Cancer Care Ontario

ColonCancerCheck
Recommendations for Post-Polypectomy Surveillance

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Acronyms and Abbreviations

CAG	Canadian Association of Gastroenterology
CCC	ColonCancerCheck
CI	confidence interval
FAP	familial adenomatous polyposis
FIT	fecal immunochemical test
HRA	high risk adenoma
LRA	low risk adenoma
mm	millimeter
OAG	Ontario Association of Gastroenterology
RR	relative risk
SIR	standardized incidence ratio
SSA	sessile serrated adenoma
TSA	traditional serrated adenoma
USMSTF	U.S. Multi-Society Task Force on Colorectal Cancer

Executive Summary

Colorectal cancer is the second most common cancer and the second leading cause of cancer-related mortality in Ontario (1). Some people with a history of pre-cancerous polyps have an increased risk of developing colorectal cancer, depending on the number, size and histology of the polyps (2,3). The purpose of post-polypectomy colonoscopy surveillance is to reduce this risk by removing incident polyps. However, colonoscopies may lead to infrequent but serious harms (4), so the benefits of the procedure must be weighed against its potential harms.

ColonCancerCheck (CCC) is Ontario's province-wide organized colorectal cancer screening program, which has the goal of reducing death from colorectal cancer. When CCC was established in 2008, the program adopted the U.S. Multi-Society Task Force on Colorectal Cancer (USMSTF) 2006 post-polypectomy surveillance guidelines (5). Since then, new evidence has emerged, and as a result, CCC began a process to review and update its post-polypectomy surveillance guidelines.

To determine the best management of people with a history of polyps, CCC assembled a panel of experts in gastroenterology, pathology and colorectal surgery. Under the guidance of this expert panel, CCC conducted a literature search of English language post-polypectomy surveillance guidelines published from 2007 to 2014 using PubMed (see Appendix 1). Following the evidence review, the expert panel decided to use the same polyp classification framework as the USMSTF (2) and the Canadian Association of Gastroenterology (6), which classifies adenomas into high and low risk.

There was a lack of consensus among guidelines from other jurisdictions about the management of low risk adenomas (LRAs), which are defined as one to two tubular adenomas less than 10 millimeters in diameter without high-grade dysplasia. To address this gap, a systematic review and meta-analysis was conducted to evaluate the risk of incident high risk adenomas, colorectal cancer and of colorectal cancer-related death in people with LRAs at their initial colonoscopy following an abnormal screening result (7).

CCC's recommendations have been reviewed by national and international experts in the field and their feedback has been incorporated. The recommendations are designed using the guiding principle that the benefits of surveillance colonoscopies should outweigh the potential harms for people who undergo the procedure. Therefore, CCC no longer recommends colonoscopy surveillance for people with LRAs. Instead, these people should be screened again with the fecal immunochemical test (FIT) beginning five years after their initial colonoscopy. In addition, because the approach to surveillance needs to be adjusted over time according to the findings of each subsequent procedure, CCC now includes recommendations based on findings from both the initial and subsequent colonoscopy.

Cancer Care Ontario

Table 1. ColonCancerCheck (CCC) Recommendations for Post-Polypectomy Surveillance

Initial colonoscopy			Subsequent colonoscopy		
Findings	**Next test[1]**	**Time until next test**	**Findings**	**Next test[1]**	**Time until next test**
No polyps Hyperplastic polyp(s)[2] in rectum or sigmoid	FIT	10 years	Not applicable		
Low risk adenoma(s)[2]	FIT	5 years	Not applicable		
High risk adenoma(s)[2]	Colonoscopy	3 years	No polyps, or hyperplastic polyp(s) in rectum or sigmoid, or low risk adenoma	Colonoscopy	5 years
			High risk adenoma(s)	Colonoscopy	3 years
>10 adenomas	Clearing colonoscopy[3]	≤1 year	<3 years at endoscopist discretion[3]		
Any sessile serrated adenoma(s)[2] <10 mm without dysplasia	Colonoscopy	5 years	At endoscopist discretion[4]		
Sessile serrated adenoma(s) ≥10 mm Sessile serrated adenoma(s) with dysplasia Traditional serrated adenoma	Colonoscopy	3 years			
Large sessile polyp removed piecemeal	Colonoscopy to check polypectomy site	≤6 months			
Serrated polyposis syndrome[2]	Colonoscopy	1 year	1 – 2 years at endoscopist discretion		

Notes:

1 – In cases where the next recommended test is colonoscopy, neither FIT nor flexible sigmoidoscopy is required between surveillance intervals.

2 - See page seven for definitions.

3 - People with >10 adenomas should undergo genetic assessment for familial adenomatous polyposis syndromes. The subsequent surveillance interval will depend on the results of the genetic assessment and whether the colon is cleared of polyps. If there is no familial adenomatous polyposis syndrome and after the colon is cleared, surveillance recommendation is colonoscopy in less than three years.

4 - Sessile serrated adenomas and traditional serrated adenomas require surveillance, but there is currently insufficient evidence to make specific recommendations on surveillance intervals.

Background

ColonCancerCheck (CCC) is Ontario's province-wide organized colorectal cancer screening program, which has the goal of reducing death from colorectal cancer. Colorectal cancer is the second most common cancer and the second leading cause of cancer-related mortality in Ontario (1). Colorectal cancer screening has been shown to significantly reduce the risk of being diagnosed with colorectal cancer and dying from colorectal cancer (8).The purpose of colorectal cancer screening is to find cancer at an early stage when it is easier to treat. Screening can also sometimes help prevent cancer by finding polyps that could turn into cancer.

A history of pre-cancerous polyps may be associated with an increased risk of developing colorectal cancer, depending on the number, size and histology of the polyps (2,3). The purpose of post-polypectomy colonoscopy surveillance is to reduce this risk by removing incident polyps.

When CCC was established in 2008, the program adopted the U.S. Multi-Society Task Force on Colorectal Cancer (USMSTF) 2006 post-polypectomy surveillance guidelines (5). Because our understanding of colorectal cancer risk continues to evolve as new evidence emerges, post-polypectomy surveillance recommendations must be periodically updated to reflect the most recent evidence.

CCC's updated post-polypectomy surveillance recommendations categorize polyp findings into high risk and low risk lesions based on the future probability of colorectal cancer. Since colonoscopies involve infrequent but serious harms, including perforation, bleeding and, in rare cases, even death (4), CCC's recommendations are designed to ensure that the benefits of surveillance colonoscopies outweigh the potential harms for people undergoing the procedure. In addition, because the approach to surveillance needs to be adjusted over time according to the findings of each subsequent test, CCC now includes recommendations based on findings from both the initial and subsequent colonoscopy.

The recommendations in this document assume that the initial colonoscopy was complete and of high quality, and that all polypectomies were complete. High-quality colonoscopy and high-quality polypectomy minimize the likelihood of missed or incompletely removed lesions and therefore reduce the likelihood of a subsequent colorectal cancer (3,9).

CCC will continue to monitor emerging evidence and consider when the recommendations need further updates.

Methodology

CCC's post-polypectomy surveillance recommendations were developed under the guidance of a panel of experts in gastroenterology, pathology and colorectal surgery. CCC conducted a literature search of English language post-polypectomy surveillance guidelines published from 2007 to 2014 using PubMed (see Appendix 1).

Following the evidence review, the expert panel opted to use the same polyp classification framework as the 2012 USMSTF (2) and the 2013 Canadian Association of Gastroenterology (6) guidelines, which classify adenomas (pre-cancerous polyps) into high risk and low risk. While European guidelines (10) include an intermediate risk category, the expert panel decided to align with the high and low risk classifications most familiar to Ontario physicians.

In the literature, there was a lack of consensus in guidelines from other jurisdictions about the management of low risk adenomas (LRAs). To address this gap, a systematic review and meta-analysis was conducted to evaluate the risk of incident advanced adenomas, colorectal cancer and colorectal cancer-related death in people with LRAs at their initial colonoscopy (7).

CCC's draft recommendations were sent to national and international stakeholders for feedback and commentary. All of the feedback received and CCC's responses can be found in Appendix 4.

Recommendations

ColonCancerCheck's (CCC's) post-polypectomy surveillance recommendations are based on the size and histology of the most advanced lesions. The recommendations assume that a high-quality colonoscopy was complete to the cecum, that there was a careful examination of the colonic mucosa, and that the bowel preparation was adequate to detect polyps five millimeters in size. In the case of incomplete screening and/or surveillance-related colonoscopy (for example, due to inadequate bowel preparation), a repeat colonoscopy should be performed within 12 months, given that incomplete colonoscopies are associated with an increased risk of post-colonoscopy colorectal cancers (3).

The following definitions / understandings are used in this document:

- **Colorectal adenomas:** lesions in the colon or rectum that contain unequivocal intraepithelial neoplasia (dysplasia).
- **Low risk adenomas (LRAs):** One to two tubular adenomas less than 10 millimeters in diameter without high-grade dysplasia.
- **High risk adenomas (HRAs)** (also called advanced adenomas)**:** One or more tubular adenomas 10 millimeters or greater, three or more adenomas of any size, or adenomas with villous histology, or adenomas with high-grade dysplasia.
- **Serrated adenomas:** Either sessile serrated adenomas (SSA) (also called "sessile serrated polyps" [SSP] or "sessile serrated adenoma/polyp" [SSA/P]) or traditional serrated adenoma (TSA). Most serrated polyps will not have any dysplasia; serrated polyps with dysplasia are considered advanced. Traditional serrated adenomas are uncommon and are often protuberant and left-sided (11–13).
- **Hyperplastic polyps:** hyperplastic polyps are very common and usually occur as diminutive (less than five millimeters) nondysplastic polyps in the rectum and sigmoid colon. These polyps are not associated with an increased risk of colorectal cancer and are therefore not considered to be screen-relevant lesions.
- **Serrated polyposis syndrome:** At least five serrated polyps proximal to the sigmoid colon, two of which are greater than 10 millimeters in diameter; any number of serrated polyps occurring proximal to the sigmoid colon in someone who has a first-degree relative with serrated polyposis; or more than 20 serrated polyps of any size distributed throughout the colon (14).
- **Clearing colonoscopy**: Repeat procedure performed to ensure that all neoplasia has been removed from the colon. A clearing colonoscopy is performed earlier than a surveillance colonoscopy.

