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Sociodemographic Disparities in Colorectal Cancer Screening, Interval Colorectal Cancers and Quality of Colonoscopy

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Sociodemographic Disparities in Colorectal Cancer Screening, Interval Colorectal Cancers and Quality of Colonoscopy

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An abstract of

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ABSTRACT

Use of recommended colorectal cancer (CRC) screening tests in the United States is well below nationwide goals, especially among racial/ethnic minorities and individuals with lower socioeconomic status (SES). Recent changes in health insurance policy and increasing use of organized screening approaches are expected to improve CRC screening coverage; however how these changes affect socioeconomic and racial/ethnic disparities in receipt of screening is not known. In addition, some screened persons may develop the so-called "interval CRCs", which are defined as cancers that develop after a negative colonoscopy but before the next recommended test. Little is known if the risk of interval cancers differs by race/ethnicity.

The goal of this dissertation was to examine CRC screening utilization and interval CRC occurrence by sociodemographic factors. This goal was achieved addressing three specific aims. Aim 1 was to examine CRC screening prevalence before and after the enactment of an Affordable Care Act (ACA) provision that removed costs for CRC screening tests. Aim 2 was to evaluate the time to receipt of CRC screening in newly age-eligible adults within Kaiser Permanente Northern California's (KPNC) organized screening program. Aim 3 was to assess variations in interval CRC incidence according to race/ethnicity.

Data from the National Health Interview Surveys (NHIS, 2008,2013), KPNC medical records (2007-2012), and Surveillance Epidemiology and End Results (SEER)-Medicare linked data (2002-2011) were used in this dissertation. Three different study designs (cross-sectional for Aim 1, retrospective cohort for Aim 2, matched case-control for Aim 3) with multivariable statistical models were used to examine research questions.

Increases in CRC screening after the ACA removed cost-sharing were observed in only blacks and whites, but not in Hispanics; changes were modest and not statistically significant after adjusting for other sociodemographic factors. Among adults newly eligible to be screened in KPNC's organized screening program, over 70% of enrollees initiated screening within 2 years of their 50^{th} birthday and relative to whites and the likelihoods of completing CRC screening were similar in blacks, 5% lower in Hispanics and 13% higher in Asians. In terms of interval CRCs, compared to whites, interval CRC incidence was significantly higher in blacks, after accounting for a quality of colonoscopy metric and other sociodemographic factors.

These studies suggest that policies aimed at increasing CRC through waiver of costs have only marginally improved CRC screening overall and may not have eliminated sociodemographic disparities, though racial disparities in CRC screening initiation among newly eligible adults within an organized program were modest. Furthermore, even if equitable rates of screening rates are achieved, the incidence of blacks may be greater than whites as a result of interval CRCs.

Racial/Ethnic and Socioeconomic Disparities in Colorectal Cancer Screening, Interval Colorectal Cancers and Quality of Colonoscopy

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Chapter 1 Introduction

Colorectal Cancer and Colorectal Cancer Screening

Colorectal cancer (CRC) is the third most common cancer and the second leading cause of cancer-related death in the US.[1] In 2016, an estimated 134,490 people will be diagnosed with colorectal cancer (CRC) and 49,190 will die from the disease.[1] Approximately 70-95% of CRCs occur sporadically and a smaller proportion (5-10%) are due to inherited genetic syndromes.[2] Relatively common behavioral, lifestyle, and dietary are risk factors for sporadic CRC and include smoking cigarettes, obesity, and consumption of red meat and alcohol. [3, 4 5-8] CRC is a heterogeneous disease with multiple pathways; however, nearly all malignant tumors arise from precancerous polyps in the mucosal layer of the colon and rectum. The presence of these precancerous polyps is one key feature of CRCs that make it amenable to prevention and early detection through screening.

The main categories of recommended CRC screening options include stool tests, endoscopic procedures and imaging studies. The available stool tests include guaiac-based fecal occult blood tests (FOBT), fecal immunochemical tests (FIT), and DNA tests. Colonoscopy, the most common form of CRC screening in the US, is an endoscopic examination of the entire colon and rectum, and if polyps are found they are removed and sigmoidoscopy is another endoscopic test, but is less commonly used and only reaches from the rectum to sigmoid colon. Imaging tests are infrequently used and include barium enema, which is an older form of screening that uses an x-ray to examined the colon and rectum for polyps, and computed tomography (CT) colonography, a newer form of

screening that uses a low-dose CT scan of the colon and rectum for polyps. These screening tests have been shown to reduce overall CRC risk and mortality though the estimated effectiveness of CRC screening varies by the type of test, adherence to these tests, and location of the tumor. [9-16] Based on this evidence and microsimulation modeling, the US Preventive Services Task Force (USPSTF) and several other public health and professional organizations recommend colonoscopy every 10 years, FIT/FOBT every year, or sigmoidoscopy every 5 years with FIT/FOBT every 3 years for average risk adults between 50 and 75 years.[17] Despite these recommendations and increasing CRC screening utilization in the past 15 years, only 57.2% of screening eligible adults were up to date for CRC screening in 2013. This estimate is considerably lower than the corresponding prevalence of cervical (80.8%) and breast (65.9%) cancer screening.[18]

Disparities in Colorectal Cancer Screening by Race/Ethnicity and Socioeconomic Status

In addition to the overall underutilization of CRC screening in the US, substantial disparities exist in CRC screening by race/ethnicity as well as socioeconomic status (SES).[19 20] The reason for these disparities is multifactorial as there are several economic, healthcare social and cultural barriers to cancer prevention and early detection among racial and ethnic minorities. Differences in screening by race/ethnicity are often examined within the context of socioeconomic disparities as racial and ethnic minorities are more likely to live in poverty, have lower educational attainment, lower access to care, and unique cultural and social barriers to healthcare utilization.[21]

Inequalities in healthcare utilization by SES and racial disparities may be magnified for CRC screening relative to other preventive health activities because CRC screening depends on an encounter with and recommendation from a health care professional. Further, even among people with insurance, the direct and indirect cost of colonoscopy is relatively high compared to other cancer screening tests. These direct costs in terms of co-pays, deductibles, as well as indirect costs, including lack of paid time off work, transportation, and inability to find a chaperone following a colonoscopy, may contribute to the disparities CRC screening by SES and race/ethnicity.[22] Fatalistic beliefs, believing a test is not necessary in absence of symptoms, and overall lack of awareness of the tests has also been noted for certain race/ethnic groups. [20 23 24, 25] Language barriers may be a particular challenge for Hispanic and Asians populations as they are more likely to have recently immigrated to the US. [20 23 24, 25]

CRC incidence and mortality rates are also significantly higher among blacks compared to non-Hispanic whites and a large proportion of these differences have been attributed to lower CRC screening rates among blacks. [26] Although differences in CRC incidence and mortality among Asians and Hispanics relative to whites are less pronounced than the corresponding differences for blacks, incidence and mortality rates have declined more slowly in these groups compared to non-Hispanic whites.[27] Furthermore, certain Asian and Hispanic subgroups have similar CRC incidence as non-Hispanic whites and CRC incidence is increasing among certain Asian subgroups.[28 29, 30] Furthermore, screening in this population is important the risk of CRC may be greater an in future generation with the adoption of Western lifestyle. [29, 31]

Although screening clearly reduces CRC risk and mortality, some people are diagnosed with CRCs following a negative colonoscopy. [32] The term "interval cancer" is used to describe the occurrence of CRC between screening and approximately 3-8% all CRCs in the US are interval cancers. [32] The majority of interval cancers are attributed to polyps that should have been removed but were missed by the surgeon or gastroenterologist during a colonoscopy. [32] Adenoma detection rate (ADR), calculated as the number of adenomas detected by a physician divided by the number of colonoscopies performed, is a useful overall quality measure that may reflect other metrics such as cecal intubation rates, withdrawal time, and bowel preparation.[33] Polypectomy detection rate (PDR), which can be more easily measured and captured in administrative data, has been proposed as a surrogate measure for ADR. [34]

Previous studies on the quality of colonoscopy have noted variations in PDR or ADR by physician characteristics.[35, 36] However, there is a paucity of data on whether or not patients from racial/ethnic minority groups are more or less likely to receive a colonoscopy from a physician with high ADR or PDR and if this might influence the increased risk of interval CRCs among racial and ethnic minorities..[37]

Limitations of Current Knowledge

There are numerous initiatives and efforts aimed at improving CRC screening utilization at the national, region, health-system and local level that would ostensibly mitigate socioeconomic and racial/ethnic disparities in CRC screening. In October 2010, the

Affordable Care Act required private health insurers to cover USPSTF recommended services with "A" or "B" ratings and remove patient cost-sharing, including deductibles, co-insurance and co-pays. The Center for Medicare and Medicaid Services has also removed cost-sharing for CRC screening tests under its authority. [38] The ACA cost-sharing provision aimed to reduce financial barriers for preventive services, including CRC screening, among privately and Medicare insured persons. Whether the provision has affected CRC screening prevalence is unknown. There is a need to investigate if CRC screening prevalence among privately and Medicare insured adults changed before and after this ACA provision and if these potential changes vary by race/ethnicity and SES. At a regional level, Kaiser Permanente Northern California (KPNC), a health insurer that operates an integrated health system, implemented one of the only organized CRC screening program in the US where their members are mailed FIT kits that are free of charge and receive reminders, removing logistical and economic barriers. Following KPNC's program implementation, CRC screening prevalence increased to nearly 77%, yet, racial/ethnic disparities in CRC screening were not reduced[39]. It is not known whether these differences began once people became eligible for CRC screening or not. Investigating potential racial differences in CRC screening among newly eligible adults is an important aspect in understanding and addressing these disparities especially given that previous cancer screening practices predict future cancer screening and helps identify populations in need of targeted intervention. [40] With increasing use of colonoscopy for CRC screening, factors related to interval cancers and quality of colonoscopy have gained attention in recent years. While most research has focused on physician level variations in adenoma or polyp detection rate, adjusting for patient mix, few studies have

examined potential disparities in quality of colonoscopy and how it relates to interval cancers by race/ethnicity.

Specific Aims

The overarching themes of this dissertation were sociodemographic disparities in CRC screening, in relation to recent policies and programs aimed at improving CRC screening utilization, and quality of colonoscopy, the most common form of CRC screening. Specifically,

Aim 1 examined if the ACA provision that eliminated cost sharing for CRC screening, among privately and Medicare insured persons, influenced CRC screening prevalence by race/ethnicity and socioeconomic status in the National Health Interview Survey (NHIS) data.

Aim 2 examined whether there are differences in CRC uptake among adults who are newly eligible for CRC screening by race/ethnicity in an integrated health system with an organized screening program in Kaiser Permanente Northern California.

Aim 3 examined variations in interval CRC incidence according to race/ethnicity and if quality of colonoscopy, as measured by PDR, accounts for these potential differences in a case-control study using SEER-Medicare data.

Chapter 2 Literature Review

Public Health Impact and Epidemiology of Colorectal Cancer (CRC)

The colorectal cancer (CRC) incidence rate in developed countries is 36.3 per 100,000 person years, which is significantly higher than the corresponding rate of 13.7 per 100,000 person years reported in the developing countries. [41] Incidence rates are highest in New Zealand, Australia, Europe, and North America and lowest in Africa and South Central Asia. [41] Differences in CRC occurrence by country and global region are largely attributed to variations in health behaviors and lifestyle factors.[41] CRC mortality is also higher in developed compared to developing countries where mortality rates are 14.6 and 7.8 per 100,000 person years, respectively. .[41]

In the US, CRC is the third most incident cancer and the second leading cause of cancer-related death. In 2016, an estimated 134,490 people will be diagnosed with CRC and 49,190 will die from the disease.[1] Overall, incidence rates in the US have steadily decreasing over time; between 2003 and 2012 colon cancer incidence has declined by approximately 3.3% per year and rectal cancer has declined by 2.2% per year. [42] Incidence rates per 100,000 person years are highest in the proximal colon (18.9) followed by the rectum (12.3) and then distal colon (10.3) [27] and increase with age. The majority (70%) of CRC cases are diagnosed in people 60 years of age and older, though substantial proportions of CRC cases occur in the 50- to 59-year age group (19%) and in those under the age of 50 (11%). [27] CRC incidence is higher in males compared to females, though the gender differences in CRC incidence have decreased over time across all race/ethnicities. Overall declines in incidence have been greater among non-

Hispanic whites compared blacks and other races/ethnicities. **(Figure 2.1)** In the most recent time period, blacks have 22-27% higher incidence rates compared to non-Hispanic whites whereas Asians and Hispanics have lower CRC incidence rates. [42] (**Table 2.1**)

CRC mortality has also declined over time; between 2003 and 2012 mortality has decreased by approximately 2.8% per year. [42] Similarly to incidence patterns, CRC mortality rates increase with age and are higher in males compared to females. Mortality declines have been greater for whites compared to blacks **(Figure 2.2)**. [42] In the most recent time period, race/ethnicity, CRC mortality is higher among blacks and is lower among Asians and Hispanics compared to whites (**Table 2.1**). Additionally, death rates are much higher among people with lower educational attainment, regardless of race/ethnicity.[43]

