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ORIGINAL ARTICLE

Increasing Colorectal Cancer Incidence Before and After Age 50: Implications for Screening Initiation and Promotion of "On-Time" Screening

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Abstract

Background Early onset colorectal cancer (CRC) incidence is rising under age 50, with a birth cohort effect for increasing incidence among individuals born 1950 and later. It is unclear whether increasing incidence trends will confer increased risk beyond age 50, the previously most commonly recommended age to initiate screening, when screening availability might modify incidence trends.

Aim Evaluate US trends in colorectal cancer (CRC) for ages 40–59 years.

Methods We analyzed counts and incidence rates for CRC, including by anatomic subsite, using the US Cancer Statistics dataset covering 100% of the population 2003–2017. Joinpoint regression was used to quantify Average Annual Percent Change (AAPC) in cancer incidence by age subgroup.

Results 470,458 CRC cases were observed age 40–59, with absolute numbers of rectal ($n=4173$) and distal cases ($n=3327$) per year for age 50–54 approaching age 55–59 cases for rectal ($n=4566$) and distal ($n=3682$) cancer by 2017. Increasing early onset rectal cancer incidence per 100,000 occuring under age 50 was observed to extend to age 50–54, from 4.9 to 6.3 for age 40–44 (AAPC 2.1; 95% CI 1.5–2.7), 9.3 to 12.0 for age 45–49 (AAPC 1.5; 95% CI 1.1–1.4), and from 16.7 to 19.5 for age 50–54 (AAPC 1.0; 95% CI 0.7–1.3).

Conclusions CRC trends suggest observed increased risks under age 50 are also present after age 50, despite prior availability of screening for this group. Recent CRC trends support initiation of screening earlier than age 50, and promotion of "on-time" screening initiation.

Keywords Colorectal cancer screening · Epidemiology · Early onset colorectal cancer · Young onset colorectal cancer · On-time screening

Drs. Cho and Siegel contributed equally to this research, and share co-first authorship.

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Introduction

Colorectal cancer (CRC) incidence rates among adults younger than 50 years are increasing, and have been attributed to a birth cohort effect after 1950 [1]. Since 2011, CRC incidence rates have also been increasing by 1% per year among ages 50–64 years [2]. These observations have led to recommendations to lower the screening initiation age to 45 years from the previously recommended 50 years, and to concerns regarding how to promote "on-time" screening at guideline-recommended ages to initiate screening [2–8]. Differences by anatomic subsite have implications for understanding risk factors and informing cancer prevention and control strategies [1, 9]. Anatomic distribution of increases among adults aged < 50 years and changes in absolute numbers of cases have not been reported in detail by 5-year age

group. To address these evidence gaps, we examined recent CRC incidence trends, stratified by anatomic subsite, among individuals age 40–59. The age range examined was just before and after age 50 years—the historically most commonly recommended initiation age for CRC screening [5–7].

Methods

We analyzed CRC incidence data from United States Cancer Statistics (USCS), which provides 100% coverage of cancer incidence for all 50 states and the District of Columbia, utilizing the Centers for Disease Control and Prevention (CDC) National Program of Cancer Registries and the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program [10]. Cancer subsites were defined as proximal (C18.0, C18.2–C18.5), distal (C18.6–C18.7), and rectal (C19.9, C20.9), and limited to primary colorectal adenocarcinomas [11]. Incidence rates were calculated using SEER*Stat v8.3.5, with rates expressed per 100,000 persons and age-adjusted to the 2000 U.S. standard population. The Joinpoint Regression Program (v4.8.0.1) was used to quantify Average Annual Percent Change (AAPC). AAPCs different from zero at $p < 0.05$ were considered to have a statistically significant "increase" or "decrease," and otherwise were considered "stable."

Table 1 Cases, rates, and fixed-interval trends of colorectal cancer subsites by age, adults aged 40–59 years, US Cancer Statistics, 2003–2017

