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# Updated guidelines on colonoscopy surveillance

New information suggests that more frequent colonoscopy surveillance should be reserved for individuals with high-risk precancerous lesions.

**ABSTRACT:** Precancerous colorectal lesions may develop along an adenomatous or serrated pathway. These lesions are further classified as low or high risk based on their size, number, and histologic characteristics. Recent evidence has demonstrated that individuals with low-risk precancerous lesions that are resected during colonoscopy are not at significant risk of future colorectal cancer compared with the general population and do not require intense colonoscopy surveillance. Conversely, individuals with high-risk precancerous lesions that are removed appear to benefit from surveillance colonoscopy. This new information has led to updated colonoscopy surveillance guidelines in British Columbia and other jurisdictions.

**W**hile the benefits of colon screening are firmly established, the impact of colonoscopy surveillance following removal of precancerous lesions from the colon and rectum is not as clear. Guidelines that recommended surveillance were based largely on expert consensus and studies that used surrogate outcomes. However, over the past 5 years, several large cohort studies have demonstrated that the risk of future colorectal cancer is similar to or lower than that of the general population and for those with a history of low-risk precancerous lesions. This has led to updated surveillance guidelines from the British, European, American, and Asian endoscopic societies. In response to this new evidence and in keeping with other guidelines, the British Columbia Guidelines and Protocols

Advisory Committee also revised its colonoscopy surveillance recommendations, which the BC Colon Screening Program has adopted.<sup>1</sup>

## Pathogenesis of colorectal cancer

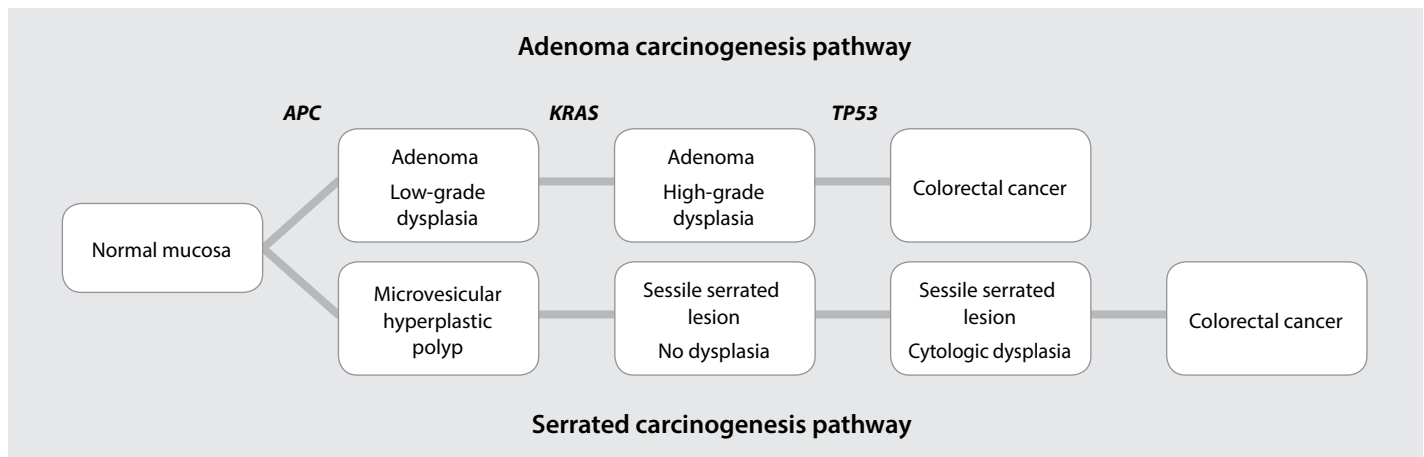
There are three pathways along which colorectal cancer may develop: progression from conventional adenomas (60%); the serrated pathway (15% to 30%), comprising hyperplastic polyps, sessile serrated lesions, and traditional serrated adenomas [Table 1];<sup>2</sup> and hereditary predisposition syndromes (e.g., Lynch syndrome; 3% to 5%). The adenoma-to-carcinoma pathway has been well described, with accumulation of genetic mutations leading to sequential histologic changes.<sup>3</sup> The genetic alterations in the serrated pathway are not yet completely understood, but mutations

