

Kaiser Permanente Research Brief

Colorectal Cancer

This brief summarizes the contributions of Kaiser Permanente Research since 2007 on the topic of colorectal cancer.

Colorectal cancer refers to cancers that start in the colon or rectum, the lower parts of the digestive system.¹ The incidence of these cancers in the U.S. has declined over the past several decades, due to improved uptake of screening through endoscopic methods or stool tests.¹ Nevertheless, colorectal cancer is the fourth most common cancer and the second leading cause of cancer death in the United States.² Colorectal cancer is caused by a mix of avoidable risk factors (such as smoking) and factors that cannot be avoided (such as genetics), but individuals can decrease their chances of developing colorectal cancer through a variety of actions, including regular screening.¹ The National Cancer Institute estimates that more than 1 in 25 U.S. men and women will be diagnosed with colorectal cancer in their lifetime.² In 2017, there were an estimated 135,430 new cases of colorectal cancer and more than 50,000 deaths.²

Colorectal cancer is an active area of study for Kaiser Permanente Research. Scientists across the program have used our rich and comprehensive longitudinal data to advance knowledge in the areas of understanding risk, improving patient outcomes, and translating research findings into policy and practice. We have published 391 articles related to colorectal cancer since 2007.³ Together, these articles have been cited more than 13,000 times.

These articles are the product of observational studies, randomized controlled trials, meta-analyses, and other studies led by Kaiser Permanente

Kaiser Permanente Publications Related to Colorectal Cancer since 2007



Source: Kaiser Permanente Publications Library and PLUM metrics, as of 23 March 2018.

a Number of citing journal articles, according to Scopus.

b Number of references in PubMed guidelines.

c Citations in DynaMed Plus, a point-of-care clinical reference tool.

This brief summarizes a selection of the publications contained within the Kaiser Permanente Publications Library, which indexes journal articles and other publications authored by individuals affiliated with Kaiser Permanente. The work described in this brief originated from across Kaiser Permanente's 8 regions and was supported by a wide range of funding sources including internal research support as well as both governmental and non-governmental extramural funding.

scientists. Our unique environment – a fully integrated care and coverage model in which our research scientists, clinicians, medical group, and health plan leaders collaborate – lets us contribute generalizable knowledge on colorectal cancer, and many other topics of research.

Understanding Risk

Who is at risk for developing colorectal cancer?

National statistics show that men experience an overall higher risk than women, and risk increases with age. Specific risk factors for developing colorectal cancer that have been studied by our researchers include age and race;⁴ lifestyle factors such as diet,⁵⁻⁷ metabolic phenotype,⁸ weight,⁹ and tobacco use;¹⁰⁻¹² hyperinsulinemia (abnormally high insulin);¹³ and hereditary cancer-syndrome-related risks.¹⁴⁻¹⁸ However, the evidence for some of these risk factors is inconsistent.^{5,12,19} There is evidence that the risk of colorectal cancer may be linked to select genetic traits,²⁰⁻²⁶ some of which may interact with lifestyle factors.⁶ We have also studied protective factors that reduce colorectal cancer risk, such as levels of plasma vitamin B6²⁷ and flavonoids,²⁸ and daily low-dose aspirin^{29,30} (generally taken as part of a cardiovascular disease prevention strategy).

LIFESTYLE-RELATED RISK FACTORS FOR COLORECTAL CANCER		
MEAT EATING	SMOKING	OBESITY
<p>ODDS RATIO</p> <p>1.41</p> <p>(95% CI: 1.29-1.55)</p> <p>People in the highest quartile of meat eating compared to the lowest⁵</p>	<p>HAZARD RATIO</p> <p>1.95</p> <p>(95% CI: 1.10-3.47)</p> <p>Current smokers compared to never smokers in the Women’s Health Initiative⁹</p>	<p>ODDS RATIO</p> <p>2.16</p> <p>(95% CI: 1.13-4.14)</p> <p>BMI ≥ 30 at time of colonoscopy compared to normal weight people¹²</p>

