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ORIGINAL ARTICLE

Updated Assessment of Colorectal Cancer Incidence in the U.S. by Age, Sex, and Race/Ethnicity

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Abstract

Background Whether recent updates to colon cancer screening guidelines benefit men and women or all race/ethnic groups equally is not clear.

Aims The aim of this study is to evaluate age-, sex-, and race/ethnicity-specific trends in CRC incidence and disease burden among adults.

Methods Using 2000–2014 surveillance, epidemiology, and end results database, annual CRC incidence (per 100,000 persons/year) among U.S. adults was categorized by age (using 10-year age intervals) and stratified by sex and race/ethnicity. Comparison of incidence between groups utilized the z-statistic with $p < 0.05$ indicating statistical significance.

Results Overall, CRC incidence was the highest among patients aged ≥ 80 years (330.8 per 100,000 persons/year), which was significantly higher in men versus women (377.2 vs. 304.3 per 100,000 persons/year, $p < 0.001$). CRC incidence in younger individuals was 22.8 per 100,000 persons/year (age 40–49) and 6.8 per 100,000 persons/year (age 30–39). CRC incidence was significantly higher in African Americans compared to non-Hispanic whites. From 2000 to 2014, CRC incidence declined in all age groups over age 60, remained stable in age 50–59, and demonstrated proportional increases in among age 20–49 years. While CRC incidence in all race/ethnic groups aged ≥ 60 years declined, Hispanics aged 50–59 increased 21.9%, but remained stable in other race/ethnic groups. Race/ethnicity-specific disparities in CRC incidence in patients aged 20–49 were also observed.

Conclusions While CRC incidence has declined among U.S. adults aged ≥ 60, increasing incidence among patients aged < 50 is concerning. Identifying risk factors among "average-risk" patients is needed to better implement targeted screening of individuals not currently meeting CRC screening criteria.

Keywords Colon cancer · SEER · Epidemiology · Race/ethnicity

Abbreviations

CRC	Colorectal cancer
U.S.	United States
SEER	Surveillance, epidemiology, and end results
APC	Annual percentage change
BAPC	Biannual percentage change

Introduction

Colorectal cancer (CRC) is the third leading cause of cancer-related deaths in both men and women in the United States (U.S.) [1]. Annually in the U.S., approximately 50,630 Americans die of CRC, accounting for approximately 8.3% of all cancer deaths [2]. From 1970 to 2015, CRC mortality has decreased by 52% among U.S. adults. However, despite rapid declines observed in older age groups, CRC death rates have increased slightly in individuals younger than 55 years since the mid-2000s [3].

Along with declines in CRC mortality, overall CRC incidence has also demonstrated significant declines. These declines in CRC incidence have been attributed to historical changes in risk factors (i.e., decreased smoking and red meat consumption and increased use of aspirin) as well as effective implementation of CRC screening tests

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for detection and removal of early adenomatous lesions prior to adenocarcinoma transformation [4]. CRC screening guidelines published by the United States Preventive Services Task Force in 1998 recommended initiation of routine CRC screening at age 50 among adults at average risk of CRC [5]. Based on data demonstrating increased risk of CRC among African Americans at an age earlier than 50, in 2008 the American College of Gastroenterology published guidelines recommending initiating routine average-risk CRC screening at age 45 for African Americans and at age 50 for non-African Americans [6]. Since that time, several studies have further evaluated CRC epidemiology among individuals less than 50 years old. In a study using U.S. population-based surveillance epidemiology and end results (SEER) data from 1975 to 2010, Bailey et al. observed a trend toward increasing CRC incidence in adults < 50 years old. Further, the authors used a predictive model based on annual percentage change to predict the incidence rate for patients aged less than 50 with newly diagnosed CRC in 2020 and 2030. By 2030, the investigators predict that 10.9% of all colon and 22.9% of all rectal cancers will be diagnosed in patients under the screening age of 50 compared to 4.8% and 9.5%, respectively, in 2010 [7]. In a study using data from the California Cancer Registry, Singh et al. also demonstrated similar trends in adults ages 20–39, or young adults, in California. Using this database, biannual percentage changes were used to find statistically significant trends of CRC incidence in young adults from 1988 to 2009, which include increases in distal colon cancer among Hispanic females aged 20–29 by 15.9% and Hispanic males aged 30–39 by 10.4%. Large biannual percentage changes were also seen among Hispanic females aged 20–29 for rectal cancer (+ 10.5%) and Caucasian males aged 20–29 for rectal cancer (+ 9.4%). Further, the investigators found that young adults had a greater proportion of CRC diagnosed at distant stage than other age groups. The distribution for each age range by stage (local, regional, and distant, respectively) was 20–29 (21.9%, 48.6%, 29.5%), 30–39 (26.5%, 46.1%, 27.4%), 40–49 (30.1%, 44.3%, 25.6%), 50–59 (36.8%, 40.8%, 22.5%), 60–69 (38.6%, 40.9%, 20.5%), 70–79 (39.7%, 41.5%, 18.8%), and 80 or older (38.2%, 43.4%, 18.4%) [8].

In May 2018, the American Cancer Society adopted a qualified recommendation to initiate routine average-risk CRC screening at age 45, regardless of race/ethnicity [9]. However, more data are needed to further understand CRC epidemiology in those under age 50 particularly among different race/ethnic groups. We aim specifically to evaluate age-specific and race/ethnicity-specific trends in CRC incidence in the U.S. with a focus on cancer incidence among individuals age less than 50 years using a large national cancer registry.

Methods

All adults (age 20 years and older) with CRC from 2000–2014 were identified using the National Cancer Institute's surveillance, epidemiology, and end results (SEER) population-based cancer registry, maintained by the National Cancer Institute, with data obtained from participating state and regional cancer registries. The 2000–2014 SEER includes data from 18 regions in the U.S. (San Francisco-Oakland, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Natives, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey, and Greater Georgia) and represents approximately 28% of the U.S. population. Data included in the national SEER registry is compiled together based on state and regional cancer registries. Cancer data collected by the database registrars are based on the available data provided by the clinical providers and the health systems and hospitals that are within each registrar's region [10].