Characteristic	Period of diagnosis				2003–2017		
	2003		2017				
	Count	Rate (95% CI)	Count	Rate (95% CI)	Count	Rate (95% CI)	AAPC (95% CI)
Total	29,047	35.4 (35.0–35.8)	32,155	34.8 (34.4–35.2)	470,458	34.4 (34.3–34.5)	− 0.1 (− 0.4–0.3)
Diagnosis age, y							
40–44	3069	13.4 (12.9–13.9)	3,099	15.8 (15.3–16.4)	47,148	14.8 (14.7–14.9)	1.3 (1.0–1.6)*
45–49	5383	24.8 (24.1–25.5)	6,087	29.1 (28.4–29.8)	87,622	26.7 (26.5–26.8)	1.1 (0.8–1.4)*
50–54	9104	47.7 (46.7–48.7)	10,512	49.2 (48.3–50.2)	154,123	47.9 (47.6–48.1)	0.3 (0.0–0.7)
55–59	11,491	72.7 (71.3–74.0)	12,457	56.7 (55.7–57.7)	181,565	61.8 (61.5–62.0)	− 1.8 (− 2.2–− 1.3)*
Rectum	10,224	12.5 (12.2–12.7)	12,484	13.6 (13.4–13.9)	174,713	12.9 (12.8–12.9)	0.5 (− 0.2–− 1.3)
Diagnosis age, y							
40–44	1,123	4.9 (4.6–5.2)	1,239	6.3 (6.0–6.7)	18,447	5.8 (5.7–5.9)	2.1 (1.5–2.7)*
45–49	2011	9.3 (8.9–9.7)	2506	12.0 (11.5–12.5)	34,714	10.6 (10.5–10.7)	1.5 (1.1–2.0)*
50–54	3189	16.7 (16.1–17.3)	4173	19.5 (19.0–20.2)	57,240	17.6 (17.6–17.9)	1.0 (0.7–1.3)*
55–59	3901	24.7 (23.9–25.5)	4566	20.8 (20.2–21.4)	64,312	21.9 (21.7–22.0)	− 1.2 (− 2.2–− 0.1)*
Distal Colon	8818	10.8 (10.5–11.0)	9986	10.9 (10.7–11.1)	143,803	10.6 (10.5–10.6)	0.2 (− 0.7–1.1)
Diagnosis age, y							
40–44	936	4.1 (3.8–4.4)	1,039	5.3 (5.0–5.6)	14,699	4.6 (4.5–4.7)	2.0 (1.5–2.4)*
45–49	1646	7.6 (7.2–8.0)	1938	9.3 (8.9–9.7)	26,847	8.2 (8.1–8.3)	1.5 (1.1–1.8)*
50–54	2900	15.2 (14.6–15.7)	3327	15.6 (15.1–16.1)	48,891	15.2 (15.0–15.3)	0.4 (− 0.2–1.1)
55–59	3336	21.1 (20.4–21.8)	3682	16.8 (16.2–17.3)	53,366	18.2 (18.0–18.3)	− 1.7 (− 2.6–− 0.7)*
Proximal Colon	10,005	12.2 (11.9–12.4)	9685	10.3 (10.1–10.5)	151,942	11.0 (11.0–11.1)	− 1.2 (− 2.1–− 0.3)*
Diagnosis age, y							
40–44	1010	4.4 (4.1–4.7)	821	4.2 (3.9–4.5)	14,002	4.4 (4.3–4.5)	− 0.1 (− 0.6–0.4)
45–49	1726	7.9 (7.6–8.3)	1643	7.9 (7.5–8.2)	26,061	7.9 (7.8–8.0)	0.0 (− 0.3–0.4)
50–54	3015	15.8 (15.2–16.4)	3012	14.1 (13.6–14.6)	47,992	14.9 (14.8–15.0)	− 0.6 (− 1.0–− 0.3)*
55–59	4254	26.9 (26.1–27.7)	4209	19.2 (18.6–19.8)	63,887	21.7 (21.6–21.9)	− 2.3 (− 2.8–− 1.8)*

Source: United States Cancer Statistics

Abbreviation: AAPC = Average Annual Percent Change

Rates for ages 40–59 years are per 100,000 persons and age-adjusted to the 2000 U.S. standard population. Trends were measured with AAPC and were considered to increase or decrease if the 95% CI excluded 0 ($p < 0.05$); otherwise, trends were considered stable

*Indicates significant AAPC

Results

From 2003 to 2017, 470,458 cases of CRC were recorded among ages 40–59 years (Table 1). For all ages combined, rates were stable, with overall CRC incidence per 100,000 observed to be 35.4 in 2003 and 34.8 in 2017 (AAPC − 0.1; 95% CI: − 0.4–0.3). By age, overall CRC incidence per 100,000 increased between 2003 and 2017 from 13.4 to 15.8 for ages 40–44 years (AAPC 1.3; 95% CI 1.0–1.6) and from 24.8 to 29.1 for ages 45–49 years (AAPC 1.1; 95% CI 0.8–1.4). CRC incidence between 2003 and 2017 was stable for ages 50–54 years (AAPC 0.3; 95% CI: 0.0–0.7) and decreased from 72.7 to 56.7 for ages 55–59 years (AAPC − 1.8; 95% CI − 2.2–− 1.3).