Figure 2.1 CRC Incidence Rates by Race, SEER9 1975-2012

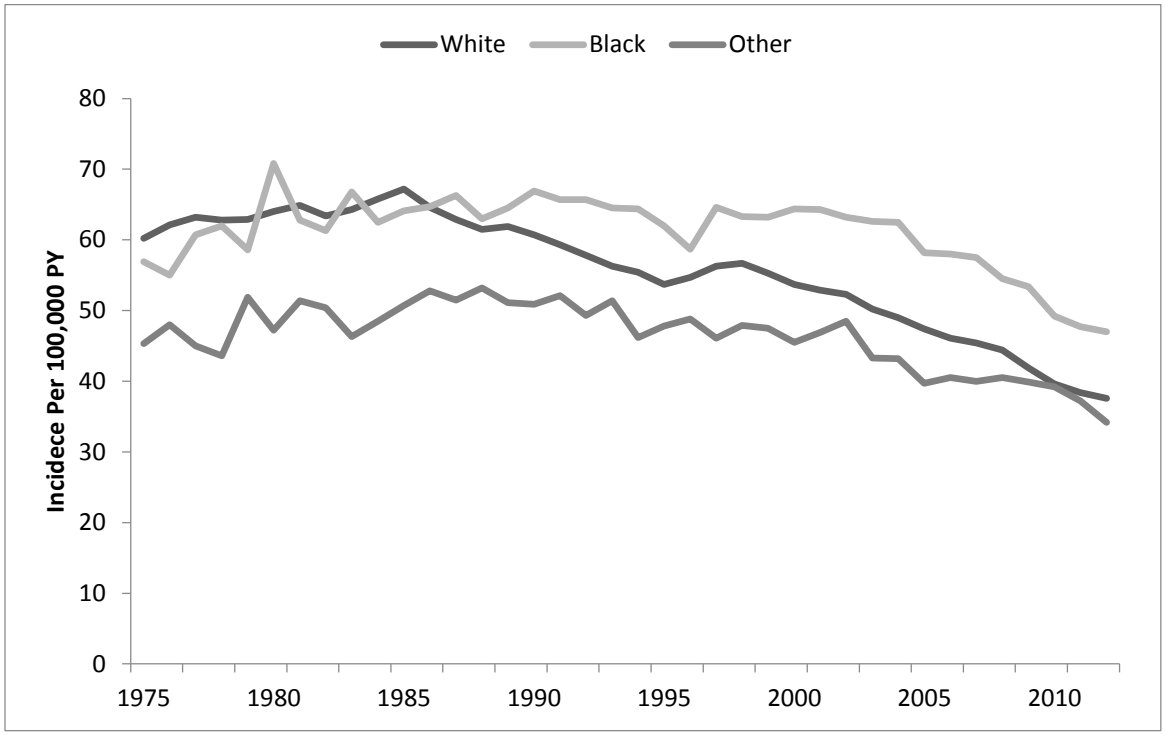


Figure 2.2 CRC Mortality Rates by Race, SEER9 1975-2012

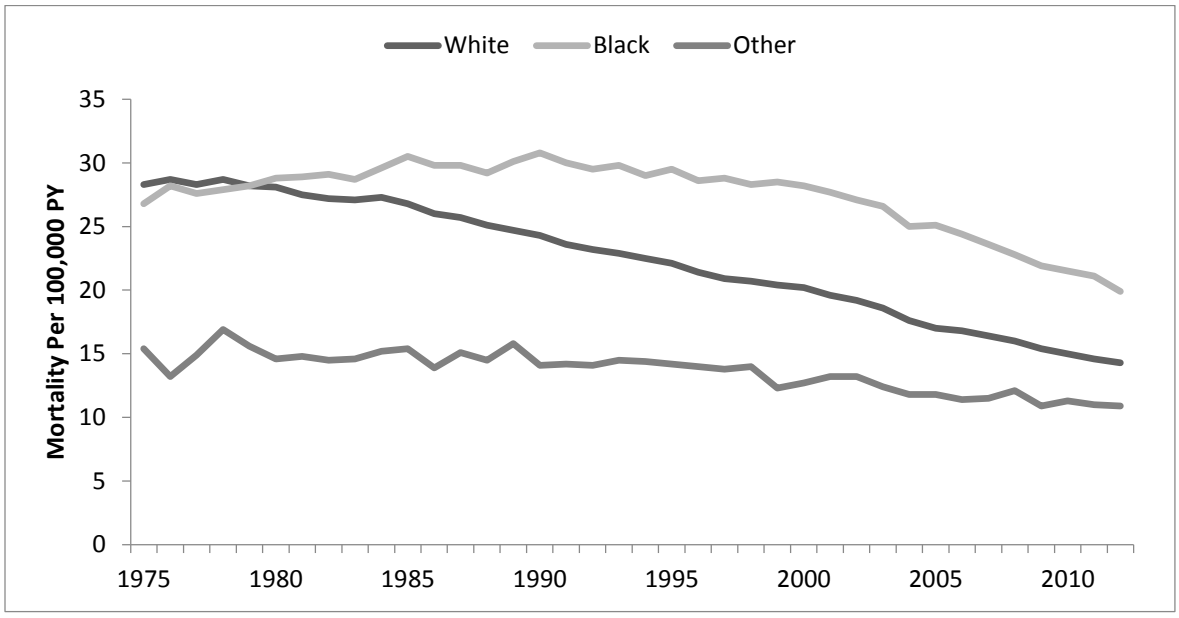


Table 2.1 Age Adjusted Incidence and Mortality Rates by Race/Ethnicity, SEER18 2008-2012

	Incidence Rate Per 100,000	**Mortality Rate Per 100,000**
All Races	42.2	15.5
Non-Hispanic White	42.4	15.2
Black	52.3	21.4
Asian/Pacific Islander	36.1	11.0
American Indian/Alaska Native	40.3	12.5
Hispanic	35.8	12.2

Approximately 44.0% of CRC cases are diagnosed at an early stage, 35.1% with regional stage and 21.0% are diagnosed with distant stage disease. The overall 5-year relative survival for CRC is 64.9%, varying substantially by stage, from 13.1% in distant disease to 90.1% in cases with localized cancer. Overall relative survival for distal cancer, including rectal cancer, is similar to that of proximal tumors. [27] CRC survival is slightly higher for Asian/Pacific Islanders (69.3%) and non-Hispanic whites (65.4%) compared to Hispanic (64.2%), American Indian/Alaska Natives (62.7%) and considerably lower than in non-Hispanic blacks (58.7%). [27]

Natural History of Colorectal Cancer and Risk Factors

CRC is a heterogeneous disease with multiple pathways. The malignancy may occur either sporadically or due to inherited genetic syndromes. Inherited genetic syndromes [Family adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer

(HNPCC)] are highly penetrant but rare (accounting for 5-10% of CRCs) and cause CRC in about 90-100% of people with these conditions.[2] Peutz-Jeghers, Juvenile polyposis syndrome, and *MUTYH*-associated polyposis are other inherited syndromes that increased CRC risk, but are less penetrant than HNPCC or FAP. [44] The majority (70-95%) of CRCs are sporadic [45] and are adenocarcinomas arising from the mucosal layers of the colon and rectum. As noted above, the largest proportion of CRCs are located in the proximal colon (transverse colon through the splenic flexure), followed by the rectum and the distal colon (including the descending and sigmoid colon). Tumor location has screening implications and is discussed in further detail in the screening section of this chapter.[27]

Studies of patients with HNPCC and FAP provided valuable insight into the natural history of familial CRC, as well as sporadic cancers, as these tumors develop through similar, but unique, pathways. Polyps vary in their gross appearance, architecture, frequency, histology and potential to progress to CRC.[44] Historically, polyps were classified into two broad categories, adenomas and hyperplastic polyps (HP). Adenomas were thought to be the only type of polyp with carcinogenic potential whereas HPs were presumed harmless, however, research studies suggest that HPs, particularly those in the proximal colon, may lead to serrated polyps and further advance to CRC.[46] With this information, the World Health Organization proposed a new classification that includes two broad categories of polyps-adenomas and serrated lesions. Adenomas are the most common polyp type, representing 50-66% of all polyps, and are more commonly located in the proximal colon compared to the distal colon.[47] Adenomas may have pedunculated

(stalk-like) or sessile (flat) appearance. Histologically, adenomas are subdivided into tubular, tubulovillous, and villous based on the microscopic architecture of the polyp. Serrated polyps have a saw-toothed appearance, are often sessile, and vary in their carcinogenic potential. There are three main histologic types of serrated polyps: 1) sessile serrated adenomas (SSA), 2) traditional serrated adenomas, which are both cancerous and 3) HP serrated polyps, which are non-cancerous.[44]

Numerous tumor suppressor, oncogenes and mismatch repair genes are involved in CRC pathogenesis. Initially, CRC was thought to develop in separate, distinct parallel pathways, however, in recent years it became clear that these pathways largely overlap.[48] Jass et al proposed five pathways, based on several defining features including the presence of Microsatellite Stability (MSI), chromosomal instability (CIN), methylation of CpG Island methylator phenotype (CIMP), as well as other characteristics as depicted in **Table 2.2**. Tumors can be MSI-stable (MSS), low MSI (MSI-L), or high MSI (MSI-H). MSI-H status is a result of impaired mismatch repair (MMR) genes; it confers more favorable prognosis and better response to certain treatments.[49 50] Tumors with high CIMP methylation usually have mutations in the BRAF oncogene and are often associated with a strong positive family history for CRC. Chromosome instability is a result of an imbalance in chromosome numbers and loss of heterozygosity and is accompanied by Adenomatous Polyposis Coli (APC), K-RAS, TP53, and loss of alleles in 18q gene. The precursors to these various pathways vary as noted in **Table 2.2**.[48]

Table 2.2 Summary of Colorectal Cancer Pathways

Group Number	% of CRCs	Polyp Type	MSI	CIMP Methylation	CIN	Other mutations/Methlyation	Sporadic or Inherited?
1	12%	Serrated	High	High	Stable	BRAF mutation	sporadic
2	8%	Serrated	Stable or Low	High	Stable	BRAF mutation	sporadic
3	20%	Adenoma or serrated	Stable or Low	Low	Stable	MGMT methylation	sporadic
4	57%	Adenoma	Stable	Negative	Instable	APC/KRAS/Other mutations	FAP or sporadic
5	3%	Adenoma	High	Negative	Stable	BRAF negative	Familial

There are several lifestyle and behavioral factors as well as comorbidities that are associated with the risk of sporadic CRC. According to the World Cancer Research Fund (WCRF), there's convincing evidence abdominal and body fatness, attained adult height, and consumption of red and processed meat increases CRC risk. WCRF considers alcohol consumption as convincingly increasing risk for men and a probable risk factor for women. Physical activity and consumption of fiber are convincingly associated with a decreased risk of CRC and garlic, milk and calcium consumption are probable protective factors. [3] Other established risk factors include age, personal history of inflammatory bowel disease or polyps, family history, as well as tobacco use. [51]

Types and Effectiveness of Colorectal Cancer Screening

CRC is a cancer that can be prevented through screening tests due to the presence of precancerous polyps in the colon and rectum. There are several tests that are used to

screen for CRC. They are usually divided into three types-the first provide endoscopic examination of the colon and rectum for polyps and tumors using sigmoidoscopy and colonoscopy. The second type of tests are stool-based tests, which are collected at home and include guaiac fecal occult blood tests (gFOBT), fecal immunochemical tests (FIT), and stool-based DNA tests (sDNA). The third type are imaging tests that include barium enema and CT colonography. The various CRC screening tests (structural and stool-based) are described in more detail below:

Sigmoidoscopy

Sigmoidoscopy is an endoscopic procedure that reaches from the rectum to the sigmoid colon (bottom third of the colon) and if polyps are found they are removed, however, because of sigmoidoscopy's limited reach, polyps located in the proximal part of the colon will not be detected. Patients receive one or two enemas an hour prior to the procedure to empty the colon and rectum. Sigmoidoscopy doesn't require sedation and may also be performed by non-gastroenterologist physicians. Risks and complications of sigmoidoscopy include bleeding, diverticulitis, perforation, though the occurrence of these complications is rare. [52, 53]

Colonoscopy

Colonoscopy is a longer tube that reaches the cecum, and if polyps are found they are removed. Compared to sigmoidoscopy, bowel preparation for colonoscopy is more extensive and requires patients to eliminate solid foods and darker liquids from their diet 1 to 2 prior to the test, as well as drink a laxative the evening before the test. Abstaining from drinking liquids 6-8 hours before the test is also recommended. Patients may also choose to be sedated, requiring a chaperone following the procedure. Colonoscopies are

typically performed by gastroenterologist or physicians with surgical training. Complications of colonoscopy include cardiopulmonary events associated with sedation, discomfort, perforation, bleeding. [54]

gFOBT

gFBOT contains guaiac, which turns blue with peroxidase activity of heme, thereby detecting blood in the stool. gFOBT does not specifically detect blood from colorectal polyps and may react to peroxidase from other sources (e.g., red meat, certain fruits and vegetables, blood from hemorrhoids or upper gastrointestinal conditions).[55] High doses of vitamin C, aspirin, and other medications, interfere with the peroxidase reaction, increasing the probability of a false negative result, so people are instructed to avoid these products prior to the test.[56] To improve the sensitivity of gFOBT, 2 samples from 3 stools are typically collected. If a gFOBT is positive, follow-up with colonoscopy is required to complete the screening process.

FIT

FIT is a newer stool based test that uses an antibody to detect human globin, which is part of the hemoglobin molecule. Because FIT detects globlin, which degrades throughout the gastrointestinal tract, it is a more reliable source of lower gastrointestinal bleeding and requires only one sample. Additionally, FIT does not rely on peroxidase activity, so there are fewer dietary restrictions associated with FIT. [56] Similar to gFBOT, there are few complications associated with the test and follow-up with colonoscopy is required if the test is positive.

sDNA

sDNA is the most recent stool-based screening test, approved by the FDA in late 2014.[57] sDNA tests examine the stool for genetic mutations associated with CRC and microsatellite instability. Unlike FOBT and FIT, a full stool sample is required for the sDNA tests. sDNA test does not require dietary restrictions and similar to other stool-based tests, require follow-up colonoscopy if the test is positive.

CT colonography

CT colonography is a newer CRC screening test and is a low-dose CT scan of the interior of the colon. It has similar bowel preparation as colonoscopy, and does not involve sedation. If a polyp is found during CT colonography, a follow-up colonoscopy to remove the polyp is required. Complications include perforation and radiation exposure, which is relatively low for one-time screening, but higher if multiple CT colonographies are performed.[58]

Barium Enema (BE)

Barium enema is an older CRC screening test. Prior to the test a barium solution injected into a patient's rectum and an x-ray is taken of the colon and rectum. Similar to CT colonography and endoscopic tests, the colon must be clean prior to the test and sedation is not required. If a polyp is found during the procedure, a follow-up colonoscopy is required. Compared to other forms of CRC screening, BE is rarely used in the United States.[59]

Effectiveness of CRC Screening Tests

Three randomized controlled trials (RCTs) demonstrated that annual or biannual FOBT reduces CRC incidence and mortality by 20% 15-31%, respectively. [9-11] There are no RCTs evaluating the effectiveness of FIT and there will likely not be RCTs of FIT given its superior sensitivity and specificity to detect colorectal cancers and adenomas compared to gFOBT. [56, 60] Four RCTs report decreased CRC incidence by 18-23% and mortality by 12-31% with a one-time flexible sigmoidoscopy or flexible sigmoidoscopy every 3-5 years. [12-15] The benefits of sigmoidoscopy are mainly in preventing the incidence and mortality from left sided-tumors given its limited reach into the colon.[12-15] Among the imaging tests, there's evidence that compared to CT colonography, BE is a less sensitive imaging test.[61]

The effectiveness of colonoscopy for average-risk adults has not been examined in RCTs, though two RCTs are currently underway and several observational studies have examined the association of CRC screening with CRC occurrence, late stage of disease and mortality.[16, 62-66] A recent case-control study reported lower risk of incident late stage cancer among average-risk adults receiving colonoscopy within 10 years of diagnosis compared to people not screened within this timeframe (OR=0.29, 95% CI 0.15,0.58). [16] Additionally, a cohort study with 22 years of follow-up reported reduced incidence and mortality after self-reported one-time colonoscopy screening compared to never screening among average-risk adults in the distal and proximal colon.[67] Observational studies have generally shown that the inverse association of CRC screening with distal cancer is stronger than that for proximal tumors. [65] A Canadian case-control studies utilizing administrative health claims linked with cancer registry data, reported a

protective effect of one-time colonoscopy on CRC mortality in distal, but not proximal tumors. [65] A US-based study using SEER-Medicare data reported a stronger association between one-time colonoscopy for distal compared to proximal CRC deaths.[66] The utility of cohort and case-control studies in examining the effectiveness of cancer screening, particularly colonoscopy which is often used for non-screening reasons, is limited due to the inability to differentiate between a true screenings versus diagnostic tests.[68, 69] The effectiveness of CRC screening by race/ethnicity has not been examined in experimental studies. A SEER-Medicare claims-based study indicates similar associations of one-time colonoscopy compared to not having received a colonoscopy for whites, blacks and other race/ethnicities for all CRC sites combined, though the effect of colonoscopy was closer to the null in blacks compared to whites for distal colon cancer.[66]

Colorectal Screening and Surveillance Recommendations

In addition to the aforementioned studies examining the effectiveness of various CRC screening tests, microsimulation models examining the benefits and cost of various CRC screening have informed the USPSTF CRC screening recommendations. The USPSTF currently recommends colonoscopy every 10 years, at-home FOBT or FIT annually, or flexible sigmoidoscopy every 5 years with FOBT every 3 years for average risk adults 50-75 years.[70] Time intervals between CRC screening tests are based on the sensitivity and specificity of the tests, natural history, and sojourn time. For example, it is estimated that it takes 10-15 years for an adenoma to progress to a CRC [71, 72] with an estimated sojourn time between 4.5 and 5.8 years.[73] These recommendations, updated in 2016, state there is inconclusive evidence to recommend CT colonography and sDNA. [70] Other organizations, including the American Cancer Society, have issued recommendations that

are similar to those of the USPSTF, but do not set a specific upper age-limit on screening and some endorse CT colonography and sDNA. [74, 75] For people at higher risk, including those with a personal history of polyps, colorectal cancer, inflammatory bowel disease as well as a strong family history of CRC or polyps, more frequent and earlier CRC screening is recommended. [74] For people with rare, high penetrance genetic mutations (FAP or HPNCC), it is recommended that CRC screening begins much earlier (before the age of 10-12 years for FAP and 20-25 years for HPNCC).