Overall CRC incidence among adults (age ≥ 20 years) was presented as cancer incidence per 100,000 persons/year, which was standardized to the year 2000 U.S. population. Given our specific focus on age-specific trends in CRC incidence, we utilized 10-year age groups (20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and 80 years and over) to evaluate age-specific CRC incidence overall and across annual time periods. Additional sub-analyses were performed by sex and race/ethnicity (non-Hispanic white, African American, Asian, and Hispanic). Year-specific trends in CRC incidence were also evaluated overall as well as stratified by age, sex, and race/ethnicity. Comparisons of incidence rates between groups utilized the z-statistic using standard equations. In addition to comparisons of cancer incidence, we also attempted to evaluate and understand the total cancer burden by assessing the total number of CRC cases overall as well as across time periods and age-, sex-, and race/ethnicity-specific groups. Statistical analyses were performed using SEER*Stat software (version 8.3.4, Surveillance Research Program, National Cancer Institute, Bethesda, MD, USA), and a two-tailed p value < 0.05 indicated statistical significance [11, 12]. This study was reviewed and determined to qualify for exempt status from the Alameda Health System Institutional Review Board.

Results

Overall CRC Incidence

Overall, CRC incidence increased with increasing age, and adults aged 80 years and over had the highest incidence of cancer compared to younger age groups (330.8 per 100,000/year) (Table 1). When stratified by sex, while CRC incidence was similarly low in men and women aged < 40 years, beginning in the age 40–49 years category, cancer incidence in men began to increase more rapidly than women, such that among adults aged > 50 years, CRC incidence in men was significantly higher than women (Table 1). When stratified by race/ethnicity, a few key observations were noted. Firstly, across all race/ethnic groups aged < 40 years, CRC incidence was generally low. However, beginning in the age 40–49 years category, race/ethnicity-specific disparities in CRC incidence began to emerge. African Americans consistently had significantly higher CRC incidence than all race/ethnic groups, and this higher incidence persisted across all age categories above 40 years (Table 1). This is in contrast to CRC incidence in Asians and Hispanics, which while significantly lower than African Americans and non-Hispanic whites, also demonstrated age-specific increases in CRC incidence. When race/ethnic groups were further stratified by sex, males had significantly higher CRC incidence than females across all race/ethnic groups, and the highest CRC incidence was observed in African American men and the lowest was among Hispanic and Asian women (Table 1).

Time-Specific Trends in CRC Incidence

Figure 1 illustrates annual age-specific trends in CRC incidence overall and stratified by sex and race/ethnicity. While individuals aged 80 years and over had the highest CRC incidence among all age groups, this group demonstrated the greatest decline in CRC incidence (421.9 per 100,000 persons/year in 2000 to 247.9 per 100,000 persons/year in 2014, 33.3% decrease (Figs. 1a and 2a). Similar declines in CRC incidence were observed in adults 70–79 years old (289.6 per 100,000 persons/year in 2000 to 172.7 per 100,000 persons/year in 2014, 40.4% decrease) and 60–69 years old (163.9 per 100,000 persons/year in 2000 to 108.1 per 100,000 persons/year in 2014, 34.0% decrease). CRC incidence among individuals aged 50–59 years remained stable from 2000 to 2014 (65.7 per 100,000 persons/year in 2000 to 65.9 per 100,000 persons/year in 2014, 0.3% increase). While overall CRC incidence among individuals aged < 50 was lower than older age cohorts, a relative increase in CRC incidence was observed for these younger cohorts. For example, CRC incidence among individuals aged 40–49 years increased from 20.9 per 100,000 persons/year in 2000 to 25.1 per 100,000 persons/year in 2014 (20.1% increase) (Figs. 1a and 2a)

When stratified by sex, while CRC incidence was higher in men compared to women across all age groups, similar trends in declining CRC incidence were observed (Figs. 1b, c, and 2a). While CRC incidence was highest among males and females aged 80 years and over, these groups experienced the greatest decline in overall CRC incidence (males aged 80 years and over: 496.4 per 100,000 persons/year in 2000 to 282.8 per 100,000 persons/year in 2014, 43.0% decrease; females aged 80 years and over: 383.2 per 100,000 persons/year in 2000 to 226.4 per 100,000 persons/year in 2014, 40.9% decrease (Figs. 1b, c, and 2a). Similar declines in CRC incidence were observed among adults aged 60–79. CRC incidence among the 50–59 years cohort remained stable in both men and women (males: 75.7 per 100,000 persons/year in 2000 to 75.8 per 100,000 persons/year in 2014, 0.1% increase; females: 56.2 per 100,000 persons/year in 2000 to 56.4 per 100,000 persons/year in 2014, 0.4% increase). Among men and women, while CRC incidence was lower among individuals aged < 50 years, relative increases in cancer incidence were observed from 2000 to 2014 (Figs. 1b, c, and 2a).

When stratified by race/ethnicity, similar age-specific trends in CRC incidence were observed (Figs. 1d–g and 2b). While CRC incidence was highest among African Americans and lowest among Hispanics, among all race/ethnic groups, CRC incidence among individuals aged 60 years and older declined in all race/ethnic groups. However, when evaluating the age 50–59 years group, while non-Hispanic whites, African Americans, and Asians all demonstrated declines in CRC incidence, a significant increase was observed in Hispanics (47.1 per 100,000 persons/year in 2000 to 57.4 per 100,000 persons/years in 2014, 21.9% increase) (Fig. 2b). In the next younger cohort of individuals aged 40–49 years, the greatest relative increase in CRC incidence was observed in non-Hispanic whites (20.6 per 100,000 persons/year in 2000 to 27.5 per 100,000 persons/year in 2014, 33.5% increase), whereas much smaller increases in CRC incidence were observed in African Americans, Asians, and Hispanics. While CRC incidence was much lower in younger age cohorts, these younger cohorts demonstrated relative increases in CRC incidence during the study period (Fig. 2b)

Burden of Disease Distribution

When evaluating the total number of CRC cancers diagnosed, the major burden of CRC is seen in individuals aged 60 years and over, which contributes to over 70% of all new CRC cases diagnosed, whereas individuals aged < 50 years