Absolute number of rectal cancer cases per year increased from 1123 to 1239 for ages 40–44 years, 2011 to 2506 for ages 45–49 years, 3189 to 4173 for ages 50–54 years, and 3901 to 4566 for ages 55–59 years between 2003 and 2017 (Fig. 1). Rectal cancer incidence per 100,000 was stable for all ages combined between 2003 and 2017 (AAPC 0.5; 95% CI: − 0.2–1.3), but increased from 4.9 to 6.3 for ages 40–44 years (AAPC 2.1; 95% CI 1.5–2.7), 9.3 to 12.0 for ages 45–49 years (AAPC 1.5; 95% CI 1.1–1.4), and 16.7 to 19.5 for ages 50–54 years (AAPC 1.0; 95% CI 0.7–1.3). Incidence per 100,000 decreased from 24.7 to 20.8 for ages 55–59 years (AAPC − 1.2; 95% CI − 2.2–− 0.1; Fig. 2 and Table 1).

Absolute number of distal colon cancer cases per year increased from 936 to 1039 for age 40–44, 1646 to 1938 for ages 45–49 years, 2900 to 3327 for ages 50–54 years, and 3336 to 3682 for ages 55–59 years between 2003 and 2017 (Fig. 1). From 2003 to 2017, distal colon cancer incidence per 100,000 was stable for all ages combined between 2003 and 2017 (AAPC 0.2; 95% CI: − 0.7–1.1), but increased from 4.1 to 5.3 for ages 40–44 years (AAPC 2.0; 95% CI 1.5–2.4), and from 7.6 to 9.3 for ages 45–49 years (AAPC 1.5; 95% CI 1.1–1.8). Distal colon cancer incidence per 100,000 between 2003 and 2017 was stable for ages 50–54 years (15.2 in 2003 vs 15.6 in 2017, AAPC 0.4, 95% CI − 0.2–1.1) and decreased from 21.1 to 16.8 for ages 55–59 years (AAPC − 1.7; 95% CI − 2.6–− 0.7; Fig. 2 and Table 1).