The following section summarizes CCC's recommendations for surveillance based on polyps detected at the initial colonoscopy, as well as for the subsequent colonoscopy interval, if appropriate. In cases where the next recommended test is colonoscopy, CCC recommends against the use of fecal tests or flexible sigmoidoscopy during the surveillance interval.

Initial colonoscopy findings: no polyps or hyperplastic polyps in rectum or sigmoid colon

In alignment with the U.S. Multi-Society Task Force on Colorectal Cancer (USMSTF) (2) and Canadian Association of Gastroenterology (CAG) (6) guidelines, CCC recommends that people who have an initial colonoscopy with either no polyps or one or more hyperplastic polyps in the rectum or sigmoid colon return to average risk screening **10 years** after the initial colonoscopy. As per CCC's average risk screening recommendations, screening should then be performed with the fecal immunochemical test (FIT) every two years.

Initial colonoscopy findings: low risk adenomas (LRAs)

The USMSTF (2) and CAG (6) guidelines recommend surveillance with a colonoscopy five to 10 years after an initial colonoscopy finds LRAs. However, guidelines from other jurisdictions do not recommend any colonoscopy surveillance for these people (10). To determine the best management of LRAs, CCC

conducted a systematic review of the primary literature on the risk of high risk (advanced) adenomas (HRAs), colorectal cancer and colorectal cancer-related death among people with LRAs (7).

The systematic review identified 11 observational studies that met the inclusion criteria (15–25). Importantly, the comparison groups differed in these studies with some comparing to those with normal initial colonoscopy and some comparing to the general population.

Compared to a normal baseline colonoscopy:

Eight cohort studies examined the risk of HRAs in people with LRAs compared to people with a normal initial colonoscopy (17,19–25). The pooled five-year cumulative incidence of HRA was 3.3% (95% confidence interval [CI] 1.8–0.1%) if the baseline colonoscopy was normal and 4.9% (95% CI 3.2–7.0%) if the baseline colonoscopy revealed LRAs, but this difference was not statistically significant. In contrast, if the baseline colonoscopy showed HRAs, the cumulative five year incidence of HRA was 17.1% (95% CI 12.0–23.0%) (7). In a meta-analysis of these studies, there was a small, but statistically significant, increase in the relative risk of HRAs in people with LRAs, as compared to those with a normal baseline colonoscopy (relative risk [RR] 1.55, 95% CI 1.24–1.94) (7).

Subsequent to the publication of the systematic review, the long-term follow up of a large cohort of participants from the prostate, lung, colon, and ovarian (PLCO) cancer screening trial found that the risks of colorectal cancer and colorectal cancer death in people with LRAs are comparable to those with a normal baseline colonoscopy (26). The study showed that people with nonadvanced adenomas (defined as any number of tubular polyps less than 10 millimeters without high-grade dysplasia) had a comparable risk for colorectal cancer to those with no adenoma at baseline colonoscopy (9.1 incidence rate per 10,000 person-years [95% CI 6.7–11.5] versus 7.5 [95% CI 5.8–9.7], respectively). Furthermore, the study showed that the risk of dying from colorectal cancer was not significantly different between the two groups (RR of colorectal cancer death in those with non-advanced adenomas 1.2 [95% CI 0.5–2.7]) (26).

Compared to the general population:

One cohort study (16) and one case-control study (15) compared the risk of colorectal cancer in people with LRAs to the risk of colorectal cancer in the general population (which includes those who have not had any screening). Both studies showed that people with LRAs have a significantly lower risk of colorectal cancer than the general population (standardized incidence ratio 0.68 [95% CI 0.44–0.99] at a median 7.7 years of follow up in the cohort study [16] and odds ratio 0.4 [95% CI 0.2–0.6] at 5 years in the case-control study [15]).

One large study compared the risk of colorectal cancer-related mortality in people with LRAs to the risk in the general population (18). It found that people with LRAs have a significantly lower risk of dying from colorectal cancer than the general population (standardized mortality ratio 0.75 [95% CI 0.63–0.88] at a median 7.7 years of follow up) (18).

Rationale for recommendation:

When compared to those with normal baseline colonoscopy, people with LRA have a similar risk of colorectal cancer or colorectal cancer death. When compared to the general population, people with LRAs are at lower risk of colorectal cancer and death from colorectal cancer. Therefore, the current literature does not support the practice of performing routine surveillance colonoscopy in people with LRAs, and doing so would unnecessarily expose people with LRAs to the risks and inconveniences of colonoscopy. As people with LRAs at their initial colonoscopy are at lower risk than the general population, in whom FIT is the recommended screening test in Ontario, CCC recommends that people with LRAs at their initial colonoscopy should not undergo colonoscopy surveillance. Instead, people with LRAs should return to the average risk screening strategy with FIT every two years, starting five years after the colonoscopy. The recommendation that people with LRAs should return to screening five years after the initial colonoscopy, as opposed to the 10 year recommendation for those with a normal baseline colonoscopy, is to account for the small but statistically significant increased relative risk of HRAs observed in the meta-analysis.

For further information on the evidence that informed this recommendation, see Appendix 2.

Initial colonoscopy findings: high risk adenomas (HRAs)

In alignment with the USMSTF (2) and CAG (6) guidelines, CCC recommends surveillance with colonoscopy in **three years** for people with HRAs found at their initial colonoscopy.

The results of the subsequent colonoscopy will influence the subsequent surveillance interval as follows:

- **Subsequent colonoscopy findings: normal colonoscopy (i.e., no polyps or hyperplastic polyps in the rectum or sigmoid colon) or LRAs**

  In alignment with the USMSTF (2) and CAG (6) guidelines, CCC recommends that the subsequent surveillance interval be lengthened to **five years** for people whose second colonoscopy reveals either no polyps, hyperplastic polyps in the rectum or sigmoid colon, or LRAs.

- **Subsequent colonoscopy findings: HRAs**

  In alignment with the USMSTF (2) and CAG (6) guidelines, CCC recommends that the surveillance interval be maintained at **three years** for people whose second colonoscopy reveals HRAs.

Initial colonoscopy findings: more than 10 adenomas

When developing the recommendation for people with more than 10 adenomas, the expert panel took into consideration the American College of Gastroenterology guidelines for genetic testing and management of hereditary gastrointestinal cancer syndromes (27), which acknowledge the need for a genetic assessment for familial adenomatous polyposis syndromes, as well as the importance of clearing the colon of all polyps. Therefore, CCC recommends that people with 10 or more adenomas at their initial colonoscopy undergo genetic assessment for familial adenomatous polyposis syndromes and receive a clearing colonoscopy within **one year**.

The subsequent surveillance interval depends on the results of the genetic assessment. For people with no familial adenomatous polyposis syndrome, surveillance colonoscopy is recommended within **three years** of the clearing colonoscopy. This recommendation is in alignment with the USMSTF guideline (2).

For people with a familial adenomatous polyposis syndrome, the American College of Gastroenterology guidelines for genetic testing and management of hereditary gastrointestinal cancer syndromes (27) should be followed.

Initial colonoscopy findings: sessile serrated adenomas greater than 10 millimeters without dysplasia

Sessile serrated adenomas greater than or equal to 10 millimeters should be followed as if they were HRAs. In alignment with the USMSTF (2) and CAG (6) guidelines, CCC recommends surveillance with colonoscopy at **five years** for people with one or more sessile serrated adenomas less than 10 millimeters without dysplasia found at their initial colonoscopy.

CCC acknowledges that these North American guidelines differ from the most recent European Society of Gastrointestinal Endoscopy (ESGE) guideline, which considers small (<10mm) sessile serrated adenomas to be low risk and does not recommend surveillance for such lesions (10). CCC will continue to monitor future evidence of the clinical outcomes in people with small sessile serrated adenomas without dysplasia.

Due to the lack of evidence on the management of findings from the subsequent colonoscopy, subsequent surveillance recommendations are at the endoscopist's discretion.

Initial colonoscopy findings: sessile serrated adenomas greater than or equal to 10 millimeters

In alignment with the USMSTF (2) and CAG (6) guidelines, CCC recommends surveillance with colonoscopy at **three years** for people with one or more sessile serrated adenomas equal to or greater than 10 millimeters found at their initial colonoscopy.

Due to the lack of evidence regarding appropriate management of findings from the subsequent colonoscopy, subsequent surveillance recommendations are at the endoscopist's discretion.

Initial colonoscopy findings: sessile serrated adenomas with dysplasia

The presence of any dysplasia in a sessile serrated adenoma is an indication that the lesion is advanced. Therefore, in alignment with the USMSTF (2) and CAG (6) guidelines, CCC recommends surveillance with colonoscopy at **three years** for people with one or more sessile serrated adenomas with dysplasia found at their initial colonoscopy.

Due to the lack of evidence regarding appropriate management of findings from the subsequent colonoscopy, subsequent surveillance recommendations are at the endoscopist's discretion.

Initial colonoscopy findings: traditional serrated adenomas

In alignment with the USMSTF (2) and CAG (6) guidelines, CCC recommends surveillance with colonoscopy at **three years** for people with one or more traditional serrated adenomas found at their initial colonoscopy.

Due to the lack of evidence regarding appropriate management of findings from the subsequent colonoscopy, subsequent surveillance recommendations are at the endoscopist's discretion.

Initial colonoscopy findings: any large sessile polyp removed piecemeal

In alignment with the USMSTF (2) and CAG (6) guidelines, CCC recommends a colonoscopy to check the polypectomy site within **six months** for people with one or more large sessile polyps removed piecemeal during their initial colonoscopy.