Table 1 Overall incidence of colorectal cancer 2000–2014

	20–29 Years incidence	95% CI	30–39 Years incidence	95% CI	40–49 Years incidence	95% CI	50–59 Years incidence	95% CI	60–69 Years incidence	95% CI	70–79 Years incidence	95% CI	80 Years and over incidence	95% CI
Overall	1.6	1.5–1.7	6.8	6.7–7.0	22.8	22.6–23.0	64.9	64.5–65.3	129.5	128.8–130.2	233.3	232.1–234.5	330.8	329–332.5
Sex														
Male	1.7	1.6-1.7	7.2	7.0–7.4	24.4	24.1–24.7	75.0	74.4–75.6	156.7	155.6–157.8	277.0	275.1–279.0	377.2	374.1–380.4
Female	1.6	1.5–1.6	6.5	6.3–6.6	21.2	20.9–21.5	55.3	54.8–55.9	105.2	104.3-106.0	199.1	197.6–200.5	304.3	302.2–306.5
Race/ethnicity														
Non–Hispanic white														
Overall	1.8	1.7–1.9	7.2	7.1–7.4	23.1	22.8–23.4	62.7	62.2–63.7	127.5	126.6–128.3	238.4	237.0–239.8	340.5	338.4–342.5
Male	1.9	1.7–2.0	7.7	7.4–7.9	24.9	24.5 - 25.3	73.2	72.4–73.9	154.3	152.9–155.6	281.0	278.7 – 283.3	387.9	384.3–391.5
Female	1.7	1.6–1.9	6.8	6.5–7.0	21.5	21.1–21.9	52.8	52.2–53.4	103.4	102.4–104.4	205.2	203.5–207.0	315.0	312.6–317.5
African American														
Overall	1.5	1.4-1.7	7.7	7.3-8.1	29.5	28.8-30.3	91.6	90.2-93.1	174.5	171.9-177.1	276.9	272.4-281.4	355.7	348.7-362.7
Male	1.5	1.3–1.8	7.7	7.2–8.3	31.4	30.3–32.5	103.2	101.0–105.5	209.5	205.2 - 213.9	330.2	322.5–338.0	434.6	421.0–448.5
Female	1.5	1.3–1.8	7.8	7.3–8.3	28.0	27.0–29.0	82.1	80.3–84.0	148.0	144.7–151.2	242.5	237.1–248.0	320.1	312.2–328.2
Asian														
Overall	1.4	1.2–1.6	6.3	5.9–6.6	21.4	20.7–22.1	59.3	58.1–60.6	111.5	109.3–113.7	183.3	179.7–187.0	261.9	256.1–267.9
Male	1.6	1.3–1.8	6.8	6.3–7.4	23.8	22.7–24.8	69.0	67.1–71.1	140.1	136.4–143.8	226.4	220.2–232.7	298.8	288.8–309.1
Female	1.2	1.0–1.5	5.8	5.4–6.3	19.4	18.5–20.3	51.4	49.8–53.1	88.8	86.2–91.5	152.4	148.0–156.9	240.3	233.1–247.7
Hispanic														
Overall	1.3	1.2–1.4	5.7	5.5–6.0	17.9	17.4–18.4	56.0	55.0–57.1	114.7	112.7–116.8	193.7	190.1–197.4	268.4	262.5–274.5
Male	1.4	1.2–1.5	6.0	5.7–6.4	19.2	18.5–19.9	65.2	63.6–66.9	142.9	139.5–146.3	248.7	242.4–255.1	315.3	304.7–326.1
Female	1.3	1.1–1.5	5.4	5.1–5.8	16.5	15.9–17.2	47.1	45.8–48.5	89.6	87.1–92.1	150.4	146.2–154.6	236.3	229.2–243.5

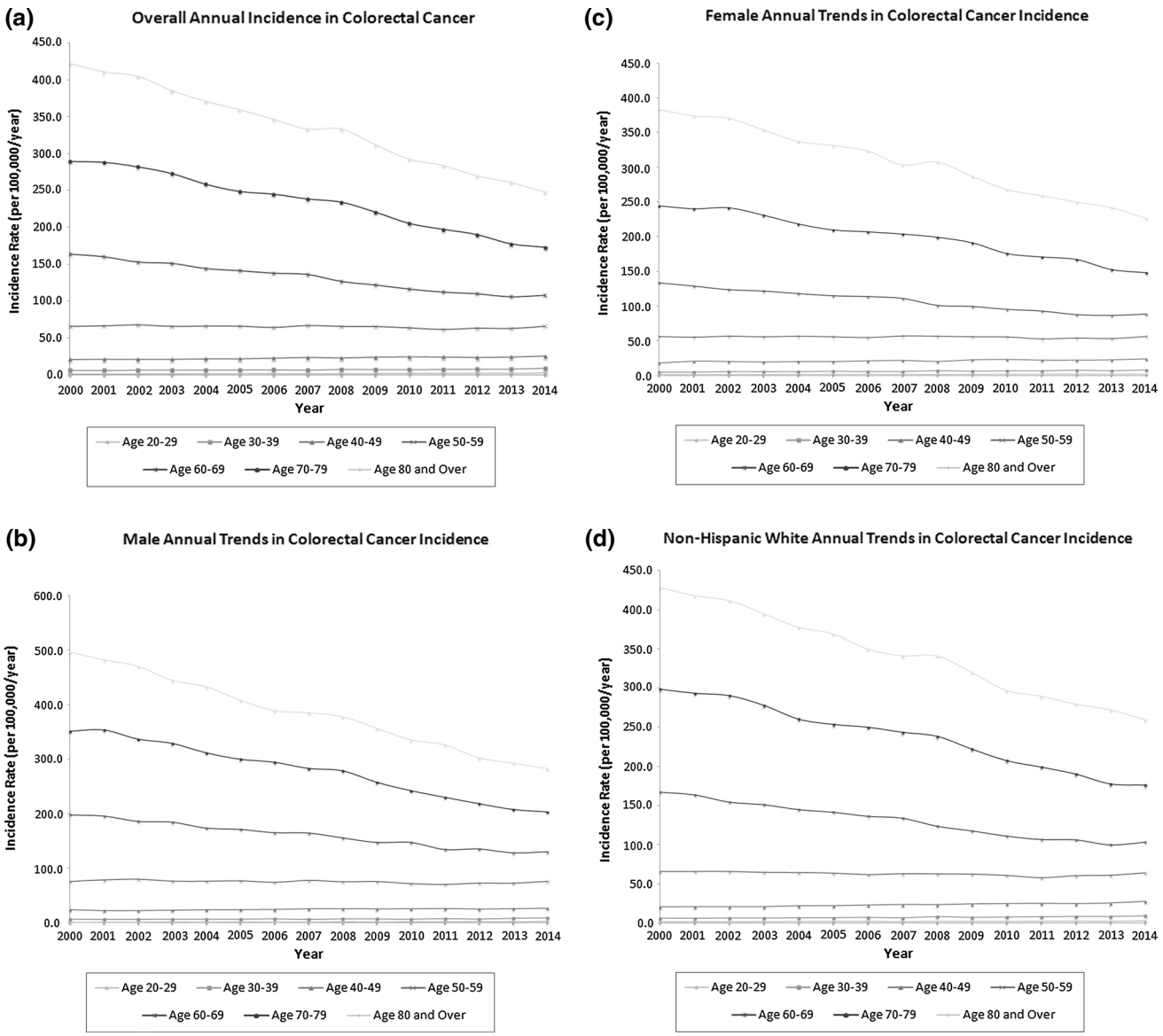
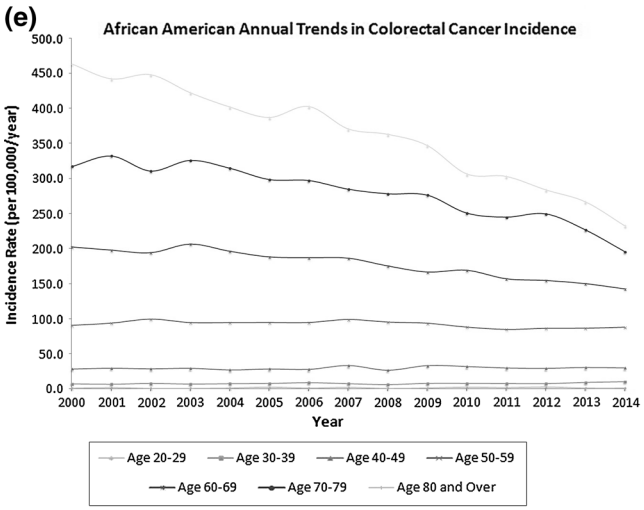


