Age to Start Colorectal Cancer Screening in Canada: Watching Brief

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Rabeneck L, Brenner DR, Coldman A, Antle S, Dixon C, Du Plessis H, Kilfoil E, Kohle M, McGrath J, Stewart M, Stein B, Stogios C, Telford J, Tinmouth J, Yang H, Baines N, Costa S, Dworkin S, Birago A for the National Colorectal Cancer Screening Network

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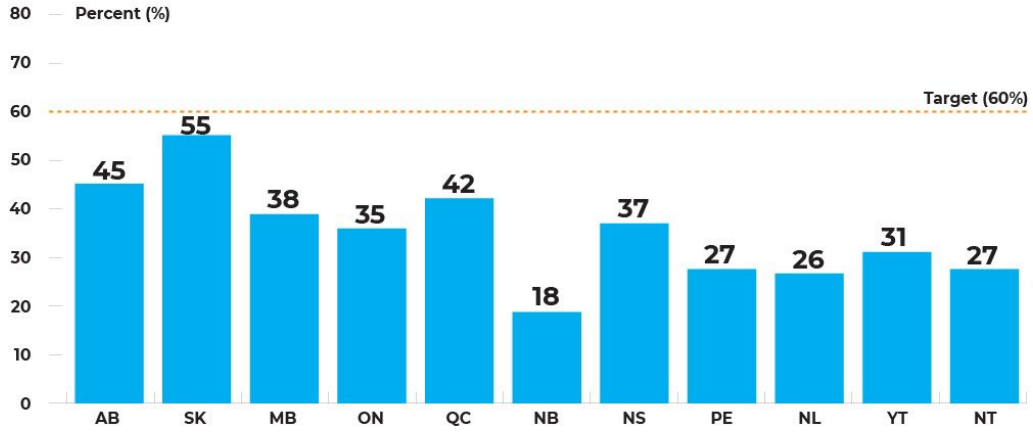
Introduction

Colorectal Cancer (CRC) is the third most commonly diagnosed cancer and second leading cause of cancer deaths in Canada.[1] Evidence shows that CRC screening is associated with a reduction in CRC incidence and CRC mortality.[2] Based on this evidence, beginning in 2008, Canadian provinces and territories have implemented CRC screening of asymptomatic average-risk (no first-degree family history of CRC or personal history of adenoma) individuals aged 50 to 74 years. Screening is done using the fecal immunochemical test (FIT) every two years.[3] Most CRC screening programs in Canada are population-based and administered through provincial and territorial organizations.[4] However, CRC screening participation in Canada falls short of the target of 60%.[3] Figure 1 shows overall participation in the pre-pandemic period, which ranges from 18% to 55%.[3]

Figure 1. Colorectal Cancer Screening Percent Participation Among Canadians Aged 50-74, Who Were Screened with a Fecal Test, By Jurisdiction (2017-2019)