To provide more detailed guidance, the following principles were developed by the expert panel:

- There is no universally accepted size criterion for large sessile polyps.
- Location (proximal to the sigmoid colon) is a risk factor associated with colorectal cancer that should be considered in addition to size.
- All polypectomies should be complete. The endoscopist should carefully examine the polypectomy site to ensure that all neoplastic tissue has been removed. Several techniques, such as the submucosal injection of saline and dyes (e.g., methylene blue) to clearly delineate the edges of the polyp and the application of soft coagulation at the edges of the polypectomy site, are associated with safer and more complete polypectomies (28).
- Submucosal ink should be injected two to three centimeters from the site of large, sessile polypectomies for future localization.
- Large or complex polyps that the endoscopist considers too challenging to remove should not be referred directly to surgery. All such cases should be reviewed by colleagues with expertise in therapeutic endoscopy (e.g., polyp adjudication committee). This review will serve to ensure that only polyps that are truly not resectable endoscopically are managed surgically, as surgical management of polyps has been shown to lead to a higher risk of mortality (29).

Due to the lack of evidence regarding appropriate management of findings from the subsequent colonoscopy, subsequent surveillance recommendations are at the endoscopist's discretion.

Initial colonoscopy findings: serrated polyposis syndrome

In alignment with the USMSTF (2) and CAG (6) guidelines, CCC recommends surveillance with colonoscopy at **one year** for people with serrated polyposis syndrome found at their initial colonoscopy.

Subsequent surveillance should be every **one to two years** based on the endoscopist's discretion.

Conclusion

Compared to the 2006 U.S. Multi-Society Task Force on Colorectal Cancer (USMSTF) post-polypectomy surveillance recommendations (5) adopted by ColonCancerCheck (CCC) in 2008, CCC's updated recommendations include guidance based on findings made at both the initial and subsequent colonoscopy.

CCC no longer recommends colonoscopy surveillance for people with low risk adenomas (LRAs). This recommendation is a departure from the 2012 USMSTF (2) and 2013 Canadian Association of Gastroenterology (6) guidelines, both of which recommend that those with a personal history of colorectal adenomas undergo colonoscopy surveillance. However, a systematic review and meta-analysis of the literature from 2006 to 2015 on the risks of colorectal neoplasia in people with LRAs demonstrated that these people are at a lower risk of colorectal cancer and colorectal cancer mortality than the general population, for whom FIT is recommended.

Moreover, the recently published long-term follow up from the PLCO study revealed that the risk of colorectal cancer and colorectal cancer mortality in people with LRAs is comparable to that of people with no adenomas at baseline colonoscopy (26). Because of this new evidence that people with LRA have a risk of colorectal cancer and colorectal cancer-related death that is similar to those who had no adenomas at their initial colonoscopy, it is logical that they be screened with FIT. This recommendation aligns those made by the ESGE in 2013 (10). However, due to the small but significant increased risk for HRA among people with LRA, CCC recommends that screening be resumed five years after the initial colonoscopy, unlike the ESGE which recommends 10 years (10). When screening is resumed, CCC's average risk screening recommendations should be followed, which recommend screening with the fecal immunochemical test (FIT) every two years until age 74.

CCC's post-polypectomy surveillance recommendations provide evidence-based guidance according to the size and histology of the most advanced detected lesion. These recommendations will help endoscopists and primary care providers in Ontario deliver high-quality care that maximizes the benefits of surveillance, while reducing the potential harms caused by unnecessary exposure to colonoscopy.

Appendix 1: List of Guidelines Reviewed

Guideline Source	Title	Year
Alberta Colorectal Cancer Screening Program	Post Polypectomy Surveillance Guidelines (30)	2013
British Society of Gastroenterology and Association of Coloproctology for Great Britain and Ireland	Guidelines for colorectal cancer screening and surveillance in moderate and high risk groups (31)	2010
Canadian Association of Gastroenterology	Colorectal cancer surveillance after index colonoscopy: guidance from the Canadian Association of Gastroenterology (6)	2013
Cancer Council Australia	Clinical Practice Guidelines for Surveillance Colonoscopy - in adenoma follow-up; following curative resection of colorectal cancer; and for cancer surveillance in irritable bowel disease (32)	2011
ColonCheck, CancerCare Manitoba	Screening, Surveillance and Follow up Recommendations (33)	2011
European Commission	European guidelines for quality assurance in colorectal cancer screening and diagnosis (34)	2010
European Society of Gastrointestinal Endoscopy	Post-polypectomy colonoscopy surveillance: European Society of Gastrointestinal Endoscopy (ESGE) Guideline (10)	2013
Expert Panel Convened by the National Institutes of Health (Rex et al)	Serrated lesions of the colorectum: review and recommendations from an expert panel (35)	2012
Guidelines and Protocols Advisory Committee (British Colombia)	Follow-up of Colorectal Polyps or Cancer (36)	2013
New Zealand Guidelines Group	Guidance on Surveillance for People at Increased Risk of Colorectal Cancer (37)	2011
National Institute for Health and Clinical Excellence (NICE)	Colonoscopic Surveillance for Prevention of Colorectal Cancer in People with Ulcerative Colitis, Crohn's Disease or Adenomas (38)	2011
Mayo Clinic	Recommended Intervals Between Screening and Surveillance Colonoscopies (39)	2013
U.S. Multi-Society Task Force on Colorectal Cancer	Colonoscopy Surveillance after Colorectal Cancer Resection: Recommendations of the U.S. Multi-Society Task Force on Colorectal Cancer (2)	2012

Appendix 2: Low Risk Adenoma Evidence Snapshot

ColonCancerCheck's (CCC) recommendation that people with low risk adenomas (LRA) no longer receive colonoscopy surveillance but instead return to screening with the fecal immunochemical test (FIT) beginning five years after the initial colonoscopy was informed by a growing body of evidence. The following section presents a snapshot of key evidence that informed CCC's recommendations for people with LRAs, as well as two large studies that were published after CCC conducted a systematic review and meta-analysis.[1]

Study 1:

Risk of advanced adenoma, colorectal cancer and colorectal cancer mortality in people with low risk adenomas at baseline colonoscopy: A systematic review and meta-analysis

By: Dubé C, Yakubu M, McCurdy BR, Lischka A, Kone A, Walker MJ, et al.
Pulished in: The American Journal of Gastroenterology. 2017;112(12):1790–801.

The objective of this systematic review and meta-analysis was to determine the risks of advanced adenomas, colorectal cancer and colorectal cancer-related mortality among people with LRAs and non-advanced adenomas (defined as any number of tubular adenomas less than 10 millimeters with no high-grade dysplasia) at baseline (initial) colonoscopy. PubMed and Embase were searched for English-language, peer-reviewed studies published between January 2006 and July 2015 that met the following criteria:

- Population: Adults at average risk for colorectal cancer with LRAs or non-advanced adenomas at baseline colonoscopy
- Comparator: Adults with normal baseline colonoscopy or the general population
- Outcomes: Advanced adenomas, colorectal cancer incidence, colorectal cancer mortality
- Follow-up: Greater than or equal to three years

The quality of each study was rated using the Newcastle-Ottawa Scale (40). The quality and strength of the evidence overall was assessed using the GRADE framework (41). Eleven observational studies were included in the analysis. The key findings are described below.

Risk of High Risk Adenomas (Advanced Adenomas) in People with LRAs (8 studies, n=10,139)

A meta-analysis showed a small but statistically significant increase in the relative risk of advanced adenomas (AA; interchangeably called high-risk adenomas) in people with LRAs compared to those with a normal baseline colonoscopy (RR 1.55 [95% CI: 1.24–1.94]; P=0.0001; I^2=0%). However, the cumulative incidence of AA remains comparable to those with a normal baseline colonoscopy. By contrast, the cumulative incidence of AA in people with AA at the baseline colonoscopy was about three times greater, as demonstrated in Table 2.

Baseline findings	5-year incidence advanced adenoma (95% confidence interval)
Normal colonoscopy	3.3% (1.8–5.1%)
LRA	4.9% (3.2–7.0%)
AA	17.1% (12.0–23.0%)

Table 2. Cumulative Incidence of AA based on baseline colonoscopy findings (7)

Risk of Colorectal Cancer in People with LRAs (3 studies, n=11,831)

Compared to the general population, people with LRAs had a lower risk of colorectal cancer (standardized incidence ratio [SIR]: 0.68 [95% CI: 0.44–0.99; median 7.7 years follow-up] and odds ratio 0.4 [95% CI: 0.2–0.6]; 3–5 years follow-up).

[1] The following acronyms are used when presenting the evidence:
n: Number of participants; **P**: P-value; **CI**: Confidence interval; **RR**: Relative risk; **I^2**: I-square

Risk of Colorectal Cancer Mortality in People with LRAs (1 study, n=40,826)

One large cohort study from Norway reported colorectal cancer mortality among people who had colorectal adenomas removed between 1993 and 2007 without subsequent colonoscopy surveillance. Compared with the general population, people with LRAs had a 25% lower rate of colorectal cancer mortality (standardized mortality ratio 0.75 [95% CI: 0.63–0.88]; median 7.7 years follow-up).

Study 2:

Adenoma surveillance and colorectal cancer incidence: a retrospective, multicentre, cohort study

By: Atkin W, Wooldrage K, Brenner A, Martin J, Shah U, Perera S, et al.
Published in: The Lancet Oncology. 2017;18(6):823–34.a

This multicentre retrospective study followed 11,944 patients who had been diagnosed with intermediate risk adenomas following an initial colonoscopy and polypectomy. The authors define intermediate risk adenomas as one or two large (greater than or equal to 10 millimeters) adenomas, or three to four small adenomas (which would be considered high risk adenomas under the US Multi-Society Task Force on Colorectal Cancer (2) and the Canadian Association of Gastroenterology's (6) classification system). The patients were followed for a median 7.9 years.