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**TABLE 1.** Features of serrated lesions in the colon and rectum.<sup>2</sup>

Lesion type	Hyperplastic polyp	Sessile serrated lesion	Traditional serrated adenoma
Prevalence	20%	15%	< 1%
Location	Rectum and sigmoid	Proximal to splenic flexure	Distal to splenic flexure
Size	Small	Small	Large
Morphology	Flat or sessile	Flat or sessile	Pedunculated
Histology	Upper crypt serration	Crypt base serration Boot-shaped crypt	Columnar epithelium Eosinophilic cytoplasm



**FIGURE 1.** Adenoma and serrated colorectal cancer pathways.

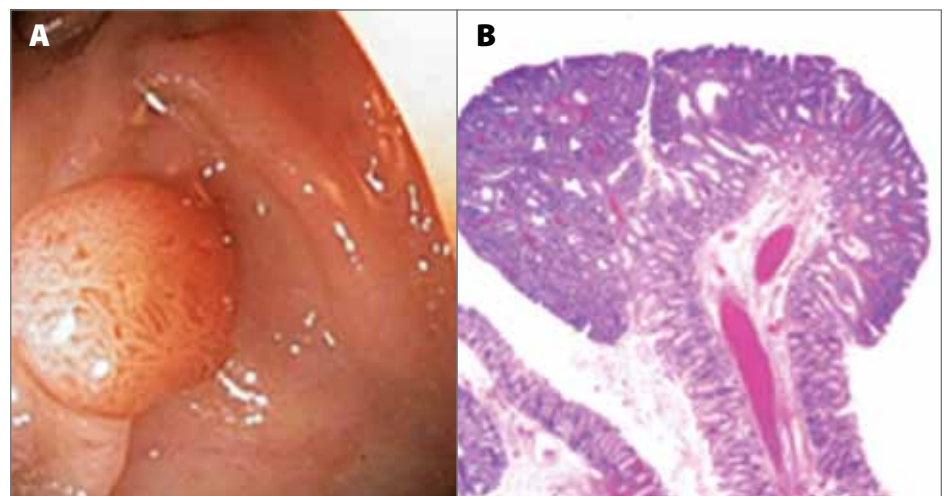
in *BRAF* and *KRAS* play a prominent role [Figure 1].<sup>4</sup> Each of the overarching pathways gives rise to molecularly distinct colorectal cancers.<sup>4,5</sup>

### Adenomatous lesions

All colonic adenomas consist of dysplastic epithelium and are classified as benign neoplasms [Figure 2]. Depending on the extent of the villous component, an adenoma may occur as one of three subtypes: tubular, villous, or tubulovillous.

Carcinomas develop in the geographic centres of adenomas and spread centrifugally, replacing the adenomatous epithelium. Several factors predispose to carcinoma development, including adenoma size, growth pattern, dysplasia grade, and patient age. Both growth pattern and dysplasia grade correlate with lesion size. Small adenomas have the lowest risk of malignant transformation, but the risk is not completely negligible. Adenomas less than 10 mm in diameter usually demonstrate only low-grade dysplasia and have a very low potential for malignant transformation.

Colorectal cancer that has invaded into but not beyond the submucosa (T1) is associated with low rates of lymph node metastases and excellent outcomes. A subset of patients can be successfully managed with endoscopic resection alone, thus avoiding the risks associated with surgical resection.<sup>6</sup> Identification of appropriate candidates for endoscopic resection depends



**FIGURE 2.** Endoscopic (A) and histologic (B) images of a colon adenoma.

on the absence of certain high-risk histopathologic features that are associated with lymphatic spread.<sup>7,8</sup> Therefore, it is essential for an experienced pathologist to assess the metastatic risk of early colorectal cancer that has been resected at colonoscopy and communicate these findings clearly to the clinician to guide further therapy.

