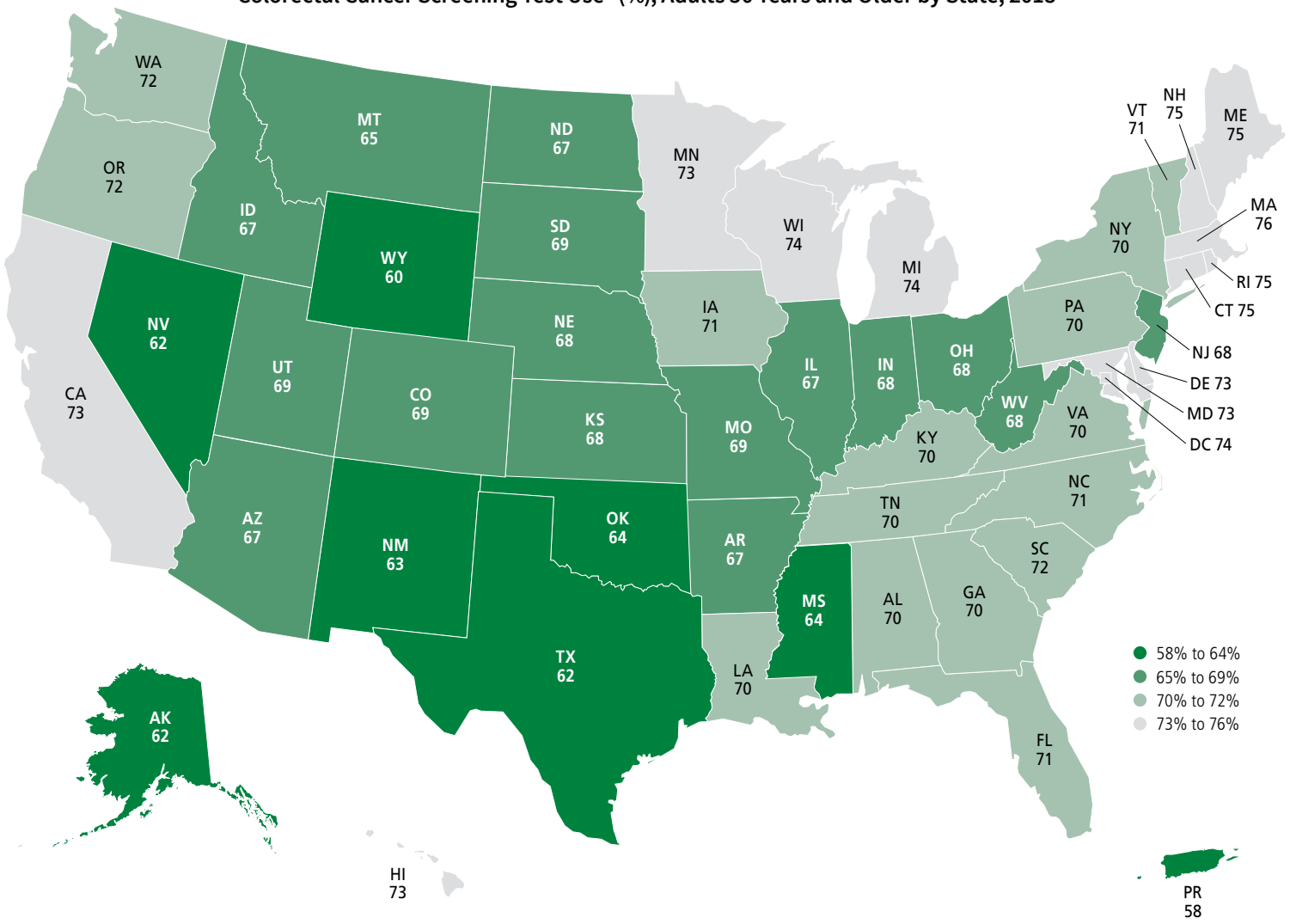
American Cancer Society®

Colorectal Cancer
Facts & Figures 2020-2022

Colorectal Cancer Screening Test Use* (%), Adults 50 Years and Older by State, 2018



*Blood stool test, sigmoidoscopy, or colonoscopy in the past 1, 5, and 10 years, respectively.
Note: Estimates are age adjusted to the 2000 US standard population and do not distinguish between examinations for screening and diagnosis.
Source: Behavioral Risk Factors Surveillance System, 2018. See Sources of Statistics (page 32) for complete citation and more information.

Contents

This publication attempts to summarize current scientific information about colorectal cancer. Except when specified, it does not represent the official policy of the American Cancer Society.

Suggested citation: American Cancer Society. *Colorectal Cancer Facts & Figures 2020-2022.* Atlanta: American Cancer Society; 2020.

Global Headquarters: American Cancer Society Inc.
250 Williams Street, NW, Atlanta, GA 30303-1002
404-320-3333

Colorectal Cancer Basic Facts

What is colorectal cancer?

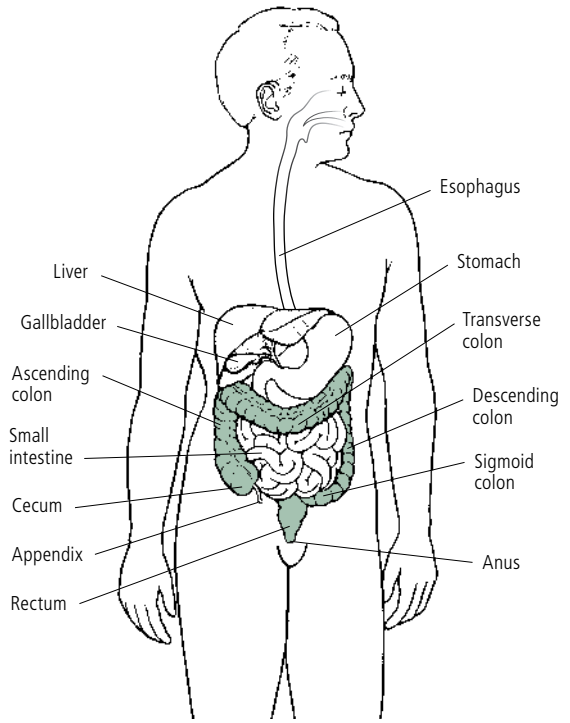
Cancer is a disease characterized by the unchecked division of abnormal cells. When this type of growth occurs in the colon or rectum, it is called colorectal cancer (CRC). The colon and rectum (colorectum), along with the anus, make up the large intestine, the final segment of the gastrointestinal (GI) system. The large intestine is sometimes called the large bowel, which is why CRC is sometimes referred to as bowel cancer. The function of the large intestine is to absorb water and electrolytes from food matter and eliminate feces. As depicted in Figure 1, the first part of the large intestine is the colon, a muscular tube about 1.5 meters (5 feet) long and 5 centimeters (2 inches) in diameter that is divided into 4 sections:

- The *ascending colon* begins with the cecum (a pouch where undigested food is received from the small intestine) and extends upward on the right side of the abdomen.
- The *transverse colon* crosses the body from right to left, and is referred to collectively with the ascending colon as the proximal, or right, colon.
- The *descending colon* descends on the left side.
- The *sigmoid colon*, named for its "S" shape, is the final portion of the colon and is referred to collectively with the descending colon as the distal, or left, colon.

Waste passes from the sigmoid colon into the rectum – the final 15 centimeters (6 inches) of the large intestine – and is then expelled through the anus (2-3 centimeters or 1 inch). Despite their anatomic proximity, cancers in the anus are classified separately from those in the rectum because they usually originate from different cell types, and thus have different characteristics.

However, tumors within the colorectum also vary in their molecular, biological, and clinical features, and in their association with risk factors.[1,2] For example, physical inactivity is associated with increased risk of cancer in the colon, but not in the rectum. In addition, patients are more likely to be diagnosed with tumors in the proximal colon if they are older (versus younger), black (versus white), or female (versus male).[3,4]

Figure 1. Anatomy of the Gastrointestinal System



What is a colorectal polyp?

CRC almost always begins as a polyp, which is a noncancerous growth that develops in the mucosal layer (inner lining) of the colon or rectum. Polyps are common, detected in about half (including serrated polyps) of average-risk individuals 50 years of age or older undergoing colonoscopy, with higher prevalence in older age groups and among men compared to women.[5] However, fewer than 10% of polyps are estimated to progress to invasive cancer,[6,7] a process that usually occurs slowly over 10 to 20 years and is more likely as polyps increase in size.[8-10]

Polyps are classified based on their growth pattern as adenomatous (i.e., adenoma), which is the most common cancer precursor, or serrated, so-called because of its saw-toothed appearance under a microscope.[11] Serrated

polyps are further subdivided based on biological characteristics into sessile serrated polyps (SSPs), traditional serrated adenomas (TSAs), and hyperplastic polyps (HPs). Similar to adenomas, SSPs, TSAs, and large HPs are associated with an increased risk for CRC. SSPs are the most difficult to detect during colonoscopy because they are usually flat, covered with a mucous cap, and colored like the surrounding tissue. These features likely contribute to their role as precursors for a large proportion of cancers diagnosed prior to the next recommended colonoscopy (interval or post colonoscopy cancers).[12]

What are the stages of colorectal cancer?

Once a polyp progresses to cancer, it can grow into the wall of the colon or rectum where it may invade blood or lymph vessels that carry away cellular waste and fluid (Figure 2). Cancer cells typically spread first into nearby lymph nodes, which are bean-shaped structures that help fight infections. They can also be carried via blood vessels to other organs and tissues, such as the liver or lungs,[13] or be shed directly into the peritoneum (membrane lining the abdomen).[14] The spread of cancer cells to parts of the body distant from where the tumor started is called metastasis.

The extent to which cancer has spread at the time of diagnosis is described as its stage. Staging is essential for determining treatment choices and assessing prognosis (prediction of disease outcome). The two most common cancer staging systems are the American Joint Committee on Cancer (AJCC) tumor, node, and metastasis (TNM) system, typically used in clinical settings, and the Surveillance, Epidemiology, and End Results (SEER) summary staging system, used for descriptive and statistical analysis of tumor registry data. In this document, we will describe CRC stages using the SEER summary staging system:

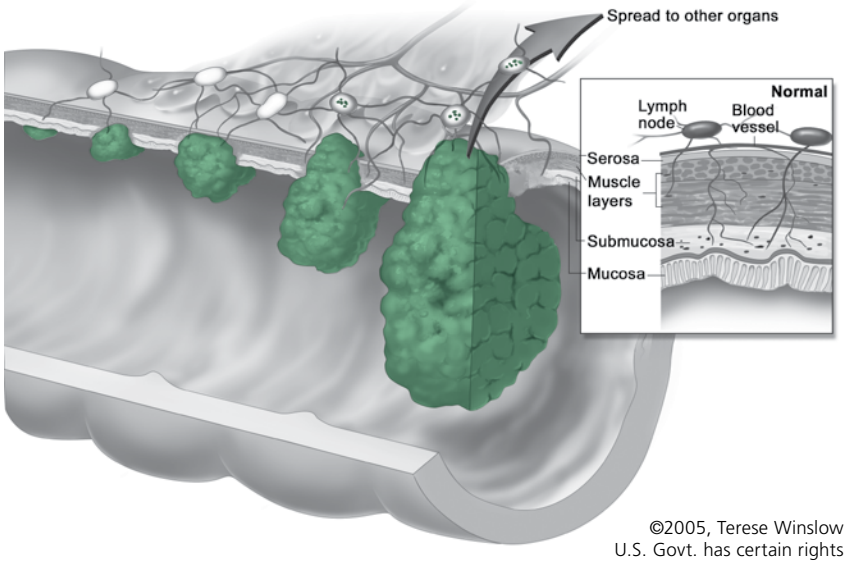
- **In situ:** Cancers that have not yet begun to invade the wall of the colon or rectum; these preinvasive lesions are not included in the cancer statistics provided in this report
- **Local:** Cancers that have grown into the wall of the colon or rectum, but have not extended through the wall into nearby tissues
- **Regional:** Cancers that have spread through the wall of the colon or rectum and have invaded nearby tissue, or that have spread to nearby lymph nodes
- **Distant:** Cancers that have spread to other parts of the body, such as the liver or lung

What are the symptoms of colorectal cancer?

Early CRC often has no symptoms, which is one of the reasons screening is so important. As a tumor grows, it may bleed or block the intestine. The most common symptoms are:

- Bleeding from the rectum
- Blood in the stool or in the toilet after having a bowel movement
- Dark or black stools

Figure 2. Stages of Colorectal Cancer Growth



- A change in bowel habits or the shape of the stool (e.g., more narrow than usual)
- Cramping, pain, or discomfort in the lower abdomen
- An urge to have a bowel movement when the bowel is empty
- Constipation or diarrhea that lasts for more than a few days
- Decreased appetite
- Unintentional weight loss

In some cases, blood loss from the cancer leads to anemia (low number of red blood cells), causing symptoms such as weakness, excessive fatigue, and sometimes shortness of breath. Timely evaluation of symptoms consistent with CRC is essential for all individuals, regardless of age, given the increasing incidence in young adults (see page 6).

Colorectal Cancer Occurrence

How many new cases and deaths are estimated to occur in 2020?

In 2020, there will be an estimated 104,610 new cases of colon cancer and 43,340 cases of rectal cancer diagnosed in the US (Table 1). Although the majority of CRCs are in adults ages 50 and older, 17,930 (12%) will be diagnosed in individuals younger than age 50, the equivalent of 49 new cases per day.

An estimated 53,200 people will die from CRC in 2020, including 3,640 men and women younger than age 50. Unfortunately, reliable statistics on deaths from colon and rectal cancers separately are not available because almost 40% of deaths from rectal cancer are misclassified as colon cancer on death certificates.[15] The high level of misclassification is partly attributed to the misconception among some that the terms colon cancer and colorectal cancer are synonymous because of the widespread use of "colon cancer" to refer to both colon and rectal cancers in educational messaging. To help mitigate the issue and be more explicitly inclusive of rectal cancer patients, several organizations have publicly ended this practice.[16] The ability to study these deaths separately is increasingly important given the steep rise in rectal cancer incidence among younger adults.[17]

Table 1. Estimated Number of Colorectal Cancer Cases and Deaths in the US in 2020 by Age

	Cases			Deaths*
Age	Colorectum	Colon	Rectum	Colorectum
0-49 years	17,930	11,540	6,390	3,640
50-64 years	50,010	32,290	17,720	13,380
65+ years	80,010	60,780	19,230	36,180
All ages	147,950	104,610	43,340	53,200

Estimates are rounded to the nearest 10 and exclude in situ carcinoma.
*Deaths for colon and rectal cancers are combined because a large number of rectal cancer deaths are misclassified as colon.

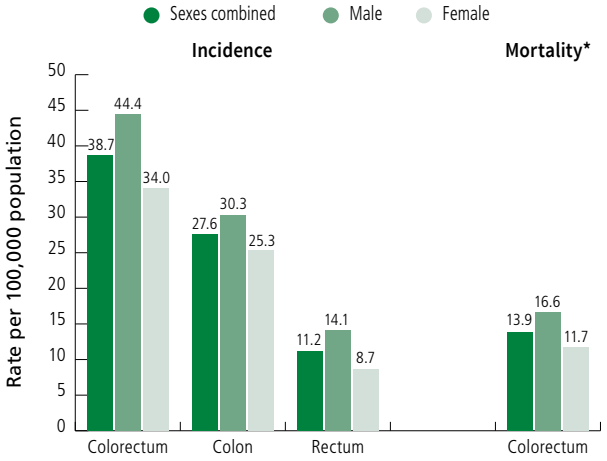
How many people who have been diagnosed with colorectal cancer are alive today?

As of January 1, 2019, there were 776,120 men and 768,650 women alive in the US with a history of CRC.[18] About one-third (35%) of these individuals were diagnosed within the preceding 5 years, and more than half (56%) were ages 65-84 years. Some of these people were cancer-free, while others still had evidence of cancer and may have been undergoing treatment.

What is the risk of developing colorectal cancer?

Approximately 4.4% of men (1 in 23) and 4.1% of women (1 in 25) will be diagnosed with CRC in their lifetime.[19] Lifetime risk is similar in men and women despite higher incidence rates in men because women have longer life expectancy. In addition to sex, age and race/ethnicity also have a large influence on risk.

Figure 3. Colorectal Cancer Incidence (2012-2016) and Mortality (2013-2017) Rates by Subsite and Sex, US



Rates are age adjusted to the 2000 US standard population. *Mortality rates by anatomic subsite are not available because a large number of rectal cancer deaths are misclassified as colon.

Sources: Incidence – North American Association of Central Cancer Registries (NAACCR), 2019. Mortality – National Center for Health Statistics (NCHS), 2019.

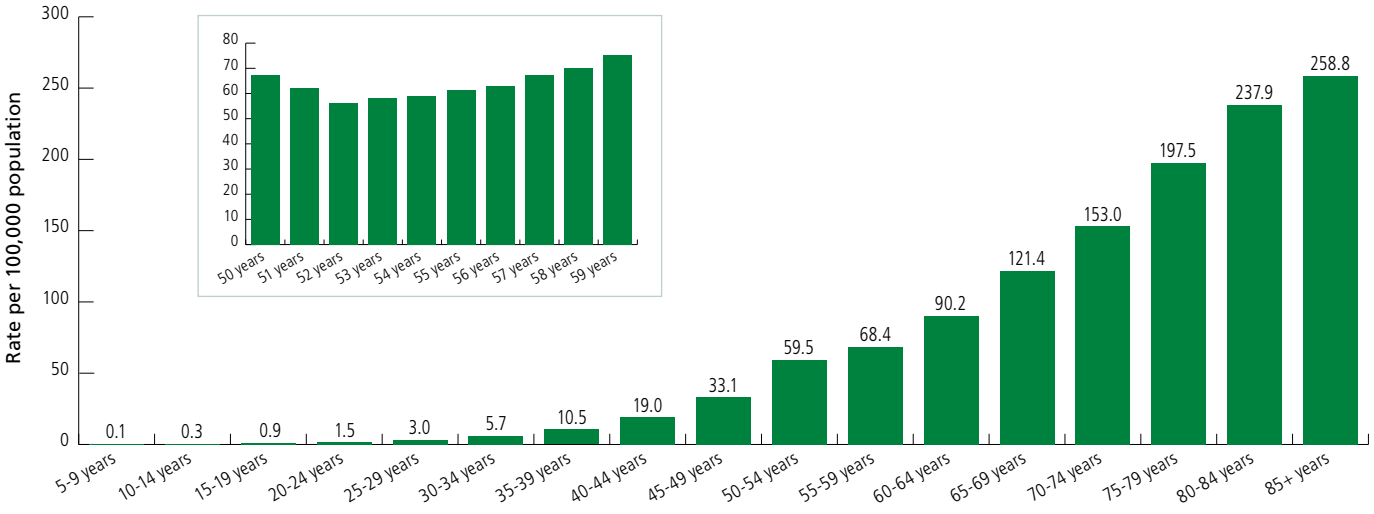
Sex

CRC incidence rates are 30% higher in men than in women, with a larger disparity for rectal cancer (60% higher) than for colon cancer (20% higher; Figure 3). As expected, women also have a lower prevalence of both adenomas overall and of advanced adenomas.[20, 21] However, among individuals 50 and older, women are more likely than men to develop adenomas in the proximal colon,[20] which are less efficiently detected through screening.[22] Gender disparities likely reflect differences in exposures to risk factors (e.g., cigarette smoking) and sex hormones, as well as complex interactions between these influences.[23] Notably, CRC incidence rates in men and women younger than 45 years are comparable.

Age

Like most types of cancer, the risk of CRC increases with age. For every subsequent 5-year age group, the incidence rate approximately doubles until age 50, and thereafter increases by about 30% (Figure 4). The exception is ages 50-54 years versus ages 55-59 years, for which there is only a 15% difference (60 versus 68 per 100,000, respectively), partly because the natural age-associated influence on risk is disrupted by first-time CRC screening in the younger age group. The screening effect is magnified in current rates by single year of age (Figure 4), which are actually higher in individuals ages 50-51 years than in those ages 52-55 years. This phenomenon is absent in incidence rates during the 1970s, prior to the uptake of screening.

Figure 4. Age-specific Colorectal Cancer Incidence Rates, US, 2012-2016



Source: Main figure: NAACCR, 2019. Inset: Surveillance, Epidemiology, and End Results (SEER) Program, 2019.

The median age at CRC diagnosis is 66 years in men and 69 years in women, but is younger for rectal cancer (age 62 and 63, respectively) than for colon cancer (age 67 and 71, respectively).[24] CRC patients overall are increasingly younger, shifting from a median age of 72 years for diagnoses in the early 2000s to 66 years today.[25] This is because incidence is increasing in younger adults and declining in older age groups.[17]

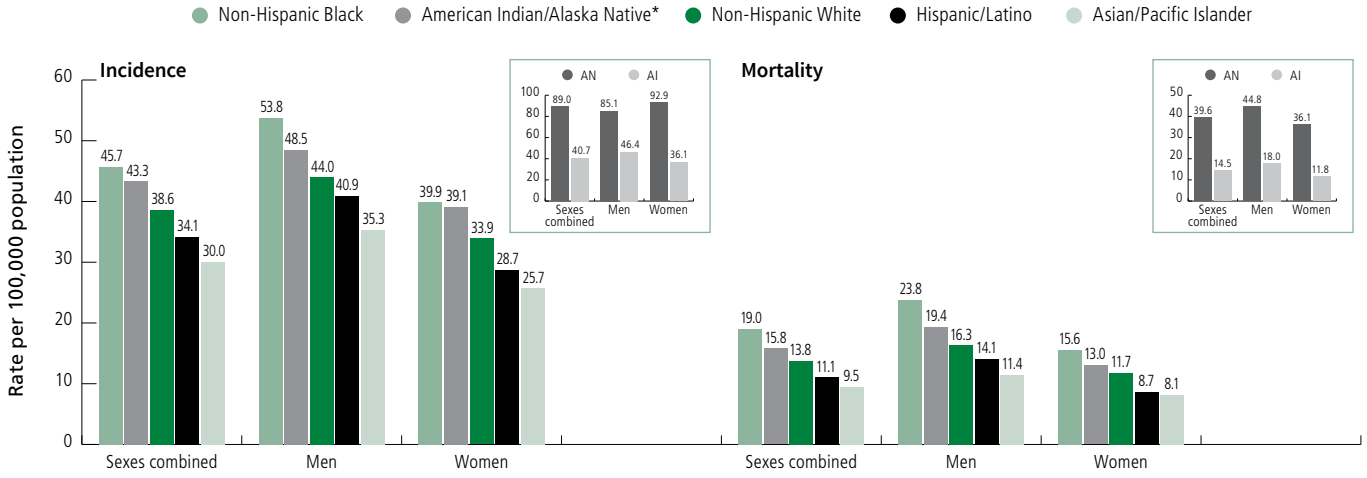
Race/ethnicity

Among broadly defined racial and ethnic groups, CRC incidence and mortality are highest in non-Hispanic blacks (hereafter, blacks), followed closely by American Indians and Alaska Natives (AIANs), and lowest in Asians/Pacific Islanders (APIs; Figure 5). During 2012-2016, CRC incidence rates in blacks were about 20% higher than those in non-Hispanic whites (NHWs) and 50% higher than those in APIs. The disparity for mortality is twice that for incidence; CRC death rates in blacks are almost 40% higher than those in NHWs and double those in APIs.

Reasons for racial/ethnic disparities in CRC are complex, but largely reflect differences in risk factor prevalence and health care access, both of which are related to socioeconomic status.[26] In 2018, the median family income was $41,361 among blacks compared to $70,642 among NHWs, with 21% and 8%, respectively, living in poverty.[27] People with the lowest socioeconomic status are 40% more likely to be diagnosed with CRC than those with the highest socioeconomic status.[28] Close to half (44%) of this disparity is attributed to differences in the prevalence of risk factors associated with CRC (e.g., smoking, obesity)[29] and a similar proportion is due to differences in CRC screening.[30] After controlling for differences in risk factors, black individuals are no more likely than whites to develop adenomas or CRC, but are less likely to receive timely follow-up of a positive screening test and/or high-quality colonoscopy.[31, 32] Higher CRC mortality among blacks may also reflect a larger proportion of tumors in the proximal colon.[3]

Importantly, the broad racial and ethnic groups to which cancer statistics are generally limited mask striking differences within these heterogeneous populations. For example, although CRC incidence in API men overall is 25% lower than in NHW men, rates in Japanese men are 23% higher.[33] Even more alarming is the burden among Alaska Natives, who have the highest CRC incidence (89 per 100,000) and mortality (40 per 100,000) rates in the US, double those in blacks (46 and 19, respectively). CRC

Figure 5. Colorectal Cancer Incidence (2012-2016) and Mortality (2013-2017) Rates by Race/Ethnicity and Sex, US



AI: American Indian, excluding Alaska; AN: Alaska Native. Rates are age adjusted to the 2000 US standard population. *Statistics based on data from Purchased/Referred Care Delivery Area (PRCDA) counties. AI/AN incidence rates exclude data from Kansas and Minnesota. Incidence rates for Alaska Native men and women are not statistically significantly different.