Analysis revealed that there were sub-groups of patients with intermediate risk adenomas. One sub-group had, as expected, an increased risk of colorectal cancer compared to the general population (which includes those who have not had any screening) and this future risk was reduced through one or two surveillance colonoscopies. However, authors also found that about a third of people with intermediate risk adenomas had a lower incidence of colorectal cancer compared to the general population (SIR 0.51 [95% CI 0.29-0.84]). This lower risk of colorectal cancer was associated with polyps either localised distal to the descending colon, less than two centimeters in size, without high-grade dysplasia and in the context of good quality bowel preparation.

These findings suggest that, even within a group of people that have higher risk lesions than LRA, some may have a lower risk of colorectal cancer than the general population. This highlights the need to concentrate post-polypectomy colonoscopy surveillance efforts on those who are truly at increased risk of colorectal cancer compared to the general population.

Study 3:

Association of colonoscopy adenoma findings with long-term colorectal cancer incidence

By: Click B, Pinsky PF, Hickey T, Doroudi M, Schoen RE.
Published in: JAMA. 2018;319(19):2021–31.

These authors prospectively followed the 15,935 participants in the Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) randomized controlled trial of flexible sigmoidoscopy who underwent colonoscopy following their first positive flexible sigmoidoscopy result. Participants were followed for over 15 years for colorectal cancer incidence and colorectal cancer mortality. There was no significant difference in colorectal cancer risk between people whose colonoscopy revealed nonadvanced adenomas (defined as any number of tubular polyps <10 millimeters without high-grade dysplasia) versus no adenomas (colorectal cancer incidence rates per 10,000 person-years 9.1 [95% CI 6.7-11.5] versus 7.5 [95% CI 5.8-9.7], respectively). Similarly, the risk of dying from colorectal cancer was not significantly different between the two groups (RR 1.2 [95% CI 0.5-2.7]). By contrast, those with advanced adenomas at the initial colonoscopy had a significantly increased risk of colorectal cancer (incidence rate of 20.0 per 10,000 person years [95% CI 15.3-24.7]) and of dying from colorectal cancer (RR 2.6 [95% CI 1.2-5.7]).

This study adds to the evidence supporting CCC's surveillance recommendations for people with LRA.

Appendix 3: Reporting Considerations

To inform surveillance recommendations, the colonoscopy report should include the following elements:

- Number of polyps
- Location of each polyp by colonic segment (i.e., cecum, ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon, sigmoid colon, rectum)
- Polyp size and morphology
    - Maximum diameter in millimeters, particularly if less than 10 millimeters (small) or 10 millimeters or greater. For simplification, polyps five millimeters or less may be referred to as diminutive
    - Morphology and mucosal pattern: ideally using the Paris Classification (42) and NBI International Colorectal Endoscopic (NICE) Classifications, (43) respectively
- Modalities used for excision
- Completeness of excision as judged by the endoscopist
- Whether all removed polyps were retrieved

Additionally, all excised polyps should be retrieved and submitted to pathology.

In cases where the endoscopist's recommendation for surveillance differs from the CCC's post-polypectomy surveillance recommendations, a justification for this deviation (e.g., inadequate bowel preparation) should also be stated.

For details on specimen submission refer to the Pathology Quality Management Program Standards (44).

Appendix 4: Comments and responses to reviewer feedback

Cancer Care Ontario greatly values the input provided by each reviewer. The following table summarizes the feedback received from the reviewers and Cancer Care Ontario's responses. With the reviewers' permission, comments have been lightly edited for length and clarity.

Jurisdiction	Reviewer	Comment	Response
Italy	Dr. Cesare Hassan Member Society Council, European Society of Gastrointestinal Endoscopy (ESGE) Gastroenterologist, Nuovo Regina Margherita Hospital	Fully agree with return to the fecal immunochemical test (FIT) for low risk adenomas (LRAs).	
		I would consider justifying why you have not applied the Atkin et al discrimination between intermediate and high risk adenomas (HRAs).	In addition to low and high risk classification, European guidelines also have an intermediate risk category. ColonCancerCheck's (CCC) recommendations include the polyps described by Atkin et al. as intermediate risk (3) in the definition of high risk adenomas. The expert panel decided to use the simple dichotomy of low and high risk adenoma to align with the classification system most familiar to Ontario physicians. This has been clarified in the document.
		I would also include early T1 surveillance after endoscopic resection.	This was outside of the scope of the review.
Netherlands	Dr. Ernst Kuipers Chairman, Erasmus MC European Lead in Colorectal Cancer Screening, World	The statement, "people with a history of pre-cancerous polyps have an increased risk of developing colorectal cancer," seems far too broad. The Atkin et al. study showed that people who had undergone a high-quality colonoscopy and had no proximal or advanced polyps had a lower colorectal cancer risk than the general population (SIR 0.51, 95% CI 0.29-0.84).	This has been clarified it in the document. Multiple recent publications demonstrate that people with LRAs (18,26) and some people with intermediate risk (3) are at lower risk for colorectal cancer and colorectal cancer death than the general population.

	Endoscopy Organization Member of the Program Committee, National Screening Program for Colon Cancer Member, Health Council of the Netherlands	If your program uses fixed ages for FIT screening (for example, every two years beginning at age 50), then adopting a five year interval for people with LRAs to return to FIT would cause them to screen with FIT at uneven years compared to the general population.	CCC does not currently have fixed year screening intervals, as screening is initiated by the primary care provider.
		With respect to the recommendation to return to screening with FIT 10 years after the baseline colonoscopy for those who had no polyps or hyperplastic polyps in rectum or sigmoid: the maximal preventive effect of FIT has to build up with repeated screens. As such, one may argue that it is a suboptimal approach to wait the final end of the colonoscopy surveillance interval before starting with FIT. If you want to have a smoother transition with less intermediate risk increase, one may argue that for instance restarting with FIT might be done at 8 years, and then from there every two years.	This will be considered in the future.
		With respect the recommendations for subsequent colonoscopy “at endoscopist discretion”: I realize that it is difficult to give any evidence-based recommendations for surveillance (for example, somebody who had a non-dysplastic serrated polyp smaller than 10 millimeters), but to leave it completely to the endoscopist discretion without further framework might lead to unnecessary uncertainty and overuse of colonoscopy.	There is growing evidence to suggest that small sessile serrated adenomas without dysplasia may be similar to LRA with respect to the risk of colorectal cancer and colorectal cancer death. At the time of this review, there was insufficient evidence about the risks associated with sessile serrated adenomas, and so the expert panel chose to remain aligned with USMSTF (2) and CAG (6) guidelines. The expert panel recognizes that the recommendation leaving it to endoscopist

			discretion may lead to an overuse of colonoscopy. However, CCC will continue to monitor future evidence of the clinical outcomes in people with small sessile serrated adenomas without dysplasia in order to determine whether the present recommendations should be revised.
United Kingdom	Dr. Matt Rutter Chair, European Society of Gastrointestinal Endoscopy quality improvement committee Clinical Director, Tees Bowel Cancer Screening Centre Chair, National Bowel Cancer Screening Programme Evaluation Group	The recommendations look very sensible. The UK is also moving in the same direction and we are currently updating our guidelines.	
		I think your recommendation for people with any non-advanced serrated polyp to return to colonoscopy in five years is out of kilter with your recommendation that people with LRAs should return to FIT in five years.	There is growing evidence to suggest that small sessile serrated adenomas without dysplasia may be similar to LRA with respect to the risk of colorectal cancer and colorectal cancer death. At the time of this review, there was insufficient evidence about the risks associated with sessile serrated adenomas, and so the recommendations remain aligned with USMSTF (2) and CAG (6) guidelines. CCC will continue to monitor future evidence of the clinical outcomes in people with small sessile serrated adenomas without dysplasia in order to determine whether the present recommendations should be revised.
		I suggest clarifying whether your recommendation for people with large sessile polyps removed piecemeal to return to colonoscopy within six months refers to a colonoscopy site check.	The document has been clarified to specify that the follow-up is a colonoscopy to check the polypectomy site within six months for large sessile polyps removed piecemeal.
United States	Dr. Douglas Robertson Chief, Gastroenterology	Generally speaking, I don't have any major concerns. The approach here seems reasonable.	
		The recommendations on serrated lesions is difficult because there is not as much data in	At the time of this review, there was insufficient evidence about the risks associated with

	White River Junction VA Medical Center Professor, Geisel School of Medicine at Dartmouth & The Dartmouth Institute	that area. But certainly, the approach is consistent with other groups and reasonable based up one what we know.	sessile serrated adenomas, and so the recommendations remain aligned with USMSTF (2) and CAG (6) guidelines. CCC will continue to monitor future evidence of the clinical outcomes in people with sessile serrated adenomas in order to determine whether the present recommendations should be revised.
		Currently, if you have two diminutive tubular adenomas, the recommendation is to return to FIT in five years. However, if you add one additional diminutive tubular adenoma, the recommendation becomes much more aggressive (colonoscopy in three years). This is problematic for the following reasons: One tiny adenoma should not change guidance so substantially. Patient preparation is variable, and there could be missed small adenomas that would cause the person to move into the HRA recommendations. There is little data in this area. Some papers distinguish between one to two small adenomas and three to four small adenomas or between having diminutive polyps alone and diminutive polyps and small polyps. Your recommendation that people with LRAs return to FIT in five years seems reasonable because this is a more intensive approach than the average risk population.	The difference to which the reviewer refers relates to the distinction between LRAs, which is defined as one to two small adenomas, versus nonadvanced adenomas, which is not defined by the number of small adenomas. The systematic review did not find a difference in risk between LRAs and nonadvanced adenomas (7). Click et al. demonstrates that the number of small adenomas is not a strong predictor of advanced neoplasia (26). However, the evidence on the risk of multiple adenomas remains mixed. Recently, Kim et al. found that three or more non-advanced diminutive adenomas had a borderline increased risk of metachronous advanced neoplasia compared with patients with low risk adenomas (45). When developing our recommendations, the expert panel erred on the conservative side in recommending that three of more adenomas of any size be considered high risk. Additionally, the expert panel identified that it was important to limit the classification of adenomas into low and high risk, rather than

			introducing the intermediate risk category which is less familiar in the Canadian context. CCC will continue to monitor future evidence in order to determine whether the present recommendations should be revised.
United States	Dr. Samir Gupta Lead reviser USMSTF guidelines on follow up after normal colonoscopy and polypectomy[1] Chief, GI Section, San Diego Veterans Affairs Healthcare System Associate Professor of Clinical Medicine Division of Gastroenterology, Moores Cancer Center University of California San Diego 1 – Reviewer wishes to note that his comments represent his personal view and not those of the US Multi-Society Task Force.	I agree that recent literature supports that individuals with one to two polyps less than 10 millimetres are a low risk group, with similar rates of advanced neoplasia and incident colorectal cancer on follow up as individuals with normal colonoscopy. Further, I agree that recent literature has strengthened evidence that individuals with adenoma one centimeter or larger, or containing villous/tubulovillous histology or high-grade dysplasia are at increased risk for advanced neoplasia and incident cancer on follow up, and warrant close surveillance.	
	Dr. Robert Schoen	Overall, I agree with the approach.	
		You may want to consider extending the timeframe for people with more than 10	This recommendation was extended to twelve months to enhance the feasibility of