The most critical prognostic factor is the presence or absence of invasion into the submucosa; without invasion through the muscularis mucosae, there is no risk for lymph node metastasis. Therefore, as per the BC Colon Screening Program Pathology Standards, these cases are retained within the high-grade dysplasia category, and the terms “intramucosal carcinoma” and “carcinoma in situ” should not be used,

because this may lead clinicians to misinterpret the lesion as colorectal cancer and could result in overtreatment of the patient. This is supported by publications that have documented identical outcomes for lesions that were reported as having high-grade dysplasia, intramucosal carcinoma, or carcinoma in situ.<sup>9</sup>

### Serrated lesions

Interpreting studies that have assessed serrated lesions is challenging due to several factors, including the subtle endoscopic appearance of the lesions and their histologic similarity to benign-behaving hyperplastic polyps, and sessile serrated lesions have proven difficult to detect at colonoscopy and diagnose at pathology.<sup>10</sup> Furthermore, the

terminology for these lesions is inconsistent and has changed several times over a short period. Although hyperplastic polyps are generally regarded as lacking malignant potential, the microvesicular subtype has emerged as the likely precursor to sessile serrated lesions.<sup>11</sup> Thus, while small hyperplastic polyps in the rectum and sigmoid are still considered harmless, all other lesions should be removed, and large hyperplastic polyps are managed as sessile serrated lesions.

In the BC Colon Screening Program, among individuals who underwent colonoscopy to follow up a positive fecal immunochemical test, 2.8% had at least one sessile serrated lesion removed and 0.1% had at least one traditional serrated adenoma removed.<sup>12</sup> As seen in other jurisdictions, the sessile serrated lesion detection rate among BC physicians varies (median: 7%; 10th, 90th percentiles<sup>4,10</sup>) and is associated with physician specialty.<sup>13</sup>

### Risk stratification of colorectal precancerous lesions

Individuals who undergo colonoscopy with the removal of precancerous lesions can be divided into those with high-risk findings and those with low-risk findings. High-risk findings could refer to either the removal of one or more high-risk precancerous lesions or the removal of multiple low-risk precancerous lesions [Table 2].<sup>1</sup> High-risk precancerous lesions are defined as being larger than 10 mm or by histologic characteristics. This includes advanced adenomas, a term that is falling out of use, and high-risk serrated lesions. An individual who has 10 or more precancerous lesions removed cumulatively during their lifetime may have an inherited predisposition to colorectal cancer and is eligible for assessment by the BC Hereditary Cancer Program.<sup>14</sup>

Several large retrospective cohort studies have shown that individuals with a high-risk adenomatous lesion have an increased incidence of metachronous colorectal cancer and colorectal cancer mortality compared with individuals with no adenomas at colonoscopy, individuals with

**TABLE 2. Classification of low- and high-risk precancerous colorectal lesions.<sup>1</sup>**

Feature	Low risk	High risk
Size	≤ 10 mm	> 10 mm
Number	1 to 4	≥ 5
Histology	<ul style="list-style-type: none"> <li>• Adenoma with low-grade dysplasia</li> <li>• Sessile serrated lesion with no dysplasia</li> </ul>	<ul style="list-style-type: none"> <li>• Adenoma with high-grade dysplasia</li> <li>• Adenoma with villous features</li> <li>• Sessile serrated lesion with dysplasia</li> <li>• Traditional serrated adenoma</li> </ul>

low-risk adenomas, and the general population.<sup>15-18</sup> Undergoing one surveillance colonoscopy appears to reduce the incidence of metachronous colorectal cancer to that of the general population; a second surveillance colonoscopy reduces the incidence of colorectal cancer below that of the general population.<sup>19</sup>

In contrast, following the removal of one or two low-risk adenomas, colorectal cancer incidence and mortality are lower than those of the general population, either in the absence of surveillance colonoscopies or statistically controlling for surveillance colonoscopies.<sup>15-20</sup> In addition, several studies have shown a reduced risk of colorectal cancer, irrespective of how many low-risk adenomas were resected. These findings have led the guideline committees, in varying degrees, to recommend no surveillance or less-intensive colonoscopy surveillance for these individuals. The evidence for high- and low-risk serrated lesions is less robust but follows a similar pattern to that of adenomatous lesions.<sup>16</sup>