Guidelines for polyp removal during a colonoscopy and surveillance following polyp removal have also been published. All adenomas should be removed according to the American Gastroenterologist Association. [76] According to US Multi-Society Task Force on Colorectal Cancer, serrated polyps located in the proximal part of the colon and serrated polyps >5mm located in the rectosigmoid should be removed. [46, 76] It is also recommended that patients who had their polyps removed should receive surveillance colonoscopy with varying durations (1 to 10 years) based on the type, number and size of the polyp. Patients with >10 adenomas in a single colonoscopy are recommended to receive a surveillance colonoscopy within 3 years whereas patients with only small hyperplastic polyps are advised to follow CRC guidelines for average-risk adults (ie they should receive a colonoscopy in 10 years). [74]

Interval Colorectal Cancers and Quality of Colonoscopy

Overall, there's substantial evidence that CRC screening reduces CRC risk and mortality. However, some people are diagnosed with CRCs following a negative colonoscopy. The term "interval cancer" is used to describe the occurrence of CRC between screenings,

whereas “detected cancers” is a term used to describe to CRCs detected with screening. Interval CRCs account for approximately 3-8% of all in the US and account for a higher proportion of proximal CRCs than distal CRCs.[32]

According to Singh et al, reasons for interval CRCs include 1) missed lesions, a function of inadequate examination (poor bowel preparation, a colonoscopy that did not reach the entire colon, failure of the physician not recognizing a lesion) 2) incomplete resection of dysplastic polyps 3) rapidly forming cancers, referred to as “de novo” cancers and 4) failure of the biopsy to identify lesions. At least two studies have attempted to quantify reasons to interval cancers and estimate that 52-58% are due to missed lesions, 19-20% due to incomplete resection, 13-24% due to de novo cancers, and 5-9% as missed during biopsy.[77, 78] Compared to detected CRCs, interval cancers are less likely to be diagnosed at an advanced stage, though there’s no difference in tumor grade and mixed results regarding interval CRC survival compared to detected CRC survival.[32]

Because the largest proportion of interval cancers are thought to be due to missed lesions, the quality of colonoscopy, which is discussed in sections below, has received growing amount of attention from researchers and gastrointestinal organizations. Interval cancers are more common among patients whose colonoscopies were performed by a non-gastroenterologist (internal medicine physicians, general surgeons or family practitioners) compared to patients whose colonoscopies were performed by a gastroenterologist. [32] In several studies, quality metrics of a physician who performed the colonoscopy preceding CRC diagnosis have been inversely associated with interval CRCs.[32, 35, 37, 79]

There are several patient level factors positively associated with interval cancers. According to a recent meta-analysis of 12 studies, interval cancers are more likely to occur in people who are older (OR=1.15 95%CI 1.02-1.30 comparing 65-75 years with <65 years), have a family history (OR=1.64, 95%CI 1.40-1.90), have more comorbidities (OR=2.00, 95%CI 1.77-2.27 comparing high vs low comorbidity score) and in those with diverticulitis (OR=4.25, 95%CI 2.58-7.00).[32] Clinical and biological factors, including CpG island methylator phenotypes as well as MSI, are associated with interval CRCs and as mentioned above, tumors in the proximal colon are more likely to be interval cancers compared to distal colon. [32]

Data on the risk or prevalence of interval cancers by race/ethnicity are scant as most previous studies on this issue were conducted in people of European decent.[32] A previous study conducted by Cooper and colleagues using SEER-Medicare data, reported similar odds of interval cancer compared to detected cancers among Hispanic, Asian Americans and other race/ethnicities relative to non-Hispanic whites, but a higher odds of interval cancers among blacks (OR=1.24, 95%CI 1.09-1.41).[37] The authors adjusted the results for patient sociodemographic, clinical factors, and quality of colonoscopy, as measured by polyp detection rate (PDR), however, their goal was to describe predictors of interval cancer more generally and they therefore, did not investigate how much physician quality compared to clinical factors contributed to black-white differences in CRC interval cancer prevalence. [37] Further, the Cooper et al study was conducted between 1994 and 2005, a time period that preceded the endorsement of quality measures by medical

societies, and it is unclear if there are differences in colonoscopy quality by race/ethnicity. Lastly, Cooper et al investigate the probability of interval given a CRC was diagnosed and investigating the incidence of interval CRCs given that someone had a colonoscopy may be palatable for public-health and cancer control efforts.

The role of disease-related factors versus health care utilization in explaining black-white CRC outcomes has been investigated previously.[80] Several studies report an earlier age at onset and higher incidence of proximal tumors among blacks compared to whites.[81, 82] A recent study noted lower prevalence of BRAF mutations among blacks compared to whites, suggesting lower prevalence of serrated polyps; however, other studies showed no differences in CRC tumors characteristics.[83, 84] Studies on racial differences in MSI status are equivocal, where a population-based study found no difference in MSI status between blacks and whites, though study with a limited number of patients reported a higher prevalence of MSI status among blacks compared to whites.[85, 86] A previous study using data from the Prostate, Lung, Colorectal and Ovarian (PLCO) cancer prevention trial reports similar adenoma detection yields in blacks and whites undergoing follow-up colonoscopy after a positive flex-sigmoidoscopy, suggesting similar biological factors in adenoma development, however, blacks were less likely to undergo a diagnostic evaluation, which lends support that health care utilization may account for black-white differences in CRC occurrence.[80]

Quality of Colonoscopy

Previous studies have note the limitations of colonoscopy at detecting proximal adenomas and serrated polyps in clinical practice, which may increase the risk of interval cancers in the right colon.[32, 65, 87] In order to reduce missed adenomas and serrated polyps, several quality metrics have been proposed. These metrics include: cecal intubation rates, withdrawal time, quality of bowel preparation, adenoma detection rate (ADR), serrated polyp detection rate (SDR), and overall polyp detection rate (PDR).[33] Cecal intubation rate is a measure of visualization of the entire colon (all the way to the cecum). Withdrawal time is the time it takes for a gastroenterologist to view the colon and an average withdrawal time (not including polyp removal) of 6 to 9 minutes is recommended by the US Multi-Society Taskforce for Colorectal Cancer.[88] Quality of bowel preparation is a patient-related quality metric of how adequate the colon and rectum has been cleared prior to colonoscopy.

Adenoma detection rate (ADR), as measured by the number of adenomas detected by gastroenterologist divided by the number of colonoscopies performed, captures cecal intubation rates, withdrawal time, and bowel preparation. ADR was initially recommended as a quality benchmark by the American Society for Gastrointestinal Endoscopy in 2006 and was updated in 2015.[89, 90] The 2006 guidelines recommended an ADR of >15% and >20% in female and male patients, respectively and the 2015 guidelines have updated ADR's to >20% in females and >30% in males.[89, 90] ADR has also been proposed as a quality metric by the Centers for Medicare and Medicaid Services. Using data from over 300,000 colonoscopies and 136 gastroenterologists in Kaiser Permanente Northern California's (KPNC) integrated health system Corley and

colleagues reported lower hazard of interval cancers (HR=0.52, 95%CI 0.39-0.69), advanced stage disease (HR=0.43, 95%CI 0.29-0.64), and CRC death (HR=0.38, 95%CI 0.22-0.65) among patients whose colonoscopy was performed by gastroenterologists in the highest, compared to the lowest, ADR quintile. [91] These findings motivated the most recent ADR recommendations.

Several single institutional studies and a study of a large multi-practice health maintenance organization (HMO) report variations in ADR's by physician. [36, 92-94] ADRs could only be estimated using time-intensive medical chart and pathology review as adenoma detection is not captured in claims-based datasets. [95] In an effort to more easily measure ADR's, polypectomy detection rate (PDR), which can be measured in claims data, has been proposed as a surrogate measure for ADR and thus quality of colonoscopy. [34]

Two previous studies noted increased odds of interval CRC compared to screened detected CRC among patients who had a screening colonoscopy completed by a physician with a low PDR compared to a higher PDR. [37, 79] The first study used administrative health insurance data and was conducted in Canada, where the proportion of gastroenterologists performing colonoscopy is lower than that in the US. [51] The second study utilized SEER-Medicare data to identify patient and provider factors that are related to interval cancers, defined as having a CRC diagnosis 6-36 months following a colonoscopy. [53] PDR in that study was measured in the non-cancer sample only, and it is unclear what minimum number colonoscopies was used for PDR calculations. Further,

the definition of an interval cancer up to 36 months may have been conservative based on the estimated sojourn time of CRCs.[96] Compared to patients with colonoscopies performed by physicians with the lowest PDR quartile (0-24%), patients whose colonoscopies were performed by physicians in the second (OR=0.84, 95%CI 0.76, 0.93), third (OR=0.80, 95%CI 0.72-0.89), and fourth (OR=0.70, 95%CI 0.63-0.78) quartiles had lower odds of interval cancer versus a screen detected cancer.

Previous studies on the quality of colonoscopy have noted variations in PDR or ADR by physician and most reported that these measures may be related to the characteristics of each physician's patient population. [36, 97, 98] For example, these studies have found that the probability of finding a polyp or adenoma increases with age, is greater for males compared to females, but does not vary substantially by race/ethnicity. [36] On the other hand, a recent study examining this issue reported that adjusting for the characteristics of the patient population did not affect the physician ADR rankings, for example, most low-ADR physicians remained in the lowest quintile after adjusting for patient characteristics .[36] Potential variations in the quality of colonoscopy by race/ethnicity have not been investigated, though racial disparities in quality of colonoscopy are plausible because such disparities have been found in breast cancer screening studies. It is reported that, compared to their white women, black women less frequently receive breast cancer screening from high-quality facilities, are more likely to have false-negative mammograms, and have higher risk of interval breast cancers. [99, 100]

Temporal Patterns of Colorectal Cancer Screening

Nationwide CRC screening prevalence estimates are largely based on self-reported measures from the National Health Interview Survey (NHIS) or the state-based Behavioral Risk Factor Survey (BRFSS). [101] [102] Results from these surveys indicate that screening prevalence varies widely over time, and by demographic and socioeconomic factors, as well as healthcare characteristics.

Despite recommendations, CRC screening prevalence is relatively low. In 2013, only 57.2% of screening eligible adults were up to date for CRC screening compared to 65.9% and 80.8% for breast and cervical cancer, respectively.[18] The most common form of CRC screening is colonoscopy (54.6%), followed by FOBT/FIT screening (8.8%).[20] Less than 2% of people use other forms of CRC screening (sigmoidoscopy, CT colonography and barium enema).[20]

According to 1992 NHIS 17.3% of adults aged 50 years and older received FOBT in the previous year. [103] During this time, <10% of adults aged 50 years and older had a sigmoidoscopy in the past 3 years [103] and colonoscopy was rarely used for CRC screening. Between 2000 and 2005, the proportion of adults who were up-to-date with CRC screening increased rapidly (from 38% to 47%), mainly due to increased use of colonoscopy. [59, 104, 105] Part of this increase was attributed to changes Medicare reimbursement policy for CRC screening tests, which was expanded in July 2001 to cover up to 80% of the cost of colonoscopy for average-risk adults. [104] [106] Prior to that time, Medicare covered FOBT for average risk and colonoscopy only for high-risk adults.

While the increase in CRC screening was greatest in people over 65 years and older, it also increased for people 50-64 years of age.[59] Between 2005 and 2008, CRC screening prevalence continued to increase from approximately 47% to 54%.[20, 107]

Disparities in Colorectal Cancer Screening Utilization by Race/Ethnicity and Socioeconomic Status

In addition to the overall underutilization of CRC screening in the US, substantial disparities by race/ethnicity status exist.[19] [20] CRC screening is particularly underutilized in Hispanics, blacks and Asians compared to non-Hispanic whites. [23, 59, 104] Differences in CRC screening are greater for Asians and Hispanics compared to blacks, however, the black-white screening disparity has garnered more attention as CRC incidence and mortality rates are considerably higher in this group. [108] [26] Using a microsimulation model, Lansdorp-Vogelaar and colleagues estimated that CRC screening accounted for 40% of black-white differences in CRC incidence and 55% of the black-white difference in CRC mortality, in part due to later stage at diagnosis among blacks .[26] [109, 110] Such wide disparities in incidence and mortality for CRC is not observed for Hispanics and Asians, which may be in part due to historically lower prevalence of risk factors, lifestyle patterns and SES.[27] Nonetheless, disparities in CRC screening in these populations are important as declines in CRC incidence has not been as rapid among Asian and Hispanics, and is in fact increasing in certain subgroups of Asians.[27] [105] Further, a substantial proportion of Asian and Hispanics have recently immigrated to the US and the risk for CRC may increase as these populations adopt a Western lifestyle, conferring greater CRC risk.[29, 31]

Differences in screening by race/ethnicity are often examined within the context of socioeconomic disparities as racial and ethnic minorities are more likely to live in poverty, have lower educational attainment, lower access to care, and though there are unique cultural and social barriers to healthcare utilization among minorities as well.[21] Income and education levels are also strongly tied to CRC screening use where people whose annual household earnings are <$35,000 have 50% lower CRC screening prevalence compared to people whose annual household income is >$100,000.[18, 20] A recent study reports that socioeconomic status and lack of access to health care account for the majority of the disparities in receiving a physician recommendation for CRC screening, which is one of the most important predictors of screening receipt. [111] For example, Blacks and Hispanics are more likely to be uninsured or Medicaid insured, where CRC screening prevalence estimates are 40 and 25% lower than privately insured adults, respectively.[18, 107]

Although people who are uninsured or Medicaid insured have especially suboptimal CRC screening use, the majority of people who are in need of CRC screening have private or Medicare insurance, as most people 50 years and older have these insurance types. [112] Unfortunately, disparities are observed in these groups as well studies of elderly Medicare recipients and people treated at Veterans Affairs clinics, with presumably equal access to care, report lower CRC screening adherence among black and Hispanics relative to whites. [113, 114 115]. Some of these differences may be explained or attenuated after adjustment for socioeconomic status as black and Hispanics have lower educational attainment and income, which independently influences CRC screening even among the

insured. [113, 114] For example, O'Malley reported higher odds of CRC screening for white compared to black Medicare enrollees after adjusting for age and sex (OR=1.51, 95%CI 1.31-1.72); however, after adjusting for socioeconomic factors the association was no longer evident (OR=1.04, 95%CI 0.89-1.22). Additionally, black-white disparities were attenuated after Medicare coverage for CRC screening was expanded, whereas Hispanic-non Hispanic disparities in screening have persisted. [115] [114]

Studies of integrated health systems and private insurance data have reported mixed results examining the association between race/ethnicity and CRC screening. A recent study reported lower CRC screening among blacks and Hispanics compared to Non-Hispanic whites in an organized KPNC screening program where FIT kits were mailed to eligible enrollees (ages 50-75).[91] Another recent study by Wernli et al examined the cumulative incidence of CRC screening uptake for enrollees who turned 50 years in a mixed model health system (Group Health in Washington) by race/ethnicity, however, the large majority (80%) of study participants were non-Hispanic whites and only small numbers of Hispanics (n=2,578) and blacks (n=2,781) were included. [116] Insurance and policies related to CRC screening are expounded upon in subsequent sections.