	Professor of Medicine & Epidemiology. Chief, Division of Gastroenterology, Hepatology and Nutrition, University of Pittsburgh	adenomas to receive a colonoscopy to 6 to 12 months.	implementing the recommendation and to align with the CAG recommendations (6).
		I am surprised that the recommendations only mention genetic testing for FAP. This recommendation requires further clarification: does everyone with more than 10 polyps need FAP testing? At what age should testing cease? What about MUTYH-associated polyposis?	This was clarified in the document. There are multiple familial adenomatous polyposis syndromes. CCC's recommendations for genetic testing align with the ACG clinical guidelines (27). A review of this evidence was out of scope for this initiative.
		The recommendations state that CCC recommends no fecal tests or flexible sigmoidoscopy during the surveillance interval. However, FIT is recommended for those with normal colonoscopy and LRAs. I would clarify this.	This has been clarified in the document.
		In the Loberg et al. paper, the lower risk of people with LRAs compared to the general population is because the general population includes people who did not have colonoscopy. I think you need to make this clearer. Whether it is the removal of the LRA or the identification of a low risk person, or possibly both, the point remains that these people do not need surveillance.	The general population is indeed very heterogeneous, as it includes screened and unscreened individuals. This has been clarified in the document. The general population is most comparable to the "average risk population."
		The Paris classification is not in general use beyond dedicated endoscopists. Sessile and pedunculated polyps are readily understood but likely not pit patterns and the various types.	There are a number of initiatives occurring in Ontario to raise awareness and build endoscopist capacity for optical diagnosis. A reference to the NBI International Colorectal Endoscopic (NICE) Classifications (43) as well as the Paris Classification (42) has been added to provide additional information to healthcare providers.
		I am surprised by the inclusion of more than three non-advanced adenomas as HRA. It would seem that they might merit their own category. Perhaps the recommendation for	In developing the recommendations, the expert panel adopted the low and high risk adenomas classification systems of the

		these people would be similar to sessile serrated polyps (repeat colonoscopy in five years). The Click et al. study did not identify significant long term risk of colorectal cancer with more than three non-advanced adenomas but the numbers were small and the confidence interval was wide. However, considering them HRA might be overkill.	USMSTF and CAG, which are most familiar to clinicians in Canada. There is a distinction between LRAs, which is defined as one to two small adenomas versus nonadvanced adenomas, which is not defined by the number of small adenomas. The systematic review did not find a difference in risk between LRAs and nonadvanced adenomas (7). Click et. al demonstrates that the number of small adenomas is not a strong predictor of advanced neoplasia (26), however these data are limited, as noted by the reviewer. The evidence on the risk of multiple adenomas remains mixed. Recently, Kim et al. found that three or more non-advanced diminutive adenomas had a borderline increased risk of metachronous advanced neoplasia compared with patients with low risk adenomas (45). When developing our recommendations, the expert panel erred on the conservative side in recommending that three of more adenomas of any size be considered high risk. CCC will continue to monitor future evidence in order to determine whether the present recommendations should be revised.
		For the recommendation for large sessile polyps removed piecemeal, I would relax the recommendation to a 6–12 month follow up. It is unusual to see a cancer within one year.	The phrasing of the recommendation has been updated to clarify that the next test is a colonoscopy to check the polypectomy site within six months. This timeframe was included in the recommendation to ensure the

			completeness of the polypectomy, which should be apparent within six months.
		The document should cite specific studies analyzed by the meta-analysis, not the meta-analysis as a whole.	This has been updated in the document.
		Traditional serrated adenomas are rare but often sessile. You should cite literature to support your definition.	Additional references have been added to the definition.
		Many consider non-advanced sessile serrated adenomas an LRA. In your recommendations, a three millimeter sessile serrated polyps in getting screened by colonoscopy, while people with LRA will return to FIT. I understand that there is a lack of data, but I suggest clarifying this in the text so it is clear that the recommendation is due to the uncertainty, not because sessile serrated polyps are a higher risk lesion than LRA.	There is growing evidence to suggest that small sessile serrated adenomas without dysplasia may be similar to LRA with respect to the risk of colorectal cancer and colorectal cancer death. At the time of this review, there was insufficient evidence about the risks associated with sessile serrated adenomas, and so the expert panel chose to remain aligned with USMSTF (2) and CAG (6) guidelines. Additional information has been added to clarify the rationale for the recommendation. CCC will continue to monitor future evidence of the clinical outcomes in people with sessile serrated adenomas in order to determine whether the present recommendations should be revised.
		I suggest that you add that sessile serrated polyps greater than 10 millimeters are being followed as if they are HRA.	This has been added to the document.
Canada	Dr. Frances Tse Chair, Practice Affairs, Canadian	**1. The systematic review and meta-analysis (Dube et al. AJG 2017) in fact showed a statistically significant and clinically relevant increased risk of**	The reviewers primarily object to CCC's post-polypectomy recommendations because of issues relating to the quality of the literature. The reviewers focus on studies comparing subjects with LRA to those with normal

	Association of Gastroenterology Dr. Gregoris Leontiadis Chair, Clinical Affairs, Canadian Association of Gastroenterology	**advanced adenoma (AA) in people with LRAs.** According to Dube et al: "*A meta-analysis of eight cohort studies (n =10,139, 3 to 10 years' follow-up) showed a small but statistically significant increase in the incidence of AA in individuals with LRAs compared with those with a normal baseline colonoscopy (RR 1.55; 95%CI 1.24–1.94); P =0.0001; I^2 = 0%). The pooled 5-year cumulative incidence of AA was 3.28% (95%CI 1.85–5.10%), 4.9% (95%CI 3.18–6.97%), and 17.13% (95%CI 11.97–23.0%) for the no adenoma, LRA, and AA baseline groups, respectively."* The first analysis (incidence of AA), which pooled **within-study** comparisons, showed a statistically significant result. **Arguably, a 55% increase in the incidence of AA in individuals with LRAs cannot be described as "small" and "not clinically relevant".** The second analysis (pooled five-year cumulative incidence of AA) did not show a difference, and therefore appeared to contradict the results of the first analysis. However, the second analysis is much weaker and much more likely to be confounded, because it is a **between-study** comparison. It is a comparison of two "proportion analyses": the incidences of AA for the no-adenoma group from each study are pooled in one analysis, while the incidences of AA for the LRA group from each study are pooled in a separate analysis, and the two pooled results are then compared to each other; i.e., the within-study	baseline colonoscopy and they discuss the potential sources of bias in the literature. As in most areas of medicine, the quality of the literature is imperfect. The strength of the evidence on the impact of surveillance colonoscopy in people with LRA will likely improve in time, particularly once studies such as the European Polyp Surveillance (EPoS) trial have been completed and published. Nevertheless, there has been a growing body of evidence on the long-term outcomes of people post-polypectomy, with several new studies published since the 2013 CAG surveillance guidelines. All long-term post-polypectomy observational studies reveal that the risk of colorectal cancer and colorectal cancer death in people with LRA is lower than that of the general population (15,16,18,26). This lower risk is not attributable to surveillance. Loberg et al demonstrate that in a large Swedish cohort who did not have access to any surveillance colonoscopy, colorectal cancer mortality in people with LRA was significantly lower than that of the general population (18), which is most comparable to the average-risk population. The evidence shows that the risk of colorectal cancer in people with LRA is lower than that for the average risk population, for whom fecal testing is recommended by CCC and the Canadian Task Force on Preventive Health Care (46). Recommending that people with LRAs, who are at lower risk than the average

		comparisons are ignored). For this reason, if the two approaches produced contradicting results, the first analysis (within-study comparison, eight cohort studies) should trump the second analysis (proportion analysis). **2. Risks of AA, colorectal cancer (CRC) and CRC-related death were probably underestimated in people with LRAs.** It is important to note that the overall certainty of evidence, assessed using GRADE, was judged to be low to very low for the outcomes assessed in the above systematic review.[2] Due to the non-randomized nature of the included studies, important biases may have existed. First, the surveillance intervals in many of these studies (particularly for those with LRAs or AA) were left to the physician's discretion. As a result, individuals with adenomas (LRAs or AA) might have received surveillance more frequently than those with normal colonoscopy. Indeed, in one study, 53% of patients with LRAs underwent first surveillance colonoscopy within three years (earlier than the currently recommended five to 10 year surveillance interval).[3] It is	risk population, receive periodic colonoscopies is therefore inconsistent with screening policies and would result in undue exposure of these individuals to the risks and inconveniences of colonoscopy. The risk of colorectal cancer is never zero, and in any population, over the long-term, there will be individuals that develop colorectal cancer and die of the disease. The goal of CCC's post-polypectomy surveillance recommendations is to balance the risks of colorectal cancer and colorectal cancer death with the risks of exposure to colonoscopy to ensure that colonoscopy is undertaken in those most likely to benefit from it.