Source: Incidence – NAACCR, 2019. Mortality – NCHS, 2019.

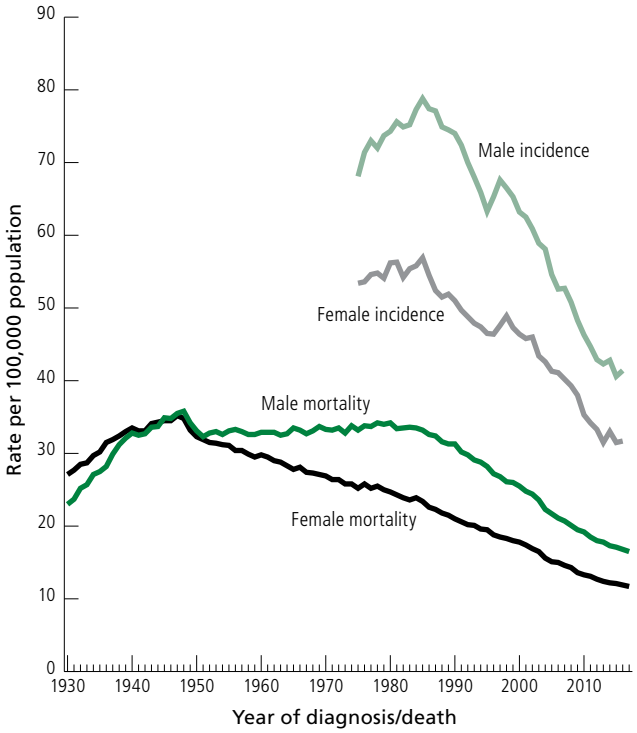
has been the most commonly diagnosed cancer in Alaska Natives since the early 1970s for reasons that are unknown, but may include a higher prevalence of CRC risk factors, such as a diet high in animal fat and low in fruits and vegetables, vitamin D deficiency, smoking, obesity, and diabetes.[34, 35] In addition, Alaska Natives, particularly rural residents, have a high prevalence of *Helicobacter pylori* (*H. pylori*),[36] a bacteria associated with inflammation and cancer of the stomach that may also be associated with CRC risk.[37, 38] Despite a disproportionately high burden of advanced adenomas among Alaska Natives,[39] the availability of endoscopic services in much of Alaska is inadequate.[40, 41] A recent study found that Alaska had the lowest county-level CRC screening prevalence in the nation.[42] In addition, the primary mode of screening at Indian Health Service facilities is stool testing, which has a limited capacity for cancer prevention and requires timely follow-up with colonoscopy for positive tests. Notably, AIANs are the only racial and ethnic group for which CRC mortality rates are not declining (see page 8).

How has colorectal cancer occurrence changed over time?

Incidence

Despite higher incidence in men than in women, trends over time are very similar by sex (Figure 6). CRC incidence rates increased from 1975 through the mid-1980s, but since have generally decreased. The decline prior to 2000 is attributed equally to changing patterns in risk factors (e.g., reductions in smoking) and the uptake of CRC screening.[43] However, the accelerated decline that began during the late 2000s is thought to predominantly reflect widespread uptake of CRC screening with colonoscopy, which increased among adults ≥50 years of age from 20% in 2000 to 61% in 2018.[44] There is about a decade of lag time between the detection and removal of precancerous polyps through screening and its reflection on CRC incidence rates.[9, 45] Notably, however, declines in CRC incidence have decelerated in the most recent 5 data years (2012-2016), perhaps reflecting a slowing in first-time screening,[46] changing risk factors exposures, such as obesity, or a combination thereof.

Figure 6. Trends in Colorectal Cancer Incidence (1975-2016) and Mortality (1930-2017) Rates by Sex, US



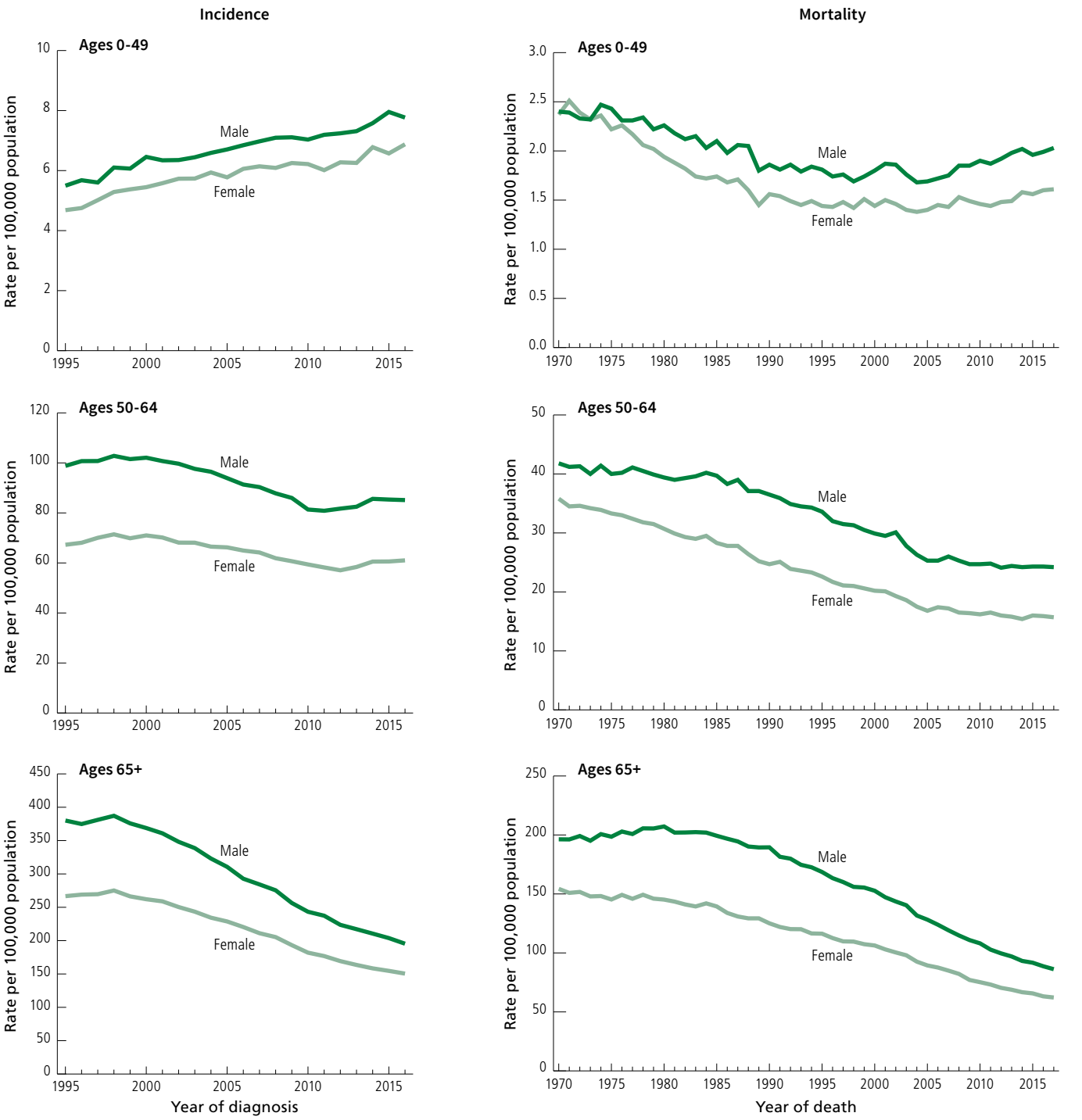
Rates are age adjusted to the 2000 US standard population. Incidence rates are adjusted for delays in reporting and exclude appendix. Due to changes in International Classification of Diseases (ICD) coding, numerator information for mortality has changed over time.

Source: Incidence – Surveillance, Epidemiology, and End Results (SEER) Program, 2019. Mortality – US Mortality Volumes 1930 to 1959, US; Mortality Data 1960-2017, NCHS, 2019.

Age-specific incidence trends

CRC trends overall reflect the majority of cases that occur in older age groups, masking trends in young adults. CRC incidence rates have been increasing since the mid-1980s in adults ages 20-39 years and since the mid-1990s in adults ages 40-54 years, with younger age groups experiencing the steepest increase.[17] This pattern is called a *birth cohort effect* because generations of individuals with higher incidence carry the elevated risk with them as they age. Indeed, after decades of decline, incidence rates have also begun to increase in ages 50-64 years. During the most recent five data years (2012-2016), incidence rates increased by 2.2% annually in individuals younger than 50 years and by 1% annually in those ages 50-64 years, a sharp contrast to declines of 3.3% per year in adults ages 65 and older (Figure 7). Although a similar incidence pattern

Figure 7. Trends in Colorectal Cancer Incidence (1995-2016) and Mortality (1970-2017) Rates by Age and Sex, US



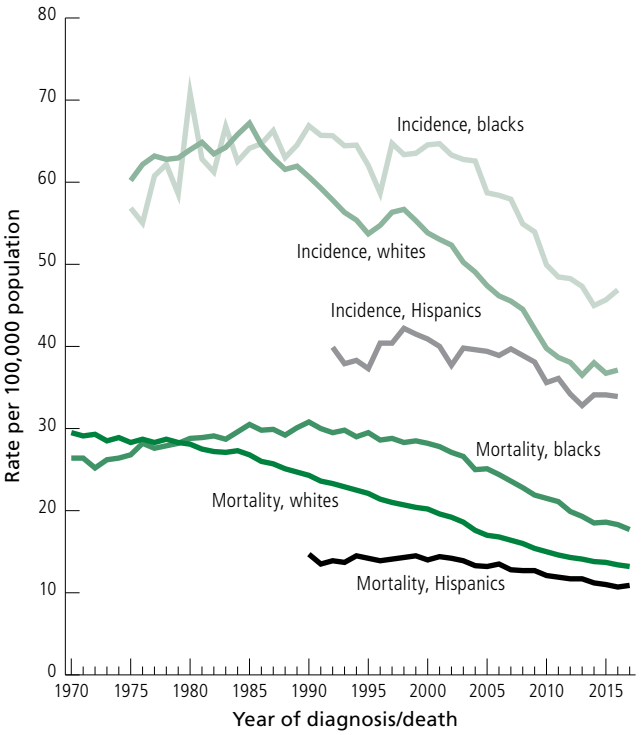
Rates are age adjusted to the 2000 US standard population. Incidence rates are adjusted for reporting delays and exclude appendix.
Source: Incidence – NAACCR, 2019. Mortality – NCHS, 2019.

has been reported in many other high-income countries,[47] reasons for the increasing trend in younger age groups are unknown. It may reflect changes in established risk factors, such as a more sedentary lifestyle and/or unfavorable dietary patterns, or other exposures whose association with CRC risk is yet unknown.

Racial/ethnic incidence trends

Historical cancer incidence data in the US are available only for the categories white, black, and other race. CRC incidence was similar in whites and blacks until the mid-1980s, when rates began declining in whites while remaining stable in blacks (Figure 8). These trends created a widening racial gap until the mid-2000s and likely reflect a combination of earlier access to and more rapid uptake of CRC screening tests among whites, as well as changing patterns in the prevalence of CRC risk factors.[48] Since the mid-2000s, CRC incidence rates decreased by about 1%-3% per year in all broadly defined racial/ethnic groups, although the pace appears to be slowing in recent years.[24] Notably, the steepest increase in early-onset CRC is among NHWs and AIANs.[49] As a result, incidence rates in NHWs ages 20-49 years are now equivalent to those in blacks (14.1 per 100,000 during 2015-2016), despite being 40% higher in blacks during 1995-1996.[50]

Figure 8. Trends in Colorectal Cancer Incidence (1975-2016) and Mortality (1970-2017) Rates by Race, US



Rates are age adjusted to the 2000 US standard population. Incidence rates are adjusted for reporting delays and exclude appendix. White and black race are not mutually exclusive from Hispanic ethnicity.

Source: Incidence – SEER program, 2019. Mortality – NCHS, 2019.

Mortality

CRC death rates have been decreasing since 1947 in women, but only since 1980 in men (Figure 6). This inconsistency likely reflects sex differences in incidence trends because of variable patterns in CRC risk factors, although population-based incidence data are not available prior to 1975. Trends over the past three decades are very similar by sex. Declines in mortality through 2000 are attributed to improvements in treatment (12%), changing patterns in CRC risk factors (35%), and screening (53%).[43] However, screening likely played an even larger role in more recent trends given its steep increase since 2000.[52] Rapid declines in CRC death rates of about 3% per year from 2002 to 2012 slowed to 2% per year from 2012 to 2017.

Age-specific mortality trends

Like incidence, CRC mortality trends vary by age (Figure 7). Among older adults, decades of rapid declines have slowed, from 1% annually during 2004-2013 to 0.6% during 2013-2017 in those ages 50-64 years and from 3.3% to 2.6%, respectively, in those ages 65 and older. In contrast, CRC death rates have increased in individuals younger than 50 years of age by 1.3% per year since 2004.

Racial/ethnic mortality trends

CRC death rates in whites began a slow decline in the early 1970s that accelerated over time. In contrast, death rates in blacks increased from the early 1970s until 1990, then decreased sluggishly during the 1990s before matching the decline in whites in the early 2000s (Figure 8). As a result of these divergent trends, although CRC death rates in blacks were 10% lower than those in whites in the early 1970s, they were almost 50% higher in 2005. The widening racial disparity was largely driven by trends for distant-stage disease, which declined in whites while remaining stable in blacks through the mid-2000s.[53] About half of the racial disparity in mortality is attributed to a combination of less screening and lower stage-specific survival rates among blacks.[30] Since the early 2000s, CRC death rates have declined consistently by 1.8% per year in Hispanics and APIs and by 2.8% per year in blacks; however, rates were stable in AIANs during this time, and in whites declines slowed from 2.5% per year during

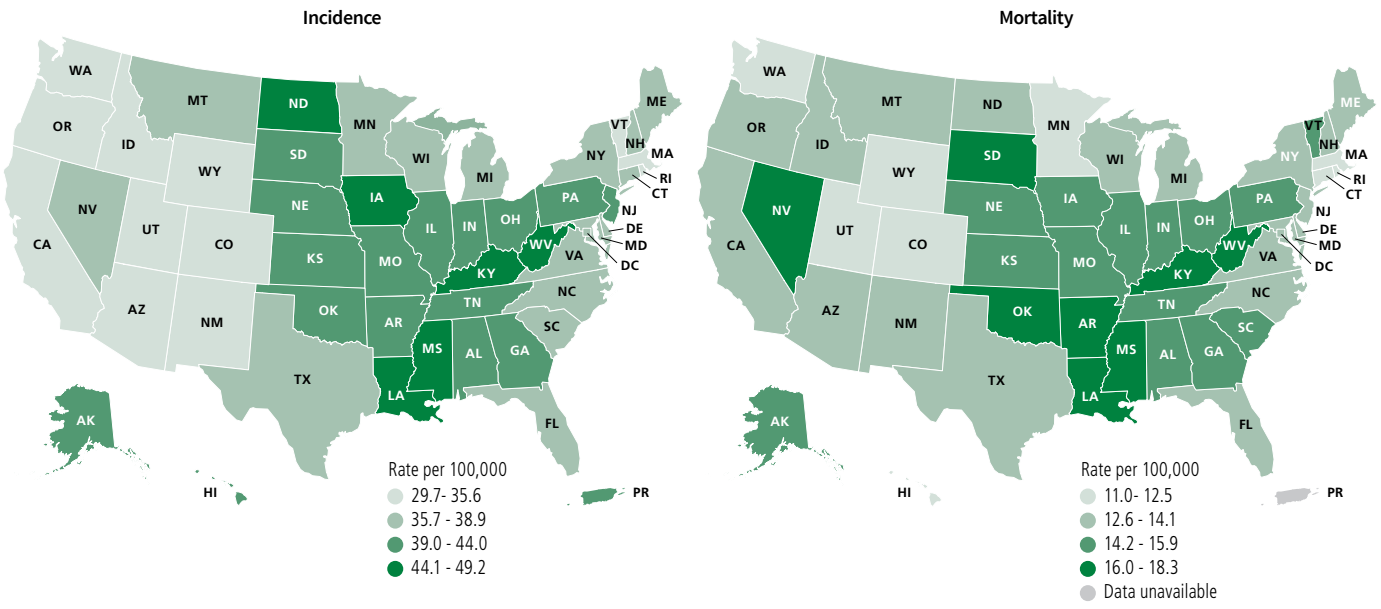
2005-2012 to 1.6% per year during 2012-2017. As a result, the black-white gap has slowly begun to narrow.

How does colorectal cancer occurrence vary by state?

The geographic pattern of CRC has changed dramatically over the past several decades. In contrast to the 1970s and 1980s, when the burden was highest across the Northeast and lowest in the South,[54] today it is highest in parts of the South, Midwest, and Appalachia and lowest in the West and Northeast. Current incidence rates range from 49 (per 100,000) in Kentucky to 30 in Utah, while death rates range from 18 in Mississippi and West Virginia to 11 in Connecticut and Utah (Figure 9). This shift is consistent with the racial and socioeconomic crossover in disease burden that occurred during the latter half of the 20th century because of changes in dietary and smoking patterns, as well as differences in access to early detection and high-quality treatment.[55] For example, CRC mortality among residents of poor counties was 20% lower than that among residents of affluent counties in the early 1970s, but is currently 30% to 40% higher.[54, 56] Geographic patterns are generally similar for blacks and whites, particularly for mortality, highlighting the importance of socioeconomic status over race in cancer disparities.[57]

Table 2 shows state-level incidence and death rates by race/ethnicity. Consistent with overall incidence, rates in NHWs and blacks are lowest in the West and highest in the South and Midwest. However, among Hispanics there is no clear pattern, perhaps reflecting geographic heterogeneity within this population in terms of place of birth and duration of residence, both of which influence CRC risk. Although data for AIANs are too sparse to provide by state, a recent study found that incidence rates for those living in Alaska (approximately 95 per 100,000) were more than two-fold higher than those living in the East and Southwest regions (30 to 40 per 100,000) of the US during 2010-2015.[58] Factors that may contribute to this disparity include differences in diet and the prevalence of obesity and smoking, as well as access to medical services, including screening. Among some more isolated groups (e.g., Alaska Natives), genetic differences may also play a role. (See page 5 and page 6 for more information about CRC in Alaska Natives.)

Figure 9. Colorectal Cancer Incidence (2012-2016) and Mortality (2013-2017) Rates by State, US



Nevada and the District of Columbia did not meet NAACCR high-quality incidence data standards for one or more years during 2012-2016. Incidence rates for the District of Columbia are based on data years 2012-2014. Rates are age adjusted to the 2000 standard population.

Sources: Incidence – NAACCR, 2019. Mortality – NCHS, 2019.

Table 2. Colorectal Cancer Incidence (2012-2016) and Mortality (2013-2017) Rates* by Race/Ethnicity and State, US

	Incidence						Mortality					
	Men			Women			Men			Women		
State	Non-Hispanic white	Non-Hispanic black	Hispanic	Non-Hispanic white	Non-Hispanic black	Hispanic	Non-Hispanic white	Non-Hispanic black	Hispanic	Non-Hispanic white	Non-Hispanic black	Hispanic
Alabama	49.4	58.9	27.6	36.3	44.6	25.5	18.5	26.4	†	12.0	17.7	†
Alaska	37.0	†	†	33.1	†	†	13.3	†	†	11.5	†	†
Arizona	37.8	33.5	41.9	29.2	33.1	26.2	15.3	18.2	15.3	10.9	16.4	8.8
Arkansas	50.1	58.2	29.4	36.5	45.8	32.0	19.4	26.0	†	13.0	19.5	†
California	40.4	48.5	38.4	32.4	39.4	27.7	14.9	21.9	13.9	11.7	16.0	8.8
Colorado	35.5	48.8	44.7	29.5	34.6	33.5	13.4	19.5	16.8	10.4	11.5	11.3
Connecticut	40.8	46.1	49.4	31.5	36.1	32.9	13.0	16.7	12.8	9.5	10.9	7.1
Delaware	42.8	51.0	34.9	32.2	38.4	42.8	17.5	17.1	†	10.2	15.7	†
Dist. Of Columbia‡,§	29.2	61.7	†	27.8	44.6	†	7.9	26.9	†	7.3	17.8	†
Florida	41.3	48.9	43.5	31.3	36.7	31.6	15.5	20.6	14.6	10.9	14.0	9.6
Georgia	47.8	57.3	37.3	34.5	41.4	30.9	17.6	25.7	10.4	11.5	15.1	5.6
Hawaii	42.2	44.5	46.5	37.3	†	42.5	12.3	†	19.7	13.0	†	†
Idaho	39.4	†	31.4	32.3	†	24.0	15.4	†	11.9	11.4	†	†
Illinois	50.3	64.4	37.5	36.8	45.9	28.5	17.5	29.1	12.4	12.4	19.0	6.8
Indiana	48.7	52.6	35.7	38.0	41.4	31.1	18.0	24.4	10.5	12.9	17.0	6.3
Iowa	50.5	57.8	36.2	39.7	37.5	19.1	17.3	18.0	†	12.7	16.2	†
Kansas	45.2	56.6	44.8	34.9	38.5	24.7	17.8	25.3	16.8	12.2	16.4	8.9
Kentucky	57.8	59.4	32.8	42.4	45.0	21.5	20.2	24.6	†	13.9	16.7	†
Louisiana	51.6	65.8	28.9	36.9	47.8	22.3	18.5	28.5	†	13.0	18.2	†
Maine	41.9	†	†	33.8	†	†	14.7	†	†	11.4	†	†
Maryland	40.0	47.8	28.4	33.1	35.6	22.3	15.4	22.5	7.5	11.5	13.9	5.2
Massachusetts	39.6	44.6	33.1	31.6	33.4	23.2	14.1	16.3	8.5	10.5	11.4	7.5
Michigan	40.7	55.3	36.1	32.4	40.8	25.3	15.8	23.6	11.6	11.5	17.0	9.4
Minnesota	42.1	47.9	33.6	33.4	40.0	43.5	14.3	13.2	†	10.7	13.2	12.6
Mississippi	52.9	70.4	†	37.8	48.9	†	20.2	30.5	†	13.9	18.0	†
Missouri	47.6	56.6	29.8	35.1	41.8	23.7	17.3	26.1	†	12.0	16.1	†
Montana	42.1	†	63.0	32.2	†	†	15.5	†	†	10.6	†	†
Nebraska	49.0	70.8	36.9	37.5	38.5	33.9	17.5	27.8	†	12.5	20.7	†
Nevada‡	42.3	47.1	35.2	33.5	33.3	25.5	19.9	30.4	13.6	14.9	17.0	9.1
New Hampshire	42.2	†	†	33.2	†	†	14.1	†	†	11.8	†	†
New Jersey	48.1	54.1	43.8	36.9	41.5	32.9	17.1	24.2	12.4	12.4	14.5	8.1
New Mexico	33.7	32.0	42.5	27.8	32.3	30.8	14.7	†	18.8	10.5	†	12.1
New York	44.8	50.7	43.6	34.8	36.6	29.1	15.3	18.2	13.6	11.3	13.7	8.2
North Carolina	41.7	51.6	27.8	32.0	36.3	24.2	15.3	23.2	6.4	10.6	14.8	6.0
North Dakota	51.9	†	†	36.8	†	†	16.5	†	†	11.0	†	†
Ohio	47.1	48.1	33.0	36.2	37.3	21.1	18.2	23.2	7.4	13.0	15.8	7.3
Oklahoma	46.8	54.6	37.3	35.2	40.6	33.0	20.3	28.4	14.1	13.7	15.6	6.7
Oregon	38.6	40.3	35.8	30.6	31.4	29.0	15.3	21.0	11.2	11.6	†	6.2
Pennsylvania	48.5	52.7	40.3	36.0	41.3	26.9	17.6	23.4	13.5	12.3	15.4	9.0
Rhode Island	38.5	35.7	35.3	31.4	25.2	23.0	14.9	†	†	11.5	†	†
South Carolina	42.5	54.5	29.0	32.4	37.3	30.4	16.0	24.8	†	11.1	14.9	†
South Dakota	46.4	†	†	36.2	†	†	19.5	†	†	12.5	†	†
Tennessee	45.7	56.9	21.4	35.2	41.4	17.4	17.7	28.3	†	12.5	18.0	†
Texas	44.5	56.4	46.0	32.1	40.9	28.0	17.2	26.6	17.2	11.4	16.3	8.9
Utah	32.9	58.7	38.7	25.6	†	32.2	12.7	†	12.5	9.6	†	9.1
Vermont	37.3	†	†	33.2	†	†	16.4	†	†	13.9	†	†
Virginia	39.2	49.4	25.5	31.3	38.2	24.0	15.8	24.4	9.1	10.9	15.2	6.3
Washington	39.2	42.6	36.0	32.5	33.8	26.1	14.7	17.1	9.5	10.9	13.3	6.5
West Virginia	52.0	50.1	†	41.5	43.6	†	20.4	30.6	†	15.8	15.8	†
Wisconsin	41.5	64.0	28.9	31.9	43.7	25.6	15.0	24.7	11.7	11.0	16.9	6.8
Wyoming	36.9	†	41.7	28.6	†	32.6	14.1	†	†	10.0	†	†
US	**44.0**	**53.8**	**40.8**	**33.9**	**39.9**	**28.7**	**16.3**	**23.8**	**14.1**	**11.7**	**15.6**	**8.7**

*Rates are per 100,000 and age adjusted to the 2000 US standard population. †Statistics not displayed due to fewer than 25 cases or deaths. ‡Incidence data for these states are not included in US combined incidence rates because data did not meet inclusion standards for all years during 2012-2016 according to the North American Association of Central Cancer Registries (NAACCR). §Rates are based on cases diagnosed during 2012-2014.

