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Original Article

Colorectal Cancer Incidence Among Young Adults in California

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Purpose: Colorectal cancer (CRC) incidence has decreased over the past three decades, due largely to screening efforts. Relatively little is known about CRC incidence among the young adult (YA) population ages 20–39, as screening typically commences at age 50 for average-risk individuals. We examined CRC incidence with a focus on YAs in order to identify high-risk subgroups.
Methods: We analyzed 231,544 incident CRC cases from 1988–2009 (including 5617 YAs 20–39 years of age) from the California Cancer Registry. We assessed age-specific incidence rates by race/ethnicity, gender, and colorectal tumor location, and calculated the biannual percent change (BAPC) to monitor change in incidence over the 22-year study period.
Results: The absolute incidence of CRC per 100,000 was low among YAs 20–29 and 30–39 years old (ranging from 0.7 per 100,000 among Hispanic and African American females aged 20–29 up to 5.0 per 100,000 among Asian/Pacific Islander males aged 30–39). However, we observed increasing CRC incidence rates over time among both males and females in the YA population, particularly for distal colon cancer in Hispanic females aged 20–29 (BAPC = +15.9%; $p < 0.042$).
Conclusion: The absolute incidence of CRC remains far lower for YAs than among adults aged 50 and over. However, CRC incidence is increasing among young adults, in contrast to the decreasing rates observed for adults in the screened population (aged 50 and above). More research is needed to better characterize YAs at increased risk for CRC.

Keywords: colorectal cancer, CRC, health disparities, incidence, race/ethnicity, young adults

Colorectal cancer (CRC) is the third most common cancer diagnosis and second most common cancer cause of death in the United States.[1] It is largely a disease of older populations; less than 10% of diagnoses occur in individuals under 50 years of age.[2] For young adults at standard risk of CRC (i.e., those without a strong family history of CRC or a known hereditary condition), there are no recommended screening programs in the United States. CRC incidence has been declining since 1975, and began to decrease at a faster rate in 1998.[3] This decline is largely attributed to the utilization of CRC screening for premalignant polyps by those 50 and older.[3] Current guidelines indicate that CRC screenings should begin at age 50 for average-risk individuals.[4] As the vast majority of young adults (YAs, aged 20–39) are thus not screened in the United States, much less is known about CRC incidence in young adults. Despite observed declines in overall CRC incidence, several recent studies have reported a concerning increase in CRC incidence among adults younger than 50 (i.e., pre-screening age adults, which for the purposes of this paper will be considered as adults aged 20–49).[5–8] Possible explanations for this observation are the lack of screening in younger populations, delayed diagnosis due to lack of insurance, a low index of suspicion from physicians, and/or a higher prevalence of predisposing risk factors that allow for accelerated tumorigenesis in younger patients.[2]

As overall CRC incidence has declined, disparities between racial/ethnic groups have been revealed, with substantial variations in race/ethnicity-specific incidence and mortality rates.[3] Multiple studies have demonstrated lower screening rates among ethnic minorities, which likely accounts for some of the observed differences in risk.[9,10] Several studies have indicated that age-adjusted incidence and mortality rates for CRC are highest amongst African Americans[3,11,12] and lowest amongst Hispanics and Asians.[12,13] Other studies have shown that CRC risk may vary by tumor subsite location within the colorectum, and that biologic behaviors of tumors may differ based on subsite location. As an example, our group has previously investigated

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differential effects on CRC progression based on colorectal tumor subsite location,[14] and we have identified differential risks of second primary CRC based on tumor subsite location of the first colorectal cancer.[15] This theory is plausible as the right and left colon derive from different embryologic structures (the midgut and hindgut, respectively). To our knowledge, no prior study has assessed CRC risk in prescreening age adults among the four major United States race/ethnicities (Caucasians, African Americans, Hispanics, Asian/Pacific Islanders) while also accounting for tumor subsite location. Therefore, despite the fact that the absolute risk of CRC is low among individuals in the 20–39 year-old YA population compared with populations aged 50 and older, we sought to investigate differences in age-specific CRC incidence rates by anatomic subsite among the major race/ethnicity populations in California. We hypothesized that CRC incidence may be low in terms of absolute incidence, but increasing over time in YAs. We specifically addressed CRC risk among YAs and focused on the Hispanic population, a major race/ethnicity in the State of California and a group that has often been inextricable from other populations in previous studies.

Methods

Study population

Case data were obtained from the California Cancer Registry (CCR) Statistical Extract, for which case ascertainment is considered complete for diagnosis years 1988 through 2009. The CCR is a geographically contiguous population-based cancer database with reporting rules similar to the Surveillance, Epidemiology and End Results (SEER) database. The entire statewide CCR database was eventually adopted as part of SEER in 2000. A total of 231,544 CRC cases diagnosed between 1988 and 2009 from the four major race/ethnicities were identified from the CCR database.

