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Early-onset colorectal cancer

The BC Guideline for colorectal cancer screening encourages physicians to evaluate younger adults with symptoms or a family history of colorectal cancer by using colonoscopy.

ABSTRACT: Globally, colorectal cancer is the third-most-diagnosed cancer and the second-leading cause of cancer death. Historically, the population at risk has been over 50 years of age, but over the past 2 to 3 decades, there has been increasing recognition of the rise in incidence before age 50. Although the percentage rise is notable, the absolute numbers of early-onset cancer remain much lower than for conventional late-onset individuals. There is a difference in clinical presentation and pathology in early-onset colorectal cancer. Currently, population screening strategies in British Columbia remain unchanged, but recognition of possible early-onset colorectal cancer requires the vigilance of health care providers.

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Many risk factors for the development of colorectal cancer have been proposed, but the most consistently recognized is advancing age, with incidence rising abruptly after age 50 **[Figure 1]**.[1,2] Hence, most screening guidelines suggest initiation of screening for and consideration of a diagnosis of colorectal cancer in individuals over 50 years of age.[3,4] However, over the past 2 to 3 decades, several countries, including Canada, have noted a rise in the incidence of colorectal cancer in adults younger than 50 years of age **[Figure 2, 3]**. Colorectal cancer arising before age 50 is considered "early onset."[5] This recognition has led to research into understanding the mechanisms and risks of early-onset colorectal cancer and has provoked discussion about

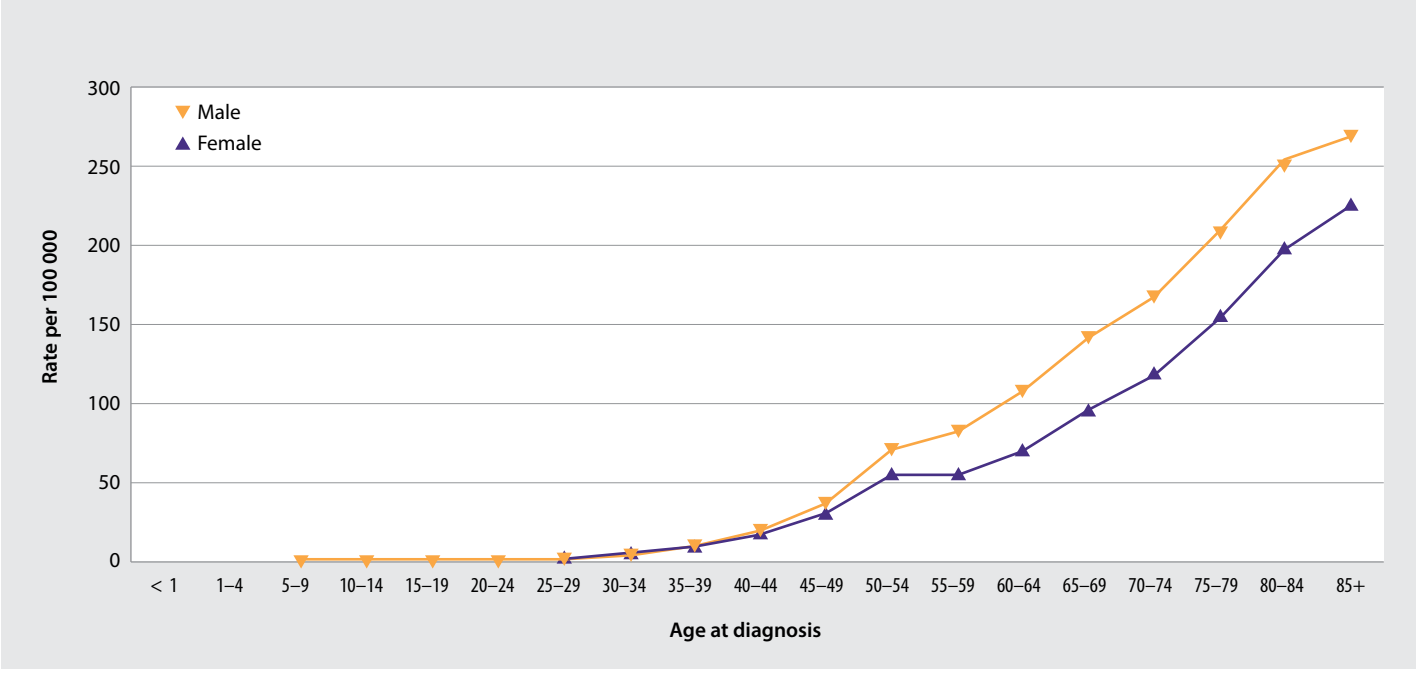

FIGURE 1. Incidence rates of colorectal cancer, by age and sex, in the United States, 2015–2019.
(Source: https://seer.cancer.gov/statfacts/html/colorect.html)