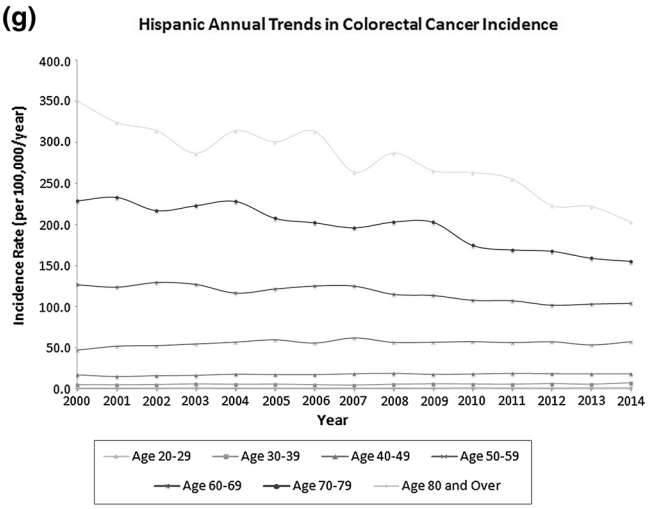
Fig. 1 Age-specific annual trends in colorectal cancer incidence overall by sex and by race/ethnicity

account for 10% (Fig. 3a). From 2000 to 2014, the total number of new CRC cases diagnosed decreased by 22.3% in those aged 80 years and over and decreased by 31.2% in those aged 70–79 years, whereas the total number of CRC cases diagnosed increased for all other age groups (Fig. 4a).

When stratified by sex, similar trends in age-specific disease burden were observed with adults aged 60 years and over representing 70.1% and 74.2% of all new CRC cases diagnosed in men and women, respectively (Fig. 3b, c). From 2000 to 2014, the total number of new CRC cases among men decreased by 16.3% in those aged 80 years and over and decreased by 29.2% in those aged 70–79 years. Among women, the total cases of CRC decreased by 26.3% in those aged 80 years and over and decreased by 33.3% in those aged 70–79 years (Fig. 4a). The total number of CRC cases among those aged < 70 years increased among men and women across all age groups from 2000 to 2014 (Fig. 4a).

When stratified by race/ethnicity, the major burden of CRC was observed in individuals aged 60 years and over, which contributes to over 60% of all new CRC cases among all race/ethnic groups (Fig. 3d–g). From 2000 to 2014, among patients aged 80 years and older, non-Hispanic whites (decrease of 28.6%) and African Americans (decrease of 32.1%) both experienced a decline in the total number of CRC diagnosed from 2000 to 2014 (Fig. 4b). However, among Asians and Hispanics aged 80 years and older, the total number of CRC patients diagnosed increased





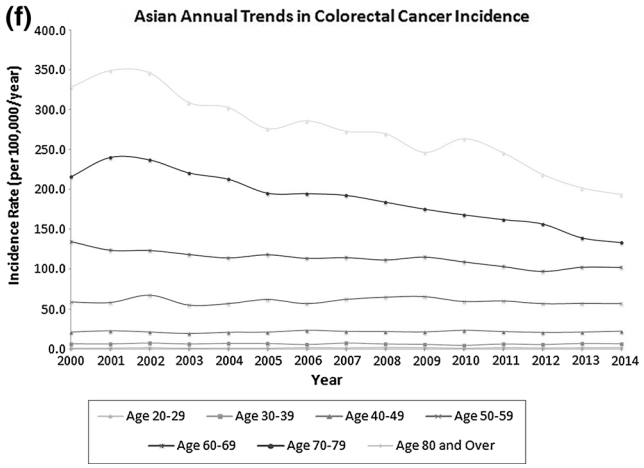


Fig. 1 (continued)

by 44.0% and 41.2%, respectively (Fig. 4b). Similarly among the age 70–79 years group, non-Hispanic whites and African Americans both experienced declines in the total number of CRC, whereas Asians and Hispanics experienced increases in CRC cases diagnosed. Among younger cohorts, nearly all race/ethnicity groups across all age categories experienced increases in the total number of CRC cases diagnosed, with the greatest proportional increase observed in Hispanics aged 50–59 years old (164.8% increase) (Fig. 4b).