Tumors were determined to be colorectal in origin based on the SEER Site Recode of ICD-O-3 codes and were classified accordingly by anatomic subsite.[16] Proximal colon tumors were defined as originating in the cecum, ascending colon, transverse colon, or splenic flexure; distal colon tumors were defined as originating in the descending colon or sigmoid colon. Rectal cancer was defined as originating in the rectosigmoid junction or rectum. Individuals with appendiceal tumors were excluded from analysis as these are typically considered distinct tumor types. We included individuals of all ages with incident malignant colorectal tumors and the following histologies with respective ICD-O-3 codes: adenocarcinoma (8010, 8020–8022, 8140–8145, 8210, 8211, 8220, 8221, 8230, 8231, 8255, 8260–8263, 8310, 8320, 8323, 8380, 8400, 8410, and 8490), mucinous adenocarcinoma (8470, 8480, 8481, 8440, 8441, 8460, 8461, and 8482), and colorectal carcinoma-not otherwise specified (8050–8052, 8070–8076, 8081–8083, 8500, 8507, 8510, 8550, 8560, 8570, 8571, 8573, and 8574). Disease stage at diagnosis was assigned to one of three categories according to SEER staging protocols: local disease, regional disease, or distant metastasis.

The available CCR race/ethnic categories are ''Hispanic exclusive,'' such that all other named race/ethnicities do not include Hispanics.[17] The same is true for the population data

Table 1. Demographic and Disease Characteristics, California Cancer Registry Colorectal Cases, 1988–2009

	Caucasian n *(%)*	*African American* n *(%)*	*Hispanic* n *(%)*	*Asian/Pacific Islander* n *(%)*	*Total* n *(%)*
Total	164,100 (71%)	15,662 (7%)	28,946 (12%)	22,836 (10%)	231,544 (100%)
Gender					
Male	82,340 (50%)	7175 (46%)	15,511 (54%)	11,810 (52%)	116,836 (50%)
Female	81,760 (50%)	8487 (54%)	13,435 (46%)	11,026 (48%)	114,708 (50%)
Age at diagnosis (years)					
Mean age (SD)	70 (13)	66 (13)	64 (14)	66 (14)	69 (13)
20–29	400 (0.2%)	57 (0.4%)	343 (1.2%)	152 (0.7%)	952 (0.4%)
30–39	2298 (1.4%)	384 (2.4%)	1284 (4.4%)	699 (3.1%)	4665 (2%)
40–49	8924 (5.4%)	1444 (9.2%)	3113 (11%)	2122 (9.3%)	15,603 (7%)
50–59	21,787 (13%)	3105 (20%)	5701 (20%)	4317 (19%)	34,910 (15%)
60–69	37,948 (23%)	4143 (26%)	7452 (26%)	5690 (25%)	55,233 (24%)
70–79	50,676 (31%)	3933 (25%)	6856 (24%)	6043 (26%)	67,508 (29%)
$\geq$80	42,067 (26%)	2596 (17%)	4197 (15%)	3813 (17%)	52,673 (23%)
Tumor stage					
Local	60,477 (36.8%)	4979 (31.8)%	9828 (34.0)%	7861 (34.4)%	83,145 (35%)
Regional	65,390 (39.8)%	5949 (38.0)%	11,757 (40.6)%	9634 (42.2)%	92,730 (40%)
Distant	30,742 (18.7)%	3839 (24.5)%	6120 (21.1)%	4335 (19.0)%	45,036 (19%)
Unknown	7491 (4.6)%	895 (5.7)%	1241 (4.3)%	1006 (4.4)%	10,633 (5%)
Anatomic subsite					
Proximal colon	68,804 (42%)	7432 (47%)	10,592 (37%)	7022 (31%)	93,850 (41%)
Distal colon	43,868 (27%)	4218 (27%)	8176 (28%)	7830 (34%)	64,092 (28%)
Rectum	46,455 (28%)	3472 (22%)	9379 (32%)	7447 (33%)	66,753 (29%)
Colon—NOS	4973 (3%)	540 (3%)	799 (3%)	537 (2%)	6849 (3%)

NOS, not otherwise specified; SD, standard deviation.

used. We examined individuals from the four largest race/ethnicities in the United States: Caucasian, African American, Hispanic, and Asian/Pacific Islander. Individuals of American Indian ancestry ($n = 754$) were excluded due to small numbers and consequent instability of rates. Individuals of an unknown race/ethnicity ($n = 1595$) were also excluded due to the lack of corresponding population data by which to estimate incidence rates. Race/ethnicity classification in the CCR is based on data within medical records and is enhanced by comparison to the 1980 United States Census list of surnames thought to denote Hispanic or Asian/Pacific Islander heritage. Population data are annual mid-year population estimates by age, race/ethnicity, and gender released by the Demographic Research Unit of the California Department of Finance and the Population Estimates Program of the United States Census Bureau in collaboration with the National Center for Health Statistics.[15,18] In total, 231,544 cases met our inclusion/exclusion criteria and comprised our study population.

This study was approved by the University of California, Irvine Institutional Review Board as exempt.