[2] Dube C, Yakubu M, McCurdy BR, et al. Risk of Advanced Adenoma, Colorectal Cancer, and Colorectal Cancer Mortality in People With Low-Risk Adenomas at Baseline Colonoscopy: A Systematic Review and Meta-Analysis. Am J Gastroenterol 2017;112:1790-1801.

[3] Chung SJ, Kim YS, Yang SY, et al. Five-year risk for advanced colorectal neoplasia after initial colonoscopy according to the baseline risk stratification: a prospective study in 2452 asymptomatic Koreans. Gut 2011;60:1537-43.

		conceivable that shorter surveillance intervals with identification and removal of small adenomas may have reduced the risks of AA, CRC and CRC-related death during the subsequent follow-up in individuals with LRAs compared to those with normal colonoscopy or the general population. Second, self-selection of patients into screening programs in many of the included studies, particularly among those who returned for surveillance exams, could have generated “healthy-adherer effect” (adherence bias) with better outcomes than expected in the general population. **Therefore, the apparent finding of “lower than average risk” in individuals with a history of LRAs is almost certainly erroneous, due to the effectiveness of earlier and more frequent surveillance colonoscopies as well as the confounding effects of “adherence bias”.** Third, follow-up of most included studies (especially the larger studies that contribute most to the effect estimates) was short (less than or equal to five years) with significant loss to follow-up (77% loss to follow-up in the largest observational study). The included studies should therefore be considered at high risk of bias. **3. Serious imprecision in the effect estimates of CRC and CRC-related death in people with LRAs.**	

		Due to low event rates, there was serious imprecision in the effect estimates for CRC and CRC-related death with very wide confidence intervals. In one cohort study, the results could be consistent with either a 17% reduced risk or up to 400% (or four-fold) increased risk of CRC in people with LRAs compared to those with normal baseline colonoscopy (RR 1.92, 95% CI 0.83-4.42).[4] In the prostate, lung, colon, and ovarian (PLCO) cancer screening trial, it was concluded that people with LRAs had the same risk for CRC and CRC-related death than those with no adenomas at the initial colonoscopy.[5] However, the confidence intervals for the effect estimates were also very wide, and the results could be consistent with either a 20% reduced risk or up to 70% increased risk of CRC (RR 1.2, 95% CI 0.8-1.7); and a 50% reduced risk or up to 300% (or three-fold) increased risk of CRC-related death (RR 1.2, 95% CI 0.5-2.7) in individuals with LRAs compared with no adenoma.[6] It is very possible that this lack of difference may be due to type II error. As such, **absence of a statistically significant difference should not be interpreted as evidence of absence of difference. Arguably, a possible 70% increased risk of CRC and a 300% increased risk of**	

[4] Lieberman DA, Weiss DG, Harford WV, et al. Five-year colon surveillance after screening colonoscopy. Gastroenterology 2007;133:1077-85.
[5] Click B, Pinsky PF, Hickey T, et al. Association of Colonoscopy Adenoma Findings With Long-term Colorectal Cancer Incidence. JAMA 2018;319:2021-2031.
[6] Katsoula A, Paschos P, Haidich AB, et al. Diagnostic Accuracy of Fecal Immunochemical Test in Patients at Increased Risk for Colorectal Cancer: A Meta-analysis. JAMA Intern Med 2017;177:1110-1118.

		CRC-related death in people with LRAs compared with no adenoma are not clinically irrelevant. **4. Uncertain benefits/harms of FIT vs. colonoscopy surveillance for people with LRAs.** CCC's recommendation to use FIT instead of colonoscopy at five years after the initial colonoscopy for people with LRAs has not been compared to surveillance colonoscopy at five years or other time intervals. Although FIT has been shown to be highly sensitive (86%; 95% CI 31-99%) and specific (91%; 95% CI 89-93%) for detection of colorectal cancer (vs. colonoscopy as reference standard); the sensitivity for detection of advanced neoplasia (composite outcome of either colorectal cancer or advanced adenomas) was disappointingly low (46%; 95% CI 37-56%).[7] CCC stated that "since colonoscopies involve infrequent but serious risks, including perforation, bleeding, and in rare cases, even death, CCC's recommendations are designed to ensure that the benefits of surveillance colonoscopies outweigh the potential harms for people undergoing the procedure". However, this document does not provide any details on the incidence of harm from colonoscopy or missed AA or CRC from false negative FIT so the recommendations do not appear to be based on consideration	

		of both benefits and harms of both strategies. In summary, we have serious concerns about the interpretation of the evidence with respect to the risks of AA, CRC, and CRC-related death in people with LRAs at baseline colonoscopy. The very low quality evidence in fact showed a statistically significant and clinically relevant increased risk of incident AA in people with LRAs compared to those with normal colonoscopy or general population. Furthermore, the seriously imprecise estimates of CRC and CRC-related death in people with LRAs (with the confidence intervals spanning moderately reduced risks to markedly increased risks compared to people with normal colonoscopy or general population) are insufficient to support a strong recommendation to rescreen these patients as average risk populations. Considering the very low certainty of evidence, we are therefore very uncertain whether a change in surveillance strategy from colonoscopy to FIT for people with LRAs would improve or worsen the outcomes of AA, CRC, and CRC-related death. There remains a real possibility this change in strategy may lead to more harms. Further studies are therefore needed before a judgment can be made. If a recommendation is to be made for a change in strategy in this patient population, consideration should be taken for this to be a conditional / weak recommendation given the very low certainty in evidence.	

		5. Further clarification for individuals with family history of CRC is needed. Finally, family history of CRC has been recognized as an important risk factor for the development of CRC. It is important to note that studies forming the evidentiary base of the post-polypectomy guidelines have not specifically evaluated the outcomes of patients with a family history of CRC or inherited CRC syndromes. Based on very low quality evidence, the CAG guidelines suggests colonoscopy as the preferred screening test over no screening or all other screening modalities, and five to 10 year screening intervals.[7] Accordingly, it is prudent that CCC provides guidance and clarification on whether the post-polypectomy surveillance recommendations also apply to individuals with a family history of CRC or inherited CRC syndromes.	The scope of the present recommendations was not to evaluate the impact of family history and CCC's position does not differ from CAG's post-polypectomy recommendations in that regard.
Alberta	Dr. Clarence Wong[1] Associate Professor of Medicine, University of Alberta Division of Gastroenterology, Royal Alexandra Hospital Medical Director, Endoscopic Ablation Program	Overall, the literature review was rigorous. Given some gaps in evidence, I believe decisions were made with the best possible evidence available. These recommendations are a paradigm shift in Canada, so my congratulations to your program for making such a bold step.	
		With respect to FIT surveillance after finding LRA on initial colonoscopy: • We agree with this recommendation. Long term cohort studies and the meta-analysis did not show an increase in colorectal cancers or	A statement has been added to indicate that incomplete procedures (for example, due to poor bowel preparation), should be repeated in 12 months as incomplete procedures have been linked to an increased risk of post-colonoscopy colorectal cancer (3).

[7] Leddin D, Lieberman DA, Tse F, et al. Clinical Practice Guideline on Screening for Colorectal Cancer in Individuals With a Family History of Nonhereditary Colorectal Cancer or Adenoma: The Canadian Association of Gastroenterology Banff Consensus. Gastroenterology 2018;155:1325-1347 e3

	Provincial Medical Lead, Alberta Colorectal Cancer Screening Program 1 – Reviewed in conjunction with Alberta Colorectal Cancer Screening Program Team	deaths. While there was a slight relative increase in five year AA in the LRA versus normal colonoscopy group, the absolute numbers were comparable. While a screening program can prevent cancers with adenoma detection, the bottom line is still cancer prevention or stage shifting so earlier cancers are found. • I agree with the interval of 5 years. Given that a negative colonoscopy on an average risk individual would be given a 10 year interval, five years after an LRA is removed is reasonable. • The recommendations do hinge on a high quality colonoscopy. In our analysis of post-colonoscopy colorectal cancers in Alberta, we found that unsatisfactory bowel preparations and non-adherence to post-polypectomy intervals were key causes of post-colonoscopy colorectal cancers. Thus, you may want to add a statement on a reasonable time to repeat a colonoscopy after an unsatisfactory bowel preparation. • The FIT surveillance interval for LRAs should also have a footnote of using a FIT with a sensitive cutoff. I would not be comfortable with the recommended LRA guideline if the FIT cutoff was high, and thus would not have a sufficient positivity rate. This could compromise external	As the reviewer mentions, the literature demonstrates that people with LRAs have a significantly lower risk of colorectal cancer than the general population (7). Since CCC recommends that the general population (i.e., people at average risk for colorectal cancer) be screened with FIT, it follows that those who are at lower risk for colorectal cancer than the general population also be screened with FIT, using the same quantitative cutoff set for the general population.

		validity and trust in a setting of a low sensitivity for FIT or high cutoff.	
		The main premise in this guideline is an in individual who may be FIT-positive, have no high risk history (e.g., no family history) and only had LRAs on colonoscopy. However, what if this was a repeat colonoscopy on an individual with prior LRAs? There may be confusion in outlining an initial versus subsequent colonoscopy. There will be a large population already undergoing surveillance colonoscopy. Will there be any recommendations for this cohort? You may need to clarify this.	Post-polypectomy guidelines typically have not made these types of distinctions. The recommendations are meant to guide decisions, but ultimately clinical judgement must be applied for patients who have already undergone surveillance colonoscopy several times.
		I fully support a recommendation to look for a polyposis syndrome and refer to genetics for people with more than 10 adenomas. In Alberta, we have certainly found asymptomatic FAP, AFAP and MAP patients through FIT screening. Lynch patients have also been identified. Given the recent American Cancer Society recommendations to lower the average risk screening age, newer guidelines need to highlight the importance of identifying high risk individuals such as family history or genetic predisposition. My concern would be if an endoscopist only focused on colonoscopy follow-up, rather than referring for genetic testing. Your footnotes under Table 1 are critical to highlight.	
		I support the initial recommendations if serrated sessile serrated adenomas/polyps are found on the initial colonoscopy. However, the recommendations on subsequent colonoscopy are vague. I would	There is growing evidence to suggest that small sessile serrated adenomas without dysplasia may be similar to LRA with respect to the risk of colorectal cancer and colorectal cancer death.