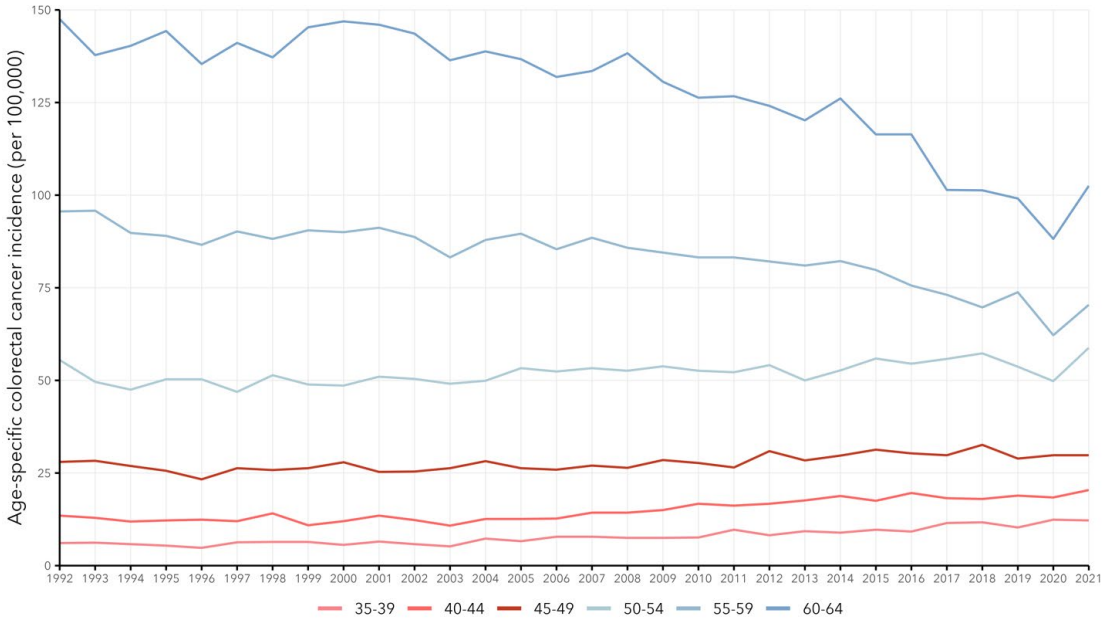
In 2017 a report drew attention to a major shift in the epidemiology of CRC in the US.[5] The reported rise in CRC incidence in younger persons has now been observed in many countries, including Canada.[6] Figure 2 shows temporal trends in age-specific CRC incidence in Canada. What this shows is that the older age groups (in blue), have higher incidence rates than the younger age groups (in red). And, whereas the incidence rates are falling among those over 55, following the implementation of screening in these ages, they are rising in the younger age groups not currently eligible for screening.[a] More detailed analyses (not shown here) that compare rates across birth cohorts estimates that those Canadians born after 1970 have significantly higher CRC incidence rates than those born earlier, and those born after 1980 are approaching 2x the risk of developing CRC compared with those born in 1950.[7] In addition, across Canada, CRC incidence varies considerably and generally follows an east west gradient, with the highest incidence in the Atlantic provinces and the lowest incidence in BC (Figure 3).

While the number and proportion of CRCs diagnosed in Canada before the age of 50 has increased in Canada (Figure 4), CRC incidence among those younger than 50 is considerably lower than for those over age 50. For the past 10 years the incidence for 50-54-year-olds has been greater than 50 cases per 100,000 annually while age groups under 50 range from approximately 12 to 32 cases per 100,000. Of note are the steady increases in ages <45, which has also been observed in multiple countries. The

[a] There is insufficient lead-time for screening conducted in the 50-54 age group to reduce their risk of CRC.

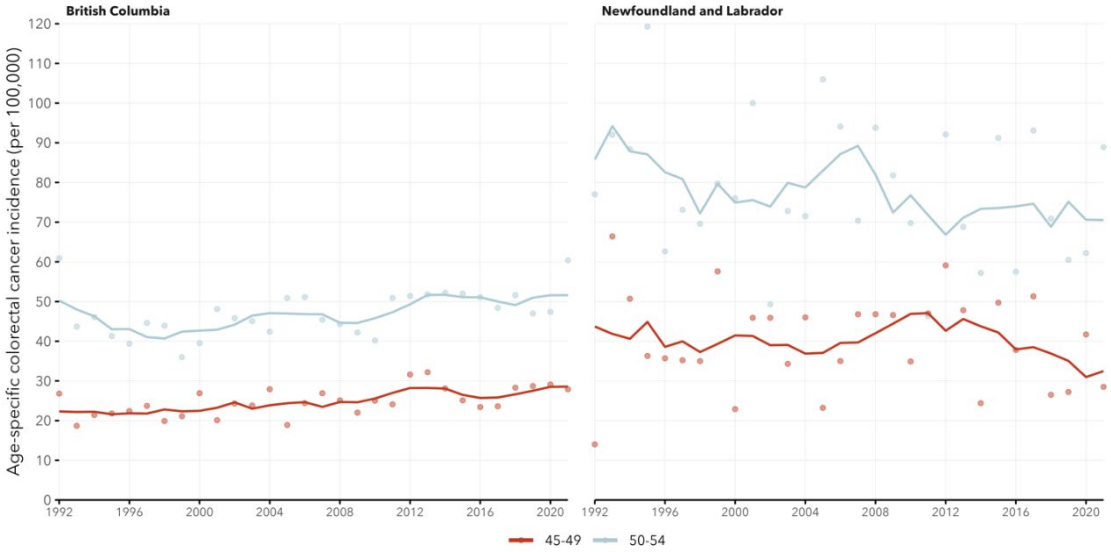
cause of these increases among all younger populations is not yet clear but is currently the focus of intensive study.