Statistical analyses

Associations in contingency tables were tested by the likelihood-ratio chi-square. Age was categorized into seven age groups (20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and ≥ 80) for determining gender-, race/ethnicity-, and age-specific incidence rates. Rates were averaged over the entire study period and by year in order to examine changes over time. These rates were calculated by dividing the age-specific number of incident CRC cases by the appropriate age specific person-years at risk, as determined from the California population stratified by race/ethnicity and gender.[18] Exact Poisson 95% confidence intervals for these rates were calculated in SAS version 9.2 (SAS Institute, Cary, NC).[19]

The biannual percent change (BAPC) in incidence was used to assess the statistical significance of changes in age-specific rates over time.[20] BAPCs were calculated using a regression model of the natural log of the annual incidence rate as a function of the year of diagnosis; such models were run independently for each combination of race/ethnicity and gender. The slope of the line provided by the model was used to

Table 2. Average Annual Age-Specific CRC Incidence Rates per 100,000 Population Among Males, by Anatomic Subsite, California Cancer Registry, 1988–2009

	Total CRC rate (95% CI)	*Proximal colon cancer rate (95% CI)*	*Distal colon cancer rate (95% CI)*	*Rectal cancer rate (95% CI)*
Caucasian				
20–29	0.9 (0.8–1.0)	0.3 (0.2–0.4)	0.2 (0.1–0.2)	0.4 (0.3–0.5)
30–39	4.4 (4.1–4.6)	1.6 (1.4–1.7)	1.0 (0.9–1.1)	1.6 (1.5–1.8)
40–49	16.8 (16.4–17.3)	5.0 (4.7–5.2)	4.6 (4.3–4.8)	6.9 (6.6–7.2)
50–59	57.1 (56.1–58.1)	16.2 (15.7–16.7)	17.8 (17.2–18.3)	21.8 (21.2–22.5)
60–69	140.7 (138.9–142.6)	46.7 (45.6–47.7)	43.4 (42.4–44.5)	47.3 (46.2–48.4)
70–79	235.6 (232.8–238.5)	97.0 (95.2–98.9)	66.1 (64.6–67.6)	66.5 (64.9–68.0)
≥ 80	298.2 (293.6–302.9)	145.0 (141.8–148.3)	72.0 (69.7–74.3)	69.1 (66.8–71.3)
African American				
20–29	0.8 (0.5–1.1)	0.4 (0.2–0.6)	s	s
30–39	4.7 (4.1–5.5)	1.6 (1.3–2.1)	1.2 (0.9–1.6)	1.7 (1.3–2.1)
40–49	22.8 (21.2–24.5)	9.7 (8.6–10.8)	5.3 (4.5–6.1)	7.3 (6.4–8.3)
50–59	72.2 (68.7–75.8)	30.2 (28.0–32.6)	20.6 (18.7–22.6)	19.3 (17.5–21.3)
60–69	155.5 (148.9–162.3)	66.3 (62.0–70.8)	45.1 (41.5–48.8)	39.3 (36.0–42.8)
70–79	231.7 (220.9–243.0)	108.2 (101.0–116.0)	65.5 (59.8–71.6)	49.0 (44.1–54.3)
≥ 80	293.4 (273.6–314.3)	156.1 (141.7–171.6)	73.2 (63.4–84.0)	50.0 (42.0–59.1)
Hispanic				
20–29	0.8 (0.7–0.9)	0.3 (0.2–0.4)	0.2 (0.1–0.3)	0.3 (0.2–0.4)
30–39	3.2 (3.0–3.5)	1.2 (1.0–1.3)	0.7 (0.6–0.9)	1.2 (1.1–1.4)
40–49	12.6 (12.0–13.2)	3.6 (3.3–4.0)	3.4 (3.1–3.7)	5.3 (4.9–5.7)
50–59	45.9 (44.4–47.5)	12.9 (12.1–13.8)	13.3 (12.5–14.2)	18.6 (17.6–19.6)
60–69	112.6 (109.3–116.1)	34.8 (32.9–36.7)	34.7 (32.9–36.7)	40.6 (38.6–42.7)
70–79	184.1 (178.1–190.1)	67.2 (63.6–70.9)	50.8 (47.7–54.0)	60.7 (57.3–64.2)
≥ 80	225.8 (215.4–236.5)	96.4 (89.6–103.5)	58.0 (52.8–63.6)	62.3 (56.9–68.1)
Asian/Pacific Islander				
20–29	1.2 (1.0–1.5)	0.3 (0.2–0.5)	0.3 (0.2–0.5)	0.5 (0.3–0.7)
30–39	5.0 (4.5–5.5)	1.5 (1.2–1.8)	1.3 (1.0–1.6)	2.1 (1.8–2.4)
40–49	18.0 (16.9–19.1)	4.5 (4.0–5.1)	5.2 (4.7–5.8)	7.9 (7.2–8.6)
50–59	54.9 (52.6–57.2)	11.7 (10.7–12.8)	18.7 (17.4–20.1)	23.4 (21.9–24.9)
60–69	124.8 (120.4–129.2)	30.0 (27.9–32.3)	46.9 (44.2–49.6)	45.3 (42.7–48.0)
70–79	211.1 (203.9–218.6)	64.1 (60.1–68.2)	74.3 (70.0–78.7)	68.5 (64.4–72.8)
≥ 80	262.5 (250.3–275.1)	93.5 (86.3–101.2)	88.7 (81.7–96.2)	69.8 (63.6–76.4)

Note. Figures are rounded to nearest tenth.
Note. ''s'' denotes a rate based on fewer than 15 cases, and therefore not shown.
CI, confidence interval; CRC, colorectal cancer.

calculate the BAPC.[21] The biannual percent change was used instead of the annual percent change to allow for stable estimates due to relatively small sample sizes in specific cohorts.