Discussion

Using a comprehensive national cancer registry, we observed significant declines in overall CRC incidence from 2000 to 2014 among U.S. adults. However, significant sex-specific and race/ethnicity-specific trends in CRC incidence were observed.

In a recent study by Bailey et al., the investigators retrospectively evaluated NCI SEER data from 1975 to 2010 to evaluate age-specific trends in CRC incidence. While overall annual percent change (APC) in CRC incidence declined by 0.92%, this decline was primarily noted among individuals aged 50 years and over. Among those less than 50 years of age, the investigators observed an increase in CRC incidence (age 35–49, APC 0.41% increase; age 20–34, APC 1.99% increase) [7]. Singh et al. further utilized California Cancer Registry data of CRC cases from 1988 to 2009 to evaluate age-specific trends in CRC incidence in California, U.S. Using biannual percentage change (BAPC), adults aged 20–29, 30–39, and 40–49 experienced significant increases in CRC incidence among both males and females. The greatest increase in BAPC was seen in Hispanic males aged 30–39 years at 4.9% followed by Hispanic females aged 20–29 at 7.8% [8]. Our study observed similar findings, with CRC incidence declining among individuals aged 60 years and older, remaining stable for

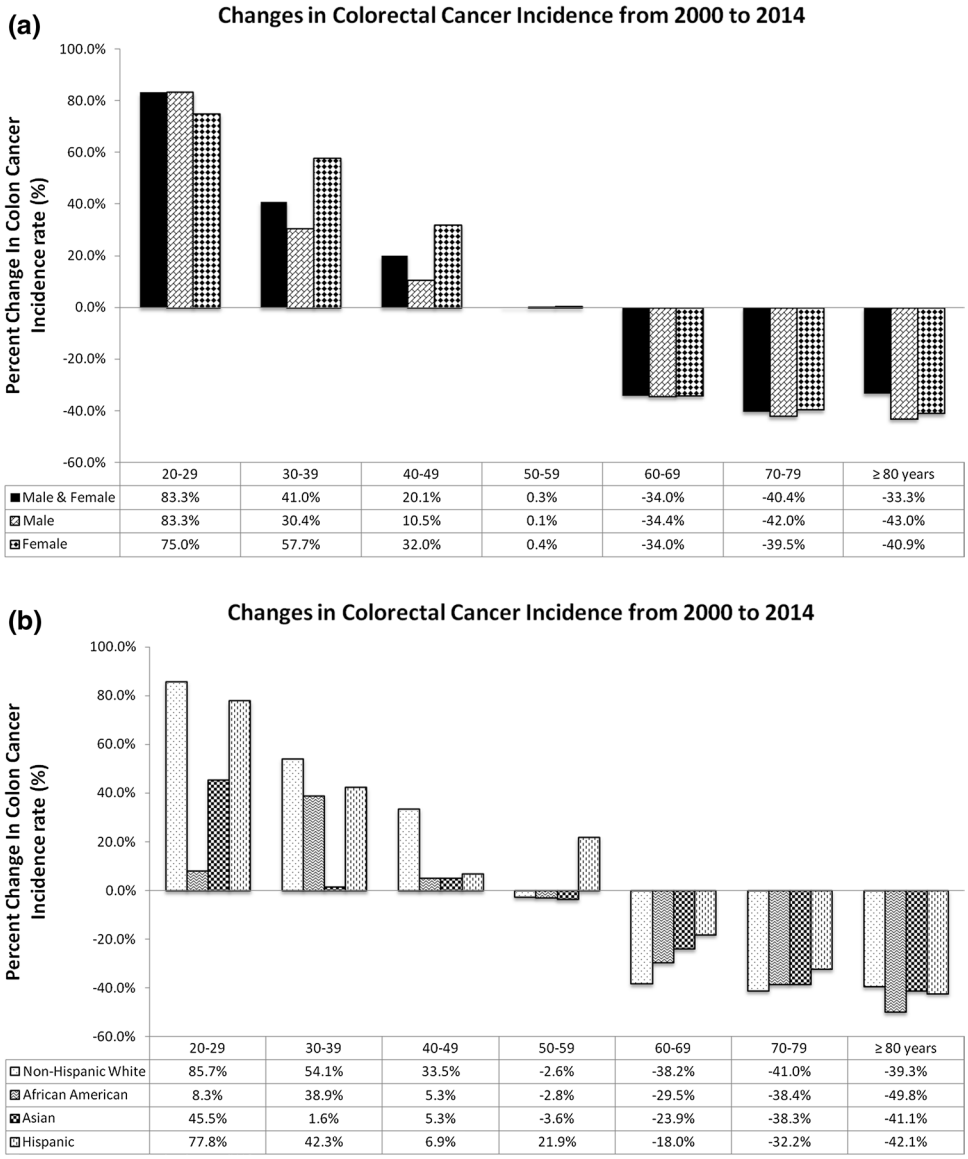


Fig. 2 Proportional changes in colorectal cancer incidence from 2000 to 2014

those aged 50–59 and demonstrating relative increases in CRC incidence among those aged 20–49 years (Fig. 2a). In examining CRC incidence changes stratified by sex, we observed similar declining trends in those aged 50 years and older, regardless of sex (Fig. 2b). When stratified by race and ethnicity, we observed that despite all other race/ethnicities demonstrating declines in CRC incidence from 2000 to 2014 in the age 50–59 group, Hispanics experienced a 21.9% relative increase in CRC incidence. While our study observed the highest incidence of CRC among individuals aged > 80 years, it is important to interpret these findings cautiously, as the current database does not provide information on important variables such as family history of colon cancer, and similarly important, whether an individual had completed prior CRC screening tests, the findings of those testing, and whether continued surveillance was completed (e.g., surveillance colonoscopy after adenomatous polyps had been removed). Another important factor to consider when interpreting these findings are that while the highest CRC incidence is seen in the oldest age groups, colonoscopy is procedure that carries inherent risks and for frail elderly individuals with multiple medical co-morbidities, poor performance status, or limited life expectancy, the benefit of screening or surveillance colonoscopy may not always outweigh the potential risks of the examination itself. Thus, the decision to implement guideline which recommended CRC screening and surveillance particularly among older individuals aged > 75 must be individualized with the primary care physician–patient discussion.

