomas without high-grade dysplasia (HGD).

For surveillance intervals for clinically significant serrated polyps with synchronous low risk conventional adenomas see First surveillance intervals following removal of serrated polyps ( $\pm$  conventional adenomas)

## 4.9.2 Background

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The 2011 edition of this guideline recommended surveillance at 5 years for individuals following removal of 1-2 small (<10mm) tubular adenomas without HGD,<sup>[1]</sup> although recognising that the risk of metachronous advanced neoplasia (MAN) in this group was likely to be no greater than that of the average population. The 2018 recommendations are based on systematic review, non-systematic review of relevant literature, international recommendations and expert opinion.

## 4.9.3 Evidence

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*What should be the first surveillance interval following removal of low risk conventional adenomas only? [SAD1]*

### 4.9.3.1 Systematic review evidence

The systematic review included studies published since 2010 of colonoscopy procedures performed from 2002. The evidence base for low-risk individuals, particularly high quality studies with long-term outcomes, using modern endoscopy technique, is limited (see Technical report). Data relating to surveillance colonoscopy in patients with low-risk adenomas were reported from one level III-2 prospective cohort analysis of a randomised controlled trial,<sup>[2]</sup> four level II prospective cohort studies<sup>[3][4][5][6]</sup> and nine level III-2 retrospective cohort studies.<sup>[7][8][9][10][11][12][13][14][15]</sup> Six cohort studies had a low risk of bias, one a moderate risk of bias and seven a high risk of bias.

Outcomes reported included incidence and risk of metachronous colorectal cancer (CRC), metachronous adenoma (MA) and metachronous advanced adenoma (MAA). The 11 cohort studies reporting incidence of metachronous cancer and advanced adenoma tended to fall within the 3-5 year surveillance range. Studies tended to report incidence of cancer closer to 5 years. No included studies reported follow up at 10 years or mortality. There was consistency in the outcomes of metachronous CRC and MAA, but not MA. Most studies were from Asian populations not necessarily directly generalisable, but probably applicable to the Australian population. The incidence of metachronous CRC, reported in 11 studies,<sup>[2][3][4][5][6][16][12][14][15][11][9]</sup> was  $\leq 1\%$  in all studies.

The incidence of MAA, reported in 11 studies<sup>[2][3][4][5][6][16][12][14][15][11][9]</sup> with surveillance intervals of 3-5 years, ranged from 1.35-8.04% in 10 of these studies.<sup>[2][3][4][5][6][16][12][14][15][11]</sup>

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## 4.9.3.2 Overview of additional evidence (non-systematic review relevant literature)

### 4.9.3.2.1 Long-term follow up from earlier studies

Four level III-2 studies included long term outcomes in groups of low risk patients but were not included in the systematic review as they did not fit the criteria, particularly as they included colonoscopies performed prior to 2002.

Two level III-2 studies reported long-term CRC incidence:

- Cottet et al<sup>[17]</sup> reported on a French retrospective cohort (n=5779). Participants had incident adenomas removed between 1990 and 1999 and were followed up using registry data until 31/12/2003, for a median of 7.7 years (inter-quartile range 5.2–10.5). The standardised incidence ratio for CRC was 0.68 (0.44–0.99) regardless of surveillance colonoscopy. The 10-year cumulative probability of CRC was 0.76% (0.39–1.48) with surveillance colonoscopy and 1.37% (0.70–2.65) without surveillance colonoscopy.
- Brenner et al<sup>[18]</sup> performed a large case-control study in Germany, identifying cases of CRC (n=2582) and matched controls (n=1798) from the population registry. Patients who had undergone a colonoscopy with removal of a polyp without high risk features had a reduced adjusted odds ratio (OR) of CRC at any site, proportional to time since polypectomy: 0.2 (0.1–0.2) for <3 years, 0.4 (0.2–0.6) for 3–5 years and 0.8 (0.4–1.5) for 6–10 years, compared with no colonoscopy (OR 1.0).

Two level III-2 studies reported CRC-specific mortality:

- Zauber et al<sup>[19]</sup> compared CRC-specific mortality in participants (n=2602) who had low- and high-risk adenomatous polyps removed in the National Polyp Study between 1980 and 1990 with standardised incidence-based CRC-specific mortality in the general population using data from the US Surveillance Epidemiology and End Results (SEER) program. The proportion of participants with non-advanced adenomas was 43%, with 81% having 1–2 adenomas only. Median follow-up was 15.8 years, with maximum of 23 years. Overall, the standardised mortality rate (SMR) was 0.47 (0.26–0.80, p=0.008). The risk of CRC mortality of those with adenomas removed was the same as those with non-adenomatous polyps at 10 years. Cumulative CRC-specific mortality at 20 years was 0.8% for the National Polyp Study patients, compared with 1.5% in the general population (significance level not reported). Mortality reduction was similar for the first 10 years of follow-up at 0.44 (0.14–1.06, p=0.09) compared with 10 or more years at 0.49 (0.23–0.93, p=0.04).
- Løberg et al<sup>[20]</sup> followed n=40,826 individuals after adenoma removal from between 1993 and 2007 and compared CRC-specific mortality with the general population up to 2011, with a median follow-up of 7.7 years (maximum 19 years). In those with low-risk adenomas who did not undergo any surveillance colonoscopy, as per Norwegian guidelines, the SMR was 0.75 (0.63–0.88).

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#### **4.9.3.2.2 Diminutive adenomas**

Diminutive adenomas (defined as <6mm) are of great interest due to their increased detection with high-quality endoscopy.

It was reported in a Chinese study<sup>[15]</sup> that the incidence of MAA following removal of diminutive adenomas was 1.8% and small adenomas 3.2%, compared with 3.1% in those with no adenomas at baseline, at follow-up between 1 and 5 years.

The risk of MAA among patients undergoing first follow-up colonoscopy after removal of adenomas <10mm was assessed in an Israeli study<sup>[13]</sup> (median follow-up 32 months), a hazard ratio of 3.49 (1.6–7.6) was reported in small adenomas compared with diminutive adenomas.

#### **4.9.3.2.3 Comorbid metabolic syndrome**

The influence of the metabolic syndrome on MAN is increasingly recognised, with consistent evidence showing that it increases risk. The risk is greatest following the removal of low risk adenomas at baseline colonoscopy and in males.<sup>[5][8][21][22]</sup> There are many definitions of metabolic syndrome.<sup>[23][24]</sup> According to the most commonly used definition, that of the US National Cholesterol Education Program Adult Treatment Panel III,<sup>[25]</sup> three or more of the following are required:

- Abdominal obesity: waist circumference  $\geq 102$ cm in men and  $\geq 88$ cm in women
- Hypertriglyceridemia:  $\geq 1.695$ mmol/L
- Low HDL-C:  $< 2.2$ mmol/L in men and  $< 2.8$ mmol/L in women
- High blood pressure (BP):  $> 130/85$ mmHg
- High fasting glucose:  $> 6.1$ mmol/L.

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#### **4.9.3.2.4 Clinical practice guidelines from other countries**

Many countries have published recommendations for surveillance after adenoma removal (Table 4)<sup>[26][27][28][29][30][31][32][33]</sup> and most classify polyps as being either low or high risk. However, there is an increasing trend to further stratify risk. The US-Multi Society Taskforce guidelines endorsed by the American Gastroenterological Association (AGA) 2012<sup>[27]</sup> include the low risk category as 1–2 tubular adenomas <10mm without HGD, and recommended a surveillance interval of 5–10 years for patients with low-risk polyps. Recent commentaries have called for a clear message advocating screening for this group according to the strategy for the average-risk population, and advocating consideration of risk-profiling to stratify patients within the low-risk group.<sup>[34]</sup> As average-risk screening differs between countries, the actual recommendation can also differ.

The Canadian Association of Gastroenterology (CAG) guidelines<sup>[33]</sup> have the same definition of low risk as the AGA, with a recommendation for return to average-risk screening (colonoscopy at 10 years in Canada) unless there are personal or familial risk factors that increase risk, in which case a colonoscopy at 5 years is



appropriate. The European Society of Gastrointestinal Endoscopy guidelines 2013<sup>[26]</sup> have the same definition of low risk as the AGA and CAG, with a clear surveillance recommendation for the low-risk group of returning such patients to a screening programme (if present in the individual country) or a screening colonoscopy at 10 years. This is similar to the low-risk group in the European guidelines developed by the International Agency for Research on Cancer.<sup>[31]</sup> New Zealand national guidelines<sup>[30]</sup> use the same low-risk definition and recommend clinicians to consider a colonoscopy at 5 years.

The British Society of Gastroenterology guidelines,<sup>[28]</sup> which take into consideration the UK National Institute for Health and Clinical Excellence recommendations,<sup>[29]</sup> are the only guidelines to define low risk differently and purely on the basis of size. All adenomas <10mm in size, regardless of dysplasia and villosity, are considered 'low-risk' and the recommendation for surveillance is either no surveillance or, in the presence of other factors, to consider colonoscopy at 5 years.

In Norway, follow-up is not recommended in the low-risk group, 1-2 adenomas, >75 years of age, hyperplastic polyps and no remaining adenomas/remnants or unknown histology.<sup>[35]</sup> A 5-year surveillance interval is recommended for those with  $\geq 3$  adenomas or 1-4mm adenomas left in situ.

Løberg et al<sup>[20]</sup> recently published long-term SMR data from a Norwegian registry of n=40,826 patients who had had adenomas removed. The number of adenomas and histology was available, but size was not. Even with a strategy of 'no surveillance', the low-risk group had a CRC-specific SMR of 0.75 (0.63-0.88).

The Dutch surveillance programme has undergone two changes. The most recent recommendations from 2013 are based on the work of van Heijningen<sup>[36]</sup> and use a risk score range of 0-5, incorporating number of adenomas, size  $\geq 10$ mm, villosity and proximal location. Recommendations are no surveillance for those with a risk score of 0, surveillance at 5 years for those with a risk score of 1-2, and surveillance at 3 years for those with a risk score of 3-5.

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#### **4.9.3.2.5 Summary of international guidelines**

Based on the best available evidence, expert international guidelines agree that, following removal of 1-2 small (<10mm) tubular adenomas without HGD, most individuals are at no greater risk of CRC than the general population.

Recommendations worldwide include no surveillance colonoscopy or return to average-population screening in many cases, with colonoscopy at an interval of 10 years where screening colonoscopy is used. In the Australian context, average risk population screening would be faecal occult blood test as per the National Bowel Cancer Screening Program (NBCSP).

The importance of high-quality colonoscopy is recognised, as is the fact that there may be a sub-group who will benefit from a surveillance interval of 5 years, with intervals of 5-10 years accordingly recommended. In the British guidelines,<sup>[28]</sup> patients with 1-2 adenomas <10mm with villous and HGD are also included in the low-risk group with a similar recommendation.

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## 4.9.4 Evidence summary and recommendations

Evidence summary	Level	References
The incidence of metachronous colorectal cancer following removal of low-risk conventional adenomas only was $\leq 1\%$ , with the majority of studies performing surveillance at 3–5 years.	II, III-2	[12], [3], [37], [14], [11], [6], [7], [9], [4], [5]
Incidence of any adenoma following removal of low-risk conventional adenomas only ranged from 27.48% to 53.48% amongst the nine cohort studies reporting this outcome. Surveillance intervals mainly ranged between 3 and 5 years.	II, III-2	[12], [37], [11], [6], [7], [9], [4], [5]
The incidence of metachronous advanced adenomas following removal of low-risk conventional adenomas only ranged from 1.35% to 8.04% with a surveillance interval of 3–5 years in 10 of 11 studies that reported this outcome.	II, III-2	[12], [3], [37], [14], [11], [6], [7], [9], [4], [5]

Evidence-based recommendation	Grade
<p><i>Low-risk individuals – conventional adenomas only</i></p> <p>First surveillance intervals should be no sooner than 5 years following the complete removal of low-risk conventional adenomas only (1–2 small [<math>&lt;10\text{mm}</math>] tubular adenomas without high-grade dysplasia).</p>	<b>D</b>

Consensus-based recommendation
<p><i>Low-risk individuals – conventional adenomas only</i></p> <p>First surveillance interval of 10 years is appropriate for most individuals following complete removal of low-risk conventional adenomas only (1–2 small [<math>&lt;10\text{mm}</math>] tubular adenomas without high-grade dysplasia).</p>

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**Practice point**

Consistently high-quality colonoscopy is imperative for optimal cost effectiveness and for implementation of uniform surveillance guidelines.

**Practice point**

Polyp/adenoma size as per the endoscopist documentation should be used for determining surveillance intervals. All endoscopists should ensure size measurements are accurate using a reference standard (eg an open biopsy forceps or snare).

**Practice point**

Surveillance intervals should be determined after the colon has been cleared of all significant neoplasia, once histology is known and in the context of individualised assessment of benefit to the patient.

**Practice point**

A shorter surveillance interval of 5 years could be considered for men who fit the criteria for the metabolic syndrome, because they may have increased risk of metachronous advanced neoplasia following removal of low-risk adenomas.

**Practice point**

Return to the National Bowel Cancer Screening Program with a faecal occult blood test after 4 years, is an appropriate option and should be discussed with the patient.

#### Practice point

Patients with 1–2 diminutive (<6mm) low-risk adenomas have a very low risk of metachronous neoplasia and should be returned to the NBCSP after 4 years unless there are significant extenuating factors.

#### Practice point

Individuals with a significant family history of colorectal cancer should be assessed according to current Australian clinical practice guidelines for the prevention, early detection and management of colorectal cancer (see Risk and screening based on family history) in addition to these recommendations, and the shorter interval used.

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### 4.9.4.1 Notes on the recommendations

The systematic review evidence does not support colonoscopy within 5 years but does not offer guidance for longer intervals. Evidence from general literature review indicates that the long-term risks of CRC and of CRC-specific mortality are similar to, or lower, than those of the general population following removal of 1–2 small (<10mm) tubular adenomas without HGD based on studies from an era of lesser quality colonoscopy. The risk is even lower for diminutive adenomas. Risk is likely to be further reduced in the current era of high quality colonoscopy.

Based on the best available evidence, expert international guidelines agree that following removal of 1–2 small (<10mm) tubular adenomas without HGD, most individuals are at no greater risk of CRC than the general population.

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### 4.9.5 Health system implications

#### 4.9.5.1 Clinical practice

These surveillance guidelines will result in substantial change to which health care providers will need to adjust. Table 3 and colour-coding in this section aims to facilitate transition from the old to new guidelines. An educational program and simple decision aids, such as wall charts and online decision tools, would help healthcare provider become familiar with the recommendations for surveillance intervals. These could be developed, promoted and distributed in conjunction with the relevant professional bodies and healthcare providers in the public and private domains.

### 4.9.5.2 Resourcing

The management of surveillance following removal of adenomas is critical in terms of health outcomes, demand for colonoscopy and cost. Recently, the Cancer Research Division, Cancer Council NSW used the Australian developed and validated model Policy1-Bowel<sup>[38]</sup> to compare the new and previous surveillance guidelines specifically related to the National Bowel Cancer Screening Program. Preliminary results demonstrate comparable health outcomes, reduced number of surveillance colonoscopies and similar program-related costs (see the preliminary results report on the Modelled comparison of proposed surveillance recommendations for the NBCSP).

There is likely to be an increased cost for pathologic assessment if a substantial proportion of health care providers do not currently submit all polyps removed for pathologic assessment or do not separate specimens.

### 4.9.5.3 Barriers to implementation

The main barriers to implementation of these recommendations will be dissemination across Australia and familiarisation for healthcare providers. This will be facilitated by a coordinated implementation and evaluation program.

**Table 3. Summary of recommendations for first surveillance intervals following removal of conventional adenomas only**

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**Table 4 Summary of international surveillance guidelines**

	10Y (or routine screening)	5Y	3Y	1Y
Australian (2011) <sup>[1]</sup>		1-2 small (<10mm) tubular adenomas without HGD	3-4 adenomas ≥10mm with HGD or villosity	≥5 adenomas
AGA (2012) <sup>[27]</sup>	No polyps or small (<10mm) hyperplastic polyps in the rectum or sigmoid		3-10 tubular adenomas ≥10mm	>10 adenomas (<3Y)
	1-2 small (<10mm) tubular adenomas <sup>a</sup>		Villous or HGD	
		SSP <10mm with no dysplasia	SSP ≥10mm OR with dysplasia OR Serrated adenoma	Serrated polyposis syndrome

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Canadian (2013) <sup>[33]</sup>	1-2 small (<10mm) tubular adenomas with LGD <sup>b</sup>		3-10 tubular adenomas ≥10mm Villous, HGD	>10 adenomas
		SSA <10mm with no dysplasia	SSP ≥10mm OR with dysplasia OR traditional serrated adenoma	Serrated polyposis syndrome
ESGE (2013) <sup>[27]</sup>	1-2 small (<10mm) tubular adenomas with LGD <sup>c</sup>		≥10mm HGD Villous ≥3 adenomas	
	Serrated <10mm with no dysplasia		Serrated ≥10mm or dysplasia	
BSG (2010) <sup>[28]</sup> NICE (2011) <sup>[29]</sup> (BCSP) <sup>[28]</sup>	1-2 small (<10mm) adenomas <sup>d</sup>		3-4 small (<10mm) adenomas ≥10mm	≥5 small adenomas ≥3 adenomas with at least one ≥10mm
European (2010) <sup>[31]</sup>	1-2 tubular adenomas <10mm, LGD		3-4 adenomas Any 10-19mm HGD, villous	≥5 adenoma ≥20mm within 1Y
New Zealand (2012) <sup>[30]</sup>		1-2 tubular adenomas <10mm, LGD (consider) <sup>e</sup> Consider at 5Y	1-2 adenomas ≥10mm 3-4 adenomas <10mm HGD, villous	≥5 adenomas 3-4 adenomas if ≥10mm
			Villous, HGD,	

## Clinical practice guidelines for surveillance colonoscopy

Korean (2012) <sup>[9]</sup>		1-2 small (<10mm) tubular adenomas, LGD	≥10mm ≥3 adenomas Serrated ≥10mm	
Dutch (2013) <sup>[36]</sup>	PRS 0	PRS 1-2	PRS 3-5	
	PRS: one point each for: 2-4 adenomas, size ≥10mm, villous histology, proximal location; two points if ≥5 adenomas			
Norwegian (1996) <sup>[35]</sup>	No routine surveillance if:  1-2 small tubular adenomas with LGD  HPP  Age >75 years  No remaining adenomas/remnants or unknown histology	≥3 adenomas  1-4mm adenomas left in situ		
	10 years if:  HGD  Villous  ≥10mm			
Japanese (2014) <sup>[32]</sup>	Follow-up colonoscopy should be repeated within 3 years after polypectomy			
Chinese	No recommended surveillance guidelines			

AGA: American Gastroenterological Association; BCSP: [UK] Bowel Cancer Screening Programme; BSG: British Society of Gastroenterology; ESGE: European Society of Gastroenterology; HGD: high-grade dysplasia; HPP: hyperplastic polyp; LGD: low-grade dysplasia NICE: National Institution of Clinical Excellence; PRS: personalised risk score; SSP: sessile serrated polyp; TSA: traditional serrated adenoma; Y: year(s).

<sup>a</sup>Guideline states: 'The evidence supports a surveillance interval of longer than 5 years for most patients'. <sup>b</sup>Guideline states: 'Clinicians may want to individualise the surveillance interval based on adenoma size, family history and patient preference. There are data suggesting that 10 years may be appropriate for most individuals'. <sup>c</sup>Guideline states: 'Surveillance is not indicated in the low risk group'. <sup>d</sup>Guideline states: 'Consider at 5 years if age, comorbidity, family history, accuracy and completeness of examination relevant'. <sup>e</sup>Guideline recommends clinicians consider surveillance colonoscopy at 5 years for this group.

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## 4.9.7 Appendices

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## 4.10 First surveillance intervals following removal of high-risk conventional adenoma

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## 4.10.1 Definition

Individuals at high risk are those who have had one or more conventional (tubular, tubulovillous or villous) adenomas removed at the baseline colonoscopy with one or more of the following four features:

- size  $\geq 10\text{mm}^*$
- high-grade dysplasia (HGD)
- villosity
- 3-4 adenomas.

\*Adenomas  $\geq 20\text{mm}$  are more likely to be excised piecemeal. For surveillance intervals for patients following removal of adenomas  $\geq 20\text{mm}$ , see First surveillance intervals following removal of large sessile or laterally spreading adenomas.

For surveillance intervals for patients following removal of  $\geq 5$  conventional adenomas, see First surveillance intervals following removal of  $\geq 5$  conventional adenomas only (SAD5).

For surveillance intervals for clinically significant serrated polyps with or without synchronous conventional adenomas, see First surveillance intervals following removal of serrated polyps ( $\pm$  conventional adenomas).

## 4.10.2 Background

The 2011 edition of this guideline<sup>[1]</sup> recommended surveillance at 3 years for individuals following removal at baseline colonoscopy of adenomas with any of the following characteristics: size  $\geq 10\text{mm}$ , HGD, villosity, 3-4 adenomas. The 2018 recommendations are based on systematic review, non-systematic review of relevant literature, international recommendations and expert opinion.

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## 4.10.3 Evidence

*What should be the first surveillance interval following removal of high-risk conventional adenomas only (size  $\geq 10\text{mm}$ , HGD, villosity and/or 3-4 adenomas)? [SAD2]*

### 4.10.3.1 Systematic review evidence

The systematic review included studies published since 2010 of colonoscopic procedures performed from 2002.

Four level II prospective<sup>[2][3][4][5]</sup> and ten level III-2 retrospective cohort studies<sup>[6][7][8][9][10][11][12][13][14][15]</sup> were included. Nine studies had a high risk of bias and five studies had a moderate risk of bias. Outcomes reported included incidence and risk of metachronous colorectal cancer (CRC), metachronous adenoma (MA) and metachronous advanced adenoma (MAA). Surveillance intervals ranged from less than 3 years to 3–5 years. None of the included studies reported follow up at 10 years or CRC mortality. Most studies consistently reported the risk of metachronous colorectal cancer and MA. The reporting of MAA was more variable. The evidence was probably generalisable to the Australian population and applicable to the Australian healthcare system with some caveats.

At variable surveillance intervals less than 3 years and between 3–5 years:

- Incidence of metachronous CRC ranged from 0–1.52%
- Incidence of MAA varied within the range of 2.40–24.24%

The evidence base is limited for outcomes in individuals after removal of high-risk adenomas, particularly high-quality studies with long-term outcomes using modern endoscopy techniques.

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#### 4.10.3.2 Overview of additional evidence (non-systematic literature review)

##### 4.10.3.2.1 Long-term outcomes

Five level III-2 studies reported long-term CRC incidence and mortality following adenoma removal in high-risk groups (Table 5) but were not included in the systematic review as they did not fit the criteria, particularly as they included colonoscopies performed prior to 2002.

Three level III-2 studies reported long-term CRC incidence:

- Cottet et al<sup>[16]</sup> reported on a French retrospective cohort (n=5779). Participants had incident high-risk adenomas removed between 1990 and 1999 and were followed up using registry data until 31/12/2003, for a median of 7.7 years (interquartile range [IQR] 5.2–10.5). The overall standardised incidence ratio (SIR) of CRC was 2.23 (1.67–2.92): 1.10 (0.62–1.82) with surveillance colonoscopy and 4.26 (2.89–6.04) without. The 10-year cumulative incidence of CRC was 2.05% (1.14–3.64) with and 6.22% (4.26–9.02) without surveillance colonoscopy.
- Brenner et al<sup>[17]</sup> performed a large case-control study in Germany, identifying cases of CRC (n=2582) and controls (n=1798) from the population registry matched for age, sex and location. Patients who had had a colonoscopy with removal of a polyp with high-risk features had a reduced adjusted odds ratio (OR) of CRC at any site, proportional to time since polypectomy: 0.3 (0.3–0.7) for <3 years, 0.5 (0.3–0.8) for 3–5 years and 1.1 (0.5–2.6) for 6–10 years, compared to no colonoscopy (OR 1.0).
- Atkin et al<sup>[18]</sup> looked at long-term incidence of CRC in those with 3–4 small adenomas and 1–2 adenomas at least one of which was  $\geq 10$ mm (n=11,944) and compared it to age- and sex-standardised incidence from the general population. Years of entry were 1990–2010, with censoring in 2014 and median follow-up of 7.9 years (IQR 5.6–11.1). After adjustment for baseline risk factors, CRC incidence in the whole cohort was not

significantly different from that of the general population (SIR 1.09, 95% confidence interval [CI] 0.91–1.30). Compared with no surveillance (hazard ratio [HR] 1), one surveillance visit at median 2.9 years (IQR 1.3–3.4) was associated with a significant reduction in colorectal cancer incidence (HR 0.57, 95% CI 0.40–0.80), two visits HR 0.51 (0.31–0.84) and three or more visits HR 0.54 (0.29–0.99);  $p=0.0029$  for any surveillance visit, compared with no surveillance.

Two level III-2 studies reported CRC-specific mortality:

- Zauber et al<sup>[19]</sup> compared CRC-specific mortality in participants ( $n=2602$ ) who had adenomatous polyps removed in the US National Polyp Study between 1980 and 1990 with standardised incidence-based CRC-specific mortality in the general population using Surveillance Epidemiology and End Results (SEER) data. Patients with low- and high-risk adenomas were included, with 57.3% advanced adenomas and 19.3%  $\geq 3$  adenomas. Median follow-up was 15.8 years, with maximum of 23 years. Overall, standardised mortality ratio (SMR) was 0.47 (0.26–0.80). The risk of CRC mortality of those with adenomas removed was the same as those with non-adenomatous polyps at 10 years. Cumulative CRC-specific mortality at 20 years was 0.8% for the National Polyp Study patients versus 1.5% in the general population. Mortality reduction was similar for the first 10 years of follow-up at 0.44 (0.14–1.06,  $p=0.09$ ) compared with 10 or more years at 0.49 (0.23–0.93,  $p=0.04$ ).
- Løberg et al<sup>[20]</sup> followed  $n=40,826$  individuals after adenoma removal during 1993–2007 and compared CRC-specific mortality with the general population up to 2011, with a median follow-up of 7.7 years (maximum 19 years). As per Norwegian Guidelines, a surveillance of 10 years is recommended for those with high-risk adenomas. The CRC-specific SMR was 1.16 (1.02–1.31).

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### **4.10.3.2.2 Influence of high-risk features (size $\geq 10$ mm, HGD, villosity, 3-4 adenomas)**

#### **4.10.3.2.2.1 Size**

Size distinguishes low risk ( $<10$ mm) and high risk ( $\geq 10$ mm) for metachronous adenoma (MA), with further division more recently into adenomas of 6–9mm (small) and 1–5mm (diminutive). Size correlates with advanced histology (villosity and/or HGD).

A recent review highlights the variability in the literature but summarises findings as “adenoma size  $\geq 10$ mm appears to be associated with future advanced neoplasia and the magnitude of risk increases for larger adenomas  $\geq 20$ mm in size.”<sup>[21]</sup> A meta-analysis<sup>[22]</sup> reported an OR for metachronous neoplasia (MN) of 2.24 (1.4–3.59) comparing various smaller adenomas with those  $\geq 10$ mm, generally at median follow-up intervals between 17 months and 16 years. On multivariate analysis, Atkin et al<sup>[18]</sup> found that adenoma size 10–19mm (HR 1.97; 1.01–3.81) and  $\geq 20$ mm (HR 2.28; 1.16–4.50) was associated with increased incidence of CRC when compared with  $<10$ mm, at median follow-up of 7.9 years. Potential difficulty in interpreting the literature may arise from inconsistency in the measurement of adenoma size, which has been shown to be inconsistent among endoscopists.<sup>[23]</sup>

#### **4.10.3.2.2.2 High-grade dysplasia**

The question of whether HGD is associated with MN has been challenged by histologic consistency of reporting, separating the influence of size and villosity and population heterogeneity. Accordingly, the British guidelines do not incorporate HGD when considering surveillance intervals.<sup>[24]</sup> Despite some variability, recent literature indicates an independent association between HGD and MN. A meta-analysis<sup>[22]</sup> reported a multivariate relative risk (RR) of 2.04 (1.10–3.78) for HGD in the index adenoma predicting MN at median follow-up between 17 months and 16 years. Facciorusso et al<sup>[25]</sup> reported a multivariate OR of 4.25 (2.11–7.5) for MAA at 3 years, whereas van Heijningen et al<sup>[26]</sup> reported a RR for metachronous advanced neoplasia (MAN) of 1.9 (1.3–2.7) on univariate but 1.3 (0.9–1.9) on multivariate analysis at median follow up of 35 months. Taniguchi<sup>[27]</sup> reported an OR 2.4 (1.51–3.83) for HGD versus low-grade dysplasia (LGD) in the largest adenoma for MA at follow up within 2 years on multivariate analysis. Another systematic review<sup>[21]</sup> reported a small and variable association of HGD with risk of metachronous advanced neoplasia in a systematic review. Most recently, Atkin et al<sup>[18]</sup> found a HR of 1.69 (1.21–2.36) for HGD versus LGD for incident CRC following removal of intermediate risk adenomas at median follow-up of 7.9 years. High-grade dysplasia is less common in diminutive polyps, with an incidence of around 0.1–0.3%, and 0.3–0.8% in small adenomas.<sup>[28][29][30]</sup> The metachronous neoplasia risk is unclear, but is likely to be low.

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#### **4.10.3.2.2.3 Villosity**

The association of villosity with MN has been complicated by factors that make it difficult to compare outcomes between studies. These include variability in histologic diagnosis (the change in the World Health Organization definition in 2010 of 'villosity' from 20% to 25% villous component being particularly relevant),<sup>[31]</sup> and different outcome definitions (sometimes tubulovillous and villous, at other times one or the other). Differing length of follow-up may also partially explain variation. Such is the uncertainty about the significance of villosity, that the British guidelines do not incorporate villosity when considering surveillance intervals.<sup>[24]</sup>

Recent literature generally indicates that villosity is an independent predictor for MN. A meta-analysis<sup>[32]</sup> reported a multivariate-adjusted OR 1.77 (1.16–2.71) for MN at median follow-up of between 17 months and 16 years, whilst another<sup>[21]</sup> concluded that villous histology within an adenoma may have a small association with future advanced neoplasia but this was not seen uniformly across all studies. In individual studies:

- Facciorusso et al<sup>[33]</sup> reported an OR for MAA of 1.49 (0.47–5.18) on univariate analysis and 1.73 (0.68–4.45) on multivariate analysis at 3 years.
- Taniguchi<sup>[27]</sup> reported an OR of 2.07 (1.59–2.70) on univariate analysis but 1.56 (0.98–2.52) on multivariate analysis at follow-up within 2 years.
- van Heijningen found villous histology significant on univariate and multivariate analysis at follow-up intervals of between less than 4 years and more than 6 years, with an OR of 2.3 (1.4–3.6).
- Atkin et al<sup>[18]</sup> did not find villosity to be associated with metachronous CRC, with a HR of 1.16 (0.71–1.91) on multivariate analysis at median 7.9 years follow-up.

#### **4.10.3.2.2.4 Multiplicity**

Increasing number of adenomas at baseline is associated with MN. A recent meta-analysis reported a RR of 2.32 (95% CI 1.81, 2.98) when comparing 1 to  $\geq 2$  baseline adenomas.<sup>[22]</sup> An often-quoted large study of pooled trial data from 2009<sup>[34]</sup> described a relatively high risk of MAA within 3–5 years at 8.6%, 12.7%, 15.2%, 19.6% and 24.1% for one, two, three, four and five adenomas, respectively. Of note, the included trials recruited from the 1980s and 1990s in the era of lower quality colonoscopy.

More recent studies have shown much lower rates of MAA. In one study the incidence of MAA was 5.8% following removal of 3–4 non-advanced adenomas at baseline colonoscopy (n=291) at  $4.0 \pm 1.3$  years.<sup>[35]</sup> Another showed the incidence of MAA to be 3.5% after removal of 1–2 diminutive adenomas, compared with 6.3% after 3–9 diminutive adenomas; and 9.8% following removal of both 1–2 and 3–9 small (6–9mm) adenomas at a median of 32 months (IQR 13–48).<sup>[36]</sup> In another study, the risk of MAA was 11.9% in patients with 3–10 adenomas after follow-up of 4.0 years.<sup>[37]</sup>

Although the relationship between number at baseline colonoscopy and MN is consistent across most literature,<sup>[36][11][35][37]</sup> Atkin et al<sup>[18]</sup> demonstrated a non-significant ( $p=0.12$ ) multivariate HR of 0.58 (95% CI 0.31–1.11) for 3 or 4 adenomas compared to 1, perhaps suggesting an effect of higher quality colonoscopy with the detection of more adenomas.

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#### **4.10.3.2.2.5 3-4 small adenomas or 1-2 adenomas with one $\geq 10$ mm without advanced histologic features**

Several recent papers have investigated at whether, following removal of high-risk adenomas, a sub-group of patients may be at lesser risk. In the first study,<sup>[11]</sup> institutional data from 2002–2012 were analysed, finding a 1.8% risk of MAA following removal of 3–4 adenomas all less than 10mm; compared with a risk of 8.6% at a mean of  $3.28 \pm 1.75$  years, when the size of at least one adenoma was  $\geq 10$ mm.

In the second study, Atkin et al<sup>[18]</sup> assessed long-term outcomes of standardised CRC incidence against a population reference in patients following removal of 3–4 small adenomas or 1–2 adenomas, one of which was  $\geq 10$ mm (these included advanced histologic features as per British guidelines). Colorectal cancer incidence in these patients, regardless of follow-up, was not significantly different from that of the general population (SIR 1.09, 95% CI 0.91–1.30).

A retrospective, multicentre cohort study included patients recruited between 2007 and 2008 with  $\geq 3$  adenomas or one or more adenomas  $\geq 10$ mm, stratified according to the British Guidelines.<sup>[35]</sup> In the group with 3–4 non-advanced adenomas (n=291), at  $4.0 \pm 1.3$  years the incidence of MAA was 5.8% and CRC 0.3%.

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#### **4.10.3.2.2.6 Cumulative risk in patients with multiple high-risk factors detected**

Several groups have recently looked at the impact of multiple high-risk findings. A group from Korea<sup>[8]</sup> retrospectively (2005–2009) analysed data for 862 individuals, with high-risk factors: size  $\geq 10$ mm, HGD, villosity and  $\geq 3$  adenomas. The cumulative incidence of MAN was associated with the number of high-risk findings. At 5 years, MAN rates were 8.5% with no high-risk findings, 18.7% with one, 26.3% with two, and 37.2% with three or four high-risk findings, with the number needed to treat to find a single MAA at 3 years being 8.4, 6.5 and 4.1 for one, two and three to four factors, respectively. At 1 and 2 years for those with three to four factors, needed to treat was 12.5 and 6.6, respectively.

A Japanese group combined metabolic factors (age  $\geq 65$  years, BMI  $> 25$ , fasting blood glucose  $> 126$  mg/dL) and adenoma predictors (HGD, villosity, right sided location, largest adenoma diameter  $\geq 10$ mm, number removed  $\geq 3$ ) into a risk score from 0–10 points. The risk of adenoma recurrence increased as the risk score increased, with an OR of 7.07 for those with a score of 0–2 compared with those with a score of 3–10 (95% CI 5.30–9.43).<sup>[38]</sup>

van Heijningen et al<sup>[26]</sup> developed a simple risk score from 0 to 5 which was predictive of MAN and incorporated into the Dutch Surveillance Guidelines. The score consists of characteristics contributing 1 point (size  $\geq 10$ mm, villous histology, proximal location, having 2–4 adenomas) or 2 points (having  $\geq 5$  adenomas). Although not yet externally validated, the score has been modelled with a c-statistic of 0.71, which is better than that of the British Society of Gastroenterology (BSG) (2010) guidelines (0.674; 0.634–0.713) and American Gastroenterological Association (AGA) (2012) guidelines (0.664; 0.625–0.703).

The risk for diminutive adenomas with advanced histologic features is poorly defined but seems low. Such adenomas are very rare.

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#### 4.10.3.2.2.7 Expert opinion and clinical practice guidelines from other countries

The definition of ‘high risk’ varies amongst clinical practice guidelines from other countries, with previous Australian guidelines having both moderate- and high-risk categories.<sup>[1]</sup> Similarly, in the BSG, European and New Zealand guidelines, 3–4 adenomas are split from  $\geq 5$  adenomas, with the BSG and NZ guidelines including 3–4 adenomas with at least one  $\geq 10$ mm in the highest risk category.

A comparison of the AGA versus BSG guidelines using pooled trial data<sup>[39]</sup> showed a risk of MAN at 1 year of 18.7% (14.8–22.5%) in this highest risk group. By contrast, Lee reports the 12-month follow-up of the high-risk group from the UK National Health Service Bowel Cancer Screening Programme, where the risk of MAN was lower, at 6.6%.<sup>[14]</sup> The European guidelines<sup>[40]</sup> incorporate  $\geq 5$  adenomas and size  $\geq 20$ mm in the highest risk group, giving no special consideration to the  $\geq 10$  adenomas group. More than 10 adenomas are recognised in the AGA guidelines<sup>[41]</sup> and Canadian Association of Gastroenterology guidelines<sup>[42]</sup> as requiring surveillance at 1-year recommendation.

The Norwegian guidelines<sup>[43]</sup> recommend surveillance at 10 years for patients with 1–2 adenomas, despite the presence of HGD or villous features or size  $\geq 10$ mm.

A recent study based on long-term data from the Norwegian registry<sup>[20]</sup> reported SMR for 40826 patients who had had adenomas removed. For, the high-risk group, CRC-specific SMR was 1.16 (1.02-1.31) implying a surveillance interval of 10 years was adequate to reduce the SMR to just above average population risk, but inadequate to reduce it to or below average population risk.

In the Dutch surveillance programme, based on the personalised risk score developed by van Heijningen et al<sup>[26]</sup> a surveillance interval of 3 years is recommended for those with a score of 3–5, while a surveillance interval of 5 years is recommended for those with a risk score of 1–2.

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### 4.10.4 Evidence summary and recommendations

Evidence summary	Level	References
The nine cohort studies of high-risk patients in whom surveillance was performed at 3–5 years reported an incidence of metachronous CRC of 0.00% to 1.52%.	II, III-2	[10], [2], [4], [11], [9], [5], [7], [3], [15]
Surveillance time primarily ranged between 3 and 5 years amongst the seven cohort	II, III-	[10], [9], [5],

Evidence summary	Level	References
studies that reported incidence of any adenoma in patients with high-risk adenomas. Adenoma incidence ranged from 36.63% to 69.71% across the seven studies.	2	[7], [3], [4], [15]
Incidence of metachronous advanced adenoma was not consistent among the 10 cohort studies and ranged from 2.40% to 24.24%. Surveillance time varied across these studies, with five studies reporting surveillance within 3 years, and seven studies reporting surveillance within 3-5 years.	II, III-2	[10], [2], [11], [9], [5], [7], [3], [4], [15], [12]

Evidence-based recommendation	Grade
<p><i>High-risk individuals - conventional adenomas only</i></p> <p>First surveillance intervals should be within 5 years following removal of high-risk conventional adenomas only, i.e. those with one or more of the following features:</p> <ul style="list-style-type: none"> <li>■ size <math>\geq 10</math>mm</li> <li>■ high-grade dysplasia</li> <li>■ villosity</li> <li>■ 3-4 adenomas.</li> </ul>	<b>D</b>

Consensus-based recommendation
<p><i>High-risk individuals - conventional adenomas only</i></p> <p>First surveillance intervals following removal of high-risk conventional adenomas only should be stratified according to the type and number of high-risk features (size <math>\geq 10</math>mm, high-grade dysplasia (HGD), villosity, 3-4 adenomas):</p> <p>A surveillance interval of 5 years is recommended for patients with either of the following:</p> <ul style="list-style-type: none"> <li>* 1-2 tubular adenomas with HGD or tubulovillous or villous adenomas (with or without HGD), all of which are <math>&lt; 10</math>mm</li> <li>* 3-4 tubular adenomas without HGD, all of which are <math>&lt; 10</math>mm</li> </ul> <p>A surveillance interval of 3 years is recommended for patients with any of the following:</p> <ul style="list-style-type: none"> <li>* 1-2 tubular adenomas with HGD or tubulovillous or villous adenomas (with or without HGD), where the size of one or both is <math>\geq 10</math>mm</li> </ul>

### Consensus-based recommendation

- \* 3-4 tubular adenomas, where the size of one or more is  $\geq 10\text{mm}$
- \* 3-4 tubulovillous and/or villous adenomas and/or HGD, all  $< 10\text{mm}$

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### Practice point

Surveillance intervals should be determined after the colon has been cleared of all significant neoplasia, once histology is known, and in the context of individualised assessment of benefit to the patient.

### Practice point

Consistently high-quality colonoscopy is imperative for optimal cost effectiveness and for implementation of uniform surveillance guidelines.

### Practice point

Polyp/adenoma size as per the endoscopist documentation should be used for determining surveillance intervals. All endoscopists should ensure size measurements are accurate using a reference standard (eg an open biopsy forceps or snare).

### Practice point

Polyps removed at colonoscopy should be sent separately for histology to guide surveillance recommendations.

### Practice point

Clinicians should accurately include features relevant to surveillance intervals in their procedure reports so that individualised surveillance recommendations can be made.

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#### 4.10.4.1 Notes on the recommendations

The systematic review supported surveillance within 5 years following removal of high-risk conventional adenomas but did not offer guidance on intervals within this broad timeframe. General review of the literature assessed high-risk features and suggested that combinations of these features might guide further stratification relevant to clinical practice.

The recommendations are based on the expectation that endoscopists in Australia are performing high-quality colonoscopy with complete adenoma excision and are supported by accurate pathology reporting.

The consensus-based recommendations are supported by the following key findings in the literature:

- Following removal of high-risk conventional adenomas, individuals require surveillance to reduce CRC incidence and CRC-specific mortality to levels at or just above population level.
- Whilst combinations of high-risk features are associated with an increased risk of metachronous neoplasia, subgroups of high-risk individuals seem to be at lesser risk. These lesser risk sub-groups include:

(i) those in whom 3–4 small tubular adenomas without HGD have been removed, and

(ii) those in whom 1–2 tubular adenomas without HGD have been removed, one of which is  $\geq 10$ mm.

The recommendation for a 5-year surveillance interval following the removal of 3–4 low-risk adenomas without HGD is consistent with this recognition and attempts to counteract the 'paradoxical' impact that high quality colonoscopy (with detection of multiple small adenomas) would otherwise have on the number of and intervals between surveillance procedures. It represents a reduction in frequency, compared with the 2011 Australian clinical practice guidelines for surveillance colonoscopy.<sup>[1]</sup>

Expert opinion and guidelines from other countries vary in their definitions of the high-risk group, with a trend towards separating off an intermediate risk group from those at highest risk (Table 4 Summary of international surveillance guidelines). Associated with this, there is variability in the corresponding surveillance interval recommendations. For the highest-risk group (albeit variably defined), a shorter surveillance interval of 1 year is recommended. Otherwise, a 3-year interval is recommended.

The British guidelines<sup>[24]</sup> differ in that they make surveillance recommendations based on size and number alone.

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**Table 3. Summary of recommendations for first surveillance intervals following removal of conventional adenomas only**

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## 4.10.5 Health system implications

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### 4.10.5.1 Clinical practice

These surveillance guidelines will result in substantial change to which health care providers will need to adjust. The aim of Table 3 and colour-coding in this section is to facilitate transition from the old to new guidelines. An educational program and simple decision aids, such as wall charts and online decision tools, would help healthcare provider become familiar with the recommendations for surveillance intervals. These could be developed, promoted and distributed in conjunction with the relevant professional bodies and healthcare providers in the public and private domains.

### 4.10.5.2 Resourcing

The management of surveillance following removal of adenomas is critical in terms of health outcomes, demand for colonoscopy and cost. Recently, the Cancer Research Division, Cancer Council NSW used the Australian developed and validated model Policy1-Bowel<sup>[44]</sup> to compare the new and previous surveillance guidelines specifically related to the National Bowel Cancer Screening Program. Preliminary results demonstrate comparable health outcomes, reduced number of surveillance colonoscopies and similar program-related costs (see the preliminary results report on Modelled comparison of proposed surveillance recommendations for the NBCSP)

There is likely to be an increased cost for pathologic assessment if a substantial proportion of health care providers do not currently submit all polyps removed for pathologic assessment or do not separate specimens.

### 4.10.5.3 Barriers to implementation

The main barrier for implementation of these recommendations will be dissemination across Australia and familiarisation for healthcare providers. This will be facilitated by a coordinated implementation and evaluation programme.