		feel more comfortable if some time frames were recommended. Despite the lack of evidence, it may be reasonable to survey small sessile serrated polyps without dysplasia every five years. FIT does not detect sessile serrated polyps reliably. For the higher risk groups such as sessile serrated polyps with dysplasia or traditional serrated adenomas, it may be prudent to follow a schedule similar to HRAs. This would also be practical for endoscopists to follow.	At the time of this review, there was insufficient evidence about the risks associated with sessile serrated adenomas, and so the expert panel chose to remain aligned with USMSTF (2) and CAG (6) guidelines. However, CCC will continue to monitor future evidence of the clinical outcomes in people with small sessile serrated adenomas without dysplasia in order to determine whether the present recommendations should be revised.
		People with large sessile polyps removed piecemeal can be considered high risk patients. There should be emphasis on initial endoscopic resection by a therapeutic endoscopist on lateral spreading lesions (LSLs). These lesions are at a high risk of recurrence and one repeat colonoscopy in six months may not be sufficient. A graduated schedule such as six months, one to three years, may be a safe approach.	This will be considered in the future.
		Recommendations for post-polypectomy surveillance are difficult, if not impossible, to follow if the initial polypectomies are not documented correctly. In Alberta, we have mandatory reporting elements on polyps as well. Despite this, we still have ongoing discrepancies that affect providing a safe recommendation. Most of these are due to insufficient documentation or improper specimen handling. I would suggest that you also add that all polyps need to be submitted in separate jars, and not just a count. I agree with using Paris and NICE as qualitative descriptors. Last, the retrieval rate post-	The reporting considerations section has been updated to suggest that the number of polyps removed and retrieved be documented. A reference to the Pathology Quality Management Partnership Standards (44) has been added to provide additional details on specimen collection and management.

		polypectomy is a quality indicator; thus, lost polyps should be documented.	
Newfoundland	Dr. Jerry McGrath Medical Director, Newfoundland and Labrador Colon Cancer Screening Associate Professor of Medicine, Memorial University	These are extremely well written and thought out. I agree with the recommendations. The evidence is clear and the United Kingdom has been following the LRA up with stool testing for a while.	
Nova Scotia	Dr. Donald MacIntosh Medical Director, Nova Scotia Colon Cancer Prevention Program National Co-lead, CAG Skills Enhancement for Endoscopy Program Professor of Medicine, Dalhousie University, Halifax NS	I congratulate the authors upon the development of an updated, evidence-based, rational overview of polyp surveillance in the setting of widespread availability of FIT for screening. Colonoscopy is not an unlimited resource and over screening of colorectal cancer has potential for harm. Having a coherent approach to the low risk adenoma should lead to a more appropriate use of surveillance colonoscopy.	
		A questions which still needs to be answered is the dividing line between 1-2 LRA's having minimal increased risk versus normal colonoscopy and 3-4 LRA's which require three-year surveillance interval (similar to an advanced adenoma). To my mind, this should be a five-year interval.	The difference to which the reviewer refers relates to the distinction between LRAs, which are defined as one to two small adenomas, versus nonadvanced adenomas, which are not defined by the number of small adenomas. The systematic review did not find a difference in risk between LRAs and nonadvanced adenomas (7). Click et. al demonstrates that the number of small adenomas is not a strong predictor of advanced neoplasia (26).

			However, the evidence on the risk of multiple adenomas remains mixed. Recently, Kim et al. found that three or more non-advanced diminutive adenomas had a borderline increased risk of metachronous advanced neoplasia compared with patients with low risk adenomas (45). When developing our recommendations, the expert panel erred on the conservative side in recommending that three of more adenomas of any size be considered high risk. Additionally, the expert panel identified that it was important to limit the classification of adenomas into low and high risk, rather than introducing the intermediate risk category which is less familiar in the Canadian context.
Ontario	Ontario Association of Gastroenterology (OAG) Board of Directors	The OAG is very concerned about this document as it pertains to low risk adenoma (LRA) surveillance. The CCC recommendations are not consistent with any published post-polypectomy surveillance guidelines. The Canadian Association of Gastroenterology (CAG) Guidelines[8], British Columbia (BC Guidelines post colorectal polyps)[9] and Alberta Colorectal Cancer Screening Program (ACRCSP)[10] all have consistent recommendations that are quite different than the CCC recommendations. Notably, the ASGE, AGA, ACG all combined together to issue the U.S. Multi-society Task	The guidelines from Canadian Association of Gastroenterology (6), British Colombia (36), Alberta (30), and the US Multi-Society Task Force (USMSTF) (2) are all from 2013 or earlier. Since this time, new prospective studies have been published about the risk of colorectal cancer and colorectal cancer death in people with LRAs (Click et al. [26]) and intermediate risk adenomas (Atkin et. al [3]). Guidelines must be periodically updated to reflect the best available evidence. The USMSTF is currently updating their guidelines in light of these new publications.

[8] Leddin D et al. Colorectal cancer surveillance after index colonoscopy: guidance from the Canadian Association of Gastroenterology. CJAG. 2013;27(4):224-8
[9] British Columbia Guidelines, Post polypectomy and colon cancer surveillance. January 2013
[10] Alberta Colorectal Cancer Screening Program (ACRCSP). June 2013

		Force Guidelines (MSTFG)[11] which are in line with the CAG, BC and Alberta guidelines. The European Guidelines (ESGE) don't specifically recommend FIT, but rather, they recommend repeat colonoscopy at 10 years for LRA surveillance. All of Canadian provincial, national and international surveillance guidelines recommend repeat colonoscopy in 5 to 10 years for LRA. There are no guidelines that support nor recommend using FIT for surveillance post LRA. Moreover, there are no studies or evidence that have used the CCC guidelines to assess its value or risk.	The European Society of Gastrointestinal Endoscopy (ESGE) published in 2013 does not recommend repeat colonoscopy at 10 years for LRA surveillance (10). Rather, they recommend that people with LRAs participate in existing national screening programs 10 years after the initial colonoscopy (10), which in Europe, generally means returning to screening with fecal based tests, including FIT (47). The ESGE recommends a colonoscopy after 10 years only if there is no national screening program available (10). Cancer Care Ontario's recommendation is more conservative than this as the recommendation is to return to screening in five years, rather than 10 years.
		The decision to change the recommendation for LRA post-polypectomy surveillance is based on the meta-analysis done by Dr. Dubé. That study showed a statistical increased risk of high risk adenoma (HRA) in LRA patients on subsequent colonoscopy tests, something that the FIT test would not necessarily pick up. In addition, Dr. Dubé notes that having LRA reduces the risk of cancer to below risk of colon cancer in the general population. This is not only counterintuitive but in fact justifies colonoscopy as the better test for subsequent surveillance. In addition she states that LRA patients have a lower rate of risk of dying from colon cancer than the	The systematic review and meta-analysis demonstrated that people with LRAs have a significantly lower risk of colorectal cancer than the general population (standardized incidence ratio 0.68 [95% CI 0.44–0.99] at a median 7.7 years of follow [16] and odds ratio 0.4 [95% CI 0.2–0.6] at 5 years [15]) (7). The ColonCancerCheck program recommends that the general population (i.e., people at average risk for colorectal cancer) be screened with FIT. It follows that those who are at lower risk for colorectal cancer than the general population should not be exposed to a more intensive surveillance procedure that can lead to rare, but serious harms (4).

[11] Lieberman DA et al. Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by UMSTF on Colorectal Cancer. Gastroenterology 2012;143(3):844-57

		general population, again supporting the concept that colonoscopy is an important screening and surveillance procedure. If patients with LRA develop further LRA, the FIT test will not identify this. There is no data to support the recommendation for FIT at 5 years after LRA detection. This recommendation is a totally arbitrary and not based on fact or studies to support this specific recommendation. This recommendation is dangerous and puts patient's health and safety at risk. It compromises what is best for patients.	Since the systematic review and meta-analysis was published, new evidence has emerged that people with LRA have the same risk of colorectal cancer than those who had no adenomas at their initial colonoscopy (26). This evidence further supports the recommendation that people with LRA should not be subjected to colonoscopy surveillance. The expert panel took a conservative approach to the recommendation for people with LRA to return to screening with FIT in five years, rather than aligning with the ESGE's recommendation that people with LRAs should return to screening through national screening programs in 10 years (10). The reason for this is that the systematic review showed a very small, but statistically significant relative risk of HRA in people with LRAs compared to those with a normal colonoscopy. Despite the fact that the cumulative risk was not significantly increased between the two groups, and therefore this risk may not be clinically relevant, the expert panel wanted to err on the side of caution in recommending that people with LRAs returning to FIT in a shorter timeframe than those with a normal colonoscopy result (7).
		Neither FIT nor colonoscopy is 100% perfect in finding neoplasia. It follows that more frequent colonoscopy testing would be helpful. There are miss rates for adenomas detection from index colonoscopy. "Back-to-back" colonoscopies have shown significant miss rates of 27% for small adenomas (less than five millimeters) and 6% for adenomas	The benefits of colonoscopy must be weighted against the potential harms, which include perforation, bleeding and, in rare cases, even death (4). In a randomized control trial, people of average risk for colorectal cancer who received screening colonoscopies had a significantly higher rate of complications,

		of more than 10 millimeters diameter.[12] There are potential incomplete polypectomy resulting from the initial index colonoscopy. Rates of incomplete resection for diminutive polyps are 29% for conventional biopsy and 17% for hot biopsy[13,14]. Residual polyp tissue is more likely to remain after resection of sessile polyps and risk increases with polyp size. Rates of 17% for polyps of 10–20 millimeters and 7% for lesions of five to nine millimeters have been quoted. Based on this data, programmatic screening which aims to optimize high quality of endoscopy serves patients much better, than recommendations that deprive patients of the best screening and preventative testing available. Individuals found to have colonic polyps are at increased risk of advanced neoplasia in the future[15,16,17,18]. This risk may be due to a number of mechanisms: missed lesions at the initial colonoscopy; incomplete removal of adenomatous tissue at initial colonoscopy; and the individual's propensity to colonic	compared those who received screening via FIT (48). The quality of the colonoscopy procedure is indeed very important. Endoscopists should state in the colonoscopy report whether the prep was adequate; if it was inadequate, a repeat procedure is required. But concern about poor preparation, which occurs in a small minority of procedures, is not sufficient justification to support colonoscopy in all persons with LRA. Similarly, endoscopists should follow evidence-based polypectomy techniques that ensure completeness of the resection. However, poor procedure quality cannot be the rationale to recommend colonoscopy for a specific population when the clinical evidence shows little benefit. As recommended in CCC's post-polypectomy surveillance recommendations, endoscopists should indicate the reasons for deviations from the recommendations in their reports, when applicable.