Sources: Incidence – NAACCR, 2019. Mortality – NCHS, 2019.

Colorectal cancer survival

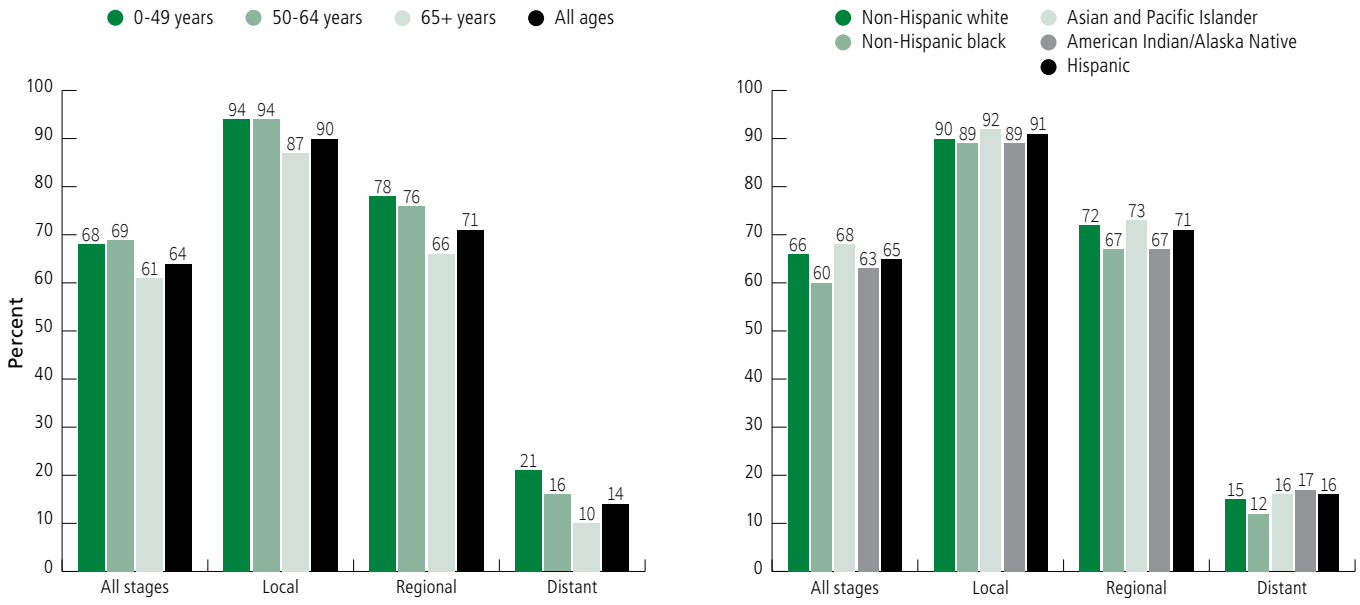
The relative survival rate for CRC is 64% at 5 years following diagnosis and 58% at 10 years.[59] The most important predictor of CRC survival is stage at diagnosis. The 5-year survival rate is 90% for the 39% of patients diagnosed with localized-stage disease, but declines to 71% and 14% for those diagnosed with regional and distant stages, respectively (Figure 10 and Figure 11). Rectal cancer is diagnosed at a localized stage slightly more often than colon cancer, 41% versus 38%, likely due to the earlier appearance of symptoms and partly explaining the higher overall 5-year relative survival (67% versus 63%). Factors associated with advanced-stage CRC diagnosis include low socioeconomic status, black race, and young age.[60, 61]

Factors associated with CRC survival in addition to stage include age at diagnosis, the presence of other illnesses, and other tumor and patient characteristics, such as race/ethnicity and socioeconomic status.[62] For reasons that are not explained by tumor differences or other known factors, women are slightly more likely than men to survive after a CRC diagnosis.[63] There is some evidence that patients with tumors located in the proximal colon have lower survival rates than those with tumors in the distal colon,[64] but this association may be confined to distant-stage diagnoses.[65]

Age

Although CRC patients younger than age 50 have higher 5-year relative survival rates than their older counterparts for every stage of diagnosis (Figure 10), overall survival among patients younger than age 50 (68%) is similar to that in ages 50-64 years (69%) because of a later stage at diagnosis. Approximately 26% of CRCs are diagnosed at a distant stage among patients younger than age 50, compared to 23% in ages 50-64 years and 19% among those ages 65 and older (Figure 11). Despite having the highest proportion of early-stage diagnoses, however, individuals ages 65 and older have the lowest overall 5-year relative survival (61%) because their stage advantage is outweighed by age-related disadvantages, such as additional health issues.

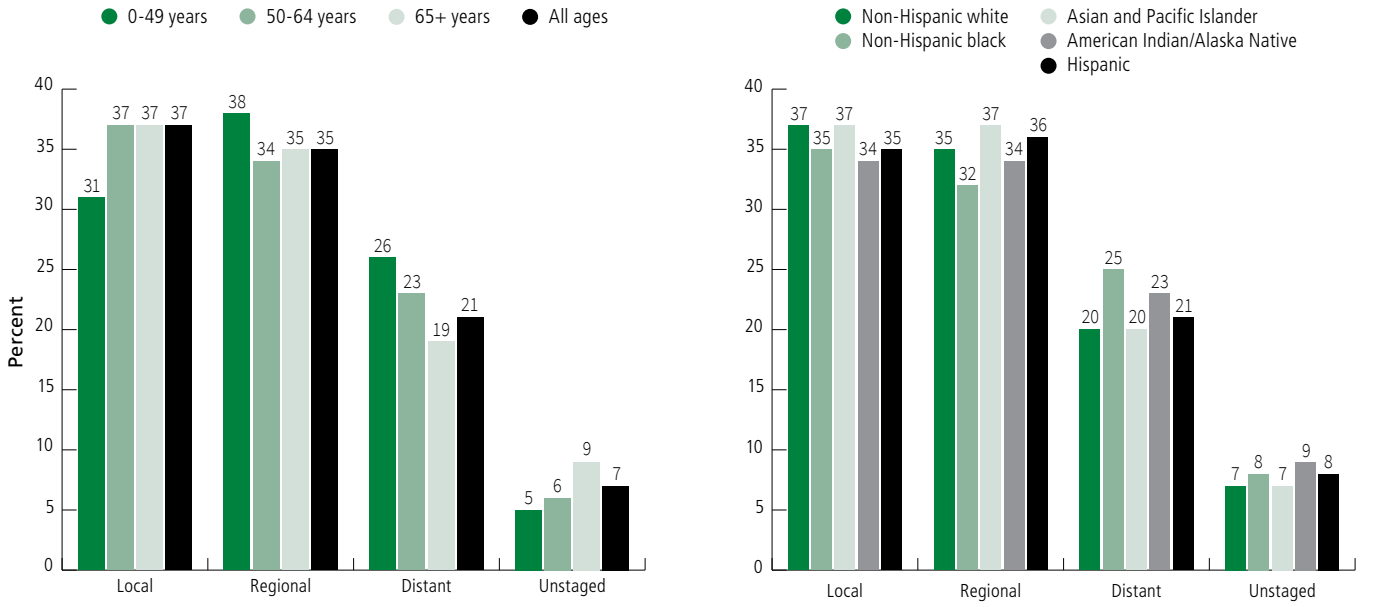
Figure 10. Colorectal Cancer Five-year Survival (%) by Age and Race/Ethnicity, 2009-2015



*Cause-specific survival rates are the probability of not dying from colorectal cancer within 5 years of diagnosis. Rates are based on cases diagnosed from 2009 to 2015, all followed through 2016. Rates for American Indians/Alaska Natives are based on small case numbers, particularly for distant-stage disease.

Source: SEER Program, 2019.

Figure 11. Colorectal Cancer Stage Distribution (%) by Age and Race/Ethnicity, 2012-2016



Source: NAACCR, 2019.

Race/ethnicity

Outcomes among racial/ethnic minorities are described in terms of cause-specific survival because life expectancy data for minority groups are inadequate to calculate relative survival. The highest CRC survival rates are for APIs (68%) and the lowest are for blacks (60%; Figure 10), one-quarter of whom are diagnosed with distant-stage disease (Figure 11). As described earlier, disparities in CRC outcomes are largely driven by socioeconomic inequalities that result in differences in access to early detection and receipt of timely, high-quality treatment.[61,66] Access to care is directly related to stage at diagnosis, which plays the largest role in racial/ethnic survival disparities.[67] Notably, when CRC is diagnosed at localized stage, 5-year survival is relatively similar (89%-92%) across racial/ethnic groups.

A recent nationwide study found that more than one-half of the black-white survival disparity is explained by differences in insurance status and one-quarter is due to differences in tumor characteristics (e.g., grade, location).[3] There is also compelling evidence that black patients are less likely to receive prompt follow-up after an abnormal CRC screening test[32] and appropriate surgery, adjuvant chemotherapy, and radiation treatments.[3,68-70] Although a recent study found no evidence of treatment delays in an equal-access health system,[71] equal cancer treatment does not eliminate the racial survival disparity.[72,73] Thus, equity in care across the cancer continuum, from prevention to early detection to clinical-trial participation and individualized treatment, is necessary to eliminate these disparities.[74]

Changes over time

The 5-year relative survival rate for CRC has increased moderately from 50% in the mid-1970s to 64% during 2009-2015.[24] However, recent advances in the treatment of metastatic disease, including improved surgical methods and the development of targeted therapies,[75-77] have rapidly extended survival for these patients. For example, the 2-year relative survival rate for distant-stage disease increased from 21% for patients diagnosed during the mid-1990s to 37% for those diagnosed during 2009-2015, with a larger jump for rectal cancer (22% to 41%) than for colon cancer (21% to 36%). Although progress is evident across race and age,[78] gains are most prominent among white and non-elderly patients.[79]

Colorectal Cancer Risk Factors

In the United States, more than half (55%) of all CRCs are attributable to lifestyle factors, including an unhealthy diet, insufficient physical activity, high alcohol consumption, and smoking.[80] These behaviors are traditionally associated with high-income countries, where CRC rates are highest. On a global scale, increasing CRC incidence is considered a marker of economic transition.[81] Importantly, however, numerous studies have shown that people with healthy lifestyle behaviors have a 27% to 52% lower risk of CRC compared to those without these behaviors.[82]

Nonmodifiable factors that increase risk are related to heredity and medical history, including a personal or family history of CRC or adenomas (precancerous polyps) and a personal history of long-term chronic inflammatory bowel disease. Most people at increased risk because of a medical or family history should begin CRC screening before age 45. (For more information on CRC screening guidelines, please see page 30.) The following sections present current knowledge about factors associated with CRC risk.

Heredity and family history

Up to 30% of CRC patients have a family history of the disease, making this one of the most important and actionable risk factors.[83-85] People with a first-degree relative (parent, sibling, or child) who has been diagnosed with CRC have 2 to 4 times the risk of developing the disease compared to people without this family history, with higher risk for diagnosis before age 50 and/or multiple affected relatives (Table 3).[84] However, a history of CRC among more distant relatives also increases risk,[86] as does a family history (first- or second-degree relatives) of adenomas.[87] Much of the CRC clustered in families is thought to reflect interactions between lifestyle factors and the cumulative effect of relatively common genetic variations that increase disease risk, referred to as high prevalence/low penetrance mutations.[88]

Identification of families with a history of CRC, especially high-burden families with undiagnosed genetic syndromes (i.e., low prevalence/high penetrance mutations, described below), offers substantial opportunity to lessen cancer incidence and mortality through increased surveillance with colonoscopy. However, patient family history in medical records continues to be incomplete. One study found that less than half of primary care physicians documented information about family members other than first-degree relatives, and age at cancer diagnosis was rarely collected.[89] Another study found that only 22% of CRC patient medical records had family history information sufficient to identify individuals who should be referred for genetic counseling and/or testing.[90]

Table 3. Relative Risks for Established Colorectal Cancer Risk Factors

	Relative risk*
Factors that increase risk:	
Heredity and medical history	
Family history[84]	
CRC	
1 or more first-degree relatives	2.2
1 or more first-degree relatives diagnosed before age 50	3.6
2 or more first-degree relatives	4.0
1 or more second-degree relatives	1.7
Adenoma	
1 or more first-degree relatives	2.0
Inflammatory bowel disease[115]	1.7
Type 2 diabetes[124]	
Male	1.4
Female	1.2†
Modifiable factors	
Heavy alcohol (daily average >3 drinks)[195]	1.3
Obesity (body mass index ≥30 kg/m^2)[146]	1.3
Colon, male	1.5
Colon, female	1.1
Rectum, male	1.3
Rectum, female	1.0†
Red meat (100 g/day)[166]	1.1
Processed meat (50 g/day)[166]	1.2
Smoking[190]	
Current vs. never	1.5
Former vs. never	1.2
Factors that decrease risk:	
Physical activity[138]	0.7
Dairy (400 g/day)[166]	0.9

*Relative risk compares the risk of disease among people with a particular "exposure" to the risk among people without that exposure. Relative risk for dietary factors compares the highest with the lowest consumption. If the relative risk is more than 1.0, then risk is higher among exposed than unexposed persons. Relative risks less than 1.0 indicate a protective effect.
†Relative risk was not statistically significant.

Hereditary syndromes

A recent study found that 5% of CRC patients have an inherited gene mutation (germline mutation) associated with a known high-risk hereditary condition, and an additional 5% have mutations associated with moderately increased risk.[91]

Lynch syndrome

The most common hereditary risk factor for CRC is Lynch syndrome, which accounts for about 3% of all CRCs.[91] People with Lynch syndrome are also at increased risk for many other cancers, including endometrial, ovarian, small intestine, stomach, urinary bladder, and female breast.[92] These individuals have a mutation in certain genes that hinders the cell's ability to correct errors introduced during DNA replication. These mistakes result in additional mutations that can ultimately lead to cancer,[93] the likelihood of which is dependent on which gene is affected. Among the 80% of Lynch syndrome patients with high-risk gene (*MLH1* or *MSH2*) mutations, 19% to 25% will develop CRC by age 50 and 40% will develop the disease by age 70.[94] The median age at CRC diagnosis among Lynch syndrome patients is 61 years of age,[95] and 8% of CRCs that occur in adults younger than age 50 are caused by Lynch syndrome.[96]

Although an estimated 1.2 million Americans (1 in 279) have Lynch syndrome,[97] the vast majority are undiagnosed because identification is dependent on a cancer diagnosis. However, there is increasing recognition of the need for a more proactive approach because rigorous colonoscopy surveillance leads to early-stage diagnosis and high survival in Lynch syndrome patients.[98] Numerous organizations, including the National Comprehensive Cancer Network and American Society for Clinical Oncology, recommend testing for Lynch snydrome in all patients with colorectal or endometrial cancer.[99, 100] Although implementation of universal testing has been slow in the community hospital setting,[101] most major public and private insurers cover the screening.[102]

Polyposis syndromes

Polyposis syndromes are another type of hereditary condition associated with increased CRC risk, the most common of which is familial adenomatous polyposis (FAP), which accounts for about 1% of all CRCs.[91] FAP is characterized by the development of up to thousands of colorectal polyps in the second and third decade of life. It is typically caused by a mutation in the adenomatous polyposis coli (APC) gene, which normally prevents uncontrolled cell growth and division.[103] These mutations are usually inherited, but occur spontaneously in 10% to 25% of affected people so there is not always a family history of the condition.[104] Disease severity ranges from severe (classic FAP) to mild (attenuated FAP), with the latter associated with later age at onset and fewer polyps (<100), but still high lifetime CRC risk.[105] Surgery is the standard method of cancer prevention for people with FAP once adenoma development is beyond the control of colonoscopy. MUTYH-associated polyposis (MAP) is a more recently recognized syndrome with large variability in clinical features, but in which patients typically develop a similar number of polyps as those with attenuated FAP.[103] Other colorectal polyposis syndromes include Peutz-Jeghers syndrome, juvenile polyposis syndrome, and serrated polyposis syndrome.[106]

BRCA1 and *BRCA2*

Approximately 1% of CRC patients have heritable mutations in the breast cancer susceptibility genes *BRCA1* and/or *BRCA2*,[91] which are among the most well-studied cancer predisposing genes. A gene panel study of CRC patients younger than age 50 also found a 1% prevalence.[96] In addition to breast cancer, these mutations confer increased risk for cancers of the ovary, prostate, and pancreas.[107] Although their influence on CRC risk is not well studied, a recent review reported an association limited to *BRCA1* mutation carriers, who have about a 50% increased risk of the disease compared to individuals without the mutation.[108]

Personal medical history

People with a personal history of CRC are more likely to develop a subsequent cancer in the colon or rectum, especially when the initial diagnosis was at a young age;[109] however, only 2% of patients will develop a second primary CRC.[110] A history of adenomatous polyps also increases CRC risk, especially multiple or large polyps.[111]

CRC risk is also increased among individuals with a history of other cancer types because of the carcinogenic effects of some treatments. Examples include childhood cancer survivors, especially those who received pelvic or abdominal or total-body radiotherapy, or certain drugs (e.g., cisplatin, procarbazine);[112] men treated with radiotherapy for prostate cancer;[113] and men treated with platinum-containing chemotherapy for testicular cancer.[114]

Chronic inflammatory bowel disease

Chronic inflammatory bowel disease (IBD) is a lifelong condition, usually diagnosed in early adulthood, in which the gastrointestinal tract is inflamed over a long period of time. People with IBD have almost double the risk of developing CRC compared to people in the general population.[115] The most common forms of IBD are ulcerative colitis and Crohn disease. Cancer risk increases with the extent, duration, and severity of disease,[115, 116] but has decreased over time, likely due to the increased use of medications to control inflammation and screening surveillance to detect premalignant lesions.[117] Although the efficacy of anti-inflammatory drugs for limiting IBD-related cancer occurrence remains unclear, two recent meta-analyses reported reduced CRC risk of 33% to 50% among individuals with ulcerative colitis, but no effect for those with Crohn disease.[118, 119] CRC patients with IBD are about 15 years younger than those without IBD and 70% more likely to die from their cancer after accounting for age and stage at diagnosis.[120] IBD has been diagnosed in an estimated 3.1 million Americans and is most common among non-Hispanic whites, women, and those with the least education.[121] Although surveillance data in the US are sparse, prevalence appears to have increased in recent years.[122]

Diabetes

People who have type 2 (adult onset) diabetes have a slightly increased risk of CRC that appears stronger in men than in women.[123, 124] The association between type 2 diabetes and CRC remains even after accounting for shared risk factors (physical activity, body mass index, and waist circumference).[125] Although some studies suggest that metformin, a drug commonly used to lower blood glucose levels in diabetic patients, independently reduces CRC incidence,[126-130] a randomized controlled trial found no association.[131] CRC patients with diabetes are no more likely to die from their cancer than those without diabetes, despite higher rates of cancer recurrence, as well as mortality from other causes.[132]

The prevalence of Americans with a history of diabetes has more than doubled over the past two decades.[133] Although type 2 diabetes is rare among children and adolescents (ages 0-19 years), incidence rates increased by 7% per year between 2002 and 2012, from 9.0 cases per 100,000 in 2002-2003 to 12.5 in 2011-2012.[134] According to the Centers for Disease Control and Prevention, 30.3 million people (9.4% of the population) were diabetic in 2017, including 7.2 million who were undiagnosed and one-quarter of whom were 65 years of age and older.[135]

H. pylori

Results from earlier studies evaluating the link between infection with *H. pylori*, a bacteria strongly associated with excess stomach cancer risk, and CRC occurrence were inconsistent.[136] However, this may be because the association is confined to specific subtypes of the bacterium. A recent large study found that increased CRC risk is limited to individuals with a history of infection with particular *H. pylori* strains, and that this association is strongest among black Americans.[137]

Modifiable risk factors

Physical inactivity

Physical activity is strongly associated with a reduced risk of colon cancer, but not rectal cancer. Studies consistently show that the most physically active people have about a 25% lower risk of developing both proximal and distal colon tumors than the least active people.[138, 139] Being physically active from a young age may further lower risk.[140] Likewise, people who are the most sedentary (e.g., spend the most hours watching TV) have a 25% to 50% increased risk of colon cancer compared to those who are least sedentary.[141] However, sedentary people who become active later in life may reduce their risk.[142] Additionally, people who were more physically active before a CRC diagnosis are less likely to die from the disease than those who were less active.[143] Based on these findings, as well as

the numerous other health benefits of regular physical activity, the American Cancer Society and the Centers for Disease Control and Prevention recommend that adults engage in at least 150 to 300 minutes of moderate-intensity activity or 75 to 150 minutes of vigorous-intensity activity each week (or a combination of these), preferably spread throughout the week, and limit time spent sedentary in activities like watching television.