Two randomized trials underway in Europe (EPoS trial NCT02319928) and the United States (FORTE NCT05080673) are comparing colonoscopy surveillance intervals for individuals with low-risk precancerous lesions; however, the results will not be available for many years.<sup>21,22</sup>

### Baseline colonoscopy

An individual's future risk of colorectal cancer must be taken in the context of their baseline colonoscopy. It is well established that the quality of the baseline colonoscopy is associated with an individual's risk of colorectal cancer incidence and mortality.<sup>23</sup>

Experts have questioned whether it is the baseline colonoscopy that provides protection against colorectal cancer rather than the subsequent surveillance.<sup>24</sup> While previous surveillance guidelines were developed prior to widespread adoption of colonoscopy quality assurance and improvement, new guidelines assume a high-quality baseline colonoscopy exam with a high precancerous lesion detection rate and complete resection.

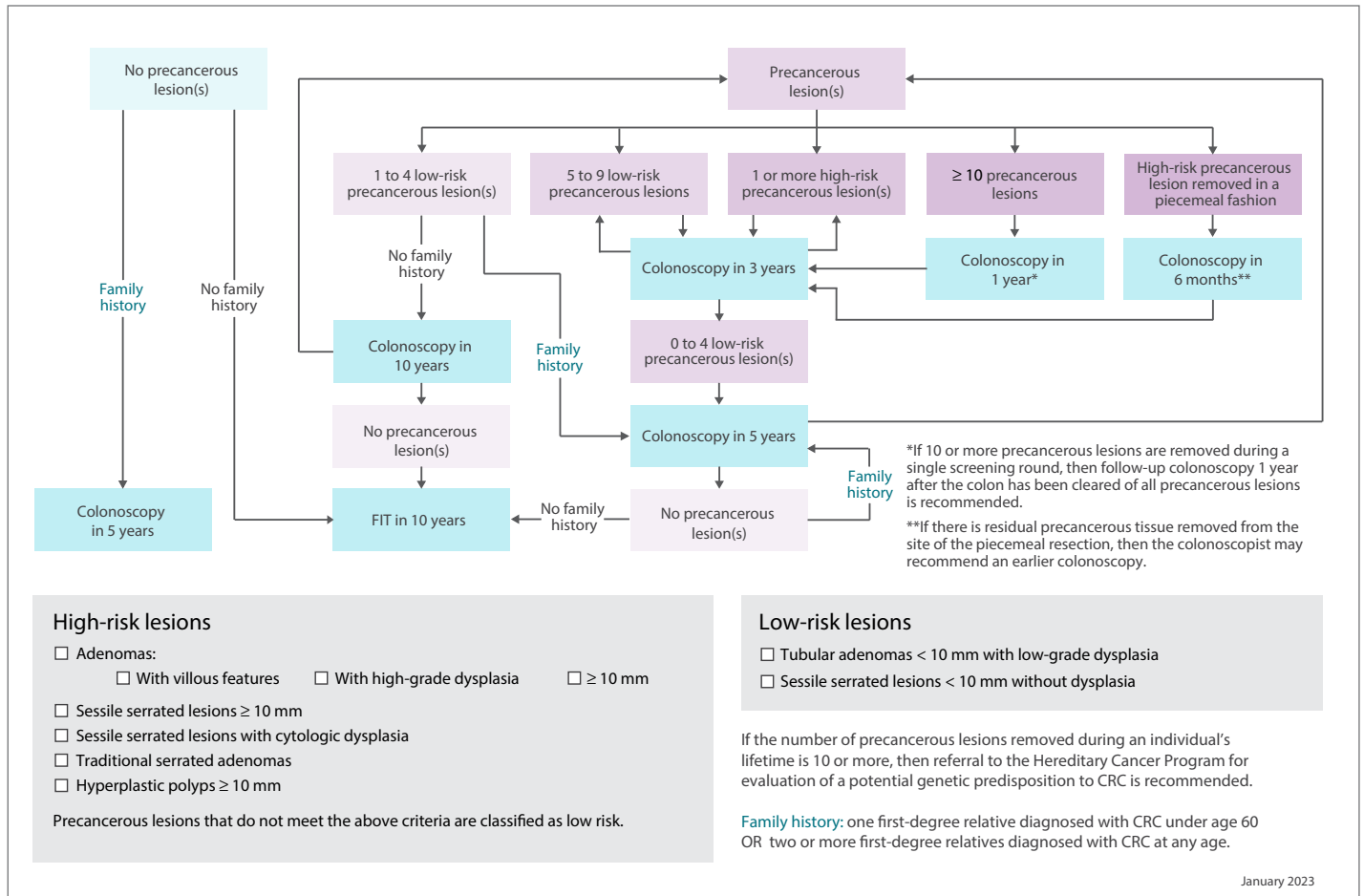
### Colonoscopy surveillance recommendations

