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 United States 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 getting 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]

Kaiser Permanente Publications Related to Colorectal Cancer since 2007

Source: Kaiser Permanente Publications Library and PlumX metrics, as of December 30, 2020.

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.

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 577 articles related to colorectal cancer since 2007.[3] Together, these articles have been cited nearly 19,000 times.

These articles are the product of observational studies, randomized controlled trials, meta-analyses, and other studies led by Kaiser Permanente scientists. Our unique environment – a fully integrated care and coverage model in which our research scientists, clinicians, medical groups, and health

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 nongovernmental extramural funding.

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] muscle abnormalities,[9] weight,[10] and use of tobacco [11-13] or alcohol;[14] hyperinsulinemia (abnormally high insulin);[15] polyp characteristics;[16] and hereditary cancer-syndrome-related risks.[17-21] However, the evidence for some of these risk factors is inconsistent.[5,13,22] There is evidence that the risk of colorectal cancer may be linked to select genetic traits,[23-38] 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 B6[39] and flavonoids,[40] and long-term use of metformin[41] and daily low-dose aspirin[42-44] (generally taken as part of a cardiovascular disease prevention strategy).

There are well-documented disparities in colorectal cancer risk by race, ethnicity, and socioeconomic status.[2,45] 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 more refined interpretations of 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[46-52] and the timeliness of diagnostic workup following positive results on screening tests.[52-54] Our researchers have found that the interpersonal relationships and quality of communication between doctors and patients are factors that partially explain the differences observed in colorectal cancer screening participation.[46] Other work has studied socioeconomic disparities[55,56] and patient factors[57-59] in relation to screening participation.

Increased Risks Of Colorectal Cancer Associated with Lifestyle Factors

MEAT EATING	SMOKING	OBESITY
41%	**95%**	**116%**
People in the highest quartile of meat eating compared to the lowest[5]	Current smokers compared to never smokers in the Women's Health Initiative[10]	BMI > 30 at time of colonoscopy compared to normal weight people[13]

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. Models incorporating a broader set of risk factors appear to outperform family history models based on the current screening guideline, suggesting that individualized colorectal cancer screening algorithms may be appropriate.[60,61] More recent work has explored different thresholds for defining a positive FIT (fecal immunochemical test) as a strategy for personalizing screening.[62]

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,[63] and that many failures in the screening process are preventable, such as fewer visits to primary care physicians and failure to follow up abnormal screening results.[52] 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, sex, and comorbidities)[64-66] and health behaviors.[67] Those who are obese, those with low muscle mass or density, and those who have metabolic syndrome have a higher risk of colorectal cancer death.[68-73]

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.[74] 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.[75-78] These persistent concerns among those who have survived more than 5 years after diagnosis highlight the challenges of long-term survivorship.[75,79] 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.[80-85]

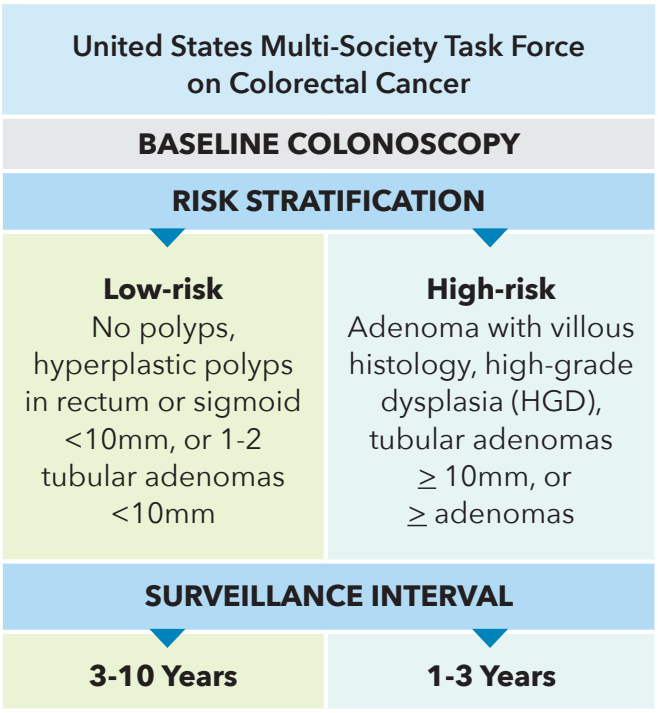
Improving Patient Outcomes

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 after age 50.[86] More than 80% of Kaiser Permanente members between the ages of 50 and 75 are screened for colorectal cancer,[87,88] which far exceeds the national average screening rate of 63%.[89,90] Our researchers have studied the factors associated with nonuse of FIT kits, leading to suggested changes in FIT kit contents to improve uptake of this screening method.[91] 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.[92-103]