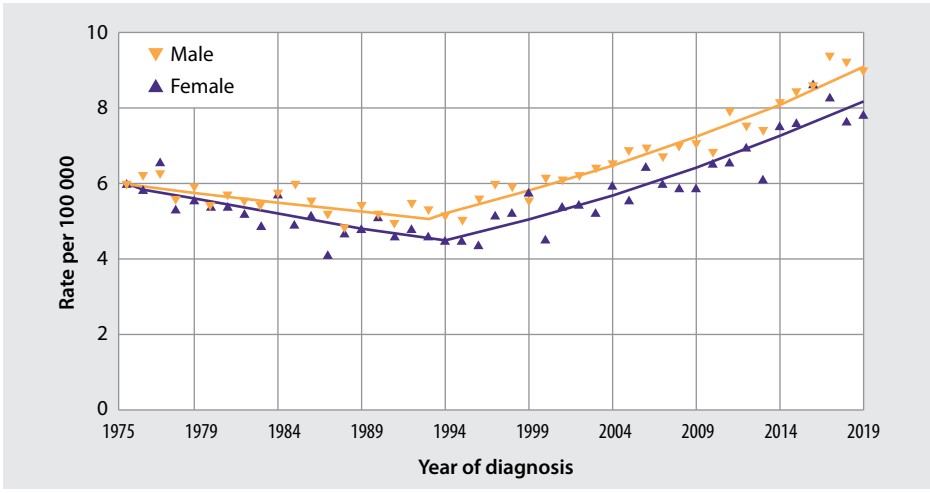

FIGURE 2. Incidence rates of colorectal cancer in those younger than 50 years of age, by sex, in the United States, 1975–2019.
(Source: https://seer.cancer.gov/statfacts/html/colorect.html)

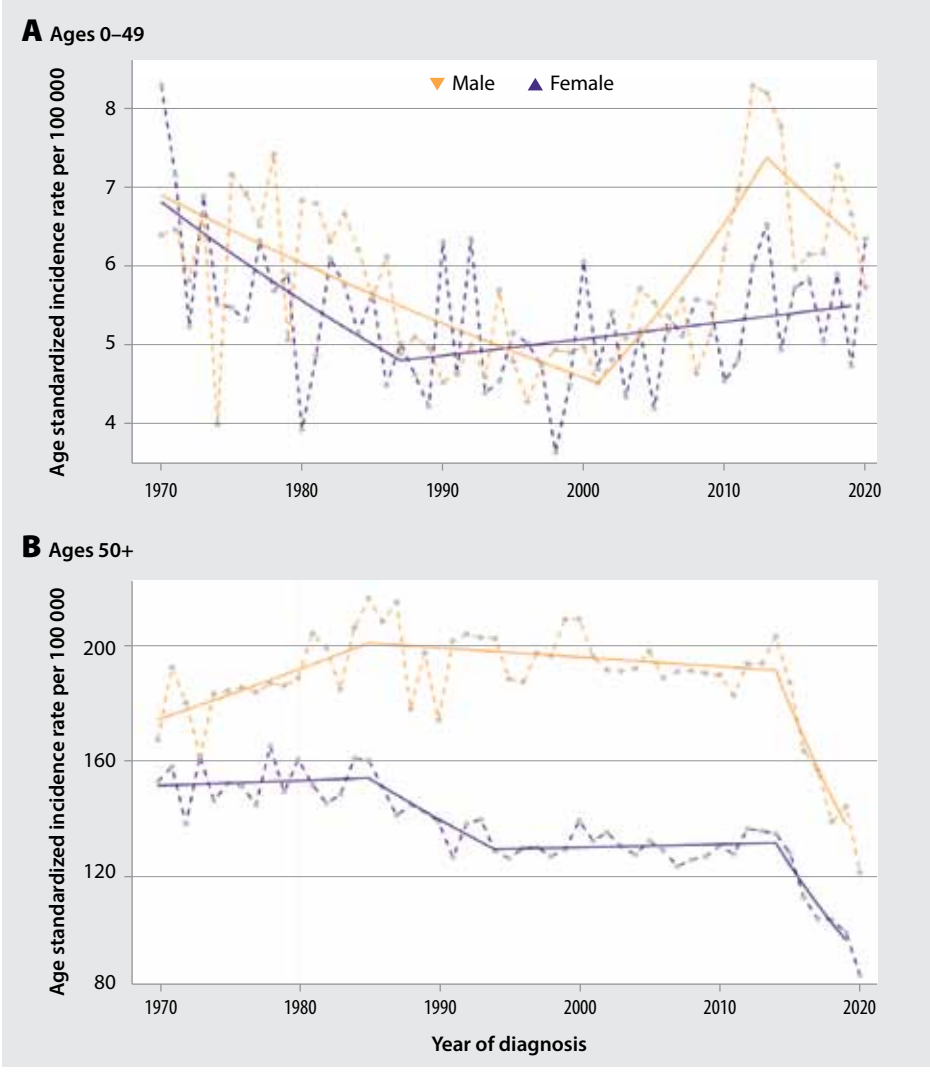

FIGURE 3. Incidence of colorectal cancer in British Columbia by age and gender. A: Ages 0–49. B: Ages 50+.
(Source: BC Cancer)