Overweight and obesity

Excess body weight increases the risk of CRC, even among those who are physically active.[144, 145] Compared to people who are normal weight, obese men have about a 50% higher risk of colon cancer and a 25% higher risk of rectal cancer, whereas obese women have about a 10% increased risk of colon cancer and no increased risk of rectal cancer.[146] Excess risk is also associated with higher abdominal fat, measured by waist circumference or waist-to-hip ratio, and fat stored within the abdominal cavity, independent of body mass index and waist circumference.[147] Thus, abdominal fat specifically may be more important than overall body weight in influencing CRC risk.[148] The timing of exposure may also be a factor, with studies suggesting a stronger influence for excess body weight during adolescence and young adulthood among women, but later in life for men.[149] Higher body weight, even within the normal range, appears to increase risk of early-onset CRC (before age 50), at least among women.[150] In addition, high body mass index measured prior to diagnosis reduces the likelihood of CRC survival.[147, 151] Excess body weight can have a negative impact on the proper functioning of many biochemical processes in the body (metabolic health), and studies indicate that poor metabolic health may be related to CRC incidence and survival independent of obesity.[152-154]

Diet

Differences in CRC incidence globally, as well as the relatively rapid changes in risk among immigrant populations in the United States, have long suggested that diet is linked to CRC occurrence.[155] Dietary patterns likely influence risk both indirectly, through excess calories and obesity, and directly through specific dietary elements. For example, diet has a large influence on the composition of the gut microbiome, which is the trillions of microorganisms, including the 1,000+ different strains of bacteria, that inhabit the large intestine. High levels of specific bacteria in the microbiome are associated with CRC risk.[156, 157] The microbiome is a very active area of research because it is thought to play a dual role in both preventing and promoting CRC and many other diseases through its influence on immune response and inflammation.[158-162] Diets with greater amounts of certain foods, such as refined carbohydrates, processed sugar, and red meat, have a higher potential to increase inflammation and are associated with increased CRC risk.[163]

However, the direct role of specific food items in cancer occurrence is extremely challenging to study for many reasons, including 1) difficulty defining and measuring intake, such as challenges in the accuracy of self-reported food questionnaires; 2) differences in the sources of dietary constituents (e.g., cereal grains, fruits, and vegetables all contribute to fiber intake); 3) the strong link between dietary patterns and other health behaviors; and 4) a constantly changing food supply. The following is a summary of current scientific evidence for dietary elements linked to CRC:

Dairy/Calcium: Most studies find that calcium consumption from dairy foods and/or supplements is associated with a decreased risk of developing adenomas and CRC,[164-166] although the mechanism remains unclear. Adequate calcium intake (approximately 700-1,000 mg/day) seems to confer protection, with limited additional benefit for higher consumption.[164] The relationship appears to require years of follow-up to observe;[167] be confined to cancers in the distal colon/rectum and particular molecular subtypes;[168, 169] and perhaps be moderated by other dietary factors.[164, 170]

Whole grains/Fiber: Although it is highly plausible that dietary fiber decreases risk of CRC for many reasons, including less exposure to carcinogens because of higher stool volume and faster transit time, study results, including those from randomized controlled trials, remain inconclusive and protective associations are weak.[164] The evidence for whole grains specifically is stronger than for overall fiber; two recent meta-analyses found that CRC risk was decreased by about 5% for every 30 grams/day of whole-grain intake.[166, 171] Importantly, the

overall health benefit of a diet high in whole grains is clear,[172] and the American Cancer Society and the World Cancer Research Fund both advocate a diet high in plant foods, including whole grains, fruits, and vegetables for the prevention of cancer and other diseases.[173, 174]

Folate: Folate intake, consumed through diet or supplements, appears to have a complex relationship with CRC risk, potentially promoting growth of preexisting tumors, while inhibiting formation of new tumors in healthy tissue.[164] There has been speculation that increased folate levels among Americans as a result of mandatory fortification of enriched flour and cereals in 1998 were responsible for the unexplained uptick in CRC incidence rates in the late 1990s (Figure 6).[175] However, this hypothesis is not supported by an analysis of data from randomized controlled trials that found no association between five years of folic acid supplementation and CRC risk.[176] Additional prospective studies conducted post-fortification found that the highest level of folate intake was associated with reduced risk of CRC.[177]

Fruits and vegetables: Results from numerous studies specifically evaluating the association between fruit and vegetable intake and CRC risk are inconsistent.[164] Two recent meta-analyses found no relationship for fruit and a possible slightly reduced risk for the highest versus lowest vegetable consumption.[166, 171] Any protective effect appears to be for moderate compared to low consumption, with high consumption providing little additional benefit.[178, 179]

Red and processed meat: Consumption of red and/or processed meat increases the risk of CRC, with a stronger association for colon cancer than rectal cancer and for processed meat than red meat.[166, 180] A recent synthesis of evidence for the World Cancer Research Fund found that the risk of CRC is increased by 18% for every 50 grams/day of processed meat (approximately 2 slices of lunchmeat) and by 12% for every 100 grams/day of red meat (marginally significant).[166] In 2015, the International Agency for Research on Cancer classified processed meat as "carcinogenic to humans" and red meat as "probably carcinogenic to humans," largely based on the evidence related to CRC risk.[181] The reasons for this association remain unclear, but may be related to the constituents of meat and/or to carcinogens (cancer-causing substances) that form during high-temperature cooking, curing, and/or smoking.[182] Although there is concern about rising consumption of processed foods overall, intake of processed meat appears to have remained stable over the past two decades.[183]

Vitamin D: Higher blood levels of vitamin D may be associated with lower risk of CRC, although research findings remain inconsistent.[164] Clinical trials have not found an association between daily supplementation with vitamin D and risk of adenomas[167] or CRC.[184] However, a recent study of pooled data from 17 cohort studies indicated that higher blood levels of vitamin D (25[OH]D up to 100 nmol/L) were associated with reduced CRC risk among women, and deficiency was associated with a 37% increased risk.[185] Forthcoming data from additional clinical trials evaluating the effect of vitamin D supplementation on cancer prevention may help clarify this association,[186, 187] although study design modifications may be necessary to reconcile the current controversy.[188]

Smoking

In November 2009, the International Agency for Research on Cancer reported that there is sufficient evidence to conclude that tobacco smoking causes CRC.[189] In the US, approximately 12% of CRCs are attributed to cigarette current or former smoking, with CRC risk in current smokers about 50% higher than that in never smokers.[80, 190] Most studies find differences in the association by anatomic and molecular subtypes of CRC.[2, 191, 192] Smoking is also associated with lower CRC-specific survival, particularly for current smokers.[193, 194]

Alcohol

An estimated 13% of CRCs in the US are attributed to alcohol consumption.[80] Although there is strong evidence that heavy consumption increases risk, the magnitude of excess risk and the association with smaller quantities is less certain. A recent meta-analysis reported that light-to-moderate alcohol consumption (up to two drinks per day) was associated with a slightly lower (8%) risk than no consumption/occasional consumption, whereas very heavy drinking (more than 3 drinks per day) was

associated with a 25% higher risk.[195] However, other studies find excess risk with just one drink per day, rising to 44% for the heaviest drinking.[166, 196] The association appears stronger in men, especially for heavy consumption, perhaps because women are less likely to drink heavily and/or because of hormone-related differences in alcohol metabolism.

Medications

Nonsteroidal anti-inflammatory drugs

There is extensive evidence that long-term regular use of aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) lowers risk of CRC.[197-199] The reduction in risk appears to be stronger among individuals younger than age 70 and without excess body weight.[200] Aspirin users who do develop CRC appear to have less aggressive tumors and better survival compared to non-aspirin users,[201, 202] although the survival benefit may be limited to certain tumor subtypes.[203, 204] The American Cancer Society has not conducted a formal evidence review, but currently does not recommend the use of NSAIDs for cancer prevention in the general population because of the potential side effects, namely serious gastrointestinal bleeding. However, the US Preventive Services Task Force currently recommends daily low-dose aspirin for the prevention of cardiovascular disease and CRC for certain individuals in their 50s who are at increased risk for cardiovascular disease; the evidence for individuals in their 60s is less convincing.[205] Decisions about aspirin use should be made after discussion with a health care provider. Visit uspreventiveservicestaskforce.org for more information about their recommendation.

Hormones

The evidence regarding the association between steroid hormones, both endogenous (naturally occurring within the body) and exogenous (e.g., hormone replacement therapy and oral contraceptives), and CRC is inconsistent.[206] Some studies have found that higher natural levels of estrogen among postmenopausal women are associated with reduced CRC risk,[207] while others have found no association.[208] Reduced risk associated with hormone replacement therapy appears to be confined to use of combined estrogen and progesterone formulations.[209, 210] Recent studies do not support an association between oral contraceptive use and CRC risk.[2, 211, 212]

Antibiotics

Emerging evidence suggests that oral antibiotic use may be associated with increased risk of CRC.[213, 214] Antibiotics might influence risk by disrupting the critical balance of the gut microbiome. For more information on the microbiome, see Diet on (page 16).

Other drugs

Oral bisphosphonates, which are used to treat and prevent osteoporosis, may reduce CRC risk.[215, 216]

Colorectal Cancer Screening

The typically slow course of growth from precancerous polyp to invasive cancer to advanced-stage disease provides a unique opportunity for the prevention and early detection of CRC.[8] Screening can prevent cancer through the detection and removal of precancerous growths and detect the disease at an early stage, when treatment is usually more successful. As a result, screening reduces CRC mortality both by decreasing incidence and increasing survival.

The 2018 American Cancer Society CRC screening guideline recommends that adults ages 45 years and older undergo regular screening with a high-sensitivity stool-based test or visual examination (described below), depending on patient preference and test availability.[217] As part of the screening process, all positive results on non-colonoscopy screening tests should be followed up with a timely colonoscopy because delays in follow-up of abnormal results increase the risk of advanced CRC and CRC death.[218, 219] The age to initiate CRC screening was

lowered from 50 to 45 years because incidence rates are increasing in younger populations, and modeling studies demonstrated that the balance of benefit to harm was more favorable for beginning screening at age 45 than at 50.[220, 221] Although health insurance coverage for screening those at average risk before age 50 remains variable, the American Cancer Society is working aggressively to educate insurers, lawmakers, and other stakeholders about the evidence in support of screening those ages 45-49 years and the importance of expanding coverage for this group. Screening before age 45 is recommended for those at an increased risk of CRC because of family history or certain medical conditions (see page 13), with age to initiate and rescreening intervals dependent on individual circumstances. Everyone should have a conversation with their health care provider about CRC screening that includes information about cancer family history well before age 45.[221] Visit cancer.org/cancer/colon-rectal-cancer/early-detection/acs-recommendations for more information, including specific guidelines for screening individuals at increased or high risk.

Recommended options for colorectal cancer screening

There are several recommended methods for CRC screening, including both visual examinations, which are performed at a health care facility, and high-sensitivity stool-based tests, which are collected at home (Table 4). All tests have a comparable ability to improve life expectancy when performed at the appropriate time intervals and with the recommended follow-up.[222] Patients should be given information about the benefits and limitations of each screening test, and choose one based on their health, medical history, and preferences with advice from a health care professional as needed. A growing body of evidence demonstrates that offering patients different test options substantially increases adherence to screening recommendations.[223] As a result, and because one-third of eligible adults are not up to date with CRC screening, including half of those ages 50-54 years, the American Cancer Society and the US Preventive Services Task Force guidelines do not emphasize any one test and stress that all recommended tests can help save lives.[217, 224]

Visual examinations

Visual tests allow doctors to see the lining of the colon and rectum through an endoscope or on radiological images.

Colonoscopy

Colonoscopy is the most commonly used CRC screening test in the US. This procedure, which is usually performed by a gastroenterologist (a doctor who specializes in the digestive system) or surgeon, allows for direct visual examination of the entire colon and rectum. It can be used as a singular screening test, or may be performed as a follow-up to abnormal results from stool and other visual tests to complete the screening process. Colonoscopy has the longest rescreening interval of all test options, 10 years for average-risk individuals with normal results.

Before undergoing a colonoscopy, patients are instructed to take special laxative agents to cleanse the colorectum completely so the intestinal lining can be thoroughly examined. During the exam, the colon is inflated with either air or carbon dioxide. Then a long, slender instrument called a colonoscope is inserted into the anus and moved slowly through the rectum to the cecum (beginning of the colon). The colonoscope has a light and small video camera on the end to allow for the detection and removal of most polyps with a wire loop or electric current. Sedation is usually provided during examinations in the US, although it is used less frequently in some European countries (e.g., Norway and Poland).[225]

While data are not yet available from randomized controlled trials evaluating the effectiveness of colonoscopy,[226] results from several trials of flexible sigmoidoscopy, a similar test discussed in the next section, provide indirect support for the benefits of colonoscopy. In addition, observational studies suggest that colonoscopy can help reduce CRC incidence by about 40% and mortality by about 60%.[227-229]

Like all screening tests, colonoscopy has limitations and potential harms. For example, it can lead to unnecessary procedures, such as the removal of small polyps that would not have progressed to cancer.[230] A recent study found that although >90% of polyps can be safely

Table 4. Characteristics of Recommended Colorectal Cancer Screening Tests

	Benefits	Performance & Complexity*	Limitations	Test Time Interval
Visual Examinations				
Colonoscopy	• Examines entire colon • Can biopsy and remove polyps • Can diagnose other diseases • Required for abnormal results from all other tests	**Performance:** Highest **Complexity:** Highest	• Full bowel cleansing • Can be expensive • Sedation usually needed, necessitating a chaperone to return home • Patient may miss a day of work. • Highest risk of bowel tears or infections compared with other tests	10 years†
Computed tomographic colonography (CTC)	• Examines entire colon • Fairly quick • Few complications • No sedation needed • Noninvasive	**Performance:** High (for large polyps) **Complexity:** Intermediate	• Full bowel cleansing • Cannot remove polyps or perform biopsies • Exposure to low-dose radiation • Colonoscopy necessary if positive • Not covered by all insurance plans	5 years
Flexible sigmoidoscopy	• Fairly quick • Few complications • Minimal bowel preparation • Does not require sedation or a specialist	**Performance:** High for rectum & lower one-third of the colon **Complexity:** Intermediate	• Partial bowel cleansing • Views only one-third of colon • Cannot remove large polyps • Small risk of infection or bowel tear • Slightly more effective when combined with annual fecal occult blood testing • Colonoscopy necessary if positive • Limited availability	5 years
Stool Tests (Low-sensitivity stool tests, such as single-sample FOBT done in the doctor's office or toilet bowl tests, are not recommended.)				
Fecal immuno-chemical test (FIT)	• No bowel cleansing or sedation • Performed at home • Low cost • Noninvasive	**Performance:** Intermediate for cancer **Complexity:** Low	• Requires multiple stool samples • Will miss most polyps • May produce false-positive test results • Slightly more effective when combined with a flexible sigmoidoscopy every five years • Colonoscopy necessary if positive	Annual
High-sensitivity guaiac-based fecal occult blood test (gFOBT)	• No bowel cleansing or sedation • Performed at home • Low cost • Noninvasive	**Performance:** Intermediate for cancer **Complexity:** Low	• Requires multiple stool samples • Will miss most polyps • May produce false-positive test results • Pre-test dietary limitations • Slightly more effective when combined with a flexible sigmoidoscopy every five years • Colonoscopy necessary if positive	Annual
Multitargeted stool DNA test (Cologuard®)	• No bowel cleansing or sedation • Performed at home • Requires only a single stool sample • Noninvasive	**Performance:** Intermediate for cancer **Complexity:** Low	• Will miss most polyps • More false-positive results than other tests • Higher cost than gFOBT and FIT • Colonoscopy necessary if positive	3 years, per manufacturer's recommendation

*Complexity involves patient preparation, inconvenience, facilities and equipment needed, and patient discomfort. †For average-risk individuals, e.g., does not apply to those who have a history of adenoma.

removed during colonoscopy, elective surgery to remove nonmalignant polyps, which has a higher risk of harms, increased by more than 50% from 2000 to 2014.[231] Other limitations of colonoscopy include a higher risk of complications compared to other screening tests, such as bowel tears and bleeding, especially when a polyp is removed or patients are older.[230, 231] Although these side effects are rare, serious bleeding occurs in 1 to 2 of every 1,000 colonoscopies.[225, 232, 233] In addition, colonoscopy sometimes misses adenomas, especially those that are located in the proximal colon; those that occur in high-risk patients; and those that are flat (sessile adenomas), from which 20% to 30% of CRCs are thought to originate.[226, 234] The quality of colonoscopy, which is variable in the US, is also associated with missed lesions, which sometimes progress to CRC before the next scheduled exam (i.e.,

interval cancer).[235, 236] Low-quality colonoscopy (measured as low adenoma detection rate) is associated with a higher likelihood of interval CRC and CRC death.[236]

Flexible sigmoidoscopy

Sigmoidoscopy was a common screening test before 2000, but current availability is limited because it has mostly been replaced by colonoscopy (see page 23 for current prevalence of sigmoidoscopy and other screening tests). These tests are very similar except colonoscopy can examine the entire colon whereas sigmoidoscopy can only visualize the rectum and distal one-third of the colon, and must be repeated more often (Table 4). Simple bowel cleansing, usually with enemas, is sufficient to prepare the colon, and the procedure is often performed without sedation in a general health care practitioner's office. If there is a polyp or tumor present, the patient should be referred for a colonoscopy so that the entire colon can be examined.

Recent analysis of data from randomized controlled trials with up to 17 years of follow-up shows that sigmoidoscopy is associated with about a 20%-25% reduction in CRC incidence and a 25%-30% reduction in CRC mortality, with greater reductions in men than women.[237-239]

Computed tomographic colonography (CTC)

Also referred to as virtual colonoscopy, CTC is an imaging procedure that provides 2- or 3-dimensional views of the entire colon and rectum with the use of a special x-ray machine linked to a computer.[230] Although a full bowel cleansing is necessary for a successful examination, sedation is not required. A small, flexible tube is inserted into the rectum in order to allow carbon dioxide, or sometimes air, to inflate the colon; then the patient passes through the CT scanner, which creates multiple images of the interior of the colon. CTC is less invasive than colonoscopy or sigmoidoscopy and typically takes approximately 10 to 15 minutes to complete.[240] Patients with adenomas larger than 5 millimeters or other abnormal results are referred for colonoscopy, optimally on the same day in order to alleviate the necessity of a second bowel preparation.

Studies have shown that the performance of CTC is similar to colonoscopy for the detection of invasive cancer and advanced adenomas, but has lower sensitivity for smaller adenomas.[241] Potential harms include cumulative radiation exposure from regular examinations, and unnecessary tests and/or treatment due to incidental benign findings outside the colorectum. There is less evidence on the benefits and harms of this test compared to others because it is relatively new and remains uncommon.[224] This may be because it is not covered by Medicare and commercial insurance coverage is variable; in 2019, 37 states mandated that commercial plans cover this test.[242]

Stool tests

Most cancerous tumors and some large adenomas bleed intermittently into the intestine. This blood, which may not be visible, can be detected in stool with special tests. Modeling studies suggest that annual screening with high-sensitivity stool tests and timely follow-up of abnormal results will result in a reduction in mortality similar to that achieved by colonoscopy over a lifetime of screening.[243] Except for the multitargeted stool DNA test, which is recommended every 3 years, stool tests should be repeated annually. However, adherence to yearly testing and timely follow-up with a colonoscopy after a positive test remains a challenge, especially in low-resource settings where stool tests are more common.[244-247]

Guaiac-based fecal occult blood test (gFOBT)

These tests use a chemical reaction to detect blood in the stool. Bleeding from cancers or adenomas may be sporadic or undetectable, so accurate results require annual testing of samples from 3 consecutive bowel movements. Patients are typically instructed to avoid nonsteroidal anti-inflammatory drugs and red meat for 3 days prior to the test because they can lead to a positive test result when no cancer is present (false positive); gFOBT detects blood from any source, including meat in the diet. Vitamin C and large amounts of citrus juices should also be avoided because they can lead to a negative test result when cancer is present (false negative). Only high-sensitivity gFOBT are recommended for CRC screening.

Data from a large clinical trial indicated that the regular use of FOBT reduced the risk of CRC death by 32% after 30 years of follow-up.[248] FOBT has also been shown to decrease CRC incidence by 20% by detecting large precancerous adenomas.[249]

Fecal immunochemical test (FIT)

The FIT (also sometimes referred to as the immunochemical FOBT, or iFOBT) uses antibodies against hemoglobin to specifically detect human blood in the stool and is about twice as likely as most gFOBT products to detect both advanced adenomas and cancer.[250, 251] Many individuals prefer FIT over gFOBT because of its convenience, lack of dietary restrictions, and collection of fewer stool samples.[252]

Multitargeted stool DNA (Cologuard®)

This test is referred to as "multitargeted" because it not only detects blood in the stool, but also multiple genetic mutations in the DNA of cells that are shed into the stool by large adenomas and CRC. Cologuard® has been shown to detect cancer and precancerous lesions more often than FIT, but also results in more false-positive tests, which can lead to unnecessary colonoscopies.[253] However, because it is a relatively new test, data are still accumulating on performance characteristics in community settings. Although it is recognized as an acceptable screening option by the American Cancer Society and the US Preventive Services Task Force[224] and is covered by Medicare, some private insurance companies may not cover this test. Patient navigation services, which include phone calls and reminder letters in multiple languages to support test completion, are embedded in the cost of the test, although the services do not extend to colonoscopy follow-up of abnormal results.[254]

Non-recommended tests for colorectal cancer screening

There are several tests for CRC screening that are not recommended by the American Cancer Society or other organizations because of poorer performance. These include in-office stool tests, in which a single-stool sample is collected during a digital rectal exam and placed on an FOBT card, and "toilet bowl tests," which are over-the-counter guaiac-based tests that are often promoted as a type of FOBT. Despite recommendations against in-office FOBT, some primary care physicians continue to offer the test.[255] Toilet bowl tests have not been evaluated in the types of rigorous clinical studies done on the guaiac-based FOBT and FIT.

Double-contrast barium enema, also called barium enema with air contrast, is a test that takes an x-ray of the colon after barium sulfate is introduced. This test is no longer recommended because it has lower sensitivity for detecting CRC than other tests.

There are also emerging technologies that are not currently recommended for CRC screening because there was insufficient data on their performance compared to other recommended options at the time the guidelines were issued. These include blood-based tests that measure circulating genetic abnormalities associated with colorectal adenomas and cancer, and capsule endoscopy, in which the patient undergoes bowel cleansing and swallows a pill-sized device containing tiny encapsulated cameras that transmit images of the colon and rectum to a recording device.

Use of colorectal cancer screening

According to the National Health Interview Survey (NHIS), CRC screening in accordance with guidelines increased rapidly among adults ages 50 and older from 2000 (38%) to 2010 (59%), but more slowly in the past decade, reaching 66% in 2018 (Table 5).[44] The most recent NHIS data collected in 2018 contain a mix of respondents surveyed before and after the release of the American Cancer Society CRC screening guideline in mid-2018. Approximately 56% of those ≥45 years of age and 21% of those ages 45-49 years reported being up to date with CRC screening in 2018.