2012 Recommendations for Surveillance And Screening Intervals in Individuals with Baseline Average Colorectal Cancer Risk[165]



Screening colonoscopy can offer preventive benefit because it allows for identification of precancerous polyps, which can be removed before they progress to cancer.[104] One Kaiser Permanente study estimated that screening colonoscopy (versus no endoscopic screening) was associated with a 65% reduction in risk of death for right-sided colon cancers and a 75% reduction for left-sided colon and rectal cancers among average-risk adults,[105] while another estimated that organized screening efforts within Kaiser Permanente were associated with large reductions in cancer-related mortality over a 15-year period.[88] 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.[106,107] Screening programs that leverage multiple screening methods[108-110] and age-specific screening intervals[111] have been shown in our research to be cost-effective, as has the removal of cost sharing for low-income persons eligible for screening.[112]

How does early identification of colorectal cancer affect outcomes?

Organized screening programs can result in early detection of colorectal cancer,[113] 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.[114,115]

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.[49,116]

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, including timely colonoscopy,[117] is an essential component of effective care.[118,119] Our research has shown that primary care physicians play a critical role in achieving appropriate follow-up after positive FIT or FOBT.[120] However, some patients do not receive appropriate follow-up; in one study about 20% of patients with a positive result did not complete follow-up within the recommended 3 months.[120] Reasons for not receiving follow-up are complex. In 2014, our researchers reported that one barrier to follow-up of positive results was 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).[121]

Primary Care Importance in Colorectal Cancer Screening[120]

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)

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.[122] Another survey found that half of colorectal cancer survivors have unmet needs following treatment; these needs are particularly pronounced among younger survivors, those with lower levels of education, and those with racial or ethnic minority backgrounds.[123]

Personalized medicine, a growing trend in cancer care, is relevant to colorectal cancer treatment and is the subject of much interest.[123,124] Some hereditary cancers have specific mutations that can be identified with tumor marker testing. Our studies have analyzed genetic associations with exposures (such as alcohol consumption or smoking) and found a series of significant relationships, but the researchers caution that their results require additional replication and valida-

tion.[125,126] Personalized medicine and the link between genetic, lifestyle, and environmental factors is an area that requires further study.