There are well-documented disparities in colorectal cancer risk by race, ethnicity, and socioeconomic status.² Kaiser Permanente researchers have characterized differences in prevalence of colorectal tumors by age, sex, and

race, and found demographic differences that have implications for both screening programs (such as what type of screening is optimal for different demographic groups) and for case mix adjustment in quality measures related to colonoscopy performance.⁴ Disparities in colorectal cancer risk are linked to differences in underlying risk factors (such as diet or tobacco use), and also reflect differences in screening uptake.³¹⁻³⁶ Our researchers have found that the interpersonal relationship and quality of communication between doctors and patients is one factor that partially explains the differences observed in colorectal cancer screening participation.³¹

Our researchers have published several studies characterizing colorectal cancer risk for people with specific risk profiles. A recent analysis evaluated the performance of a colorectal cancer risk prediction model that incorporated lifestyle and environmental factors, and genetic variants. The authors found that models incorporating a broader set of risk factors outperformed family history models based on the current screening guideline, and suggest that individualized colorectal cancer screening algorithms may be appropriate.³⁷

What other health risks do people with colorectal cancer face?

The primary health risk for people with colorectal cancer is death. Our research has estimated that more than half of colorectal cancer deaths are attributable to patients not being screened.³⁸ Among people with colorectal cancer, prognosis is linked to characteristics of the tumor (such as tumor type and tumor stage) and to patient characteristics (such as age, race, gender, and comorbidities).³⁹ There is also evidence regarding the relationship between obesity, metabolic syndrome, and colorectal cancer death, with evidence suggesting an association that varies with the degree of overweight or obesity.⁴⁰⁻⁴³

Survivors of colorectal cancer also face health and quality of life challenges related to cancer treatments. Patients who need surgical

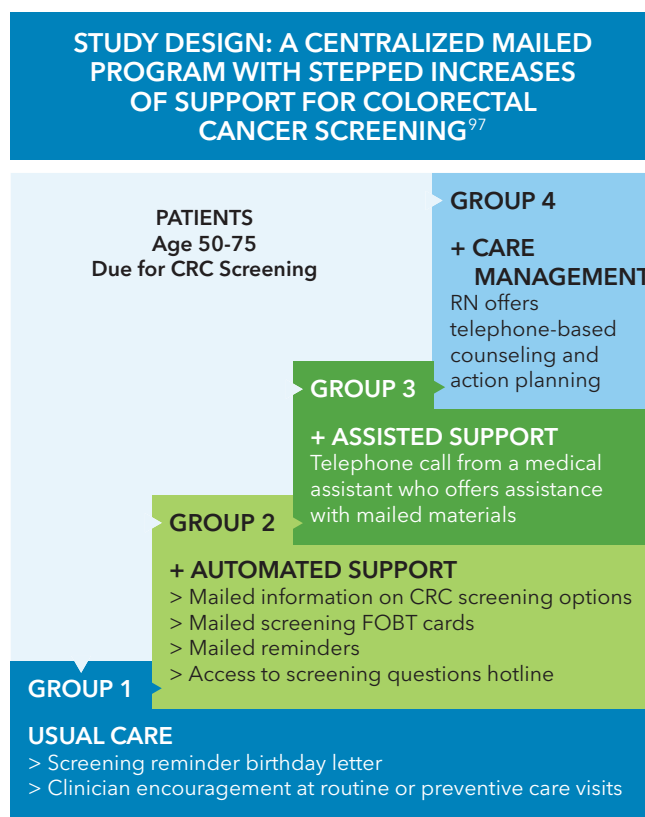
treatment for colorectal cancer may lose portions of their intestine and receive a temporary or permanent ostomy (a surgically-created opening in the abdomen for passage of bodily waste), which frequently leads to bowel dysfunction and other issues. Our researchers have studied quality of life and psychosocial adjustment for patients with ostomies after colorectal cancer.⁴⁴ They found that people who have a permanent ostomy have worse social well-being than colorectal cancer patients who do not have an ostomy, and that women suffer more in terms of both physical and psychosocial well-being after ostomy than men.⁴⁵⁻⁴⁸ These persistent concerns among those who have survived more than 5 years after diagnosis highlight the challenges of long-term survivorship.^{45,49} Our researchers have also studied long-term quality of life for rectal cancer survivors, noting the impact of cancer and cancer treatment on many aspects of survivors' lives.⁵⁰⁻⁵⁵

Improving Patient Outcomes

What strategies are effective in preventing colorectal cancer?

Lifestyle modifications to mitigate risk, combined with regular screening (via endoscopic methods or stool tests) are the primary approaches to preventing colorectal cancer.