Figure 2. Temporal Trends in Colorectal Cancer Incidence in Canada. Age-specific Incidence of Colorectal Cancer By 5-year Age Groups in Canada (excluding Quebec) 1992-2021



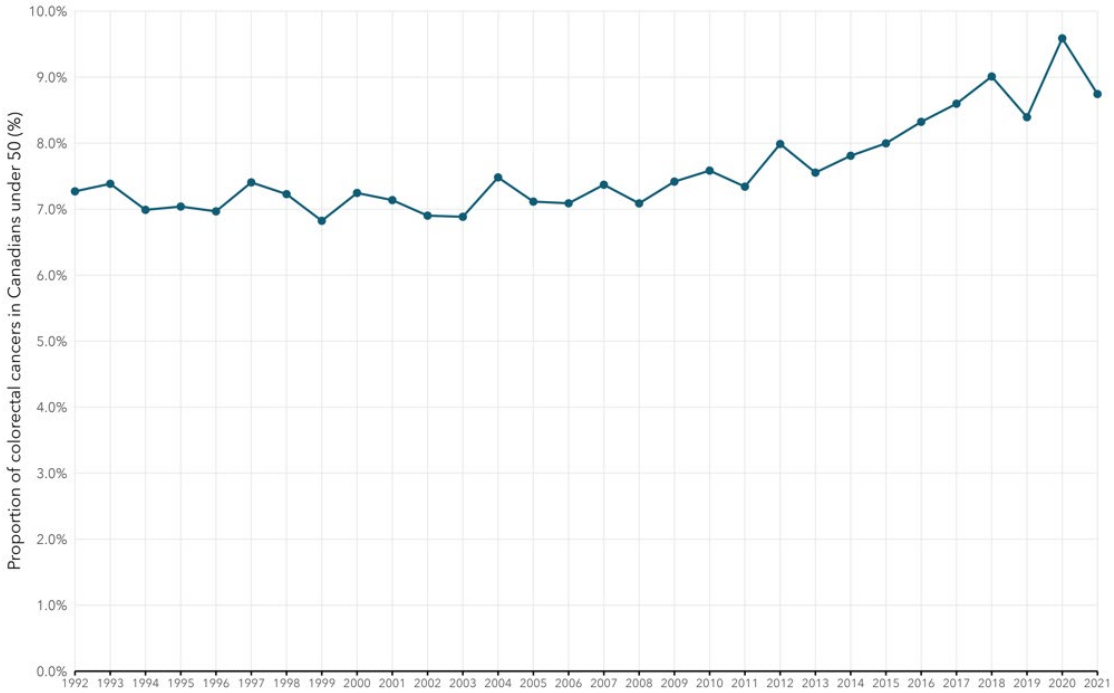
Footnote: Data Source: Centre for Population Health Data, Statistics Canada

Figure 3: Temporal Trends in Colorectal Cancer Incidence in Newfoundland and Labrador and in BC Among People 5 Years Above and Below 50 years of Age



Footnotes: Line represents 5-year age-specific incidence of CRC by 5-year age groups in Canada (excluding Quebec) 1992-2021. Data Source: Centre for Population Health Data, Statistics Canada