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## 4.10.6 Colorectal cancer incidence and mortality after adenoma removal

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**Table 5. Colorectal cancer incidence and mortality after adenoma removal**

Author	Study	Years	Population	Follow-up	Outcomes	
Brenner 2012 <sup>[45]</sup>	German Case-control III-2	2003- 2010	2582 cases  1798 controls	Up to 10 years	Adjusted OR for CRC incidence at follow-up after polypectomy:  <3 years: 0.2 (0.2-0.3), 3-5 years: 0.4 (0.3- 0.6)  6-10 years: 0.9 (0.5-1.5) for low- and high- risk adenomas	
Cottet 2012 <sup>[16]</sup>	French Retrospective cohort and registry  III-2	Incident adenomas:  1990- 1999  Follow up:  31/12 /2003	n=5779	Median follow-up  7.7 years  IQR 5.2- 10.5	Non-advanced adenomas:  n=3236  SIR 0.68 (0.44-0.99) regardless of follow-up;  SIR 0.60 (0.30-1.07) with a single follow-up colonoscopy  10-year cumulative probability of CRC was 0.76% (0.39-1.48) with and 1.37% (0.70-2.65) without surveillance colonoscopy.	Advanced adenomas:  n=1899  SIR 2.23 (1.67- 2.92): 1.10 (0.62- 1.82) with follow-up 4.26 (2.89-6.04) without;  10-year cumulative probability 2.05% (1.14-3.64) with 6.22% (4.26-9.02) without surveillance colonoscopy
Atkin 2017 <sup>[18]</sup>	UK Retrospective cohort study  III-2	Incident adenomas 1990- 2010  Follow-up through 2014	n=11,944	Median follow-up  7.9 years  IQR 5.6- 11.1.	3-4 small adenomas or 1-2 adenomas, at least one of which is $\geq 10$ mm  After adjustment for baseline risk factors, CRC incidence in the whole cohort was not significantly different from that of the general population (SIR 1.09, 95% CI 0.91-1.30); compared with no surveillance, one surveillance visit at median 2.9 years (IQR 1.3-3.4), was associated with a significant reduction in CRC incidence rate (HR 0.57, 95% CI 0.40-0.80).	
		1993- 2007		Median follow-up	Low-risk group (no surveillance colonoscopy)	High-risk group (surveillance colonoscopy every 10 years)

Løberg 2014 <sup>[20]</sup>	Norway Registry III-2	Mortality 2011	40826	7.7 years (maximum 19)	SMR 0.75 (0.63–0.88)	SMR 1.16 (1.02– 1.31)
Removal of the first adenoma						
1993–1999: SMR 1.17 (1.03–1.33) vs. 2000– 2007: 0.76 (0.65–0.89)						
Zauber 2012 <sup>[19]</sup>	USA Cohort (NPS) III-2	1980– 1990	2602	Median follow-up  15.8 years	SMR 0.47 (0.26–0.80) cumulative mortality at 20 years 0.8 vs. 1.5% in general population. The risk of CRC mortality of those with adenomas removed was the same as those without adenomas at 10 years.	
<i>Abbreviations:</i> CI: Confidence interval; CRC: colorectal cancer; HR: hazard ratio; IQR: interquartile range; OR: odds ratio; SIR: standardised incidence ratio; SMR: standardised mortality ratio; UK: United Kingdom; USA: United States of America						

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## 4.10.8 Appendices

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## 4.11 First surveillance intervals following removal of $\geq 5$ adenomas (conventional adenoma)

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### 4.11.1 Definition

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Patients in whom  $\geq 5$  conventional (tubular, tubulovillous or villous) adenomas have been detected and removed are in a separate risk category from those with fewer adenomas. For surveillance intervals following removal of  $\geq 5$  conventional adenomas with synchronous clinically significant serrated polyps see First surveillance intervals following removal of serrated polyps ( $\pm$  conventional adenomas)

### 4.11.2 Background

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In the 2011 Australian clinical practice guidelines for surveillance colonoscopy,<sup>[1]</sup> a surveillance interval of 1 year (5–9 adenomas) or within a year ( $\geq 10$  adenomas) was recommended for individuals following the removal of  $\geq 5$  conventional adenomas at the index colonoscopy. Although the association of risk for metachronous advanced adenoma (MAA) and increasing numbers of adenomas detected and removed at index colonoscopy remains, in the era of high quality endoscopy, the magnitude of this risk may not be as great as previously.

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### 4.11.3 Evidence

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*What should be the surveillance interval following removal of  $\geq 5$  conventional adenomas only? [SAD5]*

#### 4.11.3.1 Systematic review evidence

The systematic review reported outcomes from three level III-2 studies.<sup>[2][3][4]</sup> One was at low<sup>[2]</sup> and two at moderate risk of bias.<sup>[3][4]</sup> Two studies were from Korea and the third from the USA, with a marked over-representation of males. Overall, although the evidence may not be directly generalisable, it could probably be sensibly applied to the Australian healthcare environment. In general, reported outcomes included metachronous adenomas (MA), metachronous advanced adenomas (MAA), metachronous colorectal cancers (CRC), metachronous advanced neoplasia (MAN) and metachronous neoplasia (MN) at follow-up of around 3 and 5 years. The three studies had different inclusions, thus limiting direct comparisons (see Table 6). There were no reports of long-term outcomes. In all studies, metachronous CRC was uncommon with a risk of 0–0.8% in those with both 5–9 and  $\geq 10$  adenomas. The risk of MAA varied according to the number and other index adenoma features such as size and follow-up duration. The risk of MAA reported in these studies was:

- 5% in those with at least 5 adenomas all  $< 10$ mm of any histology (n=169) after 3 years follow-up<sup>[2]</sup>
- 9.1% for those with 5–9 non-advanced adenomas removed at index colonoscopy (n=99) after a mean follow-up of 4 years<sup>[3]</sup>
- 11.9% for those with 3–10 adenomas ( $> 60\%$  advanced) removed at index colonoscopy (n=975) after a mean follow up of 4.0 years<sup>[4]</sup>
- 16.3% in those with at least 5 adenomas with 1  $\geq 10$ mm (n=123) after 3 years follow-up<sup>[2]</sup>
- 26.6% in those with  $> 10$  adenomas ( $> 60\%$  advanced) removed at index colonoscopy (n=214) after a mean follow-up of 4.3 years.<sup>[4]</sup>

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### 4.11.3.2 Overview of additional evidence (non-systematic literature review)

#### 4.11.3.2.1 Metachronous advanced neoplasia according to size of prior adenomas removed

One level III-2 study<sup>[5]</sup> investigated MAN after the removal of 3–9 non-advanced adenomas at index colonoscopy according to size (n=130). The incidence of MAN was 6.3% in the group with 3–9 adenomas sized 1–5mm (n=79) and 9.8% in the 3–9 adenomas sized 6–9mm (n=51) with a median follow-up of 32 months (interquartile range 13–48).

**Table 6. Summary of studies with ≥5 adenomas - metachronous neoplasia**

Author and design	n	Patient group at index colonoscopy	Outcome and follow-up time			
			Advanced adenoma	CRC	Advanced neoplasia	
Park <sup>[3]</sup> Retrospective multicentre 2007–2008 n=1394	99	5–9 NAA	9.1% 4Y	0%	AR 3Y	AR 5Y
					1.2% (1.17–1.22)	6.4% (6.34–6.46)
Park <sup>[4]</sup> Retrospective multicentre 2009–2011	975	3–10 adenomas (mean 4.5±1.9), 60% advanced adenomas	11.9% 4.0±1.2Y	0.1%	AR 3Y 3.0% (1.8–4.1)	AR 5Y 16.2% (12.3–20.1)
	214	>10 adenomas (mean 14.2±0.3), 68.2% advanced adenomas	26.6% 4.3±1.5Y	0	6.8% (2.9–10.7)	28.7% (20.8–36.5)
Vemulapalli <sup>[2]</sup> Secondary analysis of a database 2002–2012 n=1859	143	5–10 All <10mm, any histology		0.6%	5% (1068 days, SD 529)	
	103	5–10 at least one ≥10mm, any histology		0.8%	16.3% (737 days, SD 553)	

	n	Patient group at index colonoscopy	Follow up years		Incidence/rate per 1000 /per annum HR (95% CI)
Sneh-Arbib <sup>[5]</sup>					
2005–2013	130	3–9 NAA	282	<0.2%	7.7%/35.5/NA
Single centre		All <10mm			
1–9mm with LGD	79	3–9 NAA	193		6.3%/25.9/1
n=1192	51	3–9 NAA 6–9mm	89		9.8%/56.2/2.4 (0.69–8.36)

**Abbreviations:** AR: absolute risk; CRC: colorectal cancer; HR: hazard ratio; LGD: low grade dysplasia; SD: standard deviation; NA: not applicable NAA: non advanced adenoma; Y: years.

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#### 4.11.3.2.2 Expert opinion and clinical practice guidelines from other countries

International recommendations demonstrate considerable variability (Table 7) and Table 4 Summary of international surveillance guidelines).

**Table 7. International recommendations for multiple adenomas**

International recommendation	Adenoma description	Recommended surveillance interval
American Gastroenterological Association <sup>[6]</sup>	3–10 tubular adenomas	3 years
	>10 adenomas	<3 years
British Society of Gastroenterology <sup>[7]</sup>	≥5 adenomas	1 year
Canadian Association of Gastroenterology <sup>[8]</sup>	3–10 tubular adenomas	3 years
	>10 adenomas	<3 years
European Society of Gastroenterology <sup>[6]</sup>	≥3 adenomas	3 years
New Zealand <sup>[9]</sup>	≥5 adenomas	1 year

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#### 4.11.4 Evidence summary and recommendations

Evidence summary	Level	References
In patients with 5-9 non-advanced adenomas at index colonoscopy, metachronous neoplasia was detected in almost 80% of patients at follow-up of 4.0±1.5 years. In the same group of patients, 100% had developed metachronous neoplasia at 6-7 years after index colonoscopy.	III-2	[3]
In a group of 214 patients with >10 adenomas at index (14.2 ± 0.3 adenomas; 68.2% with advanced adenomas at index) neoplasia was detected in almost 90% of patients after a mean follow-up of 4.3 years. In the same group, metachronous neoplasia was detected in 100% of patients 8 years after index colonoscopy.	III-2	[3]
In patients with 5-9 non-advanced adenomas at index (n=99), metachronous advanced adenoma was reported in 9.1% after a mean follow-up of 4 years.	III-2	[3]
In patients with >10 adenomas at index (14.2±0.3 adenomas, 68.2% with advanced adenomas at index, n=214), metachronous advanced adenomas were reported in 26.6% after a mean follow-up of 4.3 years.	III-2	[4]
The risk of metachronous advanced neoplasia was similar to that of advanced adenomas, and was 16.3% after 3 years of follow-up.	III-2	[2]
Only one case of metachronous colorectal cancer was reported across two studies (n=551) in patients with no advanced adenomas at index.	III-2	[3], [2]
Only one case of metachronous colorectal cancer was reported across two studies (n=1312) in patients with advanced adenomas at index.	III-2	[3], [2]
Those with at least 5 adenomas with one ≥10mm had a detection rate of 2.4%, compared to no findings in those with 5 adenomas all ≤10mm, after 3 years follow-up.	III-2	[2]
Those with at least 5 adenomas with 1 ≥10mm had a detection rate of MAN of 1.6%, compared to 0.6% in those with 5 adenomas all ≤10mm at index, after 3 years follow-up	III-2	[2]
Those with at least 5 adenomas with 1 ≥10mm had a detection rate of 11.4% for tubular adenoma ≥10mm verse 3.7% for those with 5 adenomas all ≤10mm at index.	III-2	[2]
Absolute risk of metachronous advanced adenoma was reported in one study in patients with 5-9 non-advanced adenomas at index (n=99) at 3 years (AR=1.2%, CI=1.17-1.22) and 5 years (AR=6.4%, CI=6.34-6.46) follow-up. In another study it	III-2	[3], [2]



Evidence summary	Level	References
was reported that the risk of metachronous advanced adenomas in those patients with at least 5 adenomas all <10mm at index (OR=3.1, CI 1.2-8.2, p=0.021) with 1068±529 days follow-up.		
At follow-up of 737±553 days after index colonoscopy, the risk of metachronous advanced neoplasia was significantly greater in patients with at least 5 adenomas with 1 ≥10mm, than in those with 1-2 adenomas all < 10mm (OR=10.8, CI=4.5-25.7, p<0.001).	III-2	[2]
In a single study that reported outcomes in patients with >10 adenomas, the risk of metachronous neoplasia at follow-up of 4.3±1.5 years was significantly higher in those with >10 adenomas at index colonoscopy than in those with 3-10 adenomas at index colonoscopy (odds ratio 3.46; 95% CI 1.90-6.28).	III-2	[4]
In a single study that separately reported the rate of metachronous advanced adenomas, the risk at follow-up of 4.3±1.5 years was higher in those with >10 adenomas at index colonoscopy than in those with 3-10 adenomas at index colonoscopy (odds ratio 2.25; 95% CI 1.49-3.38).	III-2	[4]

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Evidence-based recommendation	Grade
<p><i>≥5 conventional adenomas only</i></p> <p>First surveillance intervals following complete removal of ≥5 conventional adenomas only, should be no longer than 3 years.</p>	<b>D</b>

Consensus-based recommendation
<p><i>≥5 conventional adenomas only</i></p> <p>First surveillance intervals should be within 3 years and stratified based on the number, size and histology following complete removal of ≥5 adenomas only.</p> <p>For those with 5-9 adenomas, recommended surveillance intervals are:</p> <ul style="list-style-type: none"> <li>* 3 years if all tubular adenomas &lt;10mm without high grade dysplasia (HGD)</li> <li>* 1 year if any adenoma ≥10mm or with HGD and/or villosity</li> </ul>

**Consensus-based recommendation**

For those with  $\geq 10$  adenomas, the recommended surveillance interval is 1 year, regardless of size or histology.

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**Practice point**

Surveillance intervals should be determined after the colon has been cleared of all significant neoplasia, once histology is known, and in the context of individualised assessment of benefit to the patient.

**Practice point**

Consistently high-quality colonoscopy is imperative for optimal cost effectiveness and for implementation of uniform surveillance guidelines.

**Practice point**

Polyp/adenoma size as per the endoscopist documentation should be used for determining surveillance intervals. All endoscopists should ensure size measurements are accurate using a reference standard (eg an open biopsy forceps or snare).

**Practice point**

Polyps removed at colonoscopy should be sent separately for histology to guide surveillance recommendations.

#### Practice point

Clinicians should accurately record adenoma features relevant to surveillance intervals so that individualised surveillance recommendations can be made.

#### Practice point

An underlying familial predisposition to colorectal cancer should be considered in all individuals with  $\geq 10$  polyps removed. Referral to a familial cancer clinic should be considered, along with appropriate psychological support.

Separate screening and surveillance recommendations apply to patients with diagnosed or likely familial syndromes (see Should family history affect surveillance intervals?).

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#### 4.11.4.1 Notes on the recommendations

The systematic review supported surveillance within 3 years following removal of  $\geq 5$  conventional adenomas but did not offer guidance on intervals within this broad timeframe. General review of the literature offered further information to guide clinical practice and inform the current recommendations which are consistent with international guidelines.

The recommendations are based on the expectation that endoscopists in Australia are performing high quality colonoscopy with complete adenoma excision and are supported by accurate pathology reporting.

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Table 3. Summary of recommendations for first surveillance intervals following removal of conventional adenomas only

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## 4.11.5 Health system implications

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### 4.11.5.1 Clinical practice

These surveillance guidelines will result in substantial change to which health care providers will need to adjust. The aim of Table 3 and colour-coding in this section is to facilitate transition from the old to new guidelines. An educational program and simple decision aids, such as wall charts and online decision tools, would help healthcare provider become familiar with the recommendations for surveillance intervals. These could be developed, promoted and distributed in conjunction with the relevant professional bodies and healthcare providers in the public and private domains.

### 4.11.5.2 Resourcing

The management of surveillance following removal of adenomas is critical in terms of health outcomes, demand for colonoscopy and cost. Recently, the Cancer Research Division, Cancer Council NSW used the Australian developed and validated model Policy1-Bowel<sup>[10]</sup> to compare the new and previous surveillance guidelines specifically related to the National Bowel Cancer Screening Program. Preliminary results demonstrate comparable health outcomes, reduced number of surveillance colonoscopies and similar program-related costs (see the preliminary results report on Modelled comparison of proposed surveillance recommendations for the NBCSP). There is likely to be an increased cost for pathologic assessment if a substantial proportion of health care providers currently do not submit all polyps removed for pathologic assessment or do not separate specimens.

### 4.11.5.3 Barriers to implementation

The main barrier for implementation of these recommendations will be dissemination across Australia and familiarisation for healthcare providers. This will be facilitated by a coordinated implementation and evaluation programme.

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## 4.11.6 References

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## 4.12 First surveillance intervals following removal of serrated polyps ( $\pm$ conventional adenoma)

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### 4.12.1 Definition

Serrated polyps (SPs) include the premalignant lesions sessile serrated adenomas (SSAs) and traditional serrated adenomas (TSAs) and the usually benign hyperplastic polyps. SSAs, TSAs and large ( $\geq 10$ mm) hyperplastic polyps are clinically significant serrated polyps.

This section considers first surveillance intervals following removal of clinically significant SPs only and with synchronous conventional adenomas.

For surveillance intervals following removal of conventional adenomas only see First surveillance intervals following removal of low-risk conventional adenomas only (SAD1) and First surveillance intervals following removal of high-risk conventional adenomas only (SAD2).

For information and guidance on serrated polyposis syndrome, see Serrated polyposis syndrome.

## 4.12.2 Background

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At the time of the previous edition of these guidelines (Australian clinical practice guidelines for surveillance colonoscopy),<sup>[1]</sup> there was insufficient evidence to differentiate follow-up protocols for SPs from those for standard adenoma follow-up. Since then, the 2010 World Health Organization classification has become well established, with reduced variability among histopathologists in applying these diagnostic criteria.<sup>[2]</sup> In addition, there has been improved endoscopist recognition of proximal serrated polyps although there is still great variability.<sup>[3]</sup> Although the evidence base remains limited, there is now sufficient information to allow specific recommendations.

### 4.12.2.1 Sessile serrated adenomas

Sessile serrated adenomas (SSAs) are expected to be diagnosed in over 5% of colonoscopies and undoubtedly have malignant potential.<sup>[3]</sup>

Predominantly found in the proximal colon, SSAs are subtle, sessile lesions and this may make it difficult to define the edges of the lesion to ensure complete resection.

The natural history of SSAs is still imperfectly understood but recent evidence suggests SSAs without dysplasia are indolent lesions with a mean dwell time of over 15 years.<sup>[4]</sup> If cytological dysplasia does develop, the dwell time is thought to be short and carcinoma may develop in less than one year.<sup>[4][5][6][7]</sup>

### 4.12.2.2 Traditional serrated adenomas

Traditional serrated adenomas (TSAs) are rare, accounting for only approximately 1% of all polyps. They are typically polypoid lesions in the distal colon and their molecular features suggest they should be treated like advanced conventional adenomas, with a significant risk of progression to malignancy if not resected.<sup>[4]</sup>

Due to their rarity, there are no meaningful data regarding the risk of metachronous neoplasia (MN) after their removal and international guidelines are based solely on expert opinion.

### 4.12.2.3 Hyperplastic polyps

Hyperplastic polyps (HP) are common. Small, distal HPs have no significant malignant potential.

Proximal HPs are early stage lesions unlikely to progress unless they develop features of an SSA. However, a true proximal HP is unlikely to be over 1cm in size; such lesions should be reviewed by an expert histopathologist to confirm the histopathological diagnosis.<sup>[4]</sup>

### 4.12.2.4 Advanced serrated polyps

Advanced serrated polyps (ASP) refer to a sessile serrated adenoma  $\geq 10$ mm in size and/or with associated conventional dysplasia, or traditional serrated adenomas of any size.

#### 4.12.2.5 Serrated polyposis syndrome

Serrated polyposis syndrome is described in detail in Clinical practice guidelines for the prevention, early detection and management of colorectal cancer<sup>[8]</sup> (see Serrated polyposis syndrome). No genetic cause has been established and it is possible there is a continuum between patients with multiple sporadic SSAs and those meeting the definition of serrated polyposis. This is particularly the case for patients meeting the World Health Organization definition of at least 5 serrated polyps proximal to the sigmoid colon with  $\geq 2$  of these being  $>10\text{mm}$  and the count being cumulative.

When serrated polyposis syndrome is first diagnosed, several colonoscopies may be required within 1–2 years to clear the colon of significant polyps. If this can be achieved, there is expert consensus that the risk of cancer justifies ongoing surveillance colonoscopy every 1 to 3 years with the aim of removing all polyps  $\geq 5\text{mm}$  and that, if this is impossible, colectomy and ileorectal anastomosis should be considered. This is supported by direct evidence.<sup>[9][10][11]</sup>

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### 4.12.3 Evidence

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*What is the appropriate first surveillance interval following complete removal of serrated polyps? [SAD4]*

#### 4.12.3.1 Systematic review evidence

The systematic review identified one level II study from Argentina with a high risk of bias<sup>[12]</sup> and two level III-2 studies from the USA with a low risk of bias.<sup>[13][14]</sup> Overall, the evidence is not necessarily generalisable to the Australian healthcare environment, but can probably be sensibly applied. Importantly, the colonoscopies in these studies were performed between 2004 and 2011 and histopathology was meticulously assessed. Although colonoscopy quality parameters were included, the SSA detection rates were still lower than the 5% anticipated with high quality colonoscopy (suggesting a level of missed lesions).<sup>[3]</sup> The outcomes assessed were various combinations of the incidence of metachronous colorectal cancer (CRC), advanced conventional adenomas, SSAs and ASPs.

The quality of the three studies was low. Limited power precluded definitive conclusions.

The systematic review findings are summarised in Table 10 below.

##### 4.12.3.1.1 Risk of metachronous colorectal cancer

Three of four cohort studies reported no incidences of colorectal cancer within 3–5 years for those classified at index as having clinically significant serrated polyps, SSAs or serrated adenomas with or without non-advanced or advanced adenoma. For those with SSAs coexisting with high risk adenoma at index, a 1.00% incidence of colorectal cancer (one case) at a mean and standard deviation of 3.54 ( $\pm 1.43$ ) years was reported.

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#### **4.12.3.1.2 Risk of metachronous advanced conventional adenoma**

The US study by Macaron et al<sup>[14]</sup> found that having an SSA as well as either low-risk or high-risk conventional adenoma did not significantly change the risk of metachronous advanced adenoma (MAA) during surveillance compared with not having an SSA. In their study, the risk was 27% at 3 years in the group with both high-risk adenoma with SSA, and 0% in the group with both low-risk adenoma and SSA.

In the Argentinian study by Pereyra et al,<sup>[12]</sup> there was no increased risk of MAA for synchronous low-risk adenoma and SSA, compared to low-risk adenoma alone.

In contrast, there was an increased risk of MAA in individuals with both high-risk adenoma and SSA, compared to high-risk adenoma alone (35.7% risk of MAA at 3 years for high-risk adenoma with synchronous SSA at baseline colonoscopy and 17.9% risk of MAA at 3 years for high-risk adenoma alone).

The US study of Melson et al<sup>[13]</sup> had a composite end-point including both MAA and metachronous advanced serrated polyps, so the incidence of MAA alone could not be determined with respect to the initial baseline findings. The findings suggest that the presence of an initial SSA increased the rate of metachronous advanced neoplasia, compared with conventional adenomas alone.

In subgroups of individuals with SSAs only at baseline colonoscopy, the 5-year risk of MAA was 12.8% in one study<sup>[14]</sup> and 8.3% in another,<sup>[12]</sup> but could not be determined in the third study. This is similar to the risk with low-risk adenoma at baseline.

#### **4.12.3.1.3 Risk of metachronous ‘advanced neoplasia’**

The study of Melson et al<sup>[13]</sup> used the end point of metachronous ‘advanced neoplasia’ during surveillance and defined this as MAA and/or SSA >1cm or SSA with high-grade dysplasia (HGD). Over a mean follow-up of 3.86 years, individuals with SSAs alone had an incidence of 6.31% of metachronous ‘advanced neoplasia’. Over a mean follow-up of 3.63 years, patients with 1 or 2 adenomas (including SSAs, if present) with each polyp <1cm had an incidence of 6.67% of advanced neoplasia. Over a mean follow-up of 1.98 years individuals with ≥3 adenomas (including SSAs if present) or an adenoma ≥1cm or with HGD or villous histology had an incidence of metachronous ‘advanced neoplasia’ of 18.75%. In all groups combined, the presence of an initial SSA increased the rate of metachronous ‘advanced neoplasia’ from 11.1% to 26.3%.

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#### **4.12.3.1.4 Risk of metachronous serrated polyps**

In the two US studies,<sup>[13][14]</sup> subjects without SSA at baseline had a very low incidence of any SSA during surveillance (<6%). Data addressing this could not be extracted from the Argentinian paper. In the study of Melson et al<sup>[13]</sup> the incidence of metachronous SSA was 33.3% over 3.94 years for individuals with SSAs with or

without low-risk adenoma at baseline and was 32.98% over 3.54 years for individuals with high risk SSAs alone ( $\geq 1$ cm or dysplastic or  $\geq 3$ ) or SSA combined with high-risk adenoma. The incidence of metachronous SSA in individuals with SSA at baseline was 42.67% at 4 years in the Argentinian study.<sup>[12]</sup> It should be noted that the prevalence of SSA at baseline colonoscopy in these studies was  $<5\%$  and some of these 'metachronous' SSAs were probably missed lesions. It will be interesting to determine the incidence of metachronous SSA when studies are published with a high prevalence of SSA at baseline colonoscopy.

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#### 4.12.3.1.5 Risk of metachronous advanced serrated polyps

It is of major interest to determine if ASPs at baseline predict a higher risk of metachronous ASPs. These were not reported by the Argentinian study.<sup>[12]</sup> Melson et al<sup>[13]</sup> defined ASP as: SSA  $\geq 1$ cm or with HGD, but included these with MAA as a composite end point of metachronous 'advanced neoplasia', making it difficult to calculate the separate risks. Macaron et al<sup>[14]</sup> defined ASP as: SSA or HP  $>1$ cm, SSA with conventional dysplasia or TSA of any size (Table 8). When comparing patients with SSA  $<10$ mm in size to those with ASPs at baseline colonoscopy, the incidences of metachronous ASP at 3 years were 0% and 6.5%, respectively, and at 5 years were 4.3% and 11.5%. These findings demonstrate a nonsignificant trend ( $p=0.11$ ) towards an increased incidence of metachronous ASP over time in those with ASP at baseline.<sup>[14]</sup> The study may have been underpowered to detect a difference in metachronous ASP rates, as only 12 of the 157 patients had ASPs.

The Argentinian study<sup>[12]</sup> found no statistically significant increase in risk of metachronous SSA according to characteristics at baseline of: size  $>10$ mm (relative risk [RR] 1.82, confidence interval [CI] 0.40–9.34,  $p=0.59$ ), cytologic dysplasia (RR 1.00, CI 0.15–4.32,  $p=1.00$ ), right sided location (RR 2.12, CI 0.47–11.53,  $p=0.48$ ) and more than three SPs (RR 1.69, CI 0.06–20.00,  $p=0.65$ ). Again, power was limited by small numbers.

##### 4.12.3.1.5.1 Cumulative incidence of metachronous advanced serrated polyp

Baseline findings	SSA or TSA only	SSA or TSA and LRA	SSA or TSA and HRA
3 years	2%	4.85%	9%
5 years	7%	11%	9%

HRA: high-risk adenoma; LRA: low-risk adenoma; SSA: sessile serrated adenoma; TSA: traditional serrated adenoma

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## 4.12.3.2 Overview of additional evidence (non-systematic literature review)

### 4.12.3.2.1 Other longitudinal data

US Data from the New Hampshire Colonoscopy Registry published after the completion of the systematic review period<sup>[15]</sup> provides further evidence that the combination of SSA and/or TSA with high-risk adenoma at baseline colonoscopy predicts a higher risk of metachronous high-risk adenoma. Over a median follow-up of 4.9 years, individuals with high-risk adenoma combined with either SSA or TSA at baseline had a 16.04-fold increased risk of metachronous high-risk adenoma compared with individuals with no polyps at baseline. Those with high-risk adenoma but no SSA or TSA had a 3.86-fold increased risk. The risk for the combination of low-risk adenoma and SSA or TSA at baseline was 2.88 (1.67–7.13) compared with those with no polyps, similar to that of those with low-risk adenoma alone, 1.93 (1.41–2.62).

This study also provided further evidence that having an SSA or TSA at baseline was associated with a significant risk of metachronous serrated polyps  $\geq 1$ cm (9.6% over 4.9 years). The risk was present in those with serrated polyps alone or combined with either low-risk adenoma or high-risk adenoma. Of note, the SSA detection rate at baseline was  $<4\%$  and some of the metachronous serrated polyps may have been missed lesions. The risk of metachronous serrated polyps  $\geq 1$ cm was highest in those who had high-risk adenoma and serrated polyps  $\geq 1$ cm at baseline, compared with individuals with no polyps (RR 17.45). In contrast, individuals without an SSA or TSA at baseline had a very low risk of metachronous serrated polyps  $\geq 1$ cm.

There is evidence that serrated polyps  $\geq 10$ mm are more frequently associated with synchronous advanced neoplasia.<sup>[16][17]</sup> This evidence supports recommendations for earlier repeat surveillance in these patients in several clinical practice guidelines.<sup>[18][19][3][20]</sup>

There is strong evidence that SSAs with dysplasia have a high chance of becoming malignant and there have been numerous reports of SSAs 'caught in the act' of transitioning to conventional dysplasia and then to invasive carcinoma.<sup>[4][5][6][7]</sup> The relative rarity of these lesions compared with the proportion of cancers bearing the molecular hallmarks of the serrated pathway and the similarity of the mean ages of patients with SSA with dysplasia and with serrated pathway cancers suggests that SSAs with dysplasia have a short dwell time before malignant conversion.<sup>[4]</sup> Based on this evidence, several guidelines recommend earlier repeat surveillance in these patients.<sup>[18][19][3][20]</sup>

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### 4.12.3.2.2 Clinical practice guidelines from other countries

Guideline recommendations are summarised in Table 11 below.

In 2012, the update of the guidelines for surveillance after polypectomy by the US Multi-Society Task Force (USMTF) on Colorectal Cancer was published.<sup>[19]</sup> The recommendations on serrated polyps were based on low quality evidence available up to 2011. These guidelines recommended surveillance colonoscopy in 5 years for SSAs <10mm without dysplasia and in 3 years for SSAs ≥10mm or with dysplasia. In the same year an expert panel published a consensus opinion with similar recommendations, but with additional advice that if there were 3 or more SSAs <10mm without dysplasia the interval should be 3 years, and with dysplasia the interval should be 1 to 3 years.<sup>[20]</sup>

The European Society of Gastrointestinal Endoscopy (ESGE) guidelines published in 2013 again noted the low quality of evidence and recommended patients with SSAs ≥10mm or with dysplasia should be considered similar to those with high-risk conventional adenomas, and should be offered surveillance colonoscopy at 3 years.<sup>[18]</sup> The ESGE guidelines regarded other SSAs as similar to in risk to low-risk conventional adenomas, recommended surveillance colonoscopy at 10 years in these patients.

Most recently, the British Society of Gastroenterology (BSG)<sup>[3]</sup> published a position statement on serrated polyps, in which they recommended that patients with SSAs ≥10mm or with conventional dysplasia should be offered surveillance colonoscopy at 3 years, but that other patients with SSAs should not be offered surveillance unless they meet criteria for serrated polyposis.

None of the above guidelines makes recommendations for combined serrated polyps and conventional adenomas, with the BSG stating the groups should be considered separately. The BSG<sup>[3]</sup> and USMTF<sup>[20]</sup> guidelines recommended surveillance at 3 years for all TSAs. All other guidelines recommended surveillance at 3 years for TSA ≥10mm, with other intervals varying from 'return to routine population screening' or colonoscopy at 5 or 10 years.

The question of the potential of large HPs is acknowledged by the BSG, US Consensus Panel and ESGE in that they are included in the guidelines, with a 3-year surveillance interval recommended in two of the three guidelines and 5-year intervals in one for HPs ≥10mm. The US Consensus Panel goes further, recommending that patients with proximal small HPs (defined as proximal to the sigmoid and <10mm) should undergo surveillance depending on size and number.

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#### 4.12.4 Evidence summary and recommendations

Evidence summary	Level	References
Three of four cohort studies reported no incidences of colorectal cancer within 3–5 years for those classified at index as having clinically significant serrated adenomas, sessile serrated adenomas or serrated adenomas with or without non-advanced or advanced adenoma.	II, III-2	[21], [14], [13], [12]

Evidence summary	Level	References
<p>For those with sessile serrated adenomas coexisting with high-risk adenoma at index, a 1.00% incidence of colorectal cancer (one case) at a mean and standard deviation of 3.54 (<math>\pm</math>1.43) years was reported.</p>		
<p>For those with sessile serrated adenomas at index, incidence of conventional adenoma was 34.67% after surveillance at 4.0<math>\pm</math>1.17 years.</p>	II	[12]
<p>In subgroup analysis according to adenoma risk at index colonoscopy, incidences of conventional adenoma were:</p> <ul style="list-style-type: none"> <li>■ 59.09% after follow-up of 3.94<math>\pm</math>1.39 years among those with sessile serrated adenoma and low-risk adenomas</li> <li>■ 68.09% after follow-up of 3.54<math>\pm</math>1.43 years among those with sessile serrated adenoma and high-risk adenomas.</li> </ul>	III-2	[13]
<p>Index features significantly associated with an increase in risk for metachronous conventional adenoma at an overall follow-up of 4.0<math>\pm</math>1.17 years were:</p> <ul style="list-style-type: none"> <li>■ sessile serrated adenoma with cytological dysplasia (RR 9.03; 95% CI=1.03–16.03, p=0.04)</li> <li>■ sessile serrated adenoma with synchronous conventional adenoma (RR 7.03; 95% CI 1.68–31.51, p=0.004).</li> </ul>	II	[12]
<p>The cumulative incidence of advanced adenoma at 1–5 years increased at a similar rate for patients with index serrated adenoma only (0.0–10.0%) and those with both serrated adenoma and non-advanced adenoma (0.0–7.0%).</p> <p>For those with serrated adenoma with advanced adenoma, cumulative incidence increased from 8.3–27.0% at 1–2 years and remained steady at 27.0% at 2–5 years.</p>	III-2	[14]
<p>There were no statistically significant differences in cumulative incidence of advanced serrated adenoma over 1–5 years between patients with index features of sessile serrated adenomas &lt;10mm, and those with hyperplastic polyp or sessile serrated adenoma <math>\geq</math>10mm, traditional serrated adenoma or sessile serrated adenoma with low grade dysplasia (p=0.59).</p>	III-2	[14]
<p>One study reported that, after 6 years follow-up, patients with an index sessile serrated adenoma only had a cumulative advanced neoplasm-free rate of 91.7% over the same period (6 years).</p>	II	[12]

Evidence summary	Level	References
<p>For those with an index sessile adenoma and synchronous low-risk adenomas, the cumulative advanced neoplasm-free rate was 100%.</p> <p>For those with index sessile serrated adenomas and synchronous high-risk adenomas, the cumulative advanced neoplasm-free rate was 0%.</p>		
<p>For those with sessile serrated adenomas at index, the incidence of sessile serrated adenoma was 42.67% after follow-up 4.0±1.17 years.</p>	II	[12]
<p>In subgroup analysis according to adenoma risk status at index colonoscopy, incidences of sessile serrated adenoma were:</p> <ul style="list-style-type: none"> <li>■ 33.33% among those with sessile serrated adenoma and low-risk adenoma, at follow-up of 3.94 ±1.39 years</li> <li>■ 32.98% among those with sessile serrated adenoma and high-risk adenomas, at follow-up of 3.54 ±1.43 years.</li> </ul>	III-2	[13]
<p>In the one study that reported metachronous sessile serrated adenoma as an outcome, there was no significant evidence to suggest an increase in risk at an overall mean follow-up time of 4 (±1.17) years based on the following index features:</p> <ul style="list-style-type: none"> <li>■ flat morphology</li> <li>■ right side location</li> <li>■ &gt;10mm</li> <li>■ &gt;3 in number</li> <li>■ cytological dysplasia</li> <li>■ synchronous conventional adenoma</li> <li>■ synchronous advance adenoma.</li> </ul>	III-2	[13]
<p>The incidence of advanced serrated polyps for those with index serrated adenoma only was 5.41% at a mean follow-up time of 3.86 (±1.39) years.</p>	III-2	[14]
	II	[14]

<p>Among patients with serrated adenomas at index and advanced serrated polyps at follow-up:</p> <ul style="list-style-type: none"> <li>■ the incidence of advanced serrated polyps differed minimally according to adenoma status: 10.00% at follow-up of 3.63±1.47 years among those with both serrated adenoma and non-advanced adenoma at index, and 12.50% at follow-up of 1.98±1.41 years among those with both serrated adenoma and advanced adenoma at index.</li> <li>■ all patients across all groups at follow-up had sessile serrated adenomas ≥10mm</li> <li>■ proximal sessile serrated adenomas were detected at follow-up in two-thirds of patients with serrated adenomas only at index or both serrated adenoma and non-advanced adenomas at index, and in half of patients with both serrated adenoma and advanced adenomas at index</li> <li>■ at follow-up, hyperplastic polyps ≥10mm occurred in one-third of patients with both serrated adenoma and non-advanced adenoma at index, and in half of those with serrated adenoma only, or with both serrated adenoma and advanced adenoma at index.</li> </ul>		
<p>The cumulative incidence of advanced serrated polyps at 1–5 years increased at a similar rate for patients with index serrated adenoma only (0.0–7.00%) and those with both serrated adenoma and non-advanced adenoma (0.0–11.00%).</p> <p>For those with serrated adenoma with advanced adenoma, cumulative incidence of advanced serrated polyps remained steady at 9.00% from 2–5 years.</p>	II	[14]
<p>There were no evidence to suggest statistically significant differences in the cumulative incidence of advanced serrated polyps over 1–5 years between patients with index features of sessile serrated adenomas &lt;10mm, and those with hyperplastic polyp or sessile serrated adenoma ≥10mm, traditional serrated adenoma or sessile serrated adenoma with low-grade dysplasia (p=0.11).</p>	II	[14]

<b>Evidence-based recommendation</b>	<b>Grade</b>
<p><i>Sessile and traditional serrated adenomas (with or without conventional adenomas)</i></p> <p>First surveillance intervals should be no greater than 5 years and should be based on features of synchronous conventional adenomas (if present) following complete removal of sessile and traditional serrated adenomas.</p>	<b>D</b>

### Consensus-based recommendation

#### *Sessile and traditional serrated adenomas (with or without conventional adenomas)*

First surveillance intervals should be based on the number, size and presence of dysplasia in the serrated polyps and synchronous conventional adenomas (if present) following complete removal of sessile and traditional serrated adenomas.

#### **Clinically significant serrated polyps only**

5 years for:

- ‡ 1-2 sessile serrated adenomas all <10mm without dysplasia.

3 years for:

- ‡ 3-4 sessile serrated adenomas, all <10mm without dysplasia
- ‡ 1-2 sessile serrated adenomas  $\geq$ 10mm or with dysplasia, or hyperplastic polyp  $\geq$ 10mm
- ‡ 1-2 traditional serrated adenomas, any size.

1 year for:

- ‡  $\geq$ 5 sessile serrated adenomas <10mm without dysplasia
- ‡ 3-4 sessile serrated adenomas, one or more  $\geq$ 10mm or with dysplasia
- ‡ 3-4 traditional serrated adenomas, any size.

#### **Clinically significant serrated polyps and synchronous conventional adenomas**

5 years for:

- ‡ 2 in total, sessile serrated adenoma <10mm without dysplasia.

3 years for:

- ‡ 3-9 in total, all sessile serrated adenomas <10mm without dysplasia
- ‡ 2-4 in total, any serrated polyp  $\geq$ 10mm and/or dysplasia
- ‡ 2-4 in total, any traditional serrated adenoma.

1 year for:

- ‡  $\geq$ 10 in total, all sessile serrated adenomas <10mm without dysplasia
- ‡  $\geq$ 5 in total, any serrated polyp  $\geq$ 10mm and/or dysplasia
- ‡  $\geq$ 5 in total, any traditional serrated adenoma.



### Consensus-based recommendation

#### **Synchronous high-risk conventional adenoma (tubulovillous or villous adenoma, with or without HGD and with or without size $\geq 10\text{mm}$ )**

3 years for:

- ✦ 2 in total, sessile serrated adenoma  $< 10\text{mm}$ , without dysplasia
- ✦ 2 in total, serrated polyp  $\geq 10\text{mm}$  and/or dysplasia
- ✦ 2 in total, any traditional serrated adenoma.

1 year for:

- ✦  $\geq 3$  total adenomas, sessile serrated adenoma any size with or without dysplasia
- ✦  $\geq 3$  total adenomas, one or more traditional serrated adenoma.

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### Practice point

Surveillance is recommended for 'clinically significant' serrated polyps:

- ✦ sessile serrated adenomas
- ✦ traditional serrated adenomas
- ✦ hyperplastic polyps  $\geq 10\text{mm}$ .

### Practice point

High-quality endoscopy is imperative to identify accurately and to completely remove sessile and traditional serrated adenomas and synchronous conventional adenomas.

**Practice point**

Polyp/adenoma size as per the endoscopist documentation should be used for determining surveillance intervals. All endoscopists should ensure size measurements are accurate using a reference standard (eg an open biopsy forceps or snare).

**Practice point**

Polyps removed should be submitted separately for histologic assessment to inform surveillance recommendations.

**Practice point**

High-quality pathology interpretation is critical to correctly diagnose sessile and traditional serrated lesions and advanced serrated polyps.

**Practice point**

High-quality reporting from endoscopists and pathologists is required to allow accurate risk stratification for surveillance interval recommendations.

**Practice point**

Surveillance intervals should be determined after the colon has been cleared of all significant neoplasia, once histology is known and in the context of individualised assessment of benefit to the patient.

#### Practice point

Small, particularly distal, true hyperplastic polyps do not require surveillance.

#### Practice point

Clinicians should be aware of the cumulative serrated polyp count and diagnostic criteria for serrated polyposis syndrome and recommend surveillance. See *Clinical practice guidelines for the prevention, early detection and management of colorectal cancer*, Serrated polyposis syndrome for diagnostic criteria and recommended surveillance.

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### 4.12.4.1 Notes on recommendations

The systematic review, although limited, demonstrated differences in the risk of metachronous neoplasia dependent on features of the SSAs and TSAs and the presence of synchronous conventional (tubular, tubulovillous and villous) adenomas, suggesting surveillance should occur within 5 years.

These recommendations are conservative, but prudence is warranted at present. The consensus-based recommendations to guide clinical practice are also informed by potentially prognostic features of serrated adenomas recognised in the general literature review:

- The risk of MAA is increased when an individual has both SSA and high-risk conventional adenoma at baseline colonoscopy, compared with high-risk conventional adenomas alone.
- The risk of metachronous SSA is much higher in those who have had an SSA alone, or SSAs synchronous with low or high risk conventional adenomas, than in those with conventional adenomas without SSAs at baseline colonoscopy.
- The risk of metachronous ASPs seems to increase over time for those with SSA or TSA at baseline colonoscopy. Studies are underpowered to determine if the characteristics of serrated polyps at baseline can predict a clinically significant risk of metachronous advanced serrated polyps.
- The risk of metachronous 'advanced neoplasia' including both advanced adenomas and ASPs seems to be higher in those with combined SSA and conventional adenomas at baseline.
- There is variability in international guidelines with acknowledgement of the limited evidence base. Expert opinion regarding the importance of serrated polyps of large size, associated with dysplasia and multiplicity has led to these factors being incorporated into existing international guidelines.
- Expert opinion recognises the unclear potential of large ( $\geq 10$ mm) hyperplastic polyps.
- Expert opinion and some direct evidence supports increased surveillance when the number of serrated polyps meets the definition of serrated polyposis.

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#### **4.12.4.1.1 Summary of recommendations for first surveillance intervals following removal of clinically significant serrated polyps (with or without conventional adenomas)**

**Table 9. Summary of recommendations for first surveillance intervals following removal of clinically significant serrated polyps ( $\pm$  conventional adenomas)**

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#### 4.12.4.2 Health system implications

##### **4.12.4.2.1 Clinical practice**

These guidelines are the first ever to separate conventional and serrated adenomas. There will be a learning curve for health care providers. The aim of the tables and colour-coding in this section is to facilitate transition from the old to new guidelines. An educational program and simple decision aids, such as wall charts and online decision tools, would help healthcare provider become familiar with the recommendations for surveillance intervals. These could be developed, promoted and distributed in conjunction with the relevant professional bodies and healthcare providers in the public and private domains.

The importance of high-quality endoscopy and pathology reporting cannot be overstated. Training and accreditation programmes should reflect these needs.

##### **4.12.4.2.2 Resourcing**

The resourcing implications of these guidelines are unclear but important to establish. There is likely to be an increased cost for pathologic assessment if a substantial proportion of health care providers currently do not submit all polyps removed for pathologic assessment or do not separate specimens.

##### **4.12.4.2.3 Barriers to implementation**

The main barrier for implementation of these recommendations will be dissemination across Australia and familiarisation for health care providers. This will be facilitated by a coordinated implementation and evaluation program.