Other factors related to racial and ethnic barriers to cancer screening include lack of awareness, fear of finding cancer, fear of the test, as well as cultural barriers, such as fatalism. For example, among low income women, black women were less likely to report having received a colonoscopy in the past 10 years and lower awareness of the

need for CRC screening than whites. [117] Additionally, language barriers may be a particular issue for minorities whose first language is not English. Studies examining reasons for not being screened among Asian Americans report that lack of awareness and "not having any health problems/symptoms" were the most common reasons for not being screened; foreign-born Asian Americans are especially prone to view cancer screening as response to symptoms/problems as opposed to a preventive measure.[118, 119] Additionally, Asian Americans may seek healthcare from traditional practitioners or physicians that speak the same language, who may be less likely to recommend CRC screening.[120] Of note, lower screening among Asian Americans may be more likely attributed to factors other than access to care, such as cultural and language barriers, as they are more likely to have more recently immigrated to the US. [23] Specific barriers described among Hispanics include embarrassment and fear of tests as well as perceptions that screening is not needed in the absence of symptoms.[121] [122, 123] In previous studies, Latinos were more likely than whites to report that they would delay stool-based testing if a doctor gave it to them. [124]

Other Individual Factors Related to Colorectal Cancer Screening

Overall, CRC screening adherence is similar in males and females, [20, 59] though at least one study reports higher CRC screening among elderly men compared to women of similar age and another report indicates lower CRC screening uptake among younger females in an integrated health system.[125] [116]

CRC screening use increases with age. For example, in 2010, 52.0% of 50-59 year-olds were up-to-date with CRC screening compared to 64.0% in people 60-69 years of age and 66.2% for people 70-75 years of age. [59] CRC screening prevalence in people aged 50-54 years is particularly low (43%) compared to people 55 years and older (62%).[108] The lower screening prevalence among younger populations has been gaining more attention with recent reports indicating increasing CRC rates among people 50-55 years, which is in contrast to generally declining CRC incidence in other age groups.[126] It is possible that younger individuals are more likely to be uninsured or have Medicaid insurance, have fewer encounters with healthcare providers, less awareness of the need for CRC screening, and have more logistical barriers such as taking time off work.[127-130] Younger adults are less likely to receive adhere to physician recommendation for CRC screening.[111, 131] Additionally, older people have had a longer window or more time for opportunistic endoscopic tests whether for CRC screening or related to symptoms.

Studies of the association between CRC risk factors and CRC screening receipt reported mixed results. A meta-analysis of 23 studies found no overall association between BMI and CRC screening, though among white females, CRC screening was significantly lower in obese females (OR=0.87 to 0.73 for class I-III obesity) compared to women with normal weight.[132] People with self-reported diabetes also have lower CRC screening utilization compared to people without this condition.[133] CRC screening was found to be higher among former smokers but lower in current smokers.[133, 134] People with family history of CRC are more likely to be screened[135], but family history does not appear to mediate the association between other covariates and CRC screening.[116] Previous cross –

sectional studies report higher CRC screening among non-CRC cancer survivors compared to people who have not been diagnosed with cancer, [136-139] though, at least two studies, one of survivors of hematopoietic transplants and another of breast cancer survivors, reported no association.[140, 141]

Lack of awareness is one of the most common patient-reported barriers for not receiving CRC screening. [20 142] It has been reported that educational tools and patient navigators may increase the knowledge and use of CRC screening. [143, 144] Other barriers include fear of finding cancer, fear of the screening tests in general and particularly of colonoscopy which is associated with discomfort and risk of colon perforation.[22, 25] As noted above, some of these behavioral and cultural factors vary and are more prominent in certain racial/ethnic minorities. Logistical barriers to CRC screening include lack of transportation, the need for a chaperone, and inability to take time off of work, all of which may vary by socioeconomic status. [22, 25]

National, State and Local Policies Related to Colorectal Cancer Screening

There are national, state, and local policies that influence CRC screening. First, national policies will be discussed followed by state and local strategies. The majority of national policies on CRC screening have addressed coverage of CRC screening among Medicare patients and more recently, coverage among privately insured adults. Such policies have the potential to influence a large number of people, especially considering that over 65% of people who are in need of CRC screening have either private or Medicare insurance. [112]

In January 1998, Medicare, the health insurer of over 95% of people 65 years and older, began covering stool-based testing and barium enemas for average-risk adults and screening colonoscopy for enrollees who had higher CRC risk, including those with family history.[145] In July 2001, Medicare expanded coverage for screening colonoscopies to average-risk adults, though enrollees were still responsible for up to 20% of the cost of colonoscopy, a substantial expense for some enrollees, especially those with fixed incomes. For example, in 2008, the Medicare average allowable charge for colonoscopy was $642- $842 [146]. Among Medicare recipients ≥65 years, people without supplementary insurance have lower odds of CRC screening (endoscopy OR=0.42, 95%CI 0.35-0.51, FOBT OR=0.71, 95%CI 0.54-0.92) compared to those with supplementary insurance.[147]

Among privately insured adults, the coverage and cost of colonoscopy may vary more widely. For example, a colonoscopy may cost over $2,000 as reimbursement may vary widely across geography, insurers, providers, and indication.[148] The direct costs in terms of co-pays, deductibles, as well as indirect costs, including lack of paid time off work, transportation, and inability to find a chaperone following a colonoscopy, may contribute to the disparities CRC screening by SES and race/ethnicity.[22] Income is also an independent predictor of CRC screening regardless of insurance status[20] as financial barriers have been noted even among the insured and may contribute to racial/ethnic disparities in CRC screening as well. [113, 147] Additionally, people with higher SES may have greater awareness of and place higher value on cancer screening compared to people with lower SES.[113, 149 115]

In 2010, the Affordable Care Act (ACA) was enacted in an attempt to improve access to and reduce the cost of healthcare in the United States. [150] The ACA had three main provisions that may influence CRC screening. The first is the creation of federal health insurance marketplaces to allow people who do not qualify for Medicaid or employer-based private health coverage to purchase insurance. Second, the ACA expanded Medicaid, though states were allowed to opt out of this expansion. These two provisions were recently rolled out (January 2014), and it is too early to determine how this might influence CRC screening. The third provision required private health insurers to cover US Preventive Services Task Force (USPSTF) recommended services with "A" or "B" ratings and remove patient cost-sharing, including deductibles, co-insurance and co-pays. This provision was extended to new and renewed private health plans after September 2010 and cost-sharing was eliminated on January 1, 2011. The Center for Medicare and Medicaid Services (CMS) has also removed cost-sharing for CRC screening tests under its authority.[151] It is unknown if uptake of CRC screening has changed since the ACA's cost provision went into effect.

There are several state-level CRC screening policies and programs that may influence CRC screening by race/ethnicity and SES. CRC screening policies vary across Medicaid plans, state-administered programs that provide insurance for disabled and low-income adults. Some Medicaid programs may only cover stool-based tests and Medicaid reimbursement rates for CRC screening, which has been shown to moderately increase CRC screening use, also varies substantially by state. [152] Whether these state-level

policies influence racial disparities is not clear. The poverty threshold for Medicaid-eligibility also varies by state, for example Connecticut's poverty threshold is 155% compared to 18% in Alabama, and some states have opted out of expanding Medicaid, which may lead to increasing racial disparities in CRC screening in these states.[153] Additionally, some states may have state cancer control plans with varying programs and policies covering CRC screening for uninsured adult. For example, beginning in 2003, Delaware funded a program to pay for CRC screening tests and nurse navigators for the uninsured, increasing the percentage of individuals who had ever received colonoscopy. [154] In 2009, the Center for Disease Control launched their Colorectal Cancer Control program, which provided funding to 29 states and tribes over 5 years to increase CRC screening in lower SES individuals. Data on whether this has influenced disparities by race/ethnicity and/or SES has not yet been reported. [155]

Local-CRC screening policies may also influence CRC screening. For example, New York City formed a city-wide coalition in 2003 to increase CRC screening use, primarily with colonoscopy.[156] There were several facets of this program, including campaigns to increase CRC awareness among patients, educational tools for healthcare providers, patient navigation programs, outreach to specific communities and a direct colonoscopy referral line. During this time, CRC screening prevalence increased from 42% in 2003 to 70% in 2014 and racial/ethnic disparities were diminished.[156]

System Barriers and Population Health Management Approaches to CRC Screening

There are several system or organizational-level barriers within healthcare systems that influence CRC screening. Many of these factors interact with the dynamic screening process within an organized setting, and a brief overview of this process is provided below. [157, 158 159] The screening process begins with recruitment of an eligible patient which may occur during a healthcare visit (typically a primary care visit) or through reminders or self-referral. From this point, a person can either be screened outside or within a visit. Screening outside a healthcare visit may occur if healthcare providers mail patients stool-based kits or within a visit if a person is given a stool kit complete at home and return via mail. If one of these tests is positive, patients complete the screening process with a colonoscopy to identify and remove suspected pre-cancerous lesions. If the initial screening procedure is colonoscopy, patients are typically referred to a specialist after a primary care visit. An appointment with a specialist must be made and kept and the test must be performed. Sigmoidoscopy can occur within an office visit, but if lesions are found, patients are referred for a colonoscopy.[74] If a benign or malignant neoplasm is identified and removed via endoscopy, recommended surveillance tests need to be planned and conducted.

Screening with a population health management (PHM) approach may address some of the organizational barriers to CRC screening. There are several definitions of PHM, but it is often described as a coordinated and preventive approach to health care with an aim to increase population health.[160] An organized approach to preventive care is a key component of PHM as is a focus on preventive (as opposed to reactive) care.

In order for a PHM approach to work, an organization must be able to identify patients who are in need of CRC screening, which may be problematic for some healthcare systems that do not have the resources to identify and track patients. Further, reminder systems increase screening uptake and directly mailing stool-based kits to patients in a systemic fashion has been shown to improve adherence to recommendations.[159, 161] Physician recommendation is one of the most important predictors of CRC screening. The value of physician recommendation can be further enhanced by using electronic reminder systems, visits devoted to preventive health, as well as payment incentives.[120, 162] Because inter-organizational coordination is necessary for colonoscopy, there are more opportunities for system break downs, which can create additional barriers to screening. FIT and gFOBT can either be given to patients during a visit and be done at home or be mailed to patients, bypassing a referral or even a healthcare visit. This approach lends itself to fewer barriers, however, a healthcare organization must be equipped to handle this process. [159]

Research on physician pay-for-performance incentives indicate that individual incentives are more effective than group incentives.[159] For example, CRC screening referrals were found to increase when physicians were given an end of the year bonus for screening referrals in a managed care plan.[163] The influence of other organizational factors including the volume of patients and the number of physicians within a healthcare practice is not clear.[159]

Most CRC screening procedures in the US are opportunistic; i.e. these procedures are associated with a healthcare encounter or physicians visit, and are not as part of an organized or PHM approach. This may contribute to some variations in CRC screening by race/ethnicity and socioeconomic status as racial/ethnic minorities and persons with lower income and education are less likely to have insurance, a usual source of care and have fewer healthcare encounters.[164]

In the United States, Kaiser Permanente health systems in both Southern and Northern California launched organized screening programs in 2006 and 2007, respectively. The program involves mailing fecal immunochemical test (FIT) kits to the homes of screening eligible enrollees annually, and use of patient and provider reminder systems At Kaiser Permanente Northern California (KPNC), CRC screening adherence increased from 37% in 2005 to 79% in 2011, resulting in one of the highest screening prevalence estimates in the nation.[165] However, a recent study[39, 91] reported that despite overall high level of coverage within KPNC the CRC screening overall, colonoscopy and FOBT use were lower among blacks and Hispanics compared to Non-Hispanic whites. The disparities actually grew following the program implementation.

Summary

In summary, colorectal cancer screening is an important aspect in preventing and detecting CRC, one of the most common cancers in the United States. However, CRC screening utilization is suboptimal, particularly in racial and ethnic minorities and in individuals who have lower SES.[19, 20, 23, 59] There are numerous initiatives and efforts aimed at improving CRC screening utilization at the national, regional, health-system and

local level that would ostensibly mitigate socioeconomic and racial/ethnic disparities in CRC screening. However, information regarding response to these programs in different racial/ethnic and SES-specific groups is limited. Among people who are regularly screened for CRC there is a small, but appreciable, risk of interval cancers. An important determinant of interval cancer is the quality of the last colonoscopy. To-date few studies have examined the relationship between race/ethnicity and interval cancers, as well as quality of colonoscopy in different racial and ethnic groups.[32]

Chapter 3 Data Sources and Study Framework

Specific Aims and Data Sources

This dissertation is a comprehensive examination of sociodemographic disparities in CRC screening, interval cancers and quality of colonoscopy. The first two aims examined disparities in CRC screening by sociodemographic factors. *Aim 1* examined whether there were changes in CRC screening prevalence by race/ethnicity and socioeconomic status in response to the Affordable Care Act's provision to remove costs among privately and Medicare insured adults. *Aim 2* examined if there were racial/ethnic disparities in CRC screening uptake among newly eligible enrollees of KPNC, an integrated health system with an organized approach to screening. The main factor of interest in this Aim is race/ethnicity. *Aim 3* examined if the risk of interval CRC varies by race/ethnicity and if quality of colonoscopy, as measured by a physician's polyp detection rates (PDR), accounts for some of these variations.

Three different data sources and study designs were used for each aim. Aim 1 was a cross-sectional analysis of the National Health Interview Survey data. Aim 2 was a retrospective cohort study of KPNC enrollees. Aim 3 was a case-control study using linked SEER-Medicare data. Each Aim is discussed in further detail below and directed acyclic graphs (DAGs) are used to describe the potential associations, confounding and intermediate factors in each aim.[166] The specific statistical analyses, variables used as well as limitations for each study for each study are discussed in Chapters 4, 5, and 6.

Data Source for Aim 1: National Health Interview Survey

Data from 2008 and 2013 NHIS was used for Aim 1. The NHIS is a cross-sectional, household, in-person survey measuring general health metrics among non-institutionalized adults. The survey is conducted annually by the US Department of Human Services since 1957.[108] NHIS is an area-based probability survey designed to be representative of its target population which is defined as dwelling units where civilian non-institutionalized people reside. This target population is divided into 1,900 geographically defined called primary sampling units (PSU's), which may represent metropolitan areas, counties or groups of counties. The current NHIS design samples 428 of these 1,900 PSU's in order to reduce costs and improve efficiency of in person-interviews. Households are then sampled from each PSU and a household questionnaire is administered to collect information on household characteristics, including household composition. A separate family component of the survey includes questions on the family member characteristics, family structure, and household income. One adult from the household is then randomly selected to obtain a representative weighted sample. The core sections of the adult survey include demographics, socioeconomic factors including income and education, access to care, general health functioning and diagnosis, and utilization of healthcare. Cancer control supplements, which are funded and designed by the National Cancer Institute, include questions on cancer prevention behaviors such as diet, nutrition, smoking, as well as cancer screening. The cancer control supplement is conducted every 5 years (e.g., 2000, 2005, and 2010) and an abbreviated cancer control supplement is administered 3 years later (e.g., 2003, 2008, and 2013).

In 2013 the household response rate was 75.7%, and the family response rate was 99.0%. Among families that responded, 81.7% of adults completed the interview leading to a total response rate of 61.2%. Household non-response may be due to inability to contact after multiple attempts, refusals, and language barriers. Adult's non-response was due to time constraints, privacy concerns, and hard refusals (e.g., people were not interested, or did not want to be bothered). [167]

The primary outcome of this study is self-reported receipt of guideline-concordant CRC screening defined as colonoscopy in the past 10 years, at-home fecal occult blood test (FOBT) in the past year, or flexible sigmoidoscopy in the past 5 years with FOBT every 3 years for people aged 50-75.[17] Respondents are initially asked if they have ever received a colonoscopy, stool based test or sigmoidoscopy and subsequently asked about the timing and reason for these tests.