Figure 4. The Proportion of Colorectal Cancers in Canada Diagnosed in Those Younger Than Age 50 (1992-2021)



Data Source: Centre for Population Health Data, Statistics Canada

In 2018, in response to the changing epidemiology of the disease, the American Cancer Society recommended lowering the age to start CRC screening from 50 to 45 years.[8] In 2021 the US Preventive Services Task Force (USPSTF), and in 2022 the US Multisociety Task Force (USMSTF) also lowered the recommended age to 45 to start CRC screening.[9,10] The National Health and Medical Research Council of Australia also recommended lowering the age to start screening to age 45 in 2023.[11]

In 2016 the Canadian Task Force on Preventive Health Care (CTFPHC) recommended CRC screening in adults 50-74 years.[12] However, these recommendations have not been updated. Should the recommended age to start CRC screening be lowered in Canada, as has occurred in the US and Australia? The need for guidance was identified as a top priority by the National Colorectal Cancer Screening Network (NCCSN) at its meeting in June 2023.

Approach

In July 2023, the Canadian Partnership Against Cancer (the Partnership) convened an Age to Start CRC Screening Working Group (the "Working Group") to guide the Watching Brief project. The purpose of this project is to summarize and contextualize the evidence on the age to start CRC screening to inform provincial and territorial decision making on lowering the age to start to CRC screening.

Why a Watching Brief?

Recognizing that the body of evidence on the topic is evolving rapidly – in part because of the US experience in screening younger persons that is well underway – the Working Group recognizes the need to update this document as the evidence evolves. Hence the term **Watching Brief**, to indicate that the Working Group is tracking the evidence as it accumulates and will update this document as needed.

The Project

The project consists of two parts. In the first part, the Partnership engaged the Canadian Agency for Drugs and Technology in Health (CADTH) (now Canada's Drug Agency, CDA) to conduct an independent Health Technology Review. When the Working Group convened to discuss the results of the review, it concluded that modeling would be helpful to provide additional insights to support provincial and territorial decision making. In the second part of the project, Dr. Darren Brenner at the University of Calgary, in collaboration with the Partnership's OncoSim team, led a modelling analysis.

CADTH Health Technology Review

The CADTH Health Technology Review was completed in December 2023 and the full report is available.[13]

Research Questions

The Working Group set four questions to be addressed by the CADTH Health Technology Review:

1. What is the effectiveness of colorectal cancer screening in average-risk individuals younger than 50 years versus those aged 50 to 75 years on the incidence of and mortality from colorectal cancer?
2. What is the effectiveness of colorectal cancer screening versus no screening in average-risk individuals younger than 50 years on the incidence of and mortality from colorectal cancer?
3. What is the cost-effectiveness of screening average-risk individuals younger than age 50 years for colorectal cancer?
4. What are the evidence-based guidelines regarding screening average-risk individuals younger than age 50 years for colorectal cancer?

CADTH Health Technology Review Findings

Empirical Evidence

Overall, empirical data describing observations in younger persons of the effectiveness of screening regarding CRC incidence, mortality, and harms were limited. This was attributed to the widespread and longstanding recommendations in most jurisdictions limiting CRC screening to those aged 50 years and older. In fact, as stated in the CADTH report "the dearth of available evidence may have resulted in no eligible studies of relevance identified using observed, empirical data in answer to the second of this report's research questions regarding the effectiveness of colorectal cancer screening versus no screening in individuals of average risk younger than 50 years."

Models

Because of the lack of empirical evidence, CADTH found that published guidelines had based their recommendations about CRC screening in individuals of average risk younger than 50 years on modeling. The models estimate that CRC screening in persons younger than 50 years may produce benefits in

terms of life-years gained, a reduction in CRC incidence and CRC deaths, but this would be accompanied by an increase in lifetime colonoscopies, and potentially an increase in adverse events/harms related to screening.