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#### 4.12.4.3 Summary of findings from studies reported in systematic review

<b>Table 10. Findings of the studies reported in the systematic review</b>			
			<b>Baseline colonoscopy findings</b>

Study	Design	Outcome	Low-risk/ non-advanced conventional adenoma	High-risk/ advanced conventional adenoma	Isolated serrated polyps	Combined serrated polyp and low- risk conventional adenoma	Combined serrated polyp and high-risk conventional adenoma
Macaron 2015 <sup>[14]</sup> (USA)	Single centre retrospective 2004–2007 n=157 TSA 17 /157=10.8%	Advanced adenoma	NAA (n=69) 6/69=8.7% FU 56.9±16.7m	AA (n=29) 6 /29=20.7% FU 34.3±20.8m	SP* only (n=111) 3.86 (±1.39) Y 46.3±16.7m 6.31%	SP with NAA (n=30) 3.63 (±1.47) Y 43.6±17.6m 6.67%	SP with AA (n=16) 1.98 (±1.41) Y 23.8±16.9m 18.75%
		Advanced serrated polyps <sup>†</sup>	1/69=1.4%	0/29=0%	6/111=5.4%	3/30=10%	2/16=12.5%
Pereyra 2016 <sup>[12]</sup> (Argentina)	Single centre prospective 4 /2007–12 /2009 n=75 SPs	Advanced neoplasia	NAA (n=140) 11 /140=7.9% FU 53.96m	AA (n=87) 20/87=23% FU 45.32m	SSA only (n=47) 4 (±1.17) Y 45.36m 3/47=6.4%	SSA with LRA (n=14) 4 (±1.17) Y 49.85m 0/14=0%	SSA with HRA (n=14) 4 (±1.17) Y 46.42m 7/14=50% RR 4.88 (1.05–26.9, p=0.02)
Melson 2016 <sup>[13]</sup> (USA)	Single centre retrospective 1/2005–12 /2011 n=166	“Advanced neoplasia” 3 CRC	LRA (n=370) 29/370=7.8% FU 53.9±22.1m CRC 2 (6.9%)	HRA (n=252) 40 /252=15.9% 40.1±20.9m	SSA <sup>^</sup> only (n=106) 26 /106=24.5% Low risk SP only 10 /56=17.9% (p=0.024)	LRA including SSAs: (n=66) FU 3.94 (±1.39) 47.3±16.7m 12/66=18.2% (p=0.019) LRA with SSA	HRA including SSAs (n=94) FU 3.54 (±1.43) 42.5±17.2m n=94 30/94=31.9% CRC 1 (1 /94=3.3%)

	^TSA 6 /166=3.6% (excluded in MAN analysis)				High risk SP only <sup>‡</sup> 16 /50=32%	2/10=20%	HRA with SSA  14/44=31.8%
		SSA	LRA 16 /370=4.3%	HRA 15 /252=6.0%		22/66=33.3% (p=0.001)	31/94=33.0% (p=0.001)
<p>*SP at baseline: SSA±dysplasia, TSA, HP≥10mm AA: ≥10mm/villous/HGD NAA: &lt;10mm without HGD or villosity; <sup>†</sup>ASP: SSA or HP ≥10mm, SSA with dysplasia or TSA of any size; <sup>‡</sup>High-risk SP: TSA and SSA with dysplasia LRA with SSAs - included <b>either</b> a low-risk SSA and a low-risk adenoma <b>or</b> only a low-risk SSA; LRA only included 1-2 TA &lt;10mm without dysplasia.</p> <p>AA: advanced adenoma; ASP: advanced serrated polyp; CRC: colorectal cancer; HRA: high-risk adenoma; LRA: low-risk adenoma; m: months; MAN: metachronous advanced neoplasia; NAA: non-advanced adenoma; SP: serrated polyp; SSA: sessile serrated adenoma; TSA: traditional serrated adenoma; Y: years.</p>							

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#### 4.12.4.4 International guidelines for surveillance after removal of serrated polyps at baseline colonoscopy

Guideline	Serrated Polyp Category									SP	Associated conventional adenoma
	HP				SSA			TSA			
	Location	Sized <5mm	5-9mm	≥10mm	Dysplasia	Sized <10mm	Sized ≥10mm	Sized <10mm	Sized ≥10mm		
Cancer Council Australia (2011) <sup>[1]</sup>	Any	No surveillance			N/A			N/A		1 Y	N/A
BSG (2017) <sup>[3]</sup>	Any	No surveillance		3 Y	3 Y	No surveillance	3 Y	3 Y		1 Y	Consider each group separately
ESGE (2013) <sup>[18]</sup>	Any	Screening or 10 Y		3 Y	3 Y	Screening or 10 Y	3 Y	Screening or 10 Y	3 Y	N/A	N/A
	Proximal	10 Y if ≤3				5 Y if 1-2	3 Y				

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US consensus panel (2012) <sup>[19]</sup>	to sigmoid	5 Y if $\geq 4$	5 Y	5 Y	1-3 Y	3 Y if $\geq 3$	1-3 Y if $\geq 2$	5 Y if 1-2	3 Y	1 Y	N/A
	Distal	10 Y	10 Y								
USMTF/AGA (2012) <sup>[22]</sup>	Proximal to sigmoid				3 Y	5 Y if 1	3Y	3 Y	3 Y	1 Y	N/A
	Distal					3 Y if $\geq 2$					
European (2010) <sup>[23]</sup>		10 Y if distal to rectosigmoid						10 Y	1-3 Y if $\geq 3$	3 Y	NR N/A

HP: Hyperplastic polyp; N/A: non-applicable; NR: not recorded; SPs: serrated polyp; Y: years. SSAs: sessile serrated adenoma; TSA: traditional serrated adenoma.

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## 4.12.6 Appendices

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## 4.13 First surveillance intervals following removal of large sessile or laterally spreading adenoma

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### 4.13.1 Definition

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Large sessile and laterally spreading lesions (LSLs) are defined as those that are broadly attached to the mucosa. In general, the height of the lesion does not exceed 50% of the base and is usually much less. The Paris system is the accepted international standard for the classification of lesion morphology (see Figure 1, Colonoscopic surveillance after polypectomy – Introduction).<sup>[1][2]</sup> LSLs  $\geq 10$ mm are subdivided based on their height above the mucosa as 0–11a (flat  $< 2.5$ mm above the mucosa), 1s (sessile  $> 2.5$ mm above the mucosa) or 0–11a + 1s (lesions with a combination of both morphologies). The uncommon 0–11b lesions (not elevated and completely flat) are also within this subgroup. The surface features of LSLs are further characterised as granular and non-granular. This has important implications for the risk of submucosal invasive disease (cancer), presence of submucosal fibrosis and ease of resection.<sup>[3][2][4]</sup>

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### 4.13.2 Background

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The 2011 Australian national clinical practice guidelines for surveillance colonoscopy<sup>[5]</sup> recommended follow-up colonoscopy at 3–6 months and again at 12 months following piecemeal removal of large and sessile adenomas to ensure complete removal.

Approximately 5% of colonic polyps encountered during colonoscopy are LSLs  $\geq 10$  mm. They may exhibit extensive growth along the bowel wall before developing an invasive component.<sup>[6]</sup> Large ( $\geq 20$  mm) LSLs are considered high-risk precursors of colorectal cancer (CRC). However, the majority are non-invasive and the absence of lymphatics in the colonic mucosa precludes lymph node metastasis enabling even very extensive LSLs to be completely resected and cured within a structured surveillance program, by endoscopic mucosal resection (EMR).<sup>[7]</sup> All LSLs are candidates for definitive management by EMR.

EMR is an outpatient day procedure, which is proven as a safe and effective alternative to surgery for most LSLs. Prospective multicentre studies have defined the therapeutic capacities and limitations and highlighted the dramatic mortality and cost reduction when compared to surgery.<sup>[8][9]</sup> Excellent long-term outcomes have been demonstrated<sup>[10][11][12]</sup> including an approximately 4% risk of late recurrence at 18 months in individuals with EMR scars that are clear at first colonoscopic surveillance at 4–6 months.

Adverse events have been reported. Post-EMR bleeding occurs in 5–6% of patients. It is rarely life-threatening, but can be managed by supportive measures alone in two thirds with endoscopic intervention reserved for those with ongoing bleeding.<sup>[13]</sup> The main risk factor is right colon location with an odds ratio of 3–4 compared with those in the left colon.<sup>[14]</sup> Perforation occurs in 1–2%, but if it or its stigmata are recognised intra-procedurally by validated imaging criteria then endoscopic closure can be effected without sequelae.<sup>[15][16]</sup>

The major limitation of colonic EMR is the high rate of adenoma recurrence of approximately 15–30% encountered at first surveillance colonoscopy.<sup>[7][11][12]</sup> This risk is closely related to the need for multi-piece excision. As size increases the possibility of single piece excision diminishes and it is rarely possible by EMR for

LSLs >20mm. Endoscopic submucosal dissection (ESD) may achieve en-bloc resection, but is time-consuming, technically demanding, more expensive, mandates multiday hospital admission and in long term follow up offers no demonstrable clinical benefit over EMR for the overwhelming majority.<sup>[17][18]</sup> Fortunately, EMR recurrences are usually small, and easily treated at scheduled surveillance colonoscopy.<sup>[7][12]</sup> A structured surveillance protocol is a proven effective long-term strategy for eradication of recurrence.

Invisible, residual microscopic adenoma present at the resection margin may account for most recurrence encountered following EMR. The Complete Adenoma Resection (CARE) study clearly demonstrated that, even for smaller lesions, incomplete resection with biopsy proven residual adenoma at the edges occurs frequently (10%) and that increasing lesion size correlates with higher incomplete resection rates of up to 23.3% for lesions 15–20mm.<sup>[19]</sup> Extra-wide field EMR involves wider excision at the edges of the lesion including at least 5mm of normal-appearing tissue. This technique was not effective in reducing recurrence, most likely due to residual, endoscopically invisible microscopic adenoma at the lesion margin particularly in the areas between sequential snare placements.<sup>[20]</sup> Full publication of an Australian multicentre randomised controlled trial of complete thermal ablation of the entire EMR defect margin is awaited.<sup>[21]</sup>

Risk factors for recurrence after EMR include lesion size  $\geq 40$  mm, piecemeal resection and the presence of high-grade dysplasia (HGD) in the resected specimen.<sup>[7][11][22][23][24]</sup> Operator technique is also likely to be very important as can be inferred from the CARE study where there was a 4-fold difference in residual adenoma amongst endoscopists even though they knew their performance was being monitored.<sup>[19]</sup> Utilising a standardised imaging protocol incorporating narrow band imaging, even subtle recurrence is readily detected during follow-up.<sup>[25]</sup>

LSLs frequently have significant synchronous advanced pathology, including other LSLs, advanced adenomas, early cancers and serrated polyposis syndrome.<sup>[26]</sup> When an advanced lesion is found, a careful assessment of the entire mucosal surface of the colon is mandatory.

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### 4.13.3 Evidence

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*What is the appropriate colonoscopic surveillance after the removal of large sessile or laterally spreading adenomas? (SAD3)?*

#### 4.13.3.1 Systematic review evidence

The systematic review reported outcomes from 13 studies over 16 articles<sup>[10][7][24][27][28][29][30][31][32][33][34][35][36][37][38][39]</sup> examining surveillance colonoscopy for patients with large ( $\geq 20$  mm) sessile and/or laterally spreading adenomas. There were seven prospective cohort studies and six retrospective cohort studies. Study types differed based on outcome.

For surveillance, there were 11 studies that were of aetiological type with all seven level II prospective studies and all six level III-2 retrospective studies, and level III-3 retrospective prognostic study. For cohort study outcomes, nine studies were at low risk of bias, no studies were at moderate risk of bias, and three studies were at high risk of bias.

For cohort study risk factor outcomes, only a single study had a low risk of bias, three studies had a moderate risk of bias, and the remaining nine studies were at high risk of bias.

Generalisability to the Australian population and healthcare environment varied between studies. Interpretation of the outcomes is genuinely uncertain due to a lack of consistency in the studies.

In summary, the systematic review did not demonstrate any additional information to guide decision-making. Accordingly the recommendations and practice points are based on consensus expert opinion.

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#### 4.13.4 Evidence summary and recommendations

Evidence summary	Level	References
<p>Three-month residual/recurrent adenoma incidence by patient varied between 9.86% and 30.13%, and residual/recurrent neoplasm incidence was 31.91%. By adenoma, 3 month residual/recurrent adenoma incidence was 22.22%. Incidence based on resection type was either not consistent or could not be determined, while patient numbers between studies varied in size.</p>	<p>II, III-2</p>	<p>[27], [34], [40], [39], [29]</p>
<p>The incidence of residual/recurrent adenoma within 4–6 months varied between three studies reporting by patient with incidences of 4.92% and 28.00% for those undergoing piecemeal resection and 0.00% and 18.75% for those undergoing en bloc resection. All three studies had fewer than 100 patients. In one study that reported by adenoma, the incidence at 4–6 months was 11.11% for those that underwent piecemeal resection and 9.09% (n=342) for those that underwent en bloc resection (n=55).</p>	<p>II, III-2</p>	<p>[36], [28], [33], [41]</p>
<p>For other studies with dissimilar surveillance times or that could not be compared, residual/recurrent adenoma incidences by patient were 25.00% at &gt;6 months and 0.00% at ≥9 months. The incidence of residual/recurrent neoplasm was 23.53% at 15 months. By adenoma, incidences at 12 and 36 months were 11.11% and 0.00%.</p>	<p>II, III-2</p>	<p>[28], [38], [42]</p>
<p>There was no significant difference between &lt;12 and &gt;12 months surveillance for residual/recurrent adenoma (by patient; p=0.266) nor when adenoma size was adjusted (OR=0.42, 95% CI=0.11–1.65, p=0.213).</p> <p>Similarly, there was no evidence to suggest significant differences between en bloc and piecemeal resection for residual/recurrent adenoma, nor when adjusted for adenoma size (OR=1.70; 95% CI 0.46–6.27; p=0.423) as well as location, shape, histology and ablation used (OR=1.13; 95% CI 0.4–3.3; p=0.82).</p> <p>This was also the case when EMR and ESD were compared (OR=2.14; 95% CI 0.18–24.74; p=0.544).</p>	<p>II, III-2, III-3</p>	<p>[31], [37], [29]</p>

Evidence summary	Level	References
The risk between en bloc and piecemeal resection types was found to be almost 3.5 times greater for patients undergoing piecemeal (compared to en bloc) resection at minimum 4–6 months, which was statistically significant when adjusted (HR=3.4; 1.5–7.6; p=0.002).	II	[35]
Cumulative incidence of residual/recurrent adenoma was reported to be 16.1%, 20.4%, 23.4% and 28.4% at 6, 12, 18 and 24 months and for those with sessile serrated adenomas/polyps this was 6.3% at 6 months and 7.0% at 12, 18 and 24 months. The overall cumulative incidence of sessile serrated adenomas/polyps were found to be significantly lower than adenomas over time (p<0.001).	II	[35]
There were no studies that reported cancer incidence relating to the population of interest.		

#### Consensus-based recommendation

##### *Large sessile and laterally spreading lesions*

First surveillance interval should be approximately 12 months in individuals who have undergone **en-bloc** excision of large sessile and laterally spreading lesions.

#### Consensus-based recommendation

##### *Large sessile and laterally spreading lesions*

First surveillance interval should be approximately 6 months in individuals who have undergone **piecemeal** excision of large sessile and laterally spreading lesions.

#### Practice point

Consideration should be given to referring large sessile and laterally spreading lesions to experienced clinicians trained in and regularly undertaking high quality EMR to reduce the risk of recurrence.

**Practice point**

Patients with large sessile and laterally spreading lesions should be informed of the requirement for scheduled surveillance before proceeding to EMR.

**Practice point**

At surveillance following piecemeal or en-bloc excision of large sessile and laterally spreading lesions, the EMR scar should be identified, photodocumented and systematically evaluated for recurrence, including biopsies. These individuals are at high risk for synchronous and/or metachronous lesions and require very careful evaluation of the remaining colon at the same time.

**Practice point**

Endoscopic mucosal resection (EMR) of large sessile and laterally spreading lesions (>20mm) is usually piecemeal and all lesions that undergo piecemeal excision are at higher risk of recurrence and require scheduled surveillance. Risk factors for recurrence after EMR are piecemeal excision, larger lesion size (>40mm) and the presence of high-grade dysplasia in the resected specimen.

**Practice point**

In patients who have undergone piecemeal excision of large sessile and laterally spreading lesions (in whom the first surveillance colonoscopy at 6 months is clear), the next surveillance colonoscopy should be considered around 12–18 months, especially in those who had large lesions (>40mm) or high-grade dysplasia at index EMR.

**Practice point**

Consideration should be given to tattooing all lesions which may need to be identified subsequently. Those that may need surgical resection should be tattooed distal to the lesion in three locations around the circumference of the bowel to facilitate recognition.

**Practice point**

Consistently high-quality colonoscopy is imperative for optimal cost effectiveness and for implementation of uniform surveillance guidelines.

**Practice point**

Polyp/adenoma size as per the endoscopist documentation should be used for determining surveillance intervals. All endoscopists should ensure size measurements are accurate using a reference standard (eg an open biopsy forceps or snare).

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#### 4.13.4.1 Notes on the recommendations

High-quality scientific evidence to determine the optimal surveillance interval following removal of large sessile and LSLs is limited. There are no randomised controlled trials comparing one surveillance interval with another.

There is no high-quality evidence to guide the timing of second surveillance colonoscopy. [Back to top](#)

### 4.13.5 Health system implications

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#### 4.13.5.1 Clinical practice

Implementation of these recommendations would not significantly affect current practice.

#### 4.13.5.2 Resourcing

Implementation of these recommendations would not require additional resources.

### 4.13.5.3 Barriers to implementation

No barriers to the implementation of these recommendations are envisaged.

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### 4.13.6 References

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## 4.14 Family history and surveillance intervals

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- 2 Evidence
  - 2.1 Systematic review evidence
  - 2.2 Overview of additional evidence (non-systematic literature review)
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## 4.14.1 Background

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A family history of colorectal cancer (CRC) occurs in 3–12% of the population.<sup>[1][2]</sup> Increased risk of CRC is graded and proportional to the number of relatives affected, age at onset and relatedness.<sup>[1]</sup> Detecting those at increased risk is important, although Australian work has demonstrated family history recording is inconsistent.<sup>[3]</sup> Higher risk individuals undergoing screening have an increased prevalence of adenomas found compared to those without a family history.<sup>[1]</sup>

At the time of the previous edition of these guidelines (Australian clinical practice guidelines for surveillance colonoscopy, 2011)<sup>[4]</sup> there was no consistent evidence that surveillance recommendations for patients with adenomas should differ for those with a family history unless a syndrome is suspected.

For guidance on family history screening recommendations from the Clinical practice guidelines for the prevention, early detection and management of colorectal cancer (2017), refer to Recommendations for risk and screening based on family history of colorectal cancer.

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## 4.14.2 Evidence

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### 4.14.2.1 Systematic review evidence

Two level II studies at high risk of bias<sup>[5][6]</sup> and one level III-3 study<sup>[7]</sup> at moderate risk of bias were included in the systematic review. The three studies compared outcomes of metachronous adenoma (MA), metachronous advanced adenoma (MAA) and metachronous advanced neoplasia (MAN) in those with and without a family history of CRC. The studies were consistent and although the population was not directly generalisable, the evidence can be sensibly applied and is relevant in the Australian healthcare context. Overall, the studies demonstrated no significant difference in the risk of metachronous adenoma, advanced adenoma or advanced neoplasm in those with a family history of CRC compared to those without.

### 4.14.2.2 Overview of additional evidence (non-systematic literature review)

The literature distinguishing between different risks of family history is sparse outside of known or likely syndromes. One group<sup>[8]</sup> randomised those with a family history of CRC (one first-degree relative [FDR] aged <50 years or two FDRs at any age) to surveillance at 3 or 6 years following baseline colonoscopy at which  $\leq 2$  adenomas were found. Advanced adenoma at the baseline colonoscopy was associated with MAA, but type of family history (reference 1 FDR age <50 years), age and sex were not. In Australian work by Good et al,<sup>[9]</sup> the non-adjusted odds ratio for MAN in those with 1 FDR and age <55 years was significant at 1.75 (1.18–2.61) when compared to those with a personal history of adenoma and no family history. This level of increased risk is considered insufficient to modify surveillance intervals based on the personal history of adenomas. A Swedish study<sup>[10]</sup> also demonstrated an increased risk of MAA in those with two close relatives with relative risk of 2.19 (1.68–2.87) but not one close relative age <50 years, with RR 1.46 (0.89–2.31), both age-adjusted.

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### 4.14.3 Evidence summary and recommendations

Evidence summary	Level	References
The presence of a family history of colorectal cancer did not alter the risk of any metachronous adenoma within 5 years of polypectomy, following surveillance colonoscopy.	II, III-3	[6], [7]
The presence of a family history of colorectal cancer did not alter the risk of metachronous advanced adenoma within 5 years of polypectomy, following surveillance colonoscopy.	II, III-3	[6], [7], [11]
No studies reported colorectal cancer risk or incidence in those with a family history of colorectal cancer and previous adenoma(s).		

Evidence-based recommendation	Grade
<p><i>Family history of CRC</i></p> <p>First surveillance intervals following adenoma removal in those with a family history of colorectal cancer should be based on patient factors and the adenoma history, unless a genetic syndrome is known or suspected.</p>	<b>D</b>

Practice point
<p>To identify those who may have an increased familial risk of colorectal cancer, a family history of colorectal cancer and associated malignancies including number of affected relatives, relatedness and age of onset should be taken and updated every 5 to 10 years.</p>

#### Practice point

In individuals who are undergoing screening colonoscopy for colorectal cancer based on family history, adenoma surveillance and screening recommendations should be compared and the shorter interval used. Refer to Clinical practice guidelines for the prevention, early detection and management of colorectal cancer (2017) (see Recommendations for risk and screening based on family history of colorectal cancer).

#### Practice point

To address individual's concerns, clinicians should take adequate time to explain the relationship of family history to recommended surveillance intervals and refer for counselling where appropriate.

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## 4.14.4 References

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## 4.14.5 Appendices

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## 4.15 Subsequent surveillance colonoscopies

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### 4.15.1 Definitions

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Subsequent surveillance intervals herein refer to intervals for colonoscopies a patient would undergo following the baseline and first surveillance colonoscopies.

In this section

- 1st colonoscopy refers to the baseline colonoscopy (initial, not surveillance)
- 2nd colonoscopy refers to the first *surveillance* colonoscopy
- 3rd colonoscopy refers to the second *surveillance* colonoscopy.

‘High-risk findings’ refers to advanced adenoma (size  $\geq 10$  mm, high-grade dysplasia [HGD], villosity) or  $\geq 3$  conventional adenomas.

Conventional adenomas include tubular, tubulovillous and villous adenomas.

Clinically significant serrated polyps include sessile serrated adenomas (SSAs), traditional serrated adenomas (TSAs), and large ( $\geq 10$  mm) hyperplastic polyps (HPs).

### 4.15.2 Background

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The 2011 Australian Clinical practice guidelines for surveillance colonoscopy<sup>[1]</sup> highlighted inconsistency in the literature guiding intervals for 2nd and subsequent surveillance colonoscopies. The importance of considering patient factors and colonoscopy history, most particularly whether the previous adenomas removed were low or high risk, was emphasised.

Generally, recommendations were tailored to risk determined by findings at the 1st and 2nd colonoscopy, with repeat of the high-risk surveillance interval for high-risk findings and in the setting of normal or low-risk findings, stopping surveillance or extending the surveillance interval as determined by the clinician on an individualised basis. No clear recommendations were given for second and subsequent colonoscopies for  $\geq 5$  adenomas, nor for serrated polyps.

In this section, intervals for conventional (tubular, tubulovillous and villous) adenomas and clinically significant serrated polyps (with or without synchronous conventional adenomas) are considered separately.

Understanding of the current literature base must consider dates of the colonoscopies performed (the quality of earlier procedures may falsely elevate incidence of metachronous neoplasia) and the lack of separate categorisation of serrated polyps.

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### 4.15.3 Overview of evidence (non-systematic literature review)

Four level III-2 studies with a high level of bias were identified.<sup>[2][3][4][5]</sup> Three studies were from Korea, with high proportions of males, and one was from the USA, with similar demographics to the Australian population. Although not directly generalisable, the results could be sensibly applied to the Australian population and healthcare system. Large numbers were included in most of the studies. Note is made of the wide range of results for risk of metachronous findings among studies in many settings mentioned below. The findings are summarised in Table 12.

In those who had low risk findings at 1st colonoscopy, the incidence of high risk findings at the 3rd colonoscopy ranged from 2.3–50.0%, depending on the findings of the 2nd colonoscopy. In those with low-risk 1st colonoscopy findings and a normal 2nd colonoscopy, it was 4.5–6.8%. The risk was only slightly higher (2.3–13.8%) in those with low risk findings on both 1st and 2nd colonoscopies. The greatest risk was in those with low risk 1st and high risk 2nd colonoscopy findings (18–50%).

In those who had high risk findings at 1st colonoscopy, the incidence of high risk findings at the 3rd colonoscopy had a similar range (9.6–50%) as when the 1st colonoscopy findings were low risk (2.3–50.0%). Within each risk category of 2nd colonoscopy findings, however, risk was elevated in high-risk 1st versus low-risk 1st colonoscopy findings. In those with high-risk 1st colonoscopy findings and a normal 2nd colonoscopy, it was 9.6–20.8%; in those with low-risk 2nd colonoscopy findings, it was 14–17.6%. The risk was greatest in those who had high risk findings on both 1st and 2nd procedures (15.8–50%).

No contemporary literature guides procedures following the 3rd colonoscopy. It is clear from the studies above that neoplasia decreases over time. Reasonably speaking, it is prudent to consider findings from the two most recent colonoscopies to recommend subsequent surveillance intervals thereby reducing complexity for clinicians. There is no literature base to inform recommendations on clinically significant serrated polyp surveillance. Therefore, the same principles as for conventional adenomas are suggested for subsequent surveillance interval recommendations.

#### 4.15.3.1 Incidence of high risk findings at third colonoscopy relative to findings at first and second colonoscopies

**Table 12. Incidence of high risk findings at the 3<sup>rd</sup> colonoscopy relative to findings at 1<sup>st</sup> and 2<sup>nd</sup> colonoscopies**

High risk findings are classed as  $\geq 3$  or advanced adenoma (size  $\geq 10$ mm, high-grade dysplasia or villosity)

Study details	Morelli (2013) <sup>[2]</sup>	Chung (2013) <sup>[3]</sup>	Park (2015) <sup>[4]</sup>	Suh (2014) <sup>[5]</sup>
	N=965	N=131	N=4143	N=852
	1985–2010	1997–2011	2001–2011	2002–2009
	<sup>a</sup> 29.1±17.7 to			<sup>a</sup> 19.2±8.8 to

Time to 2 <sup>nd</sup> colonoscopy		<sup>b</sup> 38.3±21.22m <sup>c</sup>	17 (6–101) m <sup>d</sup>	2.1y (1.7) <sup>e</sup>	<sup>b</sup> 37.1±16.9m <sup>c</sup>
Time to 3 <sup>rd</sup> colonoscopy		<sup>a</sup> 32.6±15.1 to <sup>b</sup> 46.2±18.4m <sup>c</sup>	24 (6–90) m <sup>d</sup>	2.8y (2.5) <sup>e</sup>	<sup>a</sup> 23.0±9.9 to <sup>b</sup> 33.0±15.0m <sup>c</sup>
<i>1<sup>st</sup> colonoscopy findings</i>	<i>2<sup>nd</sup> colonoscopy findings</i>	<i>3<sup>rd</sup> colonoscopy incidence of high risk findings</i>			
Low risk	Normal	6.6%		6.8%	4.5%
	Low risk	13.8%	2.3%	10.6%	8.2%
	High risk	18.0%	50%	24.3%	22.9%
High risk	Normal	9.6%		17.7%	20.8%
	Low risk	14.0%	17.5%	16.4%	17.6%
	High risk	22.0%	50%	38.2%	15.8%
<sup>a</sup> High-risk group; <sup>b</sup> low-risk group; <sup>c</sup> mean ± standard deviation (SD) (m: months); <sup>d</sup> median (min-max) months; <sup>e</sup> mean (inter-quartile range) years (y).					

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#### 4.15.4 Practice Points

##### Practice point

The findings of the previous two colonoscopies predict high-risk findings on the subsequent colonoscopy and should be considered when recommending subsequent surveillance intervals.

##### Practice point

For individuals who have undergone two or more colonoscopies, the surveillance interval for the next (3rd) colonoscopy should be based on the reports and histology from the two most recent procedures (1st and 2nd colonoscopies) as per Tables 14–16 (see Table 13 as a quick reference guide).

**Table 13 Colonoscopy findings and surveillance intervals: reference guide to Tables 14–16**

		<b>3<sup>rd</sup> colonoscopy</b>
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1 <sup>st</sup> colonoscopy findings	2 <sup>nd</sup> colonoscopy findings	surveillance interval
Conventional adenomas only	Normal colonoscopy or conventional adenomas only	Table 14
	Clinically significant serrated polyps <i>without</i> synchronous conventional adenomas	Table 15a
	Clinically significant serrated polyps <i>with</i> synchronous conventional adenomas	Table 15b
Clinically significant serrated polyps <i>with or without</i> synchronous conventional adenomas	Normal colonoscopy or conventional adenomas only	Table 16
	Clinically significant serrated polyps <i>without</i> synchronous conventional adenomas	Table 15a
	Clinically significant serrated polyps <i>with</i> synchronous conventional adenomas	Table 15b

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#### 4.15.4.1 Notes on the recommendations

Clinicians should make every effort to obtain procedure reports and histology from previous colonoscopies to inform whether a surveillance colonoscopy is indicated and the appropriate surveillance interval. If information is not available, first surveillance intervals should be used as per Table 3 (Conventional adenomas only) or Table 9 (Clinically significant serrated polyps ± conventional adenomas), although this will lengthen the surveillance interval for those with 2nd colonoscopy low-risk findings if 1st colonoscopy findings were high-risk.

#### 4.15.4.2 Recommended surveillance intervals for 3rd colonoscopy

**Table 14. Recommended surveillance intervals for 3rd colonoscopy - conventional adenomas only at 1st and 2nd colonoscopy**

**Table 15. Recommended surveillance intervals for 3rd colonoscopy.** a. (top) clinically significant serrated polyps only at 2nd colonoscopy. b. (bottom) clinically significant serrated polyps with synchronous conventional adenomas at 2nd colonoscopy.

**Table 16. Recommended surveillance intervals for 3rd colonoscopy - clinically significant serrated polyps at 1st colonoscopy, no adenomas or conventional adenomas only at 2nd colonoscopy**

## 4.15.5 Health system implications

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### 4.15.5.1 Clinical practice

These guidelines are the first ever to separate conventional adenomas and clinically significant serrated polyps. There will be a learning curve for health care providers. The aim of the tables and colour-coding in this section is to facilitate transition from the old to new guidelines. An educational program and simple decision aids, such as wall charts and online decision tools, would help healthcare provider become familiar with the recommendations for surveillance intervals. These could be administered in conjunction with the relevant professional bodies and healthcare providers in both the public and private domains.

### 4.15.5.2 Resourcing

The resourcing implications of these guidelines are unclear and ideally would be assessed in a research forum.

### 4.15.5.3 Barriers to implementation

The main barrier for implementation of these recommendations will be dissemination across Australia and familiarisation for health care providers. This will be facilitated by a coordinated implementation and evaluation programme.

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## 4.15.6 References

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## 4.16 The elderly and stopping rules

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  - 2.2 Surveillance recommendations for individuals age  $\geq 75$  years
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### 4.16.1 Background

Australia has an ageing population and life-expectancy continues to rise making the question of when to stop surveillance colonoscopy increasingly important. Although the incidence of CRC or pathology at screening or diagnostic colonoscopy increases with age,<sup>[1]</sup> there is no evidence that metachronous neoplasia is greater in the elderly. It must also be remembered that colonoscopy and adenoma removal is highly protective for lengthy periods, that most polyps do not develop into CRC and that the lead time for progression of an adenoma to CRC is perhaps 10–20 years. Therefore, there may be minimal benefit in offering surveillance for most elderly individuals. Importantly, there is also increased risk associated with performing colonoscopy in the elderly. The elderly have more co-morbidities, reduced organ reserve and increased morbidity and mortality following procedures.<sup>[1][2]</sup> The 2011 Australian Clinical Practice Guidelines for Surveillance Colonoscopy<sup>[3]</sup> concluded that most individuals aged 75 years or older would not benefit from surveillance.

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## 4.16.2 Overview of evidence (non-systematic literature review)

Systematic review was not undertaken for this question. Non-systematic review of the general literature was undertaken with limited results. The literature on colonoscopy in the elderly is mostly from the US and focuses on the role of screening colonoscopy in the elderly rather than surveillance. Some parallels can be made in terms of procedure-related complications, however.

The area of decision-making in the elderly is not well-researched in terms of surveillance colonoscopy, although one study<sup>[4]</sup> looked at understanding decision-making around recommending surveillance colonoscopy in the elderly. Importantly, specialist recommendation markedly influenced primary-care providers recommending surveillance. Other influences were life expectancy, patient preferences, safety of the procedure and previous findings.

One older review of 1199 colonoscopies on patients  $\geq 80$  years (of which 227 (19.3%) were done for surveillance), demonstrated the risk of advanced adenoma was 14% and CRC 1%.<sup>[5]</sup> A more recent paper<sup>[6]</sup> looked at the incidence of CRC in patients undergoing surveillance colonoscopy and compared findings in those aged 50–74 years with those  $\geq 75$  years of age. In the older group, the rate of CRC was 0.24 per 1000 person-years vs 3.61 per 1000 person-years in the younger group,  $p < 0.001$ . In Cox regression analysis, the HR for CRC in the elderly patients compared with the younger group was 0.06 (95% CI, 0.02–0.13,  $p < 0.001$ ), after adjusting for comorbid illness, sex, and ethnicity. This result seems counter-intuitive but may be indicative of the protection afforded by colonoscopy over time.

Life expectancy decreases with age and co-morbidity, a validated measure of which is the Charlson score,<sup>[7]</sup> which can be quickly calculated via online calculators or downloadable Apps. A single centre study followed 404 patients  $\geq 75$  years of age after colonoscopy for varying indications including surveillance and screening until death.<sup>[8]</sup> Mortality was predicted by age (HR 1.16 for each year after 75 years, 95% CI 1.07–1.3,  $p = 0.0003$ ) and Charlson score (HR 8.3 for each point increase, 95% CI 1.4–48.5,  $p = .02$ ). The median survival of patients age 75–79 years was  $> 5$  years if the Charlson score was  $\leq 4$ . Among patients age  $\geq 80$  years, the median survival was  $< 5$  years regardless of Charlson score.

A comprehensive review of the literature in terms of the elderly was recently published<sup>[2]</sup> and highlighted that the elderly are more likely to experience a poor bowel preparation, (regardless of compliance and preparation type) and that increasing age may be related to reduced completion rates. Most importantly, age was a critical factor in the occurrence of adverse events, with a 34.8 per 1000 colonoscopies composite rate (perforation, bleeding, cardiovascular and pulmonary events) in those  $\geq 80$  years. Octogenarians experienced a 70% increased risk of adverse events compared with those who were younger. The consequences of non-fatal events were noted as “more severe and protracted.”

In a large retrospective cohort study in the US, patients  $\geq 50$  years of age undergoing surveillance colonoscopy between 2001 and 2010,<sup>[6]</sup> 4834 patients  $\geq 75$  years of age were compared with 22,929 age 50–74 years. After adjustment for multiple factors, the elderly were more likely to be hospitalised post-procedure, RR 1.28 (1.07–1.53),  $p = 0.006$ , with a Charlson score of  $\geq 2$  being an independent predictor when compared with a score of 0 or 1, (adjusted OR 2.54 [2.06–3.14]).

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#### 4.16.2.1 Expert opinion and guidelines from other countries

The Norwegian Guidelines<sup>[9]</sup> for surveillance are the only international recommendations to have an age cut-off of  $\geq 75$  years of age for surveillance.

##### 4.16.2.1.1 Practice Points

###### Practice point

Careful assessment and shared decision-making should be utilised when considering surveillance colonoscopy in the elderly, most of whom will have no significant findings and will not benefit.

###### Practice point

Surveillance colonoscopy in those  $\geq 75$  years should be considered based on age, co-morbidity and the preferences of the patient. The reproducible and validated Charlson score is useful to assess life expectancy and could be implemented to assist decision-making (see Tables 17 and 18 below).

###### Practice point

In obtaining consent for colonoscopy for an elderly patient, complication rates should reflect the individual risk based on age and comorbidity rather than 'standard' figures.

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#### 4.16.2.2 Surveillance recommendations for individuals age $\geq 75$ years

**Table 17. Surveillance recommendations for individuals age  $\geq 75$  years**

Age (years)	Charlson score <sup>a</sup>	
	$\leq 4$	$> 4$
75–80	Surveillance colonoscopy to be considered <sup>b,c</sup>	Surveillance colonoscopy not recommended
$> 80$	Surveillance colonoscopy not recommended	

<sup>a</sup>Charlson for colonoscopy benefit can be simplified as per Table 18; <sup>b</sup>colonoscopy should be considered an option dependent on a clear conversation about the low risk of significant colorectal pathology, taking the patient's wishes into consideration; <sup>c</sup>consent for colonoscopy should include age appropriate statistics on risk.

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#### 4.16.2.3 Charlson score for colonoscopy benefit

**Table 18. Charlson score for colonoscopy benefit**

Age	Medical conditions
75–79 years (3 points for age)	<p><b>May have <i>one</i></b> of these conditions only (1 point each):</p> <ul style="list-style-type: none"> <li>Mild liver disease</li> <li>Diabetes without end-organ damage</li> <li>Cerebrovascular disease</li> <li>Ulcer disease</li> <li>Connective tissue disease</li> <li>Chronic pulmonary disease</li> <li>Dementia</li> <li>Peripheral vascular disease</li> <li>Congestive heart failure</li> <li>Myocardial infarction</li> </ul> <p><b>May not have <i>any</i></b> of these medical conditions (<math>\geq 1</math> point each):</p> <ul style="list-style-type: none"> <li>Moderate/severe liver disease</li> <li>Diabetes with end-organ damage</li> <li>Hemiplegia</li> <li>Moderate or severe renal disease</li> <li>AIDS</li> <li>Metastatic or non-metastatic solid organ or haematopoietic malignancy</li> </ul>
80 years (4 points for age)	May not have any of the above medical conditions

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#### 4.16.3 References

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## 4.17 Malignant polyps

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### 4.17.1 Definition

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A malignant polyp (MP) is an adenoma in which neoplastic cells have invaded through the muscularis mucosa into the submucosa. It is therefore a colorectal cancer, and such invasion is associated with the possibility of spread to locoregional lymph nodes and distant organs.<sup>[1]</sup> Lesions without submucosal invasion, even in the presence of high-grade dysplasia (HGD), have negligible potential for distant spread and are not considered MPs. Previously, terms such as ‘intramucosal carcinoma’ and ‘carcinoma in situ’ were occasionally used to describe HGD. These terms should no longer be used, due to the therapeutic confusion they may create and the potential for unnecessary surgery and over-surveillance. Such lesions are not MPs.<sup>[2]</sup>

### 4.17.2 Background

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Malignant polyps constitute less than 5% of all colorectal adenomas and approximately 40–60% of stage I colorectal cancers.<sup>[3][4][5]</sup> Their occurrence is expected to rise as the proportion of stage I cancer increases, in the setting of the National Bowel Cancer Screening Program. The clinicopathological significance of the MP usually arises after endoscopic polypectomy, when histology confirms invasive malignancy. The question becomes whether endoscopic resection alone is sufficient treatment or if surgical resection of the affected bowel segment with lymph node clearance is necessary. Ultimately, the treatment decision is based on an estimated risk of residual cancer, risk of surgical complications and informed patient choice.

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### 4.17.3 Overview of evidence (non-systematic literature review)

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#### 4.17.3.1 Endoscopic considerations

Invasive disease is rare in polyps < 10mm. Recognising the endoscopic appearances of early submucosal invasion (SMI) is important to optimise treatment outcomes. Suspicion of SMI may dictate a change in the therapeutic strategy to optimise the possibility of en-bloc and R0 excision, including endoscopic mucosal resection, endoscopic sub-mucosal dissection (ESD) or surgery. Whilst large pedunculated polyps may contain cancer, this is often not evident or recognised prior to endoscopic resection and because the lesion’s pedicle provides a natural resection margin, conventional polypectomy proceeds as it generally would, ensuring adequate clearance from the neoplastic head of the lesion. Lesion assessment is thus most important for flat and laterally spreading lesions. It is divided into an overview and focal interrogation phase.<sup>[6]</sup>

In overview, lesions are classified according to the Paris system 1 and surface morphology which allows broad stratification for the risk of SMI. Homogeneous flat (0–11a) granular lesions have a low risk of SMI of <1%, whilst the less frequent flat non-granular lesions with a depressed component (0–11a + c) or nodule (0–11a + 1s) are at increased risk for SMI, generally >20%. Gross features that suggest SMI include presence of ulceration, firm or hard surface, friability and effacement or distortion of the surrounding colonic folds.<sup>[7][1][8]</sup> Increasing size is generally associated with an increased risk of SMI, but the use of this parameter alone is too simplistic and even very extensive lesions can be non-invasive, for example, homogeneous granular 0–11a laterally spreading lesions (LSLs) of the proximal colon.

Once overview assessment is complete, focal interrogation is used to examine areas of depression or nodularity looking for a disruption in the mucosal pit or microvascular pattern. Benign lesions should generally have a homogeneous surface pattern. With SMI one may identify a demarcated zone of altered or disrupted pit or microvascular pattern (e.g. Kudo pit pattern type V).<sup>[9][10]</sup> Approximately 50% of large sessile and laterally spreading polyps with cancer do not disclose overt features of SMI, so called “covert SMI”. In a large multicentre Australian study of over 2000 lesions, once overt SMI cases were excluded, features associated with covert SMI were rectosigmoid location, protuberant morphology (Paris 0-Is and 0-IIa+Is) and increasing size (>40mm).<sup>[6]</sup> Lesions suspected of harbouring SMI may not be suitable for endoscopic excision. Piecemeal resection prevents histopathological assessment of complete excision and interferes with the prediction of lymph node metastasis.<sup>[9]</sup> In experienced hands, ESD may be an option but formal surgical resection is often required.

If malignant histology is suspected, tattoo placement to enable precise future localisation of the polypectomy site is recommended. Tattoo placement may also be useful for hard-to-see polyps being referred for expert endoscopic removal; in this instance, the tattoo must be sufficiently distant to avoid encroachment and potential fibrosis at the polyp base.

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#### 4.17.3.2 Pathologic considerations

Although the endoscopist decides if endoscopic/macrosopic resection is complete at the time of polypectomy, histological features are the most important determinant of the risk of residual disease. Given evidence of significant interobserver variation, review by a second pathologist with special interest in gastrointestinal pathology should be considered, especially where the diagnosis is unclear or difficult.<sup>[11]</sup> Consistently, the most important parameters suggesting a risk of lymph node involvement are an inadequate margin, poorly differentiated carcinoma grade and lymphovascular invasion.<sup>[1][12][13]</sup> Each of these factors alone may confer a risk of 5-20% for lymph node involvement. Other parameters reported to be important include depth of invasion (especially for sessile lesions), tumour width, tumour budding, cribriform architectural pattern, distal location (distal colon and rectum) and mucinous histology. Multiple high-risk features often coexist in a given case. Assessment of high-risk parameters can be especially difficult with sessile polyps, which present difficulties with orientation and are often fragmented. Many of the important parameters (e.g. depth of invasion by Haggitt classification for pedunculated polyps and Kikuchi classification for sessile polyps), are not routinely reported by all laboratories, yet are prognostically important.<sup>[3]</sup> Synoptic reporting assists standardisation. Variation amongst reported series means estimating absolute risk based on histopathologic findings is also difficult, but co-existent unfavourable features increases risk.

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#### 4.17.3.3 Who needs formal surgical resection?

The evidence basis for managing MPs relies entirely on retrospective series, with no available randomised trials. Nonetheless, low-risk lesions, characterised by superficial submucosal invasion (<1000 microns), clear resection margins, well- or moderate- degrees of histological differentiation (i.e., not poor) and absence of lymphovascular invasion, are best served by endoscopic resection alone, which is almost always curative.<sup>[1][13]</sup> In these cases, the risks of surgical complications far outweigh the chance of residual lymph node involvement.

There is significant recent support for a resection margin of  $\geq 1\text{mm}$  (as opposed to  $\geq 2\text{mm}$ ) as being adequate.<sup>[3]</sup><sup>[14][15][16][17]</sup> However, there remains controversy in cases where clearance at the margin is uncertain; a population-based series from The Netherlands found the only independent risk factor predicting long term cancer recurrence to be a positive resection margin<sup>[5]</sup> whilst a Brisbane series found that in the absence of other high risk histological factors, a positive resection margin may only require further local excision rather than oncological colonic resection.<sup>[18]</sup>

Whilst defining low risk MPs is now clear, the recent literature continues to show some variation in identifying high risk factors for residual cancer. For instance, the Brisbane series identified greater width and depth of malignant invasion, poor differentiation and a cribriform architecture as high risk features,<sup>[18]</sup> an English series found depth of invasion, but not lymphovascular invasion, to be important,<sup>[3]</sup> a Japanese series did not find depth of invasion per se to be important<sup>[19]</sup> and a population-based series from Modena found lymphovascular invasion to be important.<sup>[20]</sup> Tumour budding was considered an important risk factor in a single-centre Polish study<sup>[17]</sup> and a systematic review found lymphatic invasion, depth of invasion, tumour budding and poor differentiation all to be important factors, each with a relative risk of approximately 5-fold for lymph node invasion.<sup>[21]</sup>

Even in the presence of high risk pathological criteria, over 70-85% of surgical resections will offer no clinical benefit as the absolute risk of residual cancer is small. In the Brisbane series of 239 consecutive MPs, 59% of cases ultimately underwent surgical resection due to high risk indications and, of these, only 6.4% had residual disease in bowel wall and 8.6% were found to have lymph node involvement (1% had disease in both bowel wall and lymph nodes). Thus, approximately 85% of operated cases may not have needed surgery.<sup>[18]</sup> Furthermore, a proportion of cases, who undergo surgery and presumably adjuvant therapy, will still develop metastatic cancer, as can be expected for nodal colorectal cancer (stage III).<sup>[5][20]</sup> The series from England also found that 1% of MP cases already had distant metastases at diagnosis.<sup>[3]</sup>

The recommended surgery when high-risk pathologic criteria are identified is a complete oncological resection with appropriate lymph node clearance. However, the decision for surgery must balance the risk of residual cancer, which only involves the minority of cases, with patient co-morbidities. Cardiopulmonary factors are an important cause of mortality in long term follow-up of patients treated for MPs as shown in New Zealand.<sup>[22]</sup> Whilst a US population-based series using the Surveillance, Epidemiology and End Results (SEER) database showed surgery to improve cancer-free survival compared to endoscopic therapy alone,<sup>[23]</sup> no difference in overall survival was seen in an earlier population-based series with the SEER database involving a different patient set<sup>[24]</sup> or in a Korean series.<sup>[16]</sup> However, selection bias does not permit accurate causal attribution of survival to any therapeutic strategy per se, especially as surgery is likely to be avoided in patients with substantial co-morbidities.

