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Time Trends in Colorectal Cancer Incidence From 1992 to 2016 and Colorectal Cancer Mortality From 1980 to 2018 by Age Group and Geography in Canada

Kathleen M. Decker, PhD[1,2,3], Pascal Lambert, MSc[2,3], Jen Bravo, MSc[3], Alain Demers, PhD[4] and Harminder Singh, MD, MPH[1,2,5]

INTRODUCTION: **Several reports have highlighted increasing colorectal cancer (CRC) incidence among younger individuals. However, little is known about variations in CRC incidence or mortality across age subgroups in different geographical locations. We aimed to examine time trends in CRC incidence and mortality in Canada by age group and geography in this population-based, retrospective cohort study.**

METHODS: **Individuals diagnosed with CRC from 1992 to 2016 or who died of CRC from 1980 to 2018 in Canada were studied. Geography was determined using an individual's postal code at diagnosis from the Canadian Cancer Registry or province or territory of death from the Canadian Vital Statistics Death Database. Geography was categorized into Atlantic, Central, Prairies, West, and Territories. Canadian Cancer Registry data were used to determine CRC incidence from 1992 to 2016. Canadian Vital Statistics Death data were used to determine CRC mortality from 1980 to 2018.**

RESULTS: **Among all age groups, CRC incidence was highest in Atlantic Canada, was lowest in Western Canada, and increased with age. CRC incidence increased over time for individuals aged 20–44 years and was stable or decreased for other age groups in all regions. CRC mortality was highest in Atlantic Canada and lowest in the Prairies and Western Canada. CRC mortality decreased for individuals in all age groups and regions except among individuals aged 20–49 years in the Territories.**

DISCUSSION: **Most of Canada has not yet seen an increase in CRC burden in the age group of 45–49 years, which is a reason to not lower the start age for CRC screening in Canada. Targeted CRC screening should be considered for individuals younger than 50 years who live in the Territories.**

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/AJG/C725

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INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer worldwide (1) and in North America and is the second and the third most common cause of cancer-related deaths among men and women, respectively (2). CRC incidence shows large variations in time trends and between age groups depending on jurisdiction. Several reports have highlighted increasing incidence among individuals younger than 50 years in North America (3–8). In the United States, early-onset CRC has been reported to be increasing most rapidly among White individuals in western states (9). However, the population structure, CRC screening, and healthcare delivery are different in Canada than those in the United States. For example, rates of obesity have been lower among Canadians than Americans, particularly among young women. In the United States, most of the non-White population is Black or Hispanic, whereas among non-White Canadians, the largest group comprises individuals of East/Southeast Asian heritage (10). The increasing rate of obesity is one of the proposed factors responsible for the increase in CRC risk among the young, and CRC risks vary by ethnic/racial background (11).

Little is known about the variation in CRC incidence across age groups in different areas in Canada. There are also limited data about CRC mortality across age groups by regions in Canada.

A detailed analysis of CRC epidemiology is essential to guide studies on CRC etiopathogenesis (gene, lifestyle, and environment interactions) and to target CRC screening activities. The United States has moved to initiate CRC screening at age 45 years due to increasing early-onset CRC incidence (12). Additional data on CRC epidemiology in Canada are essential to guide any changes. The objective of this study was to examine

[1]Department of Community Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada; [2]CancerCare Manitoba Research Institute, Winnipeg, Manitoba, Canada; [3]Department of Epidemiology and Cancer Registry, CancerCare Manitoba, Winnipeg, Manitoba, Canada; [4]Public Health Agency of Canada, Ottawa, Ontario, Canada; [5]Department of Internal Medicine, University of Manitoba, Winnipeg, Manitoba, Canada. **Correspondence:** Kathleen M. Decker, PhD. E-mail: kdecker@cancercare.mb.ca.

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time trends in CRC incidence and mortality in Canada by age group and geography.