Absolute number of proximal colon cancer cases per year between 2003 and 2017 decreased from 1010 to 821 for ages 40–44 years, 1726 to 1643 for ages 45–49 years, 3015 to 3012 for ages 50–54 years, and 4254 to 4209 for ages 55–59 years (Fig. 1). From 2003 to 2017, proximal cancer incidence per 100,000 decreased for all ages combined (AAPC − 1.2; 95% CI: − 2.1–− 0.3), but was stable for ages 40–44 years (4.4 vs 4.2 in 2017; AAPC − 0.1; 95% CI − 0.6–0.4) and for ages 45–49 years (7.9 vs 7.9 in 2017; AAPC 0.0; 95% CI − 0.3–0.4; Fig. 2). Incidence of proximal cancer per 100,000 decreased from 15.8 to 14.1 for ages 50–54 years (AAPC − 0.6; 95% CI − 1.0–− 0.3) and from 26.9 to 19.2 for ages 55–59 years (AAPC − 2.3; 95% CI − 2.8–− 1.8) between 2003 and 2017.
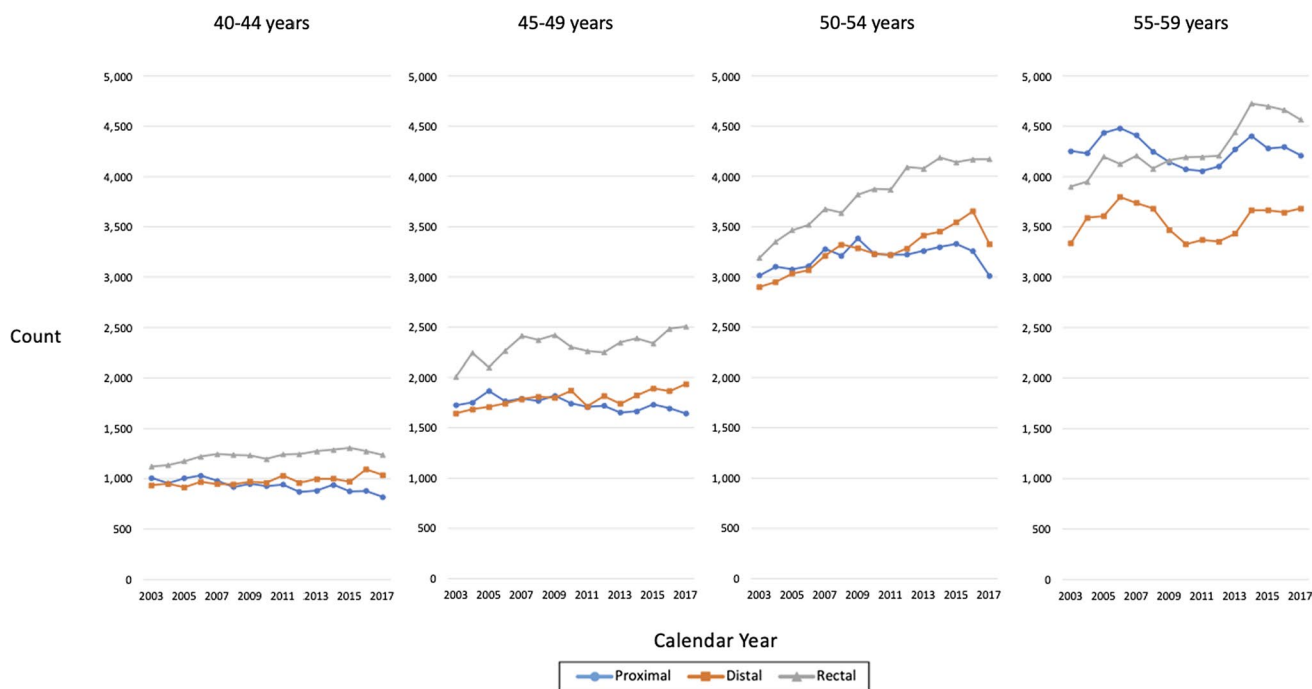
Fig. 1 Colorectal cancer cases by 5-year age groups and anatomic subsite, United States Cancer Statistics, 2003–2017
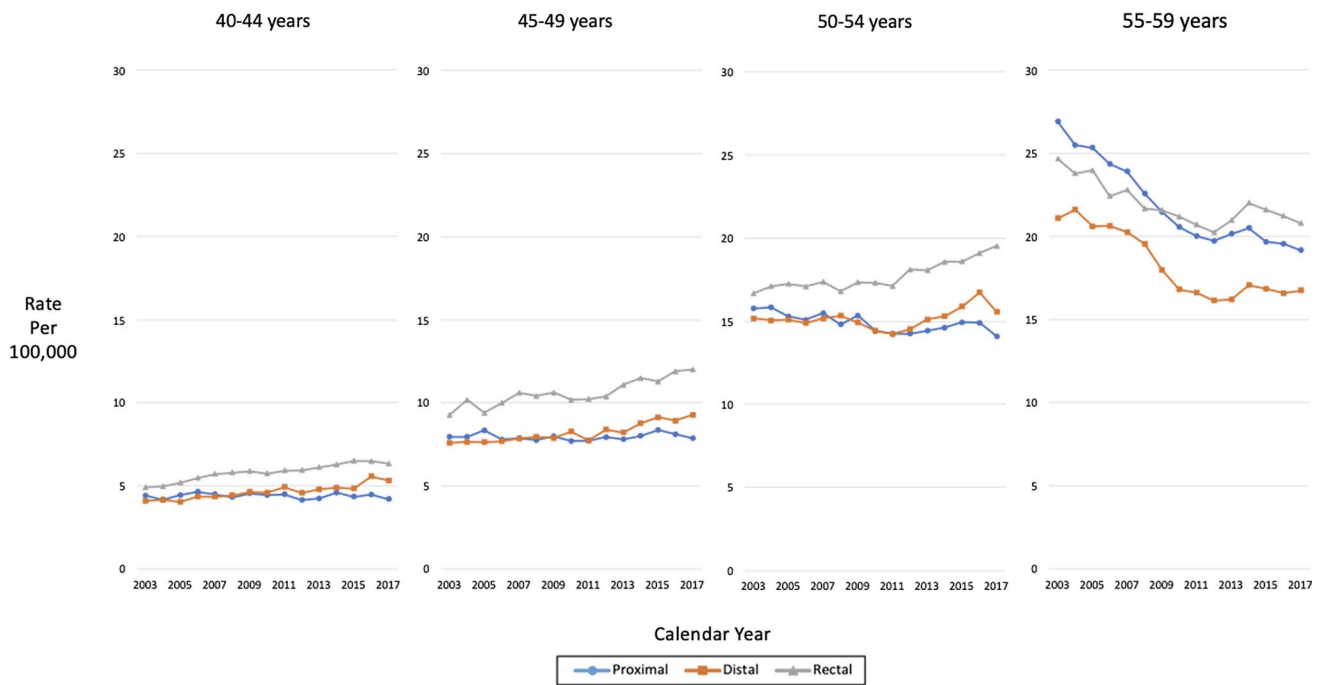
Fig. 2 Colorectal cancer incidence rates by 5-year age groups and anatomic subsite, United States Cancer Statistics, 2003–2017. Rates are per 100,000 persons and age-adjusted to the 2000 US standard population, 2003–2017