All calculations were performed for each of the seven age groups. Statistical significance was defined as a *p*-value less than α of 0.05, or when 95% confidence intervals excluded a value of 1. The criterion for statistical significance was not adjusted for the number of comparisons made.

Results

Demographics and disease characteristics

A total of 5617 YAs were observed among the 231,544 CRC cases in this study (952 aged 20–29 and 4665 aged 30–39; Table 1). The study population was predominantly Caucasian (71%), but also included Hispanics (12%), Asian/Pacific Islanders (10%), and African Americans (7%; Table 1). The numbers of male and female cases were equal for each group. The mean age of all study participants at diagnosis was 69 years old. Caucasians had a mean age of 70; lower mean ages were observed in the African American (66), Hispanic (64), and Asian/Pacific Islander (66) groups.

Forty-one percent of all CRC cases had proximal colon subsite location, compared to 28% in the distal colon and 29% in the rectum. African Americans had the highest proportion of CRC diagnoses in the proximal colon—notable at 47%. Information on tumor stage at diagnosis was available for 95% of the study population. Regional disease stage was the most common stage in all examined race/ethnicity and age groups (Table 1), though YAs had a greater proportion of CRC diagnosed at distant stage than each of the 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%).

Age-specific CRC incidence rates and anatomic subsite

As expected, all other populations were observed to have substantially higher CRC incidence rates among both males (Table 2) and females (Table 3) than the YA age groups

Table 3. Average Annual Age-Specific CRC Incidence Rates per 100,000 Population Among Females, by Anatomic Subsite, California Cancer Registry, 1988–2009

	Total CRC rate (95% CI)	*Proximal colon cancer rate (95% CI)*	*Distal colon cancer rate (95% CI)*	*Rectal cancer rate (95% CI)*
Caucasian				
20–29	0.8 (0.7–1.0)	0.2 (0.2–0.3)	0.3 (0.2–0.4)	0.3 (0.2–0.4)
30–39	3.7 (3.5–3.9)	1.1 (1.0–1.2)	1.2 (1.1–1.3)	1.3 (1.2–1.5)
40–49	14.5 (14.0–14.9)	4.1 (3.9–4.3)	4.5 (4.3–4.8)	5.5 (5.3–5.8)
50–59	40.5 (39.7–41.4)	13.0 (12.6–13.5)	13.1 (12.6–13.5)	13.6 (13.2–14.1)
60–69	94.3 (92.8–95.7)	39.1 (38.2–40.0)	26.4 (25.7–27.2)	26.7 (25.9–27.5)
70–79	177.9 (175.7–180.1)	87.6 (86.0–89.1)	43.3 (42.3–44.4)	41.9 (40.8–42.9)
≥80	263.0 (259.8–266.2)	143.6 (141.3–146.0)	53.1 (51.7–54.6)	53.3 (51.9–54.7)
African American				
20–29	0.7 (0.5–1.0)	s	s	s
30–39	4.6 (3.9–5.3)	1.9 (1.5–2.3)	1.5 (1.2–1.9)	1.1 (0.8–1.5)
40–49	19.0 (17.6–20.5)	7.5 (6.7–8.5)	6.3 (5.5–7.2)	4.7 (4.0–5.5)
50–59	62.4 (59.3–65.6)	28.4 (26.3–30.6)	18.4 (16.8–20.2)	13.9 (12.5–15.5)
60–69	128.4 (123.0–134.1)	65.2 (61.3–69.2)	36.0 (33.1–39.0)	25.0 (22.6–27.6)
70–79	210.6 (201.9–219.5)	111.5 (105.2–118.0)	51.7 (47.4–56.2)	39.8 (36.1–43.8)
≥80	306.5 (292.4–321.0)	166.8 (156.5–177.6)	64.7 (58.3–71.6)	54.4 (48.6–60.7)
Hispanic				
20–29	0.7 (0.6–0.9)	0.2 (0.1–0.3)	0.2 (0.2–0.3)	0.3 (0.2–0.4)
30–39	3.4 (3.1–3.7)	0.9 (0.7–1.0)	1.1 (1.0–1.3)	1.2 (1.1–1.4)
40–49	11.4 (10.9–12.0)	3.2 (2.9–3.6)	4.1 (3.8–4.5)	3.8 (3.5–4.2)
50–59	32.1 (30.9–33.4)	10.5 (9.8–11.2)	11.0 (10.3–11.8)	10.1 (9.4–10.8)
60–69	70.4 (68.0–72.9)	28.9 (27.4–30.5)	20.0 (18.7–21.3)	20.2 (18.9–21.5)
70–79	120.2 (116.1–124.4)	55.6 (52.8–58.5)	30.2 (28.1–32.3)	31.5 (29.4–33.7)
≥80	178.2 (171.1–185.4)	94.8 (89.7–100.2)	35.9 (32.8–39.2)	38.6 (35.4–42.1)
Asian/Pacific Islander				
20–29	1.0 (0.8–1.3)	0.3 (0.2–0.5)	0.2 (0.1–0.4)	0.4 (0.3–0.6)
30–39	4.5 (4.1–5.0)	1.2 (1.0–1.5)	1.5 (1.2–1.8)	1.7 (1.5–2.1)
40–49	16.0 (15.0–17.0)	3.7 (3.3–4.2)	6.2 (5.6–6.9)	5.9 (5.3–6.5)
50–59	44.3 (42.4–46.3)	11.0 (10.0–11.9)	18.1 (16.9–19.4)	14.4 (13.3–15.5)
60–69	82.5 (79.3–85.7)	28.4 (26.6–30.3)	28.0 (26.2–30.0)	24.6 (22.9–26.4)
70–79	140.9 (135.7–146.2)	55.9 (52.7–59.3)	44.4 (41.5–47.4)	37.0 (34.4–39.7)
≥80	217.9 (208.6–227.5)	96.7 (90.6–103.2)	62.9 (58.0–68.1)	50.2 (45.8–54.9)