Among adults ages 50 and older in 2018:

- 61% reported having a colonoscopy in the past 10 years, and 3% and 1% reported having a sigmoidoscopy or CT colonography, respectively, in the past 5 years.
- Approximately 11% reported a recent stool test; 9% reported an FIT or FOBT in the past year and 3% reported stool DNA testing in the past 3 years.[44]

Table 5. Colorectal Cancer Screening (%), Adults 45 Years and Older, US, 2018

	Stool test*	Colonoscopy†	Up to date‡	
	≥50 years	≥50 years	≥50 years	50-75 years
Overall	11	61	66	67
Gender				
Males	12	62	67	67
Females	10	60	64	66
Age (years)				
50-64	10	56	61	62
50-54	9	42	48	–
55-64	10	63	68	–
65+	12	66	71	77
75+	10	60	63	–
Race/ethnicity				
White	10	63	68	69
Black	12	60	65	66
Hispanic	15	52	59	59
American Indian/Alaska Native	12	53	59	56
Asian	15	47	55	58
Sexual orientation				
Gay/Lesbian	18	68	76	76
Straight	11	61	66	67
Bisexual	25	49	58	§
Education				
Less than high school	11	46	52	53
High school diploma	10	57	62	63
Some college	11	62	68	68
College graduate	11	68	73	73
Immigration status				
Born in US	10	63	68	69
Born in US territory	§	76	80	84
In US fewer than 10 years	§	20	26	30
In US 10+ years	14	49	56	58
Income level				
<100% FPL	12	49	55	57
100 to <200% FPL	12	48	55	57
≥200% FPL	11	65	70	70
Insurance status				
Uninsured	5	26	30	30
Private	9	60	65	65
Medicare or Medicare & Medicaid	14	61	67	73
Private & Medicare	11	71	74	80
Medicaid or Other state plan	14	44	53	54

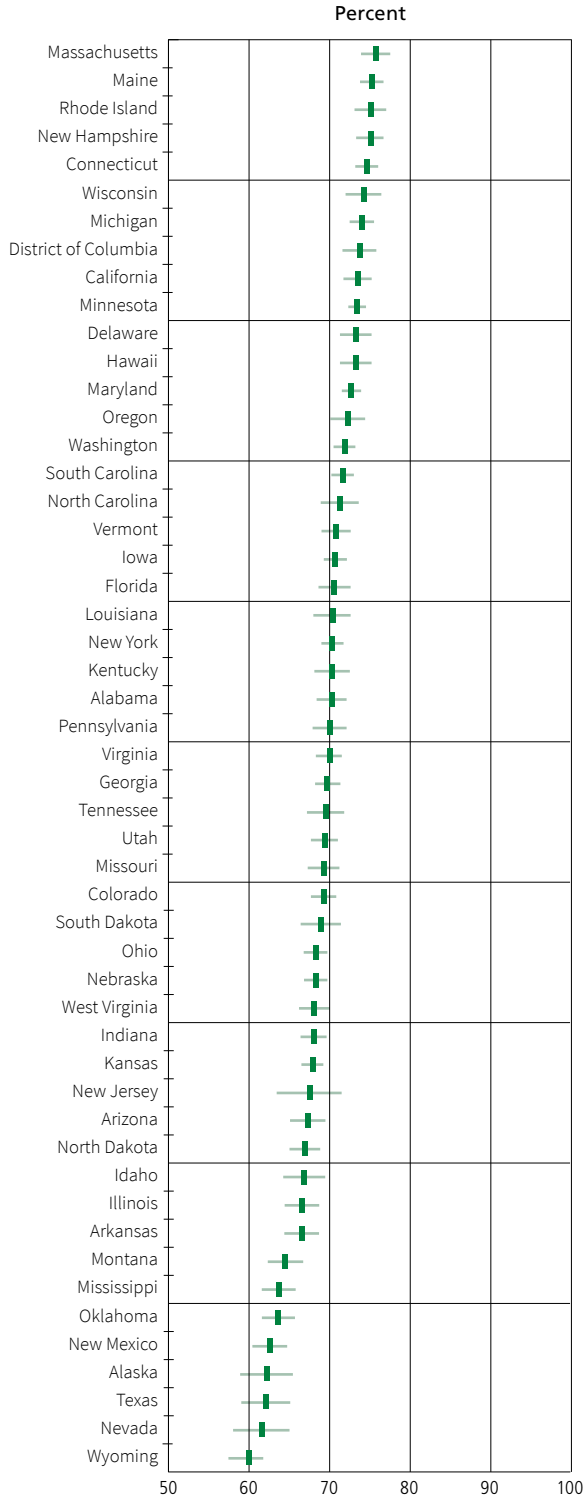
FPL: federal poverty level. *Fecal occult blood test (FOBT) OR fecal immunochemical test (FIT) in the past 1 year OR stool DNA (sDNA) test in the past 3 years. †In the past 10 years. ‡For ages ≥45 and ≥50 years: FOBT/FIT, sigmoidoscopy, colonoscopy, computed tomographic colonography (CTC), or sDNA test in the past 1, 5, 10, 5 and 3 years, respectively. For ages 50-75 years: FOBT/FIT, sigmoidoscopy, colonoscopy, CTC, or sDNA test in the past 1, 5, 10, 5 and 3 years, respectively, OR sigmoidoscopy in past 10 years with FOBT/FIT in past 1 year. §Estimate not shown due to instability. Note: Estimates do not distinguish between examinations for screening and diagnosis. All estimates except for age and insurance status are age adjusted to the 2000 US standard population.

Source: National Health Interview Survey, 2018.

- Screening was lowest among ages 50-54 years (48%); Asian Americans (55%); individuals with less than a high school education (52%); the uninsured (30%); and recent (<10 years) immigrants (26%).

The prevalence of CRC screening also varies substantially among US states and territories (see cover). According to data from the 2018 Behavioral Risk Factor Surveillance System (BRFSS):[256]

Figure 12. Colorectal Cancer Screening* (%), Adults 50 Years and Older by State, 2018



*Blood stool test, sigmoidoscopy, or colonoscopy in the past 1, 5, and 10 years, respectively. Note: Estimates are age adjusted to the 2000 US standard population and do not distinguish between examinations for screening and diagnosis.

Source: Behavioral Risk Factors Surveillance System, 2018. See Sources of Statistics (p. 32) for complete citation and more information.

- Screening utilization ranged from 58% in Puerto Rico and 60% in Wyoming to 76% in Massachusetts (Figure 12 and Table 6).
- In all states, screening prevalence is substantially lower in people ages 50-64 years than in those age 65 and older, with the largest absolute difference in Puerto Rico (22%) and Florida, Mississippi, and Oklahoma (all 19%).

Strategies to overcome screening barriers

Screening utilization for CRC remains lower than that for breast and cervical cancers despite the large body of evidence supporting its effectiveness for reducing cancer incidence and mortality.[257] Use of CRC screening is influenced by numerous individual, provider, health system, and community factors, as well as public policy. Barriers to screening include no usual source of care, inadequate insurance coverage, lack of provider recommendation, logistical factors (e.g., transportation, scheduling, and language), fear, and lack of knowledge.[258-263] These barriers are more prevalent among people with fewer financial resources, lower educational attainment, and among racial/ethnic minorities, resulting in disparities in screening prevalence and outcomes.[264]

Interventions to help overcome these barriers include increasing individual patient awareness (e.g., education and reminders), ease of access (e.g., providing transportation, reducing out-of-pocket expenses, mailed FIT kits, patient navigators), provider delivery (e.g., provider reminders, assessment, and feedback), and community demand (e.g., media campaigns).[265] Multi-component interventions are recommended because they are more effective at increasing CRC screening utilization than a single approach.[265, 266] Additionally, adherence to CRC screening guidelines increases when patients are offered a variety of tests.[222, 223, 267, 268] Importantly, however, the effectiveness of screening is compromised without timely follow-up of abnormal results. Follow-up of colonoscopy among adults with a positive stool test may be increased through the use of patient navigators and provider-level interventions, such as physician reminders and performance data, although evidence for effective strategies remains sparse.[269]

Table 6. Colorectal Cancer Screening* (%), Adults 50 Years and Older by State, 2018

	All races				Non-Hispanic white	Non-Hispanic black
	≥50 years	50 to 64 years	≥65 years	50 to 75 years	≥50 years	≥50 years
United States (median)	**70**	**63**	**75**	**69**	**71**	**71**
Range	*60-76*	*50-72*	*66-82*	*58-77*	*61-80*	*63-84*
Alabama	70	63	76	70	71	67
Alaska	62	52	70	60	62	†
Arizona	67	59	76	66	69	75
Arkansas	67	58	74	66	67	69
California	73	64	82	72	80	77
Colorado	69	62	74	69	71	76
Connecticut	75	71	78	75	76	76
Delaware	73	67	78	72	75	71
District of Columbia	74	69	78	74	77	73
Florida	71	61	80	69	74	67
Georgia	70	61	78	68	71	71
Hawaii	73	69	75	75	78	†
Idaho	67	59	72	66	68	†
Illinois	67	61	70	67	67	74
Indiana	68	61	73	68	69	67
Iowa	71	66	74	71	71	84
Kansas	68	60	74	67	69	66
Kentucky	70	63	76	69	70	70
Louisiana	70	64	76	69	71	70
Maine	75	69	79	75	76	†
Maryland	73	67	78	73	73	77
Massachusetts	76	72	78	77	77	82
Michigan	74	69	77	74	75	71
Minnesota	73	68	77	73	75	66
Mississippi	64	54	73	62	64	65
Missouri	69	62	75	69	69	71
Montana	65	56	71	64	65	†
Nebraska	68	62	72	68	70	67
Nevada	62	52	69	60	67	67
New Hampshire	75	70	78	75	75	†
New Jersey	68	59	75	67	69	76
New Mexico	63	55	66	64	66	†
New York	70	65	75	70	72	70
North Carolina	71	64	77	71	73	69
North Dakota	67	61	72	67	68	†
Ohio	68	61	75	67	69	68
Oklahoma	64	54	73	62	65	68
Oregon	72	66	77	72	72	†
Pennsylvania	70	66	72	72	71	68
Rhode Island	75	70	79	76	77	75
South Carolina	72	62	80	70	72	71
South Dakota	69	63	74	69	70	†
Tennessee	70	60	77	69	71	63
Texas	62	53	71	60	68	68
Utah	69	63	73	70	72	†
Vermont	71	65	72	71	71	†
Virginia	70	63	75	70	70	72
Washington	72	65	77	72	73	71
West Virginia	68	61	74	67	69	66
Wisconsin	74	69	77	75	75	82
Wyoming	60	50	67	58	61	†
Puerto Rico	58	48	70	55	†	†

*Blood stool test, sigmoidoscopy, or colonoscopy in the past 1, 5, and 10 years, respectively. †Estimate not presented due to instability. Note: Estimates are age adjusted to the 2000 US standard population and do not distinguish between examinations for screening and diagnosis. Puerto Rico not included in ranges or medians.

Source: Behavioral Risk Factor Surveillance System, 2018.

The National Colorectal Cancer Roundtable (NCCRT), a coalition of public, private, and voluntary organizations and individuals established in 1997 by the American Cancer Society and the CDC to promote CRC screening, has produced evidence-based toolkits for policy makers, communities, health systems, and health care providers to help improve CRC screening uptake.[270, 271] Other efforts include the CDC's Colorectal Cancer Control Program (CRCCP), which uses multicomponent interventions to increase CRC screening among low-income, underinsured, or uninsured individuals and certain racial and ethnic groups, in particular. During its first year (2015-2016), CRC screening prevalence increased by 4.4% in clinics receiving CRCCP funds, resulting in an additional 24,100 people screened.[272] Integrated health systems have improved CRC screening participation and reduced CRC incidence and mortality by implementing patient reminders and mailed FIT kits.[273] Mailed outreach FIT programs may also be effective in community health center settings, which historically have low CRC screening rates and limited resources.[274]

On a broader scale, provisions of the Patient Protection and Affordable Care Act (ACA) removed some barriers to screening. For example, CRC screening increased faster in states that adopted the ACA provision to expand Medicaid eligibility compared to those that did not.[275] The ACA also reduced or eliminated out-of-pocket screening costs for those who are insured, although loopholes remain.[276] All recommended screening options, including colonoscopy, are covered without cost sharing for people with Medicare insurance and most commercial insurance plans. However, the required follow-up colonoscopy for a positive stool test is often coded as a diagnostic procedure, resulting in out-of-pocket costs for patients. In addition, Medicare still imposes cost sharing on beneficiaries who have a polyp removed during a screening colonoscopy, undermining efforts to improve CRC screening, particularly among low-income patients who are at highest risk for CRC.[277]

Visit cancer.org/colonmd for more information on programs and resources aimed at increasing CRC screening.

Colorectal Cancer Treatment

Treatment for CRC has advanced rapidly over the past several decades, particularly for advanced disease.[76, 278] However, it has also become increasingly clear that outcomes vary widely based on tumor-specific molecular features, tumor location, and patient characteristics.[279-281] Treatment decisions are made by patients with their physicians after considering the best options available for their tumor characteristics along with the risks and benefits associated with each.

Colon cancer

Most people with colon cancer will have some type of surgery to remove the tumor. Adjuvant chemotherapy (given after surgery) may also be used. Radiation is used less often to treat colon cancer.

Carcinoma in situ

Carcinoma in situ is malignant cancer that has not spread beyond the layer of cells in which it began. Surgery to remove the growth of abnormal cells may be accomplished by polyp removal through a colonoscope (polypectomy) or more invasive surgery. Resection of a segment of the colon may be necessary if the tumor is too large to be removed by local excision or if cancer cells are found after the polyp is removed.

Localized stage

Localized stage refers to invasive cancer that has penetrated into (but not completely through) the wall of the colon. Surgical resection to remove the cancer, together with a length of normal colon on either side of the tumor and nearby lymph nodes, is the standard treatment.

Regional stage

Regional stage describes cancers that have grown through the wall of the colon and/or spread to nearby lymph nodes. If the cancer has not spread to nearby lymph nodes, surgical resection to remove the tumor and nearby colon and surrounding lymph nodes may be the only treatment needed. If the cancer is likely to come back because it has spread to other tissues or has high-risk characteristics, chemotherapy may also be recommended. If the cancer has spread to nearby lymph nodes, surgical resection is usually followed by chemotherapy. Adjuvant chemotherapy based on the drug fluorouracil (5-FU) is typically used in patients with stage III or high-risk stage II disease who are in otherwise good health.[282] Oxaliplatin is often part of adjuvant chemotherapy as well.[283] However, some patients may not tolerate this regimen given its toxicity, and there is growing appreciation for the need to confine its use to patients who are most likely to benefit.[76, 284, 285] Adjuvant chemotherapy for colon cancer is as effective in patients ages 70 and older (almost half of all patients) who are otherwise as healthy as in younger patients, although certain drugs (e.g., oxaliplatin) may be avoided to limit toxicity. However, studies indicate that individuals 75 years of age and older are far less likely than younger patients to receive this treatment.[76, 286]

Distant stage

At this stage, the cancer has spread to distant organs and tissues, such as the liver, lungs, peritoneum (lining of the abdomen), or ovaries. When surgery is performed, the goal is usually to relieve or prevent blockage of the colon and to prevent other local complications. If there are only a few metastases to the liver or lungs, surgery to remove these, as well as the colon tumor, may improve survival.

Chemotherapy and targeted therapies may be given alone or in combination to relieve symptoms and prolong survival. A number of targeted therapies have been approved in recent years by the US Food and Drug Administration to treat metastatic CRC. Some of these drugs inhibit new blood vessel growth to the tumor by targeting a protein called vascular endothelial growth factor (VEGF). Others interfere with cancer cell growth by targeting the epidermal growth factor receptor (EGFR) or other proteins. Genetic testing of tumors is important because those with certain mutations (e.g., KRAS, NRAS, or BRAF) largely do not respond to these drugs.[287] Immunotherapy drugs are also now approved to treat a small portion of CRCs.

Rectal cancer

Surgery is usually the main treatment for rectal cancer, often accompanied by chemotherapy and radiation before and/or after surgery to reduce the risk of spread and recurrence. The chemotherapy drugs used in the treatment of rectal cancer are largely the same as those used for colon cancer.

Carcinoma in situ

Treatment options include polypectomy (polyp removal), local excision, or full-thickness rectal resection. This resection may be carried out through the anus. No further treatment is needed.

Localized stage

At this stage, the cancer has grown through the first layer of the rectum into deeper layers, but has not spread outside the rectal wall. Some small localized rectal cancers may be treated by removal through the anus, without an abdominal incision. For other tumors, depending on the location, surgery may involve removal of the cancer and some surrounding normal tissue through one or more small abdominal incisions. For cancers close to the anus, surgery may require removal of the anus and the sphincter muscle, so a permanent colostomy is needed (see next section for information about colostomy). In most cases, no further treatment is needed unless the tumor has high-risk features. Patients who are not candidates for surgery may be treated with radiation therapy.

Regional stage

At this stage, the cancer has grown through the wall of the rectum, and may have spread into nearby tissues and/or lymph nodes. Patients with regional-stage disease

are increasingly treated with chemotherapy and radiation (chemoradiation) before surgery. Some patients also receive chemotherapy after surgery, although the potential benefits are debated.[288-290]

Distant stage

At this stage, the cancer has spread to distant organs and tissues, such as the liver or lung. In rare cases, the cancer can be successfully treated by removing all of the tumors with surgery, along with other treatments. Otherwise, palliative treatments (surgery, chemotherapy, and/or radiation therapy) are used to relieve, delay, or prevent symptoms and prolong life. Similar to colon cancer, a number of targeted therapies have been approved to treat select metastatic rectal cancers, including VEGF and EGFR inhibitors.

Colostomy

When a section of the colon or rectum is removed during surgery, the healthy parts can usually be reconnected, allowing the patient to eliminate waste normally. When reconnection is not immediately possible, the surgeon connects the colon to an opening (stoma) that is made in the skin of the abdomen, allowing waste to leave the body. The surgical procedure to create an opening in the body for the elimination of waste is called an ostomy. When the stoma is connected to the colon it is called a colostomy; when the stoma is connected to the small intestine it is called an ileostomy. Usually a flat bag, held in place by a special adhesive, fits over the stoma to collect waste.

Most patients with CRC who require a colostomy need it only temporarily, until the colon or rectum heals from surgery. After healing takes place, usually in 6 to 8 weeks, the surgeon reconnects the ends of the colon and closes the stoma. A permanent colostomy is necessary more often for rectal than for colon cancer patients.

A person with an ostomy learns to care for it with help from doctors, nurses, and enterostomal therapists (health professionals trained to care for people with stomas). If surgery is expected to result in an ostomy, an enterostomal therapist will often visit the patient before surgery to explain what to expect and how to care for the ostomy. They also provide information about lifestyle issues, including emotional, physical, and sexual concerns, as well as resources and support groups.

Side effects of colorectal cancer treatment

Although many side effects that occur during cancer treatment are temporary, some persist after treatment has ended (long-term effects) and others do not arise until several years later (late effects). Side effects should be discussed with a clinician because treatment options are often available. For example, antiemetic drugs can prevent or lessen nausea and vomiting following chemotherapy. To manage the long-term and late effects of treatment, the American Cancer Society has established guidelines to aid primary care clinicians in delivering risk-based care to CRC survivors (see sidebar).[291] Short- and long-term effects of specific modes of CRC treatment are briefly described in the following sections. For more information on late and long-term effects of cancer and its treatment, visit cancer.org/treatment/treatments-and-side-effects.html.

Surgery

The time needed to heal after surgery is different for each person. Patients often have some pain for the first few days that can usually be controlled with medication. It can take a few days to be able to eat normally again. About 25% of patients experience a delay in bowel function (postoperative ileus) because of bowel stress caused by surgical manipulation, which may require an extended hospital stay.[292] Patients are monitored for signs of bleeding, infection, or other problems that require immediate treatment.

Other side effects from surgery for CRC may include fatigue, possibly for an extended period of time; frequent or urgent bowel movements, diarrhea, constipation, gas, and/or bloating, particularly among rectal cancer patients; a temporary or permanent colostomy; and urogenital/sexual dysfunction (e.g., erectile dysfunction in men).

American Cancer Society Colorectal Cancer Posttreatment Survivorship Care Guidelines

CRC patients have specific needs and concerns once treatment ends. In 2015, a multidisciplinary expert workgroup published evidence- and consensus-based posttreatment care guidelines for clinicians to aid in providing comprehensive, long-term care for colorectal cancer survivors. These guidelines include information on surveillance for cancer recurrence, screening for new cancers, management of chronic and late effects, and referrals for rehabilitation, psychosocial and palliative care, or other specialty care.

Visit cancer.org/health-care-professionals/american-cancer-society-survivorship-guidelines/colorectal-cancer-survivorship-care-guidelines.html for full text of the guidelines, as well as resources for clinicians.

Radiation therapy

Side effects of radiation therapy can include skin irritation, nausea, diarrhea, rectal irritation and/or painful inflammation, rectal bleeding, bladder dysfunction (irritation, pain, and/or frequent urination), fatigue, or sexual problems. Many of these side effects go away after treatments are completed, but some, like sexual problems and some degree of rectal and/or bladder irritation, may be permanent. Late effects include increased risk of bowel obstruction and fractures in the bone at the base of the spine (the sacrum). In addition, radiation to the pelvic area in women may damage the ovaries, causing infertility. Fertility counseling prior to treatment is recommended for women for whom this is a concern (see Sexual function and fertility, below). Radiation also increases the risk of developing second cancers in exposed areas.

Chemotherapy

The chemotherapy drugs most often used in the treatment of CRC are 5-fluorouracil (5-FU), capecitabine, oxaliplatin, and irinotecan. Side effects depend on the type and dosage of drugs, the length of treatment, and individual patient characteristics. Some side effects are temporary (e.g., hair loss), while others may persist after treatment (e.g., numbness in the hands or feet). Some patients may experience low blood cell counts because chemotherapy can harm the blood-producing cells of the bone marrow. This can increase the chance of infection (due to a shortage of white blood cells), bleeding or bruising after minor cuts or injuries (due to a shortage of blood platelets), and fatigue or shortness of breath.

Targeted therapy

Targeted therapy is a newer class of drugs resulting from an increased understanding of the molecular features of cancer development. Targeted drugs for CRC (e.g., EGFR and VEGF inhibitors) often have different but notable side effects compared to conventional chemotherapy drugs, such as dry skin or skin rash.

Sexual function and fertility

Many treatments for CRC directly or indirectly impact sexual function and fertility in both male and female patients.[293, 294] This is a particularly relevant issue for the increasing number of affected young adults in their reproductive years. The American Society for Clinical Oncology clinical practice guidelines recommend that fertility preservation be discussed with all new patients at the time of diagnosis because efforts such as sperm banking, embryo/oocyte cryopreservation (the freezing of fertilized or unfertilized eggs), and ovarian transposition (a surgical repositioning of the ovaries away from the field of radiation) should be started far in advance of treatment.[295] For more information, visit cancer.org/treatment/treatments-and-side-effects/physical-side-effects/fertility-and-sexual-side-effects.html.

What Is the American Cancer Society Doing about Colorectal Cancer?

Research

Colorectal cancer is an active area of scientific research; studies span the cancer continuum from prevention and early detection to treatment and beyond. As of August 1, 2019, the American Cancer Society was funding 78 grants totaling more than $25 million in colorectal cancer research. Examples of projects in which researchers in the American Cancer Society Extramural Research program are engaged include:

- Evaluating why certain colorectal cancers evade or resist treatment
- Exploring new ways to prevent colorectal cancer by manipulating gut microbiota
- Investigating whether increased consumption of cooked dry beans, which have anti-inflammatory and anti-cancer properties, could lower the risk of colorectal cancer recurrence in survivors with obesity
- Understanding barriers to colonoscopy screening in North and South Carolina

Examples of CRC research projects conducted within the American Cancer Society Intramural Research program include:

- Monitoring disparities in CRC screening, including identifying medically underserved populations and evaluating initiatives to reduce screening disparities
- Exploring the mechanisms underlying CRC development, such as gene-environment interactions
- Analyzing disparities and emerging trends in population-based CRC incidence and mortality rates
- Investigating factors associated with survival following a CRC diagnosis
- Identifying the needs of CRC survivors as they transition from active treatment and back into the community care setting
- Developing population-based systems for monitoring cancer patient-reported quality of life and treatment-related side effects

Colorectal cancer screening guidelines

Since 1980, the American Cancer Society has issued evidence-based recommendations for CRC screening in average-risk adults that are generally updated every 5 years. These recommendations are developed by an independent Guideline Development Group of experts in cancer epidemiology, primary care, and health services research with the support of American Cancer Society staff in the Center for Cancer Screening, the Intramural Research program, and an ad hoc group of clinicians with expertise in CRC. As part of the ongoing guideline development process, American Cancer Society staff monitor the medical and scientific literature for new evidence that may support a change in the current recommendations, as well as new information about CRC screening that should be conveyed to clinicians and target populations. The most recent update of the American Cancer Society guideline for CRC screening was published in 2018.[217]

Strategies to reach the 80% in Every Community nationwide goal

In 2014, the NCCRT launched the 80% by 2018 campaign to raise CRC screening rates across the nation. Although the nation as a whole did not achieve the 80% goal, it was reached and even surpassed in some hospital and community clinic settings, as well as in some health plans. 80% in Every Community is the new NCCRT campaign to continue efforts to substantially reduce CRC as a major public health problem by increasing colorectal screening rates to 80% or higher in communities across the nation. The NCCRT, established in 1997 by the American Cancer Society and the Centers for Disease Control and

Prevention, is a coalition of more than 100 member organizations and individual experts dedicated to reducing CRC incidence and mortality in the US through coordinated leadership, strategic planning, and advocacy. Over the past five years, more than 1,750 organizations have committed to the shared goal of raising CRC screening utilization. This initiative emphasizes evidence-based screening activities that respond to individualized needs, barriers, and motivations within a community. Talking points, FAQs, press materials, downloadable graphics, and more are available at nccrt.org/80-in-every-community. The American Cancer Society is committed to the 80% in Every Community goal as one of our major initiatives and is implementing several key strategies in support of this nationwide program, including playing a major role as convener and leader of the effort.