Models are sensitive to the model inputs and assumptions, the majority of which are based on US inputs, and in several an assumption of 100% screening participation was made, an ideal state that is not attained in any jurisdiction. The effect of lower rates of participation can be inferred by appropriate scaling of results.

Guidelines

CADTH found that seven of eight evidence-based guidelines made recommendations in favour of CRC screening for individuals of average risk younger than 50 years, specifically starting at age 45.

Canadian Modelling Analysis Conducted for this Watching Brief

Given the limited empirical evidence and limitations of published models, a Canadian modeling analysis was conducted to inform this Watching Brief using the Partnership's OncoSim-Colorectal Model. Due to variability in the costs of care across Canada, costs would need to be updated in the model. This was outside the scope of the Watching Brief, and therefore the modeling output did not include QALYs.

OncoSim-Colorectal Model

OncoSim-Colorectal is a microsimulation model of CRC that models the natural history and progression of adenomas (i.e., cancer precursors) and CRC.[14] The analysis estimated lifetime and program impacts of reducing the age to start CRC screening in Canada from 50 to 45 years old using FIT every 2 years. The analysis used four birth cohorts (those born in 1975-79, 1980-84, 1985-89, 1990-94) each followed until age 74 years. The clinical outcomes were CRC incidence and CRC mortality.

The model assumes the program change (lowering the screening age from 50 to 45 years) occurs in 2024 and that screening ends at age 74 years. Participation is assumed to be 43% to the first invitation based on Canadian survey data and recent clinical trial data with 80% adherence to subsequent screening. The FIT cut-off level used to define a positive test was 20µg/gm feces (a commonly used cut-off level).

Canadian OncoSim-Colorectal Model Main Findings

Lowering the age of CRC screening from 50 to 45 years old would result in fewer persons with a diagnosis of CRC and fewer deaths from CRC. It would also require additional FITs and colonoscopies.

To quantitate this, the model estimates that lowering the screening age to 45 years (compared to age 50 years) in persons born from 1970-1994 in Canada over lifetime of the cohorts (screening during 2024-2079) would result in:

- 2.8 fewer incident CRC cases per 100 additional colonoscopies
- 1.8 fewer incident CRC cases per 1000 additional completed FITs
- 1.2 fewer CRC deaths per 100 additional colonoscopies
- 0.7 fewer CRC deaths per 1000 additional completed FITs

And this would mean a total of (2024-2079):

- 12,370 fewer persons diagnosed with CRC

- 5,350 fewer CRC deaths
- 78,676 potential years of life gained

And this would require (2024-2079):

- 7,016,163 additional completed FITs
- 439,894 additional colonoscopies

Age to Start Working Group Proposes a Screening Worksheet

Given the variation in CRC incidence across Canada, the findings of the CADTH review showing limited empirical evidence and considering the findings from the Canadian modeling using OncoSim, the Working Group determined that no single blanket recommendation on lowering the age to start CRC screening would be appropriate at this time.

With that in mind, the Working Group proposes here a Worksheet (Appendix A) to aid provinces and territories to work through their decisions in a structured way by estimating the incremental effects of screening a younger age group. To use the Worksheet, the upper section entitled "Existing Screening Program Experience" is completed. Given that current programs screen those age 50-74 years using FIT, all the information described in the first row (Population Group Age 50-74) would be known by the program, i.e., the population size (N, the number of persons age 50-74 in the province or territory), the number of tests completed per year in those 50-74 (T), the annual testing rate in those 50-74 (R), the annual number of FIT+, the FIT positivity rate (F+R), number of colonoscopies performed following a positive FIT (NC), and the colonoscopy compliance rate (CCR). Note that all this information would have been observed by the program and pertains to those age 50-74.

The next step is to complete the second row in the "Existing Screening Program Experience" section, providing the same information as above, but only for those age 50-54 within the screen eligible group. Again, this information would have been observed by the program. The assumption is that the information pertaining to this (lowest) age group could be used to approximate the experience that would be observed if the age to start screening were lowered to 45-49.