Note. Figures are rounded to nearest tenth.
Note. ''s'' denotes a rate based on fewer than 15 cases, and therefore not shown.
CI, confidence interval; CRC, colorectal cancer.

(20–29 and 30–39 years old). The absolute incidence of CRC among adults aged 20–29 ranged from 0.7 (African American females and Hispanic females) to 1.2 (Asian/Pacific Islander males) per 100,000. When analyzed by tumor subsite location among individuals aged 20–29, the highest incidence in males was rectal cancer among Asian/Pacific Islanders; in females it was also rectal cancer among Asian/Pacific Islanders. The absolute incidence of CRC among adults aged 30–39 ranged from 3.4 (Hispanic females) to 5.0 (Asian/Pacific Islander males) per 100,000. Among individuals aged 30–39, the tumor subsite location with highest incidence in males was rectal cancer among Asian/Pacific Islanders, though for females it was proximal colon cancer among African Americans.

Biannual percent change of CRC incidence by gender, age, race/ethnicity, and anatomic subsite

Despite low CRC incidence, both male and female YAs (aged 20–29 and 30–39) were observed to have significant increased BAPC in CRC incidence. In fact, as shown in Table 4, the BAPC significantly *decreased* in both males and females in all four age groups ≥ 50 years old, but significantly *increased* among pre-screening age adults aged 20–29, 30–39, and 40–49. Tables 5 (males) and 6 (females) show the BAPC in age-specific CRC incidence rates by anatomic subsite location. Incidence rates varied widely by tumor subsite, race/ethnicity, and age. Of note, the greatest observed biannual percentage changes were for distal colon cancer among Hispanic females aged 20–29 (BAPC = +15.9%; $p = 0.042$) and Hispanic males aged 30–39 (BAPC = +10.4%, $p < 0.001$). Large BAPC increases were also observed among Hispanic females aged 20–29 for rectal cancer (+10.5%) and Caucasian males aged 20–29 for rectal cancer (+9.4%). Interestingly, a large decrease in BAPC (–11.9%) for rectal cancer was observed among Asian/Pacific Islander males aged 20–29. Individuals aged 40–49 were observed to have increasing BAPCs in CRC incidence for both males and females in every race/ethnicity group except African American.

Table 4. Biannual Percent Change in Age-Specific CRC Incidence Rates, by Gender, Pooled Across Caucasians, African Americans, Hispanics, and Asian/Pacific Islanders, California Cancer Registry, 1988–2009

Gender	*Age group*	*BAPC*	p-*value*	*Incident cases*	*Person-years at risk*
Male	20–29	+2.7	<0.011	514	58636525
	30–39	+3.5	<0.001	2487	60805393
	40–49	+2.7	<0.001	8341	51248632
	50–59	−1.0	0.006	19782	35613256
	60–69	−4.4	<0.001	31301	23146945
	70–79	−5.1	<0.001	34252	15140018
	≥80	−7.1	<0.001	20159	7035989
Female	20–29	+3.8	<0.008	438	53314710
	30–39	+4.5	<0.001	2178	57753130
	40–49	+2.6	<0.001	7262	51006233
	50–59	−1.4	0.025	15128	37137748
	60–69	−3.6	0.001	23932	26330944
	70–79	−4.0	0.001	33256	19788963
	≥80	−5.5	0.001	32514	12868523

Note. BAPC is rounded to the nearest tenth; probabilities are rounded to three places, with a floor of 0.001.