METHODS

Study design and population

We performed a population-based retrospective cohort study. Individuals diagnosed with CRC from 1992 to 2016 or who died of CRC from 1980 to 2018 in Canadian provinces and territories were included. Data from Québec were not available. CRC cases were determined using the *International Classification of Diseases for Oncology, Third Edition* (*ICD-O-3*) codes. The following *ICD-O-3* codes were included: C18.0 (cecum), C18.2-C18.9 (ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon, sigmoid colon, large intestine [not otherwise specified]), C19.9 (rectosigmoid junction), C20.9 (rectum), and C26.0 (malignant neoplasm of intestinal tract, part unspecified) (13). These codes are used by Canadian Cancer Statistics publications to define CRC. We excluded the following morphology codes: 905 (mesothelial neoplasms), 9140 (Kaposi sarcoma), and 9590–9992 (lymphomas). We also excluded appendix cancers as they are not affected by screening. Cause of death was determined using *ICD* version 9 codes from 1980 to 1999 and *ICD* version 10 codes from 2000 to 2018. The following *ICD* codes were used: *ICD-9* 1530–1539 (excluding 1535), 1540, 1541, and 1590; *ICD-10* C18.0–C18.9 (excluding C18.1), C19.9, C20.9, and C26.0.

Data sources

We used data (age at diagnosis and area of residence) from the Canadian Cancer Registry (CCR) to determine CRC incidence in Canada from 1992 (the year the CCR was created) to 2016. The CCR is a person-level database that includes clinical (tumor location, histological subtype, and grade) and demographic (including 6-digit postal code) information about Canadian residents diagnosed with new cases of cancer (14). The CCR was also used to determine stage at diagnosis. Stage data were available from 2010 to 2016. We used data from the Canadian Vital Statistics Death Database from 1980 to 2018 to determine CRC mortality (15). The Canadian Vital Statistics Death Database collects demographic and medical (cause of death) information and province or territory of occurrence of death on all deaths in Canada. Cause of death information was not available for 2019 or 2020. Deaths that occurred in the United States were excluded because this information was available only until 2009.

Statistical analysis

CRC incidence rates were calculated by geography (Atlantic, Central, Prairies, West, and Territories) and age group (20–29, 30–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85–89, and 90+ years) for five 5-year time periods (1992–1996, 1997–2001, 2002–2006, and 2007–2011) and one 4-year time period (2012–2016). Because of small numbers, CRC incidence rates were calculated separately for the Territories for 3 age groups (20–49, 50–74, and 75+ years). CRC incidence rates were also calculated by stage (early: stages I and II; late: stages III and IV) from 2010 to 2016 for 3 age groups (20–49, 50–74, and 75+ years). Because of the low number of cases, the Territories were excluded.

CRC mortality rates were calculated by the same geographical locations and age groups (20–29 and 30–39 age groups were combined) for seven 5-year time periods (1980–1984, 1985–1989, 1990–1994, 1995–1999, 2000–2004, 2005–2009, and 2010–2014) and one 4-year time period (2015–2018). Because of the low number of cases, CRC mortality rates were calculated for the Territories for three 10-year time periods (1980–1989, 1990–1999, and 2000–2009) and one 9-year time period (2010–2018).

The average percent change (APC) in CRC incidence and mortality over each time period by age and geography was calculated using the Joinpoint Regression Program (version 4.8.0.1 developed by Surveillance Epidemiology and End Results, National Cancer Institute, Bethesda, MD). We used the default settings (minimum of 0 Joinpoint and maximum of 1 Joinpoint, a permutation test with an overall significant level of 0.05 for model selection, and a constant variance). Analyses with *P* values less than 0.05 indicate a significant change in the APC over the time period.

To ensure confidentiality, all counts were randomly rounded to a lower or higher multiple of 5, as Statistics Canada requires for releasing tables and figures. Analyses were conducted using R (version 4.0.5; R Foundation for Statistical Computing, Vienna, Austria) and SAS (version 9.4; SAS Institute, Cary, NC). This study was approved by the University of Manitoba's Health Research Ethics Board and the Research and Resource Impact Committee at CancerCare Manitoba.

RESULTS

Incidence

There were 349,505 cases of CRC diagnosed in Canadians from 1992 to 2016. A total of 43,605 CRC cases were diagnosed among individuals who resided in Atlantic Canada, 173,250 in Central Canada, 72,330 in the Prairies, 60,320 in Western Canada (see Supplementary Table 1, http://links.lww.com/AJG/C725), and 1,040 in the Territories (see Supplementary Table 2, http://links.lww.com/AJG/C725). Figure 1 illustrates the time trend in Joinpoint-predicted CRC incidence rate per 100,000 by age group for Atlantic, Central, Prairies, and Western Canada from 1992 to 2016 and Figure 2 for the Territories. Corresponding statistics for trends are provided in the Supplementary Digital Content (see Supplementary Tables 3 and 4, http://links.lww.com/AJG/C725).