Discussion

Utilizing a national sample of over 470,000 CRC cases observed between 2003 and 2017 within the US Cancer Statistics dataset, we found that increased risk trends for CRC under age 50 are also present after age 50. Specifically, we observed that rectal cancer incidence rates increased for ages 40–54 between 2003 and 2017. By 2017, counts and rates of rectal and distal cancers for ages 50–54 approached those reported for ages 55–59. We postulate that these trends are a consequence of increasing rates of rectal and distal cancer for ages 50–54 years along with decreasing rates of distal cancer among ages 55–59 years. Our data suggest that the observed increased risk for CRC under age 50 for birth cohorts born after 1950 is also present after age 50, despite the prior availability of screening for this group. As such, availability of screening for persons age 50 and beyond does not appear to "reset" the birth cohort effect for increased CRC risk observed under age 50. Rectal cancers often require multiple modalities for treatment, including radiation, chemotherapy, and surgery, and survivors often experience significant post-treatment morbidity [12]. The observed increase in absolute number of distal and rectal cancers, and in the incidence rate of rectal cancers age 50–54, highlights importance of screening uptake to reduce morbidity and mortality. CRCs, particularly rectal cancers, are detectable and preventable with currently available screening modalities such as the

fecal immunochemical test and colonoscopy. However, in 2018, the proportion up-to-date with screening ranged from 61 to 63% for adults ages 50–64 years compared to 71–79% for adults ages ≥ 65 years [2, 13]. Furthermore, the proportion of individuals ages 50–54 years who were up-to-date with screening was just 48–50% [2, 12].

Our sample was large enough to allow for anatomic subsite-specific analysis of CRC trends, which enables observation of the drivers of increasing trends in CRC. We found changes in distal and rectal cancer incidence for individuals ages 40–44 and 45–49 years, and changes in rectal cancer incidence for individuals ages 50–54 years. We observed decreasing proximal cancer incidence for ages 50–54 and 55–59 years, and stable proximal incidence for ages 40–44 and 45–49 years. Data reported by Siegel et al., which has significant overlap with the US Cancer Statistics dataset data we used, have shown trends toward increasing CRC incidence from birth to age 49 for proximal, distal, and rectal cancer for time periods 2016 and earlier [2]. For the age group 50 to 64 years of age, Siegel et al. reported increasing incidence trends for cancers of the distal colon and rectum from 2012 to 2016, but not the proximal colon [2]. Our data confirm and extend Siegel et al.'s report by providing finer detail on incidence trends among age groups just before and after age 50. Additionally, our data emphasize that the increasing trend for the 50–64-year-old group reported by Siegel is currently driven by individuals age 50–54, underscoring the importance of promoting early initiation

of screening at age 45, and the need to increase screening uptake for 50–54-year-olds in order to address current trends, and possibly head off future, even larger increases in age-specific incidence as birth cohorts from 1950 and younger age and grow older. Further, as the embryologic origins, molecular tumor characteristics, and associated microbial milieu may differ by anatomic site, our observation of differences in trend by site highlights the importance of considering site in studies examining risk factors for early-onset CRC, as well as for CRC early in middle age just before and after age 50 [9, 14–17].

A strength of this study is the use of USCS, which provides a national assessment of case counts between 2003 and 2017. A limitation of our analysis is that we do not have data on whether increases in CRC incidence, particularly for those age 50 and older, were occurring among people exposed versus unexposed to colorectal cancer screening tests, and cannot therefore determine whether the increased risks observed were among people who were unscreened.

Taken together, increasing CRC incidence for both ages 45–49 and 50–54 years and the low prevalence of "on-time" screening at age 50 years underscore the importance of implementing interventions to increase screening for individuals age 50–54 years. A variety of interventions may be useful in increasing screening uptake in this patient population, including offering choice of tests, and organized mailed outreach invitations to complete screening [18]. Increasing CRC incidence among adults aged 45–49 and 50–54 years also supports recent American Cancer Society [4], American College of Gastroenterology [8], and United States Preventive Services Task Force [19] recommendations to initiate average risk screening at age 45, instead of age 50 [6, 7].

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