Notably, our approximately 300-strong force of health systems staff is playing a crucial role by engaging and supporting key strategic partners – such as hospitals and health systems, community health centers, state health departments, corporate partners, payers, and state and local coalitions – to encourage and support their commitment to increasing the number of individuals who are screened for colorectal cancer. Our staff work with these partners to assist them in implementing proven strategies that are known to increase CRC screening rates, such as implementing provider and patient reminders, helping providers assess and track their screening rates, implementing quality screening navigation, and using the power of the provider recommendation. The American Cancer Society Community Health Advocates implementing Nationwide Grants for Empowerment and Equity (CHANGE) program provides one avenue for health systems staff to collaborate at the community level. CHANGE provides both financial and technical assistance to federally qualified health centers (FQHCs) and other community partners to build capacity and implement interventions to increase cancer screening rates among low income, low education, and racially diverse populations. Since 2011, the American Cancer Society has awarded 252 grants to community-based partners to implement evidence-based CRC interventions, reaching over one million men and women with cancer prevention and early detection education and outreach and providing more than 332,000 CRC screening exams. CHANGE grant-funded FQHCs have been found to increase screening rates faster than nonfunded FQHCs.

Additionally, the American Cancer Society works to unify and magnify effective communication to the public about the value of CRC screening through multiple channels. These activities include the development and implementation of targeted traditional and social media strategies to motivate unscreened consumers to get screened. Finally, we lead by example, encouraging our own staff and volunteers to be up to date with recommended cancer screening tests. Through these actions, the American Cancer Society is working to leverage the energy of multiple and diverse partners to make history and achieve this remarkable public health goal.

Advocacy

Our nonprofit, nonpartisan advocacy affiliate, the American Cancer Society Cancer Action Network℠ (ACS CAN), is involved in advocacy efforts at both the federal and state levels that increase access to quality CRC screening, treatment, and care for all adults. In partnership with the American Cancer Society, the Centers for Disease Control and Prevention (CDC), and the National Colorectal Cancer Roundtable, as well as over 1,750 other organizations, ACS CAN hopes to reach the goal of achieving 80% or higher CRC screening rates in every community. Following are some of the efforts the American Cancer Society and ACS CAN are involved in to help reach that goal:

- Implementing the provisions in the Patient Protection and Affordable Care Act, more commonly referred to as the Affordable Care Act or ACA. The reforms in the ACA, which was signed into law in March 2010, represent a profound structural change in how insurance operates and how consumers and patients use the health insurance system. ACS CAN and the American Cancer Society have a significant impact at the federal and state levels through our advocacy work, which urges policy makers to implement the law to ensure that all Americans have access to

evidence-based prevention, early detection, and treatment services critical to CRC patients. In particular, ACS CAN has advocated for expansion of Medicaid in all 50 states for those individuals up to 138% of the federal poverty level, as it was originally intended by the ACA. This would ensure that low-income, uninsured, and underinsured Americans will have access to the same CRC services as those in private and other public insurances.

- Advocating for clarification on ACA-required coverage of CRC screening modalities as recommended by the United States Preventive Services Task Force (USPSTF). This includes clarifying that there should be no cost sharing requirements for a colonoscopy that is ordered to complete the screening process following a positive CRC stool-based screening test (follow-up colonoscopy), cost sharing for short interval screening following the removal of adenomatous polyps during a screening colonoscopy, and other ambiguous coverage issues related to CRC screening.
- Supporting the work and maintaining funding for the CDC's Colorectal Cancer Control Program (CRCCP), which currently provides funding to 30 grantees across the US. The CRCCP's goal is to increase CRC screening rates in targeted populations by implementing evidence-based, system-level interventions through partnerships with health systems. The program provides grants for both population-based education and awareness campaigns and efforts to improve access to vital CRC screening tests and follow-up services for at-risk low-income, uninsured, and underinsured individuals between the ages of 50 and 75.
- Advocating for passage of the Removing Barriers to Colorectal Cancer Screening Act of 2019, which will ease the financial burden of people living on a fixed income by allowing Medicare beneficiaries to receive screenings without coinsurance, even when a polyp is removed. This legislation would help increase screening rates and reduce the incidence of CRC.
- Advocating for state legislation to ensure insurance coverage in each state aligns with the American Cancer Society's evidence-based CRC guideline, which recommends average-risk adults begin screening at age 45
- Engaging governors, mayors, and state legislators to inform them about the 80% in Every Community initiative, urging them to help make CRC screening a priority. Specifically, ACS CAN is urging state and city governments to work across all sectors to increase screening rates by eliminating cost and access barriers to screening and by investing in or creating a state CRC screening and control program.

Sources of Statistics

New cancer cases. The estimated number of CRC cases in the US in 2020 was projected using a spatiotemporal model based on incidence data from 50 states and the District of Columbia for the years 2002 to 2016 that met the North American Association of Central Cancer Registries' (NAACCR's) high-quality data standards for incidence. For more information on this method, please see Zhu et al.[296]

Incidence rates. Incidence rates are defined as the number of people newly diagnosed with cancer during a given time period per 100,000 population at risk. CRC incidence rates for the US were calculated using case data from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute, the National Program of Cancer Registries of the Centers for Disease Control and Prevention, and NAACCR, and population data collected by the US Census Bureau. Incidence rates for Alaska Natives are based on cases reported by the Alaska Native Tumor Registry (ANTR) of the SEER Program; rates for American Indians excluding Alaska Natives are based on NAACCR Purchased/Referred Care Delivery Area (PRCDA) county regions excluding the ANTR. Incidence rates were age adjusted to the 2000 US standard population and adjusted for delays in reporting when possible. Trends exclude appendix.

Estimated cancer deaths. The estimated number of CRC deaths in the US in 2020 was calculated by fitting the actual number of CRC deaths from 2003 through 2017 to a statistical model that forecasts the number of deaths three years ahead. The actual number of deaths was obtained from the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention. For more information on this method, please see Chen et al.[297]

Mortality rates. Mortality rates, or death rates, are defined as the number of people who die from cancer during a given time period per 100,000 population. Mortality rates are based on counts of cancer deaths compiled by NCHS and population data from the US Census Bureau. Death rates for Alaska Natives are based on deaths occurring in the Alaska Community Health Service Delivery Area region. Due to data limitations, there may be a small degree of cross-contamination between rates for American Indians and Alaska Natives where they are presented separately. Death rates are age adjusted to the 2000 US standard population.

Survival. Relative and cause-specific (herein referred to as cancer-specific) survival rates were calculated using data from the SEER registries. Relative survival rates account for normal life expectancy by comparing overall survival among a group of cancer patients to that of people not diagnosed with cancer who are of the same age, race, and sex. Cancer-specific survival is the probability of not dying from a specific cancer (e.g., colorectal) within a specified time period following a diagnosis. Cancer-specific survival was used for rates by race and ethnicity because reliable estimates of normal life expectancy historically have not been available by Hispanic ethnicity or for Asians/Pacific Islanders and American Indians/Alaska Natives.

Screening. The national prevalence of CRC screening was estimated from the National Health Interview Survey (NHIS) 2018 data file, obtained from NCHS, released in 2019 (cdc.gov/nchs/nhis.htm). The NHIS is conducted by the US Census Bureau and is designed to provide national prevalence estimates on health characteristics such as cancer screening behaviors. Data are collected through in-person interviews.

CRC screening prevalence by state was estimated from the 2018 Behavioral Risk Factor Surveillance System (BRFSS) public use data files, obtained from the National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention. The BRFSS is a telephone survey designed to provide state prevalence estimates of health behaviors and was conducted by state health departments.

Important note about estimated cases and deaths. The projected number of new cancer cases and deaths for the current year are model based. For this reason, we discourage the use of our estimates to track cancer trends. Age-standardized incidence and mortality rates are used to track cancer incidence and mortality trends.

References

1. Lee GH, Malietzis G, Askari A, Bernardo D, Al-Hassi HO, Clark SK. Is right-sided colon cancer different to left-sided colorectal cancer? – a systematic review. *Eur J Surg Oncol*. 2015;41(3):300-308.

2. Burón Pust A, Alison R, Blanks R, et al. Heterogeneity of colorectal cancer risk by tumour characteristics: Large prospective study of UK women. *Int J Cancer*. 2017;140(5):1082-1090.

3. Sineshaw HM, Ng K, Flanders WD, Brawley OW, Jemal A. Factors That Contribute to Differences in Survival of Black vs White Patients With Colorectal Cancer. *Gastroenterology*. 2018;154(4):906-915 e907.

4. Siegel RL, Miller KD, Fedewa SA, et al. Colorectal cancer statistics, 2017. *CA Cancer J Clin*. 2017;67(3):177-193.

5. Corley DA, Jensen CD, Marks AR, et al. Variation of Adenoma Prevalence by Age, Sex, Race, and Colon Location in a Large Population: Implications for Screening and Quality Programs. *Clin Gastroenterol Hepatol*. 2013;11(2):172-180.

6. Levine JS, Ahnen DJ. Clinical practice. Adenomatous polyps of the colon. *N Engl J Med*. 2006;355(24):2551-2557.

7. Risio M. The natural history of adenomas. Best Pract Res *Clin Gastroenterol*. 2010;24(3):271-280.

8. Winawer SJ, Zauber AG. The advanced adenoma as the primary target of screening. *Gastrointest Endosc Clin N Am*. 2002;12(1):1-9, v.

9. Stryker SJ, Wolff BG, Culp CE, Libbe SD, Ilstrup DM, MacCarty RL. Natural history of untreated colonic polyps. *Gastroenterology*. 1987;93(5):1009-1013.

10. Pickhardt PJ, Kim DH, Pooler BD, et al. Assessment of volumetric growth rates of small colorectal polyps with CT colonography: a longitudinal study of natural history. *Lancet Oncol*. 2013;14(8):711-720.

11. Øines M, Helsingen LM, Bretthauer M, Emilsson L. Epidemiology and risk factors of colorectal polyps. *Best Pract Res Clin Gastroenterol*. 2017;31(4):419-424.

12. Rex DK, Ahnen DJ, Baron JA, et al. Serrated lesions of the colorectum: review and recommendations from an expert panel. *Am J Gastroenterol*. 2012;107(9):1315-1329; quiz 1314, 1330.

13. Tauriello DVF, Calon A, Lonardo E, Batlle E. Determinants of metastatic competency in colorectal cancer. *Mol Oncol*. 2017;11(1): 97-119.

14. Quere P, Facy O, Manfredi S, et al. Epidemiology, Management, and Survival of Peritoneal Carcinomatosis from Colorectal Cancer: A Population-Based Study. *Dis Colon Rectum*. 2015;58(8):743-752.

15. Yin D, Morris CR, Bates JH, German RR. Effect of misclassified underlying cause of death on survival estimates of colon and rectal cancer. *J Natl Cancer Inst*. 2011;103(14):1130-1133.

16. Colon Cancer Alliance Announces Corporate Name Change (ccalliance.org/news/press-releases/colon-cancer-alliance-announces-corporate-name-change) [press release]. Washington DC 2017.

17. Siegel RL, Fedewa SA, Anderson WF, et al. Colorectal cancer incidence patterns in the United States, 1974-2013. *J Natl Cancer Inst*. 2017;109(8).

18. Miller KD, Nogueira L, Mariotto AB, et al. Cancer treatment and survivorship statistics, 2019. *CA Cancer J Clin*. 2019;69(5):363-385.

19. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2020. *CA Cancer J Clin*. 2020;70(1):7-34.

20. Lieberman DA, Williams JL, Holub JL, et al. Race, ethnicity, and sex affect risk for polyps >9 mm in average-risk individuals. *Gastroenterology*. 2014;147(2):351-358; quiz e314-355.

21. Ferlitsch M, Reinhart K, Pramhas S, et al. Sex-specific prevalence of adenomas, advanced adenomas, and colorectal cancer in individuals undergoing screening colonoscopy. *JAMA*. 2011;306(12):1352-1358.

22. Samadder NJ, Curtin K, Tuohy TMF, et al. Characteristics of Missed or Interval Colorectal Cancer and Patient Survival: A Population-Based Study. *Gastroenterology*. 2014;146(4):950-960.

23. Murphy G, Devesa SS, Cross AJ, Inskip PD, McGlynn KA, Cook MB. Sex disparities in colorectal cancer incidence by anatomic subsite, race and age. *Int J Cancer*. 2011;128(7):1668-1675.

24. Howlader N, Noone AM, Krapcho M, et al., eds. *SEER Cancer Statistics Review, 1975-2016*. Bethesda, MD: National Cancer Institute; 2019.

25. Ries LAG, Eisner MP, Kosary CL, et al., eds. *SEER Cancer Statistics Review, 1973-1999*. Bethesda, MD: National Cancer Institute; 2002.

26. Carethers JM, Doubeni CA. Causes of Socioeconomic Disparities in Colorectal Cancer and Intervention Framework and Strategies. *Gastroenterology*. 2019.

27. Semega JL, Kollar MA, Mohanty A. Income and Poverty in the United States: 2018. In. U.S. Government Printing Office, Washington, DC: U.S. Census Bureau; 2019.

28. Doubeni CA, Laiyemo AO, Major JM, et al. Socioeconomic status and the risk of colorectal cancer: an analysis of more than a half million adults in the National Institutes of Health-AARP Diet and Health Study. *Cancer*. 2012;118(14):3636-3644.

29. Doubeni CA, Major JM, Laiyemo AO, et al. Contribution of behavioral risk factors and obesity to socioeconomic differences in colorectal cancer incidence. *J Natl Cancer Inst*. 2012;104(18):1353-1362.

30. Lansdorp-Vogelaar I, Kuntz KM, Knudsen AB, van Ballegooijen M, Zauber AG, Jemal A. Contribution of screening and survival differences to racial disparities in colorectal cancer rates. *Cancer Epidemiol Biomarkers Prev*. 2012;21(5):728-736.

31. Fedewa SA, Flanders WD, Ward KC, et al. Racial and Ethnic Disparities in Interval Colorectal Cancer Incidence: A Population-Based Cohort Study. *Ann Intern Med*. 2017;166(12):857-866.

32. Laiyemo AO, Doubeni C, Pinsky PF, et al. Race and colorectal cancer disparities: health-care utilization vs different cancer susceptibilities. *J Natl Cancer Inst*. 2010;102(8):538-546.

33. Torre LA, Sauer AM, Chen MS, Jr., Kagawa-Singer M, Jemal A, Siegel RL. Cancer statistics for Asian Americans, Native Hawaiians, and Pacific Islanders, 2016: Converging incidence in males and females. *CA Cancer J Clin*. 2016;66(3):182-202.

34. Kelly JJ, Alberts SR, Sacco F, Lanier AP. Colorectal cancer in alaska native people, 2005-2009. *Gastrointest Cancer Res*. 2012;5(5):149-154.

35. Perdue DG, Haverkamp D, Perkins C, Daley CM, Provost E. Geographic variation in colorectal cancer incidence and mortality, age of onset, and stage at diagnosis among American Indian and Alaska Native people, 1990-2009. *Am J Public Health*. 2014;104 Suppl 3:S404-414.

36. McMahon BJ, Bruce MG, Koch A, et al. The diagnosis and treatment of Helicobacter pylori infection in Arctic regions with a high prevalence of infection: Expert Commentary. *Epidemiol Infect*. 2016;144(2):225-233.

37. Sonnenberg A, Genta RM. Helicobacter pylori is a risk factor for colonic neoplasms. *Am J Gastroenterol*. 2013;108(2):208-215.

38. Butt J, Varga MG, Blot WJ, et al. Serologic Response to *Helicobacter pylori* Proteins Associated With Risk of Colorectal Cancer Among Diverse Populations in the United States. *Gastroenterology*. 2019;156(1):175-186.e172.

39. Conway AA, Gerry JM, Sacco F, Wren SM. High Prevalence of Adenomatous Polyps in Alaska Native People Aged 40-49 years. *J Surg Res*. 2019;243:524-530.

40. Day LW, Espey DK, Madden E, Segal M, Terdiman JP. Screening prevalence and incidence of colorectal cancer among American Indian/Alaskan natives in the Indian Health Service. *Dig Dis Sci*. 2011;56(7):2104-2113.

41. Carmichael H, Cowan M, McIntyre R, Velopulos C. Disparities in colorectal cancer mortality for rural populations in the United States: Does screening matter? *Am J Surg*. 2019.

42. Berkowitz Z, Zhang X, Richards TB, Nadel M, Peipins LA, Holt J. Multilevel Small-Area Estimation of Colorectal Cancer Screening in the United States. *Cancer Epidemiol Biomarkers Prev*. 2018;27(3):245-253.

43. Edwards BK, Ward E, Kohler BA, et al. Annual report to the nation on the status of cancer, 1975-2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. *Cancer*. 2010;116(3):544-573.

44. National Center for Health Statistics, Division of Health Interview Statistics. National Health Interview Survey Public Use Data File 2018. In. Centers for Disease Control and Prevention. Hyattsville, MD.2019.

45. Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. *N Engl J Med*. 1993;329(27):1977-1981.

46. Legler JM, Feuer EJ, Potosky AL, Merrill RM, Kramer BS. The role of prostate-specific antigen (PSA) testing patterns in the recent prostate cancer incidence decline in the United States. *Cancer Causes Control*. 1998;9(5):519-527.

47. Siegel RL, Torre LA, Soerjomataram I, et al. Global patterns and trends in colorectal cancer incidence in young adults. *Gut*. 2019.

48. Irby K, Anderson WF, Henson DE, Devesa SS. Emerging and widening colorectal carcinoma disparities between Blacks and Whites in the United States (1975-2002). *Cancer Epidemiol Biomarkers Prev*. 2006;15(4):792-797.

49. Siegel RL, Medhanie GA, Fedewa SA, Jemal A. State Variation in Early-Onset Colorectal Cancer in the United States, 1995-2015. *J Natl Cancer Inst*. 2019;111(10):1104-1106.

50. Surveillance, Epidemiology and End Results (SEER) Program, SEER*Stat Database: NAACCR Incidence - CiNA Analytic File, 1995-2016, for NHIAv2 Origin, Custom File With County, ACS Facts and Figures projection Project, North American Association of Central Cancer Registries. 2019.

51. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence – SEER 13 Regs Research Data with Delay-Adjustment, Malignant Only, Nov 2018 Sub (1992-2016) <Katrina/Rita Population Adjustment> – Linked To County Attributes – Total U.S., 1969-2017 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2019, based on the November 2018 submission. 2019.

52. Zauber AG. The impact of screening on colorectal cancer mortality and incidence: has it really made a difference? *Dig Dis Sci*. 2015;60(3):681-691.

53. Robbins AS, Siegel RL, Jemal A. Racial disparities in stage-specific colorectal cancer mortality rates from 1985 to 2008. *J Clin Oncol*. 2012;30(4):401-405.

54. Siegel RL, Sahar L, Robbins A, Jemal A. Where can colorectal cancer screening interventions have the most impact? *Cancer Epidemiol Biomarkers Prev*. 2015;24(8):1151-1156.

55. Liang PS, Mayer JD, Wakefield J, Ko CW. Temporal Trends in Geographic and Sociodemographic Disparities in Colorectal Cancer Among Medicare Patients, 1973-2010. *J Rural Health*. 2016;33(4):361-370.

56. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin*. 2019;69(1):7-34.

57. Siegel R, Ward E, Brawley O, Jemal A. Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA Cancer J Clin*. 2011;61(4):212-236.

58. Melkonian SC, Jim MA, Haverkamp D, et al. Disparities in Cancer Incidence and Trends among American Indians and Alaska Natives in the United States, 2010-2015. *Cancer Epidemiol Biomarkers Prev*. 2019;28(10):1604-1611.

59. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence – SEER 18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2018 Sub (2000-2016) – Linked To County Attributes – Total U.S., 1969-2017 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2019, based on the November 2018 submission. 2019.

60. Andrew AS, Parker S, Anderson JC, et al. Risk Factors for Diagnosis of Colorectal Cancer at a Late Stage: a Population-Based Study. *J Gen Intern Med*. 2018;33(12):2100-2105.

61. Ward E, Jemal A, Cokkinides V, et al. Cancer disparities by race/ethnicity and socioeconomic status. *CA Cancer J Clin*. 2004;54(2):78-93.

62. Jemal A, Ward EM, Johnson CJ, et al. Annual Report to the Nation on the Status of Cancer, 1975-2014, Featuring Survival. *J Natl Cancer Inst*. 2017;109(9).

63. Yang Y, Wang G, He J, et al. Gender differences in colorectal cancer survival: A meta-analysis. *Int J Cancer*. 2017;141(10):1942-1949.

64. Petrelli F, Tomasello G, Borgonovo K, et al. Prognostic Survival Associated With Left-Sided vs Right-Sided Colon Cancer: A Systematic Review and Meta-analysis. *JAMA Oncology*. 2017;3(2):211-219.

65. Karim S, Brennan K, Nanji S, Berry SR, Booth CM. Association Between Prognosis and Tumor Laterality in Early-Stage Colon Cancer. *JAMA Oncology*. 2017;3(10):1386-1392.

66. Bach PB, Schrag D, Brawley OW, Galaznik A, Yakren S, Begg CB. Survival of blacks and whites after a cancer diagnosis. *JAMA*. 2002;287(16):2106-2113.

67. Ellis L, Canchola AJ, Spiegel D, Ladabaum U, Haile R, Gomez SL. Racial and Ethnic Disparities in Cancer Survival: The Contribution of Tumor, Sociodemographic, Institutional, and Neighborhood Characteristics. 2018;36(1):25-33.

68. Halpern MT, Holden DJ. Disparities in timeliness of care for U.S. Medicare patients diagnosed with cancer. *Curr Oncol*. 2012;19(6):e404-e413.

69. Lai Y, Wang C, Civan JM, et al. Effects of Cancer Stage and Treatment Differences on Racial Disparities in Survival From Colon Cancer: A United States Population-Based Study. *Gastroenterology*. 2016;150(5):1135-1146.

70. Butler EN, Chawla N, Lund J, Harlan LC, Warren JL, Yabroff KR. Patterns of colorectal cancer care in the United States and Canada: a systematic review. *J Natl Cancer Inst Monogr*. 2013;2013(46):13-35.

71. Eaglehouse YL, Georg MW, Shriver CD, Zhu K. Racial Comparisons in Timeliness of Colon Cancer Treatment in an Equal-Access Health System. *J Natl Cancer Inst*. 2019.

72. Yothers G, Sargent DJ, Wolmark N, et al. Outcomes among black patients with stage II and III colon cancer receiving chemotherapy: an analysis of ACCENT adjuvant trials. *J Natl Cancer Inst*. 2011;103(20):1498-1506.

73. Haller DG, Catalano PJ, Macdonald JS, et al. Phase III study of fluorouracil, leucovorin, and levamisole in high-risk stage II and III colon cancer: final report of Intergroup 0089. *J Clin Oncol*. 2005;23(34):8671-8678.

74. Doubeni CA, Rustgi A. Racial Disparities in Colorectal Cancer Survival: Is Elimination of Variation in Care the Cure? *J Natl Cancer Inst*. 2015;107(10).

75. Kopetz S, Chang GJ, Overman MJ, et al. Improved survival in metastatic colorectal cancer is associated with adoption of hepatic resection and improved chemotherapy. *J Clin Oncol*. 2009;27(22):3677-3683.

76. Murphy CC, Harlan LC, Lund JL, Lynch CF, Geiger AM. Patterns of Colorectal Cancer Care in the United States: 1990-2010. *J Natl Cancer Inst*. 2015;107(10).

77. Piawah S, Venook AP. Targeted therapy for colorectal cancer metastases: A review of current methods of molecularly targeted therapy and the use of tumor biomarkers in the treatment of metastatic colorectal cancer. *Cancer*. 2019.

78. Surveillance, Epidemiology, and End Results (SEER) Program, SEER*Stat Database: Incidence – SEER 9 Regs Research Data, Nov 2018 Sub (1975-2016) <Katrina/Rita Population Adjustment> – Linked To County Attributes – Total U.S., 1969-2017 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2019. 2019.

79. Sineshaw HM, Robbins AS, Jemal A. Disparities in survival improvement for metastatic colorectal cancer by race/ethnicity and age in the United States. *Cancer Causes Control*. 2014;25(4):419-423.

80. Islami F, Goding Sauer A, Miller KD, et al. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. *CA Cancer J Clin*. 2018;68(1):31-54.

81. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. *Gut*. 2016.

82. Kohler LN, Garcia DO, Harris RB, Oren E, Roe DJ, Jacobs ET. Adherence to Diet and Physical Activity Cancer Prevention Guidelines and Cancer Outcomes: A Systematic Review. *Cancer Epidemiol Biomarkers Prev*. 2016;25(7):1018-1028.