Guidelines recommend regular colorectal cancer screening, although timing and frequency varies depending on screening type, family history, and other factors. Average-risk adults are generally recommended to begin regular screening at age 50.⁵⁶ More than 80 percent of Kaiser Permanente members between the ages 50 and 75 are screened for colorectal cancer,⁵⁷ which far exceeds the national average screening rate of 63 percent.⁵⁸ Our researchers have studied the factors associated with non-use of fecal immunochemical test (FIT) kits, leading to suggested changes in FIT kit contents to improve uptake of this screening method.⁵⁹ In our research, the implementation of more than one choice for screening, combined with direct patient outreach, was associated with increased screening rates in all racial and ethnic groups.^{60,61}



Screening for colorectal cancer can offer preventive benefit because it allows for identification of pre-cancerous polyps, which can be removed before they progress

to cancer. One Kaiser Permanente study estimated that screening colonoscopy (versus no endoscopic screening) was associated with a 65 percent reduction in risk of death for right-colon cancers and a 75 percent reduction for left-colon and rectal cancers among average-risk adults.⁶² Another study contributed to the evidence base for ongoing enhancements in screening quality by establishing associations between increasing polyp detection and a decreasing future risk of death from colorectal cancer.^{63,64} Our researchers have described favorable health and cost-effectiveness outcomes of screening programs that leverage multiple screening methods⁶⁵ and age-specific screening intervals.⁶⁶

How does early identification of colorectal cancer affect outcomes?

Organized screening programs can result in early detection of colorectal cancer,⁶⁷ thereby offering substantial survival benefits (because cancers are less likely to have advanced or spread). Colorectal cancer cases that are identified early also may be treatable with less invasive approaches that have fewer associated risks; our researchers have described some of these minimally invasive treatment options.⁶⁸

Disparities in colorectal cancer outcomes are complex. Our research has shown that survival disparities are related both to screening uptake (and therefore early identification of precancerous and cancerous lesions) and to treatment pathway choices after diagnosis.³⁴

What are the key factors in effective treatment of people with colorectal cancer?

Follow-Up of Positive Screenings. When a patient receives a positive result from a colorectal cancer screening test, such as FIT and fecal occult blood tests (FOBT), appropriate follow-up is an essential component of effective care.⁶⁹ Our research has shown that primary care physicians play a critical role in achieving appropriate follow-up after positive FIT or FOBT.⁷⁰ However, some patients do not receive

appropriate follow up; in one study about 20% of patients with a positive screening did not complete follow-up within the recommended 3 months.⁷⁰ Reasons for not receiving follow-up are complex. In 2014, our researchers published an article that discussed one barrier to follow-up of positive screenings, related to patient cost-sharing under the Affordable Care Act, which did not mandate coverage of follow-up colonoscopies (examination of the whole large bowel) after positive screening FOBT or sigmoidoscopy (examination of only the sigmoid or distal part of the colon).⁷¹

Person-Centered Treatment. Patients with colorectal cancer should receive whole-person treatment that varies depending on the stage of the cancer at the time of diagnosis, and is driven by patient-centered decision making that weighs the risks and benefits of the available treatment options. Our researchers have evaluated patients' experiences with cancer care using telephone surveys in the first year after diagnosis. They found that race, language, and health status were all associated with patients' ratings of care, and that Asian and Pacific Islander patients reported the poorest care experience.⁷²

Personalized medicine, a growing trend in cancer care, is relevant to colorectal cancer

Primary Care Importance in Colorectal Cancer Screening⁷⁰

Patients with ≥1 Primary Care Provider (PCP) visit had

88%
higher odds of completing screening versus those with no PCP visits
OR = 1.88
(95% CI: 1.86-1.89)

30%
higher odds of following up a positive FIT versus those with no PCP visits
OR = 1.30
(95% CI: 1.22-1.40)

treatment and is the subject of much interest.⁷³ Some hereditary cancers have specific mutations that can be identified with tumor marker testing. Our studies have analyzed genetic associations with environmental exposures (such as alcohol consumption) and found a series of significant relationships, but the researchers caution that their results require additional replication and validation.^{74,75} Personalized medicine and the link between genetic and environmental factors is an area of treatment that requires further study.