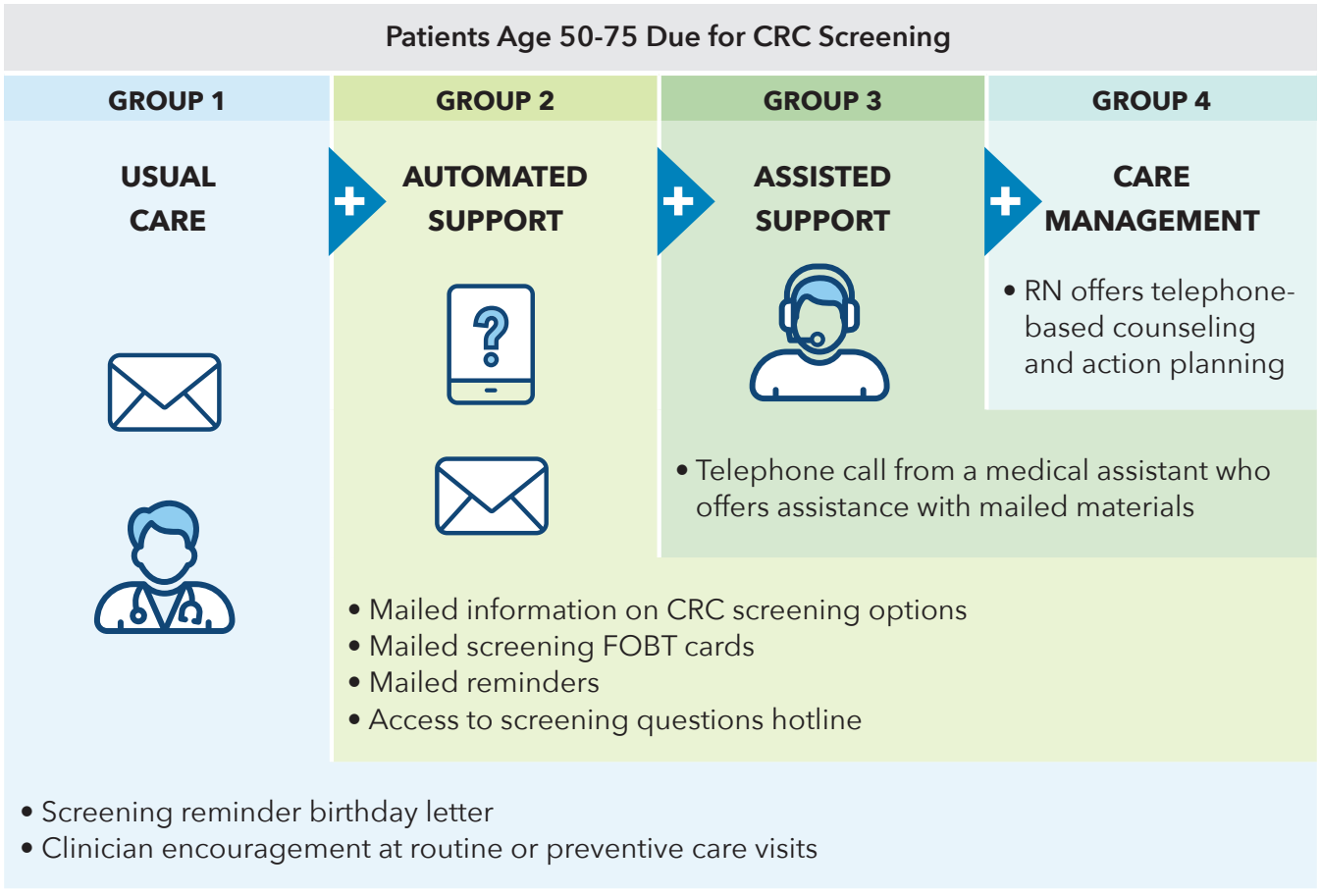
Ongoing Surveillance. Ongoing colonoscopy surveillance is recommended after polypectomy,[127] and among survivors of colon cancer, to detect new or recurrent cancers, though there is uncertainty as to the optimal timing for surveillance.[128,129] There is evidence that surveillance is underutilized by some patients and overutilized by others.[130] Our scientists have explored factors such as financial hardship which may affect patients' compliance with surveillance,[131] and have informed new, refined guidelines through estimation of post-colonoscopy risks for different polyp types.[16,132]

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.

STUDY DESIGN: A Centralized Mailed Program with Stepped Increases of Support for Colorectal Cancer Screening[152]



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,[133-143] the effectiveness of different screening methods,[144-147] and best practices for screening follow-up.[148] 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.[149-152]

Our researchers have also reported on the effects of focused efforts to improve screening among underserved populations.[153-158] 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.[159]

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 and team-based care model, an intervention that added a nurse navigator to the post-screening bundle did not have any added benefit.[148]

Kaiser Permanente research contributes to policy and practice change not only within our own delivery system, but also has advanced national understanding of colorectal cancer. Our research on colorectal cancer since 2007 has been cited more than 170 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.[160] Kaiser Permanente researchers and clinicians have also directly contributed to many consensus statements and practice guidelines. These include 6 distinct consensus statements from the U.S. Multi-Society Task Force on Colorectal Cancer,[161-167] an additional 4 consensus statements from the U.S. Preventive Services Task Force,[42,168-170] and a guideline issued by the World Endoscopy Organization.[171] 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.[165] Our scientists have also participated in Fight Colorectal Cancer, a national work group that discussed trends and research priorities in colorectal cancer diagnosis and prevention,[172] and in a CDC summit on FIT outreach strategies.[173]

Kaiser Permanente's nearly 185 research scientists and more than 1,530 support staff are based at 9 research centers. There are currently 2,355 studies underway, including clinical trials. Since 2007, our research scientists and clinicians have published nearly 19,000 articles. Kaiser Permanente currently serves approximately 12.5 million members in 8 states and the District of Columbia.

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