Finally, the lower section entitled "Estimated Added Testing" for those 45-49 who would be added to existing programs is completed for two scenarios. In the first scenario, captured in the first row of this section, the assumed behavior and outcomes in those 45-49 are the same as observed in those 50-74, in other words the annual testing rate (R), FIT positivity rate (F+R) and colonoscopy compliance rate (CCR) are assumed to be the same in those 45-49 and observed in those 50-74. In the second scenario, captured in the second row of this section, the assumed behavior and outcomes are the same as those observed in those 50-54.

In this way, each province and territory can use their existing CRC screening program experience in the current target age group (50-74) and their experience in younger persons (i.e. 50-54 years) in the current target age group to generate two estimates of the added testing (FITs, colonoscopies) that would be needed to screen those 45-49 years.

By using the Worksheet each province and territory can estimate the incremental effects of lowering the age to start screening. They can also use the Worksheet to estimate the incremental effects of increasing participation in the current target age group and contrast the two.

Take-Home Messages

1) Although empirical data describing the effectiveness of CRC screening in younger persons is quite limited at this time, the field is evolving rapidly, and it is likely that evidence will emerge in the next year or two.

2) Regarding the changing epidemiology of CRC in Canada, the most notable increase in CRC incidence rates in younger persons is among those 45-50 years. However, the incidence is also increasing among those in even younger age groups, and a lowering of the age to start CRC screening to age 45 would not address this.

3) If the age to start CRC screening is lowered to 45 years, this would lead to clinical impact in terms of a reduction in CRC incidence and CRC deaths but would require an increase in FIT kits and colonoscopies as well as staffing resources.

4) If a decision is taken to lower the age to start CRC screening, additional resources will be required to ensure this does not adversely impact access to diagnostic colonoscopy.

5) If a decision is taken to lower the age to start CRC screening, there should be a clear plan in place beforehand to monitor and to evaluate the implementation, so that a full picture of its impacts on clinical outcomes and resources can be determined.

6) Regardless of the decision whether to lower the age to start CRC screening, it is important that younger persons with large bowel symptoms, such as rectal bleeding, undergo prompt investigation.

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Appendix A. Age to Start CRC Screening Worksheet

Existing Screening Program Experience

Population Group	Population Size - **N**	Number Tests per Year - **T**	Annual Testing Rate - **R** (=T/N)	Annual Number FIT+ve - **FIT+**	FIT Positivity Rate – **F+R** (=FIT+/T)	Number colonoscopies Performed following +FIT Test - **NC**	Colonoscopy Compliance Rate – **CCR** (=NC / FIT+)
Age 50-74	N_{50-74}	T_{50-74}	R_{50-74}	$FIT+_{50-74}$	$F+R_{50-74}$	NC_{50-74}	CCR_{50-74}
Age 50-54	N_{50-54}	T_{50-54}	R_{50-54}	$FIT+_{50-54}$	$F+R_{50-54}$	NC_{50-54}	CCR_{50-54}

Estimated Added Testing

Added Population	Assumed Behaviour and Outcomes	Added Population Size – **N**	Estimated Added Number Tests per Year - **T**	Estimated Added Annual Number FIT+ve - **FIT+**	Estimated Added Number Colonoscopies after FIT+ve - **NC**
45-49	Same as 50-74	N_{45-49}	$T = N_{45-49} \times R_{50-74}$	$FIT+ = N_{45-49} \times R_{50-74} \times F+R_{50-74}$	$NC = N_{45-49} \times R_{50-74} \times F+R_{50-74} \times CCR_{50-74}$
45-49	Same as 50-54	N_{45-49}	$T= N_{45-49} \times R_{50-54}$	$FIT+ = N_{45-49} \times R_{50-54} \times F+R_{50-54}$	$NC = N_{45-49} \times R_{50-54} \times F+R_{50-54} \times CCR_{50-54}$