In the most comprehensive review to date,<sup>[1]</sup> estimates of the risk of residual cancer are presented in tabular form and include resection margin  $< 1\text{mm}$  ( $> 20\%$  risk), deep invasion ( $> 20\%$  risk), poor differentiation (8-15% risk), lymphovascular invasion (5-10% risk) and tumour budding ( $< 5\%$  risk). Online risk calculators are available, examples of which can be found at Prediction in Surgery (St Mark's Lymph Node Positivity Model) or the T1 Colorectal Cancer Working Group. Estimations such as these are necessary to counterbalance surgical risk. An excellent set of online surgical risk assessment calculators can also be found at Prediction in Surgery

and includes the Colorectal Physiologic and Operative Severity Score for the Enumeration of Mortality and Morbidity (CR-POSSUM) and Association of Coloproctology of Great Britain and Ireland (ACPGBI) calculators. A particularly difficult surgical decision arises for very low rectal lesions, where the appropriate oncological operation is an abdominoperineal resection necessitating a permanent colostomy. In such cases, a compromise is an extended local excision (e.g. transanal endoscopic microsurgery) if the only issue is an inadequate clearance margin without any other high risk feature.

Thus, the management of MPs requires review by a multidisciplinary team consisting of endoscopist, pathologist and surgeon as a minimum. In the private setting this may still occur, albeit potentially on a less formal basis. Ideally, individuals and institutions should contribute to a national prospective database. Risks of residual and nodal cancer must be estimated, surgical risk needs to be assessed and final decisions only made after open discussion with the patient.

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#### 4.17.3.4 Surveillance for malignant polyps

Post-polypectomy colonoscopic surveillance for MPs is based on limited evidence. If the resection margin is clear, follow up should not be for local recurrence but for detection of metachronous adenomas and cancer. Hence, surveillance should be consistent with that for post-operative surveillance after curative surgery.<sup>[25]</sup> If there is uncertainty about endoscopic clearance and surgery is not performed, a reasonable interval for reinspection is at 3 months.<sup>[1]</sup>

#### 4.17.4 Future directions

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A substantial majority of MPs with high risk criteria do not have residual or nodal cancer at surgery. For these patients, endoscopic polypectomy alone would have sufficed and most of these cases have therefore undergone “unnecessary” surgery. Histopathological assessment alone has been unable to differentiate those who do and do not have residual cancer. It is unlikely that prospective randomisation will add much further insights given that patients refusing or unsuitable for surgery have already provided some understanding of the natural history of high risk cases. Technological advances such as functional (not anatomical) imaging or molecular techniques (e.g. circulating tumour DNA detection) will be needed to improve patient selection for further surgery.

Improved endoscopic prediction of MPs with technological advances in endoscopic instruments and techniques may enable more successful en-bloc endoscopic polypectomies and better preservation of resection margins. Appropriate patient selection for more complex endoscopic submucosal dissection rather than the more common endoscopic mucosal resection may also improve pathological confirmation of clear resection margins.

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## 4.17.5 Practice Points

### Practice point

Endoscopists should be familiar with endoscopic appearances suggestive of a malignant polyp.

### Practice point

Removal of polyps likely to be malignant should be en-bloc or patients should be referred to a centre specialising in endoscopic excision of large and flat polyps.

### Practice point

Tattoos should be applied 2-3cm distal to the polypectomy site if future site localisation or surgery is necessary.

### Practice point

Malignant polyps should be reviewed by a second pathologist with a specialist gastrointestinal interest where histological diagnosis is unclear or difficult. Multidisciplinary review and management (endoscopist, pathologist and surgeon as a minimum) is appropriate in public and private settings although the nature may differ.

### Practice point

Standardised synoptic reporting should be used to assist clinical decision making (structured reporting protocols are available at the Royal College of Pathologists of Australasia website).

**Practice point**

Low-risk malignant polyps have all of the following features: superficial submucosal invasion (<1000 microns), moderate or well differentiated histology, no lymphovascular invasion, clear margins and no other risk features. In these cases, where the endoscopist is certain that the lesion has been completely removed, then the neoplasm should be considered cured by endoscopic polypectomy.

**Practice point**

Polyps that do not satisfy low risk criteria or have other histological risk features (often not routinely reported) including: malignant invasion depth >2mm, invasion width >3mm, tumour budding and cribriform architecture, should be considered at risk of harbouring residual bowel wall cancer or lymph node metastases. A magnitude of the risk should be estimated and the need for formal surgical resection considered.

**Practice point**

Cases considered for surgery must have an assessment of surgical risk using validated surgical risk scoring systems, e.g. Risk Prediction in Surgery.

**Practice point**

A discussion of risk of residual cancer balanced against risk of surgery must occur with the patient to determine ultimate management choice.

**Practice point**

Multi-disciplinary management and audit are important.

### Practice point

Surveillance recommendations for a T1 adenocarcinoma as per 2017 Australian Clinical practice guidelines for the prevention, early detection and management of colorectal cancer should be followed for completely resected malignant polyps.

### Practice point

A patient who has had potential incomplete endoscopic resection of a malignant polyp not undergoing surgery should undergo repeat colonoscopy to assess recurrence at an interval of 3 months.

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## 4.18 Discussion

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  - 3.2 Studies currently underway
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## 4.18.1 Surveillance intervals following the removal of conventional adenomas only

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### 4.18.1.1 Unresolved issues

Long term outcomes following the removal of conventional adenomas are not well-described in the literature in the modern era of high quality colonoscopy. It is also unclear exactly which low risk individuals may benefit from shorter surveillance intervals. Studies of outcomes and surveillance intervals in routine endoscopy practice in Australia are lacking.

### 4.18.1.2 Studies currently underway

An important set of studies, the European Polyp Surveillance (EPoS) trials<sup>[1]</sup>, have commenced and will be a step forward in addressing gaps in the evidence base.

### 4.18.1.3 Future research priorities

More prospective contemporary studies incorporating high quality colonoscopy are needed, particularly in an Australian environment. Research on the efficacy of dissemination and implementation of these guidelines along with barriers and enablers would be valuable. There is a unique opportunity with these surveillance recommendations to comprehensively assess health outcomes, colonoscopy demand and cost implications to guide the further refinement of international surveillance intervals following removal of conventional adenomas. Compulsory colonoscopy and pathology data provision to a national database would facilitate the above research priorities.

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## 4.18.2 Surveillance intervals following the removal of serrated adenomas with or without synchronous conventional adenomas

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### 4.18.2.1 Unresolved issues

The understanding of serrated adenomas in the era of modern high quality colonoscopy is evolving.

### 4.18.2.2 Studies currently underway

An important set of studies, the EPoS trials<sup>[1]</sup>, have commenced and will be a step forward in addressing gaps in the evidence base.

#### 4.18.2.3 Future research priorities

These guidelines are the first internationally to consider surveillance intervals of conventional and serrated adenomas alone and in combination. There is an opportunity to set up observational trials to assess outcomes to inform international surveillance intervals over time.

The resourcing implications of separate recommendations for serrated polyps are important to establish. Research on the efficacy of dissemination and implementation of these guidelines along with barriers and enablers would be valuable.

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### 4.18.3 Surveillance intervals following the removal of large sessile and laterally spreading adenomas

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#### 4.18.3.1 Unresolved issues

High quality data in this area is lacking.

#### 4.18.3.2 Studies currently underway

None

#### 4.18.3.3 Future research priorities

Nil new

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### 4.18.4 Surveillance intervals for second and subsequent colonoscopies

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#### 4.18.4.1 Unresolved issues

The understanding of serrated adenomas in the era of modern high quality colonoscopy is evolving.

#### 4.18.4.2 Studies currently underway

None known.

#### 4.18.4.3 Future research priorities

These guidelines are the first internationally to consider second and subsequent surveillance intervals of conventional and serrated adenomas alone and in combination. There is an opportunity to set up observational trials to assess outcomes to inform international surveillance intervals over time. The resourcing implications of these changed recommendations are important to establish. Research into the efficacy of dissemination and implementation of these guidelines along with barriers and enablers would be valuable.

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#### 4.18.5 References

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### 4.19 Surveillance colonoscopy after curative resection for colorectal cancer - Introduction

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#### Introduction

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Patients who have surgery for colorectal cancer (CRC) are at above-average risk for the development of a second, metachronous CRC (and adenomatous polyps). After surgery for CRC, the aim of patient follow-up is to improve survival by the early detection and treatment of recurrent or metachronous neoplasia. To increase the chance of early recognition of such disease, intensive post-operative follow-up is recommended. This involves a combination of clinical review, blood tests for the tumour marker carcinoembryonic antigen (CEA), colonoscopy, radiological imaging and/or abdominal ultrasound at regular intervals after resection (see Follow-up after curative resection for colorectal cancer in Clinical practice guidelines for the prevention, early detection and management of colorectal cancer).

This section of the guidelines reviews the available evidence, so that such patients can be advised about an appropriate interval for post-operative and subsequent surveillance colonoscopies.

See sections

- Pre and perioperative colonoscopy in patients with colorectal cancer undergoing resection (COL1)
- Follow-up colonoscopy after colorectal cancer resection (FUC1)
- Patient selection for surveillance colonoscopy following resection

## 4.20 Preoperative and perioperative colonoscopy in patients with colorectal cancer undergoing resection

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### 4.20.1 Background

This section focuses specifically on the use of colonoscopy in surveillance following curative resection of colorectal cancer (CRC). Complete, high-quality colonoscopy should be performed at the time of diagnosis of a CRC, to check for synchronous cancer and to clear the colon of synchronous adenomatous polyps. Surveillance colonoscopy following resection of CRC aims to improve patient outcomes by finding metachronous cancers at an early stage, detecting anastomotic or intraluminal recurrences and removing metachronous adenomas. Hence, understanding the rate of development of and risk factors associated with either metachronous neoplasia or locally recurrent cancer may be important for reducing mortality from CRC.

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### 4.20.2 Evidence

*What is the role of pre- or perioperative colonoscopy in CRC patients? (COL1)*

#### 4.20.2.1 Systematic review evidence

A systematic review of studies published since 2010 was undertaken to update the evidence on which the 2011 version of these guidelines was based.<sup>[1]</sup>

The search strategy, inclusion and exclusion criteria, and quality assessment are described in detail in the Systematic review report).

Nine studies were identified, which included prospective<sup>[2][3][4]</sup> and retrospective<sup>[5][6][7]</sup> cohort studies, and two case-series.<sup>[8][9]</sup> Five studies<sup>[2][3][5][6][10]</sup> were level III-2, two studies<sup>[4][7]</sup> were level III-3 evidence, and two studies<sup>[9][8]</sup> were level IV evidence. Three studies were at high-risk of bias,<sup>[3][6]</sup> one study was at moderate risk of bias,<sup>[9]</sup> and five studies were at low risk of bias.<sup>[2][5][7][4][10]</sup>

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##### 4.20.2.1.1 Lesion localisation accuracy

Four studies<sup>[3][2][5][7]</sup> reported the accuracy of primary colorectal tumour identified by preoperative colonoscopy with the location of the primary tumour during surgical resection. All studies reported high accuracy, varying from 81% to 96%. However, accuracy is dependent on the colonoscopy success rate, which may be hindered by tumour obstruction.

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##### 4.20.2.1.2 Preoperative imaging unable to locate tumour

Two studies<sup>[2][3]</sup> reported the percentage of patients in which preoperative imaging was unable to locate the primary colorectal tumour. Both studies reported rates of 22–23% across a combined total of 189 patients.

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##### 4.20.2.1.3 Complications

Only a single study reported complications from preoperative colonoscopy, in a cohort of 48 patients who received a self-expendable metallic stent (SEMS) placement for luminal obstruction.<sup>[9]</sup> Complications including minor bleeding (16%) and perforation (2%) were reported, and were consistent with any surveillance colonoscopy procedure in the average or symptomatic general populations.

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#### **4.20.2.1.4 Surgery requiring modification intraoperatively due to preoperative non-concordance**

Four studies reported the percentage of patients requiring a modification to planned surgery due to non-concordance with preoperative colonoscopy finding:<sup>[2][7][3][6]</sup>

- In a cohort of 111 patients, 6.3% required an altered surgical management plan.<sup>[2]</sup>
- In a large cohort of 374 patients, 2.9% required a modification of their planned operative procedure.<sup>[7]</sup>
- In another large cohort of 715 patients, 8.9% required intraoperative on-table changes in their surgical procedure.<sup>[6]</sup>
- In a small cohort of 79 patients, 1.6% required an intraoperative surgical management change.<sup>[3]</sup>

Put together, there is consistent evidence across these studies that only a small percentage of patients (<10%) required a modification to their planned tumour surgery.

#### **4.20.2.1.5 Successfully completed preoperative colonoscopy**

Consistent evidence reported that preoperative colonoscopy was highly successful, and failure to complete colonoscopy was mainly due to obstructing/stenosing tumours, or poor bowel preparation. In the study by Kim et al,<sup>[9]</sup> a gastroscope was used instead of a colonoscope when the passage of colonoscope was not feasible due to a narrow expanded lumen. Johnstone et al<sup>[3]</sup> reported 79.7% success in a cohort of 79 patients. Kim et al<sup>[9]</sup> reported 62.5% success in a cohort of 48, and the 2013 study by Lim et al<sup>[4]</sup> reported 88.9% success in a cohort of 73 patients.

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#### **4.20.2.1.6 Synchronous lesions**

Five studies report synchronous lesions rates.<sup>[9][4][6][10][5]</sup>

Three studies reported adenomas rates varying from 22–42%, across a combined cohort of 800.<sup>[9][4][6]</sup> Only Lim et al reported a high-grade dysplasia rate of 2.2% in 45 patients.<sup>[4]</sup>

Synchronous carcinoma rates reported in three studies were relatively low at 2.2–4.1%.<sup>[9][4][6]</sup> Paik et al only reported polyp numbers and the percentage of patients.<sup>[10]</sup>

Put together, synchronous adenoma rate were up to 40% in these studies, but synchronous carcinoma rates were below 5%.

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#### 4.20.2.1.7 Postoperative metachronous lesions

Two studies reported postoperative lesions detected during surveillance scopes following tumour resection.<sup>[10][8]</sup> In a study of 116 patients, polyp rates of 53% during 3–15 month follow-up were reported, and 26% of patients with neoplastic polyps detected during follow-up.<sup>[10]</sup> In a large study including over 850 patients, Couch et al<sup>[8]</sup> reported adenoma and carcinoma detection rates in two cohorts, with one cohort (Cohort 1) having up to 5 years of follow-up. Adenoma rates were higher in those who had no preoperative colonoscopy, but never reached more than 17% per year, per cohort. Carcinoma rates were much lower in both cohorts, and were below 3% per year in the 36% of patients that had a surveillance scope. The mean time to polyp detection in this cohort ranged from 12 to 40 months, depending on the cohort, or preoperative intervention.<sup>[8]</sup>

Postoperative lesions detected after surgical resection were substantial in these two studies. Adenoma rates were much greater than carcinoma rates, and were still detected up to 5 years post-surgery in those who had a surveillance colonoscopy. As not all participants had a surveillance scope, the exact recurrence rates are difficult to establish.

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### 4.20.3 Evidence summary and recommendations

Evidence summary	Level	References
<p><b>Lesion localisation accuracy</b></p> <p>Preoperative colonoscopy was highly accurate, but is dependent on its success rate, which may be hindered by tumour obstruction.</p>	III-2, III-3	[2], [3], [5], [7]
<p><b>Preoperative imaging unable to locate tumour</b></p> <p>Primary colorectal tumour could not be located during preoperative imaging in as many as 1 in every 4 or 5 patients.</p>	III-2	[2], [3]
<p><b>Complications</b></p> <p>Only minor complications were reported on preoperative colonoscopy, consistent with any surveillance scoping in the average or symptomatic general populations.</p>	IV	[9]
<p><b>Surgery requiring modification intraoperatively due to preoperative non-concordance</b></p> <p>There was consistent evidence that a small percentage of patients (&lt;10%) will require a modification to their planned tumour surgery.</p>	III-2, III-3	[2], [7], [3], [6]
<p><b>Successfully completed preoperative colonoscopy</b></p>	III-2, III-3,	[3], [9], [4]

Evidence summary	Level	References
<p>Consistent evidence reported that preoperative colonoscopy was highly successful, and failure to complete colonoscopy was mainly due to obstructing/stenosing tumours or poor bowel preparation.</p>	IV	
<p><b>Synchronous lesions</b></p> <p>Synchronous adenoma rates were up to 40% in these studies, but synchronous carcinoma rates were below 5%.</p>	III-2, III-3, IV	[9], [4], [5], [10], [6]
<p><b>Postoperative lesions</b></p> <p>Rates of lesions detected on postoperative colonoscopy following surgical resection were substantial in the two studies that reported this outcome. Adenomas rates were much greater than carcinoma rates, and were still detected up to 5 years post surgery in those who had a surveillance colonoscopy. As not all participants had surveillance colonoscopy exact recurrence rates are difficult to establish.</p>	III-2, IV	[10], [8]

Evidence-based recommendation	Grade
<p>A preoperative colonoscopy should be attempted in all patients with a newly diagnosed colorectal cancer.</p>	<b>C</b>

Evidence-based recommendation	Grade
<p>Colonoscopy should be performed 3–6 months after resection for patients with obstructive colorectal cancer in whom a complete perioperative colonoscopy could not be performed and in whom there is residual colon proximal to the location of the pre-operatively obstructing cancer.</p>	<b>C</b>

Practice point
<p>In cases of a colorectal cancer that may be difficult to identify at surgery, particularly using the laparoscopic approach, submucosal tattoo should be placed in three places approximately 2 cm distal to the lesion at the time of colonoscopy. This should be clearly documented in the colonoscopy report.</p>

#### Practice point

If the index colorectal cancer (CRC) obstructs the lumen and prevents passage of a colonoscope, consideration should be given to specific pre-operative assessment of the proximal colon by alternative means. CT colonography (CTC) can be considered. However, its role in this clinical scenario requires further analysis. It is safe to perform same-day CTC following an incomplete colonoscopy, including in patients who have had a biopsy or simple polypectomy. CTC should be delayed in patients with complex endoscopic intervention and in patients at high risk of perforation, such as those with active colitis or high-grade stricture.

#### Practice point

Proximal visualisation is unnecessary if the colon proximal to the cancer is to be included in the resection specimen. In patients with residual un-visualised colon, colonoscopy should be performed 3–6 months after surgery, providing no non-resectable distant metastases are found.

#### Practice point

In patients with a defunctioning loop ileostomy, it is preferable to undertake colonoscopy after this is reversed to enable adequate bowel preparation.

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## 4.20.4 Health system implications

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### 4.20.4.1 Clinical practice

No significant effects on clinical practice are anticipated, because the evidence-based recommendations and consensus-based recommendations have not changed.

### 4.20.4.2 Resourcing

No significant effects on resource requirements are anticipated, because the evidence-based recommendations and consensus-based recommendations have not changed.

### 4.20.4.3 Barriers to implementation

No significant barriers to the implementation of these recommendations have been identified.

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### 4.20.5 References

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## 4.20.6 Appendices

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## 4.21 Follow-up colonoscopy after colorectal cancer resection

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### 4.21.1 Background

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Given that the objectives of surveillance are early detection of metachronous cancer and timely polypectomy for metachronous adenomas, recommendations about the timing of colonoscopy after resection of colorectal cancer (CRC) should be largely based upon the natural history of metachronous colonic neoplasia. Intraluminal recurrences are infrequent and a secondary consideration.

The natural history of metachronous cancer and polyps is best estimated by studies of the yields of colonoscopy at various time points after surgery, when pre or perioperative colonoscopy has excluded synchronous cancer and cleared synchronous polyps.

### 4.21.2 Evidence

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*What should be the follow-up colonoscopy for patients after CRC resection? (FUC1)*

#### 4.21.2.1 Systematic review evidence

A systematic review of studies published since 2010 was undertaken to update the evidence on which the 2011 version of these guidelines was based.<sup>[1]</sup>

No new studies were found (see Technical report).

The systematic review undertaken in 2010 is still relevant and summarises the available evidence for this clinical question.

In the literature prior to 2005, Barillari<sup>[2]</sup> and Neugut<sup>[3]</sup> found that more than one-half of metachronous adenomas and cancers were detected within the first 24 months after surgery. In a 2000 study, Togashi et al<sup>[4]</sup> detected 22 metachronous CRCs in 19 out of 341 patients after CRC surgery, 14 (64 %) of them within 5 years of surgery. Most were small ( $\leq 10$ mm) and many had a flat endoscopic appearance. In a study of 174 patients reported by Juhl et al in 1990,<sup>[5]</sup> three-quarters of the colonoscopically detected neoplasms (adenomatous polyps and cancers) occurred within the first 24 months. In the period 12–30 months after surgery, 4 metachronous cancers and 37 advanced adenomas were detected. A retrospective review by Khoury et al<sup>[6]</sup> concluded that annual follow-up colonoscopy for 2 years after CRC surgery was beneficial and that the interval between subsequent examinations be increased depending on the result of the most recent examination.<sup>[6]</sup>

However, not all of these earlier studies advocated colonoscopy within 1 to 2 years of surgery. Among 175 patients who underwent a curative resection for CRC between 1986 and 1992, colonoscopies performed 1 year after surgery and then at 2-year intervals revealed no metachronous cancers or advanced adenomas. The authors suggested that only patients who had had synchronous adenomas at pre-operative colonoscopy should undergo follow-up colonoscopy at 3 years.<sup>[7]</sup> Similarly, Stigliano et al<sup>[8]</sup> conducted a retrospective study of 322 patients and found no metachronous cancers within the first 2 years after surgery. In their 2002 review, Berman et al<sup>[9]</sup> suggested that there were insufficient data to support the routine use of annual or more frequent colonoscopy to identify metachronous or recurrent CRC and they suggested post-operative colonoscopy be limited to every 3 to 5 years. A large retrospective audit of patients after CRC resection by McFall et al, concluded that most patients are at very low risk of developing significant colonic pathology in the 5 years after resection, but the value of this study was limited by the fact that less than one-third of the patients underwent postoperative colonoscopy<sup>[10]</sup> and the mean interval between surgery and colonoscopy was more than 4 years. Similar reservations about the need for follow-up colonoscopy earlier than 2 to 3 years were expressed by Mathew et al,<sup>[11]</sup> even though 10 out of 14 patients with neoplastic findings at surveillance colonoscopy were detected 2 years postoperatively.

A Western Australian study by Yusoff et al audited all patients who underwent surgical resection of CRC from 1989 to 2001<sup>[12]</sup> and found that no metachronous cancers (and only 1 of 11 recurrent anastomotic cancers) were found by surveillance of asymptomatic patients. The three metachronous cancers were all detected in symptomatic patients, at 4, 8 and 9 years after surgery. In a subset of their patients, the yields for adenoma were 10% at one 1 year post-operatively, 28% at 2 years and none at 3 years.

Another Australian study by Platell et al published in 2005 specifically evaluated the clinical utility of performing a colonoscopy 12 months after curative resection for CRC.<sup>[13]</sup> In 253 patients who had undergone complete colonoscopy prior to resection, 90% received their first post-operative colonoscopy at a mean of 1.1 years. Although no recurrent or metachronous cancers were found, 149 polyps were detected in 30% of patients, 42% of which were adenomas. Additionally, of the total number of polyps, 13% were villous or tubulovillous adenomas. Having observed such a high prevalence of advanced adenomas at 12 months (7.9% of patients), the authors raised the possibility that, instead of performing post-operative colonoscopy at 3 to 5 years, as recommended in then-current 2005 clinical practice guidelines for the prevention, early detection and management of CRC,<sup>[14]</sup> a variably intense colonoscopy surveillance schedule might be justifiable. Similarly, a large study from Taipei<sup>[15]</sup> concluded that a lifelong schedule of postoperative colonoscopic surveillance was necessary.

According to Hassan et al,<sup>[16]</sup> who used a decision analysis model, early surveillance colonoscopy performed 1 year following CRC resection was clinically efficient and cost-effective in terms of cancer detection and prevention of cancer-specific death.<sup>[16]</sup> Compared with 'no early colonoscopy' following surgery, the number of 1-year colonoscopies required to find one CRC was 143 and the number needed to prevent one CRC-related death was 926. In a 2007 analysis of 1002 operated CRC patients, Rulyak et al<sup>[17]</sup> concluded that surveillance colonoscopy within one year of surgery was warranted because (i) 9 of the 20 metachronous cancers detected during the study period were found within 18 months of surgery and (ii) the rate of metachronous advanced neoplasia was significantly lower if colonoscopy was performed within 18 months of surgery (6.9 %) than if colonoscopy was delayed for 3 years or more (15.5 %).

In a 2009 study from China, Wang et al compared 'intensive colonoscopic surveillance' (3-monthly colonoscopy for the first year after surgery, then 6-monthly for the following 2 years and annually thereafter) with 'routine colonoscopic surveillance' (at 6, 30 and 60 months after surgery).<sup>[18]</sup> In the intensive surveillance group, one metachronous cancer was detected in the second year of surveillance, one in the fourth year and the third more than 5 years after initial surgery. In the routine surveillance group, no metachronous cancers were found at 6 months, four were found at 30 months, one was found at 5 years and one was found thereafter. The authors concluded that the routine schedule of surveillance was acceptable, with follow-up colonoscopy at one and two years after surgery and then 3 to 5 years thereafter.

Thus, while not all of the published evidence is in agreement, most studies demonstrate a significant incidence of metachronous cancers, advanced adenomas and other types of polyps after curative resection for CRC. In many studies, a high proportion of the metachronous neoplasia was detected within the first 2 years after surgery.

Careful, high-quality colonoscopy at 12 months after surgery would be expected to detect the vast majority of metachronous neoplasia. In turn, this should improve survival in patients operated on for CRC, by finding second cancers at a stage early enough to be cured by re-operation, and by removing metachronous adenomas while still benign. As a result, the weight of evidence from the literature would seem to support performing the initial postoperative surveillance colonoscopy at an interval of 1 year. If this examination does not reveal a metachronous cancer, the intervals between subsequent colonoscopies should probably be 3 and then 5 years, depending on the number, size and histologic type of polyps (if any) removed (see Colonoscopic surveillance after polypectomy).

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### 4.21.3 Overview of additional evidence (non-systematic review relevant literature)

The US guidelines for colonoscopy surveillance after cancer resection referenced in the last clinical practice guidelines<sup>[19]</sup> have since been updated to include additional data from 2005 to 2015.<sup>[20]</sup> The literature was summarised with regard to metachronous cancer development. Reporting pooled data from over 15,000 patients, 253 (1.6%) metachronous cancers were detected, 30% of these within 2 years of the index malignancy. While it could be argued that second cancers found so soon after surgery were in many instances missed synchronous (rather than metachronous) lesions, the importance of detecting them remains undiminished. Thus, the US Guidelines' re-iterated previous recommendations to perform post-operative colonoscopy at an interval of 1 year (with subsequent colonoscopies after an interval of 3 years and then 5 years, if all surveillance examinations were normal).

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### 4.21.4 Evidence summary and recommendations

Evidence summary	Level	References
Follow-up colonoscopy reduces the mortality rate of patients after colorectal cancer (CRC) resection. Most studies demonstrate a significant incidence of metachronous cancers, advanced adenomas and other types of polyps after curative resection for CRC.	II, III-2, III-3	[15], [17], [2], [4], [21], [22], [23], [24], [25], [3], [13], [16], [18]
In many studies, a high proportion of the metachronous neoplasia occurred within the first 2 years after surgery.	III-3	[26]

Evidence-based recommendation	Grade
Colonoscopy should be performed 1 year after the resection of a sporadic cancer, unless a complete postoperative colonoscopy has been performed sooner.  <b>Recommendation unchanged from 2011 edition of clinical practice guidelines for surveillance colonoscopy.</b>	<b>C</b>



Evidence-based recommendation	Grade
<p>If the perioperative colonoscopy or the colonoscopy performed at 1 year reveals advanced adenoma, then the interval before the next colonoscopy should be guided by recommended surveillance intervals according to polyp features.</p> <p><b>Recommendation unchanged from 2011 edition of clinical practice guidelines for surveillance colonoscopy.</b></p>	<p><b>C</b></p>

Evidence-based recommendation	Grade
<p>If the colonoscopy performed at 1 year is normal or identifies no advanced adenomas, then the interval before the next colonoscopy should be five 5 years (i.e. colonoscopies at 1, 6, and 11 years after resection).</p> <p><b>Recommendation unchanged from 2011 edition of clinical practice guidelines for surveillance colonoscopy.</b></p>	<p><b>C</b></p>

Consensus-based recommendation
<p>If surveillance colonoscopy reveals adenoma, then the interval before the next colonoscopy should be guided by polyp features (evidence-based recommendation, Grade C). However, if subsequent colonoscopy is normal, then surveillance should revert back to the intervals recommended for initial cancer surveillance (colonoscopy at 6 and 11 years post resection).</p> <p><b>Recommendation unchanged from 2011 edition of clinical practice guidelines for surveillance colonoscopy.</b></p>

Consensus-based recommendation
<p>If all colonoscopies performed at 1, 6 and 11 years post resection are normal, follow-up can be with either of the following options:</p> <ul style="list-style-type: none"> <li>✦ faecal occult blood test every 2 years</li> </ul>

**Consensus-based recommendation**

\* colonoscopy at 10 years (i.e. 21 years post resection)

**Recommendation unchanged from 2011 edition of clinical practice guidelines for surveillance colonoscopy.**

**Practice point**

Patients undergoing either local excision (including transanal endoscopic microsurgery) of rectal cancer or advanced adenomas or ultra-low anterior resection for rectal cancer should be considered for periodic examination of the rectum at 6-monthly intervals for 2 or 3 years using either digital rectal examination, rigid proctoscopy, flexible proctoscopy, and/or rectal endoscopic ultrasound. These examinations are considered to be independent of the colonoscopic examination schedule described above

**Practice point**

Patients with incomplete colonoscopy pre-operatively (e.g. impassable distal lesion) should have a semi-urgent elective post-operative colonoscopy when feasible, independent of surveillance intervals.

**Practice point**

Surveillance colonoscopy in those age  $\geq 75$  years should be based on age and comorbidity as assessed by the reproducible and validated Charlson score. Charlson score is useful to assess life expectancy and could be implemented to stratify benefits of surveillance colonoscopy in the elderly (see Table 18. Charlson score for colonoscopy benefit).

**Table 18. Charlson score for colonoscopy benefit**

Age	Medical conditions
	<p><b>May</b> have <i>one</i> of these conditions only (1 point each):</p> <p>Mild liver disease</p> <p><b>May not</b> have <i>any</i> of these medical conditions</p>

<p>75–79 years (3 points for age)</p>	<p>Diabetes without end-organ damage Cerebrovascular disease Ulcer disease Connective tissue disease Chronic pulmonary disease Dementia Peripheral vascular disease Congestive heart failure Myocardial infarction</p>	<p>(≥1 point each): Moderate/severe liver disease Diabetes with end-organ damage Hemiplegia Moderate or severe renal disease AIDS Metastatic or non-metastatic solid organ or haematopoietic malignancy</p>
<p>80 years (4 points for age)</p>	<p>May not have any of the above medical conditions</p>	

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## 4.21.5 Health system implications

### 4.21.5.1 Clinical practice

No significant effects on clinical practice are anticipated, because the evidence-based recommendations and consensus-based recommendations have not changed.

### 4.21.5.2 Resourcing

No significant effects on resource requirements are anticipated, because the evidence-based recommendations and consensus-based recommendations have not changed.

### 4.21.5.3 Barriers to implementation

No significant barriers to the implementation of these recommendations have been identified.

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## 4.21.6 References

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## 4.21.7 Appendices

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## 4.22 Patient selection for surveillance colonoscopy following resection

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- 2 Overview of evidence (non-systematic literature review)
  - 2.1 Risk factors for local recurrence following resection for colorectal cancer
  - 2.2 Risk factors for metachronous neoplasia following resection for colorectal cancer
- 3 References

### 4.22.1 Background

The Clinical practice guidelines for the prevention, early detection and management of colorectal cancer updated in 2017, proposed that intensive follow-up for colorectal cancer (CRC) should be considered for patients who have had potentially curable disease. The US Multi-Society Task Force on Colorectal Cancer recommended that all patients who have undergone curative resection of either colon or rectal cancer should undergo surveillance colonoscopy.<sup>[1]</sup> A Cochrane review updated in 2016 concluded that, although intensive follow-up can detect recurrences earlier, resulting in more salvage surgery with curative intent, this was not associated with improved survival.<sup>[2]</sup> Harms related to intensive follow-up and salvage therapy were not well reported.

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### 4.22.2 Overview of evidence (non-systematic literature review)

No systematic reviews were undertaken for this topic. Practice points were based on selected evidence (see Guideline development process).

#### 4.22.2.1 Risk factors for local recurrence following resection for colorectal cancer

Recent studies suggest that follow-up after CRC resection could perhaps be customised according to a patient's individual risk.<sup>[3][4][5][6][7][8][9][10][11][12]</sup> Importantly for colonoscopic surveillance, a number of studies have determined features of a primary CRC, which increase the risk of local recurrence at the surgical anastomosis.<sup>[3][4][5][13][14]</sup> Anastomotic recurrence occurs far more often in rectal cancer patients than in colon cancer patients, and additional proctoscopy follow-up has been recommended by some for this reason.<sup>[1][5][15]</sup> Local recurrence is also more likely to occur in patients undergoing local excision (including transanal endoscopic microsurgery) of their rectal primary cancers. Unfortunately, some of these recurrences are associated with extra-colonic disease or local spread and are not curable.<sup>[3][16][17][18][19]</sup>

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#### 4.22.2.2 Risk factors for metachronous neoplasia following resection for colorectal cancer

Having developed one CRC, patients are at risk for the development of metachronous polyps and cancers. Bouvier et al reported the incidence of metachronous cancer as being 1.8% at 5 years, 3.4% at 10 years, and 7.2% at 20 years with the greatest excess risk between 1 and 5 years post-operatively.<sup>[20]</sup> Some authors have reported that the presence of synchronous polyps or cancers at preoperative colonoscopy is a risk factor for metachronous CRC<sup>[21][22][23][24][25]</sup> and for metachronous adenomatous polyps.<sup>[21][26]</sup> However, in several other studies including a large cancer registry based population-based study have failed to identify any link between synchronous adenomas and the development of subsequent metachronous CRC.<sup>[20][23][27]</sup>

Metachronous and synchronous tumours are features of Lynch syndrome, previously called hereditary non-polyposis colorectal cancer (HNPCC).<sup>[28][29]</sup> A propensity for metachronous CRCs with a predilection for the proximal colon, and development of cancer at an early age, are well recognised characteristics of Lynch syndrome.<sup>[30]</sup>

Primary tumour location is a risk factor for the development of metachronous cancer. In a study of more than 500 CRC patients from a cancer registry database, patients whose first cancer was located proximal to splenic flexure were found to be at twice the risk for developing a metachronous cancer compared to those with a first cancer in the distal colon.<sup>[13]</sup>

Thus, reported studies have disagreed about whether patients who have undergone CRC resection can be stratified with regard to their risk of future development of metachronous polyps and cancers. Even in those studies where a positive predictive factor was identified, the strength of the association with the development of future colonic neoplasia was insufficiently strong to exclude patients without the factor from colonoscopic surveillance.

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#### Practice point

Patients with hereditary colorectal cancer syndromes should have surveillance colonoscopy performed post-operatively as per the Clinical practice guidelines for the prevention, early detection and management of colorectal cancer.

### Practice point

Other clinically high-risk patients should be considered for more frequent surveillance colonoscopy after surgery than would otherwise be recommended (e.g. initial post-operative colonoscopy at 1 year and then 1-3 yearly depending on personalised estimate of risk). These include patients:

- \* whose initial diagnosis was made younger than age 40 years
- \* with suspected but un-identified hereditary colorectal cancer syndromes
- \* with multiple synchronous cancers or advanced adenomas at initial diagnosis.

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## 4.23 Colonoscopic surveillance and management of dysplasia in IBD - Introduction

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- 2 Epidemiology
- 3 Pathological characteristics

4 Colorectal cancer and dysplasia risk
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### 4.23.1 Background

Colorectal cancer (CRC) is one of the most devastating complications of chronic colitis in the setting of inflammatory bowel disease (IBD).<sup>[1]</sup>

Current strategies in the reduction or management of colitis-associated CRC are chemoprophylaxis, colonoscopy surveillance of at-risk individuals, endoscopic removal of dysplastic lesions and proctocolectomy, which is a potentially curative treatment for those with precancerous dysplasia or early cancer.

Maintaining mucosal healing may reduce colorectal carcinogenesis. Chemoprophylaxis has been proposed using mesalazine, thiopurines and ursodeoxycholic acid in the setting of IBD with and without primary sclerosing cholangitis (PSC).

There are data linking colonoscopy with a reduced risk for CRC and mortality in patients with IBD.<sup>[2]</sup> Guidelines based on case series suggest that IBD surveillance may permit earlier detection of cancers and improve prognosis.<sup>[3]</sup> In Australia, there is increasing acceptance that improved endoscopic technologies have resulted in improved identification of dysplasia and permitted resection of dysplastic lesions before resorting to proctocolectomy.<sup>[4]</sup>

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### 4.23.2 Epidemiology

Since IBD was first recognised in 1925,<sup>[5]</sup> substantial variation in the literature surrounding the incidence of CRC in patients with IBD has been reported in substantial variation in its incidence in the literature. This variation is thought to be due to referral centre bias, heterogeneity in study design and, possibly, environmental or geographical factors.<sup>[6]</sup> Furthermore, changes to the surveillance and management of dysplasia, including the improvement of endoscopic technologies in the earlier identification of pre-cancerous dysplasia, have undoubtedly affected both the reported rates and outcomes of dysplasia and CRC.

Initial data suggested a difference in risk of CRC between those with ulcerative colitis (UC) and Crohn's disease, but it is generally accepted that the risks are approximately equivalent stratifying for the extent of colonic involvement.<sup>[7][8][9][10]</sup> A meta-analysis of 116 studies including 54,478 patients derived an overall prevalence of CRC in any patient with UC to be 3.7%. The incidence was reported as 3 cases per 1,000 person-years duration (PYD).<sup>[11]</sup> When stratified for disease duration, the incidence increased from 2 per 1000 PYD (cumulative probability 2%) for the first decade to 7 per 1000 PYD (cumulative probability 8%) for the second decade and 12 per 1000 PYD (cumulative probability 18%) for the third decade. In Australia, the cumulative

incidences of CRC in UC for the first, second and third decades were 1% (95% confidence interval [CI]: 0-2), 3% (95% CI: 1-5) and 7% (95% CI: 4-10), respectively.<sup>[12]</sup> Similar findings have been recently described amongst a large Korean multicentre study<sup>[13]</sup> indicating that the cumulative incidence of CRC in IBD patients in low-prevalence countries might be similar to that of Western countries. Ongoing reductions in the incidence of CRC in IBD may continue to be seen with regular surveillance colonoscopy, improvements in imaging and adenoma detection and aggressive use of maintenance therapies to achieve mucosal healing.

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### 4.23.3 Pathological characteristics

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Intraepithelial dysplasia (superficial to the lamina propria) is the premalignant lesion in IBD associated CRC, and is classified as low grade or high grade according to histopathological features. The differentiation of low-grade dysplasia (LGD) from high-grade dysplasia (HGD) is based on the degree and extent of nuclear stratification, haphazardness and loss of nuclear polarity, nuclear atypia, nucleoli size, nuclear clumping and presence of atypical mitotic figures.

Low-grade dysplasia needs to be differentiated from reactive changes due to inflammation. The presence of neoplastic invasion is diagnostic of CRC. For the most part, IBD-associated CRC is histologically similar to sporadic CRC, although it exhibits several different pathobiological features.

Colorectal cancer in IBD, like its sporadic counterpart, is most commonly adenocarcinoma. Dysplasia in IBD is typically multifocal, and variously described as flat, indistinct, ulcerated, plaque-like, nodular, velvety, stricturing or mass-like, whereas sporadic dysplasia is more classically unifocal and associated with discrete polyp formation.<sup>[10]</sup>

Lesions arise from areas of the colon currently or previously inflamed, but may be in areas of microscopic inflammation rather than macroscopic involvement.<sup>[14]</sup> Being associated with chronic inflammation, colitis-associated dysplasia is most commonly located in the distal colon. The mean age at onset is lower in IBD than for sporadic CRC, and synchronous tumours traditionally were more common in IBD, occurring in up to 12%.<sup>[15]</sup> These adverse features, however, might arise from the more subtle lesions but also through inferior older generations of colonoscopic equipment failing to identify lesions.

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### 4.23.4 Colorectal cancer and dysplasia risk

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Risk stratification underlies the modern concept of IBD surveillance strategy. Compared to mucosal healing, the presence of objective mucosal inflammation (endoscopic or histologic) is associated with a greater risk of subsequent colorectal dysplasia. A meta-analysis reported that the odds ratio (OR) of colorectal dysplasia to be 3.5 (95% CI: 2.6-4.8) in those with any mucosal inflammation and OR of 2.6 (95% CI: 1.5-4.5) in those with histologic inflammation.<sup>[16]</sup>

Increased duration of IBD increases CRC risk.<sup>[7][11][12]</sup> CRC risk increases markedly after 10 years of disease duration in subjects with extensive colitis and somewhat later for those with limited left-sided colitis.

The age of onset might be an independent predictor for the development of CRC<sup>[8]</sup>, adjusting for disease duration appears to ameliorate this effect.<sup>[17]</sup> Calculations regarding commencement of surveillance are therefore based upon disease duration not patient age. Nevertheless, a nationwide cohort study showed that childhood onset IBD was associated with increased gastrointestinal cancers (hazard ratio 18.0; 95% CI: 14.4–22.7).<sup>[18]</sup>

Greater extent of disease also provides an increase in cumulative inflammatory insults corresponding to the increased risk of CRC<sup>[17]</sup> in those with extensive colitis or pancolitis. An Australian UC cohort study identified CRC in 24 patients of whom 1 (1.6%) had proctitis, 8 (3.8%) had left-sided colitis and 12 (6.1%) had extensive colitis at study entry.<sup>[12]</sup>

Evidence of chronic intestinal damage also is associated with the risk of developing colorectal neoplasia. Colonic strictures<sup>[19][20][21]</sup>, a foreshortened colon<sup>[19]</sup> and pseudopolyps<sup>[19][22]</sup> represent healing of severe inflammation. These endoscopic features have been shown to be associated with a higher rate of CRC in IBD.

The risk of developing colitis-associated CRC in the presence of PSC is increased. A meta-analysis performed by Soetikno et al<sup>[23]</sup> confirmed the CRC risk with PSC to be 4.8-fold the background rate seen in IBD patients. Australian data demonstrated a trend that CRC risk was increased in the presence of PSC with IBD (6%), compared with PSC without IBD (0%, P=0.08).<sup>[24]</sup> Interestingly, CRC associated with PSC and IBD tend to be predominantly located in the proximal colon.<sup>[25]</sup> CRC risk remains elevated following orthotopic liver transplant and ongoing yearly surveillance is recommended.<sup>[23]</sup>

As with sporadic CRC, family history of CRC is associated with a greater risk of developing dysplasia. For patients with IBD and a first degree relative with CRC the risk is at least two times baseline.<sup>[26][27]</sup>

For patients with UC treated with proctocolectomy and ileal pouch-anal anastomosis, the risk of pouch cancer is very rare questioning the need for selective surveillance.<sup>[28]</sup>

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#### 4.23.5 Characterisation of lesions and implications for management

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New consensus in the nomenclature used to describe dysplasia in IBDs has been developed. Modern descriptors classify lesions based on the Paris classification of endoscopically-detected lesions and whether they can be managed by endoscopic resection or not.<sup>[29]</sup>

The use of high-definition white-light endoscopy (WLE) and chromoendoscopy (Advances in technique) has resulted in greater appreciation of flat and indistinct dysplastic lesions that were previously missed on standard-definition colonoscopy. The inability to identify subtle lesions in previous decades led to the need for taking random biopsies every 10cm in the colon in an attempt to identify dysplasia. The finding of dysplasia through random biopsies was often a late event signifying the presence of widespread multifocal dysplasia. As such, many of these patients were treated by proctocolectomy, due to the high likelihood of missed invasive CRC or high risk of developing cancer.

The modern surveillance paradigm is to manage endoscopically-identified lesions by endoscopic removal of these lesions where possible. High-quality colonoscopy and the use of high-definition colonoscopes are prerequisites for identifying often subtle dysplasia. When confirmed as dysplasia without invasion, they can be removed using endoscopic resection or polypectomy, monitored through close colonoscopic surveillance, with proctocolectomy advised if there is evidence of invasion, when dysplastic lesions cannot be removed, or with multifocal dysplasia.

Individualisation of treatment is also important. The new surveillance paradigm accepts the move away from taking random biopsies towards targeted biopsies based on high-definition colonoscopy with other image-enhancement technologies. The most established image enhancement technology remains dye-spray chromoendoscopy, for which there is high-level evidence for superior yield of dysplasia identification, compared with WLE.<sup>[30]</sup>

Random biopsies typically have a low yield of dysplasia identification,<sup>[31]</sup> but are still advocated in those with high risk-factors for invisible dysplasia (those with prior dysplasia, PSC or foreshortened tubular colon).<sup>[32]</sup>

Ultimately, the primary goal of IBD management should be prevention of IBD dysplasia through improved medical management and achievement of mucosal healing. Histological remission might be an emerging treatment paradigm in the prevention of dysplasia development.<sup>[33]</sup>

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## 4.24 Initiation of surveillance in IBD

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## 4.24.1 Background

Guidelines support the commencement of surveillance colonoscopy after 8 years of onset of inflammatory bowel disease (IBD) symptoms in those with at least left-sided ulcerative colitis (UC).<sup>[1]</sup> Individuals with more extensive Crohn's colitis with prior involvement of at least one third of the colon are also recommended to commence surveillance at this time. However, in patients with primary sclerosing cholangitis (PSC), the risk of subclinical colitis and the incremental risk of colorectal cancer (CRC) support commencement of surveillance immediately upon the diagnosis of PSC.<sup>[2]</sup> Patients with limited ileal Crohn's disease or proctitis do not have increased risk of CRC over that of the general population, so participation in population-based surveillance is recommended.