whether screening guidelines should be altered to accommodate a younger population. The early-onset colorectal cancer cohort is separate from previously recognized populations with hereditary cancer syndromes such as Lynch syndrome, with a family history of premature colorectal cancer, or with long-standing inflammatory bowel disease. These groups are known to be at higher risk of colorectal cancer and have their own screening strategies.[2]

Colon screening

Colorectal cancer screening strategies for BC have recently been revised and published by the Guidelines and Protocols Advisory Committee, a joint committee of Doctors of BC and the BC Ministry of Health.[2] The recommendations include risk stratification of individuals and for those deemed average risk to begin screening at age 50 with biennial fecal immunochemical testing. Colonoscopy is reserved for those with a positive fecal immunochemical test and for individuals at higher risk of colorectal cancer. The value of these screening strategies is based on the slow progression from normal colonic mucosa to precancerous lesions to colorectal cancer. By identifying and removing precancerous lesions, colorectal cancer may be prevented.

In BC, colorectal cancer is the third-most-common cancer diagnosis for women and the second-most-common cancer diagnosis for men; it represented 10% of all new cancer cases in 2022 and 11% of all cancer deaths.[4] In general, there has been a steady decline in both colorectal cancer diagnoses and deaths over the past 20 years **[Figure 4]**.[1] This is attributed partly to screening programs that have led to the detection of colorectal cancer at an earlier stage of disease and to the removal of precancerous lesions. In addition, improvements in surgery and chemotherapy play a beneficial role in outcomes when cancer has already occurred. Lifestyle changes, including reduced smoking, increased physical activity, and achieving a healthy weight, are also important in the primary prevention of colorectal cancer.

Early-onset colorectal cancer

Despite the reduction in colorectal cancer incidence overall, the median age of diagnosis in the United States has shifted from 72 years of age in 2001–2002 to 66 years in 2015–2016, thus reflecting the presentation of this cancer in younger people.[5] Some estimates suggest that within the next decade, 25% of rectal cancers and 10% to 12% of colon cancers will be diagnosed in individuals under the age of 50.[6,7] However, while the percentage increase in younger individuals is striking, the absolute risk remains much lower than for the older population. For example, the risk for Canadian males under age 50 increased from 10/100 000 in 1971 to 12.5/100 000 in 2015, but the risk for those over age 50 was 225/100 000 in 2000.[6]

The concept of a birth-cohort effect, perhaps related to dietary factors or exposures, for those born after 1980 has been proposed as a cause of the increased risk in this group. The exact factors for this are not yet clear.[8] Early-onset colorectal cancer has features that are somewhat different from conventional late-onset colorectal cancer in terms of epidemiology, risk factors, presentation, and histology. Epidemiologically, there is increased risk of early-onset colorectal cancer among those with Caucasian ethnicity, male gender, and a first-degree relative with colorectal cancer. Obesity, hyperlipidemia, smoking, and alcohol consumption also play a role.[8] A study from Ontario identified modifiable risk factors for early-onset colorectal cancer, including sedentary lifestyle and intake of sugary drinks and fast food.[9] From a clinical standpoint, early-onset colorectal cancer presents with a longer duration of symptoms before diagnosis, more rectal cancer than colon cancer, more advanced disease at presentation, and a more aggressive histologic phenotype.[10] Early-onset colorectal cancer progresses more rapidly and aggressively than older-onset colorectal cancer. Given the higher rate of distal colon or rectal cancer in the younger population, there is an increased presentation with actual symptoms, whereas more proximal colon cancer is often asymptomatic. The most common symptoms for distal cancer in the young population are rectal bleeding (38%), abdominal or pelvic pain (33%), and a change in bowel habits (20%).[10]

Early-onset colorectal cancer progresses more rapidly and aggressively than older-onset colorectal cancer.