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[17] [No reference provided by reviewer]
[18] Anti M, Armuzzi A, Morini S, Lascone E, Pignataro G, Coco C, Lorenzetti R, Paolucci M, Covino M, Gasbarrini A, et al. Severe imbalance of cell proliferation and apoptosis in the left colon and in the rectosigmoid tract in subjects with a history of large adenomas. Gut. 2001;48:238–246.

		neoplasia (either lifestyle factors, an inherent imbalance of cell proliferation, or a combination of these).[19,20,21,22] An optimally performed double-contrast barium enema and FIT detect only half of adenomas of 5 mm or larger that are detected by colonoscopy.[23] For CRC, the miss rate for FIT25 to FIT150 was the same 21% (n=3), whereas that with FIT200 the miss rate increased to 35% (n=5). Although FIT has good specificity, the sensitivity is low, even for high risk adenoma (up to 50%). Therefore, using FIT testing to replace surveillance colonoscopy for LRA is very risky because it may not pick up interval developed adenomas or adenomatous growth from previous incomplete polypectomy. Additionally, there is great variability in endoscopy skills in Ontario endoscopists. Previous studies have demonstrated an increase in missed lesions when	Cancer Care Ontario supports a number of initiatives to improve endoscopy quality, including the Colonoscopy Quality Management Partnership with the College of Physician and Surgeons of Ontario. We respectfully disagree with the statement that all individuals with colonic polyps are at increased risk of advanced neoplasia in the future. The literature demonstrates that while some individuals with colonic polyps have an increased risk of colorectal cancer compared to the general population and to those with a normal baseline colonoscopy, others do not. This was specifically demonstrated in several multiple long-term follow up studies of large cohorts by Cottet et al. (3), Brenner et al. (15), Atkin et al. (3) and Click et al. (26). The risk of colorectal cancer in those with LRA is less than that of the general population, and therefore can be considered lower than average risk. Since CCC and the Canadian Task Force on Preventive Health Care (46)

[19] Brenner H, Chang-Claude J, Jansen L, Seiler CM, Hoffmeister M. Role of colonoscopy and polyp characteristics in colorectal cancer after colonoscopic polyp detection: a population-based case-control study. Ann Intern Med. 2012;157:225–232.
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[23] Anti M, Armuzzi A, Morini S, Lascone E, Pignataro G, Coco C, Lorenzetti R, Paolucci M, Covino M, Gasbarrini A, et al. Severe imbalance of cell proliferation and apoptosis in the left colon and in the rectosigmoid tract in subjects with a history of large adenomas. Gut. 2001;48:238–246.

		colonoscopy is done by low endoscopy volume physicians. Aside from Dr. Dubé's self-quoted study, there is no externally supported evidence, anywhere, either within our country or internationally to justify the value of FIT testing post index colonoscopy.	both recommend fecal-based testing for people of average risk, it is logical that the same would apply to people with LRA who are at lower risk than the average risk population. Recommending that people with LRAs receive surveillance colonoscopy would result in undue exposure to the risks and inconveniences of colonoscopy.
		The Alberta Health Services has a very comprehensive and balanced PPSG guidelines that is in line with physicians' practices across the country. In addition, Alberta has being screening for colon cancer with FIT and still recognizes the importance of post-polypectomy surveillance for LRA with colonoscopy. Cancer Care Ontario has yet to launch the FIT program in Ontario and is prematurely putting such confidence in the stool test and considering it superior to colonoscopy for post-polypectomy surveillance. It is completely illogical and hazardous to suggest to do a FIT test at 5 years if one is to detect new polyps and remove them to prevent growth and development of cancer. The current recommendations by CCC would not be best practice and significantly opens physicians up to potential litigation and most importantly puts our patients at undue risk of developing a preventable cancer.	The Alberta Health Services guidelines were produced before the release of recent long-term studies of the risks associated with LRA (3,16,18,20,26). There is research to show that clinicians have a low adherence to post-polypectomy surveillance guidelines (49-51). Accordingly, physician preferences and current practices should not be the basis of clinical recommendations. High-quality clinical evidence needs to drive recommendations. When promoting the uptake of these recommendations, current physician practices must be considered in developing change management strategies. For a summary of the evidence supporting the efficacy and effectiveness of FIT, please see *Colorectal cancer screening in average risk populations: Evidence summary* (8). With respect to the issue of litigation, in light of the recent evidence demonstrating that people with LRAs have a lower risk of colorectal cancer and colorectal cancer death than the general population (3) and the same risk of colorectal cancer and colorectal cancer death

			as those with normal colonoscopy findings (26), physicians could be at risk for litigation if they continue to expose their patients to the potential harms of colonoscopy without benefit to the patient.
		One wonders what is the motivation behind these CCC recommendations are? Is it controlling the number of colonoscopies to be done in the province and thus cost control? One wonders if Cancer Care Ontario is responding to provincial financial pressures for reasons to restrict and limit a more expensive but accurate procedure and for cancer prevention with colonoscopy. From the OAG perspective this CCC study is commissioned by Cancer Care Ontario and written by members whom are actively involved in the leadership of the Quality Based Procedures (QBP) and Quality Management Program (QMP). These bodies are not separate from the political and funding complexities of health issues in Ontario. We feel that the both the presence of some evidence in this field and the notable lack of evidence in key areas must be weighed together. Cancer Care Ontario must understand the potential impact of this type of document on patient specific outcomes such as interval cancer. In addition, if there is disagreement and deviation from other published guidelines, we think there needs to be more effort to explain and reassure both	Cancer Care Ontario is committed to using the best available evidence to inform recommendations to promote high quality care and patient safety while protecting the population from being exposed to unnecessary harms. Given the recent evidence shows that people with LRAs have a comparable risk of colorectal cancer and colorectal cancer death to those with normal colposcopy results (26) and the risk of colorectal cancer and colorectal cancer death is lower than the general population (2), these individuals should not be subjected to risk of periodic colonoscopy, which may include perforation, bleeding, and in rate occasions, even death (4). The recommendations were based on a review of the evidence by an expert panel of endoscopists, general surgeons, and pathologists that are affiliated with Cancer Care Ontario, including the Gastrointestinal Quality Based-Procedure (QBP) and Colonoscopy Quality Management Program (QMP). Cancer Care Ontario highly values external input and feedback; international, national and provincial experts were invited to comment on the draft recommendations. The recommendations have received strong support from the vast majority of the reviewers. Regarding the suggestion to further explain and reassure the audience regarding the

		patients and providers as to the rationale for this dramatic change. Our hope would be that instead of limited consultations with outside parties prior to publication, that Cancer Care Ontario makes every effort to meet in a more substantial manner with key stakeholder groups to understand the full effect of this document and seek feedback on this document from other national and international experts in this area. CCC's recommendations must be reviewed and critiqued by other experts in this field.	rationale for the change in recommendation for LRAs, this has been added to the document.
		The OAG cannot and will not endorse this document as it currently stands. It puts patient's health at risk. It is unproven, untested and potentially dangerous. We think this document should be viewed widely and let the public know what potential impact these recommendations could have on their health.	We respectfully disagree that these recommendations put patients at risk. There is strong evidence supporting the fact the people with LRAs are at a similar risk to people with no adenomas found at the initial colonoscopy. The overuse and overexposure to colonoscopy and poor quality colonoscopy are the drivers of patient risk. Based on the feedback received, additional information has been added to summarize the evidence supporting the change in recommendations for LRA so that the public and providers can better understand the rationale. Cancer Care Ontario is committed to using the best available evidence to inform recommendations to promote high quality care and patient safety.
Quebec	Dr. Alan Barkun	The recommendations are very logical and evidence-based for LRA, who are at an even lower risk than people of average risk never	Regarding the recommendation to return to screening with FIT after five years, this was motivated by the fact that the systematic review showed a small, but statistically

	Senior Scientist, Montreal General Hospital Chairholder, Douglas G. Kinnear Chair in Gastroenterology and Professor of Medicine, Director of Endoscopy and Therapeutic Endoscopy Training Program, Chief Quality Officer, Division of Gastroenterology, McGill University	colonoscopied. I completely agree with FIT for LRA follow-up. I initially wondered why a five year follow-up interval was selected for LRA, instead of 10 years, but then I read your rationale and agree that it is best to err on the side of caution. This will lead to a large reduction in colonoscopies. However, given the data published in the American Journal of Gastroenterology about the risk of HRA in people with LRAs after five to 10 years, perhaps you could consider recommending that people with LRAs return to FIT in 10 years, rather than five years. I realize that this data exceeds the cut-off date of the literature search but it may be worthwhile to update the recommendation to 10 years as this will be cleaner and easier for clinicians.	significant relative risk of HRA in people with LRAs compared to those with a normal colonoscopy (7). However, the cumulative risk was not significantly increased, and therefore this risk may not be clinically relevant. As a result of the slight increased relative risk of HRA for people with LRA, the expert panel chose a conservative recommendation to return to screening in five years that would be more acceptable to clinicians. More information has been added to provide the rationale for this recommendation. CCC will continue to monitor future evidence in order to determine whether the present recommendations should be revised.

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