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## 4.24.2 Systematic review evidence

*What is the appropriate time to commence surveillance in IBD patients (ulcerative colitis and Crohn's patients, and effects of primary sclerosing cholangitis or family history of CRC)? (SUR1)*

A total of 34 studies reported IBD cohorts with varying clinical manifestations including UC, Crohn's disease, or undefined colitis with and without PSC in relation to CRC prevalence, dysplasia prevalence, all-cause mortality, colitis associated neoplasia prevalence and CRC risk factors.<sup>[3][4][5][6][7][8][9][10][11][12][13][14][15][16][17][18][19][20][21][22][23][24][25][26][27][28][29][30][31][32][33][34][35]</sup> Ten studies were level III-2 evidence,<sup>[6][7][10][13][14][15][22][36][26][35]</sup> and 24 studies were level III-3 evidence.<sup>[3][4][5][8][9][11][12][16][17][18][19][20][21][23][24][36][25][27][28][29][30][31][32][33][34]</sup>

Twenty nine studies were at high-risk of bias,<sup>[4][5][6][8][9][10][12][13][14][15][16][17][18][19][21][22][23][24][36][25][27][28][29][30][31][32][33][34][35]</sup> four studies were at moderate risk of bias,<sup>[7][11][20][26]</sup> and one study was at low risk of bias.<sup>[3]</sup>

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### 4.24.2.1 Colorectal cancer prevalence

A large number of studies reported CRC rates in varying sized cohorts of patients with UC, with follow-up in some studies as long as 40 years. Rates of CRC were relatively low for the first decade after UC diagnosis, after which some studies reported significantly higher CRC rates in patients with UC, compared with the general population.<sup>[6][9][10][23][35][8][11][14][15][16][17][29][30]</sup> Increasing duration of IBD after diagnosis is associated with an increasing risk of CRC, the magnitude of which is higher in patients with Crohn's disease, compared with those with UC. The increase in CRC risk in these patients is substantial after 10 years post diagnosis.<sup>[3][20][27][29]</sup>

There is further evidence to suggest that PSC significantly increases the risk of CRC (greater than 5-fold increased risk) over IBD alone or against the general population.<sup>[7][18][26][19]</sup> Those with Crohn's disease have a greater risk of CRC than the general population from the same region. The magnitude of the increased risk varied between studies, but was consistently 1.5 to 2.0-fold greater than within 10 years of a Crohn's disease diagnosis.<sup>[6][10][36][29][8][13][14][16]</sup> There is some evidence to suggest that individuals with left-sided colitis, or pancolitis had a higher risk of CRC.<sup>[27][31][23][29]</sup>

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#### 4.24.2.2 Colorectal cancer mortality

Three studies<sup>[10][22][28]</sup> reported CRC mortality rates in those with Crohn's disease. Two studies<sup>[22][28]</sup> reported a trend towards higher mortality rates (2-fold higher) in those with Crohn's disease, while only the larger study<sup>[10]</sup> reported a statistically significant difference. Three studies reported CRC mortality rates in those with UC compared with the general population. One study reported a trend towards higher mortality rates (2-fold higher) in those with UC, while another study by Herrinton 2012 reported a statistically significant difference.<sup>[10][22][28]</sup> Only single studies reported 5-year<sup>[32]</sup> and 10-year<sup>[9]</sup> CRC survival rates in those with IBD. Five-year survival rates in a small cohort of UC patients were not different from sporadic CRC cases. Ten-year survival rates were lower in those with higher stage CRC at diagnosis.

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#### 4.24.2.3 Dysplasia prevalence

Two studies reported dysplasia prevalence in those with UC. Nowacki 2015<sup>[27]</sup> reported risk of dysplasia in a cohort of 360 UC patients based on duration of disease and followed for >15 years. Risk of dysplasia was 5% within the first 8 years of UC, increased to 7% after 9-15 years disease duration and reached 17% after 15 years of UC duration. Significant increase was only reported when comparing duration of 1-8 years and >15 years: odds ratio (OR) 4.3 (confidence interval [CI] 1.8-10.5,  $p=0.006$ ).<sup>[27]</sup> Stolwijk et al (2013) reported cumulative risk of any dysplasia, or high-grade dysplasia (HGD) specifically at 10, 15 and 20 years of follow-up post diagnosis of UC. The risk of any dysplasia was 23.5% at 10 years, 33.3% at 15 years and reached 48.3% at 20 years follow-up in a cohort of 293. The cumulative risk of HGD was 6.6% at 10 years, 12.1% at 15 years and reached 19.0% at 20 years of follow-up in the same cohort.<sup>[31]</sup>

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#### 4.24.2.4 Risk factors for colorectal cancer in IBD patients: family history

Several studies reported risk rates for CRC in IBD populations. A small ( $n=186$ ) Belgian study reported non-significant differences (5% vs 7%) in family-history of CRC positivity between IBD patient with or without a CRC diagnosis.<sup>[21]</sup> Another study reported no significant difference (4.9% vs 7.8%) in family-history of CRC positivity rates between those diagnosed with both UC and CRC ( $n=144$ ), compared to over 96,000 cases of sporadic CRC ( $p=0.190$ ).<sup>[32]</sup> A Dutch study reported no significant change (relative risk [RR] 1.90; CI 0.88-4.13) in CRC risk in an IBD cohort with a known family history of CRC in a first-degree relative or second-degree relative (RR 1.11; CI

0.40–3.03). Interestingly, this study also reported that the risk of CRC was significantly higher in IBD patients with an unknown family history of CRC (n=199) compared with IBD patients with no known family history of CRC (RR 1.72; CI 1.27–2.35).<sup>[5]</sup> A large cohort study reported risk of advanced neoplasia (HGD or CRC) in a population diagnosed with Crohn's disease (n=408) or UC (n=573) in those with a first-degree relative diagnosed with CRC, compared with those with no known family history. Family history was significantly associated with the development of advanced neoplasia in both univariate (hazard ratio [HR] 3.2; CI 1.4–7.6) and multivariate analysis (HR 3.9; CI 1.6–9.5).<sup>[25]</sup>

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#### 4.24.2.5 Risk factors for CRC in IBD patients: primary sclerosing cholangitis

Boonstra 2013<sup>[7]</sup> reported the risk of CRC in IBD patients with PSC (n=402), compared to IBD only patients (n=772), and showed a positive association (4.7% versus 0.9%) in those with PSC (standardised incidence ratio [SIR] 9.8; CI 1.9–96.6) with up to 15 years of follow up. Lindstrom 2011<sup>[18]</sup> reported CRC in Crohn's disease patients with PSC (n=28) compared with Crohn's disease only patients (n=46), and showed a positive association (11% versus 0%) in those with PSC (p=0.05). This positive association was also reported for low-grade dysplasia (p=0.02) and advanced neoplasia (HGD or CRC, p=0.016), but not HGD in the same cohort.<sup>[7]</sup> In a very large Danish study, Jess 2012<sup>[12]</sup> reported a marked increased risk of CRC in UC patients with PSC, specifically reporting a nine-fold difference in CRC risk when comparing UC patients with and without PSC (RR 9.13; CI 4.52–18.5). In contrast, there was no significant association between PSC and CRC in patients with Crohn's disease (RR 2.90; CI 0.40–20.9) or in individuals without IBD (RR 1.05; CI 0.82–1.35).<sup>[12]</sup> In a study by Baars et al (2011), the duration of PSC (0–5 years, 5–10 years and >10 years) was reported with respect to risk of CRC in an IBD cohort (n=566). A positive association was only seen after 5 years (RR 5.03; CI 2.36–10.72), and maintained after 10 year (RR 3.05; CI 1.25–7.43), but not for <5 years duration of PSC (RR 2.35; CI 0.97–5.75).<sup>[5]</sup>

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#### 4.24.2.6 Risk factors for CRC in IBD patients: ulcerative colitis or Crohn's disease

In a longitudinal study spanning three decades, Jess et al (2012)<sup>[12]</sup> reported no significant difference in the risk of CRC (RR 1.07; CI 0.95–1.21) with nearly 8,000,000 participants (n=32,911 with UC). In a comparison between patients with UC (n=288) and those with Crohn's disease (n=265), Baars et al (2011)<sup>[5]</sup> reported CRC risk was greater (39.2% versus 21.9%) in those with UC (RR 0.49; CI 0.36–0.68, p<0.001).<sup>[12]</sup> The same study reported no significant difference in the risk of CRC in 14,463 Crohn's disease patients, compared to the nearly 8 million general population in Denmark (RR = 0.85; CI 0.67–1.07).<sup>[12]</sup>

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#### 4.24.2.7 Risk factors for CRC in IBD patients: duration of IBD, degree of inflammation, or extent of IBD

Only two studies reported duration of IBD and risk of CRC. Baars et al (2011)<sup>[5]</sup> reported risk of CRC in those with less than 10 years duration of disease, compared to those with IBD for 10–20 years, or greater than 20 years. In the longer time points, diagnoses of IBD for 10–20 years (RR 2.26; CI 1.55–3.29) and >20 years (RR 4.42; CI 3.07–6.36) were associated with greater risk of CRC. Matsuoka et al (2013)<sup>[24]</sup> reported an increased risk of CRC (OR=16.7; CI 5.95–46.88) in those with UC for 70 months or more.

In a study with IBD patients (n=1018), Mooiweer et al (2013)<sup>[25]</sup> reported no significant association between risk of colitis-associated neoplasia, and degree of inflammation assessed both histologically and endoscopically with 2.6 years median follow up.

Another study compared the degree of inflammation in a cohort of IBD patients (n=565). No significant difference in risk of CRC was seen between those with mild, moderate, or severe inflammation. The only positive risk associated was found between unknown degree of inflammation and mild inflammation (RR 2.80; CI 1.77–4.41) with 15.5 years follow-up.<sup>[5]</sup> The same study reported risk of CRC in those with left-sided UC versus extensive UC, <50% segmental Crohn's disease, or >50% segmental Crohn's disease. The only positive risk association was found between left-sided UC and <50% segmental Crohn's disease (RR 0.43; CI 0.24–0.77, p<0.001) only after univariate analysis, with 15.5 years of follow-up.<sup>[5]</sup> Matsuoka et al (2013)<sup>[24]</sup> only found positive risk associated with those with active phase inflammation (RR 0.04; CI 0.01–0.11), or mild colitis (RR 5.80; CI 3.52–9.55) and not pancolitis (RR 0.72), at follow-up of 60 months.

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#### 4.24.2.8 Risk factors for all-cause mortality

Only one study reported all-cause mortality risk in 154 cases followed over 8 years, comparing those with an endoscope procedure in the past 6–36 months and those without a recent colonoscopy. After both univariate and multivariate analysis, a recent colonoscopy correlated with reduced mortality (OR 0.34; CI 0.12–0.95).<sup>[4]</sup>

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#### 4.24.2.9 Risk factors of dysplasia

Only a single study reported risk of dysplasia in a cohort with UC patients (n=293). After both univariate and multivariate analysis, pancolitis positively associated with a high risk of dysplasia (HR 1.922; CI 1.12–3.31, p=0.019), compared with distal colitis after almost 11 years of follow-up.<sup>[31]</sup>

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### 4.24.3 Evidence summary and recommendations

Evidence summary	Level	References
<p>A large number of studies reported colorectal cancer (CRC) rates in varying sized cohorts of patients with ulcerative colitis (UC), with follow-up of up to 40 years in some studies. CRC were relatively low for the first decade after UC diagnosis, after which some studies reported significantly higher CRC rates in UC patients, compared with the general population.</p> <p>There is consistent evidence to suggest that those with Crohn's disease have a greater risk of CRC than the general population from the same region. The magnitude of the increased risk varied between studies, but was consistently 1.5 to 2.0-fold greater than within 10 years of a Crohn's disease diagnosis.</p>	III-2, III-3	[6], [9], [10], [23], [35], [8], [11], [13], [14], [15], [16], [17], [29], [30], [33], [36]
<p>Increasing duration of IBD after diagnosis is associated with an increasing risk of CRC, the magnitude of which is higher in Crohn's disease patients, compared with those with UC. The increase in CRC risk in these patients is substantial after 10 years post diagnosis.</p>	III-3	[3], [20], [27], [29], [5], [24]
<p>There is consistent evidence to suggest that those with IBD and primary sclerosing cholangitis (PSC) are at significantly higher risk of CRC (greater than 5-fold increased risk) from 10–20 years post PSC diagnosis.</p>	III-2, III-3	[7], [18], [26], [19], [12], [5]
<p>There is some inconsistent evidence to suggest that a positive family history of CRC increases the risk of CRC in those with IBD.</p>	III-3	[21], [32], [5], [25]
<p>The 5-year survival rate following a diagnosis of CRC in those with IBD was 61–72%, but this might not be significantly different to that of controls. However, it would appear that IBD CRC mortality has not been decreasing.</p>	III-3	[3], [9], [32], [30]
<p>Left-sided colitis, active inflammation, or mild colitis were all associated with significant increased risk of CRC.</p>	III-3	[5], [24]
<p>CRC in patients with IBD is uncommon within 8 years of disease onset except in those with co-existing PSC or a personal family history of CRC.</p>	III-1	[37], [38], [39], [40], [41]

Evidence-based recommendation	Grade
<p>Surveillance colonoscopy should commence after 8 years of onset of inflammatory bowel disease symptoms in those with at least distal (left-sided) ulcerative colitis or Crohn's colitis with involvement of at least one third of the colon.</p>	<b>C</b>

Evidence-based recommendation	Grade
In the presence of primary sclerosing cholangitis (PSC), surveillance colonoscopy should commence upon the diagnosis of PSC.	<b>B</b>

Practice point
A family history of colorectal cancer in a first degree relative represents an intermediate risk factor. Surveillance colonoscopy may begin after 8 years of the onset of symptoms of inflammatory bowel disease, or 10 years before the age of the youngest relative with colorectal cancer of whichever is earliest.

Practice point
Those with isolated proctitis or small bowel Crohn's disease do not require surveillance colonoscopy.

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#### 4.24.3.1 Unresolved issues

Whether the modern era of treat to target can further reduce colitis associated dysplasia and CRC is unknown. However, there has not been a demonstrable trend of reduction of colitis-associated CRC mortality despite incremental improvement in IBD treatment and surveillance.

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## 4.25 Surveillance interval for IBD patients

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### 4.25.1 Risk stratification

With improvement in colonoscopic technology and attention towards high quality procedures, routine yearly to 2-yearly surveillance colonoscopy surveillance is no longer required for most patients with inflammatory bowel disease (IBD). Current guidelines recommend surveillance colonoscopy intervals to be based on risk stratification and findings on prior surveillance colonoscopies.<sup>[1]</sup>

Stratification according to risk (Table 19) is now incorporated into the Medicare Benefits Schedule reimbursement for the colonoscopy procedure, incentivising focus on quality of colonoscopy. High-risk patients are those with factors associated with greater risk for the development of colorectal dysplasia, and require more frequent surveillance procedures. Low-risk patients are those whose risk of developing dysplasia is estimated to be similar to that of the general non-IBD population. In the absence of clinical trial data, this strategy is based on expert opinion. The recommended surveillance intervals are based on the assumption that the examinations are successful, conducted on well-prepared uninflamed colons, carried out by physicians trained in the detection of dysplasia, and performed using contemporary techniques for visualisation of dysplasia and mucosal sampling.

**Table 19. Risk stratification in IBD**

<b>Risk category</b>	<b>Criteria</b>	<b>Recommended surveillance colonoscopy</b>
High	Any of: <ul style="list-style-type: none"> <li>■ primary sclerosing cholangitis</li> <li>■ ongoing chronic active inflammation</li> <li>■ prior colorectal dysplasia</li> <li>■ evidence of intestinal damage with colonic stricture</li> <li>■ pseudopolyps or foreshortened tubular colon</li> <li>■ family history of colorectal cancer (CRC) at age ≤50 years.</li> </ul>	Yearly
Intermediate	All of: <ul style="list-style-type: none"> <li>■ quiescent disease</li> <li>■ no high-risk features</li> <li>■ no history of CRC in a first-degree relative</li> </ul>	Every 3 years
Low	All of: <ul style="list-style-type: none"> <li>■ quiescent disease</li> <li>■ no other risk factors</li> <li>■ inactive disease on consecutive surveillance colonoscopies</li> </ul>	Every 5 years

There is consistency among guidelines to commence surveillance colonoscopies in both ulcerative colitis (UC) where the maximal involvement (endoscopy and histologic) extent is beyond the splenic flexure and Crohn's colitis that involved over one third of the colon length. Commencement of surveillance should be after 8 years of onset of colitis symptoms.

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## 4.25.2 Evidence

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*What is the most appropriate time interval for surveillance in IBD patients (SUR2)?*

### 4.25.2.1 Systematic review evidence

No studies published since 2010 were found that directly answer the clinical question by matching the PICO criteria for this question (see Technical report).

A total of nine studies from the systematic review to answer the related clinical question What is the appropriate time to commence surveillance in IBD patients (ulcerative colitis and Crohn's patients, and effects of primary sclerosing cholangitis or family history of CRC)? reported long term outcomes (>10 years following IBD diagnosis) were relevant to this clinical question.<sup>[2][3][4][5][6][7][8][9][10]</sup> A single study was level III-2 evidence<sup>[5]</sup> and the remaining studies were level III-3 evidence. All studies were at high risk of bias, except for one study that was at moderate risk of bias,<sup>[5]</sup> and another study that was at low risk of bias.<sup>[2]</sup> The reported outcomes were colorectal cancer (CRC) prevalence in those with UC, Crohn's disease, IBD+PSC, and in regards to duration of IBD or extent of Crohn's disease. Studies also reported the prevalence of dysplasia among those with UC, and risk factors for CRC in those with IBD (PSC, duration of IBD).

Colorectal cancer rates were relatively low for the first decade after UC diagnosis, after which some studies reported significantly higher CRC rates in UC patients compared with the general population. The risk of CRC was still significant 20–30 years after UC diagnosis.<sup>[4][7][8][10]</sup> Increasing duration of IBD is associated with an increasing risk of CRC, the magnitude of which is higher among Crohn's disease patients, compared with patients with UC, after IBD diagnosis. The increase in CRC risk in these patients is substantial after 10 years post diagnosis.<sup>[2][6]</sup> In those with Crohn's disease, CRC prevalence reached 7% 30-years post Crohn's disease diagnosis.<sup>[7]</sup>

Only a few studies reported that either those with IBD and PSC are at risk of CRC from 10–20 years post PSC diagnosis,<sup>[5]</sup> or that individuals with left-sided colitis, or pancolitis had a higher risk of CRC, and this risk was still present more than 10 years after IBD diagnosis.<sup>[2][6]</sup> Both PSC and IBD duration are major risk factors for CRC, both being substantial after 5–10 years.<sup>[3]</sup> Two studies reported that lengthening duration of UC positively correlated with a greater risk of either any dysplasia or high-grade dysplasia.<sup>[6][9]</sup>

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#### 4.25.2.2 Evidence summary and recommendations

Evidence summary	Level	References
The cumulative risk of colorectal cancer (CRC) increases with duration of IBD due to cumulative damage of the mucosa resulting from chronic inflammation. The median time to the development of CRC was 16–23 years. Accordingly, the need to perform surveillance increases over time. The risk in the first decade of symptoms is typically <0.5%, rising to 1% at 10 years after diagnosis of ulcerative colitis.	III-3	[2], [6], [4], [8], [10], [7]
Primary sclerosing cholangitis (PSC) is an additional risk factor for CRC, beyond IBD. The duration of PSC was a risk factor for CRC after 5 years. However, PSC and the colitis associated with PSC are often subclinical, meaning that they are diagnosed many years after disease onset.	III-2, III-3	[5], [3]
The risk of CRC arising in patients with proctitis or ileitis alone is low.	III-3	[6]

#### Consensus-based recommendation

**Patients with IBD at high risk of CRC** (those with PSC, ongoing chronic active inflammation, prior colorectal dysplasia, evidence of intestinal damage with colonic stricture, pseudopolyps or foreshortened tubular colon or family history of CRC at age  $\leq 50$  years) should undergo yearly surveillance colonoscopy.

#### Consensus-based recommendation

**Patients with IBD at intermediate risk of CRC** (those with quiescent disease, no high risk features or family history of CRC in a first-degree relative) should undergo surveillance colonoscopy every 3 years.

#### Consensus-based recommendation

**Patients with IBD at low risk of CRC** (those with quiescent disease and no other risk factors, and with inactive disease on consecutive surveillance colonoscopies) may undergo surveillance colonoscopy every 5 years.

### Practice point

Consider increased frequency of surveillance (intervals less than 3 years) in patients with a family history of CRC in a first-degree relative <50 years of age because this may be an additional risk factor for CRC.

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#### 4.25.2.3 Notes on the recommendations

There are no prospective controlled studies on surveillance strategy and surveillance intervals. Recommendations are based on risk factors identified on cohort studies and actual findings of dysplasia at the time of surveillance colonoscopy.

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## 4.26 Recommended surveillance techniques in IBD patients

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## 4.26.1 Background

Prevention of colorectal cancer (CRC) relies on the early and adequate detection of dysplasia. Detection of dysplasia, in turn, depends on the efficacy of endoscopic visualisation of dysplasia and the adequacy of mucosal sampling. These two differing notions reflect a recent paradigm shift in the techniques used in endoscopic surveillance for CRC in inflammatory bowel disease (IBD). There is widespread acceptance of this approach in Australia.<sup>[1]</sup>

Colonic dysplasia was previously thought to be difficult to visualise endoscopically. Therefore, the practice of taking random biopsies of the colonic mucosa was considered to be the only method of conducting a widespread survey of the colonic mucosa. Random mucosal sampling is now thought, at best, to sample only 1% of colonic mucosa.<sup>[2]</sup>

In order to improve visualisation of the mucosa for subtle dysplasia, the colon should be well prepared. In order to minimise histological confusion between inflammation and dysplasia, colitis should be in remission at the time of surveillance colonoscopy, wherever possible.

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### 4.26.1.1 Chromoendoscopy

To improve the identification of dysplasia, especially flat-dysplastic lesions associated with colitis, dye-spray chromoendoscopy is recommended. Dye-spray chromoendoscopy is the most intensively studied technique for enhancing visualisation of colonic dysplasia. Chromoendoscopy improves visualisation of discrete colonic lesions, and is also used to improve evaluation of pit pattern allowing differentiation between benign and dysplastic lesions.<sup>[3]</sup>

Two dyes commonly used are:

- methylene blue, a vital stain that is absorbed by normal colonic mucosa, but less so by inflamed or dysplastic tissue
- indigocarmine surface enhancing dye that pools in pits and folds enhancing visibility of the mucosal architecture.

These dyes have similar yields and can be sprayed topically onto the mucosal surface or via the water pump delivered through the colonoscope working channel.<sup>[4]</sup> Careful endoscopic examination is then needed to detect alteration in the colonic mucosal architecture.

The diagnostic accuracy of chromoendoscopy for dysplasia in ulcerative colitis (UC) is high.<sup>[5]</sup> Prospective controlled studies indicate a consistently increased sensitivity of chromoendoscopy versus white light endoscopy (WLE).<sup>[6][7]</sup> A meta-analysis of six studies involving 1277 patients showed the difference in dysplasia detection between chromoendoscopy and WLE to be 7% (95% confidence interval [CI] 3.2–11.3).<sup>[8]</sup> The number needed to treat to detect one extra patient with dysplasia or cancer was 14.3 for chromoendoscopy versus WLE. The absolute difference in lesions detected by targeted biopsies was 44% (95% CI 28.6–59.1) and flat lesions was 27% (95% CI 11.2–41.9), both in favour of chromoendoscopy.<sup>[8]</sup>

An Australian tandem colonoscopy study compared the yield of dysplasia for a first-pass procedure performed using high-definition WLE and the second-pass procedure with methylene blue dye spray.<sup>[9]</sup> The yield of dysplasia on first-pass WLE with targeted biopsies was 18.0% (95% CI 10.0–26.0, n=16/89 biopsies in 9 subjects), on second-pass chromoendoscopy and targeted biopsies was 13.5% (95% CI 5.7–21.3, n=10/74 biopsies in 10 subjects). Chromoendoscopy identified 8 subjects from a cohort of 52 with histological dysplasia, six of whom did not have dysplasia identified during the first-pass colonoscopy.<sup>[9]</sup>

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#### 4.26.1.2 Narrow-band imaging

Narrow-band imaging (NBI), using a light filter, may also increase dysplasia detection. The current SCENIC international consensus statement on surveillance and management of dysplasia in IBD does not advocate NBI in place of either standard- or high-definition WLE.<sup>[10]</sup> Two controlled studies found NBI not to be superior to WLE and numerically identified fewer dysplastic lesions. In a randomised parallel-group trial in 112 patients, the proportion of patients with dysplasia detected using NBI was 5 of 56 (9%) versus 5 of 56 (9%) with WLE.<sup>[11]</sup> A randomised crossover trial in 48 patients found the proportion of patients with dysplasia identified using NBI was 9 of 48 (19%), versus 13 of 48 (27%) with WLE.<sup>[12]</sup>

The SCENIC consensus statement also recommend that NBI should not replace chromoendoscopy.<sup>[10]</sup> In four controlled studies the proportion of patients with dysplasia detected was numerically higher with chromoendoscopy than with NBI (0.1–22% difference) but these differences were not statistically significant.<sup>[13][14][15][16]</sup>

An analysis of pit pattern amongst experts in IBD surveillance found that the interobserver agreement for pit pattern was significantly higher for chromoendoscopy than for NBI (0.322 versus 0.224,  $p < 0.001$ ). However, in differentiating between non-neoplastic patterns versus neoplastic patterns, NBI outperformed chromoendoscopy (kappa 0.65 versus 0.50,  $p < 0.001$ ).<sup>[17]</sup>

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### 4.26.1.3 Other technologies

The relevance of other advanced imaging technologies is under active investigation. Full Spectrum Endoscopy (FUSE) significantly reduces missed dysplasia over forward viewing colonoscopy by achieving 330° panoramic views using three contiguous cameras. In an Australian study in patients with IBD, mean dysplasia identified with conventional forward-viewing colonoscope was 0.13 versus 0.37 with FUSE ( $p=0.044$ ) with or without chromoendoscopy.<sup>[9]</sup>

Other advanced imaging techniques such as confocal laser endomicroscopy, although more accurate in providing in vivo diagnosis of dysplasia, have limited applicability for Crohn's disease surveillance.<sup>[18]</sup> Even without the use of these limited technologies, high-definition WLE with or without NBI or dye-spray chromoendoscopy may identify visible dysplasia without relying on random biopsies.

The European Crohn's and Colitis Organisation recommends that surveillance colonoscopy should take into account local expertise.<sup>[18]</sup> Chromoendoscopy with targeted biopsies has been shown to increase dysplasia detection rate. Alternatively, random biopsies (quadrantic biopsies every 10 cm) and targeted biopsies of any visible lesion should be performed if WLE is used. High-definition endoscopy should be used if available.<sup>[19]</sup>

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### 4.26.1.4 Targeted versus random biopsies

Targeted biopsies have been shown to be non-inferior to random biopsies.<sup>[20]</sup> In a tandem colonoscopy study using FUSE, the dysplasia yield of random colonic biopsies was only 0.3% (95% CI 0.0–0.7,  $n=2/687$  biopsies) with no additional unique subjects identified, versus 16.0% (95% CI 10.3–21.6,  $n=26/163$ ) for targeted biopsies ( $p<0.0001$ ).<sup>[9]</sup> Chromoendoscopy therefore increases the yield of dysplasia compared with WLE. However, chromoendoscopy increases the duration of colonoscopy by a mean of 11 minutes.<sup>[10]</sup>

Random biopsies may identify invisible dysplasia missed by high-definition colonoscopy and chromoendoscopy. Random biopsies are still recommended in patients at high risk of invisible dysplasia, i.e. those with previous colorectal dysplasia, primary sclerosing cholangitis (PSC) or tubular colon.<sup>[20]</sup>

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## 4.26.2 Evidence

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*What are the recommended surveillance strategies for surveillance in IBD patients? (SUR3)*

#### 4.26.2.1 Systematic review evidence

A total of 24 studies reported IBD cohorts with varying clinical manifestations (including UC, Crohn's disease and undefined colitis with and without PSC) in relation to surveillance endoscopy technologies for the detection of colonic neoplasia (including dysplasia, or intraepithelial neoplasia).<sup>[13][21][22][15][23][24][25][26][11][27][9][28][29][30][31][20][32][16][33][34][35][36][37][19]</sup> Seventeen studies were level II evidence<sup>[13][22][15][23][25][26][11][27][9][29][30][32][16][34][36][37][19]</sup> and six studies were level III-2 evidence.<sup>[35][31][21][28][33][20][24]</sup> Two studies were at high-risk of bias,<sup>[24][28]</sup> one study was at moderate risk of bias,<sup>[20]</sup> six studies were at low risk of bias,<sup>[9][25][36][31][33][35]</sup> seven studies were at risk of bias,<sup>[21][22][15][29][26][34][37]</sup> and eight studies had unclear risk of bias.<sup>[13][23][11][27][30][32][16][19]</sup>

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##### 4.26.2.1.1 Neoplasia detection rate

Three randomised controlled trials (RCTs) reported neoplasia detection rates comparing those receiving chromoendoscopy surveillance with those receiving NBI. In a study by Bisschops et al (2012)<sup>[13]</sup> with 68 patients, no significant difference was reported for neoplasia detection in chromoendoscopy versus NBI per patient (0.919) or per lesion ( $p=0.225$ ) analysis. Pellisé et al (2011)<sup>[16]</sup> reported no significant difference in the detection of suspicious lesions, on a per-patient ( $p=0.43$ ) or per-lesion ( $p=0.644$ ) basis. Watanabe et al (2016)<sup>[19]</sup> reported identical detections rates (2.3%) for high-grade dysplasia (HGD) or cancer in a trial in 263 patients. A single study reported no significant difference ( $p=0.50$ ) for the detection of HGD or cancer in a cohort of 369 patients when comparing high-definition endoscopy to standard-definition endoscopy.<sup>[35]</sup> Neoplasia detection was reported in a cohort of 236 comparing chromoendoscopy to WLE.<sup>[31]</sup> This study reported no significant difference between chromoendoscopy and WLE on per-patient ( $p=1.0$ ) or per-procedure analysis ( $p=0.80$ ).<sup>[31]</sup> Only one study reported neoplasia detection in a small cohort of 48 patients comparing NBI to high-definition endoscopy. On per-lesion analysis, NBI detected a significantly greater proportion of lesions than high-definition endoscopy ( $p<0.001$ ). The same significant difference was not seen ( $p=1.0$ ) for per-patient analysis.<sup>[36]</sup>

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##### 4.26.2.1.2 Neoplasia detection diagnostic accuracy

Iacucci et al (2016)<sup>[26]</sup> reported the diagnostic accuracy for high-definition endoscopy for neoplasia detection in a cohort of 75 patients. With a reported detection rate of 28%, high-definition endoscopy had a sensitivity of 93.6% and a specificity of 85%. The same study reported the diagnostic accuracy for high-definition dye-chromoendoscopy for neoplasia detection in a cohort of 75 patients. With a reported detection rate of 22.6%, high-definition dye-chromoendoscopy had a sensitivity of 86.6% and a specificity of 89.6%. The same study<sup>[26]</sup> also reported the diagnostic accuracy for high-definition virtual chromoendoscopy for neoplasia detection in a cohort of 75 patients. With a reported detection rate of 17.3%, high-definition virtual chromoendoscopy had a sensitivity of 92% and a specificity of 73.3%.

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#### 4.26.2.1.3 Dysplasia detection rate

Several studies compared two imaging technologies, and found no significant difference in dysplasia detection rates. These included chromoendoscopy versus NBI,<sup>[15]</sup> high-definition endoscopy versus standard-definition endoscopy,<sup>[21]</sup> NBI vs WLE,<sup>[11]</sup> and WLE versus NBI.<sup>[27]</sup>

Three studies reported dysplasia detection using chromoendoscopy compared with WLE. Marion et al (2016)<sup>[28]</sup> compared chromoendoscopy-targeted biopsies with either WLE-targeted, or random biopsies in a cohort of 68 patients. Chromoendoscopy-targeted biopsy detected significant greater dysplasia than random biopsies ( $p < 0.001$ ) or WLE-targeted biopsies ( $p = 0.001$ ). WLE-targeted biopsies were no better than random biopsies ( $p = 0.054$ ). Picco et al (2013)<sup>[33]</sup> did not report statistical analysis of the differences in HGD and low-grade dysplasia detection rates with chromoendoscopy and WLE in a cohort of 75 patients. Rates of dysplasia detection were similar for targeted WLE biopsies and targeted chromoendoscopy biopsies.<sup>[33]</sup> In a large cohort of 1000 IBD patients undergoing more than 35,000 biopsies. Moussata et al (2017)<sup>[29]</sup> reported that the dysplasia detection rate was almost 14 times greater with chromoendoscopy-targeted biopsy than with random biopsy.

Two RCTs reported dysplasia detection comparing high-definition chromoendoscopy to high-definition WLE. Mohammed et al (2015)<sup>[30]</sup> ( $n = 103$ ) reported that the rate of dysplasia detection per patient was significantly ( $p = 0.04$ ) greater with chromoendoscopy than WLE. Park et al (2015)<sup>[32]</sup> reported no difference in rates of colitis-associated dysplastic lesions or sporadic adenoma in a trial of 210 participants using the same endoscopy methods.

Leong et al (2017)<sup>[9]</sup> reported the dysplasia detection miss rate in a crossover RCT in 52 IBD subjects undergoing surveillance for neoplasia. Conventional high-definition forward-viewing colonoscopy missed 71.4% of dysplastic lesions on per lesion analysis, whereas FUSE missed 25.0% per lesion ( $p < 0.0001$ ). Forward-viewing colonoscopy missed 75.0% of dysplastic lesions per subject and FUSE missed 25.0% per subject ( $p = 0.046$ ).

Hlavaty et al (2011)<sup>[25]</sup> reported intraepithelial neoplasia detection in a diagnostic accuracy study of 45 participants. Combining WLE and chromoendoscopy significantly improved the detection of intraepithelial neoplasia in per-patients analysis ( $p = 0.002$ ), compared to random biopsies only. White light endoscopy alone was superior to random biopsies ( $p = 0.04$ ). All other analyses show no significant difference. Günther et al (2011)<sup>[24]</sup> reported a significant difference ( $p < 0.05$ ) in the rate of detection of flat polypoid lesions (with high-grade intraepithelial neoplasia) in 4819 biopsies taken in 150 participants by confocal endomicroscopy-guided targeted biopsies, compared with either chromoendoscopy or high-definition WLE-guided random biopsies.

Freire et al (2014)<sup>[23]</sup> reported intraepithelial neoplasia detection in a RCT with 162 participants. No significant differences ( $p > 0.05$ ) were reported between chromoendomicroscopy versus WLE.

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## 4.26.2.2 Diagnostic accuracy studies

### 4.26.2.2.1 Chromoendoscopy

Wanders et al (2017)<sup>[37]</sup> reported the diagnostic accuracy of chromoendoscopy for dysplasia detection in a cohort of 61 patients. With a reported detection rate of 9.8%, these combined techniques had a sensitivity of 28.6% and a specificity of 86.4%.

### 4.26.2.2.2 Confocal laser endomicroscopy

Rispo et al (2012)<sup>[34]</sup> reported the diagnostic accuracy for confocal laser endomicroscopy for dysplasia detection in a cohort of 51 patients. With a reported detection rate of 27%, confocal laser endomicroscopy had a sensitivity of 100% and a specificity of 90%.

Wanders et al (2017)<sup>[37]</sup> also reported the diagnostic accuracy for integrated confocal laser endomicroscopy in combination with chromoendoscopy for dysplasia detection in a cohort of 61 patients. With a reported detection rate of 9.8%, these combined technique had a sensitivity of 42.9% and a specificity of 92.5%.

Dlugosz et al (2016)<sup>[22]</sup> reported the diagnostic accuracy for probe-based confocal laser endoscopy for dysplasia detection in a cohort of 644 patients. With a reported detection rate of 3.0%, probe-based confocal laser endoscopy had a sensitivity of 89% and a specificity of 96%.<sup>[22]</sup>

### 4.26.2.2.3 High-definition endoscopy

The Dlugosz et al study<sup>[22]</sup> also reported the diagnostic accuracy for high definition endoscopy for dysplasia detection in a cohort of 644 patients. With a reported detection rate of 3.0%, high-definition endoscopy had a sensitivity of 68%, but a specificity of 97%.<sup>[22]</sup>

### 4.26.2.2.4 White-light endoscopy

Matsumoto et al (2010)<sup>[29]</sup> reported the diagnostic accuracy of WLE for dysplasia detection in a cohort of 48 patients. With a reported detection rate of 8.3%, WLE had a sensitivity of 78.6% and a specificity of 78.6%.<sup>[29]</sup>

### 4.26.2.2.5 Autofluorescence imaging

The Matsumoto et al study<sup>[29]</sup> also reported the diagnostic accuracy for auto fluorescence imaging for dysplasia detection in a cohort of 48 patients. With a reported detection rate of 8.3%, auto fluorescence imaging had a sensitivity of 100%, but a specificity of only 18.2%.<sup>[29]</sup>

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### 4.26.3 Evidence summary and recommendations

Evidence summary	Level	References
Current evidence continues demonstrate the superiority of chromoendoscopy in the detection of dysplasia in patients with IBD.	II, III-2	[6], [20], [30]
Targeted biopsies are non-inferior to random biopsies in dysplasia detection.  Invisible dysplasia is defined by histological dysplasia that is identified by random biopsies and not seen either by white light endoscopy or chromoendoscopy. Inflammatory bowel disease patients with primary sclerosing cholangitis (PSC), prior dysplasia or intestinal damage (stricture, colonic foreshortening) have increased risk of invisible dysplasia found on random biopsies.	II, III-2	[25], [20]

Evidence-based recommendation	Grade
Chromoendoscopy should be incorporated into surveillance procedures, especially in high-risk patients.	<b>A</b>

Evidence-based recommendation	Grade
Taking targeted, rather than random, biopsies is the recommended method of identifying dysplasia in patients with inflammatory bowel disease.	<b>B</b>

Evidence-based recommendation	Grade
Random biopsies are recommended in IBD patients with PSC, prior dysplasia, and intestinal damage (colonic stricture or foreshortening).	<b>C</b>

Evidence-based recommendation	Grade
Standard-definition colonoscopy is not recommended for surveillance procedures, especially in the absence of chromoendoscopy	<b>B</b>

### Consensus-based recommendation

Proceduralists performing surveillance colonoscopy in patients with IBD should be familiar with and adhere to surveillance guidelines.

### Practice point

IBD surveillance requires high-quality colonoscopy:

- ‡ performing the colonoscopy when the patient is in clinical and endoscopic remission
- ‡ excellent bowel preparation
- ‡ the use of high-definition colonoscopes
- ‡ ensuring optimal and full visualisation of the mucosal surface during slow withdrawal.

### Practice point

Dye spray chromoendoscopy can be applied with a spray catheter or by incorporating dye in the reservoir of the water pump.

### Practice point

Either methylene blue or indigo carmine is an appropriate dye for chromoendoscopy.

### Practice point

Upon identification of invisible dysplasia on random biopsies, confirmation of diagnosis and grade is required by at least two GI pathologists. Chromoendoscopy is then recommended to determine if there is multifocal dysplasia.



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#### 4.26.3.1 Considerations in making these recommendations

Emerging evidence, suggests that digital non-dye-based chromoendoscopy in combination with high definition imaging may replace dye-based chromoendoscopy in expert IBD surveillance centres and be able to reduce overall colonoscopy duration.

#### 4.26.3.2 Unresolved issues

The optimal withdrawal time for dye-spray and non-dye digital chromoendoscopy has not been identified.

Whether non-NBI non-dye digital chromoendoscopy provided by other endoscope companies provide similar benefits as NBI remains unknown.

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### 4.26.4 References

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## 4.27 Management of elevated dysplasia in IBD

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### 4.27.1 Background

Historically, an elevated lesion containing dysplasia in inflammatory bowel disease (IBD) was referred to as a dysplasia-associated lesion or mass (DALM). Such lesions were strongly associated with synchronous or metachronous colorectal cancer (CRC).<sup>[1]</sup> A diagnosis of DALM was therefore an indication for colectomy. In the present era of high-definition colonoscopy where earlier detection of dysplasia is typical, the term DALM should no longer be used (see Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients: International Consensus Recommendation [SCENIC]).<sup>[2]</sup>

Visible dysplastic lesions that can often be resected endoscopically with clear resection margins can be followed by close surveillance colonoscopy with good outcomes.<sup>[3][4][5][6][7]</sup> Conversely, if the dysplastic lesion cannot be entirely removed, or multifocal dysplasia is present indicating a more widespread 'field-effect', referral for surgical management is recommended.

Elevated dysplastic lesions should be classified as either endoscopically-resectable or endoscopically non-resectable. Endoscopically resectable methods include conventional polypectomy and endoscopic mucosal resection. Endoscopic submucosal dissection or full-thickness resection might be possible in some situations. When lesions are removed endoscopically, ensure that the surrounding flat mucosal does not harbour dysplasia either by visualisation or by biopsies. Tattooing is recommended to permit easier identification for future surveillance colonoscopies.

Endoscopically non-resectable dysplastic lesions would require surgical resection, typically by colectomy. Referral for discussion at an IBD multidisciplinary meeting involving an experienced colorectal surgeon is recommended.

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## 4.27.2 Evidence

*What should be the protocol to manage elevated dysplasia in IBD? (MNG1)*

### 4.27.2.1 Systematic review evidence

No studies published since 2010 were identified that compared management protocols for elevated dysplasia in those with IBD.

### 4.27.2.2 Overview of additional evidence (non-systematic literature review)

Long-term follow-up data are reassuring that localised dysplastic lesions in IBD can be treated effectively endoscopically followed by close surveillance follow up.<sup>[3][4][5][6][7]</sup>

A recent meta-analysis looking at the cancer risk after resection of polypoid dysplasia in patients with longstanding ulcerative colitis, found the pooled incidence of CRC to be 5.3 (95% confidence interval [CI] 2.7–10.1) per 1000 years of patient follow-up. Colorectal cancer/high grade dysplasia combined and all forms of dysplasia were 7.0 (95% CI 4.0–12.4) and 65 (95% CI 54–78) per 1000 years of patients follow up.<sup>[8]</sup>

## 4.27.3 Evidence summary and recommendations

Evidence summary	Level	References
No studies published since 2010 were identified that compared management protocols for elevated dysplastic lesions in patients with IBD.		

Evidence-based recommendation	Grade
Raised lesions containing dysplasia may be treated endoscopically provided that entire lesion is removed and there is no dysplasia in flat mucosa elsewhere in the colon.	<b>C</b>

Evidence-based recommendation	Grade
If a raised dysplastic lesion cannot be completely removed, surgical intervention is strongly recommended.	<b>D</b>

### Consensus-based recommendation

In the presence of multifocal low-grade dysplasia that cannot be removed endoscopically, at least frequent surveillance colonoscopy is required. Surgical management is also an alternative based on case-by-case discussion.

Surveillance colonoscopy with chromoendoscopy within 3–12 months should be carried out after endoscopic resection of an elevated dysplastic lesion in inflammatory bowel disease.

### Practice point

The important objective for the endoscopist performing surveillance procedures is to identify lesions that are safely and completely resectable endoscopically. This is based on endoscopic features of the identified lesion and elsewhere in the colon.

### Practice point

Nomenclature should reflect the SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease. The term 'dysplasia associated lesion or mass (DALM)' should not be used.

### Practice point

Consider referral to an experienced endoscopist to perform surveillance for inflammatory bowel disease using chromoendoscopy to exclude multi-focal dysplasia followed by endoscopic resection of the dysplastic lesion.

### Practice point

Close colonoscopic surveillance is required following endoscopic resection of dysplasia given the risk of multifocal dysplasia and metachronous dysplasia.

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## 4.28 High-grade dysplasia in IBD

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### 4.28.1 Background

Patients with inflammatory bowel disease (IBD; both ulcerative colitis [UC] and Crohn's colitis) are at increased risk of developing colorectal cancer (CRC). Appropriate colonoscopic surveillance using recommended techniques at appropriate intervals is therefore recommended so as to allow early detection of dysplasia amenable to endoscopic resection prior to onset of invasive disease. The management of high-grade dysplasia (HGD) in patients with IBD depends on whether or not the lesion is amenable to complete endoscopic resection and if the dysplasia is visible.

Traditionally, the approach to managing HGD has been surgical resection. This recommendation stemmed from early studies that indicated a high prevalence of CRC (42–67%) in the resected specimen in patients who underwent colectomy for HGD. In recent years however, the management approach in these patients has evolved away from routine colectomy due to several factors: improved lesion visualisation in the era of high-definition white light endoscopy (WLE) and chromoendoscopy, better cancer risk stratification as a result of better understanding of the natural history of dysplasia, and patients' preference for continued surveillance over colectomy.

Three factors need to be taken into consideration to determine the best management protocol for IBD patients with HGD:

- the natural history of HGD and the degree of risk that a patient will develop cancer
- comparative patient outcomes after colectomy and continued surveillance
- patients' preferences for the different treatment options.

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## 4.28.2 Evidence

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*What should be the protocol to manage high grade dysplasia in IBD? (MNG2)*

### 4.28.2.1 Systematic review evidence

The systematic review only identified a single publication meet the inclusion criteria: the SCENIC International Consensus Statement on Surveillance and Management of Dysplasia in Inflammatory Bowel Disease.<sup>[1]</sup> Dysplasia in IBD was the focus of this consensus statement which was based on a synthesis of existing literature and consensus expert opinion.

Although Australian experts were not involved in the development of these guidelines, the panel of experts from the SCENIC consensus statement development panel were all from developed countries where the health care system and patient demographics are likely to be comparable to that in Australia. For these reasons, it was thought that these guidelines are likely to be fairly representative and, therefore, applicable to Australia.