Among all age groups, CRC incidence was highest in Atlantic Canada, was lowest in Western Canada, and increased with age. CRC incidence increased over time in all regions for individuals aged 20–39 (APC Atlantic 2.3, 95% confidence interval [CI] 1.0–3.6, Central 2.1, 95% CI 1.6–2.6, Prairies 2.4, 95% CI 1.7–3.1, and West 2.0, 95% CI 0.8–3.2) and 40–44 years (APC Atlantic 0.5, 95% CI 0.06–1.6, Central for 2003–2016 3.5, 95% CI 2.2–4.7, Prairies 1.9, 95% CI 1.1–2.8, and West for 1997–2016 2.5, 95% CI 1.6–3.5), which is consistent with prior Canadian studies (7). CRC incidence rates were relatively stable for those aged 45-49 years (APCs from –0.2, 95% CI –0.9 to 0.8 in Atlantic Canada to 0.6, 95% CI –0.2 to 1.4 in the Prairies) and for those aged 50–54 years (APCs from −0.4, 95% CI −1.1 to 0.3 in Atlantic Canada to 1.0, 95% CI 0.3–1.7 in Western Canada) and decreased primarily after 2002 for individuals aged 55–74 years in all regions except for the 70–74 age group in Atlantic Canada (APC 0.2, 95% CI −0.1 to 0.6). For individuals aged 75 years and older, CRC incidence decreased or remained stable for all regions but started dropping rapidly in recent years, mostly in Central Canada (APC −26.8, 95% CI −43.9 to −4.4 for 2014–2016). In the Territories, CRC incidence rates increased steadily among those in the age group of 20–49 years (APC 6.4, 95% CI −1.7 to 15.1), decreased but not significantly since 2000–2001 in the age group of 50–74 years