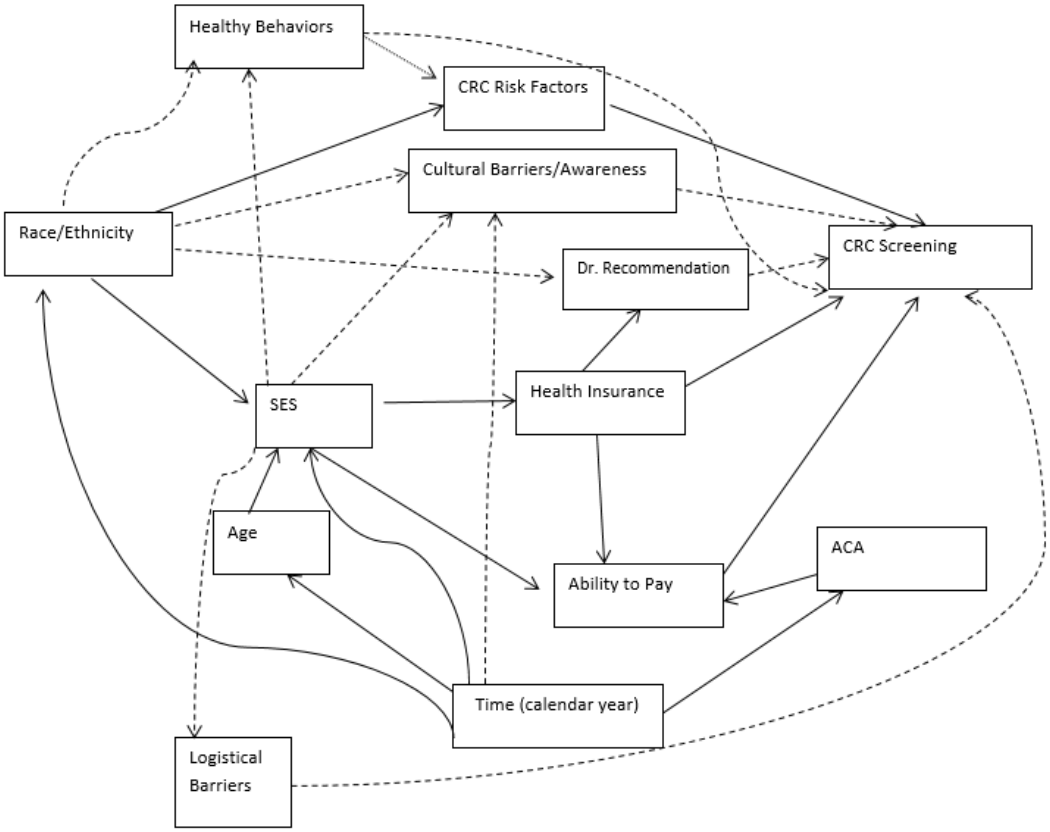
Study Population and Framework for Aim 1

The 2008 NHIS data will be used to measure cancer screening prevalence in the pre-ACA period. The 2013 data will be selected for comparison as these provide the most up to date information following the implementation of the ACA cost provision. Data from the 2010 NHIS will not be utilized as the ACA had just been enacted. The primary outcome of the study is receipt of CRC screening according to the most recent USPSTF recommendations, published in 2016.[70]

Because the ACA limited cost-sharing for privately insured and the Center for Medicare and Medicaid Services also approved this provision for Medicare recipients, analyses

were restricted to respondents with private insurance, Medicare or both at the time of the survey. Dual (Medicare and Medicaid) eligible subjects will be included in the Medicare group, as they represent a small proportion of respondents (3.1% of CRC-screening eligible) and sensitivity analyses removing dual eligible persons will be conducted. Based on the previous literature, as outlined in Chapter 2, the following DAG (**Figure 3.1)** will be used to determine confounders and unmeasured confounders in Aim 1. Unmeasured confounders and paths are indicated using dotted lines.

Figure 3.1 Proposed DAG for Aim 1



Note: Time doesn't cause SES, Race/Ethnicity or Awareness, however, these factors change over time.
Family history is included in the CRC risk factors box

---> Dotted lines indicated unmeasured confounders and confounding paths

Abbreviations:
CRC=Colorectal Cancer
ACA=Affordable Care Act
SES=Socioeconomic Status
Dr.=Doctor

Data Source for Aim 2: Kaiser Permanente Northern California

Data from Kaiser Permanente Northern California (KPNC) was used in Aim 2. KPNC is an integrated health system that annually serves approximately 3.8 million people, of those approximately 900,000 are between 50 and 80 years of age. The care is delivered in 17 medical centers across the Northern California/San Francisco Bay area. KPNC is the health insurer of 22% of Northern California's total adult population aged 25-64 years.[168] In addition to serving commercially insured enrollees, KPNC insures and provides healthcare for Medi-Cal, California's Medicaid program, and Medicare Advantage recipients. KPNC is unique in terms of its overall integrated approach to care and its organized approach to CRC screening. In 2007, KPNC launched an organized CRC screening program with a dedicated management team to identify, remind and conduct an outreach component where FIT kits are mailed to average risk adults annually. If a kit is not returned, the patient is reminded in-person during an office visit, or via telephone. There is also an in-reach component whereby records of screening-eligible adults are flagged to identify enrollees who are not up-to-date for CRC screening.

Data used in this study was extracted from the Virtual Data Warehouse (VDW), a repository of standardized data that incorporates laboratory records, enrollment information, demographics, death index, tumor registries, pharmacy, encounters (including dates of service), and vital signs. A personal identifier is used to capture information for each patient, though for the purposes of this project, all data will be de-identified. Individual level income and education are not recorded in the KPNC medical system but area-based census data on education and income are available.

Study Population and Framework for Aim 2

A retrospective cohort study design was used to examine receipt of CRC screening among KPNC enrollees who are newly screening eligible and at average-risk for CRC. KPNC enrollees who turned 50 years between January 1, 2007 and December 31, 2012 were selected from the KPNC VDW.

The DAG considered in Aim 2 is similar to that used in Aim 1. In the KPNC system where FIT kits were mailed to enrollees at no cost, and for this reason the ability to pay and logistical barriers should not play a role and were removed from the DAG (**Figure 3.2**). Further, because everyone in the study is entering at the same time, age is also removed from the DAG. Although gender is not associated with CRC screening overall, within the integrated health systems, women are less likely to be screened compared to men[116], so gender is added to the DAG for Aim 2. Physician recommendation was retained in the DAG to account for KPNC in-reach component, though the magnitude of the physician recommendation/CRC screening association is thought to be lower in the KPNC population compared to systems with opportunistic screening. Unmeasured confounders and confounding paths are indicated with dotted line.

The anticipated sample size of this study was 138,799 people with 78,728 non-Hispanic whites, 11,328 blacks, 23,386 Asians, 24,160 Hispanics, 489 Native Americans and 708 people who identified with multiple race/ethnicity groups (**Figure 3.3**). Based on preliminary calculations using the National Cancer Institute's Power V3.0, 80% power will be achieved if the ratio-based effect size for blacks, Asians, Hispanics and Other

race/ethnicities (relative to whites) is stronger than 0.94, 0.95, 0.95, and 0.80 based on the analytic study size estimates. [169]

Figure 3.2 Proposed DAG for Aim 2

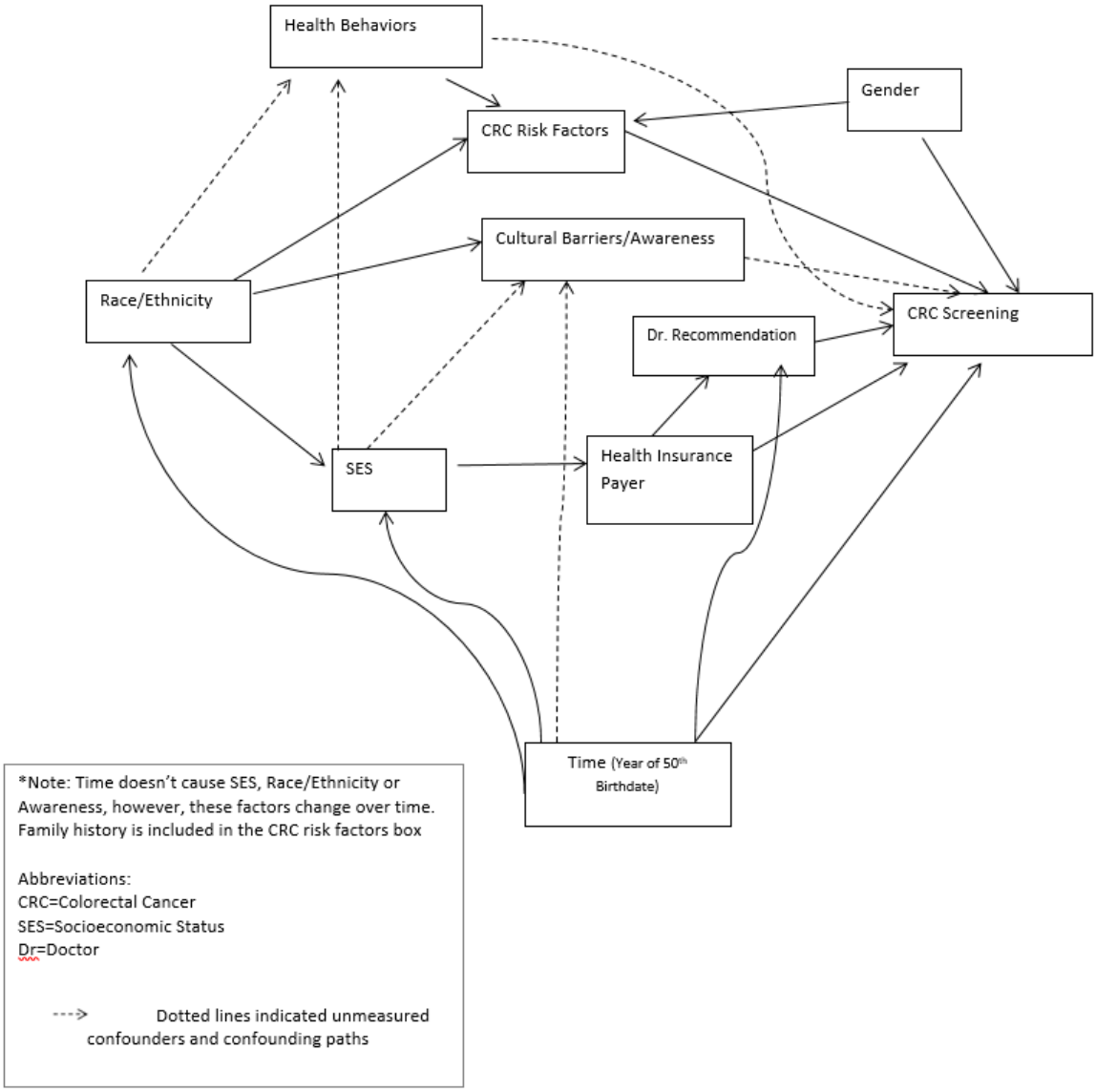
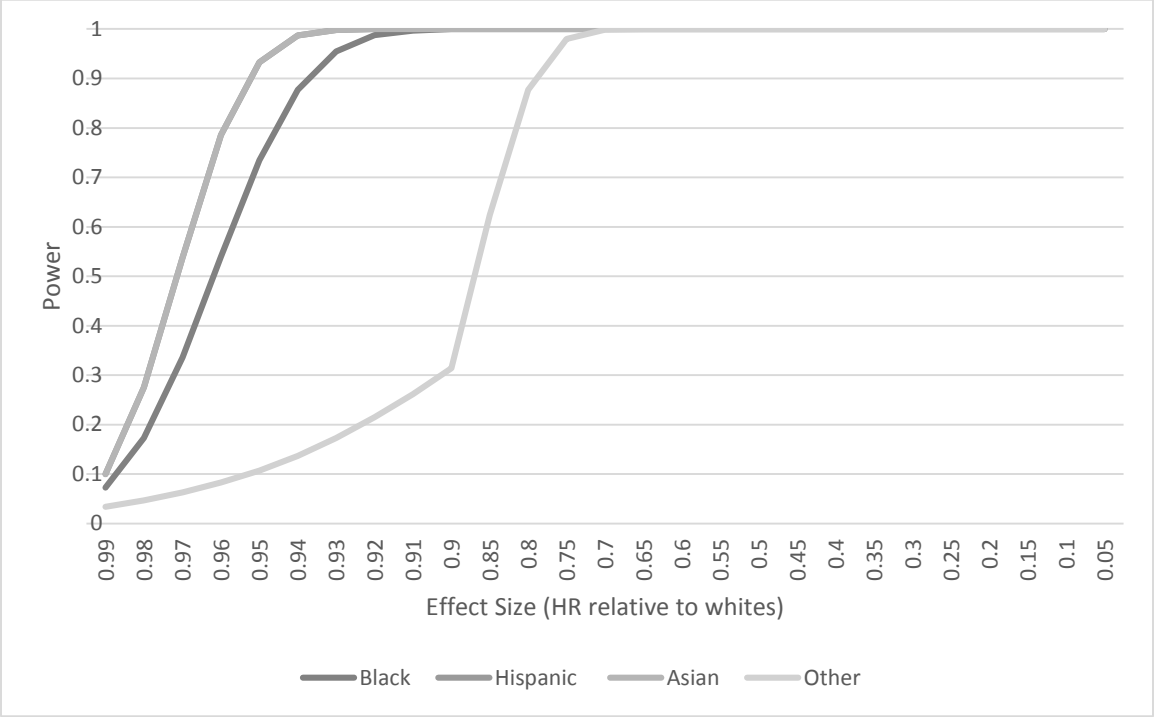


Figure 3.3 Power Calculations for Aim 2



*Note Hispanic and Asians have similar sample sizes as a result power calcualtions are very similar and line markers ovelap. Native American and multiple races also have similar sample sizes, as a result power calculations are similar and are indicated with the "other category". Abbreviation: Hazard Ratio (HR)

Data Source for Aim 3: SEER-Medicare

Aim 3 of this dissertation utilized Surveillance Epidemiology and End Results (SEER) registry data that are linked to Medicare claims data, hereafter referred to as SEER-Medicare. SEER is a collection of 18 population-based cancer registries, covering approximately 28% of the 2010 US population.[170] The SEER program began with 9 registries (Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, and Utah) in 1973-1975 and in 1992; Los Angeles, San Jose- Monterey, rural Georgia and Alaska Native registries were added (SEER13). In 2000, SEER expanded to greater California, Kentucky, Louisiana, New Jersey and greater Georgia (SEER18). SEER registries have a larger proportion of foreign born people, Native Americans, Hispanics and Asians compared to the general population of the United States.