Another recent study by Siegel et al. in which SEER data from 1974 to 2013 was analyzed using incidence rate ratios and age-period-cohort modeling; the investigators

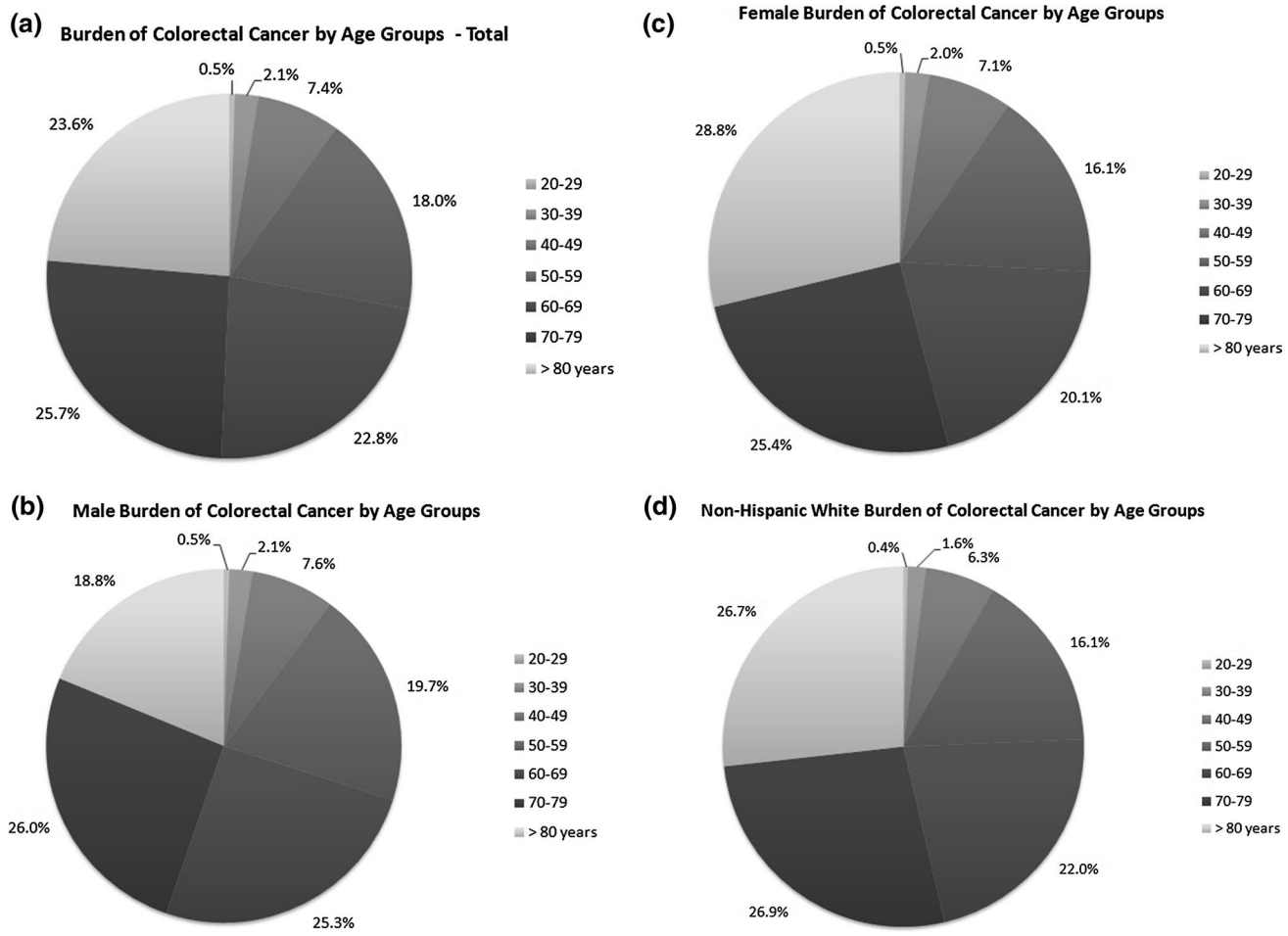


Fig. 3 Age-specific burden (number of colorectal cancer cases diagnosed) overall by sex and by race/ethnicity

demonstrated that mortality associated with CRC has increased in adults ages 20 to 54 by 1% each year from 2004 to 2014. This was in stark contrast to the fact that during the mid-1970s to the 1990s, the mortality rate in the same age population had been declining by 2% each year [13]. With the mounting evidence of increasing CRC incidence and increasing CRC-related mortality in adults aged < 50, the American Cancer Society has recently recommended lowering the age at which to begin routine CRC screening to age 45 regardless of sex or race/ethnicity [9]. With these newly adopted screening recommendations and a goal to increase screening to 70% of the target population along with risk-factor modification and treatment, CRC mortality is estimated to decline by almost 50% by the year 2020 according to a micro-simulation model by The Healthy People Consortium and the American Cancer Society [14]. While the increasing CRC incidence among younger individuals is a call for attention, it should be remembered that while increases are noted, the overall absolute incidence of CRC among these younger cohorts is far lower than those aged 50 and over, cohorts for which there are more clear guidelines to implement CRC screening. Thus, while it is reasonable to call for more study into investigating the increasing CRC incidence among young individuals, it remains more effective to target resources and education to ensure older individuals are continuing to stay up to date with CRC screening and surveillance recommendations.