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#### 4.28.2.1.1 Natural history of high-grade dysplasia

Confirmation of the grade of dysplasia is initially required, through consensus with an expert gastrointestinal pathologist. The distinction is important, because high-grade dysplasia (HGD) is indicative of a more aggressive lesion than low-grade dysplasia (LGD). Exclusion of invasion (intramucosal cancer) is required, and is often best done by en bloc resection.

The management of patients with non-resectable or resectable polypoid and non-polypoid HGD was considered separately, because the natural history of these lesions is likely to be different.<sup>[1]</sup>

##### 4.28.2.1.1.1 Non-resectable high grade dysplasia

Patients with endoscopically non-resectable HGD should undergo colectomy.<sup>[1]</sup>

#### **4.28.2.1.1.2 Resectable polypoid high grade dysplasia**

Of the studies that reported outcomes for polypoid HGD, most studies were heterogeneous in that both LGD and HGD were included.<sup>[1]</sup> Only one study reported on outcomes for patients with polypoid HGD alone. Of the six studies that reported on the incidence of CRC in patients with LGD and HGD, most patients had LGD. Over a mean follow up period of 36–82 months, 19 of 311 patients developed a CRC. The overall incidence of CRC was 6% with a range of 2–13%. Of the only study that focused on polypoid HGD, none of the nine patients developed CRC after a mean follow up period of 76.5 months (range 52–99 months).<sup>[1]</sup>

A systematic review that included data from 376 patients with resected polypoid dysplasia in 10 studies reported an annualised CRC incidence of 0.5%, which was considered comparable to that of synchronous and metachronous CRC.<sup>[1]</sup> This finding would favour to surveillance over colectomy.

#### **4.28.2.1.1.3 Resectable non-polypoid high grade dysplasia**

In patients with resectable non-polypoid HGD, it remains acceptable to offer surveillance over colectomy as most dysplasia will be visible provided that careful, high-quality colonoscopic surveillance is performed by an IBD expert using high-definition colonoscopy. The use of chromoendoscopy is required to further exclude multifocal dysplasia. However, the SCENIC suggestion to offer these patients surveillance colonoscopy rather than colectomy was conditional, given the higher risk of CRC with non-polypoid HGD and the greater difficulty in ensuring complete resection.

#### **4.28.2.1.1.4 Invisible dysplasia**

The term invisible dysplasia refers to lesions identified by random biopsies. Invisible dysplasia accounts for <10% of dysplasia.<sup>[1]</sup> Invisible dysplasia is uncommon in sporadic colorectal carcinogenesis and tends to be associated with IBD chronic colitis. The risk of invisible dysplasia is highest for patients with additional high-risk factors of primary sclerosing cholangitis, prior colorectal dysplasia, and tubular foreshortened colon. In the presence of one or more high risk factors, random colonic biopsies is required in order to identify invisible dysplasia that can be missed even with advanced imaging techniques. The yield of invisible dysplasia with random biopsies is low – approximately 0.2–0.3%.<sup>[2][3]</sup>

Four studies (each comprising more than 15 IBD patients) reported on the incidence of CRC after the diagnosis of invisible dysplasia.<sup>[1]</sup> Over a mean follow up period of 15–50 months, CRC developed in 7 of 122 (6%, range 3–9%) patients. This contrasts with earlier studies which reported a much higher incidence of synchronous CRC in the resected specimen when the colectomy was performed for invisible dysplasia. Notably, a systematic review comprising of 20 studies which included 477 patients with invisible LGD reported a CRC rate of 22% in

the resected colectomy specimen.<sup>[1][4]</sup> An even earlier (1994) systematic review found CRC in 42% (10 of 24 patients) of patients with invisible HGD.<sup>[5]</sup> Subsequent studies have echoed similar rates of CRC ranging between 45% and 67%.<sup>[6][7][8][9]</sup> However, it is likely that these high rates of CRC are related to technological issues in an era where high-definition WLE and chromoendoscopy were not available.<sup>[1]</sup> This is likely to account for the disparity between the rates of 'invisible' dysplasia reported in older studies (87%)<sup>[5]</sup> and compared to that in more recent studies (10%).<sup>[1]</sup>

The rationale for recommending surveillance colonoscopy for invisible LGD or colectomy for invisible HGD therefore no longer stands. Instead, SCENIC recommended referral to an endoscopist skilled with IBD surveillance using chromoendoscopy with high-definition colonoscopy when invisible dysplasia is diagnosed. A visible lesion should be managed according to its features (above) and, if no dysplasia is identified (i.e. true invisible dysplasia), patients should be counselled appropriately about the role of continued surveillance versus colectomy.

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#### **4.28.2.1.2 Treatment of high grade dysplasia**

No studies were found that compared endoscopic management with colectomy after endoscopic resection of lesions with HGD, whether polypoid or non-polypoid HGD.<sup>[1]</sup> Hence, the management of these lesions relies heavily on the clinician's assessment of risk in terms of cancer development and the patient's preference between surveillance versus colectomy after an informed discussion.

Exclusion of multi-focal dysplasia indicative of widespread field defect is required. Close surveillance is required after complete endoscopic resection of solitary resectable high-grade dysplastic lesions confirmed as non-invasive by a pathologist.

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#### **4.28.2.1.3 Patient preferences**

This was not part of the review undertaken for the SCENIC consensus statement, but the authors described one study in which 199 patients with UC were surveyed. The study found that patients preferred colonoscopic surveillance over colectomy unless the risk of synchronous CRC was greater than 73%.<sup>[10]</sup> No other studies were described.

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#### **4.28.2.2 Evidence summary and recommendations**

<b>Evidence summary</b>	<b>Level</b>	<b>References</b>
Following complete endoscopic resection of polypoid high-grade dysplasia (HGD), colonoscopic surveillance is preferable over colectomy.	III-1	[11], [12], [13], [14], [15],

Evidence summary	Level	References
Following complete endoscopic resection of non-polypoid HGD, colonoscopic surveillance is preferable to colectomy.		[16], [17], [18]
In the presence of invisible HGD that has been confirmed by a second expert gastrointestinal pathologist, chromoendoscopy with high-definition colonoscopy is recommended to help determine if there is multi-focal dysplasia.	IV	[6], [14], [16], [7], [9], [8], [4], [19], [20]

Evidence-based recommendation	Grade
Patients with endoscopically non-resectable high-grade dysplasia should undergo colectomy.	<b>C</b>

Evidence-based recommendation	Grade
For patients with endoscopically resectable high grade dysplasia, whether polypoid or non-polypoid, continued colonoscopic surveillance after complete resection of the lesion is recommended rather than referral for colectomy.	<b>C</b>

Consensus-based recommendation
Patients with resected high-grade dysplasia should undergo further surveillance in 3-12 months. Subsequent surveillance intervals depend on the findings of each subsequent surveillance colonoscopy.

Consensus-based recommendation
Patients with invisible high-grade dysplasia (HGD) should undergo more intensive colonoscopic surveillance than patients with visible HGD.

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### 4.28.2.3 Considerations in making these recommendations

#### 4.28.2.3.1 Surveillance intervals after complete resection of high grade dysplasia

The optimal frequency of surveillance following complete endoscopic resection of HGD is unclear. More frequent surveillance for these patients would seem sensible but the appropriate interval is not well defined. Most recommendations are extrapolated from existing post-polypectomy surveillance guidelines for non-IBD patients, as published by various societies. The SCENIC consensus statement,<sup>[1]</sup> recommended that patients with resected HGD should undergo further surveillance in 3–6 months. Patients with small (<10mm) resected HGD may return at 12 months for surveillance.

Intervals for subsequent surveillance colonoscopies depend on the findings on the initial repeat scope. Where no further dysplasia is identified on the initial repeat scope, it would seem reasonable to perform a follow-up surveillance scope in 12 months.

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## 4.29 Low-grade dysplasia in IBD

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### 4.29.1 Background

In light of the recent SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease (IBD),<sup>[1]</sup> flat mucosal dysplasia should be differentiated into visible and invisible. Invisible dysplasia cannot be visualised on high-definition white-light endoscopy (WLE) even after chromoendoscopy enhancement, making resection impossible.

The significance of low grade dysplasia (LGD) in flat mucosa is controversial.

### 4.29.2 Evidence

*What should be the protocol to manage low grade dysplasia in IBD? (MNG3)*

#### 4.29.2.1 Systematic review evidence

Tertiary referral data have generally shown that LGD is associated with progression to high-grade dysplasia (HGD) or cancer.<sup>[2][3]</sup> Of 47 patients who were diagnosed with LGD at St Mark's Hospital (London, UK), 20% eventually developed CRC and 39% developed either HGD or cancer.<sup>[2]</sup> In a cohort treated at Mount Sinai Hospital (New York, USA), the rate of progression to higher grades of neoplasia was 53% at 5 years.<sup>[3]</sup> These results contrast with other data which show progression from LGD to advanced neoplasia is slow, and is not invariable.<sup>[4][5][6]</sup>

A meta-analysis of 20 surveillance studies involving 508 cases of LGD in flat mucosa or dysplastic mass lesions found the cancer incidence to be 14 per 1000 person-years duration (PYD), and the incidence of any advanced lesion was 30 per 1000 PYD. The positive predictive value of LGD for concurrent cancer was 25% and for progression to cancer was 8%.<sup>[7]</sup> Of 159 patients with LGD followed longitudinally, 10 were found to progress to advanced dysplasia on follow up (5 HGD, 5 cancer) with an overall incidence of 1.34 cases in 100 patient-years.



Of 89 subjects with visible LGD that was completely removed (52 were identified with standard definition WLE, 17 with high-definition WLE and 20 with chromoendoscopy), 5 patients developed advanced neoplasia (0.97 cases per 100 patient-years), all of whom had undergone surveillance with standard-definition WLE.<sup>[7]</sup> These data support the use of high-definition endoscopy and/or chromoendoscopy in surveillance following detection of LGD.

More lesions can be detected by chromoendoscopy but the impact in the reduction of cancer remains less certain.<sup>[8]</sup> Patients in whom invisible dysplasia is detected should be referred to an endoscopist with expertise in chromoendoscopy surveillance for IBD. If a visible dysplasia is identified, it should be resected endoscopically, if possible. After successful endoscopic resection, initial surveillance colonoscopy should be performed in 3–6 months. There are currently no studies comparing surveillance colonoscopy with colectomy in this setting.<sup>[1]</sup>

Due to the uncertainty about the predictive value of invisible LGD, it is recommended that surgery be considered if it is multifocal. However, patients with LGD in flat mucosa who wish to avoid an operation require repeat colonoscopy at 3–6 months, preferably with chromoendoscopy, and thereafter at yearly intervals. A finding of unifocal LGD in flat mucosa is less likely to be associated with imminent cancer, and follow-up colonoscopy is reasonable within 6 months in these cases.

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#### 4.29.2.2 Overview of additional evidence (non-systematic literature review)

Two retrospective studies, including a total of 223 patients with LGD, demonstrated that rates of progression to high grade dysplasia or colorectal cancer (CRC) was generally low (5–12%) over a median follow-up period of 3–5 years. Flat dysplasia located in the distal colon is associated with higher risk of progression.<sup>[9][10]</sup> In recent data from a Dutch nationwide study, the progression of LGD to HGD and CRC was 21.9%.<sup>[11]</sup>

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### 4.29.3 Evidence summary and recommendations

Evidence summary	Level	References
The predictive value of low-grade dysplasia (LGD) in flat mucosa for future cancer is controversial, but probably higher if it is located in multiple synchronous sites.	III-2	[2], [7], [3], [4], [5], [6]
Low-grade dysplasia arising from flat mucosa should be evaluated for multifocal dysplasia typically by an expert IBD endoscopist utilising chromoendoscopy with high-definition colonoscopy.	III-3	[1], [8]
Following endoscopic resection of LGD, close surveillance is recommended due to the increased risk of synchronous and metachronous dysplasia.	III-3	[1], [8]

Evidence-based recommendation	Grade
Unifocal low-grade dysplasia should be followed by ongoing surveillance using high-definition white-light endoscopy and chromoendoscopy at 6 months. If 6-month surveillance colonoscopy is normal, surveillance should be repeated annually.	<b>C</b>

Evidence-based recommendation	Grade
Low-grade dysplasia in flat mucosa should be evaluated for multifocal dysplasia by an endoscopist with expertise in inflammatory bowel disease surveillance using high-definition white-light endoscopy and/or chromoendoscopy.	<b>C</b>

Consensus-based recommendation
Visible dysplasia should be resected endoscopically and then followed up with surveillance colonoscopy with high-definition white-light endoscopy and chromoendoscopy within 3-12 months.

Consensus-based recommendation
Consider shorter surveillance intervals for flat dysplasia located in the distal colon, as this is associated with higher risk of progression.

Practice point
When determining an individual's appropriate surveillance frequency, the risk factors for progression of low-grade dysplasia (LGD) towards high-grade dysplasia (HGD) or colorectal cancer are: older age at diagnosis of LGD (age >55 years), male sex and inflammatory bowel disease duration of >8 years at diagnosis of LGD.

### Practice point

Multifocal low-grade dysplasia is associated with a sufficiently high risk of future cancer that colectomy is usually recommended. Patients who elect to avoid surgery require follow-up surveillance at 3 months, preferably with chromoendoscopy and high-definition white-light endoscopy. If 3-month surveillance colonoscopy is normal, surveillance should be repeated annually.

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## 4.30 Indefinite dysplasia in IBD

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### 4.30.1 Background

Dysplasia in colitis surveillance is classified as low-grade dysplasia (LGD) or high-grade dysplasia (HGD). Rarely, following expert pathologist review, the histologic changes fall short of those required to make a diagnosis of LGD, and are termed indefinite dysplasia (ID). Typically, the diagnosis of ID is made when there is active colitis that might induce changes of atypia and interfere with a definitive diagnosis of dysplasia.

Frequently, repeat colonoscopy is performed following induction of mucosal healing, and repeat endoscopic biopsies are required to determine whether the ID changes have resolved, remain or progress towards LGD or HGD. It is helpful to note whether the dysplasia is within an endoscopically visible lesion, or in endoscopically normal mucosa, ideally with the assistance of enhanced endoscopic imaging. The rates of progression of ID to LGD or beyond are unknown, with a paucity of literature referring to ID and outcomes.

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## 4.30.2 Evidence

*What should be the protocol to manage indefinite dysplasia in IBD? (MNG4)*

### 4.30.2.1 Systematic review evidence

No new publications were identified that compared management protocols for ID in those with inflammatory bowel disease (IBD).

### 4.30.2.2 Overview of additional evidence (non-systematic literature review)

Lai et al followed 125 subjects diagnosed with ID from a pathology database from 1989–2004. Of 22 subjects that had resection within 6 months of diagnosing ID, the prevalence of dysplasia was 27.3% (1 LGD, 5 HGD). Of 59 subjects with ID that had follow up colonoscopy data, the progression rate to dysplasia or colorectal cancer (CRC) was 3.2 cases per 100 person years. The progression rate to dysplasia was 1.5 cases per 100 person years at risk.<sup>[1]</sup> It must be noted that cases of ID diagnosed from 1989 to 2004 relied on standard-definition colonoscopy and might have missed cases of synchronous LGD or HGD to account for this strong association of ID with dysplasia. van Schaik et al found 5 of 26 cases (19%) of ID developed advanced dysplasia after a median follow up of 24 months.<sup>[2]</sup>

If ID is diagnosed, progression to a higher grade of dysplasia or carcinoma is unusual. In a large series, at a single tertiary referral centre, 1 of 23 patients with ID (4%) eventually developed carcinoma and 5 (22%) developed LGD after 9 years of follow-up.<sup>[3]</sup> In contrast, data from New York showed that the five year rate of progression from ID to HGD or CRC was 9%.<sup>[4]</sup> If a biopsy is diagnosed as indefinite for dysplasia by two sub-specialised gastrointestinal pathologists, follow-up surveillance colonoscopy (preferably with chromoendoscopy) at 6 months is reasonable, and thereafter at annual intervals. Treatment escalation to ensure that endoscopic and histological healing takes place can clarify or help exclude the diagnosis of dysplasia severity.<sup>[5]</sup>

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## 4.30.3 Evidence summary and recommendations

Evidence summary	Level	References
The predictive value of indefinite dysplasia in flat mucosa for imminent cancer is	III-2,III-	[3], [4]

Evidence summary	Level	References
low.	3	

Evidence-based recommendation	Grade
Indefinite dysplasia in flat mucosa does not require surgery, but follow-up colonoscopic surveillance is recommended, preferably with chromoendoscopy, at more frequent intervals.	<b>D</b>

Consensus-based recommendation
Indefinite dysplasia should be reviewed by a second gastro-intestinal pathologist.

Consensus-based recommendation
After detecting indefinite dysplasia, inflammation (if present) should be treated and colonoscopy should be repeated.

Practice point
If indefinite dysplasia is detected at random biopsy, repeat colonoscopy with enhanced imaging techniques may assist in defining an endoscopically resectable lesion, or a lesion amenable to further targeted biopsies.

Practice point
If there are features of active inflammation, repeat colonoscopy following escalation of therapy may assist in further defining indefinite dysplasia.

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## 4.30.4 References

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## 4.31 Discussion

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## 4.31.1 Health system implications

### 4.31.1.1 Clinical practice

Dedicated inflammatory bowel disease (IBD) services that can provide advanced imaging techniques offering high-quality colonoscopy using advanced endoscopic imaging technologies are recommended. Expert referral centres that can perform endoscopic mucosal resection, endoscopic submucosal dissection and full-thickness resections are required to reduce the need for colectomy. Dedicated training of advanced imaging techniques used in IBD surveillance is recommended. Confirmation of dysplasia with a second experienced gastrointestinal pathologist is required to confirm diagnosis and establish the grade of dysplasia.

Endoscopic resection of dysplasia, followed by close surveillance, can reduce the need for colectomy. Treatment should be individualised according to patients' wishes. Recommendations should be provided following a multidisciplinary discussion incorporating colorectal surgeon, gastroenterologist and pathologist.

Surveillance for IBD-associated dysplasia should be performed in dedicated tertiary centres by endoscopists with expertise in IBD surveillance. These centres should have access to high-definition white-light endoscopy and chromoendoscopy. Inflammatory bowel disease patients with high risk of dysplasia, including those with concurrent primary sclerosing cholangitis or prior flat dysplasia might benefit from panoramic imaging such as full-spectrum endoscopy combined with chromoendoscopy.<sup>[1]</sup> This would ensure a standardised high level of care and constitute a platform for education and training, as well as permit data-collection and creation of centralised database of IBD-associated dysplasia.

### 4.31.1.2 Resourcing

Since the 2011 update of these guidelines, there has been an overall move away from routine colectomy in patients with high-grade dysplasia (HGD). Although the overall incidence of HGD is low, the expertise available for high-quality IBD surveillance through chromoendoscopy and high-definition colonoscopy may only be available at selected centres. And as these patients may require fairly intensive surveillance, this may translate to greater IBD surveillance workload in expert centres and therefore greater need for rural IBD patients to travel to expert centres. Notwithstanding this, these guidelines are not anticipated to alter current resourcing levels as the overall incidence of HGD is low (approximately 3.2% of all IBD patients).

Resources will need to be allocated towards:

- hiring and training of additional medical, nursing and supporting personnel to operate dedicated surveillance endoscopy lists, including expert gastrointestinal pathologists experienced in dysplasia diagnosis, and colorectal surgical units experienced in managing IBD surgery.



- purchase and installation of high-resolution endoscopes, dye and pump sets for chromoendoscopy, and endoscopy systems that can provide panoramic imaging to reduce miss rates of dysplasia behind colonic folds and in blind spots. Inflammatory bowel disease centres should be resourced to conduct advanced endoscopic resection.

#### 4.31.1.3 Barriers to implementation

Barriers to implementation of the recommendations for colonoscopic surveillance and management of dysplasia in patients with IBD include:

- poor awareness of surveillance guidelines
- low-quality surveillance colonoscopy
- too frequent surveillance colonoscopies or performing surveillance on those with a low yield of dysplasia (e.g. proctitis or ileitis)
- resource shortage
- inconsistency in knowledge of dysplasia surveillance
- lack of established IBD centres that provide dysplasia surveillance

Attitudes of gastroenterologists will determine willingness to refer patients to a centralised endoscopy unit for a service they themselves can provide

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### 4.31.2 Unresolved issues

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#### 4.31.2.1 Elevated dysplasia in IBD

IBD dysplasia nomenclature need to be standardised to allow, physicians to communicate findings effectively. Ongoing use of descriptions such as dysplasia associated lesion or mass (DALM) and ALM is impractical and does not guide management of dysplasia in IBD. Use of these terms should be discouraged.

Long term data is needed to assess the impact of endoscopic resection with close surveillance on the natural history.

#### 4.31.2.2 High-grade dysplasia in IBD

The natural history of HGD remains unclear. Overall, all studies that evaluated HGD have small numbers or form a small cohort within a much larger study of all patients with dysplasia in IBD. More longitudinal studies are needed to allow for better understanding of HGD.

More patient preference studies are needed to understand patient decision-making in the setting of dysplasia, given that the natural history of HGD is likely to remain elusive for the foreseeable future. While it is generally perceived that patients may prefer colonoscopic surveillance over colectomy, it is also well known that clinicians are poor patient surrogates. In the absence of robust data about the likelihood of developing colorectal cancer (CRC), patient preference data is needed to assist with decision making.

The appropriate frequency of surveillance after complete resection of HGD is unclear. More frequent surveillance following resection of HGD would seem sensible and is extrapolated from on existing post-polypectomy surveillance recommendations in patients without IBD. While this would seem appropriate, more studies are needed define appropriate surveillance intervals.

Surgical resection for HGD or CRC in Crohn's disease is typically a total proctocolectomy, as segmental resections might encourage the development of Crohn's disease at the anastomosis.<sup>[2]</sup> However, these recommendations are based upon small series<sup>[3][4]</sup> and in patients with limited Crohn's disease colitis and well-controlled disease, the risk of metachronous and synchronous CRC might be low.<sup>[5]</sup>

#### 4.31.2.3 Low-grade dysplasia in IBD

The recommendations for surveillance over colectomy are largely individualised. To date there are no studies comparing surveillance colonoscopy with colectomy for low-grade dysplasia, or informing the natural history of visible dysplastic lesions after endoscopic resection.

#### 4.31.2.4 Indefinite dysplasia in IBD

Histologic features of indefinite dysplasia (ID) may be present because of ongoing low grade inflammation, and it is important to evaluate ID whilst considering the extent of ongoing inflammation. Repeat examination after treating inflammation can be helpful in this case. The natural history of ID is unknown, and the risk for progression to cancer appears low. Studies on ID do not routinely report the presence of associated inflammation and, in the past, have not used current methods of classifying flat/polypoid dysplasia.

### 4.31.3 Studies currently underway

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No large prospective trials on ID are underway. Some larger units periodically report on ulcerative colitis surveillance outcomes that are collected prospectively, and these reports may add insight regarding long term outcomes of ID.

#### 4.31.4 Future research priorities

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Longitudinal cohort studies with long-term outcomes of patients undergoing endoscopic resection and surveillance is required.

Longitudinal cohort studies of outcomes from surveillance versus colectomy are necessary. The formation of a centralised database could assist in this endeavour.

Clarification of the long-term outcomes for indefinite dysplasia is required. Prospective evidence demonstrating that repeat examination with enhanced imaging techniques improves lesion detection or outcomes (or otherwise) is needed.

Longitudinal cohort studies of outcomes from surveillance versus colectomy are necessary. The formation of a centralised database could assist in this endeavour.

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## 5 Anxiety and colonoscopy: Approaches to minimise anxiety and its adverse effects

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## 5.1 Background

### 5.1.1 Potential adverse outcomes associated with anxiety

While the literature on colonoscopy is extensive, few studies explore its association with anxiety.<sup>[1]</sup> In a study investigating the procedural experience of patients undergoing endoscopic procedures,<sup>[2]</sup> researchers assessed 88 consecutive patients undergoing colonoscopy (n = 55) or gastroscopy (n = 33) 1 week prior to the investigation, while awaiting procedure commencement and 24-72 hours after recovering from sedation post procedure. Before the procedure, the colonoscopy group anticipated significantly more pain and had significantly lower pre-procedural acceptance than the gastroscopy group. However, the colonoscopy group reported lower pain and significant decreases in endoscopy concerns and anxiety after the procedure. Despite this, their acceptance of the procedure did not significantly improve after the procedure, while there was near-universal acceptance of the test in the gastroscopy group. Anticipated pain was the strongest predictor of pre-test acceptance of colonoscopy. The concern of pain associated with colonoscopy needs to be addressed by the practitioner.

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#### 5.1.1.1 Target groups for interventions to minimise anxiety

The evidence suggests two target groups for interventions to minimise anxiety: those with low socioeconomic status (SES) and those who generally tend to be anxious. In addition, women have been identified as more anxious than men in intervention research studies (see Overview of evidence section below)

##### 5.1.1.1.1 *Socioeconomic status*

Researchers have observed differences according to SES in coping with stressful medical procedures.

In a large participant subgroup (n = 3535) from the UK Flexible Sigmoidoscopy Trial,<sup>[3]</sup> anxiety and worry about bowel cancer pre-screening were higher in lower SES participants. Their worry and anxiety reduced after screening, but not to a significantly greater extent than the high-SES group. However, the low-SES subgroup did report more positive psychological consequences of screening in the post-flexible sigmoidoscopy sample (n = 40,534), with an SES gradient for anxiety but not distress measures.<sup>[3]</sup>

While patients in this study underwent screening flexible sigmoidoscopy, the results are likely to be generalisable to those undergoing surveillance colonoscopy, where there are also likely to be concerns about bowel cancer.

#### **5.1.1.1.2 Accuracy of physician estimates of anxiety**

'Trait anxiety' is the tendency to experience anxiety and is considered a stable personality trait. 'State anxiety' is temporary discomfort when feeling threatened by a situation.<sup>[4]</sup> State anxiety, but not trait anxiety, was found to be moderately increased in patients undergoing outpatient diagnostic endoscopy in a US consecutive case series.<sup>[5]</sup> State anxiety about the procedure did not differ by age, sex, source of referral, procedure type or perceived procedural knowledge.<sup>[5]</sup> Thus, people who tended to be anxious overall were also more anxious immediately before the procedure. The authors notably found that physician estimates of patient anxiety were not significantly associated with either procedural state anxiety or changes in state anxiety between baseline and the procedure, and speculated that physician estimates are unrelated due to the increases in state anxiety being small.

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## **5.2 Overview of evidence (non-systematic literature review)**

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No systematic reviews were undertaken for this topic. Practice points were based on selected evidence and guidelines (see Guideline development process).

### **5.2.1 Anxiety level before and during colonoscopy**

Overall, the evidence suggests that 16–20% of people undergoing colonoscopy have severe anxiety, usually related to pain and discomfort. A cross-sectional study<sup>[6]</sup> examined the possible relationship between state (i.e., situational) and trait (i.e., stable) anxiety in 52 gastroscopy and 46 colonoscopy outpatients. The researchers observed a small but statistically significant increase in state anxiety before elective upper gastroscopy and colonoscopy, but no changes in trait anxiety. Females had higher anxiety levels in both procedures. Overall, anxiety levels were not related to type of procedure.

A service evaluation based in the UK was conducted to determine patients' (n = 216) attitudes, preferences and expectations for day-case colonoscopy.<sup>[7]</sup> Patients attending for elective colonoscopy completed and returned a composite patient pre-procedure questionnaire comprised of Likert scale questions examining patient levels of anxiety pre-procedure and the causes of anxiety, demographic characteristics, previous colonoscopy experience, preferred staff roles and patient preferences for a single-sex colonoscopy department. A 15-point preference (ranking) scale was also included which addressed the domains of endoscopy care that were considered most important to least important as contributing to satisfactory experience. Additionally, a sample of 19 patients from the study cohort completed the 15-point ranking questionnaire post-procedure. Pre-procedure, 43.5% of patients reported none or mild anxiety, 40.3% reported moderate anxiety and 16.2% reported severe or very severe anxiety (p = 0.066). The anticipation of pain (40.8%), the nature of the results (37.3%) and potential complications and sedation (21.9%) were reported as the main sources of their anxiety. Interestingly, similar levels of moderate to severe anxiety were reported irrespective of previous experience of having a colonoscopy (59.8% versus 52.9%, p = 0.3). However, patients who reported having previous

experience of pain or discomfort during a colonoscopy (n = 64) were more likely to report moderate to severe anxiety (73.4% versus 36.5%,  $p < 0.01$ ), particularly related to procedure-associated pain (51.6% versus 19.2%,  $p < 0.01$ ) and expectation of severe or moderate pain (50% versus 19.2%,  $p = 0.01$ ). Hence, whilst the use of sedation and analgesia reduce the experience of pain during a colonoscopy, pain and discomfort are often identified as factors contributing to unwillingness to return for a repeat procedure, with associated increased anxiety prior to future examinations. This is clearly relevant to patients whose screening or surveillance entails multiple colonoscopies.

A sex- and age-matched case-control, cross-sectional study of 100 patients with inflammatory bowel disease (IBD) and 100 patients without IBD (control group) examined whether the quality and tolerance of bowel preparation was associated with anxiety levels immediately prior to colonoscopy.<sup>[8]</sup> Before their procedure, patients completed a questionnaire consisting of the Hospital Anxiety and Depression Scale (HADS-A/HADS-D), Visceral Sensitivity Index, State Trait Anxiety Inventory (STAI-S) and self-assessed their bowel preparation, and abdominal pain and nausea during it. Endoscopist-reported measures included the Mayo score, Harvey Bradshaw Index, simple endoscopic score for Crohn's disease, and the Boston Bowel Preparation Scale (BBPS). A multiple linear regression model identified that nausea ( $p = 0.0071$ ), abdominal pain during bowel preparation ( $p = 0.0029$ ) and a lower number of previous colonoscopies ( $p = 0.032$ ) were independently associated with pre-procedure anxiety (assessed by STAI-S), after controlling for age, sex and endoscopist-rated quality of bowel preparation (on the BBPS). Based on these findings, the authors suggested that taking measures to reduce anxiety could improve tolerance of bowel preparation and colonoscopy.

In some situations, patients may undergo colonoscopy without clinical consultation with an endoscopist before the day of the procedure. An observational study of 409 colonoscopy-naïve patients compared the pre-endoscopy information-seeking behaviours and levels of anxiety about the procedure (using a single question using a 10-item rating scale) of patients who did not receive clinical consultation (direct group; 34% of total sample) with those of patients who had received a pre-procedure consultation with the endoscopist (consult group).<sup>[9]</sup> The study found no differences in pre-procedure anxiety levels between the direct group (mean 4.7; 95% confidence interval [CI]: 4.3–5.2) and the consult group (5.0; 95% CI: 4.6–5.3), but found that undergoing a colonoscopy for symptoms rather than for screening was associated with greater anxiety. Furthermore, 20% of participants overall reported high pre-procedure anxiety, suggesting a need for measures to reduce anxiety including providing detailed information about the procedure.

A prospective qualitative study of 13 patients in Australia<sup>[10]</sup> examined the effect of colonoscopies on patients' anxiety about their initial colonoscopy. The researchers interviewed patients 1 week before and 1 week, 2 weeks and 12 months after their colonoscopy. Participants reported that the procedure was associated with stigma, and that discussing it was stressful, embarrassing and anxiety-provoking. The researchers reported that contributors to patient anxiety included irrational expectations of the procedure, limited perceptions of control and power imbalances with doctors. Prior to procedures, anxiety was elicited by fear of a serious diagnosis, while an unclear or functional diagnosis seemingly increased anxiety after the procedure. The authors noted that anticipating the preparation before the procedure was reportedly important to manage anxiety during this stage. The authors advocated for increased shared decision-making as part of a shift towards the biopsychosocial model of healthcare to reduce patient anxiety. Notably, they recommended developing and using neutral language for colonoscopy procedures to reduce the stigma of colonoscopies and bowel health issues.

A 2013 systematic review<sup>[11]</sup> examined patients' experiences of colonoscopy in the screening context. From 56 included studies, most patients reported that the most burdensome aspect of a colonoscopy was bowel preparation. Patients also reported anxiety, pain anticipation and feeling embarrassed and vulnerable. Obstacles to screening colonoscopies included inadequate knowledge of the procedure and fear of finding cancer. The reviewers found that physician recommendations, family history, knowing a person with cancer and perceiving the test to be accurate motivated patients to have a colonoscopy.

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### 5.2.2 Anxiety levels in children and adolescents

While colonoscopy is most frequently performed on adults, it may be used in the diagnostic evaluation of children and adolescents with colonic disease. Adolescents with IBD will usually require colonoscopy from time to time.

A study designed to compare adolescents aged 10–18 years with either IBD or functional gastrointestinal disease (FGID) undergoing their first colonoscopy recorded the levels of pain or anxiety that they experienced. These levels were assessed by means of a questionnaire recorded immediately before the procedure and a second questionnaire 48 hours later. While no differences in anxiety were reported, it was noted that children with IBD at the time of colonoscopy experienced higher levels of anxiety accompanied by higher pain scores. Adolescents with FGID experience common pain symptoms during colonoscopy and may describe more post-colonoscopy pain than those with IBD. It was concluded that anxiety is associated with severity of pain after colonoscopy in children with IBD, while not observed to be a factor in children with FGID.<sup>[12]</sup>

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### 5.2.3 Reducing anxiety about colonoscopy

Studies have investigated the efficacy of information in various formats, aromatherapy, and audio or visual distraction in reducing anxiety, increasing satisfaction and reducing pain, with variable outcomes.

### 5.2.4 Providing information

An Australian study<sup>[1]</sup> assessed the response of 80 patients to information consistent with their coping style. The researchers classified patients according to their coping style as either information seekers or information avoiders. The researchers administered an information intervention that included a general description of colonoscopy and procedural events like the potential complications of and instructions about preparing for the procedure. This information was provided orally and in writing. There was also a sensory information condition that described in depth what the patient might see, hear, or feel during each part of the procedure, such as during hospital admission procedures, in the endoscopy room, during intravenous line insertion, when affected by intravenous sedation, and during the colonoscopy and recovery. This information was also provided orally and in writing.

The researchers found that information seekers receiving sensory information (more information overall) self-reported less anxiety than information seekers receiving information on the procedure. In contrast, information avoiders receiving procedural information (less information overall) self-reported lower anxiety than avoiders receiving sensory information. Those groups who received the amount of information consistent with their preferences also reported more satisfaction with the intervention, were observed to experience less pain and exited recovery 12–16 minutes earlier. However, there were no differences on perceptions of pain or dosages of sedative medications.

A cross-sectional, mixed-methods study<sup>[13]</sup> explored the experience of anxiety in colonoscopy outpatients by evaluating whether any differences in state anxiety existed between pre- and post-colonoscopy patients, and whether problem-focused, emotion-focused, and maladaptive coping styles were significantly associated with this anxiety. The researchers recruited 26 pre-procedure participants and 24 post-procedure participants, and found a strong, positive relationship between maladaptive coping and state anxiety in the entire sample. This relationship also existed in both pre-procedure and post-procedure samples. The interviews indicated that clinicians and endoscopy nurses needed to be aware that some patients do not correctly process information about colonoscopy; specifically, the knowledge that they may be conscious or experience pain during the procedure. The study authors recommended that clinicians ensure that patients understand the standard practice of the hospital, and that more attention be given to pain management as it may not be adequate during conscious sedation.

A randomised controlled trial (RCT)<sup>[14]</sup> explored the ability of an information intervention provided before clinical procedures to improve procedural knowledge and consequently reduce anxiety related to it. The investigators randomly assigned patients to either viewing or not viewing an information video before colonoscopy. The study enlisted 150 patients; 72 video-watchers and 78 non-video-watchers. The groups were generally similar in terms of age, sex, education levels and initial anxiety scores, but female patients had higher baseline anxiety scores than male patients. Patients who had previously had colonoscopies had lower baseline anxiety scores than those with no previous experience. The authors found that patients who watched the video reported significantly less anxiety than control group participants. The intervention group reported significantly more knowledge on items assessing the purpose, details and potential complications of colonoscopies. A commentary on the RCT<sup>[14]</sup> argued that the intervention may be cost-effective by reducing cost of sedation and post-operative recovery time, although it does not appear that cost-effectiveness has been evaluated for this intervention.

In a study of 201 patients undergoing colonoscopy<sup>[15]</sup>, patients were randomised into three groups: those provided with pre-procedure information by video plus discussion, those provided with video alone and those provided with discussion alone. Patients in both groups who viewed the videos had significantly higher scores on knowledge than those in the discussion alone group, but there were no statistically significant differences in knowledge scores between the two groups viewing the video. Increased understanding of the benefits and risks of colonoscopy was not associated with increases in anxiety.



Another RCT<sup>[16]</sup> of 162 colonoscopy patients included an information video as part of pre-procedure preparation, with control patients not watching the video. The investigators found no differences between the groups on situational, pain ratings, procedure tolerability or willingness to have future colonoscopies. All staff rated outcomes in the two groups equally. The two groups did not differ in midazolam dosages, but patients in the video group used significantly higher fentanyl doses. Women had significantly higher situational anxiety ratings, and also reported less satisfaction with the procedure and more pain from it.

A non-RCT investigated the effects of written and oral information versus oral information alone on pre-colonoscopy anxiety.<sup>[17]</sup> Patients in group one (n = 51) received written and oral information and group two (n = 53) received only oral information. The written information discussed preparation, the process of colonoscopy and potential issues needing attention following the procedure. The oral information was identical to the written information. Patients completed questionnaires 24 hours before and on the day of the colonoscopy. State anxiety scores after the colonoscopy lowered, but this was not statistically significant and there were no between-group differences at either time point. The study author suggested that written information potentially increased anxiety in patients with high baseline trait anxiety, as too much detailed information made them more aware of the risks and insertion process. Furthermore, information was provided to patients a day before their procedure, which may not have allowed sufficient time for patients to adequately process the information.

Another RCT examined the impact of using information videos before colonoscopy on patient satisfaction and anxiety.<sup>[18]</sup> The authors recruited 227 patients from an endoscopy unit and randomly assigned them to either the video group (n = 124) or verbal group (n = 130). Patients in the video group viewed a 10-minute video about the colonoscopy procedure and had their questions about the procedure answered, while patients in the verbal group listened to a text version of the video spoken by physicians uninvolved in the colonoscopy procedure and subsequently also had their questions answered. Low state anxiety levels and communication by video were significantly associated with 'communication success', considered by the authors to have been achieved where patients indicated post-procedure that the procedure was similar to or better than they had been told. The state anxiety levels were notably significantly higher in women than men at baseline.

Note: Clinicians should also follow the Clinical Care Standards that apply to the preparation of patients for procedures, including informed consent (see Australian Commission on Safety and Quality in Health Care Colonoscopy Clinical Care Standards).

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### 5.2.5 Aromatherapy

An RCT<sup>[19]</sup> of the effect of aromatherapy on alleviating anxiety, stress and physiological parameters of colonoscopy randomised 27 patients into groups inhaling neroli oil (experimental group, n = 14) or sunflower oil (control group, n = 13). The researchers found no significant differences in state procedural anxiety or procedural pain scores before and after aromatherapy, although neroli oil was significantly more effective in reducing systolic blood pressure than sunflower oil.

### 5.2.6 Audiovisual distraction strategies

An RCT investigated the effects of visual and audiovisual distraction during colonoscopy on pain, anxiety, and procedure tolerance in 180 patients.<sup>[20]</sup> Participants were randomly allocated to one of three groups: Group A (n = 60) received visual distraction (DVD with no sound and earphones on), Group B (n = 60) received audio-visual distraction (DVD with sound and earphones on), and Group C (n = 60) received routine care. Before the procedure, patients were permitted to select their preferred DVD (e.g., landscape scenery, animation, comedy, Chinese Kung Fu). The groups did not differ significantly on state and trait anxiety before the procedure. The researchers observed lower pain scores in the visual and audio-visual distraction groups relative to the control group, but not to a statistically significant extent. Patients in the visual and audio-visual distraction groups reported more willingness to repeat the procedure.

An endoscopist-blinded RCT in Japan<sup>[21]</sup> assessed the intervention of relaxing visual distraction on patient pain, anxiety and satisfaction during colonoscopy. Patients (n = 60) were randomly allocated to one of two groups, with the first group (n = 28) viewing a silent movie wearing a head-mounted display and the second group (n = 29) wearing only the display. Patients in the first group reported significantly higher median post-procedural satisfaction levels than patients in the second group. In patients who had anxiety scores of 50 or higher before the procedure, the anxiety and pain scores during the procedure were significantly lower in the group receiving the visual distraction intervention.

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### 5.2.7 Anaesthesia and sedation technique

Multiple guidelines strongly recommend administering medication for endoscopic procedures<sup>[22]</sup> and, in Australia, most patients receive sedation for their colonoscopies. Frequently used approaches include deep sedation induced by propofol, or conscious sedation induced by combining benzodiazepines and opioids. Because of the deeper level of sedation/anaesthesia achieved with propofol, pain during the procedure should be minimal but there have been no studies of these two commonly used sedative regimens comparing their effects on anxiety or on anxiety associated with future colonoscopy.

An Australian RCT<sup>[23]</sup> compared an alternative approach using methoxyflurane administered via portable inhaler (Penthrox) with intravenous midazolam and fentanyl, and showed no differences between the groups in pain scores or nervousness. It should be noted that Penthrox may not be suitable for all patients, particularly those with significant anxiety disorders or visceral hypersensitivity, even though it has the potential safety advantage of lack of respiratory depression.

A prospective study<sup>[24]</sup> investigated the effects of pre-procedure anxiety on patient sedative requirements in 135 patients undergoing sedation for colonoscopy. Before the procedure, intravenous propofol was administered until patients exhibited no responses to verbal commands (loss of consciousness). Colonoscopy then began. The endoscopist assessed procedural time, spasm score and difficulty score for colonoscopy immediately after the procedure. The researchers observed no association between pre-procedural anxiety and sedative requirements for deep sedation in patients receiving colonoscopies, suggesting that the two are unrelated.

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## 5.2.8 Music

A single-blind RCT was used to assess the efficacy of music for patients undergoing colonoscopy.<sup>[25]</sup> In this study, 109 patients were randomised and fitted with mute or music-delivery headphones. Clinicians were blinded to the trial and sedation was provided if requested. Primary outcome was the measurement of pain and secondary endpoints were recorded as need for sedation, patient satisfaction and willingness to repeat the procedure. Those wearing music headphones recorded statistically significant reduction in pain and in the proportion of patients requiring sedation. Clinicians perceived less difficulty and multivariate analysis confirmed a significant beneficial effect of music. The introduction of music during colonoscopy significantly reduces discomfort.

A meta-analysis of RCTs on the effect of music on patients undergoing colonoscopy, assessed procedure time, dose of sedation, pain scores and willingness to repeat the procedure in the future. Eight studies met the criteria and observed that patients' overall experience was statistically significantly improved when music was used during the procedure. There were significant differences in pain scores, sedation levels, procedure time and willingness to repeat the procedure. The investigators concluded that music can 'improve patients' overall experience with colonoscopy'.<sup>[26]</sup>

In another randomised study in a US veterans' gastrointestinal diagnostic facility,<sup>[27]</sup> 198 patients were randomised. Ninety-eight (98) comprised a control group, who had 25 minutes of quiet time before endoscopy while the study group (100) had music selected by the investigators, who were nurses, for 25 minutes before having endoscopy. All were evaluated by the STAI-S.<sup>[28]</sup> Both groups experienced reduced anxiety scores but, after controlling for trait anxiety, there was a statistically different outcome between the groups, with those listening to music having a greater reduction in anxiety. It is suggested that music, a non-invasive nursing intervention may reduce anxiety if provided prior to gastrointestinal investigative procedures.

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## 5.2.9 Practice points

### Practice point

Providing pre-colonoscopy advice to patients by means of educational material, video and clinical explanation can assist in improving the patient experience with the procedure, and in reducing decreasing anxiety and abdominal pain during the procedure.

**Practice point**

Endoscopists should aim to control pain and discomfort during a colonoscopy procedure in order to reduce patient anxiety.

**Practice point**

Physicians should be able to provide accurate and relevant information about colonoscopy for patients who are undergoing open access colonoscopy (without prior consultation with an endoscopist).

**Practice point**

Gastroenterology clinics are recommended to evaluate shifting towards a biopsychosocial approach to healthcare and encouraging patients to participate in decision-making in order to provide them with a greater sense of control, thus reducing anxiety.

**Practice point**

The use of neutral language around colonoscopy may be useful in order to break down the stigma and taboo surrounding the procedure and bowel health issues.

**Practice point**

Clinicians should ensure that patients understand the standard practice and convey information about the procedure as clearly as possible (e.g., whether they will be conscious, whether they will experience pain, etc.).

### Practice point

Note: Clinicians should also follow the Clinical Care Standards that apply to the preparation of patients for procedures, including informed consent (see Australian Commission on Safety and Quality in Health Care Colonoscopy Clinical Care Standards).

### Practice point

Patients who receive the amount of information consistent with their preferences (information seekers versus avoiders) report lower anxiety and more satisfaction with the intervention, and experience less pain and shorter time in recovery. Colonoscopists can assess patients' desire for information by asking the patient directly, for example "how much information would you like about XX (this procedure)? Are you someone who prefers to get a lot of information or just the basics?"

### Practice point

Music provided to patients prior to and during colonoscopy may reduce their discomfort.