Note. Probabilities given for the BAPC are from tests that the slope of the regression line is zero.

BAPC, biannual percent change; CRC, colorectal cancer.

Discussion

Despite a gradually decreasing CRC incidence among the overall population of California and the low absolute incidence of CRC among young adults, we observed significant increases in CRC incidence over time among males and females in both of the YA age groups (20–29 and 30–39), as well as in individuals aged 40–49. Importantly, this observation was particularly evident among Hispanic males and Hispanic females, groups not previously identified to be at increased CRC risk. It is important to recognize that while multiple studies have shown overall rates of CRC to be declining, age-standardized incidence rates may mask rising age-specific incidence rates in certain age groups, as reported here, demonstrating the importance of also examining age-specific rates.

While an increase in CRC incidence in young populations has been previously reported,[5–8] this is the first report of incidence rates stratified by race/ethnicity and tumor location in YAs. In 2009, Siegel et al. focused on Caucasians in their analysis of SEER data on the rising incidence of CRC in individuals under 50 years of age.[5] Our findings generally support this prior report, although we also observed significant increases in rates of proximal colon cancer among most race/ethnicity groups within the YA population. The prior study also examined tumor subsite location within the colorectum, but again only evaluated Caucasians, while our study assessed all four major race/ethnicity groups in California.

Several lines of research indicate that CRC among YAs differs from CRC in adults 50 and older. Interestingly, survival outcome among surgically-resected CRC cancer patients is improved for patients < 40 versus > 40 years.[22] Also, in a small study of 37 YA CRC patients compared to CRC patients age > 50, YA CRC patients reported different symptomatology related to their cancer at diagnosis (i.e., pain, fatigue, rash, and interruptions with mood, work, and life relationships).[23] A separate study of 180 patients with CRC under age 50 at two institutions reported that the vast majority of patients (94%) were diagnosed due to cancer-related symptoms (rectal bleeding, abdominal pain, or colonic obstruction).[24] In that study, only 8% of the patients had a first-degree family member with CRC, which clearly demonstrates that using family history alone is inadequate in prognosticating risk among the YA and unscreened population. One plausible explanation for differences in symptomatology between YAs and adults 50 or older with CRC could relate to differences in tumor subsite location. Of note, the largest BAPC increases among YA patients in our study were observed on the left side (i.e., descending colon, rectum). Importantly, left-sided lesions are more likely to result in clinically-identifiable rectal bleeding due to their distal location, and also can be detected by all routine CRC screening modalities (including flexible sigmoidoscopy, which cannot be used to detect proximal [right-sided] CRC). Even though adults under age 50 are largely unscreened, efforts are underway to raise awareness among primary care physicians

Table 5. Biannual Percent Change in Age-Specific CRC Incidence Rates Among Males, by Anatomic Subsite, California Cancer Registry, 1988–2009

	Total CRC		*Proximal colon cancer*		*Distal colon cancer*		*Rectal cancer*	
	BAPC	p-*value*	*BAPC*	p-*value*	*BAPC*	p-*value*	*BAPC*	p-*value*
Caucasian								
20–29	+4.6	0.025	+6.0	0.219	−0.4	0.938	+9.4	0.006
30–39	+4.7	<0.001	+1.4	0.421	+4.4	0.002	+8.3	<0.001
40–49	+3.2	<0.001	+1.2	0.108	+2.6	0.026	+5.3	<0.001
50–59	−1.9	<0.001	−2.0	<0.001	−2.6	<0.001	−1.2	0.083
60–69	−5.3	<0.001	−2.9	<0.001	−7.4	<0.001	−5.8	<0.001
70–79	−5.6	<0.001	−3.3	<0.001	−8.2	<0.001	−6.3	<0.001
≥80	−7.5	<0.001	−5.7	<0.001	−9.2	<0.001	−9.3	<0.001
African American								
20–29	−2.3	0.651	−7.0	0.157	−3.5	0.666	−0.6	0.860
30–39	+2.8	0.234	0.0	0.993	+3.5	0.406	+4.4	0.371
40–49	−0.2	0.902	−2.3	0.168	−2.2	0.501	+5.3	0.062
50–59	−0.7	0.486	−0.5	0.592	−0.8	0.546	−1.8	0.345
60–69	−2.3	0.004	+1.8	0.121	−5.6	<0.001	−5.9	0.002
70–79	−4.5	<0.001	−2.2	0.039	−6.4	<0.001	−6.5	0.006
≥80	−4.8	0.002	−4.1	0.031	−7.9	0.005	−2.9	0.111
Hispanic								
20–29	+3.5	0.064	+3.0	0.390	+5.2	0.555	+5.0	0.217
30–39	+4.9	0.005	+4.0	0.116	+10.4	<0.001	+4.1	0.105
40–49	+4.0	<0.001	+2.4	0.095	+4.9	<0.001	+4.6	0.005
50–59	+2.2	0.015	+3.1	0.038	+3.2	0.070	+1.2	0.109
60–69	−0.8	0.079	+1.9	0.016	−0.8	0.299	−2.8	<0.001
70–79	−1.6	0.023	+0.2	0.777	−3.0	0.024	−2.4	0.007
≥80	−3.5	0.002	−2.2	0.108	−2.0	0.334	−6.8	0.002
Asian/Pacific Islander								
20–29	−2.0	0.437	−3.0	0.617	+5.8	0.136	−11.9	0.015
30–39	+0.7	0.690	+5.1	0.126	+0.4	0.921	−0.4	0.901
40–49	+3.4	0.020	−0.6	0.791	+4.7	0.018	+5.9	0.009
50–59	+1.5	0.062	+3.3	0.037	−0.1	0.950	+2.3	0.007
60–69	−2.9	0.002	+1.2	0.501	−3.2	0.033	−4.5	<0.001
70–79	−2.9	0.004	−0.5	0.695	−3.4	0.014	−4.6	<0.001
≥80	−6.4	<0.001	−3.3	0.041	−8.4	<0.001	−6.7	<0.001