83. Patel SG, Ahnen DJ. Familial colon cancer syndromes: an update of a rapidly evolving field. *Curr Gastroenterol Rep*. 2012;14(5):428-438.

84. Lowery JT, Ahnen DJ, Schroy III PC, et al. Understanding the contribution of family history to colorectal cancer risk and its clinical implications: A state-of-the-science review. *Cancer*. 2016;122(17):2633-2645.

85. Jones WF, Ahnen DJ, Schroy III PC. Improving on-time colorectal cancer screening through lead time messaging. *Cancer*. 2019.

86. Samadder NJ, Smith KR, Hanson H, et al. Increased Risk of Colorectal Cancer Among Family Members of All Ages, Regardless of Age of Index Case at Diagnosis. *Clin Gastroenterol Hepatol*. 2015;13(13):2305-2311 e2301-2302.

87. Tuohy TM, Rowe KG, Mineau GP, Pimentel R, Burt RW, Samadder NJ. Risk of colorectal cancer and adenomas in the families of patients with adenomas: a population-based study in Utah. *Cancer*. 2014;120(1):35-42.

88. Peters U, Hutter CM, Hsu L, et al. Meta-analysis of new genomewide association studies of colorectal cancer risk. *Hum Genet*. 2012;131(2):217-234.

89. Flynn BS, Wood ME, Ashikaga T, Stockdale A, Dana GS, Naud S. Primary care physicians' use of family history for cancer risk assessment. *BMC Family Practice*. 2010;11(1):45.

90. Wood ME, Kadlubek P, Pham TH, et al. Quality of cancer family history and referral for genetic counseling and testing among oncology practices: a pilot test of quality measures as part of the American Society of Clinical Oncology Quality Oncology Practice Initiative. *J Clin Oncol*. 2014;32(8):824-829.

91. Yurgelun MB, Kulke MH, Fuchs CS, et al. Cancer Susceptibility Gene Mutations in Individuals With Colorectal Cancer. *J Clin Oncol*. 2017;35(10):1086-1095.

92. Win AK, Lindor NM, Young JP, et al. Risks of primary extracolonic cancers following colorectal cancer in lynch syndrome. *J Natl Cancer Inst*. 2012;104(18):1363-1372.

93. Lynch HT, Snyder CL, Shaw TG, Heinen CD, Hitchins MP. Milestones of Lynch syndrome: 1895-2015. *Nat Rev Cancer*. 2015;15(3):181-194.

94. Moller P, Seppala TT, Bernstein I, et al. Cancer risk and survival in path_MMR carriers by gene and gender up to 75 years of age: a report from the Prospective Lynch Syndrome Database. *Gut*. 2018;67(7):1306-1316.

95. Hampel H, Stephens JA, Pukkala E, et al. Cancer Risk in Hereditary Nonpolyposis Colorectal Cancer Syndrome: Later Age of Onset. *Gastroenterology*. 2005;129(2):415-421.

96. Pearlman R, Frankel WL, Swanson B, et al. Prevalence and Spectrum of Germline Cancer Susceptibility Gene Mutations Among Patients With Early-Onset Colorectal Cancer. *JAMA Oncol*. 2017;3(4):464-471.

97. Win AK, Jenkins MA, Dowty JG, et al. Prevalence and Penetrance of Major Genes and Polygenes for Colorectal Cancer. *Cancer Epidemiol Biomarkers Prev*. 2017;26(3):404-412

98. Møller P, Seppälä T, Bernstein I, et al. Cancer incidence and survival in Lynch syndrome patients receiving colonoscopic and gynaecological surveillance: first report from the prospective Lynch syndrome database. *Gut*. 2017;66(3):464-472.

99. Gupta S, Provenzale D, Llor X, et al. NCCN Guidelines Insights: Genetic/Familial High-Risk Assessment: Colorectal, Version 2.2019. *J Natl Compr Canc Netw*. 2019;17(9):1032-1041.

100. Sepulveda AR, Hamilton SR, Allegra CJ, et al. Molecular Biomarkers for the Evaluation of Colorectal Cancer: Guideline From the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and the American Society of Clinical Oncology. *J Clin Oncol*. 2017;35(13):1453-1486.

101. Cohen SA, Laurino M, Bowen DJ, et al. Initiation of universal tumor screening for Lynch syndrome in colorectal cancer patients as a model for the implementation of genetic information into clinical oncology practice. *Cancer*. 2016;122(3):393-401.

102. Green RF, Ari M, Kolor K, et al. Evaluating the role of public health in implementation of genomics-related recommendations: a case study of hereditary cancers using the CDC Science Impact Framework. *Genet Med*. 2019;21(1):28-37.

103. Leoz ML, Carballal S, Moreira L, Ocaña T, Balaguer F. The genetic basis of familial adenomatous polyposis and its implications for clinical practice and risk management. *Appl Clin Genet*. 2015;8:95-107.

104. Aretz S, Uhlhaas S, Caspari R, et al. Frequency and parental origin of de novo APC mutations in familial adenomatous polyposis. *Eur J Hum Genet*. 2004;12(1):52-58.

105. Lynch HT, Smyrk T, McGinn T, et al. Attenuated familial adenomatous polyposis (AFAP). A phenotypically and genotypically distinctive variant of FAP. *Cancer*. 1995;76(12):2427-2433.

106. Vasen HFA, Tomlinson I, Castells A. Clinical management of hereditary colorectal cancer syndromes. *Nat Rev Gastroenterol Hepatol*. 2015;12(2):88-97.

107. Mersch J, Jackson MA, Park M, et al. Cancers associated with BRCA1 and BRCA2 mutations other than breast and ovarian. *Cancer*. 2015;121(2):269-275.

108. Oh M, McBride A, Yun S, et al. BRCA1 and BRCA2 Gene Mutations and Colorectal Cancer Risk: Systematic Review and Metaanalysis. *J Natl Cancer Inst*. 2018;110(11):1178-1189.

109. Mysliwiec PA, Cronin KA, Schatzkin A. Chapter 5: New Malignancies Following Cancer of the Colon, Rectum, and Anus. In: *New Malignancies Among Cancer Survivors: SEER Cancer Registries, 1973-2000*. Bethesda, MD: National Cancer Institute; 2006.

110. Yang L, Xiong Z, Xie QK, et al. Second primary colorectal cancer after the initial primary colorectal cancer. *BMC Cancer*. 2018;18(1):931.

111. Ren J, Kirkness CS, Kim M, Asche CV, Puli S. Long-term risk of colorectal cancer by gender after positive colonoscopy: population-based cohort study. *Curr Med Res Opin*. 2016;32(8):1367-1374.

112. Teepen JC, Kok JL, van Leeuwen FE, et al. Colorectal Adenomas and Cancers After Childhood Cancer Treatment: A DCOG-LATER Record Linkage Study. *J Natl Cancer Inst*. 2018;110(7):758-767.

113. Wallis CJD, Mahar AL, Choo R, et al. Second malignancies after radiotherapy for prostate cancer: systematic review and metaanalysis. *BMJ*. 2016;352:i851.

114. Groot HJ, Lubberts S, Wit Rd, et al. Risk of Solid Cancer After Treatment of Testicular Germ Cell Cancer in the Platinum Era. *J Clin Oncol*. 2018;36(24):2504-2513.

115. Lutgens MW, van Oijen MG, van der Heijden GJ, Vleggaar FP, Siersema PD, Oldenburg B. Declining risk of colorectal cancer in inflammatory bowel disease: an updated meta-analysis of population-based cohort studies. *Inflamm Bowel Dis*. 2013;19(4):789-799.

116. Beaugerie L, Itzkowitz SH. Cancers complicating inflammatory bowel disease. *N Engl J Med*. 2015;372(15):1441-1452.

117. Castano-Milla C, Chaparro M, Gisbert JP. Systematic review with meta-analysis: the declining risk of colorectal cancer in ulcerative colitis. *Aliment Pharmacol Ther*. 2014;39(7):645-659.

118. Bonovas S, Fiorino G, Lytras T, Nikolopoulos G, Peyrin-Biroulet L, Danese S. Systematic review with meta-analysis: use of 5-aminosalicylates and risk of colorectal neoplasia in patients with inflammatory bowel disease. *Aliment Pharmacol Ther*. 2017;45(9):1179-1192.

119. Lu MJ, Qiu XY, Mao XQ, Li XT, Zhang HJ. Systematic review with metaanalysis: thiopurines decrease the risk of colorectal neoplasia in patients with inflammatory bowel disease. *Aliment Pharmacol Ther*. 2018;47(3):318-331.

120. Jewel Samadder N, Valentine JF, Guthery S, et al. Colorectal Cancer in Inflammatory Bowel Diseases: A Population-Based Study in Utah. *Dig Dis Sci*. 2017;62(8):2126-2132.

121. Xu F, Dahlhamer JM, Zammitti EP, Wheaton AG, Croft JB. Health-Risk Behaviors and Chronic Conditions Among Adults with Inflammatory Bowel Disease – United States, 2015 and 2016. *MMWR Morb Mortal Wkly Rep*. 2018;67(6):190-195.

122. Kappelman MD, Moore KR, Allen JK, Cook SF. Recent trends in the prevalence of Crohn's disease and ulcerative colitis in a commercially insured US population. *Dig Dis Sci*. 2013;58(2):519-525.

123. Tsilidis KK, Kasimis JC, Lopez DS, Ntzani EE, Ioannidis JP. Type 2 diabetes and cancer: umbrella review of meta-analyses of observational studies. *BMJ*. 2015;350:g7607.

124. Ma Y, Yang W, Song M, et al. Type 2 diabetes and risk of colorectal cancer in two large U.S. prospective cohorts. *Br J Cancer*. 2018;119(11):1436-1442.

125. Larsson SC, Giovannucci E, Wolk A. Diabetes and colorectal cancer incidence in the cohort of Swedish men. *Diabetes Care*. 2005;28(7):1805-1807.

126. Currie CJ, Poole CD, Gale EA. The influence of glucoselowering therapies on cancer risk in type 2 diabetes. *Diabetologia*. 2009;52(9):1766-1777.

127. Libby G, Donnelly LA, Donnan PT, Alessi DR, Morris AD, Evans JM. New users of metformin are at low risk of incident cancer: a cohort study among people with type 2 diabetes. *Diabetes Care*. 2009;32(9):1620-1625.

128. Lee MS, Hsu CC, Wahlqvist ML, Tsai HN, Chang YH, Huang YC. Type 2 diabetes increases and metformin reduces total, colorectal, liver and pancreatic cancer incidences in Taiwanese: a representative population prospective cohort study of 800,000 individuals. *BMC Cancer*. 2011;11:20.

129. Ruiter R, Visser LE, van Herk-Sukel MP, et al. Lower risk of cancer in patients on metformin in comparison with those on sulfonylurea derivatives: results from a large population-based follow-up study. *Diabetes Care*. 2012;35(1):119-124.

130. Singh S, Singh H, Singh PP, Murad MH, Limburg PJ. Antidiabetic medications and the risk of colorectal cancer in patients with diabetes mellitus: a systematic review and meta-analysis. *Cancer Epidemiol Biomarkers Prev*. 2013;22(12):2258-2268.

131. Home PD, Kahn SE, Jones NP, et al. Experience of malignancies with oral glucose-lowering drugs in the randomised controlled ADOPT (A Diabetes Outcome Progression Trial) and RECORD (Rosiglitazone Evaluated for Cardiovascular Outcomes and Regulation of Glycaemia in Diabetes) clinical trials. *Diabetologia*. 2010;53(9):1838-1845.

132. Iyengar A, Gold HT, Becker DJ. Association of diabetes with colorectal cancer treatment and outcomes. *J Clin Oncol*. 2018;36(15_suppl):e18752-e18752.

133. Geiss LS, Wang J, Cheng YJ, et al. Prevalence and incidence trends for diagnosed diabetes among adults aged 20 to 79 years, United States, 1980-2012. *JAMA*. 2014;312(12):1218-1226.

134. Mayer-Davis EJ, Dabelea D, Lawrence JM. Incidence Trends of Type 1 and Type 2 Diabetes among Youths, 2002-2012. *N Engl J Med*. 2017;377(3):301.

135. Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2017. Atlanta, GA: US Department of Health and Human Services, CDC; 2017. In.

136. Burnett-Hartman AN, Newcomb PA, Potter JD. Infectious Agents and Colorectal Cancer: A Review of *Helicobacter pylori, Streptococcus bovis*, JC Virus, and Human Papillomavirus. 2008;17(11):2970-2979.

137. Butt J, Varga MG, Blot WJ, et al. Serologic Response to Helicobacter pylori Proteins Associated With Risk of Colorectal Cancer Among Diverse Populations in the United States. *Gastroenterology*. 2019;156(1):175-186.e172.

138. Boyle T, Keegel T, Bull F, Heyworth J, Fritschi L. Physical activity and risks of proximal and distal colon cancers: a systematic review and meta-analysis. *J Natl Cancer Inst*. 2012;104(20):1548-1561.

139. Robsahm TE, Aagnes B, Hjartaker A, Langseth H, Bray FI, Larsen IK. Body mass index, physical activity, and colorectal cancer by anatomical subsites: a systematic review and meta-analysis of cohort studies. *Eur J Cancer Prev*. 2013;22(6):492-505.

140. Hidayat K, Zhou H-J, Shi B-M. Influence of physical activity at a young age and lifetime physical activity on the risks of 3 obesity-related cancers: systematic review and meta-analysis of observational studies. *Nutrition Reviews*. 2019.

141. Schmid D, Leitzmann MF. Television viewing and time spent sedentary in relation to cancer risk: a meta-analysis. *J Natl Cancer Inst*. 2014;106(7).

142. Chao A, Connell CJ, Jacobs EJ, et al. Amount, type, and timing of recreational physical activity in relation to colon and rectal cancer in older adults: the Cancer Prevention Study II Nutrition Cohort. *Cancer Epidemiol Biomarkers Prev*. 2004;13(12):2187-2195.

143. Campbell PT, Patel AV, Newton CC, Jacobs EJ, Gapstur SM. Associations of recreational physical activity and leisure time spent sitting with colorectal cancer survival. *J Clin Oncol*. 2013;31(7):876-885.

144. Larsson SC, Wolk A. Obesity and colon and rectal cancer risk: a meta-analysis of prospective studies. *Am J Clin Nutr*. 2007;86(3):556-565.

145. Ortega LS, Bradbury KE, Cross AJ, Morris JS, Gunter MJ, Murphy N. A Prospective Investigation of Body Size, Body Fat Composition and Colorectal Cancer Risk in the UK Biobank. *Sci Rep*. 2017;7(1):17807.

146. Xue K, Li FF, Chen YW, Zhou YH, He J. Body mass index and the risk of cancer in women compared with men: a meta-analysis of prospective cohort studies. *European J Cancer Prev*. 2017;26(1):94-105.

147. Murphy N, Jenab M, Gunter MJ. Adiposity and gastrointestinal cancers: epidemiology, mechanisms and future directions. *Nat Rev Gastroenterol Hepatol*. 2018;15(11):659-670.

148. Aleksandrova K, Schlesinger S, Fedirko V, et al. Metabolic Mediators of the Association Between Adult Weight Gain and Colorectal Cancer: Data From the European Prospective Investigation into Cancer and Nutrition (EPIC) Cohort. *Am J Epidemiol*. 2017;185(9):751-764.

149. Kim H, Giovannucci EL. Sex differences in the association of obesity and colorectal cancer risk. *Cancer Causes Control*. 2017;28(1):1-4.

150. Liu P-H, Wu K, Ng K, et al. Association of Obesity With Risk of Early-Onset Colorectal Cancer Among Women. *JAMA Oncology*. 2019;5(1):37-44.

151. Wang N, Khankari NK, Cai H, et al. Prediagnosis body mass index and waist-hip circumference ratio in association with colorectal cancer survival. *Int J Cancer*. 2016.

152. Liang X, Margolis KL, Hendryx M, et al. Metabolic Phenotype and Risk of Colorectal Cancer in Normal-Weight Postmenopausal Women. *Cancer Epidemiol Biomarkers Prev*. 2017;26(2):155-161.

153. Myte R, Gylling B, Haggstrom J, et al. Metabolic factors and the risk of colorectal cancer by KRAS and BRAF mutation status. *Int J Cancer*. 2019;145(2):327-337.

154. Cespedes Feliciano EM, Kroenke CH, Meyerhardt JA, et al. Metabolic Dysfunction, Obesity, and Survival Among Patients With Early-Stage Colorectal Cancer. *J Clin Oncol*. 2016.

155. O'Keefe SJ. Diet, microorganisms and their metabolites, and colon cancer. *Nat Rev Gastroenterol Hepatol*. 2016;13(12):691-706.

156. Kwong TNY, Wang X, Nakatsu G, et al. Association Between Bacteremia From Specific Microbes and Subsequent Diagnosis of Colorectal Cancer. *Gastroenterology*. 2018;155(2):383-390.e388.

157. Wong SH, Yu J. Gut microbiota in colorectal cancer: mechanisms of action and clinical applications. *Nat Rev Gastroenterol Hepatol* 2019;16(11):690-704.

158. Tilg H, Moschen AR. Food, immunity, and the microbiome. *Gastroenterology*. 2015;148(6):1107-1119.

159. Brennan CA, Garrett WS. Gut Microbiota, Inflammation, and Colorectal Cancer. *Annu Rev Microbiol*. 2016;70:395-411.

160. Dejea CM, Fathi P, Craig JM, et al. Patients with familial adenomatous polyposis harbor colonic biofilms containing tumorigenic bacteria. *Science*. 2018;359(6375):592-597.

161. O'Keefe SJ, Li JV, Lahti L, et al. Fat, fibre and cancer risk in African Americans and rural Africans. *Nat Commun*. 2015;6:6342.

162. Scott KP, Gratz SW, Sheridan PO, Flint HJ, Duncan SH. The influence of diet on the gut microbiota. *Pharmacol Res*. 2013;69(1):52-60.

163. Tabung FK, Liu L, Wang W, et al. Association of Dietary Inflammatory Potential With Colorectal Cancer Risk in Men and Women. *JAMA Oncol*. 2018;4(3):366-373.

164. Song M, Garrett WS, Chan AT. Nutrients, foods, and colorectal cancer prevention. *Gastroenterology*. 2015;148(6):1244-1260 e1216.

165. Aune D, Lau R, Chan DS, et al. Dairy products and colorectal cancer risk: a systematic review and meta-analysis of cohort studies. *Ann Oncol*. 2012;23(1):37-45.

166. Vieira AR, Abar L, Chan DSM, et al. Foods and beverages and colorectal cancer risk: a systematic review and meta-analysis of cohort studies, an update of the evidence of the WCRF-AICR Continuous Update Project. *Ann Oncol*. 2017;28(8):1788-1802.

167. Baron JA, Barry EL, Mott LA, et al. A Trial of Calcium and Vitamin D for the Prevention of Colorectal Adenomas. *N Engl J Med*. 2015;373(16):1519-1530.

168. Keum N, Liu L, Hamada T, et al. Calcium intake and colon cancer risk subtypes by tumor molecular characteristics. *Cancer Causes Control*. 2019;30(6):637-649.

169. Keum N, Lee DH, Greenwood DC, Zhang X, Giovannucci EL. Calcium intake and colorectal adenoma risk: dose-response meta-analysis of prospective observational studies. *Int J Cancer*. 2015;136(7):1680-1687.

170. Zhao J, Giri A, Zhu X, et al. Calcium: magnesium intake ratio and colorectal carcinogenesis, results from the prostate, lung, colorectal, and ovarian cancer screening trial. *Br J Cancer*. 2019;121(9):796-804.

171. Schwingshackl L, Schwedhelm C, Hoffmann G, et al. Food groups and risk of colorectal cancer. *Int J Cancer*. 2018;142(9):1748-1758.

172. Wu H, Flint AJ, Qi Q, et al. Association Between Dietary Whole Grain Intake and Risk of Mortality: Two Large Prospective Studies in US Men and Women. *JAMA Intern Med*. 2015;175(3):373-384.

173. World Cancer Research Fund/American Institute for Cancer Research. Continuous Update Project Expert Report 2018. Diet, nutrition, physical activity and colorectal cancer. Available at dietandcancerreport.org.

174. Rock CL, Thomson CA, Gansler T, et al. American Cancer Society Guidelines on nutrition and physical activity for cancer prevention. *CA Cancer J Clin*. 2019.

175. Mason JB, Dickstein A, Jacques PF, et al. A temporal association between folic acid fortification and an increase in colorectal cancer rates may be illuminating important biological principles: a hypothesis. *Cancer Epidemiol Biomarkers Prev*. 2007;16(7):1325-1329.

176. Vollset SE, Clarke R, Lewington S, et al. Effects of folic acid supplementation on overall and site-specific cancer incidence during the randomised trials: meta-analyses of data on 50,000 individuals. *Lancet*. 2013;381(9871):1029-1036.

177. Stevens VL, McCullough ML, Sun J, et al. High levels of folate from supplements and fortification are not associated with increased risk of colorectal cancer. *Gastroenterology*. 2011; 141(1):98-105.

178. Aune D, Lau R, Chan DS, et al. Nonlinear reduction in risk for colorectal cancer by fruit and vegetable intake based on metaanalysis of prospective studies. *Gastroenterology*. 2011;141(1):106-118.

179. Lee JE, Chan AT. Fruit, vegetables, and folate: cultivating the evidence for cancer prevention. *Gastroenterology*. 2011;141(1):16-20.

180. Chan DS, Lau R, Aune D, et al. Red and processed meat and colorectal cancer incidence: meta-analysis of prospective studies. *PloS one*. 2011;6(6):e20456.

181. Bouvard V, Loomis D, Guyton KZ, et al. Carcinogenicity of consumption of red and processed meat. *Lancet Oncol*. 2015;16(16):1599-1600.

182. Kim E, Coelho D, Blachier F. Review of the association between meat consumption and risk of colorectal cancer. *Nutr Res*. 2013;33(12):983-994.

183. Zeng L, Ruan M, Liu J, et al. Trends in Processed Meat, Unprocessed Red Meat, Poultry, and Fish Consumption in the United States, 1999-2016. *J Acad Nutr Diet*. 2019;119(7):1085-1098 e1012.

184. Manson JE, Cook NR, Lee IM, et al. Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease. *N Engl J Med*. 2019;380(1):33-44.

185. McCullough ML, Zoltick ES, Weinstein SJ, et al. Circulating Vitamin D and Colorectal Cancer Risk: An International Pooling Project of 17 Cohorts. *J Natl Cancer Inst*. 2019;111(2):158-169.

186. Pradhan AD, Manson JE. Update on the Vitamin D and OmegA-3 trial (VITAL). *J Steroid Biochem Mol Biol*. 2016;155(Pt B):252-256.

187. Luttmann-Gibson H, Mora S, Camargo CA, et al. Serum 25-hydroxyvitamin D in the VITamin D and OmegA-3 TriaL (VITAL): Clinical and demographic characteristics associated with baseline and change with randomized vitamin D treatment. *Contemp Clin Trials*. 2019:105854.

188. Chabrol T, Wion D. Randomized clinical trials of oral vitamin D supplementation in need of a paradigm change: The vitamin D autacoid paradigm. *Med Hypotheses*. 2020;134:109417.

189. Secretan B, Straif K, Baan R, et al. A review of human carcinogens – Part E: tobacco, areca nut, alcohol, coal smoke, and salted fish. *Lancet Oncol*. 2009;10(11):1033-1034.

190. Carter BD, Abnet CC, Feskanich D, et al. Smoking and mortality – beyond established causes. *N Engl J Med*. 2015;372:631-640.

191. Murphy N, Ward HA, Jenab M, et al. Heterogeneity of Colorectal Cancer Risk Factors by Anatomical Subsite in 10 European Countries: A Multinational Cohort Study. *Clin Gastroenterol Hepatol*. 2019;17(7):1323-1331 e1326.

192. Limsui D, Vierkant RA, Tillmans LS, et al. Cigarette smoking and colorectal cancer risk by molecularly defined subtypes. *J Natl Cancer Inst*. 2010;102(14):1012-1022.

193. Yang B, Jacobs EJ, Gapstur SM, Stevens V, Campbell PT. Active smoking and mortality among colorectal cancer survivors: the Cancer Prevention Study II nutrition cohort. *J Clin Oncol*. 2015;33(8):885-893.