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## 5.1 Socioeconomic factors - Introduction

### Contents

- 1 Introduction
  - 1.1 Strategies for reducing socioeconomic inequality in surveillance colonoscopy
    - 1.1.1 Health literacy
    - 1.1.2 Shared decision-making
    - 1.1.3 Cultural competency
- 2 References

### 5.1.1 Introduction

Many socioeconomic factors influence health, including education, employment, income and wealth, family, neighbours, housing, access to services, migration and refugee status and food security.<sup>[1][2][3][4][5][6][7][8][9][10][11][12]</sup> Socioeconomic disadvantage, and its detrimental effects on health, is common in Australia.<sup>[1][13]</sup>

Social and economic circumstances are recognised determinants of access to health care and of healthcare outcomes, including for colorectal cancer (CRC).<sup>[2][3][4][14][15][16]</sup> Between 2009 and 2013, Australians living in the most disadvantaged areas had the highest age-standardised incidence for CRC.<sup>[17]</sup>

Apart from access to health services related to distance or transport, the cost of services is an additional factor, related to socioeconomic status (SES) that influences the care people receive. In 2015–2016, one in 12 (8%) Australians who needed to see a medical specialist delayed or did not attend because of the cost. Those with a long-term health condition were more likely to delay seeing or not see a medical specialist due to cost than those without (9% compared with 5%). People living in the areas of most socioeconomic disadvantage were more likely to delay seeing or not see a medical specialist due to cost than those living in areas of least disadvantage (9% compared with 6%).<sup>[18][14]</sup>

Many socioeconomic factors are beyond the capacity of individual clinicians to address. This section focuses on those modifiable SES-related factors which impact on surveillance in three settings:

- following adenoma detection;
- post curative resection for CRC;
- in the setting of dysplasia surveillance in inflammatory bowel disease.

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### 5.1.1.1 Strategies for reducing socioeconomic inequality in surveillance colonoscopy

Clinicians can address three key areas linked to SES to improve the success of surveillance, by:

- communicating information in a way that is meaningful and actionable for the patient
- sharing decision-making with the patient and their support people
- improving their own cultural competency to support effective communication with patients from different cultural groups and belief systems.

The goal should be to ensure that all patients' decisions, including whether or not to participate in surveillance colonoscopy, are well informed and freely made.

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#### 5.1.1.1.1 Health literacy

Literacy is low in Australia. In 2011, only 56% of people had the general literacy needed to cope with everyday life and work.<sup>[19]</sup>



Health literacy is defined as the skills, knowledge, motivation and capacity of a person to access, understand, appraise and apply information to make effective decisions about health and health care and take appropriate action.<sup>[20]</sup> Poor health literacy is associated with low SES<sup>[21][22][23]</sup> and is relevant to surveillance.<sup>[24][25]</sup>

Almost 60% of adult Australians have low health literacy.<sup>[26]</sup> In 2006, among those whose first language was English, 44% had a level of health literacy described as adequate or better but amongst the almost 3 million Australians aged 15–74 years who spoke English as a second language this level fell to only 25%.<sup>[27]</sup> Low health literacy is associated with low levels of knowledge and poorer health outcomes.<sup>[28]</sup>

Since 2011 all hospitals and day facility services in Australia have been required to meet the National Safety and Quality Health Service Standards for accreditation. A specific standard (the Partnering with Consumers Standard) requires demonstration of actions to improve consumer understanding and participation in decision making about their care.<sup>[29]</sup> With the introduction of the second edition of the National Safety and Quality in Health Care Standards, health service organisations will be required to communicate with consumers in a way that supports effective partnerships, in this way specifically addressing issues related to health literacy. A number of useful resources are available to assist clinicians, managers and other health professionals working outside the hospital or day facility to support improvements in health literacy and to develop information to meet the needs of patients with low health literacy.<sup>[30][31]</sup> These resources are readily accessible on a number of sites, including the National Health and Medical Research Council and Cancer Australia websites.

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#### **5.1.1.1.2 Shared decision-making**

People who are supported to make an informed decision by a healthcare professional may have better outcomes, better experiences, and less regret about their decisions.<sup>[32][33][34]</sup> Disadvantaged groups may benefit most.<sup>[35]</sup> Patient decision aids, decision support and navigation tools have been shown to increase CRC screening participation, but have not been trialled in the surveillance setting.<sup>[36][37][38][39][40][41][42]</sup> Larger studies are needed to identify which features of navigation are most effective in patients ongoing participation in CRC surveillance, particularly those from lower SES backgrounds.

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#### **5.1.1.1.3 Cultural competency**

Cultural competency is the capacity to interact with people across different cultures and requires cross-cultural communication skills. This competency is particularly important in Australia where 1 in 4 Australians is born overseas, and just under 3% identify as Aboriginal or Torres Strait Islander Australians.<sup>[43]</sup> Action at all levels of the health system is required to reduce the health inequalities that exist for many culturally and linguistically diverse background communities.<sup>[44]</sup> An important first step to reduce this source of health inequality is to

ensure that environments provide a sense of cultural safety so that people feel sufficiently comfortable to discuss their cultural identity. This then enables information and discussions about treatment options to be undertaken in a culturally sensitive manner. A number of services are available to support health services and providers including translation services, cultural guides, social services and patient advocacy groups. Online and face-to-face training in cultural competence for health professionals and the broader health workforce is also available and is now considered by many professional bodies essential training for clinicians.

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See sections

- Impact of socioeconomic factors on surveillance colonoscopy
- Colonoscopy outcomes in Aboriginal and Torres Strait Islander peoples
- Impact made by socioeconomic factors in treatment groups undergoing surveillance colonoscopy

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## 5.2 Impact of socioeconomic factors on surveillance colonoscopy

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- 2 Overview of evidence (non-systematic literature review)
  - 2.1 Prevention
  - 2.2 Participation
  - 2.3 Preparation
  - 2.4 Phasing out
- 3 References

### 5.2.1 Background

Overall, Australians from the two lowest socioeconomic status (SES) groups are 1.2 times more likely to be diagnosed with colorectal cancer (CRC) compared with those from the two highest SES groups and those from the lowest SES are 1.3 times more likely to die from CRC than those from the highest SES.<sup>[1]</sup>

Rurality also contributes to disadvantage; people living in very remote areas are less likely to be diagnosed with CRC but more likely to die from CRC than those living in other regions suggesting that this group do not reap the benefits of early CRC detection that those in major cities and regions do.<sup>[1]</sup>

It was demonstrated in a study in the United States that lower uptake of screening and treatment in low, compared to high, SES groups leads to the disparity in mortality due to CRC in these populations.<sup>[2]</sup>

The primary objective of surveillance is to reduce the incidence and mortality of subsequent CRC. There are several ways the impact of low SES on surveillance can be mitigated:

- Prevention – education to reduce adenoma or cancer occurrence/ recurrence
- Participation – engagement to ensure participation in evidence-based surveillance
- Preparation – ensuring effective bowel preparation to enable a high quality colonoscopy
- Postponement – understanding and agreement to defer colonoscopy when the risks outweigh the benefits due to comorbidities or life expectancy.

Effective communication between consumers and healthcare providers, and within healthcare teams, has been linked to improved consumer health outcomes.<sup>[3]</sup> Effective communication is relevant to all four of these aspects of surveillance.

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## 5.2.2 Overview of evidence (non-systematic literature review)

No systematic reviews were undertaken for this topic. Practice points are based on selected evidence and guidelines (see Guideline development process).

### 5.2.2.1 Prevention

Colorectal cancer is predominantly a lifestyle disease.<sup>[4][5][6]</sup> Lifestyle modification is important for the prevention of colorectal polyps, especially advanced and multiple adenomas, which are established precursors of colorectal cancer.

The key question in the context of surveillance is whether individuals identified as being at increased risk by prior colonoscopy, who are then enrolled in surveillance, can benefit from lifestyle modifications, given the time needed to show benefit. There is evidence that this is the case for some risk factors.<sup>[6]</sup> There is an obligation to inform patients of the evidence and support effective action to address these risk factors. For patients of low SES, this can be a particular challenge because of both social and economic barriers. However, the individual gains will be greater because of the higher prevalence of most risk factors for CRC among lower SES groups.<sup>[7]</sup> Beneficial changes include smoking cessation, weight reduction, increased physical activity and improved diet. The benefits will have more impact at a population than individual level.<sup>[8]</sup> For instance, data from the Nurses' Health Study and Health Professional Follow-up Study show that weight loss in men but not post-menopausal women was associated with decreased CRC risk within 4 years.<sup>[9]</sup> Low SES may be associated with a higher prevalence of these at-risk behaviours but also influence an individual's capacity to benefit from these interventions. These data are from population studies and do not provide information for familial cancer syndromes or those with inflammatory bowel disease (IBD).

Lifestyle factors also appear to be important in CRC recurrence.<sup>[10][11]</sup> Time since smoking cessation has been significantly associated with a decreased risk of some CRCs and the likelihood of synchronous cancers.<sup>[12][13][14]</sup> This finding is particularly relevant to lower SES and Indigenous populations because of their higher rates of smoking.

#### Practice point

Clinicians should advise patients that modification of lifestyle factors can reduce their risk of polyp recurrence and colorectal cancer.

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### 5.2.2.2 Participation

The doctor-patient relationship has a strong influence on acceptance of colonoscopy.<sup>[3][15]</sup> The need for colonoscopy will need to be discussed with all patients, but more specific attention will need to be directed to socio-economically deprived patients. They will benefit by being encouraged to comply with the recommendations of guidelines such as these.

Patients in the three target groups for surveillance colonoscopy covered by these guidelines will have already received treatment for their underlying condition (in adenoma follow-up or following resection for CRC) or had diagnosis of their disease (IBD). Any barriers to health system access and provision of appropriate care should have been identified in the course of initial management, allowing them to complete their primary treatment. Surveillance in these patients will in large part be fulfilled by maintaining their effective engagement. Those most at risk of being lost to follow-up should be identified and include those from low SES backgrounds.<sup>[16][17]</sup>  
[18]

Marital status has also been shown to influence likelihood of participating in surveillance, with individuals having a current partner being more likely to participate<sup>[19][20]</sup>

Aboriginal and Torres Strait Islander participants, participants who live in regional and remote regions, and participants who live in areas of lower socioeconomic status, have higher rates of positive screening results but lower rates of follow-up colonoscopies than other participants.<sup>[21]</sup>

For colonoscopy, other procedural factors also need to be considered, anticipated and managed.<sup>[22][23][15]</sup> In a Dutch study of compliance with colonoscopic surveillance among patients with familial adenomatous polyposis, poor compliance was associated significantly with perceived self-efficacy, use of sedatives during colonoscopy, pain after surveillance colonoscopy and low perceived benefits of surveillance.<sup>[24]</sup>

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### 5.2.2.3 Preparation

There is increasing recognition of the relationship between the quality of bowel preparation and adenoma detection rates.<sup>[25][26]</sup> Identifying and addressing the needs of those with poor health literacy due to education, ethnicity or comorbidities is clearly pivotal to achieving a high-quality surveillance colonoscopy, which depends on adequate bowel preparation.<sup>[27][28][29][30]</sup>

#### Practice point

Information and instructions for bowel preparation and colonoscopy need to be tailored to meet the needs of most Australians who have inadequate or poor health literacy.

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### 5.2.2.4 Phasing out

Years of public health efforts to raise awareness of the benefits of CRC screening make discussions about ceasing screening sound counter-intuitive.<sup>[31]</sup> Socioeconomic factors may influence the effectiveness of conversations about having no further colonoscopy, particularly due to low health literacy or high cultural expectations of continued surveillance. Evidence suggests that the context of these discussions may influence their success in older people.<sup>[32]</sup> A trusting relationship, communications over a long period and messages that are less direct, such as 'This test would not help you live longer', have been shown to be more effective than messages that directly address limited life expectancy.<sup>[32]</sup> Decision aids may also be useful.<sup>[33]</sup> Discussions should be based on the likely risks and benefits of the procedure for the individual and the final decision on the patient's informed preference.

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### 5.2.3 References

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## 5.3 Colonoscopy outcomes in Aboriginal and Torres Strait Islander peoples

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- 1 Background
- 2 Overview of evidence (non-systematic literature review)
  - 2.1 Colorectal cancer rates

2.2 Participation in the national bowel cancer screening program
2.3 Uptake of services for bowel health
3 Implications for health system planning
4 References

*Do rates and outcomes of colonoscopy among Aboriginal and Torres Strait Islander peoples differ from those of other Australians?*

### 5.3.1 Background

Aboriginal and Torres Strait Islander people are disadvantaged across a range of health-related and socioeconomic indicators, compared with other Australians. Many factors contribute to the gap between Indigenous and non-Indigenous health, including social disadvantage (e.g. lower education and employment rates), as well as higher smoking rates, poor nutrition, physical inactivity and poor access to health services.<sup>[1]</sup>

### 5.3.2 Overview of evidence (non-systematic literature review)

No systematic reviews were undertaken for this topic. This overview is based on selected evidence and guidelines (see Guideline development process).

#### 5.3.2.1 Colorectal cancer rates

Aboriginal people are diagnosed with bowel cancer an average of 7.2 years younger than non-Indigenous Australians (unpublished NSW Cancer Registry data). In NSW and South Australia, 20% of bowel cancer diagnosed in Aboriginal people occurs in people under the age of 50. This compares with 6% in the non-Aboriginal population.<sup>[2]</sup>

National data shows that Indigenous Australians have a slightly lower age-standardised bowel cancer rate than non-Indigenous Australians (52 versus 57 per 100,000) and bowel cancer mortality rate than non-Indigenous Australians (12 versus 15 per 10,000).<sup>[3]</sup> This lower incidence and mortality may be due to lower life expectancies in Aboriginal people, fewer diagnoses due to lower participation in cancer screening, and a larger proportion of inadequate death certification and more cancers of unknown primary site amongst Aboriginal people.<sup>[4]</sup>

#### 5.3.2.2 Participation in the national bowel cancer screening program

The National Bowel Cancer Screening Program reports much lower participation rates amongst the Indigenous than the non-Indigenous population. Indigenous Australians, who are screened are more likely to screen positive than non-Indigenous Australians (11% versus 8% non-Indigenous), but less likely to undergo diagnostic assessment (57% versus 71%). Indigenous Australians undergoing diagnostic assessment wait longer than non-Indigenous Australians (median 64 days versus 52 days).<sup>[4][1]</sup>

### 5.3.2.3 Uptake of services for bowel health

A 2005 North Queensland study reported that approximately 30% of Indigenous patients estimated to have colorectal cancer (CRC) attended for treatment. The authors recommended education for Indigenous people about CRC and establishing cancer units with Indigenous liaison officers. The study authors also highlighted the importance of health care providers having sufficient cultural competence to ensure Indigenous Australians' participation in bowel cancer prevention and treatment.<sup>[5]</sup> Training and employing more indigenous healthcare providers and working in collaboration with local Indigenous communities will also improve participation.

At a national level, achieving increased participation by Aboriginal and Torres Strait Islander people in bowel cancer surveillance also requires overcoming recognised barriers, such as incomplete enrolment in Medicare and barriers inhibiting Indigenous self-identification.<sup>[6]</sup> Currently there are limitations to the quality of data at a national level because of incomplete capture of Indigenous status. The importance of all health care providers being cultural competent has been discussed above.

### 5.3.3 Implications for health system planning

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Culturally sensitive resources are required to assist in implementation of guideline recommendations in Indigenous communities.

Carefully planned studies are also required to understand and specifically address unmet needs for surveillance colonoscopy and under-detection of CRC and possibly inflammatory bowel disease in Indigenous people.

Health system planning to improve participation in surveillance will more effectively achieve the goal of reducing bowel cancer if planning also addresses risk factors for bowel cancer of high prevalence for Indigenous people. Commonwealth and jurisdictional health plans incorporate Closing the Gap targets<sup>[7]</sup> and the Australian Institute of Health and Welfare provides regular reports on progress towards meeting these targets.<sup>[8]</sup> These reports are available to support health service planning and review.

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## 5.4 Impact of socioeconomic factors in treatment groups undergoing surveillance colonoscopy

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  - 2.2 Surveillance after diagnosis of inflammatory bowel disease
- 3 Issues requiring more clinical research study
- 4 References
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*Does lower SES have to result in poorer outcome for curative resection for colonic cancer?*

This question focuses on those modifiable socioeconomic status (SES)-related factors which impact on surveillance in the three groups being considered:

1. following adenoma detection;
2. post-curative resection for colorectal cancer (CRC); and
3. in the setting of dysplasia surveillance in inflammatory bowel disease (IBD).

### 5.4.1 Background

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Many studies have found poorer survival following a diagnosis of colorectal cancer (CRC) among people from low socioeconomic status (SES) groups compared with those from high SES groups, but with some exceptions.<sup>[1]</sup><sup>[2]</sup> Differences between health systems may account for these contradictory findings. Influences of comorbidities rather than other factors, such as treatment or patient characteristics, may also contribute to the effect of SES.<sup>[3]</sup> Further research remains to be done, but it seems that if practitioners assist their patients to access best care and promote management of comorbidities, they could promote equality of outcomes.

### 5.4.2 Overview of evidence (non-systematic literature review)

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No systematic reviews were undertaken for this topic. Practice points are based on selected evidence and guidelines (see Guideline development process).

A cohort study of white and African American males with advanced lung and colon cancer, who had not had previous chemotherapy, had their socioeconomic and biological data collected prospectively in 12 medical centres in the US Veterans Administration System (1981–1986).<sup>[4]</sup> The essential finding of the study was that lung and colon cancer outcomes "may be similar among black and white patients who have equal access to comparable medical care in spite of socioeconomic differences". This study highlights the importance of access to good clinical care in improving outcomes.<sup>[5]</sup><sup>[4]</sup> This is highly relevant to Australia.

The relationships between geographic remoteness, area disadvantage and risk of advanced colorectal cancer was looked at among people aged 20–79 years diagnosed with CRC in Queensland between 1997 and 2007. Analysis showed that patients living in inner regional areas (odds ratio [OR]=1.09, 1.01–1.19) and outer regional areas (OR=1.11, 1.01–1.22) areas were significantly more likely to be diagnosed with advanced cancer than those in major cities (P=0.045), after adjusting for individual-level variables. The authors noted that "[g]iven the relationship between stage and survival outcomes, it is imperative that the reasons for these rurality inequities in advanced disease be identified and addressed".<sup>[6]</sup> The reasons clearly relate to surveillance pre- and post-initial CRC diagnosis.

Higher SES and being married were associated with greater participation in surveillance in a large US study.<sup>[7]</sup> Patients over age 80 years and those with rectal cancer were less likely to undergo surveillance.

#### Practice point

After curative resection for colorectal cancer, survival outcomes in disadvantaged patients may be improved by clinicians and health systems by addressing the barriers and access to optimal clinical care.

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### **5.4.2.1 Surveillance after colonic polypectomy**

In the post-adenoma setting, risk reduction is related to participation in surveillance and lifestyle modifications.

A finding of the National Polyp Study<sup>[8]</sup> was that removal of adenomas with a follow-up of at least 3 years reduced the incidence of CRC recurrence. Eighty per cent compliance was achieved, but the general population compliance was not known. This study suggests that risk reduction requires effective participation in surveillance while previously mentioned studies provide strong evidence that lifestyle modification is important for the prevention of colorectal polyps, especially advanced and multiple adenomas, established precursors of colorectal cancer.

A systematic review and meta-analysis to quantify the evidence for an association between weight gain and colorectal adenoma occurrence found an increased risk of colorectal adenoma throughout the whole range of weight gain. Even a small amount of adult weight gain was related to higher odds of colorectal adenoma occurrence. The findings suggest a benefit of weight control in reducing the development of metachronous colorectal adenomas and preventing CRC. The study findings emphasise the importance of patient awareness and the clinician's ability to communicate information to patients.<sup>[9]</sup> Studies have also reported that weight loss after bariatric surgery or physical activity helped reduce the risk of CRC-related mortality<sup>[10]</sup> The key question in the context of surveillance is the time to benefit for those identified as at increased risk.<sup>[11]</sup> Further studies of general population compliance need to address SES factors and so assist in developing methods to increase compliance of patients of lower SES.

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### **5.4.2.2 Surveillance after diagnosis of inflammatory bowel disease**

There is a perception that patients with inflammatory bowel disease (IBD) are of a higher socioeconomic status and have a higher level of education than the general population. However, available research suggests that people with IBD are not of higher SES and at some time in the course of their illness, they are more likely to be out of work than the general population.<sup>[12]</sup> Recommendations to increase participation in surveillance are likely to apply equally to people with IBD as to other groups.

### **5.4.3 Issues requiring more clinical research study**

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Carefully planned studies are required to specifically address surveillance colonoscopy and colorectal cancer and possibly IBD in Aboriginal and Torres Strait Islander people.

Resources will be required to assist in implementation of guideline recommendations in Aboriginal and Torres Strait Islander communities.

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## 5.4.4 References

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## 5.4.5 Appendices

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## 5.5 Guideline development process

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### 5.5.1 Guideline development process

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## 5.5.2 Introduction

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These draft clinical practice guidelines are a revision and update of the 2011 *Clinical Practice Guidelines for Surveillance Colonoscopy*. The guidelines were originally developed in 2010 and formed an update and a substantial expansion of several specific sections of the 2005 *Clinical Practice Guidelines for the Prevention, Early Detection and Management of Colorectal Cancer*. This current revision and update was commissioned and funded by the Department of Health Commonwealth of Australia. They focus on the appropriate use of colonoscopy in colorectal cancer (CRC) prevention and address three main questions:

- when to repeat colonoscopy after removal of adenomatous polyps?
- when to repeat colonoscopy after curative resection for colorectal cancer?
- when to perform colonoscopy in those patients with inflammatory bowel disease, who have an increased risk of developing CRC?

The guideline project commenced in May 2016, and in July 2016 the National Health and Medical Research Council (NHMRC) agreed to consider approving the guideline, provided it was developed according to NHMRC procedures and requirements.

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## 5.5.3 Guidelines development group

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The Management Committee responsible for the overall management and strategic leadership of the guideline development process of the 2017 Colorectal Cancer Guidelines Revisions was approached to steer the revision of the Clinical Practice Guidelines for Surveillance Colonoscopy. This group acted as a steering committee to establish the scope of the guideline revision and ensure that all deliverables agreed in the project plan were delivered to acceptable standards in accordance with NHMRC requirements, within agreed timeframes and within the approved budget.

A wider multidisciplinary Working Party of relevant experts was then convened to develop the revised guideline and author specific sections. This was to ensure that representatives from all specialities and disciplines involved in surveillance colonoscopy were represented. Two consumer representatives were invited to be part of the Working Party.

The guideline questions were allocated to specific guideline Working Party members to act as lead authors according to their areas of expertise. Each lead author team was able to co-opt additional experts as co-authors for their allocated questions. The Management Committee assessed the suggestion of any additional co-authors including their declaration of interest.

A project team based at Cancer Council Australia conducted the systematic reviews, comprising of systematic literature searches, literature screening against pre-determined inclusion and exclusion criteria and critical evaluation and data extraction of the included literature. The project team was responsible for liaising with the Working Party members in regards to content development, content review and compiling the document.

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## 5.5.4 Guideline scope

At the start of the project, members of the Management Committee with expertise in surveillance colonoscopy were asked to review the clinical questions and sections of the 2011 guidelines and provide feedback in regards to the currency and relevance of the clinical question, suggested review approach (if the question or topic should be updated by systematic literature review or a general literature update) as well as any new clinical questions or topics to be considered. See Clinical question list that summarises the included clinical questions to be updated by systematic review as well as the topic areas that were updated by a general literature review.

The Management Committee met and decided which areas were most relevant and required systematic review. They concluded that the guideline revision would be a straightforward undertaking as the new literature between 2010 and 2017 could be integrated into the existing content and guideline structure.

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## 5.5.5 Steps in preparing clinical practice guidelines to NHMRC criteria

The clinical practice guideline was developed according to the procedures and requirements for meeting the 2011 NHMRC standard for clinical practice guidelines.<sup>[1]</sup> The development program was designed to meet the scientific rigour required by the standard for developing high quality, evidence-based clinical practice guidelines. A series of NHMRC resources and handbooks<sup>[2][3][4][5][6][7][8][9][10]</sup> guided the process and outlined the major steps and expectations involved in developing guidelines. These documents provided the definitions and protocols for developing research questions and search strategies, conducting systematic literature reviews, summarising and assessing the relevant literature and finally, formulating and grading the recommendations. They also included checklists and templates created to satisfy designated standards of quality and process. For every systematic review question the below steps were followed:

For every question the below steps were followed:

1. Develop a structured clinical question (PICO question)
2. Search for existing relevant guidelines and systematic reviews
3. Process if relevant clinical practice guideline was identified or not

<p><b>3a If no relevant clinical practice guideline was found</b></p> <p>Check if an existing systematic review of high quality exists and can be used to inform the systematic review process</p> <p>Developing the systematic review protocol and systematic literature search strategy for each PICO question</p>	<p><b>3b If a relevant clinical practice guideline was found and assessed as suitable for adaption</b></p> <p>Conduct systematic literature review update for the question of the existing clinical practice guideline</p> <p>Screening of literature update results against pre-defined inclusion and exclusion criteria</p>
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<p>Conducting the systematic literature search according to protocol</p> <p>Screening of literature results against pre-defined inclusion and exclusion criteria</p> <p>Critical appraisal and data extraction of each included article</p>	<p>Critical appraisal and data extraction of each new included article</p> <p>Update evidence table of evidence review of existing guideline with new literature update results</p>
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4. Summarise the relevant data
5. Assess the body of evidence and formulate recommendations
6. Write the content narrative

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#### 5.5.5.1 Developing a structured clinical question

During the scoping process the clinical questions included in the 2011 guideline development were assessed for clinical importance to the target audience and currency (Clinical question list).

The included clinical questions for systematic review were structured according to the PICO (populations, interventions, comparisons, outcomes) framework. The lead author and subcommittee members provided the systematic review team with feedback to refine the PICO questions.

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#### 5.5.5.2 Search for existing relevant guidelines and systematic reviews

For each PICO question, the National Guideline Clearinghouse (<http://guideline.gov>) the Guidelines Resource Centre (<http://www.cancerview.ca/>) as well as the scoping search for the PICO question were scanned for relevant clinical practice guidelines that could potentially be suitable for adaption.

No existing guideline was identified to be suitable for adaption. However, relevant guidelines that did not meet the criteria for adaption were checked for systematic reviews that could be used as a source of relevant references to inform the systematic review process for the PICO question. Full systematic reviews were then performed as outlined in the following sections.

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### 5.5.5.3 Developing a systematic search strategy

For each PICO question, systematic literature search strategies were developed by the technical team. Most searches were directed to surveillance colonoscopy as a generic base. Searches were limited or widened as necessary according to the PICO structure using keywords or MESH and subject terms. Systematic search strategies were derived from these terms for each included electronic databases. The included standard databases searched were PubMed, Embase, Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects and Health Technology Assessment for all questions. The psychosocial questions also included CINAHL and PsycINFO databases to retrieve relevant literature.

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### 5.5.5.4 Conducting the systematic literature search according to protocol

Clinical practice guidelines should be based on systematic identification and synthesis of the best available scientific evidence.<sup>[2]</sup> For each clinical question, that required a systematic literature review, literature searches were conducted systematically with the literature cut-off date of 30 June 2017. The following electronic databases were part of the systematic literature search strategy:

- **PubMed (U.S. National Library of Medicine):** bibliographic references and abstracts to articles in a range of languages on topics such as clinical medical information and biomedicine, and including the allied health fields, biological and physical sciences
- **EMBASE:** major pharmacological and biomedical database indexing drug information from 4550 journals published in 70 countries
- **Database of Abstracts of Reviews of Effects and Health Technology Assessment:** contains details of systematic reviews that evaluate the effects of healthcare interventions and the delivery and organisation of health services
- **The Cochrane Database of Systematic Reviews:** contains systematic reviews of primary research in human health care and health policy, and are internationally recognised as the highest standard in evidence-based health care
- **CINAHL:** bibliographic references and abstracts to journal articles, book chapters, pamphlets, audiovisual materials, software, dissertations, critical paths, and research instruments on topics including nursing and allied health, biomedicine, consumer health, health sciences librarianship, behavioural sciences, management, and education
- **Psychinfo:** Bibliographic references and abstracts to journal articles, book chapters, dissertations and technical reports on psychology; social, clinical, cognitive and neuropsychology; psychiatry, sociology, anthropology and education, with source material from a wide range of languages.

A search filter to retrieve relevant literature considering Aboriginal and Torres Strait Islander peoples was added to each question.

Additional relevant papers from reference lists and, where appropriate, clinical trial registries, were also identified for retrieval as part of the snowballing process.

The full detailed systematic literature search strategy for every clinical question is fully documented in the technical report of the question (see Technical report).

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#### 5.5.5.5 Screening of literature results against pre-defined inclusion and exclusion criteria

Part of the systematic review process is to screen all retrieved literature results against the pre-defined inclusion and exclusion criteria in two stages.

##### a) First screen

During the first screening round, the titles and abstracts of all retrieved literature were screened by one or two reviewers. All irrelevant, incorrect and duplicates were removed.

##### b) Second screen

A second screen was undertaken based on the full article. A reviewer assessed each article for inclusion against the pre-defined inclusion and exclusion criteria for each question. In the case of a disagreement between the reviewers, a third independent reviewer assessed the article against the inclusion and exclusion criteria. Articles that met the inclusion criteria were forwarded for quality assessment and data extraction.

#### 5.5.5.6 Critical appraisal and data extraction of each included article

Two assessors independently assessed the risk of bias of each of the included studies using a study design specific assessment tool and where necessary pre-specified criteria (see the Technical report for quality assessment tools). Any disagreements were adjudicated by a third reviewer.

For all included articles, the relevant data were extracted and summarised in study characteristics and evidence tables (Technical report).

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#### 5.5.5.7 Summary of the relevant data

For each outcome examined, the results, level of the evidence, the risk of bias due to study design and the relevance of the evidence for each included study were documented a body of evidence table. Each question was addressed by a systematic review resulting in a systematic review report. All systematic review reports are published in the technical report of the guideline. Levels of evidence are shown below.

**5.5.5.7.1 Table A1. Designations of levels of evidence according to type of research question (NHMRC, 2009)**

Level	Intervention	Diagnosis	Prognosis	Aetiology	Screening
I	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies
II	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among consecutive patients with a defined clinical presentation	A prospective cohort study	A prospective cohort study	A randomised controlled trial
III-1	A pseudo-randomised controlled trial (i.e. alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, among non-consecutive patients with a defined clinical presentation	All or none	All or none	A pseudo-randomised controlled trial (i.e. alternate allocation or some other method)
III-2	A comparative study with concurrent controls:  Non-randomised, experimental trial  Cohort study  Case-control study	A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence	Analysis of prognostic factors amongst untreated control patients in a randomised controlled trial	A retrospective cohort study	A comparative study with concurrent controls:  Non-randomised, experimental trial  Cohort study

	Interrupted time series with a control group				Case-control study
III-3	A comparative study without concurrent controls: Historical control study Two or more single arm study Interrupted time series without a parallel control group	Diagnostic case-control study	A retrospective cohort study	A case-control study	A comparative study without concurrent controls: Historical control study Two or more single arm study
IV	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard)	Case series, or cohort study of patients at different stages of disease	A cross-sectional study	Case series

Source: National Health and Medical Research Council. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. Canberra: NHMRC; 2009. ([https://www.nhmrc.gov.au/\\_files\\_nhmrc/file/guidelines/developers/nhmrc\\_levels\\_grades\\_evidence\\_120423.pdf](https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf))

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### 5.5.5.8 Assessing the body of evidence and formulate recommendations

The technical report for each question was forwarded to each lead author. The authors, in collaboration with their subcommittee members and systematic review team (who conducted the systematic reviews and provided the technical reports), assessed the body of evidence and completed the NHMRC Evidence Statement form to record the volume of the evidence, its consistency, clinical impact, generalisability and applicability and developed evidence statements (see Technical report). The process is described in NHMRC additional levels of evidence and grades for recommendations for developers of guidelines (2009).<sup>[10]</sup>



Following grading of the body of evidence and development of evidence statements, expert authors were asked to formulate evidence-based recommendations that related to the summarised body of evidence. The method of grading recommendations is shown in Table A2.

### 5.5.5.8.1 Table A2. Grading of recommendations

Component of Recommendation	Recommendation Grade			
	<b>A</b> Excellent	<b>B</b> Good	<b>C</b> Satisfactory	<b>D</b> Poor
<b>Volume of evidence</b> <sup>1**</sup>	one or more level I studies with a low risk of bias or several level II studies with a low risk of bias	one or two level II studies with a low risk of bias or a systematic review/several level III studies with a low risk of bias	one or two level III studies with a low risk of bias, or level I or II studies with a moderate risk of bias	level IV studies, or level I to III studies /systematic reviews with a high risk of bias
<b>Consistency</b> <sup>2**</sup>	all studies consistent	most studies consistent and inconsistency may be explained	some inconsistency reflecting genuine uncertainty around clinical question	evidence is inconsistent
<b>Clinical impact</b>	very large	substantial	moderate	slight or restricted
<b>Generalisability</b>	population/s studied in body of evidence are the same as the target population for the guideline	population/s studied in the body of evidence are similar to the target population for the guideline	population/s studied in body of evidence differ to target population for guideline but it is clinically sensible to apply this evidence to target population <sup>3</sup>	population/s studied in body of evidence different to target population and hard to judge whether it is sensible to generalise to target population
	directly applicable to	applicable to Australian	probably applicable to Australian healthcare	not applicable to

<b>Applicability</b>	Australian healthcare context	healthcare context with few caveats	context with some caveats	Australian healthcare context
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<sup>1</sup> Level of evidence determined from level of evidence criteria

<sup>2</sup> If there is only one study, rank this component as 'not applicable'

<sup>3</sup> For example results in adults that are clinically sensible to apply children OR psychosocial outcomes for one cancer that may be applicable to patients with another cancer.

\*\*For a recommendation to be graded A or B, the volume and consistency of evidence must also be graded either A or B.

*Source: National Health and Medical Research Council. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. Canberra: NHMRC; 2009. ([https://www.nhmrc.gov.au/\\_files\\_nhmrc/file/guidelines/developers/nhmrc\\_levels\\_grades\\_evidence\\_120423.pdf](https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf))*

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The overall recommendation grades are shown in Table A3.

### 5.5.5.8.2 Table A3. Overall recommendation grades

Grade of recommendation	Description
<b>A</b>	Body of evidence can be trusted to guide practice
<b>B</b>	Body of evidence can be trusted to guide practice in most situations
<b>C</b>	Body of evidence provides some support for recommendation(s) but care should be taken in its application
<b>D</b>	Body of evidence is weak and recommendation must be applied with caution

*Source: National Health and Medical Research Council. NHMRC levels of evidence and grades for recommendations for developers of guidelines. Canberra: NHMRC; 2009. ([https://www.nhmrc.gov.au/\\_files\\_nhmrc/file/guidelines/developers/nhmrc\\_levels\\_grades\\_evidence\\_120423.pdf](https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf))*

In addition to developing evidence-based recommendations as a result of the systematic review for a question, expert authors could also draft consensus-based recommendations in the absence of evidence after having performed a systematic review, or practice points, when a matter was outside the scope of the search strategy for the systematic review. The NHMRC approved recommendation types and definitions are shown in Table A4.

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### 5.5.5.8.3 Table A4. NHMRC approved recommendation types and definitions

Type of recommendation	Definition
<b>Evidence-based recommendation</b>	A recommendation formulated after a systematic review of the evidence, indicating supporting references
<b>Consensus-based recommendation</b>	A recommendation formulated in the absence of quality evidence, after a systematic review of the evidence was conducted and failed to identify admissible evidence on the clinical question
<b>Practice point</b>	A recommendation on a subject that is outside the scope of the search strategy for the systematic review, based on expert opinion and formulated by a consensus process

*Source: National Health and Medical Research Council. Procedures and requirements for meeting the NHMRC standard for clinical practice guidelines. Melbourne: National Health and Medical Research Council, 2011*

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### 5.5.5.9 Writing the content

For each clinical question, the assigned lead authors were asked to draft their guideline chapter using the following format:

- general introduction to the clinical question
- background to the clinical question, including its clinical importance and historical evidence, where relevant
- review of the evidence, including the number, quality and findings of studies identified by the systematic review
- evidence summary in tabular form including evidence statements, levels of evidence of included studies, and reference citations
- evidence-based recommendation(s) and corresponding grade(s), consensus-based recommendations and practice points
- implications for implementation of the recommendations, including possible effects on usual care, organisation of care, and any resource implications
- discussion, including unresolved issues, relevant studies currently underway, and future research priorities
- references.

For sections not based on systematic review, the lead author was asked to draw on high-level evidence, particularly international guidelines, consensus statements and key literature considered to be relevant to Australian practice, to develop information and practice points.

The content draft was then reviewed by subcommittee members who were available. The draft documents often underwent several iterations.

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### 5.5.5.10 Review of the draft chapters

The draft guideline sections were circulated to the Working Party members and posted on Cancer Council Australia's wiki platform. The group was asked to review the content and submit feedback. Members were asked to submit further suggestions on consensus-based recommendation and practice points.

A face-to-face meeting with all available Working Party members was held in December 2017 to review and finalise the draft guideline for public consultation. Prior to this meeting, the latest version of the draft guideline was circulated as soon as they were available. All members were asked to review the content, individual recommendations and practice points in detail, and to identify and note any controversies and points to be discussed at the group meeting.

During the meeting, each chapter/section was tabled as an agenda point and recommendations and practice points were discussed in detail. All clinical guidance was reviewed and approved by consensus, which was reached by voting. In some cases, the authors agreed on specific actions for the content or discussed further sections or amendments to be added. These were actioned by the authors. Each recommendation and practice point was approved once the eligible panellists (excluding representatives of the funding bodies and panellists who cannot vote due to conflict of interest) reached consensus. See the Administrative report for information on conflict of interest declarations and action required.

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### 5.5.6 Public consultation

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A complete draft of the guideline was sent out for public consultation from 3 April to 2 May 2018. Submissions are invited from the general public and professional societies and groups and other relevant stakeholders. The consultation was publicised by email to key stakeholders, including contacting professional societies and groups, consumer groups and other relevant parties.

All feedback on the draft received during the consultation period will be compiled and send to the relevant author and subcommittee to review their draft content, assessing and considering the submitted comments. Each additional submitted paper during public consultation will be assessed by the methodologist team against the systematic review protocol to determine if it could be included.

Another face-to-face Working Party meeting was held on 22 May 2018 to review all public consultation comments and the amended guideline content. Subsequent changes to the draft were agreed by consensus, based on consideration of the evidence. The same consensus process that was followed prior to public consultation was followed again. All changes resulting from the public consultation submission reviews will be documented and made accessible once the guideline is published.

The guideline was assessed by two independent reviewers according to the AGREEII assessment tool ([www.agreetrust.org](http://www.agreetrust.org)) before the final draft was submitted to NHMRC. Further suggestions by the independent expert reviewers were considered and integrated in the final draft.

The final draft was submitted to NHMRC for review on 23 July 2018. Further suggestions by the independent expert reviewers were considered and integrated in the final draft and then submitted to NHMRC Council for approval.

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## 5.5.7 Organisations formally endorsing the guidelines

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The following medical colleges and professional bodies may be approached to endorse the guideline:

- Australian College of Rural and Remote Medicine (ACRRM)
- Colorectal Surgical Society of Australia and New Zealand (CSS ANZ)
- Gastroenterological Society of Australia (GESA)
- Medical Oncology Group of Australia Incorporated (MOGA)
- Royal College of Pathologists of Australia (RCPA)
- Royal Australasian College of Physicians (RACP)
- Royal Australian College of Surgeons (RACS).

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## 5.5.8 Dissemination and implementation

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Cancer Council Australia have created a plan regarding the dissemination of the guideline in Australia.

The guideline will be made available online via the Cancer Council Australia Cancer Guidelines wiki. The online guideline version increases availability as well as accessibility, and usage will be tracked and analysed with a web analytics solution. Interlinking and listing the guidelines on national and international guideline portal is an important part of the digital dissemination strategy. Important Australian health websites, such as EviQ and healthdirect Australia will be approached to link to the online guideline. The guideline will also to be listed on national and international guideline portals such as Australia's Clinical Practice Guidelines Portal. The Cancer Guidelines wiki is a responsive website that is optimised for mobile and desktop access. When accessing the guidelines with a mobile and tablet device, an icon can be easily added to the home screen of mobile devices, offering easy mobile access.

In addition, the final guideline document will be launched via email alert to professional organisations, interested groups and clinical experts in the field, directing them via URL link to the online guideline and all associated resources.

The Cancer Guidelines wiki is based on semantic web technology, so the guidelines are available in a machine-readable format, which offers the possibility to easily integrate the guideline content with systems and web applications used in the Australian healthcare context.

Use of the guideline as part of core curriculum in specialty exams will be encouraged. It is recognised that a planned approach is necessary to overcome specific barriers to implementation in particular settings and to identify appropriate incentives to encourage uptake of guideline recommendations. Implementation of the guidelines will require a combination of effective strategies and may include further CME initiatives and interactive learning, the development and promotion of computer-assisted decision aids and electronic decision-support systems, and the creation of audit and other clinical tools.

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## 5.5.9 Future updates

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The incoming literature updates will continue to be monitored for each systematic review question. If there is strong evidence emerging in a specific area of surveillance colonoscopy, the Management Committee will be reconvened to assess if this warrants a guideline update (full or partial). It is recommended that the guideline be updated after 5 years.

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## 5.5.10 References

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1. ↑ National Health and Medical Research Council. *Procedures and requirements for meeting the NHMRC standard for clinical practice guidelines*. Melbourne; 2011.
2. ↑ <sup>2.0</sup> <sup>2.1</sup> National Health and Medical Research Council. *A guide to the development, evaluation and implementation of clinical practice guidelines*. Commonwealth of Australia: National Health and Medical Research Council; 1999 Jan 1 Available from: [http://www.nhmrc.gov.au/\\_files\\_nhmrc/publications/attachments/cp30.pdf](http://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/cp30.pdf).
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10. ↑ <sup>10.0</sup> <sup>10.1</sup> National Health and Medical Research Council. *NHMRC additional levels of evidence and grades for recommendations for developers of guidelines*. Canberra; 2009 Available from: [www.mja.com.au/sites/default/files/NHMRC.levels.of.evidence.2008-09.pdf](http://www.mja.com.au/sites/default/files/NHMRC.levels.of.evidence.2008-09.pdf).

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## 5.6 Clinical question list

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- 1 Advances in colonoscopy, CT colonography and other methods (section lead: Gregor Brown)
- 2 Colonoscopic surveillance after polypectomy (section lead: Karen Barclay)
- 3 The role of surveillance colonoscopy after curative resection for colorectal cancer (section leads: James Moore and Tarik Sammour)
- 4 Colonoscopic surveillance and management of dysplasia in inflammatory bowel disease (IBD) (section lead: Rupert Leong)
  - 4.1 IBD and risk of colorectal cancer
  - 4.2 Management of elevated dysplasia in IBD
- 5 Anxiety in colonoscopy: approaches to minimise anxiety and its adverse effects (section lead: Afaf Girgis)
- 6 Socio-economic factors (section lead: Anne Duggan)

This page lists the questions answered by systematic review and modelling. For full details about the reviews, including the inclusion and exclusion criteria, please see the Technical report.

### 5.6.1 Advances in colonoscopy, CT colonography and other methods (section lead: Gregor Brown)

Background chapter based on general literature summary. The 2011 content was reviewed and updated where required. Practice points were included as guidance.

### 5.6.2 Colonoscopic surveillance after polypectomy (section lead: Karen Barclay)

**Clinical Question SAD1:** What should be the surveillance colonoscopy for patients at low risk (1-2 small <10mm tubular adenomas)?

Population	Intervention	Comparator	Outcomes	Study Type	Study Design
			<ul style="list-style-type: none"> <li>■ Incidence of colorectal cancer</li> <li>■ Incidence of adenoma</li> </ul>		Systematic reviews of Level II

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Population	Intervention	Comparator	Outcomes	Study Type	Study Design
Patients diagnosed with 1 or 2 tubular adenomas <10mm in size which have been removed	Surveillance colonoscopy follow up schedule - 5 to 10 years colonoscopy	<ul style="list-style-type: none"> <li>■ Alternative colonoscopy frequency schedule(s) - &lt;5 years; or</li> <li>■ No schedule; or</li> <li>■ No comparator</li> </ul>	<ul style="list-style-type: none"> <li>■ Incidence of advanced adenoma</li> <li>■ Risk of colorectal cancer</li> <li>■ Risk of adenoma</li> <li>■ Risk of advanced adenoma</li> <li>■ Complications</li> </ul>	Intervention, aetiology	evidence, randomised controlled trials, cohort studies or case-control studies

Population	Risk factor	Outcomes	Study Type	Study Design
<p><u>Low risk population:</u></p> <p>Patients diagnosed with 1 or 2 tubular adenomas &lt;10mm in size which have been removed</p>	<ul style="list-style-type: none"> <li>■ Surveillance time</li> </ul>	<ul style="list-style-type: none"> <li>■ Incidence of colorectal cancer</li> <li>■ Incidence of adenoma</li> <li>■ Incidence of advanced adenoma</li> <li>■ Risk of colorectal cancer</li> <li>■ Risk of adenoma</li> <li>■ Risk of advanced adenoma</li> </ul>	Prognostic	Systematic reviews of Level II evidence, cohort studies

**Clinical Question SAD2:**

What should be the surveillance colonoscopy for patients at high risk (size  $\geq 10$ mm, HGD, villosity and/or 3-4 adenomas)?



Population	Intervention	Comparator	Outcomes	Study Type	Study Design
Patients who have had a polypectomy to remove: <ul style="list-style-type: none"> <li>■ three or more adenomatous polyps; or</li> <li>■ at least one adenoma is <math>\geq 10</math>mm in size; or</li> <li>■ the adenomas exhibit villous or tubulovillous histology or high-grade dysplasia</li> </ul>	Surveillance colonoscopy follow up schedule - 3 yearly colonoscopy (or any schedule given no comparator)	<ul style="list-style-type: none"> <li>■ Alternative colonoscopy frequency schedule(s) - 5 years or 5-10 years; or</li> <li>■ No comparator</li> </ul>	<ul style="list-style-type: none"> <li>■ Incidence of colorectal cancer</li> <li>■ Incidence of adenoma</li> <li>■ Incidence of advanced adenoma</li> <li>■ Risk of colorectal cancer</li> <li>■ Risk of adenoma</li> <li>■ Risk of advanced adenoma</li> <li>■ Complications</li> </ul>	Intervention, aetiology	Systematic reviews of Level II evidence, randomised controlled trials, cohort studies or case-control studies

Population	Risk factor	Outcomes	Study Type	Study Design
<u>High risk population:</u> Patients who have had a polypectomy to remove: <ul style="list-style-type: none"> <li>■ three or more adenomatous polyps; or</li> <li>■ at least one adenoma is <math>\geq 10</math>mm in size; or</li> <li>■ the adenomas exhibit villous or tubulovillous histology or high-grade dysplasia</li> </ul>	<ul style="list-style-type: none"> <li>■ High risk population (compared to low risk population*)</li> <li>■ Surveillance time</li> </ul> * Patients with 1 or 2 tubular adenomas $< 10$ mm in size	<ul style="list-style-type: none"> <li>■ Incidence of colorectal cancer</li> <li>■ Incidence of adenoma</li> <li>■ Incidence of advanced adenoma</li> <li>■ Risk of colorectal cancer</li> <li>■ Risk of adenoma</li> <li>■ Risk of advanced adenoma</li> </ul>	Prognostic	Systematic reviews of Level II evidence, cohort studies

**Clinical Question SAD3:**

What is the appropriate colonoscopic surveillance after the removal of large sessile or laterally spreading adenomas?