SEER registries collect standardized information on patient demographics, tumor characteristics, first course of treatment, and vital status (including cause of death). The National Cancer Institute (NCI) linked SEER data with Medicare claims. Medicare is a federally-funded health insurance plan for elderly adults covering approximately 97% of persons aged ≥65 years.[171, 172] The majority of Medicare recipients are enrolled due to age entitlement (84%), though people with End Stage Renal Disease or medical disability are also eligible to receive Medicare benefits. All Medicare recipients are entitled to Part A insurance benefits, which cover inpatient hospital care and 96% of Medicare recipients enroll in Part B, which covers outpatient services and requires a monthly premium payment. Medicare enrollees also have a choice between fee-for-service (FFS), and health maintenance organization (HMO) plans. In the HMO plans care is capitated, and

the data on specific services, including colonoscopies, are not captured in Medicare claims.[173] For these reasons, we will restrict our analyses to enrollees with Medicare A and B in FFS plans in order to adequately capture colonoscopy receipt. As of 2015, 71% of Medicare enrollees had FFS. [173]

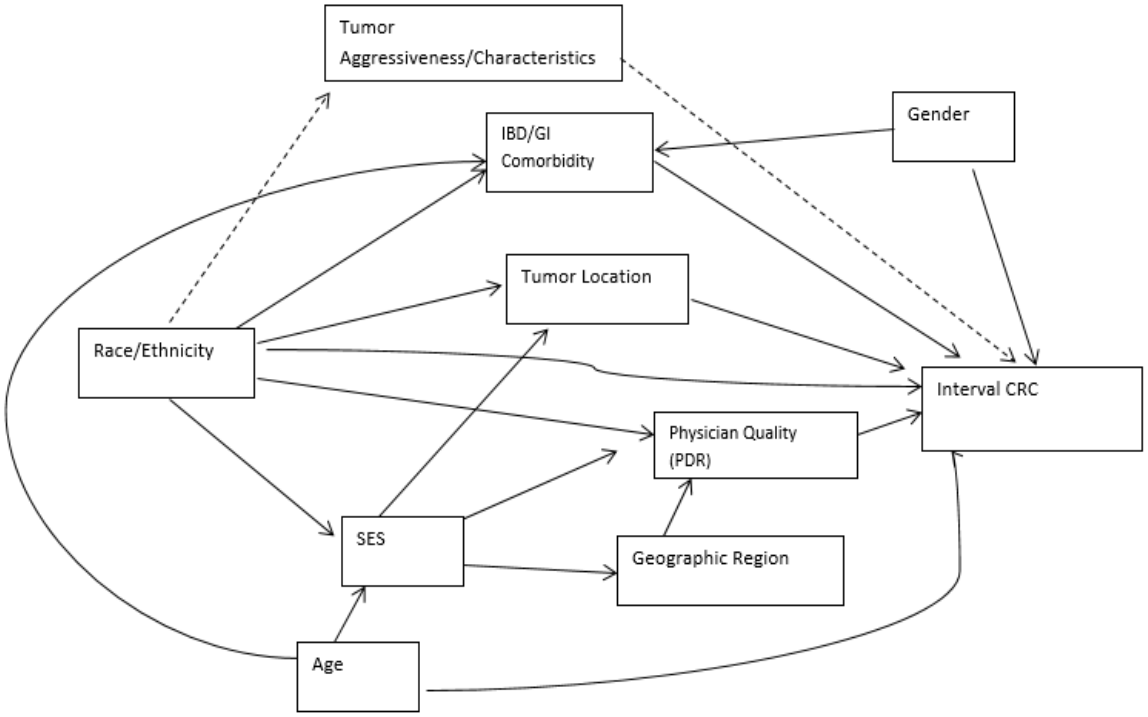
Study Population and Framework for Aim 3

SEER is linked with Medicare data based on patients' social security number, name, sex and date of birth. Among SEER cases aged ≥65 years, 94% are linked to Medicare, 3% do not have adequate information for the linkage and 3% do not have Medicare insurance. [172] The two data sources are linked every two years and in each biannual update, the SEER-Medicare dataset is rebuilt to account for newly reported cases. SEER-Medicare contains an enrollment file with monthly enrollment status, demographic and tumor characteristic information. The healthcare claims files include outpatient, physician non-institutionalized, and MEDPAR or hospitalization files. The SEER-Medicare database also maintains a 5% random sample of cancer-free Medicare FFS beneficiaries to allow comparisons with the cancer patients. The 5% random sample was updated in November 2014 and in the current sample, any persons diagnosed with any form of cancer, including CRC, through December 31, 2011 were removed. In the cancer file, there is a flag if someone was once in the 5% random sample so that they can be added back into initial disease-free cohort. There were 186,251 cancer patients initially in the 5% random sample of those 27,379 had CRC and will be added back into the sample.

This will be a case-control study, with incidence density sampling of controls, using SEER-Medicare data between 2002 and 2011. The source population is Medicare recipients with Parts A and B coverage, who are eligible for Medicare based on age (i.e., over 65 years of age), and reside in the SEER-areas. The framework for evaluating confounders and intermediates is displayed in **Figure 3.4**.

The power of this study, 2770 cases and 4 controls per case and a baseline risk of interval CRCs equals 0.00315, is displayed in **Figure 3.5** .[169] Our study will have at least 80% power to detect an effect size of 1.20 or greater among blacks, 1.70 or greater among Hispanics,1.40 or greater among Asians and other race/ethnicities.

Figure 3.4 Proposed DAG for Aim 3

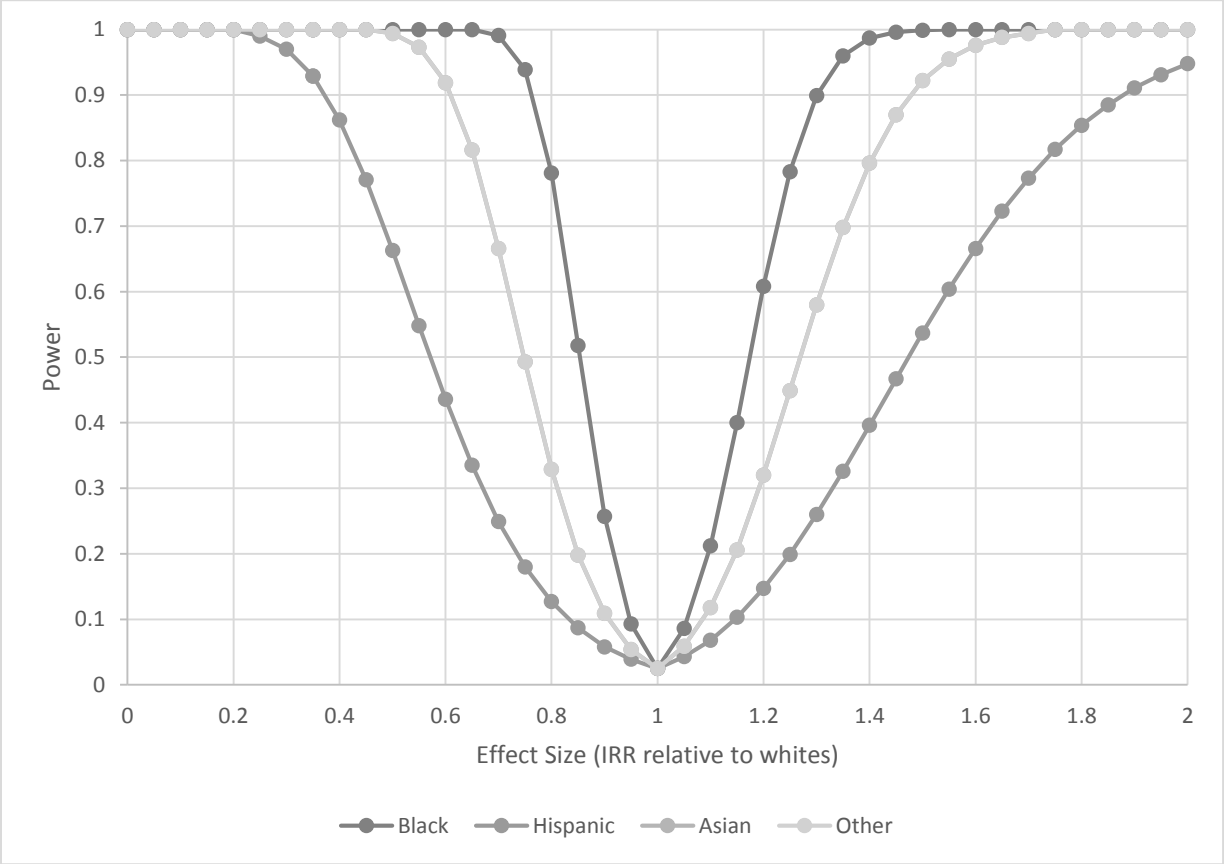


Note: Tumor Characteristics includes tumor location. Tumor aggressiveness/characteristics include MSI status, BRAF mutations. Tumor location can be measured but other characteristics are not available in SEER-Medicare.

Abbreviations:
PDR=Polyp Detection Rate
CRC=Colorectal Cancer
SES=Socioeconomic Status

---> Dotted lines indicated unmeasured confounders and confounding paths

Figure 3.5 Power Calculations for Aim 3



*Note: Lines for other races and Asians overlap due to similar sample size

Chapter 4 Changes in CRC screening before and After the Affordable Cancer Act (Aim 1)

Title: Elimination of cost sharing and receipt of screening for colorectal

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Abstract

Background: The Affordable Care Act (ACA) cost-sharing provision aimed to reduce financial barriers for preventive services, including colorectal cancer (CRC) screening among privately and Medicare insured persons. Whether the provision has affected CRC screening prevalence is unknown. This study investigated if CRC screening prevalence among privately and Medicare insured adults by race/ethnicity and socioeconomic status (SES) changed before and after the ACA.
Methods: Data on privately and Medicare insured adults from 2008 (before ACA) and 2013 (after ACA) National Health Interview Surveys (NHIS) were used. There were 15,786 adults aged 50-75 years in CRC screening analyses. Changes in guideline recommended screening between 2008 and 2013 by race/ethnicity and SES were expressed as prevalence difference (PD) and 95% confidence intervals (CI) adjusted for demographics, insurance, income, education, BMI, and having a usual provider.
Results: Overall, CRC screening prevalence increased from 57.3% to 61.2% between 2008 and 2013 ($p<0.001$). Unadjusted CRC screening prevalence increased in blacks and non-Hispanic whites, but not in Hispanics. Adjusted CRC screening prevalence during the corresponding period increased in low income (PD=5.9, 95% CI 1.8, 10.2), least educated (PD=7.2, 95% CI 0.9, 13.5), and Medicare insured persons (PD=6.2, 95% CI 1.7, 10.7) but not in high income, most educated, and privately insured respondents or in any racial/ethnic group.
Conclusions: Increases in CRC screening prevalence between 2008 and 2013 were modest and confined to respondents with lower educational attainment and income. These findings may in part reflect the ACA's removal financial barriers. However, there was no significant increases among Hispanics, likely as a result of patient-reported obstacles to CRC screening other than costs.

Introduction

The 2010 Affordable Care Act (ACA) required private health insurers to cover US Preventive Services Task Force (USPSTF) recommended services with "A" or "B" ratings and remove patient cost-sharing, including deductibles, co-insurance and co-pays. This provision was extended to new and renewed private health plans after September 2010 and cost-sharing was eliminated on January 1, 2011.[150] The Center for Medicare and Medicaid Services (CMS) has also removed cost-sharing of some preventive services for Medicare recipients under its authority.[151] Patient costs were eliminated with the hope of improving access and utilization of 45 preventive services, including screening for cancer, as cost is a recognized barrier even among the insured.[113 114, 147] The cost of some cancer screenings, particularly colonoscopy, the most common type of colorectal cancer (CRC) screening test, is substantial. For example, in 2008, the Medicare average allowable charge was $642- $842 for colonoscopy[146], though the cost of colonoscopy may be well over $2,000 as prices for these procedures vary widely across geography, insurers, provider and indication.[148] Prior to the ACA, Medicare enrollees without supplemental insurance were responsible for up to 20% of the allowable charges, and privately insured persons may have been responsible for a range of costs including co-insurance, co-pays and meeting deductibles.

In recent years, CRC screening prevalence has also stabilized after steep increases between 2000 and 2008.[20, 107] Additionally, there are several groups with lower CRC screening uptake, including those with lower incomes, educational attainment and racial/ethnic minorities.[20, 107] It is unknown if uptake of CRC screening has changed since

the ACA's cost provision went into effect. We evaluated changes in these preventive measures between 2008 and 2013 using the data from the National Health Interview Survey (NHIS) according to race/ethnicity and SES to determine if the groups who are in the most need of CRC screening benefited from this provision.

Methods

Study Population

Our study utilized data from 2008 and 2013 NHIS, a multi-staged cross-sectional household in-person interview survey administered among the non-institutionalized population of the United States.[56] We used 2008 data to measure cancer screening prevalence in the pre-ACA period. The 2013 data were selected for comparison as these provide the most up to date information following the implementation of the ACA cost provision. Data from the 2010 NHIS were not utilized as the ACA had just been enacted. There primary outcome of the study was receipt of CRC screening according to the 2008 CRC USPSTF screening recommendations, respectively.[70]

Because the ACA limited cost-sharing for privately insured and CMS also approved this provision for Medicare recipients, analyses were restricted to respondents with Private, Medicare or both (Medicare plus Private) at the time of the survey. Dual (Medicare and Medicaid) eligible subjects were included in the Medicare group, but represented a small proportion of respondents (3.1% for CRC-screening eligible). Analyses removing dual eligible persons did not alter results. There were 16,433 respondents aged 50-75 years with Medicare and/or Private insurance at the time of the interview. Those who reported

a history of CRC (n=138), were missing CRC history (n=27) or CRC screening (n=482) data were excluded, leaving 15,786 respondents available for analyses.

Measures

Receipt of guideline-concordant CRC screening was defined as: colonoscopy in the past 10 years, at-home fecal occult blood test (FOBT) in the past year, or flexible sigmoidoscopy in the past 5 years with FOBT every 3 years for people aged 50-75.[17] Primary independent variables of interest were year of survey (2013 versus 2008) and race/ethnicity (Hispanic, non-Hispanic White, non-Hispanic Black, Other) as well as socioeconomic factors (SES) including insurance type (Medicare, Private, or Medicare plus Private), annual household income (low <$35,000, medium $35,000-$74,999 and high >$75,000), and education (< High School (HS) or General Educational Diploma (GED), HS or GED only, some college, and at least a college degree). Household income cut points were determined *a priori* based on income tertiles in our study population. Several covariates were considered based on previous studies of cancer screening determinants;[174] these included age, sex, immigration status (US born vs. foreign born), having a usual source of preventive care (yes/no), and body mass index (BMI), which was classified as underweight, normal, overweight and obese according to the World Health Organization criteria.[175]

Statistical Analysis

Weighted prevalence estimates, accounting for the NHIS sample design and chi-square tests were used to assess changes in screening by year (2013 versus 2008). Adjusted prevalence difference (PD) and 95% confidence intervals (CI) of CRC

screening were estimated using logistic regression models with predicted marginal probabilities.[176] Prevalence Ratios (PR) were also estimated using predicted marginal model probabilities to present relative differences in CRC screening. Adjusted models comparing 2013 to 2008 screening prevalence were stratified by insurance, income, race/ethnicity and educational attainment to examine potential differences in PDs across these groups. We also examined whether disparities narrowed by comparing PDs within sociodemographic groups in 2008 and 2013. Collinearity among independent variables was assessed and none was detected. Model fit was assessed with Hosmer-Lemeshow test. Two-way interaction terms between survey year and each covariate was assessed and none was observed. All models were constructed using data on respondents with non-missing covariate or outcome data.

Four sensitivity analyses were conducted. First, we compared respondents who indicated their tests were for routine/preventive (as opposed to diagnostic) reasons with respondents without screening to assess if associations were similar to those observed in the primary analyses (i.e., using screening for any reason as the main exposure of interest). Second, we examined changes in screening patterns between 2003 and 2008 (i.e., in the 5 years that preceded our study) to determine if changes observed between the 2008 and 2013 surveys possibly represented a continuation of an on-going trend. Third, changes in CRC screening among our study population was compared with changes in the uninsured (n=1,723) between 2008 and 2013, as this group was not as likely to be influenced by the ACA cost-sharing provision. Fourth, we used five multiple imputations to estimate income values among respondents missing this data item according to NHIS guidelines and compared them with our main findings.[177] Imputed income was

conditional on a family's racial/ethnic composition, receipt of welfare benefits, age distribution, health insurance and numerous comorbid and activities of daily living metrics. The multiple imputation procedure accounted for both the variation in the beta estimates associated with predicted income and the uncertainty of the imputed income value. All statistical tests used 2-sided p-values with an alpha of 0.05 in accordance with previous studies examining cancer screening patterns over time using NHIS data.[20, 107] All analyses were conducted with SAS version 9.4 and *SAS callable SUDAAN* version 9.0.3.