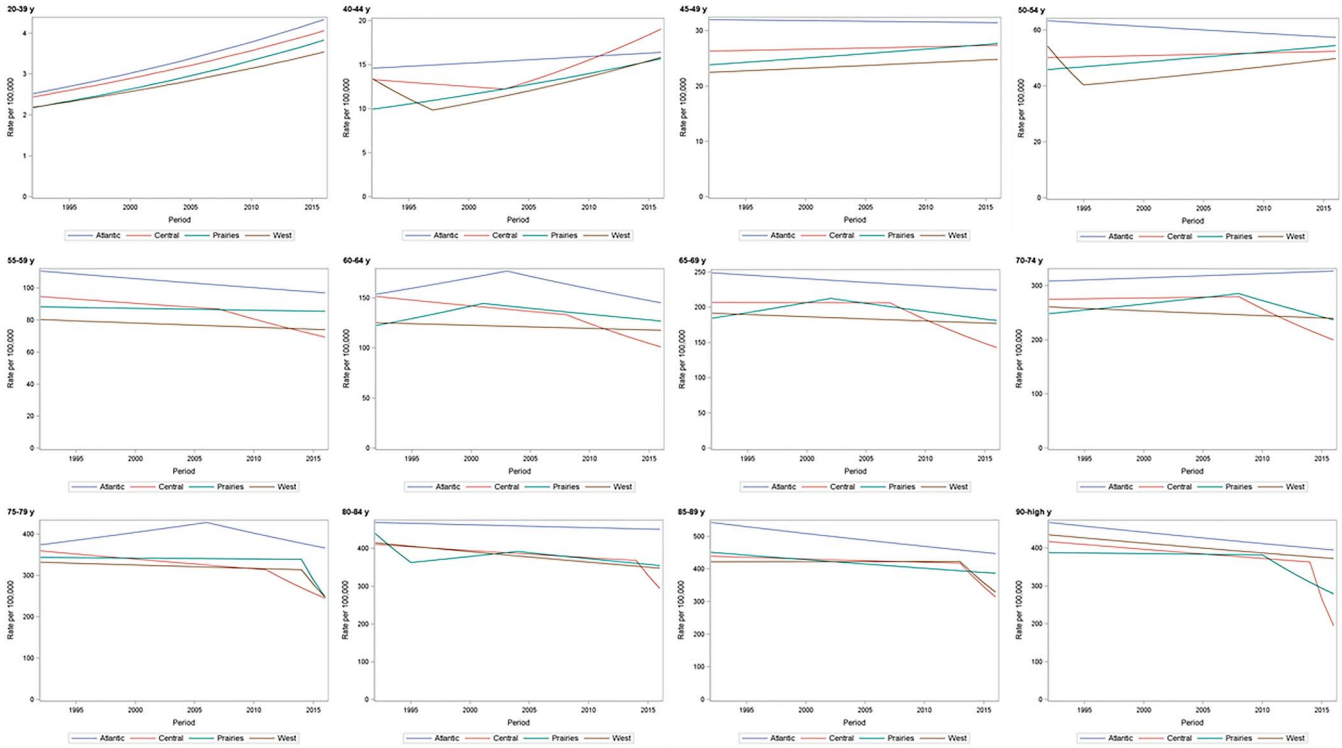

Figure 1. Time trends in CRC incidence rate per 100,000 individuals by age group for Atlantic, Central, Prairies, and Western Canada, 1992–2016. CRC, colorectal cancer.

(APC −3.0, 95% CI −10.3 to 4.9), and remained stable in the age group of 75+ years (APC 0.4, 95% CI −6.7 to 8.0).

In stratified analyses for stage, most of the patterns were not statistically significant, likely because of the small number of cases. However, there was a trend toward early-stage CRC decrease in all age groups and regions except for individuals aged 50–74 years in Western Canada and those aged 20–49 years in Atlantic Canada and the Prairies. The incidence of late-stage CRC tended to increase for the age group of 20–49 years in all regions except Atlantic Canada (see Supplementary Tables 5 and 6 and Figure 1, http://links.lww.com/AJG/C725).

Mortality

From 1980 to 2018, 268,410 individuals in Canada died of CRC. Of these individuals, 25,935 resided in Atlantic Canada, 171,205 in Central Canada, 39,040 in the Prairies, 31,790 in Western Canada (see Supplementary Table 7, http://links.lww.com/AJG/C725), and 440 in the Territories (see Supplementary Table 8, http://links.lww.com/AJG/C725). Figure 3 illustrates the time trend in Joinpoint-predicted CRC mortality rate per 100,000 by age group for Atlantic, Central, the Prairies, and Western Canada from 1992 to 2018 and Figure 4 for the Territories. Corresponding statistics for trends are provided in the Supplementary Digital Content (see Supplementary Tables 9 and 10, http://links.lww.com/AJG/C725).

For all age groups, the CRC mortality rate per 100,000 individuals was highest in Atlantic Canada and lowest in the Prairies or Western Canada. CRC mortality decreased for individuals aged 20–39 years but was significant only for those living in Central Canada (APC −10.2, 95% CI −14.7 to −5.4). The most recent trends indicate that CRC mortality significantly decreased for individuals in all other age groups in all regions. By contrast, CRC mortality among individuals aged 20–49 years increased in the Territories, although not significantly (APC 19.4, 95% CI −34.5 to 117.4). CRC mortality decreased among individuals aged 50–74 years in the Territories, but the decrease was not significant (APC −9.1, 95% CI −38.5 to 34.4). Among those older than 75 years in the Territories, CRC mortality significantly decreased (APC −14.0, 95% CI −25.0 to −1.4).

DISCUSSION

In this study, we observed that CRC incidence was highest in Atlantic Canada and lowest in Western Canada. The higher rates in Atlantic Canada were consistent in all age groups. CRC mortality was also highest in Atlantic Canada, was lowest in Western Canada, and decreased among all age groups in all regions except for individuals aged 20–49 years in the Territories. Although not statistically significant, the increasing mortality rate among younger individuals in the Territories is unique within Canada. The percentage of individuals who identify as First Nations or Inuit is 21.8% in the Yukon, 48.7% in the Northwest Territories, and 85.4% in Nunavut. Data from the United States also show that American Indian/Alaska Native individuals have an increased risk of CRC mortality compared with White individuals (16). Our results suggested that targeted CRC screening protocols should be considered for all individuals who live in the Territories, including those younger than 50 years.