Population	Intervention	Comparator	Outcomes	Study Type	Study Design
<p>Patients diagnosed with adenomas <math>\geq 20\text{mm}</math> including:</p> <ul style="list-style-type: none"> <li>■ large sessile adenomas; or</li> <li>■ laterally spreading adenomas</li> </ul> <p>which were removed by:</p> <ul style="list-style-type: none"> <li>■ en bloc resection</li> </ul> <p>Procedure performed by endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD)</p>	<p>Surveillance colonoscopy follow up schedule with colonoscopy</p>	<p>Alternative colonoscopy frequency schedule(s)</p> <p>or</p> <ul style="list-style-type: none"> <li>■ No comparator</li> </ul>	<p>*Residual /Recurrent adenoma</p> <ul style="list-style-type: none"> <li>■ Cancer incidence</li> </ul>	<p>Intervention, aetiology</p>	<p>Systematic reviews of Level II evidence, randomised controlled trials, cohort studies or case-control studies</p>
<p>Patients diagnosed with adenomas <math>\geq 20\text{mm}</math> including:</p> <ul style="list-style-type: none"> <li>■ large sessile adenomas; or</li> <li>■ laterally spreading adenomas</li> </ul> <p>which were removed by:</p> <ul style="list-style-type: none"> <li>■ piecemeal</li> </ul> <p>Procedure performed by endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD)</p>	<p>Surveillance colonoscopy follow up schedule with colonoscopy - &lt;6 months</p>	<p>Alternative colonoscopy frequency schedule(s)</p> <p>or</p> <ul style="list-style-type: none"> <li>■ No comparator</li> </ul>			

Population	Risk factor	Outcomes	Study Type	Study Design
Patients diagnosed with adenomas $\geq 20$ mm including large sessile adenomas or laterally spreading adenomas	<ul style="list-style-type: none"> <li>■ en bloc resection</li> <li>■ piecemeal resection</li> <li>■ endoscopic mucosal resection (EMR)</li> <li>■ endoscopic submucosal resection (ESD)</li> <li>■ surveillance time</li> </ul>	Residual /Recurrent adenoma <ul style="list-style-type: none"> <li>■ Cancer incidence</li> </ul>	Prognostic	Systematic reviews of Level II evidence, cohort studies

**Clinical Question SAD4:**

What is the appropriate colonoscopic surveillance after the identification of sessile serrated adenomas and traditional serrated adenomas?

Population	Intervention	Comparator	Outcomes	Study Type	Study Design
Patients diagnosed with <ul style="list-style-type: none"> <li>■ traditional serrated adenomas/polyps or;</li> </ul>	Surveillance colonoscopy		<ul style="list-style-type: none"> <li>■ Incidence and location of colorectal cancer</li> <li>■ Incidence of adenoma</li> <li>■ Incidence of advanced adenoma</li> <li>■ Incidence of SSA /TSA</li> </ul>		Systematic reviews of Level II evidence,

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Population	Intervention	Comparator	Outcomes	Study Type	Study Design
<ul style="list-style-type: none"> <li>sessile serrated adenomas/polyps or sessile serrated polyps proximal to the splenic flexure</li> </ul> +/- dysplasia +/- $\geq$ 10mm which have been removed	follow up schedule with colonoscopy - 3 years (or any schedule given no comparator)	Alternative colonoscopy frequency schedule(s) - <3, 5 or 5-10 years; or <ul style="list-style-type: none"> <li>No comparator</li> </ul>	<ul style="list-style-type: none"> <li>Incidence of advanced SSA/TSA</li> <li>Risk of colorectal cancer</li> <li>Risk of adenoma</li> <li>Risk of advanced adenoma</li> <li>Risk of TSA/SSA</li> <li>Risk of advanced TSA/SSA</li> </ul>	Intervention, aetiology	randomised controlled trials, cohort studies or case-control studies

Population	Risk factor	Outcomes	Study Type	Study Design
Patients diagnosed with sessile serrated adenomas/polyps or traditional serrated adenomas/polyps which have been removed and are undergoing surveillance	Patients with <ul style="list-style-type: none"> <li>traditional serrated adenomas/polyps or;</li> </ul>	<ul style="list-style-type: none"> <li>Incidence and location of colorectal cancer</li> <li>Incidence of adenoma</li> <li>Incidence of advanced adenoma</li> <li>Incidence of SSA /TSA</li> <li>Incidence of advanced SSA/TSA</li> </ul>	Prognostic	Systematic reviews of Level II evidence, cohort

Population	Risk factor	Outcomes	Study Type	Study Design
colonoscopy	<ul style="list-style-type: none"> <li>sessile serrated adenomas/polyps or sessile serrated polyps proximal to the splenic flexure</li> </ul> +/- dysplasia +/- ≥ 10mm	<ul style="list-style-type: none"> <li>Risk of colorectal cancer</li> <li>Risk of adenoma</li> <li>Risk of advanced adenoma</li> <li>Risk of TSA/SSA</li> <li>Risk of advanced TSA/SSA</li> </ul>		studies

**Clinical Question SAD5:**

What should be the surveillance colonoscopy for patients with adenoma multiplicity?

Population	Intervention	Comparator	Outcomes	Study Type	Study Design
Patients diagnosed with multiple (5-19): <ul style="list-style-type: none"> <li>adenomas and/or</li> <li>low risk adenomas and/or</li> <li>high risk adenomas and/or</li> <li>serrated adenomas</li> </ul> which have been removed	Surveillance colonoscopy follow up schedule with colonoscopy <ul style="list-style-type: none"> <li>1 year for five to nine adenomatous polyps</li> <li>≤1 year for ≥10 adenomatous polyps</li> <li>Any schedule given no comparator</li> </ul>	Alternative colonoscopy frequency schedule(s) <ul style="list-style-type: none"> <li>No comparator</li> </ul>	<ul style="list-style-type: none"> <li>Incidence of colorectal cancer</li> <li>Incidence of adenoma</li> <li>Incidence of advanced adenoma</li> <li>Risk of colorectal cancer</li> <li>Risk of adenoma</li> <li>Risk of advanced adenoma</li> <li>Complications</li> </ul>	Intervention, aetiology	Systematic reviews of Level II evidence, randomised controlled trials, cohort studies or case-control studies

Population	Risk factor	Outcomes	Study Type	Study Design
Patients diagnosed with adenomas that have been removed and are undergoing surveillance colonoscopy	Patients with multiple (5-19): <ul style="list-style-type: none"> <li>■ adenomas and/or</li> <li>■ low risk adenomas and/or</li> <li>■ high risk adenomas and/or</li> <li>■ serrated adenomas</li> </ul>	<ul style="list-style-type: none"> <li>■ Incidence of colorectal cancer</li> <li>■ Incidence of adenoma</li> <li>■ Incidence of advanced adenoma</li> <li>■ Risk of colorectal cancer</li> <li>■ Risk of adenoma</li> <li>■ Risk of advanced adenoma</li> </ul>	Prognostic	Systematic reviews of Level II evidence, cohort studies

### **Clinical Question SFH1:**

Is the surveillance colonoscopy recommendation different for patients with adenomas who also have a family history of CRC?

### **Intervention studies**

Population	Intervention	Comparator	Outcomes	Study Type + Design
Patients diagnosed with adenomas which have been removed  AND Presence of a family history of colorectal cancer: <ul style="list-style-type: none"> <li>■ 1 first degree relative (FDR) or second degree relative (SDR) and age (<math>\geq 55</math> or <math>\geq 60</math>) years at diagnosis; or</li> </ul>	Following a defined surveillance		Incidence of: <ul style="list-style-type: none"> <li>■ colorectal cancer</li> <li>■ adenoma</li> <li>■ advanced adenoma</li> </ul> Risk of: <ul style="list-style-type: none"> <li>■ colorectal cancer</li> </ul>	Intervention studies of level I to III-

Population	Intervention	Comparator	Outcomes	Study Type + Design
<ul style="list-style-type: none"> <li>1 FDR age (&lt;55 or &lt;60) years at diagnosis or 2 FDR or 1 FDR and 1 SDR on the same side of the family, at any age at diagnosis</li> </ul> Colonoscopy after 2002	colonoscopy schedule	Alternative surveillance colonoscopy frequency schedule(s) or No comparator	<ul style="list-style-type: none"> <li>adenoma</li> <li>advanced adenoma</li> </ul> Complications	2 evidence

### Prognostic studies

Population	Risk factor	Outcomes	Study Type + Design
Patients diagnosed with adenomas which have been removed and are undergoing surveillance colonoscopy	Presence of a family history* of colorectal cancer <ul style="list-style-type: none"> <li>1 first degree relative (FDR) or second degree relative (SDR) and age (<math>\geq 55</math> or <math>\geq 60</math>) years at diagnosis; or</li> <li>1 FDR age (&lt;55 or &lt;60) years at diagnosis or 2 FDR or 1 FDR and 1 SDR on the same side of the family, at any age at diagnosis</li> </ul>	Risk of: <ul style="list-style-type: none"> <li>colorectal cancer</li> <li>adenoma</li> <li>advanced adenoma</li> </ul>	Prognostic studies of level I to III-3 evidence

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## 5.6.3 The role of surveillance colonoscopy after curative resection for colorectal cancer (section leads: James Moore and Tarik Sammour)

### **Clinical Question COL1:**

What is the role of pre or peri-operative colonoscopy in CRC patients?

Population	Intervention	Comparator	Outcomes	Study Design
			<ul style="list-style-type: none"> <li>Diagnostic yield</li> <li>Adenoma detection rate</li> </ul>	

Population	Intervention	Comparator	Outcomes	Study Design
Patients diagnosed with colorectal cancer and planned surgery	Colonoscopy performed peri-operatively including <ul style="list-style-type: none"> <li>■ pre-operatively</li> <li>■ post-operatively</li> </ul>	N/A	<ul style="list-style-type: none"> <li>■ Synchronous cancer rate</li> <li>■ Quality of life</li> <li>■ Adenomas with advanced pathological features</li> </ul>	Cohort studies  Case /controls

**Clinical Question FUC1:**

At what time points after CRC resection should surveillance colonoscopy be performed?

**PICO Question FUC1:**

In patients who have undergone resection for colorectal cancer what is the optimal follow-up colonoscopy frequency or schedule in relation to diagnostic yield, adenoma recurrence, adenomas with advanced pathological features, and quality of life?

Population	Intervention	Comparator	Outcomes	Study Design
Patients who have undergone resection for colorectal cancer	Surveillance colonoscopy follow up frequency/schedule	An alternative surveillance colonoscopy follow up frequency/schedule	Diagnostic yield (what % of cancer was diagnosed), adenoma recurrence, adenomas with advanced pathological features, quality of life	Comparative study with or without concurrent controls

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## 5.6.4 Colonoscopic surveillance and management of dysplasia in inflammatory bowel disease (IBD) (section lead: Rupert Leong)

### 5.6.4.1 IBD and risk of colorectal cancer

**Clinical Question SUR1:**

What is the appropriate time to commence surveillance in IBD patients (ulcerative colitis and Crohn's patients, and effects of primary sclerosing cholangitis or family history of CRC)?



Population	Intervention	Comparator	Outcomes	Study Design
Patient diagnosed with Inflammatory Bowel Disease (Ulcerative colitis or Crohn's disease) with or without a family history of CRC, or primary sclerosing cholangitis	Time to commence surveillance following a diagnosis of IBD (Ulcerative colitis or Crohn's disease)	An alternative time to commence surveillance following a diagnosis of IBD	<ul style="list-style-type: none"> <li>■ Colorectal cancer prevalence</li> <li>■ Colorectal cancer mortality</li> <li>■ Dysplasia prevalence</li> </ul>	Intervention and aetiology studies of all study designs

Population	Risk factors	Outcomes	Study Design /Type
Patient diagnosed with Inflammatory Bowel Disease (Ulcerative colitis or Crohn's disease)	<ul style="list-style-type: none"> <li>■ Family History of CRC</li> <li>■ Ulcerative colitis</li> <li>■ Crohn's disease</li> <li>■ primary sclerosing cholangitis</li> <li>■ Duration of IBD</li> <li>■ Extent of bowel involvement</li> <li>■ Activity of disease (endoscopic)</li> <li>■ Activity of disease (histological)</li> <li>■ Intestinal damage</li> </ul>	<ul style="list-style-type: none"> <li>■ Colorectal cancer incidence</li> <li>■ Colorectal cancer mortality</li> <li>■ Dysplasia incidence</li> </ul>	Prognostic studies of all design

**Clinical Question SUR2:**

What is the most appropriate time interval for surveillance in IBD patients based on risk?

**Intervention studies**

Population	Intervention	Comparator	Outcomes	Study Design
Patient diagnosed with Inflammatory Bowel Disease (Ulcerative colitis or Crohn's disease)  with or without a family history of CRC, or primary sclerosing cholangitis	Frequency of surveillance following a diagnosis of IBD (Ulcerative colitis or Crohn's disease)	An alternative frequency of surveillance following a diagnosis of IBD (Ulcerative colitis or Crohn's disease)	<ul style="list-style-type: none"> <li>■ Colorectal cancer prevalence</li> <li>■ Colorectal cancer mortality</li> <li>■ Dysplasia prevalence</li> </ul>	Intervention studies of all study designs

### Prognostic studies

Population	Risk factors	Outcomes	Study Design /Type
Patient diagnosed with Inflammatory Bowel Disease (Ulcerative colitis or Crohn's disease)	<ul style="list-style-type: none"> <li>■ Family History of CRC</li> <li>■ Ulcerative colitis</li> <li>■ Crohn's disease</li> <li>■ primary sclerosing cholangitis</li> <li>■ Duration of IBD</li> <li>■ Extent of bowel involvement</li> <li>■ Activity of disease (endoscopic)</li> <li>■ Activity of disease (histological)</li> <li>■ Intestinal damage</li> </ul>	<ul style="list-style-type: none"> <li>■ Colorectal cancer incidence</li> <li>■ Colorectal cancer mortality</li> <li>■ Dysplasia incidence</li> </ul>	Prognostic studies of all design

### **Clinical Question SUR3:**

What is the recommended surveillance strategies for surveillance in IBD patients?

Population	Intervention	Comparator	Outcomes	Study Design
Patient diagnosed with Inflammatory Bowel Disease (Ulcerative colitis or Crohn's disease)	<ul style="list-style-type: none"> <li>■ High-definition endoscopy (HDE)</li> <li>■ Chromoendoscopy</li> <li>■ Confocal laser Endomicroscopy</li> <li>■ Narrow band imaging (NBI)</li> <li>■ Autofluorescence imaging</li> <li>■ Endoscopy with targeted biopsies</li> </ul>	Standard white light, standard definition colonoscopy	<ul style="list-style-type: none"> <li>■ Colorectal cancer prevalence, or</li> <li>■ Dysplasia prevalence over a specific follow-up period</li> </ul>	Intervention studies of all study design
	<ul style="list-style-type: none"> <li>■ Targeted biopsies</li> </ul>	<ul style="list-style-type: none"> <li>■ Random biopsies</li> </ul>		

Population	Index Test 1	Index Test 2	Reference standard	Outcomes
Patient diagnosed with Inflammatory Bowel Disease (Ulcerative colitis or Crohn's disease)	<ul style="list-style-type: none"> <li>■ Colonoscopy (white light endoscopy)</li> <li>■ High-definition endoscopy (HDE)</li> <li>■ Chromoendoscopy</li> <li>■ Confocal Laser Endomicroscopy (CLE)</li> <li>■ Narrow band imaging (NBI)</li> <li>■ Autofluorescence imaging</li> <li>■ Endoscopy with targeted biopsies</li> <li>■ Endoscopy with random biopsies</li> </ul>	An alternative endoscopy technique listed for Index test 2 or no 2 <sup>nd</sup> index test	Pathological histology	Diagnostic performance related to the detection of colorectal cancer or dysplasia, including <ul style="list-style-type: none"> <li>■ sensitivity</li> <li>■ specificity</li> <li>■ PPV or NPV</li> <li>■ accuracy</li> </ul>
	Targeted biopsies			

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### 5.6.4.2 Management of elevated dysplasia in IBD

#### **Clinical Question MNG1:**

What should be the protocol to manage elevated dysplasia in IBD?

#### **PICO MNG1:**

In patients who have inflammatory bowel disease (IBD) and elevated dysplasia, which management protocol achieves the best outcomes in relation to the development of colorectal cancer?

Population	Intervention	Comparator	Outcomes	Study Design
Patients who have IBD and elevated dysplasia	Management protocol for elevated dysplasia which may include: <ul style="list-style-type: none"> <li>■ endoscopic lesions</li> <li>■ surgical interventions</li> </ul>	An alternative management protocol	Development of colorectal cancer	Comparative studies with or without concurrent controls

#### **Clinical Question MNG2:**

What should be the protocol to manage high-grade dysplasia in IBD?

#### **PICO MNG2:**

In patients who have inflammatory bowel disease (IBD) and high-grade dysplasia, which management protocol achieves the best outcomes in relation to the development of colorectal cancer?

Population	Intervention	Comparator	Outcomes	Study Design
Patients who have IBD and high-grade dysplasia in flat mucosa	Management protocol for high-grade dysplasia which may include: <ul style="list-style-type: none"> <li>■ colectomy</li> </ul>	An alternative management protocol	Development of colorectal cancer	Comparative studies with or without concurrent controls

#### **Clinical Question MNG3:**

What should be the protocol to manage low-grade dysplasia in IBD?

#### **PICO MNG3:**

In patients who have inflammatory bowel disease (IBD) and low-grade dysplasia, which management protocol achieves the best outcomes in relation to the prevention of progression to a higher grade of dysplasia?

Population	Intervention	Comparator	Outcomes	Study Design
Patients who have IBD and low-grade dysplasia in flat musoca	Management protocol for low-grade dysplasia which may include: <ul style="list-style-type: none"> <li>■ colectomy</li> <li>■ chromoendoscopy</li> <li>■ surveillance</li> </ul>	An alternative management protocol	Prevent progression to a higher grade of dysplasia	Comparative studies with or without concurrent controls

**Clinical Question MNG4:**

What should be the protocol to manage indefinite dysplasia in IBD?

**PICO MNG4:**

In patients who have inflammatory bowel disease (IBD) and indefinite dysplasia, which management protocol achieves the best outcomes in relation to the progression to colorectal cancer?

Population	Intervention	Comparator	Outcomes	Study Design
Patients with IBD and indefinite dysplasia	Management protocol for low-grade dysplasia which may include: <ul style="list-style-type: none"> <li>■ chromoendoscopy</li> <li>■ surveillance</li> </ul>	An alternative management protocol	Progression to colorectal cancer	Comparative studies with or without concurrent controls

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### 5.6.5 Anxiety in colonoscopy: approaches to minimise anxiety and its adverse effects (section lead: Afaf Girgis)

Background chapter based on general literature summary. The 2011 content was reviewed and updated where required. Practice points were included as guidance.

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### 5.6.6 Socio-economic factors (section lead: Anne Duggan)

Background chapter based on general literature summary. The 2011 content was reviewed and updated where required. Practice points were included as guidance.

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## 5.7 Journal articles

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- 1 Bowel cancer
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  - 1.2 Surveillance colonoscopy
- 2 Skin cancer
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  - 2.2 Melanoma

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### 5.7.1 Bowel cancer

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Journal articles developed out of the Australian *Clinical practice guidelines for the prevention, early detection and management of colorectal cancer* and *Clinical practice guidelines for surveillance colonoscopy*.

As part of the dissemination and implementation plans for these guidelines, lead authors were encouraged to develop articles to submit to journals for publication in order to further promote the updated Australian guidance on surveillance colonoscopy and the prevention, early detection and management of colorectal cancer.

Dissemination and implementation plans:

- Clinical practice guidelines for the prevention, early detection and management of colorectal cancer
- Clinical practice guidelines for surveillance colonoscopy.

#### 5.7.1.1 Colorectal cancer

##### **Journal articles published or accepted for publication:**

Revised Australian national guidelines for colorectal cancer screening: family history *Mark A Jenkins, Driss Ait Ouakrim, Alex Boussioutas, John L Hopper, Hooi C Ee, Jon D Emery, Finlay A Macrae, Albert Chetcuti, Laura Wuellner and James B St John* (29 October 2018)

The National Bowel Cancer Screening Program: time to achieve its potential to save lives *Hooi C Ee, James St John* (31 July 2019)

#### 5.7.1.2 Surveillance colonoscopy

##### **Journal articles published or accepted for publication:**

TBC

## 5.7.2 Skin cancer

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### 5.7.2.1 Keratinocyte cancer

#### **Journal articles published or accepted for publication:**

TBC

### 5.7.2.2 Melanoma

Journal articles developed out of the Australian *Clinical practice guidelines for the diagnosis and management of melanoma*.

As part of the dissemination and implementation plan for the guideline, lead authors were encouraged to develop articles to submit to journals for publication in order to further promote the updated Australian guidance on the diagnosis and management of melanoma.

#### **Journal articles published or accepted for publication:**

When is a sentinel node biopsy indicated for patients with primary melanoma? An update of the 'Australian guidelines for the management of cutaneous melanoma' *David E Gyorki, Andrew Barbour, Mark Hanikeri, Victoria Mar, Shahneen Sandhu and John F Thompson*

Clinical practice guidelines for the diagnosis and management of melanoma: melanomas that lack classical clinical features *Victoria J Mar, Alex J Chamberlain, John W Kelly, William K Murray and John F Thompson*

Updated evidence-based clinical practice guidelines for the diagnosis and management of melanoma: definitive excision margins for primary cutaneous melanoma *Michael J Sladden, Omgo E Nieweg, Julie Howle, Brendon J Coventry and John F Thompson*

Methods of melanoma detection and of skin monitoring for individuals at high risk of melanoma: new Australian clinical practice *Nikki R Adler, John W Kelly, Pascale Guitera, Scott W Menzies, Alex J Chamberlain, Paul Fishburn, Alison E Button-Sloan, Clinton Heal, H Peter Soyer and John F Thompson*

Multidisciplinary care of cancer patients – a passing fad or here to stay? *John F Thompson and Gabrielle J Williams*

Improving diagnostic accuracy for suspicious melanocytic skin lesions: new Australian melanoma clinical practice guidelines stress the importance of clinician/pathologist communication *Richard A Scolyer, H Peter Soyer, John W Kelly, Craig James, Catriona A McLean, Brendon J Coventry, Peter M Ferguson, Robert V Rawson, Victoria J Mar, Sara L de Menezes, Paul Fishburn, Jonathan R Stretch, Stephen Lee and John F Thompson*

New treatment paradigms for clinically-apparent metastatic melanoma in regional lymph nodes *Michael A. Henderson, John Spillane, T. Michael Hughes, Andrew J. Spillane, B. Mark Smithers and John F. Thompson*

Evidence-based clinical practice guidelines for the management of patients with lentigo maligna *Mitchell Robinson, Clare Primiero, Pascale Guitera, Angela Hong, Richard A. Scolyer, Jonathan R. Stretch, Geoffrey Strutton, John F. Thompson and H. Peter Soyer*

Diagnosis and Management of Cutaneous Melanoma *Victoria Mar (20-4-2020: accepted for publication AJGP)*

New Australian melanoma management guidelines - the patient perspective *J F Thompson & Alison Button-Sloan (27-May-2020: accepted for publication MJA)*

Last updated: 6 July 2020

## 5.8 Technical report

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This Technical Report accompanies the *Clinical practice guidelines for Surveillance Colonoscopy*, developed by Cancer Council Australia.

It outlines the guideline development process and methodology, lists the clinical questions, provides all accompanying NHMRC Statement Forms, the detailed technical documentation for each question and the risk of bias assessment tools used to assess the included literature as a result of a systematic review.

### 5.8.1 Guideline development process

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### 5.8.2 Clinical question list

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### 5.8.3 Evidence statement forms, systematic review reports and modelling reports

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The following reports are for questions that were answered by a new systematic literature review or modelling. The associated technical documentation appears at the bottom of the relevant content pages.

The questions were given alphanumeric codes when they were developed, please refer to the codes below and see the Clinical question list for more detail.

**SAD1:** *What should be the surveillance colonoscopy for patients are low risk (1-2 small <10mm tubular adenomas)?*

Evidence statement form SAD1

Systematic review report SAD1



**SAD2:** *What should be the surveillance colonoscopy for patients at high risk (size  $\geq 10$ mm, HGD, villosity and/or 3-4 adenomas)?*

Evidence statement form SAD2

Systematic review report SAD2

**SAD3:** *What is the appropriate colonoscopic surveillance after the removal of large sessile or laterally spreading adenomas?*

Evidence statement form SAD3

Systematic review report SAD3

**SAD4:** *What is the appropriate colonoscopic surveillance after the identification of sessile serrated adenomas and traditional serrated adenomas?*

Evidence statement form SAD4

Systematic review report SAD4

**SAD5:** *What should be the surveillance colonoscopy for patients with adenoma multiplicity?*

Evidence statement form SAD5

Systematic review report SAD5

**SFH1:** *Is the surveillance colonoscopy recommendation different for patients with adenomas who also have a family history of CRC?*

Evidence statement form SFH1

Systematic review report SFH1

**COL1:** *What is the role of pre or peri-operative colonoscopy in CRC patients?*

Evidence statement form COL1

Systematic review report COL1

**FUC1:** *At what time points after CRC resection should surveillance colonoscopy be performed?*

Systematic review report FUC1

**SUR1:** *What is the appropriate time to commence surveillance in IBD patients (ulcerative colitis and Crohn's patients, and effects of primary sclerosing cholangitis or family history of CRC)?*

Evidence statement form SUR1

Systematic review report SUR1

**SUR2:** *What is the most appropriate time interval for surveillance in IBD patients based on risk?*

Evidence statement form SUR2

Systematic review report SUR2

**SUR3:** *What is the recommended surveillance strategies for surveillance in IBD patients?*

Evidence statement form SUR3

Systematic review report SUR3

**MNG1:** *What should be the protocol to manage elevated dysplasia in IBD?*

Evidence statement form MNG1-4

Systematic review report MNG1

**MNG2:** *What should be the protocol to manage high grade dysplasia in IBD?*

Evidence statement form MNG1-4

Systematic review report MNG2

**MNG3:** *What should be the protocol to manage low grade dysplasia in IBD?*

Evidence statement form MNG1-4

Systematic review report MNG3

**MNG4:** *What should be the protocol to manage indefinite dysplasia in IBD?*

Evidence statement form MNG1-4

Systematic review report MNG4

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## 5.9 Working party members and contributors

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  - 2.2 Colonoscopic surveillance after polypectomy
  - 2.3 The role of surveillance colonoscopy after curative resection for colorectal cancer

- 2.4 Colonoscopic surveillance and management of dysplasia in inflammatory bowel disease
- 2.5 Anxiety in colonoscopy
- 2.6 Socio-economic factors

## 5.9.1 Surveillance Colonoscopy Guidelines Working Party members and contributors

Please see the Administrative report for information on the process and criteria for selecting members.

### 5.9.1.1 Management committee

Name	Affiliation
Dr Cameron Bell (Chair)	Gastroenterologist, Royal North Shore Hospital, Sydney
Professor Timothy Price	Chair, Management Committee and Colorectal Cancer Guidelines Revision Working Party Medical Oncologist, The Queen Elizabeth Hospital, Adelaide
Professor Sanchia Aranda	CEO, Cancer Council Australia
Professor Finlay Macrae AO	Gastroenterologist, Royal Melbourne Hospital, Melbourne
Professor James St John AO	Emeritus Consultant Gastroenterologist, The Royal Melbourne Hospital; Honorary Senior Associate, Cancer Council Victoria; Honorary Clinical Professorial Fellow, The University of Melbourne
Dr Bernie Towler	Department of Health representative; Principal Medical Advisor, Population Health Division, Department of Health, Canberra
Ms Jutta Thwaites	Head, Clinical Guidelines Network (maternity leave from November 2016 - November 2017)

Note: Please see below for relevant management committee members involved in the revision of this guidelines.

### 5.9.1.2 Working party

Relevant management committee members	
Name	Affiliation
Dr Cameron	Chair, Colonoscopy Surveillance Guidelines Revision Working Party; Deputy Chair,

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<b>Relevant management committee members</b>		
<b>Name</b>	<b>Affiliation</b>	
Bell (Chair)	Management Committee; Gastroenterologist, Royal North Shore Hospital, Sydney	
Prof Timothy (Tim) Price	Chair, Management Committee and Colorectal Cancer Guidelines Revision Working Party; Medical Oncologist, The Queen Elizabeth Hospital, Adelaide	
Prof Finlay Macrae AO	Gastroenterologist, Royal Melbourne Hospital, Melbourne	
Prof James (Jim) St John AO	Gastroenterologist, Honorary Senior Associate, Cancer Council Victoria, Melbourne	
Ms Jutta Thwaites	Head, Clinical Guidelines Network (maternity leave from November 2016 - November 2017)	
<b>Guideline section leaders</b>		
<b>Name</b>	<b>Specialty</b>	<b>Section</b>
A/Prof Gregor Brown	Gastroenterology	Advances in colonoscopy, CT colonography and other methods
Dr Karen Barclay	Colorectal surgery	Colonoscopic surveillance after polypectomy
Dr James Moore	Colorectal surgery	The role of surveillance colonoscopy after curative resection for colorectal cancer (co-lead)
Dr Tarik Sammour	Colorectal surgery	The role of surveillance colonoscopy after curative resection for colorectal cancer (co-lead)
Prof Rupert Leong	Gastroenterology	Colonoscopic surveillance and management of dysplasia in inflammatory bowel disease
Prof Afaf Girgis	Psycho-oncology	Anxiety in colonoscopy
Dr Anne Duggan	Gastroenterology	Socioeconomic factors
<b>Additional working party members</b>		
<b>Name</b>	<b>Specialty</b>	
Prof Anthony Gill	Pathology representative	
Prof Andrew Clouston	Pathology representative	
Prof Jon Emery	General practice representative	
Mr Jeff Cuff	Consumer representative	

Relevant management committee members	
Name	Affiliation
Ms Jillian Arnott	Consumer representative
Prof Karen Canfell	Director, Cancer Research Division, Cancer Council NSW (Epidemiology expert)
Prof Dianne O'Connell	Senior Epidemiologist, Manager, Cancer Research Division, Cancer Council NSW (Epidemiology expert)

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### 5.9.1.3 Cancer Council Australia project team contributions

Name	Affiliation
Laura Wuellner	Project Manager, Clinical Guidelines Network (until November 2016), Acting Head, Clinical Guidelines Network, Cancer Council Australia (from November 2016 - January 2018)
Tamsin Curtis	Project Manager, Clinical Guidelines Network (from March 2018), Cancer Council Australia
Katrina Anderson	Project Manager, Clinical Guidelines Network (from November 2016 - December 2017)
Dr Albert Chetcuti	Senior Systematic Reviewer, Systematic Literature Reviews, Clinical Guidelines Network
Victoria Freeman	Research Assistant, Systematic Literature Reviews, Clinical Guidelines Network
Ben Lee-Bates	Research Assistant, Systematic Literature Reviews, Clinical Guidelines Network

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## 5.9.2 Guideline section details

\*Denotes section lead author

### 5.9.2.1 Advances in colonoscopy, CT colonography and other methods

Name	Affiliation
A/Prof Gregor Brown*	Head of Endoscopy, The Alfred Hospital; Gastroenterologist at a private Gastroenterology practice in inner Melbourne.
Dr Joshua	Head of endoscopy, Northern Health; Gastroenterologist, Royal Melbourne Hospital and Albury

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<b>Name</b>	<b>Affiliation</b>
Butt	Wodonga Health
A/Prof David Hewett	Director Endoscopy, Mater Health, Mater Misericordiae Ltd, Brisbane; Associate Professor, School of Medicine, The University of Queensland; Gastroenterologist & Therapeutic colonoscopist, Brisbane Colonoscopy
Dr Spiro Raftopoulos	Gastroenterologist, Hollywood Private Hospital; Gastroenterologist, Peel Health Campus; Gastroenterologist, Sir Charles Gairdner Hospital
Dr Mark Appleyard	Director of Gastroenterology and Hepatology Royal Brisbane and Women's Hospital
A/Prof Rajvinder Singh	Director of Gastroenterology at the Lyell McEwin and Modbury Hospitals, South Australia; Clinical Associate Professor of Medicine, the University of Adelaide
Dr Tom Sutherland	Abdominal Radiologist, St Vincent's Hospital

## 5.9.2.2 Colonoscopic surveillance after polypectomy

<b>Name</b>	<b>Affiliation</b>
Dr Karen Barclay*	Colorectal surgeon, The Northern Hospital
Prof Barbara Leggett	Gastroenterologist, Royal Brisbane and Women's Hospital; Professor of Medicine, School of Medicine, University of Queensland; Honorary Group Leader, Queensland Institute of Medical Research Berghofer
Prof Finlay Macrae AO	Gastroenterologist, Royal Melbourne Hospital, Melbourne
Prof Michael Bourke	Professor of Medicine, University of Sydney; Director Gastrointestinal Endoscopy, Westmead Hospital
Dr Hooi Ee	Gastroenterologist, Sir Charles Gairdner Hospital, Perth

### 5.9.2.3 The role of surveillance colonoscopy after curative resection for colorectal cancer

Name	Affiliation
Dr James Moore*	Clinical Director, General Surgery; Surgical Directorate, Royal Adelaide Hospital
Dr Tarik Sammour*	Associate Professor, Discipline of Surgery, University of Adelaide; Colorectal Surgeon, Department of Surgery, Royal Adelaide Hospital
Dr Andrew Luck	Colorectal surgeon, Lyell McEwin Hospital

### 5.9.2.4 Colonoscopic surveillance and management of dysplasia in inflammatory bowel disease

Name	Affiliation
Prof Rupert Leong*	Senior Staff Specialist Gastroenterologist and Director of Endoscopy, Concord Hospital, Sydney; Clinical Professor of Medicine, University of Sydney and Macquarie University, Sydney; Conjoint Professor of Medicine, University of NSW.
Dr Crispin Corte	Gastroenterologist, Royal Prince Alfred Medical Centre, Macquarie University Clinic, Concord Hospital and Concord Medical Centre
Dr Cherry Koh	Colorectal Surgeon, Royal Prince Alfred Hospital
Dr Betty Wu	Gastroenterology Fellow, St George Hospital
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### 5.9.2.5 Anxiety in colonoscopy

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### 5.9.2.6 Socio-economic factors

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## 5.10 Conflict of interest register

### Conflict of interest register and management

Conflict of interest register

## 5.11 Glossary and abbreviations

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### 5.11.1 Abbreviations

Abbreviation	Term
AN	Advanced neoplasia (advanced adenoma or colorectal cancer)
ASP	Advanced serrated polyp
AGA	American Gastroenterological Association
ACPGBI	Association of Coloproctology of Great Britain and Ireland
BMI	Body mass index
BPPS	Boston bowel preparation scale
BSG	British Society of Gastroenterology
CRC	Colorectal cancer
CCRTGE	Conjoint Committee for the Recognition of Training in Gastrointestinal Endoscopy



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CA	Conventional adenoma
DNA	Deoxyribonucleic acid
DALM	Dysplasia associated lesion mass
EMR	Endoscopic mucosal resection
ESD	Endoscopic submucosal dissection
EPoS	European Polyp Surveillance trials
ESGE	European Society for Gastroenterology
FICE	Fujinon intelligent chromoendoscopy
GESA	Gastroenterological Society of Australia
HGD	High grade dysplasia
HRA	High risk adenoma
HDL	High-density lipoprotein
HPP/HP	Hyperplastic polyp
ID	Indefinite dysplasia
IBD	Inflammatory bowel disease
KRAS	Kirsten rat sarcoma
LSL	Laterally spreading lesion/s
LGD	Low grade dysplasia
LRA	Low risk adenoma
MP	Malignant polyp
MA	Metachronous adenoma
MAA	Metachronous advanced adenoma
MAN	Metachronous advanced neoplasia
MN	Metachronous neoplasia
MMR	Mismatch repair
NHMRC	National Health and Medical Research Council
NPS	National Polyp Study
NAA	Non-advanced adenoma
OC	Optical colonoscopy
PEG	Polyethylene glycol
PICO	Population, intervention, comparison, outcome
PCP	Primary care physicians
PSC	Primary sclerosing cholangitis

RR	Relative risk
RANZCR	Royal Australian and New Zealand College of Radiologists
SP	Serrated polyp
SES	Socioeconomic status
SIR	Standardised incidence ratio
SMR	Standardised mortality ratio
STAI-S	State Trait Anxiety Inventory
SMI	Submucosal invasion
SCENIC	Surveillance for colorectal endoscopic neoplasia detection and management in inflammatory bowel disease patients: International Consensus recommendations
SEER	Surveillance, Epidemiology and End Results
TSA	Traditional serrated adenoma
TP53	Tumour suppressor p53
UC	Ulcerative colitis
UK	United Kingdom
USMTF	US Multi-Society Task Force
USA	United States of America
WLE	White light endoscopy
WASP	Workgroup serrated polyps and Polyposis
WHO	World Health Organization

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## 5.11.2 Glossary terms

<b>Term</b>	<b>Definition</b>
Abdominoperineal resection	An operation for rectal cancer. This involves removing part of the colon, rectum and anus, and creating a permanent colostomy.
Absolute risk	The risk a subject has for developing the tested disease over a stated time period.
Adenocarcinoma	A type of cancerous tumour that forms from glandular structures in epithelial tissue.
Adenoma detection rate (ADR)	The proportion of individuals undergoing a complete screening colonoscopy who have one or more adenomas, or polyps, detected. Variously defined according to context but most often defined as the proportion of patients aged 50 and over having screening colonoscopy found to have at least one adenomatous polyp.
Adenomatous Polyposis Coli	A multifunctional tumour suppressor gene. Mutations in this gene are responsible for

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(APC)	familial adenomatous polyposis and contributes to many sporadic colorectal cancers.
Adjuvant therapy	A treatment given with or shortly after another treatment to make it more effective. This usually refers to surgery followed by chemotherapy or radiotherapy.
Advanced adenoma (AA)	An adenoma that measures 10mm or more in size. Includes adenomatous polyps greater than or equal to 10 mm in size or with a significant villous component or with high-grade dysplasia.
Anterior resection	A surgical procedure to remove cancer in the rectum with the bowel being re-joined to leave a functioning anus.
Biopsy	The removal of a small sample of tissue from the body for examination under a microscope to help diagnose a disease.
Bowel cancer	Cancer of the large bowel; also known as colorectal cancer, colon cancer or rectal cancer.
Bowel preparation	The process of cleaning out the bowel before a test, scan or operation to allow the doctor to see the bowel more clearly.
Carcinoembryonic antigen (CEA)	A protein that may be found in the blood of a person with colorectal cancer.
Chemoprophylaxis	Administration of a medication or drug to prevent disease.
Colectomy	The surgical removal of all or part of the colon. The affected areas of the colon are cut out and the two ends are joined back together. Colectomies are named for the part removed. They include: right and left hemicolectomies and transverse, sigmoid, subtotal and total colectomies.
Colon	The main part of the large bowel, which absorbs water and electrolytes from undigested food (solid waste). Its four parts are the ascending colon, transverse colon, descending colon and sigmoid colon.
Colonoscopy	An examination of the large bowel using a camera on a flexible tube, which is passed through the anus.
Colorectal	Referring to the large bowel, comprising the colon and rectum.
Confidence interval (CI)	A measure that quantifies the uncertainty in measurement. When reported as 95% CI, it is the range of values within which we can be 95% sure that the true value for the whole population lies.
Confocal laser endomicroscopy (CLE)	An endoscopy procedure that uses a specialised endoscope capable of visualising the mucosal layer of the colon at very high magnification.
Consensus-based recommendation	A recommendation formulated in the absence of quality evidence, after a systematic review of the evidence was conducted and failed to identify admissible evidence on the clinical question.
	Also known as virtual colonoscopy, a medical imaging procedure that uses low dose radiation computerised tomography (CT) scanning to obtain an interior view of the colon

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CT colonography	(the large bowel) that is otherwise only seen with a more invasive procedure such as colonoscopy where an endoscope is inserted into the rectum and passed through the entire colon.
CT scan	A computerised tomography (CT) scan, in which x-ray equipment is used to create detailed digital images, or scans, of areas inside the body.
Distant metastasis	Cancer that has spread from the original (primary) tumour to distant organs or distant lymph nodes.
Electronic chromoendoscopy (EC)	An endoscopic procedure using a specialised endoscope that provides a detailed contrast enhancement image of the mucosal surface of the colon, and includes NBI, FICE or i-SCAN.
Evidence-based recommendation	A recommendation formulated after a systematic review of the evidence, indicating supporting references.
Faecal occult blood test	A test that can detect microscopic amounts of blood in stools. The most common type of FOBT is the immunochemical FOBT (iFOBT), which directly detect haemoglobin using antibodies specific for the globin moiety of human haemoglobin.
Familial adenomatous polyposis (FAP)	An autosomal dominant inherited condition in which numerous polyps form mainly in the colon.
Familial syndromes	Genetic disorders in which inherited genetic mutations in one or more genes predispose a person to developing cancer, particularly at an early age.
First degree relative (FDR)	An individual's full siblings, parents or children.
Flexible sigmoidoscopy	A procedure to examine the inner lining of the rectum and lower portion of the colon using a flexible tube, usually a colonoscope (unlike the colonoscopy that examines the entirety of the colon). The tube is approximately 60 cm long, has a small light and a camera attached at the tip of the tube.
Full spectrum endoscopy (FUSE)	An endoscope with a viewing angle of 330°.
Functional gastrointestinal disease (FGID)	Also known as functional gastrointestinal disorders. A group of bowel disorders which are characterised by persistent and recurring gastrointestinal symptoms in the absence of demonstrable organic pathology.
General practitioner (GP)	A medical professional who treats acute and chronic illnesses and provides preventive care and health education to a wide range of patients.
Hazard ratio (HR)	A measure of how often a particular event happens in one group compared to how often it happens in another group, over time. In cancer research, hazard ratios are often used in clinical trials to measure survival at any particular moment in a group of patients who have been given a specific treatment or a placebo.
Imaging	Using scans, including nuclear medicine, to create images of the interior of a body for clinical analysis and medical intervention.

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Incidence	An epidemiological term reporting number of new cases in a population within a specified period.
Interval cancer (IC)	A cancer whose presence is diagnosed in the time between scheduled screening tests or surveillance procedures.
Laparoscopic approach	A procedure where small multiple incisions are made to perform an operation, rather than making a large open incision.
Local recurrence	The reappearance of cancer at a site that was previously treated and responded to therapy.
MAPK pathway	A chain of proteins in the cell that communicates a signal from a receptor on the surface of the cell to the DNA in the nucleus.
Metabolic syndrome	Metabolic syndrome is a collection of conditions that often occur together and increase the risk of diabetes, stroke and heart disease. The main components of metabolic syndrome include obesity, high blood pressure, high blood triglycerides, low levels of HDL cholesterol and insulin resistance.
Metastatic	Cancer that has spread from the primary site of origin (where it started) into different area(s) of the body.
mut-L homolog 1 (MLH1)	A gene commonly associated with Lynch syndrome and functions in repairing DNA mismatches.
Narrow band imaging (NBI)	A specialised type of endoscopy that uses specific blue and green wavelengths of light to enhance visualisation of the mucosal layer of the colon.
National Bowel Cancer Screening Program (NBCSP)	An Australian screening program that aims to reduce illness and death from bowel cancer through early detection or prevention of the disease.
Negative predictive value (NPV)	The probability that a subject with a negative screening test result truly does not have the condition for which they are being tested.
Odds ratio (OR)	A comparison of the odds (probability) of something happening in one group with the odds of it happening in another.
Pathology	A medical specialty that determines the cause and nature of diseases by examining and testing body tissues, for instance from laboratory examination of samples of body tissue.
Peri-operative	Measures or interventions used at or around the time of an operation to improve patient outcomes.
Polyp	A small growth protruding from a mucous membrane, such as the lining of the bowel.
Polypectomy	The removal of polyps from the bowel.
Positive predictive value (PPV)	A measure for the probability that a subject with a positive screening result truly has the disease for which they are being tested.
Practice point	A recommendation on a subject that is outside the scope of the search strategy for the systematic review, based on expert opinion and formulated by a consensus process.

Proctocolectomy	A surgical procedure to remove the colon and rectum.
Randomised controlled trial (RCT)	A study in which people are allocated at random (by chance alone) to receive one of several clinical interventions. One of these interventions is the standard of comparison or control.
Rectal endoscopic ultrasound	An imaging procedure where a probe is inserted into the rectum and high frequency sound waves (ultrasound waves) are generated to look for abnormalities in the rectum and nearby structures.
Rectum	The final section of the large bowel, ending at the anus.
Second degree relative (SDR)	Someone who shares 25% of a person's genes, such as uncles, aunts, grandparents, half-siblings
Villosity	The state of being villous, a histopathological feature of some tubular adenomas. Villous adenoma is a type of polyp found in the colon or rectum that appear as a cauliflower-like mass.

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