Results

Among the 15,786 CRC screening eligible respondents, the average age was 61.6 years, and the majority of respondents were non-Hispanic white (78.6%) and privately insured (61.8%) (**Table 4.1**). Among the CRC screening eligible population, the proportion of respondents who had Medicare insurance, higher income (≥$75,000), higher education (completed college) and who were older (60-75 years) was higher in 2013 compared to 2008 (**Table 4.1**).

Colorectal Cancer Screening Results

Overall, CRC screening prevalence increased from 57.3% in 2008 to 61.2% in 2013 ($p<0.001$) (**Table 4.2**). This increase was statistically significant among blacks (8.8% change, p-value=0.003), non-Hispanic whites (3.3% change, p-value=0.007), low (4.3% change, p=0.024) and middle (3.5% change, p=0.043) income groups, and in Medicare-only (9.8% change, p-value<0.001) and Medicare plus privately (5.9% change, p-value=0.002) insured subjects. No change was observed among privately insured or high

income respondents. In the analyses by educational attainment, CRC screening prevalence increased among respondents who had completed HS or GED only (4.1% change, p-value=0.038). Results adjusted for sociodemographic factors, BMI, usual source of preventive care and immigration status are presented in **Table 4.3**. There were no significant changes in CRC screening for any racial/ethnic after adjustment. The increase in CRC screening was evident in the low income (PD=5.9, 95% CI 1.8, 10.2), Medicare (PD=6.2, 95%CI 1.7, 10.2), and lower educational attainment (<HS PD=7.2, 95%CI 0.9, 13.5 and HS or GED PD=5.3%, 95%CI 1.2, 9.2) groups, but not among higher SES groups.

By screening modalities, overall adjusted colonoscopy use increased from 53.1% in 2008 to 60.6% in 2013 (p-value<0.001) and during the same time period, FOBT declined from 11.0% to 8.7% (p-value=0.001). The adjusted PD for colonoscopy was significantly higher in 2013 compared to 2008 for blacks (PD=8.2%), whites (PD=6.6%), and Hispanics (PD=7.0%) (**Figure 4.1**). Colonoscopy increased across education status, and the three insurance types examined in this study. During the study period, FOBT utilization did not change for respondents of any race/ethnicity, those with lower educational attainment (<HS or GED, completed HS or GED) or low and medium income respondents (**Figure 4.2**), but declined for high income (PD=-3.3, 95%CI -5.6,-0.9), privately insured (PD=-2.2, 95%CI -4.0,-0.4), private plus Medicare insured (PD=-5.4, 95%CI -8.3,-2.5) and those with higher education [(some college (PD=-5.0, 95%CI -7.5, -2.4) college graduates (PD=-3.5, 95%CI -5.9,-1.1)].

Analyses examining differences in CRC screening according to sociodemographic group are presented in **Table 4.4**. Unadjusted black-white differences in screening narrowed over time, where CRC screening was 5.9% and <1% lower in blacks than whites in 2008 and 2013, respectively, though a test for interaction was not statistically significant (p-value=0.087). (**Table 4.4**) Unadjusted CRC screening in Hispanics were 16.4% and 13.8% lower than whites in 2008 and 2013, respectively, but this change was not statistically significant (p-value=0.575) and substantial disparities remained. For people of other racial/ethnicities, CRC screening prevalence was 6.3% and 7.4% lower than whites in 2008 and 2013, respectively. Differences by income group and educational attainment also remained.

Sensitivity Analyses for CRC screening

Analyses restricted to persons reporting CRC screening for routine reasons (77.7% of those reporting CRC screening) are shown in **Table 4.5**. Between 2008 and 2013, adjusted CRC screening prevalence increased across all insurance and income groups, but there were no changes by race/ethnicity. The greatest change in CRC screening was observed among low income and Medicare-only groups, which was similar to the main analyses. In the second sensitivity analyses examining changes in CRC screening between 2003 and 2008 among privately and Medicare insured respondents (**Table 4.6**), the magnitude of change (PD=12.7, 95% CI 10.3-15.0) in the earlier period (2003-2008) was greater than the change observed during our study period (2008-2013). The changes in CRC screening between 2003 and 2008 were observed across all insurance types, income levels and education groups in the adjusted analyses. There were also significant changes in whites and blacks between 2003 and 2008, but not in Hispanics. In the third

analyses examining CRC-screening in eligible uninsured respondents there was a 2.8% (95%CI -3.1-8.7) increase between 2008 and 2013, (**Table 4.7**), which was not statistically significant, but the lack of significance could be related to the smaller sample size of this group. Results from sensitivity analyses using imputed income are shown in **Table 4.7** and were similar to our main findings for race/ethnicity, education, and insurance. However, changes in CRC screening between 2008 and 2013 were no longer statistically significant for low income individuals (PD=2.9, 95%CI -0.2,6.0).

Discussion

In this study of a nationally representative sample of Medicare and privately insured persons, there were modest gains (5.9-7.2%) in CRC screening between 2008 (pre-ACA) and 2013 (post-ACA) overall. By race/ethnicity, increases in CRC screening were observed in whites and even more so in blacks. Increases in CRC were observed among adults with low income and lower educational attainment as well as Medicare-only respondents. Higher prevalence of CRC screening in these groups was attributable to increased colonoscopy as opposed to FOBT which was stable during our study period. Colonoscopy also increased in higher SES groups, but a concomitant decrease in FOBT suggests migration from FOBT to colonoscopy among higher SES groups.[178]

Changes in CRC screening among lower SES groups may, in part, reflect the removal of costs as there are known financial barriers to cancer screening,[113, 147] and the cost of colonoscopy is substantial. [147, 179] Prior to the implementation of the ACA's elimination of cost sharing for preventive services, Medicare enrollees were responsible for up to

20% of allowable charges and along with privately insured, may have been responsible for a range of costs including co-pays and meeting deductibles, posing a challenge to receiving CRC screening,[113, 147] particularly among those with fixed incomes. While our observations are consistent with ACA's removal of financial barriers, it is also possible that increases in CRC screening among lower socioeconomic groups and in blacks may reflect continuation of increasing secular trends which have been observed nationwide as well as in private health plans.[20, 107, 116] It is worth noting that increases in CRC screening prevalence in blacks outpaced that of whites, nearly eliminating CRC differences during this time period in unadjusted analyses, however, there was no difference in CRC screening between these two groups in adjusted analyses, calling to question if such changes were as result of the ACA removal of cost-sharing provision. However, in the previous 5-year period (between 2003 and 2008), there was a significant increase in CRC screening among privately and Medicare insured, however the increase was universal across socioeconomic measures including income and educational status. By contrast, the 2008-2013 change in CRC screening was limited to subjects with lower income and lower levels of education, i.e. the population subgroup that is expected to benefit the most from the ACA. Additionally, the increase in CRC screening among lower SES persons may reflect a greater potential to improve given their lower CRC screening prevalence.

Despite increases in CRC screening for respondents with lower income, Medicare insurance and lower educational attainment, gains in CRC screening were modest, disparities still exist and CRC screening prevalence in all groups are below the 80% by 2018 target set forth by the National CRC Roundtable.[56] Patients' perception of

insurance coverage (as opposed to actual coverage) has been shown to impede cancer screening utilization,[180] which highlights the need for increased awareness of ACA's cost-sharing provision among insured people. It is important to note that some Medicare recipients may still be charged if a polyp is removed during a colonoscopy or if it's a result of a positive stool test and deemed diagnostic due to a loop-hole in this provision which states that cost sharing is removed for screening tests only.[181] Future research on how this influences individuals screening behavior is needed.

The substantially lower CRC screening prevalence in lower SES groups and in Hispanics may reflect patient-reported obstacles to CRC screening other than costs. These obstacles include embarrassment, fear, system/logistical challenges, lack of awareness, not receiving a physician's recommendation for CRC screening, and believing that it is CRC screening is not important or necessary, which need to be addressed in order to increase CRC screening uptake.[20, 25, 174, 182, 183] While these factors are not directly addressed by the ACA cost-sharing provision, some of these barriers, including beliefs that CRC screening is not important, may be indirectly influenced by this provision as the removal of cost for CRC screening may highlight the importance and societal value of on preventive services, including CRC screening. [184]

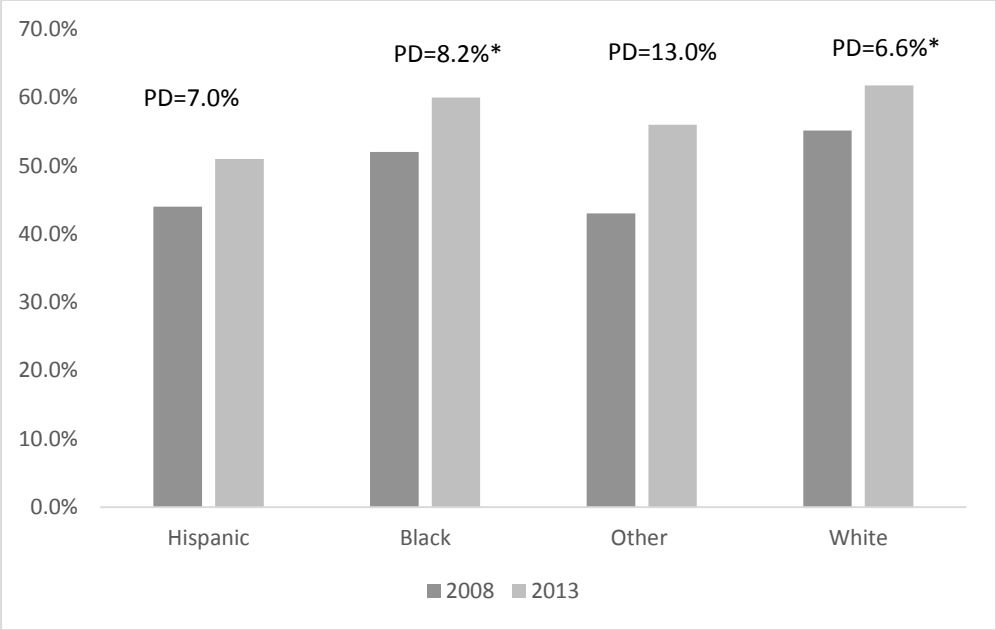
Our study has some limitations. First, we were only able to examine the initial 2 –year period following the ACA cost-sharing provision. Second, screening data were based on self-report. Validation of other survey data indicate FOBT and endoscopy may be

underreported.[185] Additionally, the reason for tests (screening versus diagnostic) was also based on self-report and has not been validated. The NHIS is cross-sectional, which limits the causal inferences that can be made from our study, and it only captures insurance and income at the time of survey and not prior to or during screening leading to possible misclassification of these factors. NHIS also lacked information on benefit structures and coverage details among privately insured persons, which is likely to vary across insurance plans and influence access to cancer screening. While the NHIS sample in our study represented 63.4 million screening-eligible adults, the analytic sample sizes in some of our stratified analyses were relatively small and lead to fairly wide confidence intervals, but our standard errors were well below and sample sizes were well above the recommended the NHIS thresholds for data suppression.[184] Additionally, we were unable to examine all race/ethnic subgroups (Asians, Native Americans) due to a lack of adequate sample size for these groups. Lastly, we excluded respondents with missing screening data from the study and those with missing covariates from adjusted results. Income was the most common independent variable with missing data and while the proportion of subjects that did not report their income was relatively small (8.1% for CRC), missing income is more common among individuals without health insurance, were born outside the US and are racial/ethnic minorities. Results from sensitivity analyses imputing income were similar to our main findings, however, changes in CRC screening were no longer statistically significant among respondents with reported and imputed low income. The lack of statistical significance is not entirely unexpected as the standard errors of these estimates account for both variations in model estimators as well

as the uncertainty of these imputed values. The percentage of respondents with missing screening data was relatively small (2.9%)and was not related to SES.

In conclusion, increases in CRC screening prevalence between 2008 and 2013 were modest. By race/ethnicity, increases in CRC screening were observed in whites and even more so in blacks. However, there were no notable increases in CRC screening among Hispanics, a group with especially low CRC screening. Increases in CRC were observed among adults with low income and lower educational attainment as well as Medicare-only respondents, though screening utilization remain well below nationwide goals. These findings reflect that financial barriers are only part of the constellation of factors, which include inconsistent physician recommendations, fear, insufficient awareness and beliefs that CRC screening is not necessary or important, [183, 186]that be addressed in order to achieve nationwide screening goals and to address barriers to CRC screening.

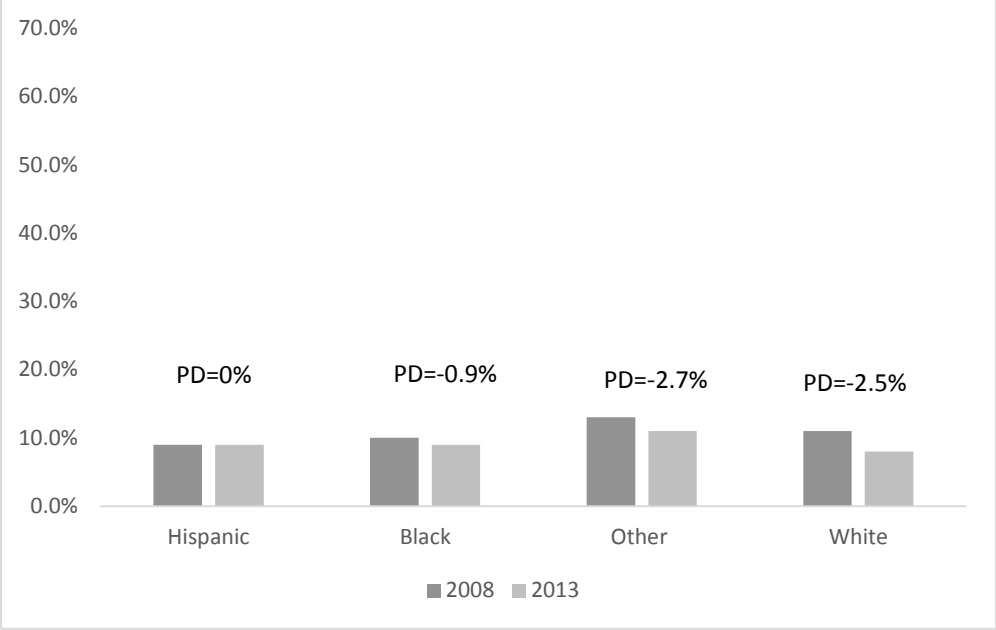
Figure 4.1 Adjusted Prevalence and Prevalence Differences of Colonoscopy between 2008 and 2013 by Race/Ethnicity among Adults 50-75 Years with Private or Medicare Insurance, NHIS 2008 and 2013



Abbreviations: National Health Interview Survey (NHIS), Prevalence Difference (PD)

*Differences between 2013 and 2008 are statistically significant. P-value for Hispanics=0.082, Blacks=0.011, Other=0.019, Whites<0.001

Figure 4.2 Adjusted Prevalence and Prevalence Differences of Stool-Based CRC Testing between 2008 and 2013 by Race/Ethnicity among Adults 50-75 Years with Private or Medicare Insurance, NHIS 2008 and 2013



Abbreviations: National Health Interview Survey (NHIS), Prevalence Difference (PD)

*Differences between 2013 and 2008 are statistically significant. P-value for Hispanics=0.885, Blacks=0.584, Other=0.370, Whites=0.002