Figure 3 outlines the updated BC colonoscopy surveillance guidelines, and Table 3 compares the BC Guidelines to those of other major societies.<sup>25-28</sup> These guidelines are informed by studies that have evaluated adults who are older than 50 years of age; therefore, the recommendations may not be appropriate for younger adults who are diagnosed with precancerous lesions, and shared decision making between physicians and their patients to determine the timing of surveillance colonoscopy is appropriate.

Because the likelihood of colonoscopy-related adverse events increases with age and efficacy decreases due to competing causes of death, surveillance colonoscopy can be discontinued between 75 and 80 years of age.<sup>29</sup>

### Potential harms of surveillance colonoscopy

The benefits of colonoscopy surveillance must be weighed against the potential harms. The risk of a serious adverse event following colonoscopy in the BC Colon Screening Program is 44 per 10 000, which generates a number needed to harm of 225.



**FIGURE 3. BC Colon Screening Program colonoscopy follow-up algorithm.** FIT = fecal immunochemical test; CRC = colorectal cancer.

(Source: BC Colon Screening Program)

**TABLE 3. Comparison of colonoscopy surveillance guidelines.**

Guideline	Publication year	High-risk findings				Low-risk findings	
		High-risk lesion(s)	Interval (years)	Multiple low-risk lesions	Interval (years)	Test	Interval (years)
BC <sup>1</sup>	2022	≥ 10 mm HGD villous	3 (then 5)	5–9	3 (then 5)	Colonoscopy	10
				≥ 10	1		
United States <sup>25</sup>	2020	≥ 10 mm HGD villous	3	3 or 4	3–5	Colonoscopy	7–10
				5–9	3		
				≥ 10	1		
Europe <sup>26</sup>	2020	≥ 10 mm HGD	3 (then 5)	≥ 5	3 (then 5)	FIT or	10
						colonoscopy	10
Britain <sup>27</sup>	2020	≥ 2 PCLs with one ≥ 10 mm HGD	3 (then FIT)	≥ 5	3 (then FIT)	FIT	When invited
Asia-Pacific <sup>28</sup>	2022	≥ 10 mm HGD villous	3	Not stated	Not stated	FIT or	2
						colonoscopy	10

HGD = high-grade dysplasia; PCL = precancerous lesion; FIT = fecal immunochemical test.



Perforation occurs in 6 per 10 000 cases, bleeding in 26 per 10 000, and death in 3 per 100 000.<sup>30</sup> In addition to fasting and consuming the bowel preparation, colonoscopy may require an individual and their accompanying adult to take time off work, arrange childcare, and make other arrangements. Last, in a setting of finite colonoscopy capacity, redirecting colonoscopy resources to those individuals who will derive the most benefit is an important consideration.

## Summary

As we strive to increase participation in colon screening, the number of individuals who undergo colonoscopy will also increase. With advances in physician skill and colonoscopy technology, the proportion of individuals diagnosed with a precancerous lesion at colonoscopy will likely exceed 70% at some point in the near future.<sup>31,32</sup> Taking the high prevalence of precancerous lesions into consideration along with the new evidence and updated guidelines, it is appropriate to reserve more frequent colonoscopy surveillance for those individuals who are at higher risk. ■

## Competing interests

Dr Schaeffer has been a consultant at Alimentiv Inc., Pfizer, Merck, Diaceutics, Astellas, and Satisfai Health Inc. Dr Telford received sessional payments as a consultant for the Guidelines and Protocols Advisory Committee in 2021–2022 as a contributing member to the colon screening guidelines.

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