Note. BAPC is rounded to the nearest tenth; probabilities are rounded to three places, with a floor of 0.001.
Note. Probabilities given for the BAPC are from tests that the slope of the regression line is zero.
BAPC, biannual percent change; CRC, colorectal cancer.

and gastroenterologists to recognize CRC-related symptomatology in patients under age 50 and promptly initiate early detection methods.[25]

Although we found Hispanics to have the lowest overall rates of CRC, this group also had the largest increase in incidence over the 1988–2009 study period. Of note, CRC incidence was observed to be declining among all age groups ≥50 years of age, except for Hispanics and Asian/Pacific Islanders 50–59 years old (as seen in Tables 5 and 6). Ideally, the population 50+ years old should be undergoing recommended CRC screening (i.e., fecal occult blood testing, fecal immunochemical testing, flexible sigmoidoscopy, colonoscopy, and/or computed tomography colonography),[4] but adherence to recommended screening guidelines is estimated to be only 50–60% among individuals age 50 and older.[26] Variation in access to healthcare between racial/ethnic groups has been well documented,[27] and it is possible that the 50–59 years old Hispanic and Asian/Pacific Islander groups with observed increases in CRC incidence may be due to differential access to screening. Data from the 2010 United States Behavioral Risk Factor Surveillance System (BRFSS) indicate differential CRC screening rates (with either sigmoidoscopy or colonoscopy) among racial/ethnic groups in the standard recommended screening population of those 50 and older: 68% of White non-Hispanics, 64% of Black non-Hispanics, 54% of Asian non-Hispanics, and 50% of Hispanics.[26] Hispanic males younger than 50 had the lowest screening rate in the 2010 BRFSS (47%) compared to other racial/ethnic and gender-specific groups.[26] A study published in 2012 showed similar risk reduction ascribed to non-invasive re-screening after an initial normal colonoscopy at age 50,[28] and this may provide a method to improve screening adherence over the next several years; however, because of the importance of the initial screening at age 50, such a change in screening practice would not likely impact those who are currently non-compliant with an initial screening. Newer methods of screening such as fecal immunochemical testing (FIT)[29] and stool DNA testing[30] have emerged as promising screening modalities with improved adherence. Despite these considerations, the YA population

Table 6. Biannual Percent Change in Age-Specific CRC Incidence Rates Among Females, by Anatomic Subsite, California Cancer Registry, 1988–2009

	Total CRC		*Proximal colon cancer*		*Distal colon cancer*		*Rectal cancer*	
	BAPC	p-*value*	*BAPC*	p-*value*	*BAPC*	p-*value*	*BAPC*	p-*value*
Caucasian								
20–29	+3.1	0.093	+5.4	0.144	+5.7	0.372	−0.2	0.924
30–39	+5.9	<0.001	+4.7	0.089	+5.2	<0.001	+7.0	0.007
40–49	+4.1	<0.001	+1.1	0.060	+5.0	<0.001	+5.8	<0.001
50–59	−2.0	0.007	−2.3	0.005	−2.3	0.005	−1.5	0.185
60–69	−4.3	<0.001	−2.6	0.003	−6.1	<0.001	−5.4	<0.001
70–79	−4.1	<0.001	−1.7	0.003	−7.3	<0.001	−6.0	<0.001
≥80	−5.5	<0.001	−3.3	<0.001	−8.7	<0.001	−7.5	<0.001
African American								
20–29	+7.0	0.297	+3.4	0.690	***	***	+3.2	0.480
30–39	+1.2	0.642	+1.9	0.470	+2.4	0.395	−1.3	0.807
40–49	−1.2	0.265	−2.6	0.139	+1.6	0.412	−2.3	0.531
50–59	−1.2	0.333	+0.4	0.764	−1.3	0.439	−3.6	0.027
60–69	−2.0	0.020	+1.0	0.229	−5.8	0.002	−4.2	0.005
70–79	−3.0	0.009	−0.6	0.643	−5.7	<0.001	−7.4	0.003
≥80	−4.3	<0.001	−2.8	0.003	−6.3	<0.001	−6.7	0.002
Hispanic								
20–29	+7.8	<0.001	−0.5	0.946	+15.9	0.042	+10.5	0.028
30–39	+4.7	<0.005	+6.5	0.004	+5.1	0.137	+4.1	0.053
40–49	+1.5	0.263	+1.8	0.507	+1.6	0.409	+1.1	0.348
50–59	+0.5	0.545	+1.9	0.254	−0.9	0.498	+0.2	0.892
60–69	−0.9	0.225	+2.6	0.173	−1.4	0.297	−3.9	<0.001
70–79	−2.0	0.004	+2.5	0.018	−6.7	<0.001	−4.4	0.012
≥80	−4.1	0.002	−2.3	0.140	−6.9	0.004	−5.6	<0.001
Asian/Pacific Islander								
20–29	−2.4	0.670	−3.9	0.444	−1.6	0.817	−8.0	0.221
30–39	+2.8	0.219	+3.5	0.312	+13.6	0.058	−1.0	0.752
40–49	+2.8	0.007	+2.5	0.237	+6.2	0.017	−0.2	0.838
50–59	+0.7	0.439	+5.1	0.005	−0.1	0.941	−1.1	0.151
60–69	−0.8	0.337	+1.4	0.202	+0.8	0.552	−4.8	<0.001
70–79	−1.2	0.155	+0.7	0.570	−2.1	0.042	−2.8	0.060
≥80	−3.7	<0.001	−0.3	0.790	−5.8	<0.001	−5.7	0.005