The United States has moved toward starting CRC screening at age 45 years among all groups, primarily based on increasing incidence among those aged 40–49 years. However, our data suggest that there is no such trend in Canada; we report that CRC incidence increased slightly or was stable for those aged 45–49 years and CRC

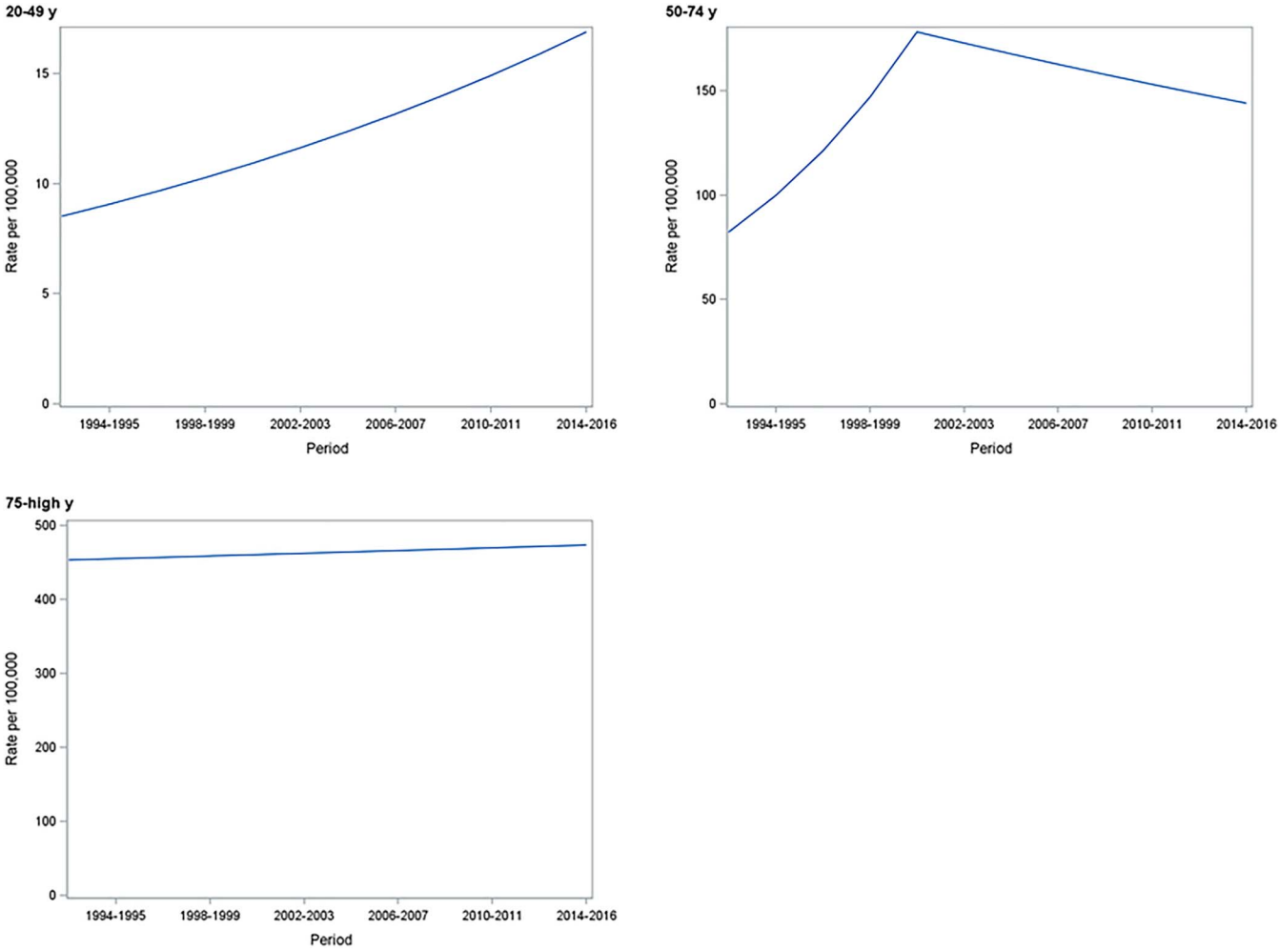

Figure 2. Time trends in CRC incidence rate per 100,000 individuals by age group in the Territories, Canada, 1992–2016. CRC, colorectal cancer.