194. Ordonez-Mena JM, Walter V, Schottker B, et al. Impact of prediagnostic smoking and smoking cessation on colorectal cancer prognosis: a meta-analysis of individual patient data from cohorts within the CHANCES consortium. *Ann Oncol*. 2018;29(2):472-483.

195. McNabb S, Harrison TA, Albanes D, et al. Meta-analysis of 16 studies of the association of alcohol with colorectal cancer. *Int J Cancer*. 2020;146(3):861-873.

196. Bagnardi V, Rota M, Botteri E, et al. Alcohol consumption and site-specific cancer risk: a comprehensive dose-response metaanalysis. *Br J Cancer*. 2015;112(3):580-593.

197. Rothwell PM, Wilson M, Elwin CE, et al. Long-term effect of aspirin on colorectal cancer incidence and mortality: 20-year follow-up of five randomised trials. *Lancet*. 2010;376(9754):1741-50.

198. Cook NR, Lee IM, Zhang SM, Moorthy MV, Buring JE. Alternate-day, low-dose aspirin and cancer risk: long-term observational follow-up of a randomized trial. *Ann Intern Med*. 2013;159(2):77-85.

199. Cao Y, Nishihara R, Wu K, et al. Population-wide Impact of Long-term Use of Aspirin and the Risk for Cancer. *JAMA Oncology*. 2016;2(6):762-769.

200. Rothwell PM, Cook NR, Gaziano JM, et al. Effects of aspirin on risks of vascular events and cancer according to bodyweight and dose: analysis of individual patient data from randomised trials. *Lancet*. 2018;392(10145):387-399.

201. Amitay EL, Carr PR, Jansen L, et al. Association of Aspirin and Nonsteroidal Anti-Inflammatory Drugs With Colorectal Cancer Risk by Molecular Subtypes. *J Natl Cancer Inst*. 2019;111(5):475-483.

202. Bains SJ, Mahic M, Myklebust TA, et al. Aspirin As Secondary Prevention in Patients With Colorectal Cancer: An Unselected Population-Based Study. *J Clin Oncol*. 2016;34(21):2501-2508.

203. Hamada T, Cao Y, Qian ZR, et al. Aspirin Use and Colorectal Cancer Survival According to Tumor CD274 (Programmed Cell Death 1 Ligand 1) Expression Status. *J Clin Oncol*. 2017;35(16):1836-1844.

204. Hua X, Phipps AI, Burnett-Hartman AN, et al. Timing of Aspirin and Other Nonsteroidal Anti-Inflammatory Drug Use Among Patients With Colorectal Cancer in Relation to Tumor Markers and Survival. *J Clin Oncol*. 2017;35(24):2806-2813.

205. Chubak J, Kamineni A, Buist DSM, Anderson ML, Whitlock EP. In: *Aspirin Use for the Prevention of Colorectal Cancer: An Updated Systematic Evidence Review for the U.S. Preventive Services Task Force*. Rockville (MD)2015.

206. Rennert G. Reproductive factors, hormones and colorectal cancer-still unresolved. *Br J Cancer*. 2017;116(1):1-3.

207. Murphy N, Strickler HD, Stanczyk FZ, et al. A Prospective Evaluation of Endogenous Sex Hormone Levels and Colorectal Cancer Risk in Postmenopausal Women. *J Natl Cancer Inst*. 2015;107(10).

208. Lin JH, Zhang SM, Rexrode KM, et al. Association between sex hormones and colorectal cancer risk in men and women. *Clin Gastroenterol Hepatol*. 2013;11(4):419-424 e411.

209. Lavasani S, Chlebowski RT, Prentice RL, et al. Estrogen and colorectal cancer incidence and mortality. *Cancer*. 2015;121(18):3261-3271.

210. Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the Women's Health Initiative randomized trials. *JAMA*. 2013;310(13):1353-1368.

211. Charlton BM, Wu K, Zhang X, et al. Oral contraceptive use and colorectal cancer in the Nurses' Health Study I and II. *Cancer Epidemiol Biomarkers Prev*. 2015;24(8):1214-1221.

212. Michels KA, Pfeiffer RM, Brinton LA, Trabert B. Modification of the Associations Between Duration of Oral Contraceptive Use and Ovarian, Endometrial, Breast, and Colorectal Cancers. *JAMA Oncology*. 2018;4(4):516-521.

213. Cao Y, Wu K, Mehta R, et al. Long-term use of antibiotics and risk of colorectal adenoma. *Gut*. 2018;67(4):672-678.

214. Zhang J, Haines C, Watson AJM, et al. Oral antibiotic use and risk of colorectal cancer in the United Kingdom, 1989-2012: a matched case-control study. *Gut*. 2019;68(11):1971-1978.

215. Thosani N, Thosani SN, Kumar S, et al. Reduced risk of colorectal cancer with use of oral bisphosphonates: a systematic review and meta-analysis. *J Clin Oncol*. 2013;31(5):623-630.

216. Vogtmann E, Corley DA, Almers LM, Cardwell CR, Murray LJ, Abnet CC. Oral bisphosphonates and colorectal cancer. *Sci Rep*. 2017;7:44177.

217. Wolf AMD, Fontham ETH, Church TR, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. *CA Cancer J Clin*. 2018;68(4):250-281.

218. Corley DA, Jensen CD, Quinn VP, et al. Association Between Time to Colonoscopy After a Positive Fecal Test Result and Risk of Colorectal Cancer and Cancer Stage at Diagnosis. *JAMA*. 2017;317(16):1631-1641.

219. Doubeni CA, Fedewa SA, Levin TR, et al. Modifiable Failures in the Colorectal Cancer Screening Process and Their Association With Risk of Death. *Gastroenterology*. 2019;156(1):63-74 e66.

220. Meester RGS, Peterse EFP, Knudsen AB, et al. Optimizing colorectal cancer screening by race and sex: Microsimulation analysis II to inform the American Cancer Society colorectal cancer screening guideline. *Cancer*. 2018;124(14):2974-2985.

221. Jones WF, Ahnen DJ, Schroy III PC. Improving on-time colorectal cancer screening through lead time messaging. *Cancer*. 2019.

222. Peterse EFP, Meester RGS, Siegel RL, et al. The impact of the rising colorectal cancer incidence in young adults on the optimal age to start screening: Microsimulation analysis I to inform the American Cancer Society colorectal cancer screening guideline. *Cancer*. 2018;124(14):2964-2973.

223. Gupta S, Halm EA, Rockey DC, et al. Comparative Effectiveness of Fecal Immunochemical Test Outreach, Colonoscopy Outreach, and Usual Care for Boosting Colorectal Cancer Screening Among the Underserved: A Randomized Clinical Trial. *JAMA Intern Med*. 2013;173(18):1725-32.

224. U. S. Preventive Services Task Force, Bibbins-Domingo K, Grossman DC, et al. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2016;315(23):2564-2575.

225. Bretthauer M, Kaminski MF, Loberg M, et al. Population-Based Colonoscopy Screening for Colorectal Cancer: A Randomized Clinical Trial. *JAMA Intern Med*. 2016;176(7):894-902.

226. Lieberman D. Colorectal Cancer Screening With Colonoscopy. *JAMA Intern Med*. 2016;176(7):903-904.

227. Zauber AG, Winawer SJ, O'Brien MJ, et al. Colonoscopic polypectomy and long-term prevention of colorectal-cancer deaths. *N Engl J Med*. 2012;366(8):687-696.

228. Nishihara R, Wu K, Lochhead P, et al. Long-term colorectal cancer incidence and mortality after lower endoscopy. *N Engl J Med*.

2013;369(12):1095-1105.

229. Doubeni CA, Corley DA, Quinn VP, et al. Effectiveness of screening colonoscopy in reducing the risk of death from right and left colon cancer: a large community-based study. *Gut*. 2018;67(2): 291-298.

230. Levin B, Lieberman DA, McFarland B, et al. Screening and surveillance for the early detection of colorectal cancer and adenomatous Polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. *CA Cancer J Clin*. 2008;58(3):130-160.

231. Peery AF, Cools KS, Strassle PD, et al. Increasing Rates of Surgery for Patients With Nonmalignant Colorectal Polyps in the United States. *Gastroenterology*. 2018;154(5):1352-1360 e1353.

232. Ko CW, Riffle S, Michaels L, et al. Serious complications within 30 days of screening and surveillance colonoscopy are uncommon. *Clin Gastroenterol Hepatol*. 2010;8(2):166-173.

233. Quintero E, Castells A, Bujanda L, et al. Colonoscopy versus fecal immunochemical testing in colorectal-cancer screening. *N Engl J Med*. 2012;366(8):697-706.

234. Zhao S, Wang S, Pan P, et al. Magnitude, Risk Factors, and Factors Associated With Adenoma Miss Rate of Tandem Colonoscopy: A Systematic Review and Meta-analysis. *Gastroenterology*. 2019;156(6):1661-1674 e1611.

235. Meester RG, Doubeni CA, Lansdorp-Vogelaar I, et al. Variation in Adenoma Detection Rate and the Lifetime Benefits and Cost of Colorectal Cancer Screening: A Microsimulation Model. *JAMA*. 2015;313(23):2349-2358.

236. Corley DA, Jensen CD, Marks AR, et al. Adenoma detection rate and risk of colorectal cancer and death. *N Engl J Med*. 2014;370(14):1298-1306.

237. Atkin W, Wooldrage K, Parkin DM, et al. Long term effects of once-only flexible sigmoidoscopy screening after 17 years of follow-up: the UK Flexible Sigmoidoscopy Screening randomised controlled trial. *Lancet*. 2017;389(10076):1299-1311.

238. Holme O, Schoen RE, Senore C, et al. Effectiveness of flexible sigmoidoscopy screening in men and women and different age groups: pooled analysis of randomised trials. *BMJ*. 2017;356:i6673.

239. Miller EA, Pinsky PF, Schoen RE, Prorok PC, Church TR. Effect of flexible sigmoidoscopy screening on colorectal cancer incidence and mortality: long-term follow-up of the randomised US PLCO cancer screening trial. *Lancet Gastroenterol Hepatol*. 2019;4(2):101-110.

240. Patel JD, Chang KJ. The role of virtual colonoscopy in colorectal screening. *Clin Imaging*. 2016;40(2):315-320.

241. de Haan MC, van Gelder RE, Graser A, Bipat S, Stoker J. Diagnostic value of CT-colonography as compared to colonoscopy in an asymptomatic screening population: a meta-analysis. *Eur Radiol*. 2011;21(8):1747-1763.

242. American College of Radiology. Patient and Provider Groups Tell Congress to Pass Medicare Virtual Colonoscopy Coverage. 2018; https://www.acr.org/Media-Center/ACR-News-Releases/2018/Patient-and-Provider-Groups-Tell-Congress-to-Pass-Medicare-Virtual-Colonoscopy-Coverage.

243. Knudsen AB, Zauber AG, Rutter CM, et al. Estimation of Benefits, Burden, and Harms of Colorectal Cancer Screening Strategies: Modeling Study for the US Preventive Services Task Force. *JAMA*. 2016;315(23):2595-2609.

244. Gellad ZF, Stechuchak KM, Fisher DA, et al. Longitudinal adherence to fecal occult blood testing impacts colorectal cancer screening quality. *Am J Gastroenterol*. 2011;106(6):1125-1134.

245. Liss DT, Petit-Homme A, Feinglass J, Buchanan DR, Baker DW. Adherence to repeat fecal occult blood testing in an urban community health center network. *J Community Health*. 2013;38(5):829-833.

246. Bharti B, May FFP, Nodora J, et al. Diagnostic colonoscopy completion after abnormal fecal immunochemical testing and quality of tests used at 8 Federally Qualified Health Centers in Southern California: Opportunities for improving screening outcomes. *Cancer*. 2019.

247. Chubak J, Garcia MP, Burnett-Hartman AN, et al. Time to Colonoscopy after Positive Fecal Blood Test in Four U.S. Health Care Systems. *Cancer Epidemiol Biomarkers Prev*. 2016;25(2):344-350.

248. Shaukat A, Mongin SJ, Geisser MS, et al. Long-term mortality after screening for colorectal cancer. *N Engl J Med*. 2013;369(12):1106-1114.

249. Mandel JS, Church TR, Bond JH, et al. The effect of fecal occultblood screening on the incidence of colorectal cancer. *N Engl J Med*. 2000;343(22):1603-1607.

250. Hassan C, Giorgi Rossi P, Camilloni L, et al. Meta-analysis: adherence to colorectal cancer screening and the detection rate for advanced neoplasia, according to the type of screening test. *Aliment Pharmacol Ther*. 2012;36(10):929-940.

251. Robertson DJ, Lee JK, Boland CR, et al. Recommendations on Fecal Immunochemical Testing to Screen for Colorectal Neoplasia: A Consensus Statement by the US Multi-Society Task Force on Colorectal Cancer. *Am J Gastroenterol*. 2016.

252. Tinmouth J, Lansdorp-Vogelaar I, Allison JE. Faecal immunochemical tests versus guaiac faecal occult blood tests: what clinicians and colorectal cancer screening programme organisers need to know. *Gut*. 2015;64(8):1327-1337.

253. Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. Multitarget stool DNA testing for colorectal-cancer screening. *N Engl J Med*. 2014;370(14):1287-1297.

254. Weiser E, Parks PD, Swartz RK, van Thomme J, Limburg P, BM B. Colorectal Cancer Screening: Compliance with Multi-target Stool DNA Testing among Medicare Beneficiaries. *Digestive Disease Week*; 2019; San Diego, CA.

255. Chido-Amajuoyi OG, Sharma A, Talluri R, Tami-Maury I, Shete S. Physician-office vs home uptake of colorectal cancer screening using FOBT/FIT among screening-eligible US adults. *Cancer Med*. 2019.

256. Centers for Disease Control and Prevention (CDC). Behavioral Risk Factor Surveillance System Survey Data. 2019; cdc.gov/brfss/. Accessed 09/04/2019.

257. Fedewa SA, Sauer AG, Siegel RL, Jemal A. Prevalence of Major Risk Factors and Use of Screening Tests for Cancer in the United States. *Cancer Epidemiol Biomarkers Prev*. 2015;24(4):637-652.

258. Beydoun HA, Beydoun MA. Predictors of colorectal cancer screening behaviors among average-risk older adults in the United States. *Cancer Causes Control*. 2008;19(4):339-359.

259. Guessous I, Dash C, Lapin P, Doroshenk M, Smith RA, Klabunde CN. Colorectal cancer screening barriers and facilitators in older persons. *Prev Med*. 2010;50(1-2):3-10.

260. Holden DJ, Jonas DE, Porterfield DS, Reuland D, Harris R. Systematic review: enhancing the use and quality of colorectal cancer screening. *Ann Intern Med*. 2010;152(10):668-676.

261. Doubeni CA, Laiyemo AO, Young AC, et al. Primary care, economic barriers to health care, and use of colorectal cancer screening tests among Medicare enrollees over time. *Ann Fam Med*. 2010;8(4):299-307.

262. Denberg TD, Melhado TV, Coombes JM, et al. Predictors of nonadherence to screening colonoscopy. *J Gen Intern Med*. 2005;20(11):989-995.

263. Laiyemo AO, Adebogun AO, Doubeni CA, et al. Influence of provider discussion and specific recommendation on colorectal cancer screening uptake among U.S. adults. *Prev Med*. 2014;67:1-5.

264. Jerant AF, Fenton JJ, Franks P. Determinants of racial/ethnic colorectal cancer screening disparities. *Arch Intern Med*. 2008;168(12):1317-1324.

265. Dougherty MK, Brenner AT, Crockett SD, et al. Evaluation of Interventions Intended to Increase Colorectal Cancer Screening Rates in the United States: A Systematic Review and Meta-analysis. *JAMA Intern Med*. 2018;178(12):1645-1658.

266. The Community Guide. Cancer Screening: Multicomponent Interventions – Colorectal Cancer. 2016; https://www.thecommunityguide.org/findings/cancer-screening-multicomponent-interventions-colorectal-cancer. Accessed 10/20/2019.

267. DeBourcy AC, Lichtenberger S, Felton S, Butterfield KT, Ahnen DJ, Denberg TD. Community-based preferences for stool cards versus colonoscopy in colorectal cancer screening. *J Gen Intern Med*. 2008;23(2):169-174.

268. Sequist TD, Zaslavsky AM, Marshall R, Fletcher RH, Ayanian JZ. Patient and physician reminders to promote colorectal cancer screening: a randomized controlled trial. *Arch Intern Med*. 2009;169(4):364-371.

269. Selby K, Baumgartner C, Levin TR, et al. Interventions to Improve Follow-up of Positive Results on Fecal Blood Tests: A Systematic Review. *Ann Intern Med*. 2017;167(8):565-575.

270. National Colorectal Cancer Roundtable. Tools & Resources – 80% by 2018. 2019; http://nccrt.org/tools/80-percent-by-2018/. Accessed October 5, 2019.

271. Sarfaty M. *How to Increase Colorectal Cancer Screening Rates in Practice: A Primary Care Clinician's Evidence-Based Toolbox and Guide 2008*. Eds. Peterson, K and Wender, R. Atlanta: The American Cancer Society, the National Colorectal Cancer Roundtable, and Thomas Jefferson University 2006, Rev 2008.

272. DeGroff A, Sharma K, Satsangi A, et al. Increasing Colorectal Cancer Screening in Health Care Systems Using Evidence-Based Interventions. *Prev Chronic Dis*. 2018;15:E100.

273. Levin TR, Corley DA, Jensen CD, et al. Effects of Organized Colorectal Cancer Screening on Cancer Incidence and Mortality in a Large Community-Based Population. *Gastroenterology*. 2018;155(5):1383-1391 e1385.

274. Coronado GD, Petrik AF, Vollmer WM, et al. Effectiveness of a Mailed Colorectal Cancer Screening Outreach Program in Community Health Clinics: The STOP CRC Cluster Randomized Clinical Trial. *JAMA Intern Med*. 2018;178(9):1174-1181.

275. Fedewa SA, Yabroff KR, Smith RA, Goding Sauer A, Han X, Jemal A. Changes in Breast and Colorectal Cancer Screening After Medicaid Expansion Under the Affordable Care Act. *Am J Prev Med*. 2019;57(1):3-12.

276. US Department of Health and Human Services. Preventive Services Covered Under the Affordable Care Act. 2010; http://www.hhs.gov/healthcare/facts/factsheets/2010/07/preventive-services-list.html. Accessed September 9, 2014.

277. Doubeni CA, Corley DA, Zauber AG. Colorectal Cancer Health Disparities and the Role of US Law and Health Policy. *Gastroenterology*. 2016;150(5):1052-1055.

278. Kennedy RH, Francis EA, Wharton R, et al. Multicenter randomized controlled trial of conventional versus laparoscopic surgery for colorectal cancer within an enhanced recovery programme: EnROL. *J Clin Oncol*. 2014;32(17):1804-1811.

279. Grothey A, Sargent DJ. Adjuvant Therapy for Colon Cancer: Small Steps Toward Precision Medicine. *JAMA Oncol*. 2016;2(9):1133-1134.

280. Kelly KJ, Alsayadnasser M, Vaida F, et al. Does Primary Tumor Side Matter in Patients with Metastatic Colon Cancer Treated with Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy? *Ann Surg Oncol*. 2019;26(5):1421-1427.

281. Loree JM, Pereira AAL, Lam M, et al. Classifying Colorectal Cancer by Tumor Location Rather than Sidedness Highlights a Continuum in Mutation Profiles and Consensus Molecular Subtypes. *Clin Cancer Res*. 2018;24(5):1062-1072.

282. Sargent D, Sobrero A, Grothey A, et al. Evidence for cure by adjuvant therapy in colon cancer: observations based on individual patient data from 20,898 patients on 18 randomized trials. *J Clin Oncol*. 2009;27(6):872-877.

283. Shah MA, Renfro LA, Allegra CJ, et al. Impact of Patient Factors on Recurrence Risk and Time Dependency of Oxaliplatin Benefit in Patients With Colon Cancer: Analysis From Modern-Era Adjuvant Studies in the Adjuvant Colon Cancer End Points (ACCENT) Database. *J Clin Oncol*. 2016;34(8):843-853.

284. Booth CM, Nanji S, Wei X, et al. Adjuvant Chemotherapy for Stage II Colon Cancer: Practice Patterns and Effectiveness in the General Population. *Clin Oncol* (R Coll Radiol). 2016;29(1):e29-e38.

285. Pahlman LA, Hohenberger WM, Matzel K, Sugihara K, Quirke P, Glimelius B. Should the Benefit of Adjuvant Chemotherapy in Colon Cancer Be Re-Evaluated? *J Clin Oncol*. 2016;34(12):1297-1299.

286. Abraham A, Habermann EB, Rothenberger DA, et al. Adjuvant chemotherapy for stage III colon cancer in the oldest old: results beyond clinical guidelines. *Cancer*. 2013;119(2):395-403.

287. Sveen A, Kopetz S, Lothe RA. Biomarker-guided therapy for colorectal cancer: strength in complexity. *Nat Rev Clin Oncol*. 2019.

288. Bosset JF, Calais G, Mineur L, et al. Fluorouracil-based adjuvant chemotherapy after preoperative chemoradiotherapy in rectal cancer: long-term results of the EORTC 22921 randomised study. *Lancet Oncol*. 2014;15(2):184-190.

289. Maas M, Nelemans PJ, Valentini V, et al. Adjuvant chemotherapy in rectal cancer: defining subgroups who may benefit after neoadjuvant chemoradiation and resection: a pooled analysis of 3,313 patients. *Int J Cancer*. 2015;137(1):212-220.

290. Kulaylat AS, Hollenbeak CS, Stewart DB, Sr. Adjuvant Chemotherapy Improves Overall Survival of Rectal Cancer Patients Treated with Neoadjuvant Chemoradiotherapy Regardless of Pathologic Nodal Status. *Ann Surg Oncol*. 2016;24(5):1281-1288.

291. El-Shami K, Oeffinger KC, Erb NL, et al. American Cancer Society Colorectal Cancer Survivorship Care Guidelines. *CA Cancer J Clin*. 2015;65(6):428-455.

292. Keller D, Stein SL. Facilitating return of bowel function after colorectal surgery: alvimopan and gum chewing. *Clin Colon Rectal Surg*. 2013;26(3):186-190.

293. Maiorino MI, Chiodini P, Bellastella G, Giugliano D, Esposito K. Sexual dysfunction in women with cancer: a systematic review with meta-analysis of studies using the Female Sexual Function Index. *Endocrine*. 2016;54(2):329-341.

294. Schneider EC, Malin JL, Kahn KL, Ko CY, Adams J, Epstein AM. Surviving colorectal cancer : patient-reported symptoms 4 years after diagnosis. *Cancer*. 2007;110(9):2075-2082.

295. Oktay K, Harvey BE, Partridge AH, et al. Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update. *J Clin Oncol*. 2018;36(19):1994-2001.

296. Zhu L, Pickle LW, Ghosh K, et al. Predicting US- and state-level cancer counts for the current calendar year: Part II: evaluation of spatiotemporal projection methods for incidence. *Cancer*. 2012;118(4):1100-1109.

297. Chen HS, Portier K, Ghosh K, et al. Predicting US- and state-level cancer counts for the current calendar year: Part I: evaluation of temporal projection methods for mortality. *Cancer*. 2012;118(4):1091-1099.

Acknowledgments

Rick Alteri; Joseph Anderson; Cammie Barnes; Durado Brooks; Lynn Butterly; Michelle DelFavero; Carol DeSantis; Ted Gansler; Eric Jacobs; Mamta Kalidas; Marji McCullough; Michael O'Brien; Alpa Patel; Scott Simpson; Robert Smith; Lindsey Torre; Dana Wagner; and Ann Zauber.

Colorectal Cancer Facts & Figures is a triennial publication of the American Cancer Society, Atlanta, Georgia.

For more information, contact:
Rebecca Siegel, MPH
Kimberly Miller, MPH
Ahmedin Jemal, DVM, PhD

The American Cancer Society's mission
is to **save lives, celebrate lives,**
and **lead the fight** for a world without cancer.

American Cancer Society®

Attacking from every angle.™

BBB ACCREDITED CHARITY
bbb.org/charity

PUTTING PATIENTS FIRST
National Health Council
Standards of Excellence
Certification Program ®