Ongoing Surveillance. Ongoing colonoscopy surveillance is recommended after polypectomy,⁷⁶ and among survivors of colon cancer, to detect new or recurrent cancers.^{77,78}

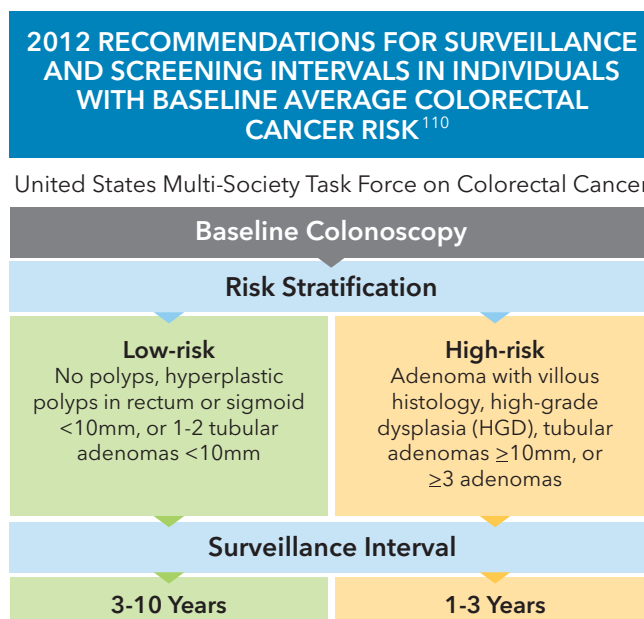
Translating Research Into Policy and Practice

How has Kaiser Permanente research on colorectal cancer contributed to changes in policy and practice?

Kaiser Permanente is a learning health care organization that works to systematically use research to inform policy and improve practice. Research, clinical, and operational partners within Kaiser Permanente have tested a range of interventions to reduce the risk of colorectal cancer and improve outcomes for patients with colorectal cancer.

Screening for colorectal cancer has been a key area in which our researchers have partnered closely with operational and clinical leaders both to measure effectiveness of screening strategies, and to improve those programs based on the evidence. Our studies have evaluated how best to engage patients in screening that meets guideline recommendations,⁷⁹⁻⁸⁸ the effectiveness of different screening methods,⁸⁹⁻⁹² and best practices for screening follow-up.⁹³ Several recent studies have examined the performance of our mail-based FIT screening programs. In a 5-year randomized controlled trial, our researchers found a high rate of screening participation over several years, demonstrating both the feasibility and effectiveness of this approach.⁹⁴⁻⁹⁷

Our researchers have also reported on the impacts of focused efforts to improve screening among underserved populations.⁹⁸⁻¹⁰³ A community-based intervention using family health histories to modify patients' risk perception was tested by our researchers, who concluded it had promise for decreasing disparities in colorectal cancer risk.¹⁰⁴



The way in which screening results are communicated to patients has also been studied by our researchers. In the context of Kaiser Permanente's integrated system and team-based care model, an intervention that added a nurse navigator to the post-screening bundle did not have any added benefit.⁹³

Kaiser Permanente research contributes not only to policy and practice change within our own delivery system, but has also advanced national understanding of colorectal cancer. Our research on colorectal cancer since 2007 has been cited more than 180 times in recent consensus statements, clinical practice guidelines, and point-of-care decision aid tools. For example, an article establishing quality thresholds for colonoscopy-based cancer screening contributed to modifications of national screening quality guidelines.¹⁰⁵ Kaiser Permanente researchers and clinicians have also directly contributed to many consensus statements and practice guidelines. These include 6 distinct consensus statements from the US Multi-Society Task Force on Colorectal Cancer,¹⁰⁶⁻¹¹² and an additional 4 consensus statements from the US Preventive Services Task Force.^{29,113-115} The most cited Kaiser Permanente article on colorectal cancer is a 2012 consensus update on colonoscopy surveillance after screening and polypectomy from the U.S. Multi-Society Task Force on Colorectal Cancer.¹¹⁰

Kaiser Permanente's nearly 170 research scientists and more than 1,600 support staff are based at 8 regional research centers and 1 national center. There are currently more than 2,500 studies underway, including clinical trials. Since 2007, our research scientists and clinicians have published more than 12,000 articles. Kaiser Permanente currently serves more than 12 million members in 8 states and the District of Columbia.

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