mortality decreased in this age group. The contrast between US and Canadian patterns suggests that each country should investigate rates by age group and region before moving toward adopting the US guidelines. In addition, the large drop in CRC mortality in this age group in most of Canada should be communicated to the public to allay fears of immediate impact of international patterns of increasing CRC incidence among the youth.

Increasing CRC incidence without a concomitant increase in CRC mortality among individuals aged 20–39 years supports the need for additional research to determine the etiopathogenesis of these changes and the need to continuously monitor the trend to assess the magnitude of CRC risks in different age groups. The use of colonoscopy has increased in all age groups (17). The incidence of late-stage CRC increased for the age group of 20–49 years in all regions except Atlantic Canada although previous research has suggested that early-age onset CRC is more often diagnosed at a later stage (18). Research examining the etiology of early-onset CRC focusing on lifestyle, environmental factors, and the microbiome is ongoing (19).

The reduction in CRC incidence and mortality rates among individuals aged 55–74 years is likely related to the increasing CRC screening in North America over the past 20 years and improved treatments. Canadian guidelines recommend CRC screening for individuals aged 50–75 years and the implementation of population-based CRC screening programs for average-risk, asymptomatic individuals (20). Organized CRC screening programs in Canada were implemented at the beginning of 2007 in Alberta and Manitoba, followed by Ontario in 2008, Saskatchewan and Nova Scotia in 2009, Prince Edward Island in 2011, Newfoundland and Labrador in 2012, British Columbia in 2013, New Brunswick in 2014, and the Yukon in 2017 (21). Organized programs are currently in the planning stages or under development in the Northwest Territories, Nunavut, and Québec (21). Before the implementation of provincial screening programs, CRC screening participation was low; in 2003, 23.5% of individuals reported any history of CRC screening (22). By 2012, screening rates had increased significantly, and the prevalence of self-reported up-to-date CRC screening in Canada was 55.2% (23). There were large differences between provinces and territories; up-to-date screening rates ranged from 41.3% in the Territories to 67.2% in Manitoba (23). The lower screening rates in the Territories, along with increased risk factors for CRC and differences in access to treatment and socioeconomic status, may be reflected in the higher CRC incidence rates observed among individuals aged 50–74 years in the Territories. Participation rates for CRC screening are lower among First Nations, Inuit, and Métis compared with non-Indigenous people in Canada, although there is considerable

