Methods (submitted as supplemental material)

We derived incidence of invasive CRC from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program from 1975 – 2014. SEER routinely collects information on patient demographics and tumor characteristics for all cancers diagnosed in defined geographic regions. SEER 9 registries include Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, and Utah, approximately 10% of the U.S. population. We estimated age-adjusted incidence (to the 2000 U.S. standard population) using SEER*Stat version 8.3.5 as incidence rates per 100,000 persons. Corresponding 95% confidence intervals were calculated as modified gamma intervals.[3]

To illustrate patterns, we plotted incidence rates across 5-year age categories (20-24 to 45-49) by time period. We divided the study period into 8 approximate 5-year time periods (1975-1979, 1980-1984, 1985-1989, 1990-1994, 1995-1999, 2000-2004, 2005-2009, and 2010-2014). In supplementary material, we report incidence rates by time period and anatomic subsite: proximal colon (cecum, ascending colon, hepatic flexure, transverse colon), descending colon (splenic flexure, descending colon, sigmoid colon) and rectum (rectosigmoid junction, rectum).

To test for time period and birth cohort effects, we conducted an age-period-cohort analysis using an analytic tool developed by the National Cancer Institute.[4] We used 5-year age groups and time periods (above) to create 13 birth cohorts (1930-35 to 1990-95). We estimated the ratio of age-specific incidence rates in each time period and birth cohort relative to the reference value (reference birth cohort=1960-64, reference time period=1990-94).

We report analyses stratified by race (white vs. black) in supplementary material.

Supplementary Table 1. Age-specific incidence (per 100,000 persons) of young-onset colorectal cancer by 5-year age group and time period, SEER 9, 1975 – 2014

| | Age group | | | | | | All ages |
	20-24	25-29	30-34	35-39	40-44	45-49	(20-49)
Time period							
1975-79	0.6	1.6	3.5	7.0	14.3	30.1	9.9
1980-84	0.6	1.1	2.9	6.2	13.4	28.3	9.1
1985-89	0.4	1.2	2.8	5.9	12.2	26.1	8.4
1990-94	0.4	1.4	3.1	6.2	12.7	24.3	8.3
1995-99	0.7	1.7	3.4	6.5	12.7	25.4	8.7
2000-04	1.0	1.8	3.9	7.6	14.3	26.9	9.6
2005-09	1.1	2.3	4.7	8.5	16.3	28.8	10.7
2010-14	1.2	2.8	5.3	9.6	18.0	31.3	11.8

NOTE: Shaded cells denote time periods during which incidence rates were lowest.

Supplementary Table 2. Age-specific incidence (per 100,000 persons) of young-onset colorectal cancer among whites by 5-year age group and time period, SEER 9, 1975 – 2014

| | Age group | | | | | | All ages |
	20-24	25-29	30-34	35-39	40-44	45-49	(20-49)
Time period							
1975-79	0.6	1.6	3.5	6.8	14.2	29.7	9.7
1980-84	0.7	1.0	2.7	6.0	12.7	28.0	8.8
1985-89	0.4	1.1	2.8	5.3	11.5	25.2	8.0
1990-94	0.4	1.3	3.0	5.7	12.0	22.9	7.8
1995-99	0.6	1.7	3.3	6.3	12.3	24.1	8.3
2000-04	1.1	1.8	3.8	7.2	13.6	25.6	9.2
2005-09	1.1	2.4	4.8	8.4	15.7	27.7	10.4
2010-14	1.4	2.8	5.3	9.6	17.8	30.2	11.6

NOTE: Shaded cells denote time periods during which incidence rates were lowest.

Supplementary Table 3. Age-specific incidence (per 100,000 persons) of young-onset colorectal cancer among blacks by 5-year age group and time period, SEER 9, 1975 – 2014

			Age group				All ages
	20-24	25-29	30-34	35-39	40-44	45-49	(20-49)
Time period							
1975-79	0.8	2.0	3.7	9.3	15.8	34.3	11.4
1980-84	0.3	1.8	4.7	8.2	20.1	31.1	11.5
1985-89	0.4	1.8	3.3	10.4	18.1	34.8	11.9
1990-94	0.5	1.7	4.0	9.9	18.0	36.8	12.3
1995-99	0.9	2.2	4.1	7.8	16.2	35.2	11.4
2000-04	0.5	1.7	4.2	9.6	18.8	35.6	12.2
2005-09	0.9	1.8	4.2	9.1	20.2	35.8	12.5
2010-14	0.6	2.5	5.3	9.7	18.7	37.8	12.9

NOTE: Shaded cells denote (first) time periods during which incidence rates were lowest.

Supplementary Figure 1. Age-adjusted (2000 U.S. standard population) incidence of young-onset colorectal cancer (ages 20-49 years) by anatomic subsite, SEER 9, 1975 – 2014

Supplementary Figure 2. Age-specific incidence of young-onset colorectal cancer by 5-year age group, overall (A) and by anatomic subsite (B-D), SEER 9, 1975 – 2014

Proximal colon (2B) includes the cecum, ascending colon, hepatic flexure, and transverse colon; distal colon (2C) includes the splenic flexure, descending colon, and sigmoid colon; rectum (2D) includes the rectosigmoid junction and rectum. Shaded regions in figure denote 95% confidence intervals