Race/ethnicity-specific disparities in CRC incidence and CRC mortality have been previously reported [15–18]. While the exact etiology explaining these differences is multifactorial, previous studies have postulated several contributing factors including differences in diet, lifestyle factors, tumor biology, healthcare access, healthcare utilization, treatment and screening outreach, and subsequent follow up [19–21]. Our study specifically focused on race/ethnicity-specific differences in age-specific trends in CRC from 2000 to 2014 in the U.S. While nearly all individuals aged 50 years and older experienced a decline in CRC across all race/ethnic groups, Hispanics in the age 50–59 cohort was the only group that demonstrated an increase in

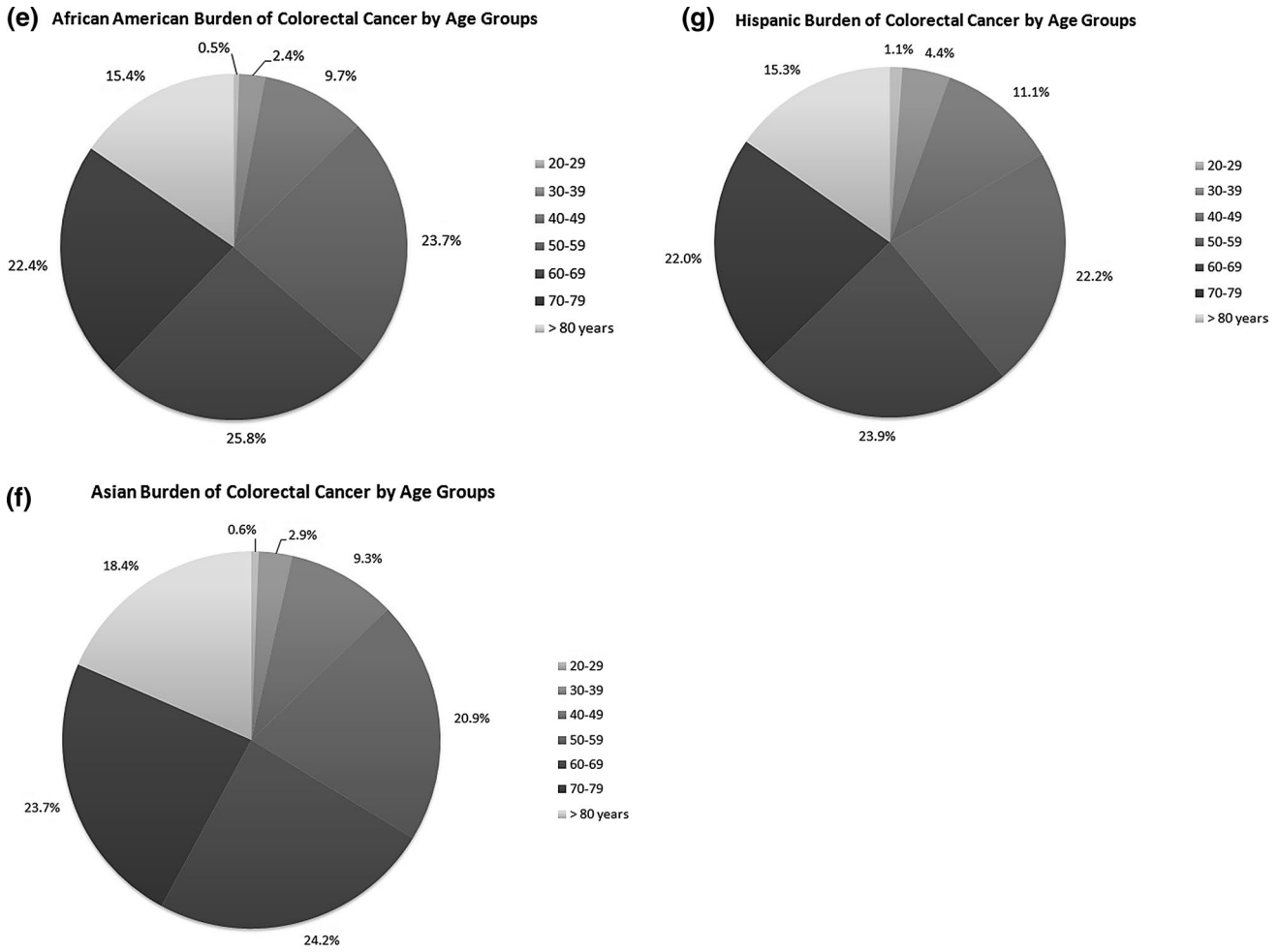
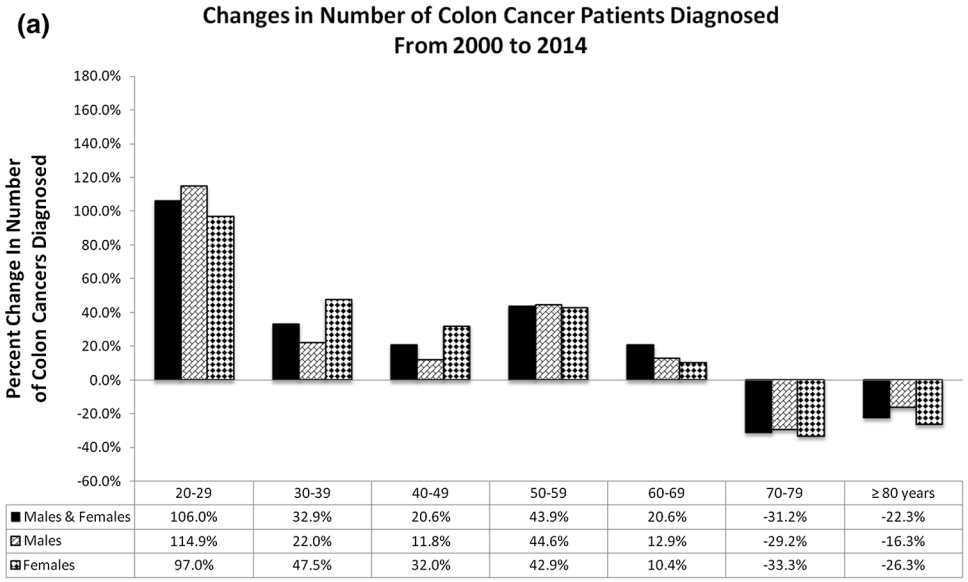


Fig. 3 (continued)

CRC from 2000 to 2014 (21.9% increase) (Fig. 2b). Wang et al. demonstrated similar findings in their analysis of Texas Cancer Registry from 1995–2010 that showed CRC incidence declining more slowly in older Hispanic adults when compared to non-Hispanic whites and African Americans [22]. While the exact etiology as to why Hispanics aged 50–59 experienced an increase in CRC incidence, previous studies have raised concerns regarding disparities in access or adherence to CRC screening recommendations among this group. For example, Nagelhout et al. demonstrated that Hispanic adults were less likely to follow up with screening recommendations from providers citing a lack of trust in their provider as the biggest determining factor to lack of adherence to CRC screening [23]. In another cross-sectional study conducted in primary healthcare clinics and community centers in New York City, it was found that 25% of Hispanic patients age 50 years and older did not adhere to physician recommendations to undergo a screening colonoscopy for CRC. In the study, it was observed that non-adherence was associated with younger ages, being born in the U.S., preference for completing interviews in English, higher acculturation, and greater reported fear of colonoscopy testing. These findings suggest that, while efforts have been made to screen this high-risk population, there are certain patient characteristics that need to be taken into account to help providers anticipate who may be less adherent and who may require additional interventions to improve CRC screening rates [24].