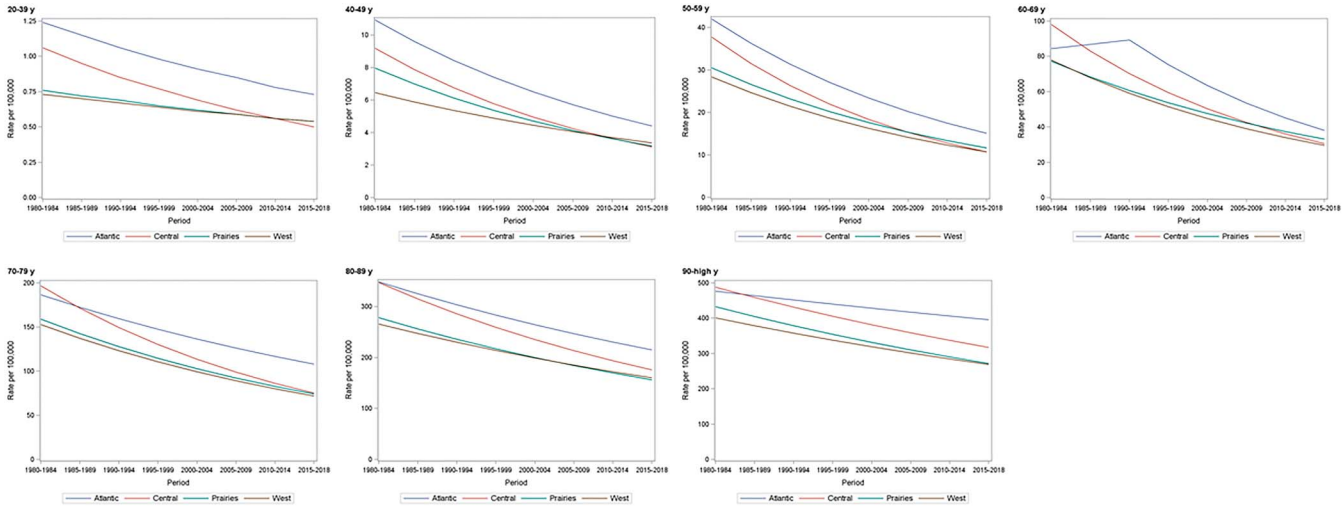

Figure 3. Time trends in CRC mortality rate per 100,000 individuals by age group in Atlantic, Central, Prairies, and Western Canada, 1980–2018. CRC, colorectal cancer.

variation by geographic location (24). As a result, most provinces and Territories have implemented strategies to connect with First Nations, Inuit, and Métis communities to increase screening

populations (21). A specific mutation in the PMS2 gene, a DNA mismatch repair gene that predisposes an individual to CRC, has been reported in a very high frequency (1 in 16 individuals) in a