Recognizing that the development of colorectal cancer from normal mucosa to precancerous lesions occurs over decades, there has been an exploration of different early-life factors that could play a role in early-onset colorectal cancer. Factors that have been examined include breastfeeding in infancy, maternal smoking, childhood obesity, and markers of onset of puberty, but no demonstrable effect has been identified so far.[11] The role of the gut microbiome and alterations related to diet or antibiotic exposure are being explored. Perhaps the strongest risk associations for those with early-onset colorectal cancer that have been determined so far are family history of colorectal cancer, sedentary lifestyle, consumption of a Western diet, and metabolic syndrome.[5] Whereas hereditary factors are present in 3% to 5% of older-onset colorectal cancer, 20% of those with early-onset colorectal cancer have at least one first-degree relative with colorectal cancer.[12]

When an individual is diagnosed with early-onset colorectal cancer, it is important to offer colon screening to their first-degree relatives, because they in turn have a tripled risk of developing colorectal cancer over that of the general population.[13]

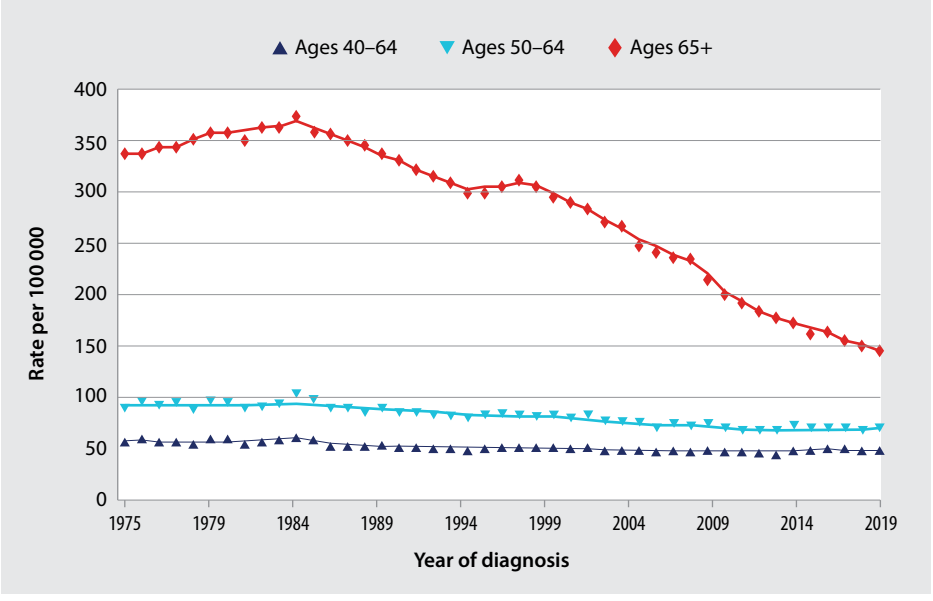

FIGURE 4. Incidence rates of colorectal cancer, by age, in the United States, 1975–2019.
(Source: https://seer.cancer.gov/statfacts/html/colorect.html)

Lowering the screening age

The increased incidence of colorectal cancer in younger adults and the benefits of colon screening in the older population have led to discussion about reducing the age of initiation of screening from 50 years of age to 45 years of age or younger.[7,14] The United States Preventive Services Task Force recommends screening individuals aged 45 to 49 years with a qualified "B recommendation" (moderate certainty of moderate net benefit), whereas screening from age 50 to 75 years is given an "A recommendation" (high certainty of substantial net benefit).[15] This earlier screening age has not been adopted by other national or provincial guidelines to date.[2]

There are several reasons for not immediately adopting an earlier screening strategy. First, the purported value of earlier screening is based on computer modeling, with several assumptions that have not yet been validated by trial data. Second, cost and resource implications need to be considered given that the proposed target population in BC that is aged 45 to 49 years numbers 322 000.[16] It would be challenging to accommodate such a large population within our current screening program. Furthermore, because the increased incidence of colorectal cancer is affecting all young adults, some could argue that screening should begin even before 45 years of age, which would dramatically increase resource use. Third, while the percentage increase in colorectal cancer among young adults may be notable, the absolute number diagnosed remains substantially lower than the number of adults over 50 years of age who are diagnosed. Finally, one must consider the ramifications of shifting resources from the existing higher-risk screening population who have yet to engage with colon screening, including, among others, rural, marginalized, and Indigenous individuals.

Summary

Approximately 40% of eligible British Columbians in the 50- to 74-year age cohort are up-to-date with screening in the Colon Screening Program, and efforts are ongoing to encourage more participation in that age group. Therefore, the updated BC Guideline for colorectal cancer screening continues to advocate for screening individuals aged 50 to 74 years without adopting an earlier initiation, but it encourages physicians to respond to younger adults who present with symptoms or have a family history of colorectal cancer by evaluating them using colonoscopy where appropriate. ■

In general, there has been a steady decline in both colorectal cancer diagnoses and deaths over the past 20 years.

Competing interests

None declared.

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