While incidence is an important measure of disease epidemiology, assessing the total number of cases of CRC diagnosed also provides important information regarding disease burden. While the overall total number of CRC diagnosed declined from 2000 to 2014 among those aged 70 years and over, those aged 50–69 experienced an increase in CRC cases diagnosed. However, when stratified by race/ethnicity, while non-Hispanic whites and African Americans aged 70 years and over both experienced declines in CRC cases diagnosed, we observed an increase in CRC diagnosed among Asians and Hispanics (Fig. 4b). Similarly the increase in number of CRC diagnosed among those aged



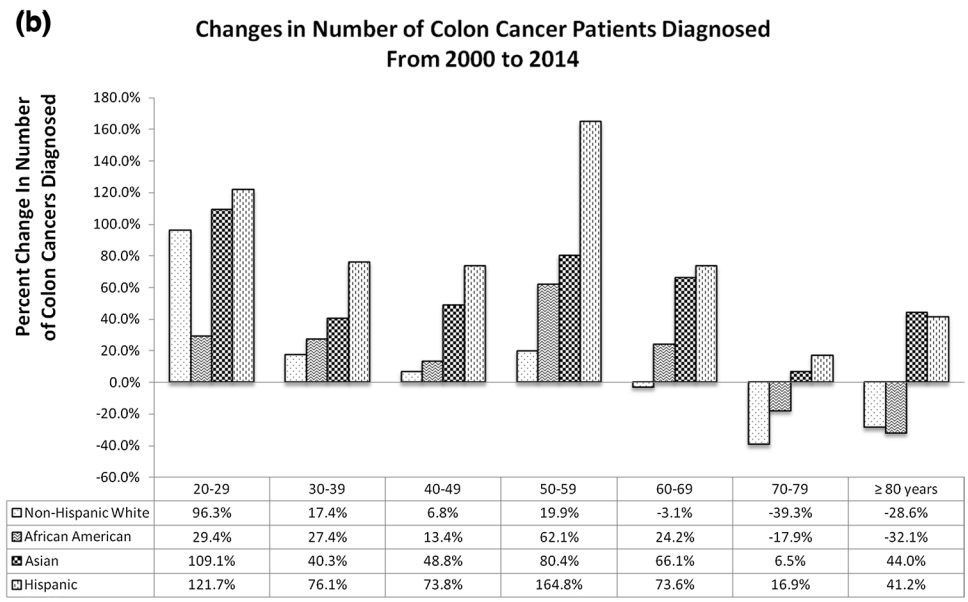


Fig. 4 Proportional changes in the total number of colorectal cancer patients diagnosed from 2000 to 2014 overall by sex and by race/ethnicity

50–69 was much greater among Asians and Hispanics than among non-Hispanic whites. Minorities are long known to be more likely to be uninsured, become stigmatized for their medical illness, be fearful or in denial of their cancer diagnoses, be more aversive to health care treatments, be untrustworthy of medical professionals and the healthcare system, and have misperceptions about cancer that ultimately interfere with ongoing management and treatment after receiving their diagnosis [25]. These challenges in minority groups may translate into lower completion of screening examinations that aimed at removing pre-cancerous lesions (adenomas), which may contribute to greater numbers of cancers developing.

The strengths of this study include high-quality data from a large U.S. population-based cancer registry over 15 years that represents a large proportion of the U.S. population. This improves the generalizability of our findings to U.S. populations. Detailed data on race/ethnicity classifications permitted detailed age, sex, and race/ethnicity-specific analyses of CRC incidence. Potential limitations inherent to large cancer registry data include potential for misclassification bias when sites are reporting CRC diagnoses, although we would not necessarily expect this bias to be discordant in nature. Furthermore, while we suspect that disparities in access to care or adherence to CRC screening contributes to these disparities, particularly among race/ethnic minorities, the current database does not include data to evaluate evaluation and management prior to the diagnosis of CRC. Furthermore, given the observational registry-based data, the inclusion of important risk factors (e.g., family history

of cancer, co-morbidities, tobacco and alcohol use, diet) was not available for analysis. Particularly, more granular data on the presence of familial-inherited colon cancer syndromes or other genetic testing data that may be associated with the age, sex, and race/ethnicity-specific disparities in CRC trends observed were not available in the SEER database for inclusion in our study.

In conclusion, despite the declines in CRC incidence observed among older age cohorts, sex-specific and race/ethnicity-specific disparities still persist. While the success of screening programs for older adults in the U.S. is encouraging, recent studies including ours raise a concern about increases among younger cohorts that are not traditionally included in screening recommendations. While overall incidence is low among these younger groups, more studies are needed to better identify high-risk groups among these "non-screening age" groups so that targeted screening interventions can be implemented for prevention of CRC as well as early diagnosis and treatment. While the recent updates from the American Cancer Society making a qualified recommendation to begin CRC screening for all average-risk adults at age 45 address some of these concerns, data are needed to evaluate how this affects CRC epidemiology and whether more targeted recommendations are needed for specific cohorts.

Author's contribution RW guarantor of the article. RW and AO: involved in study concept and design. RW involved in acquisition of data. AO, AR, BL, TB, and RW involved in analysis and interpretation of data. AO and RW involved in statistical analysis. AO and RW involved in drafting of the manuscript. AO, AR, BL, TB, and RW involved in critical revision of the manuscript for important intellectual content. RW involved in study supervision. RW had full access to all the data in the study and took responsibility for the integrity of the data and accuracy of the data analysis.

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Compliance with Ethical Standards

Conflict of interest Robert J. Wong: Advisory board, consultant, speaker's bureau, and research Grants—Gilead Sciences; Speakers bureau: Salix, Bayer; Research Grant: Abbvie. Ajay Ohri, Ann Robinson, Benny Liu, Taft Bhuket: None.

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