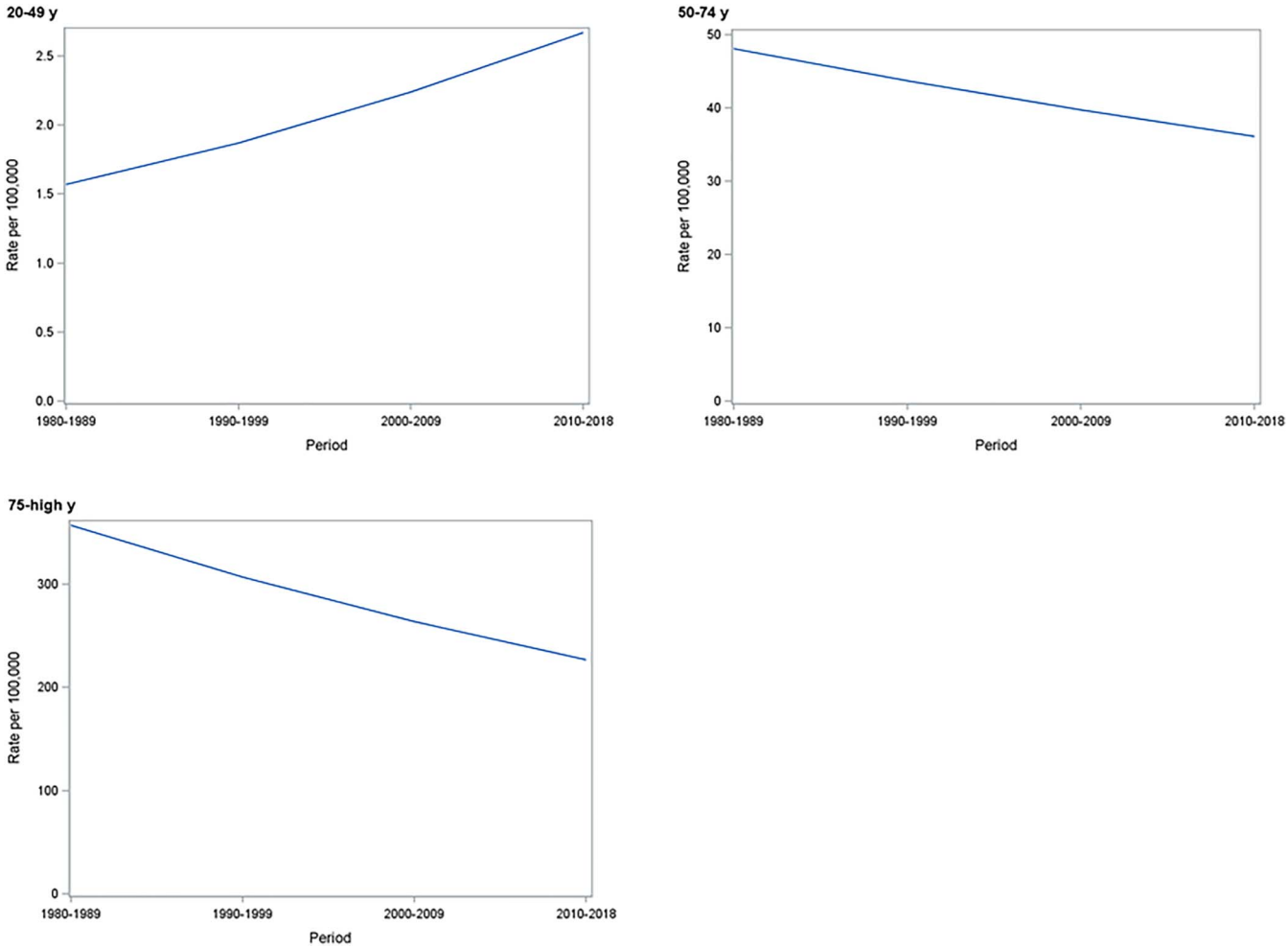

Figure 4. Time trends in CRC mortality rate per 100,000 individuals by age group in the Territories, Canada, 1980–2018. CRC, colorectal cancer.

specific area of the Territories (25). Although this alone could not be the reason for differential CRC epidemiology because the population of the affected area was only 12,090 in 2011, the widespread availability of genetic testing is essential to detect individuals with hereditary predisposition for CRC, followed by recommended surveillance. In addition to differences in CRC screening rates, ethnic and lifestyle differences across Canada could also be contributing to differences in CRC epidemiology across the country. There is a higher proportion of individuals of European descent in Atlantic Canada and from Asia in Western Canada (26). Historically, obesity and smoking rates have been higher in Atlantic Canada (27).

The results of this study should be interpreted in the context of its strengths and limitations. We used data from the CCR, the population-based database that collates information on cancer incidence from all provincial and territorial cancer registries in Canada since 1992. The quality of the data is continuously monitored to ensure that the information in the CCR meets the standards for acceptance in international publications such as Cancer Incidence in Five Continents and Cancer Incidence in North America (28). The percentage of cases that were missing postal codes at diagnosis was low. Individuals from Québec were not included because data were available only until 2010. We did not examine trends in CRC incidence or mortality rates among different age groups and geography by sex. Finally, because of rounding, estimated rates may deviate more from actual rates for subgroups with smaller counts, such as the younger age groups.

In conclusion, our study suggests that time trends of early-onset CRC are different in Canada than that previously reported in the United States, and Canada can potentially wait to reduce the age of onset of CRC screening. We have identified the Canadian Territories as an area which might benefit from targeted CRC screening. Our data on decreasing CRC mortality across the age groups across much of Canada are reassuring.

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CONFLICTS OF INTEREST

Guarantor of the article: Kathleen M. Decker, PhD.

Specific author contributions: K.M.D.: conceptualization, funding acquisition, methodology, project administration, supervision, writing original draft and review and editing. P.L.: conceptualization, formal analysis, methodology, supervision, writing—review and editing. J.B.: formal analysis, methodology, writing—review and editing. A.D.: conceptualization, funding acquisition, methodology, writing—review and editing. H.S.: conceptualization, funding acquisition, methodology, writing original draft and review and editing. All authors have read and agreed to the published version of the manuscript.

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Potential competing interests: None to report.

Institutional review board statement: This study was conducted according to the guidelines of the Declaration of Helsinki and approved by the University of Manitoba's Health Research Ethics Board (HS21853, H2018:217), Manitoba Health's Health Information Privacy Committee, Statistics Canada, and CancerCare Manitoba's Research and Resource Impact Committee. Because data were deidentified, informed consent was not required.

Study Highlights

WHAT IS KNOWN

- ✓ Colorectal cancer (CRC) incidence shows large variations in time trends and between age groups depending on jurisdiction.
- ✓ Several reports have highlighted increasing incidence among individuals younger than 50 years.

WHAT IS NEW HERE

- ✓ In Canada, CRC incidence increased over time for individuals aged 20–44 years and was stable or decreased for other age groups in all regions.
- ✓ CRC mortality significantly decreased for individuals in all age groups and regions except among individuals aged 20–49 years in the Territories.

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