Note. BAPC is rounded to the nearest tenth; probabilities are rounded to three places, with a floor of 0.001.
Note. Probabilities given for the BAPC are from tests that the slope of the regression line is zero.
Note. "***" = insufficient cases to estimate BAPC.
BAPC, biannual percent change; CRC, colorectal cancer.

is largely unscreened and little information exists to demonstrate which groups of YA patients are at highest risk, or which CRC detection methods would be preferred among YA patients.

There are multiple risk factors—including genetic, lifestyle, and environmental—that can contribute to CRC development in young populations. Adults in the prescreening age range (20–49) without a family history of hereditary CRC syndromes (such as familial adenomatous polyposis [FAP] or hereditary non-polyposis colorectal cancer [HNPCC]) are not routinely screened for CRC, and even those with a family history of these conditions may not participate in regular screening. In this study, we found that younger individuals with CRC were more likely to have distant disease at the time of diagnosis, as could be expected in an unscreened population. In a study by You et al., a large percentage of young-onset CRC patients were not insured;[8] a lack of insurance in known to hinder access to healthcare, which could in turn lead to delayed presentation and advanced disease at diagnosis. Dietary factors such as the intake of fats, red meats, fruits, and vegetables, along with lifestyle factors such as physical activity and obesity, have all been shown to modify CRC risk.[31] Current CRC screening guidelines generally recommend that routine screening begins at age 50 for average-risk individuals, but earlier for higher risk individuals.[4] For example, the American College of Gastroenterology recommends that screening begin at age 45 for African Americans[32] and the American College of Physicians recently released a guidance statement noting that African Americans should be screened starting at age 40.[33] However, the American Cancer Society and United States Preventive Services Task Force have not adopted this recommendation for earlier screening among African Americans, and race/ethnicity-specific recommendations for other groups are lacking. Among YAs, greater focus on early detection among young, symptomatic individuals may be warranted.

Our population-based analysis of CRC incidence was limited by the inability to control for family history of CRC,

which is an important risk factor for CRC. Information on family history is not available within the CCR (or SEER); therefore, if risk factors associated with a family history of CRC vary by race/ethnicity, then our observations about race/ethnicity may have been differentially influenced by genetic factors. Approximately 5% of all CRC tumors result from an inherited cancer syndrome, and this proportion is higher in younger individuals with CRC.[34–36] Importantly, hereditary syndromes increase CRC risk for individuals of all ages; for example, HNPCC has an average age range at CRC diagnosis of 50–61 years old, accounting for the large majority of cases of hereditary CRC,[34,35] while FAP, with an average age of CRC diagnosis of 40 years old, accounts for $<1\%$ of cases of CRC.[36] As such, while a small proportion of individuals in our study must be carriers of a genetic mutation that predisposed them to a higher risk of CRC, we were unable to control for this in our incidence analyses; even proxy data such as microsatellite instability was unavailable. The population-based nature of this study is a strength, particularly for this regional cancer registry which includes data from a populous, diverse region that is (unlike SEER) geographically contiguous.

Conclusion

The results of this investigation support our hypothesis that CRC incidence for YAs is low in terms of absolute incidence, but is increasing over time. We observed that despite an overall decrease in CRC incidence amongst Californians, CRC incidence rose in young adults aged 20–29 and 30–39, as well as among individuals aged 40–49. Furthermore, we found that CRC in YAs (a largely unscreened population) was more likely to be diagnosed at an advanced stage and therefore less likely to be cured. Our findings suggest that more research is needed to characterize individuals with young-onset CRC and to determine how these individuals differ from young people who do not develop CRC.

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