Table 4.1 Respondent Characteristics among Adults 50-75 Years with Private and Medicare Insurance, NHIS 2008 and 2013

	Total		2008		2013	
	n	%	n	%	n	%
TOTAL	15,786		5,853		9,933	
Insurance [a]						
Private	8,742	61.8	3,405	63.4	5,337	60.3
Medicare	3,868	19.2	1,251	16.9	2,617	21.3
Medicare+Private	3,176	19.0	1,197	19.7	1,979	18.4
Income [a]						
<$35,000	4,852	24.5	1,799	25.4	3,053	23.7
$35,000-74,999	4,909	33.7	1,868	35.3	3,041	32.4
≥$75,000	4,742	41.8	1,660	39.4	3,082	43.9
Missing	1,283		526		757	
Education [a]						
<High School	1,555	9.0	622	10.1	933	8.0
Completed HS or GED	4,325	28.1	1,671	29.2	2,654	27.1
Some College	4,510	29.6	1,609	29.3	2,901	29.9
Completed College	4,756	33.4	1,672	31.5	3,084	35.1
Missing	640		279		361	
Race/Ethnicity [a]						
Hispanic	1,538	7.4	570	7.0	968	7.7
Non-Hispanic White	11,227	78.6	4,186	79.2	7,041	78.2
Non-Hispanic Black	2,211	9.4	803	9.5	1,408	9.4
Non-Hispanic Other	810	4.6	294	4.4	516	4.7
Immigration Status [a]						
Born outside US	2,098	12.2	769	11.1	1,329	13.1
US Born	13,686	87.8	5,083	88.9	8,603	86.9
Missing	2		1		1	
Sex						
Male	6,774	46.6	2,505	46.7	4,269	46.5
Female	9,012	53.4	3,348	53.3	5,664	53.5
Age (CRC)[a]						
50-59	6,758	47.8	2,660	49.5	4,098	46.3
60-75	9,028	52.2	3,193	50.5	5,835	53.7
Usual Source of Care						
No	593	3.9	238	4.2	355	3.7
Yes	14,376	96.1	5,312	95.8	9,064	96.3
Missing	817		303		514	
BMI						
Underweight	197	1.1	67	1.1	130	1.1
Normal	4,439	29.6	1,663	29.7	2,776	29.6
Overweight	5,562	37.5	2,082	37.5	3,480	37.4
Obese	4,866	31.8	1,767	31.8	3,099	31.9
Missing	722			274	448	

a. P<0.05

Table 4.2 Prevalence and 95% CI of CRC Screening among Adults 50-75 Years with Private and Medicare Insurance, NHIS 2008 and 2013

	2008		2013		Differences between 2013 and 2008	
	%	95%CI	%	95%CI	% Change	P-value
Total	57.3	(55.7,58.9)	61.2	(59.9,62.5)	3.9	<0.001
Race/Ethnicity						
Hispanic	43.0	(38.1,48.1)	48.8	(44.7,53.0)	5.8	0.085
Non-Hispanic White	59.3	(57.5,61.1)	62.6	(61.1,64.1)	3.3	0.007
Non-Hispanic Black	53.5	(48.8,58.1)	62.3	(58.9,65.7)	8.8	0.003
Non-Hispanic Other	52.0	(45.5,58.3)	56.3	(50.4,62.0)	4.3	0.369
Insurance						
Private	55.7	(53.6,57.7)	57.6	(55.7,59.4)	1.9	0.204
Medicare	50.4	(47.1,53.6)	60.2	(57.7,62.7)	9.8	<0.001
Medicare+Private	68.4	(65.3,71.3)	74.3	(71.8,76.6)	5.9	0.002
Income						
<$35,000	51.0	(48.1,53.8)	55.3	(52.9,57.7)	4.3	0.024
$35,000-74,999	56.7	(54.2,59.2)	60.2	(58.0,62.2)	3.5	0.043
≥$75,000	62.2	(59.5,64.7)	64.9	(62.8,67.1)	2.7	0.134
Education						
<High School	47.4	(43.2,51.6)	53.1	(48.7,57.4)	5.7	0.069
Completed HS or GED	52.4	(49.5,55.3)	56.5	(54.2,58.8)	4.1	0.038
Some College	59.1	(56.3,61.8)	61.0	(58.5,63.4)	1.9	0.333
Completed College	65.7	(62.9,68.5)	68.3	(66.2,70.4)	2.6	0.170
Immigration Status						
Born outside US	48.0	(43.6,52.3)	54.7	(51.1,58.3)	6.7	0.021
Born in US	58.5	(56.8,60.1)	62.2	(60.8,63.5)	3.7	<0.001
Sex						
Male	58.1	(55.6,60.6)	59.4	(57.5, 61.4)	1.3	0.413
Female	56.6	(54.5,58.6)	62.8	(61.1,64.4)	6.2	<0.001
Age						
50-59	52.2	(49.8,54.7)	53.8	51.7	1.6	0.371
60-75	62.2	(60.2,64.2)	67.6	66.1	5.4	<0.001
Usual Source of Care						
No	48.9	(41.9,55.9)	50.8	43.3	1.9	0.711
Yes	59.4	(57.8,61.0)	63.6	62.2	4.2	<0.001
BMI						
Underweight	55.3	(40.6,69.1)	59.1	47.7	3.8	0.691
Normal	53.5	(50.7,56.3)	59.5	56.9	6	0.003
Overweight	59.1	(56.5,61.7)	61.2	59.2	2.1	0.209
Obese	59.0	(56.3,61.7)	64.1	61.8	5.1	0.006

Table 4.3 Adjusted Prevalence Difference and 95%CI of CRC Screening, 2013 versus 2008 among Adults 50-75 years with Private and Medicare Insurance by Race/Ethnicity and SES, NHIS 2008 and 2013

	2008 (95%CI)	2013 (95%CI)	PD[a] (95%CI)	P-value
Total	60.5 (58.8,62.2)	63.3 (61.8,64.7)	2.7 (0.54, 4.9)	0.016
Race/Ethnicity				
Hispanic	53.7 (47.6,59.7)	60.3 (55.1,65.4)	6.6 (-0.08, 14.1)	0.079
Non-Hispanic Black	61.4 (56.6,66.1)	66.2 (62.6,69.6)	4.8 (-1.1, 10.7))	0.116
Non-Hispanic White	61.6 (59.6,63.5)	63.7 (62.0,65.3)	2.1 (-0.5, 4.6)	0.101
Non-Hispanic Other	56.4 (48.7,63.7)	58.8 (51.0,66.1)	2.4 (-8.0,12.8)	0.650
Insurance				
Private	58.2 (56.0,60.4)	59.6 (57.6,61.6)	1.4 (-1.5, 4.3)	0.356
Medicare	57.1 (53.4,60.7)	63.3 (60.6,65.9)	6.2 (1.7, 10.7)	0.008
Medicare + Private	71.2 (67.9,74.3)	74.7 (71.9,77.2)	3.4 (-0.5, 7.3)	0.087
Income				
<$35,000	53.5 (50.5,56.6)	59.4 (56.8,62.0)	5.9 (1.8, 10.2)	0.009
$35,000-74,999	60.0 (57.3,62.6)	62.4 (60.1,64.7)	2.4 (-0.9, 5.7)	0.139
≥$75,000	64.7 (62.0,67.2)	66.0 (63.7,68.3)	1.3 (-2.4,5.0)	0.475
Education				
< High School	50.4 (45.9,55.0)	57.7 (53.3,61.9)	7.2 (0.9, 13.5)	0.022
HS or GED	53.3 (50.0,56.5)	58.6 (56.1,61.1)	5.3 (1.2, 9.2)	0.015
Some College	61.7 (58.7,64.6)	62.5 (60.0,65.0)	0.8 (-3.1, 4.7)	0.689
College Graduate	67.9 (64.9,70.8)	69.4 (67.1,71.7)	1.5 (-2.4, 5.4)	0.443

a. Model is adjusted for insurance, income, race/ethnicity, education, sex (CRC only), age, immigration status, BMI and usual source of preventive care and includes 12,678 respondents with non-missing data.

Table 4.4 Unadjusted and Adjusted Prevalence Differences and 95%CI of CRC Screening by Race/Ethnicity and Year among Adults 50-75 Years, NHIS 2008 and 2013

	Unadjusted Prevalence Difference [a]			
	2008		2013	
	PD	95%CI	PD	95%CI
Race/Ethnicity (ref: Non-Hispanic Whites) [a]				
Hispanic	-16.4	(-21.5, -11.3)	-13.8	(-17.9, -9.7)
Non-Hispanic Black	-5.9	(-10.8, -1.0)	0.0	(-3.8,3.7)
Non-Hispanic Other	-7.4	(-14.1, -0.7)	-6.3	(-12.4, -0.2)
Income (ref: high income) [b]				
Low	-11.2	(-14.9, -7.5)	-9.7	(-12.8, -6.6)
Medium	-5.4	(-8.7, -2.1)	-4.8	(-7.7, -1.9)
Education (ref: college graduates) [c]				
<HS	-18.4	(-23.3,13.5)	-15.2	(-19.9, -10.5)
HS Diploma or GED	-13.4	(-17.3, -9.5)	-11.9	(-15.0, -8.8)
Some College	-6.6	(-10.5, -2.7)	-7.3	(-10.4, -4.2)

	Adjusted Prevalence Difference[d]			
	2008		2013	
	PD	95%CI	PD	95%CI
Race/Ethnicity (ref: Non-Hispanic Whites) [e]				
Hispanic	-7.9	(-14.2-1.6)	-3.3	(-8.8, 2.2)
Non-Hispanic Black	-1.0	(-6.1,4.1)	2.6	(-1.1, 6.3)
Non-Hispanic Other	-5.2	(-12.8,2.4)	-4.9	(-12,9,3.2)
Income (ref: to high income) [f]				
Low	-8.7	(-13.4, -4.0)	-9.6	(-13.5, -5.7)
Medium	-4.1	(-7.8, -0.4)	-4.5	(-7.6, -1.4)
Education (ref: college graduates) [g]				
<HS	-16.6	(-22.5, -10.7)	-12.7	(-17.8, -7.6)
HS Diploma or GED	-13.7	(-18.4, -9.0)	-11.3	(-14.8,-7.8)
Some College	-5.4	(-9.9, -0.9)	-6.8	(-10.1,-3.5)

a. P-value for heterogeneity across survey years: Hispanic (0.575), Black (0.087), Other (0.921)

b. P-value for heterogeneity across survey years: Low income (p=0.626), medium (p=0.843)

c. P-value for heterogeneity across survey years: <HS (p=0.445), HS or GED (p=0.683), Some College (p=0.732)

d. Adjusted for insurance, income, race/ethnicity, education, sex (CRC only), age, immigration status, BMI and usual source of preventive care

e. P-value for heterogeneity across survey years: Hispanic (0.263), Black (0.415), Other (0.971)

f. P-value for heterogeneity across survey years: Low income (p=0.289), medium (p=0.644)

g. P-value for heterogeneity across survey year:s <HS (p=0.167), HS or GED (p=0.322), Some College (p=0.729)

Table 4.5 Adjusted Prevalence Difference and 95% CI of CRC Screening for Routine Reasons, 2013 versus 2008 among Adults 50-75 years with Private and Medicare Insurance by Race/Ethnicity and SES, NHIS 2008 and 2013

	PD Comparing 2013 vs 2008[a]	95%CI
Total[a]	5.2	(2.9,7.6)
Race/Ethnicity		
Hispanic	3.0	(-5.4, 11.4)
Non-Hispanic Black	5.2	(-1.5,11.9)
Non-Hispanic White	5.2	(2.4, 7.9)
Non-Hispanic Other	6.9	(-4.3,18.1)
Insurance		
Private	3.8	(0.7, 6.9)
Medicare	9.7	(4.8, 14.6)
Medicare + Private	5.9	(1.2,10.6)
Income		
<$35,000	9.0	(4.5,13.5)
$35,000-74,999	3.8	(0.1,7.5)
≥$75,000	4.5	(0.4, 8.6)
Education		
< High School	9.6	(2.3, 16.9)
HS or GED	7.2	(2.9, 11.5)
Some College	3.2	(-0.9,7.3)
College Graduate	4.9	(0.4,9.4)

a. Compares 6,037 respondents indicating their CRC screening was for routine reasons with respondents who were not guideline concordant (n=4,794). Model only includes respondents with non-missing data. Adjusted for insurance, income, race/ethnicity, education, sex, age, immigration status, BMI and usual source of preventive care

Table 4.6 Adjusted CRC Screening Prevalence Difference between 2003 and 2008 among Adults 50-75 years with Private and Medicare, NHIS 2003 and 2008

	Adjusted Prevalence and 95%CI						Adjusted PD comparing 2008 vs 2003[a]	
	2003 %	95%CI		2008 %	95%CI		PD	95%CI
Total [b]	44.0	42.4	45.8	56.8	55.1	58.5	12.7	(10.3,15.0)
Race/Ethnicity								
Hispanic	39.5	34.0	45.3	45.7	40.0	51.5	6.2	(-1.8,14.2)
Non-Hispanic Black	42.7	37.8	47.7	54.2	49.2	59.1	11.5	(4.6, 18.4)
Non-Hispanic White	45.0	43.0	46.9	58.2	56.3	60.1	13.2	(10.5,15.9)
Non-Hispanic Other	33.8	25.2	43.6	48.7	41.3	56.2	14.9	(3.3,26.4)
Insurance								
Private	41.2	39.3	43.1	53.9	51.8	56.0	12.7	(9.8, 15.6)
Medicare	42.0	38.5	45.6	51.5	47.8	55.2	9.5	(4.2, 14.8)
Medicare + Private	53.5	50.4	56.6	67.8	64.6	70.9	14.3	(9.8, 18.8)
Income								
<$35,000	40.3	38.0	42.7	52.9	49.9	55.9	12.6	(8.9,16.3)
$35,000-74,999	44.7	42.1	47.3	56.8	54.0	59.6	12.1	(8.4,15.8)
≥$75,000	46.3	43.0	49.7	59.6	56.8	62.4	13.3	(9.0,17.6)
Education								
< High School	36.8	33.1	40.7	49.6	45.1	54.0	12.8	(6.9,18.7)
HS or GED	42.7	39.7	45.6	51.7	48.5	54.9	9.0	(5.1,12.9)
Some College	43.8	40.8	47.0	58.6	55.5	61.5	14.7	(10.4,18.6)
College Graduate	48.3	45.1	51.6	63.0	59.8	66.0	14.7	(10.2,19.2)

a. The 2008 prevalence estimates in the table above do not match the prevalence estimates for 2008 in the main analyses due to changes in the skip patterns/questionnaire between 2003 and 2008. Coding of 2008 screening variables were altered to match 2003 skip patterns.
b. Includes 9,766 respondents. Adjusted for insurance, income, race/ethnicity, education, sex, age, immigration status, BMI and usual source of preventive care.

Table 4.7 Adjusted Colorectal Cancer Screening Prevalence among Adults 50-75 years without Insurance, NHIS 2003 and 2008

	2008		2013		PD comparing 2013 vs 2008[a]	
	%	95% CI	%	95% CI	% change	95% CI
CRC Screening	21.4	(17.1,26.5)	24.3	(21.0.27.9)	2.8	(-3.1,8.7)

a. Adjusted for age, sex (CRC screening only), income, education, race/ethnicity, immigration status, and BMI. Model includes 1,723

Table 4.8 Adjusted Prevalence Difference and 95% CI for CRC Screening, 2013 versus 2008 among Adults 50-75 Years with Private or Medicare Insurance, by Race/Ethnicity and Socioeconomic Status Using Imputed Income, NHIS 2008 and 2013

	2008 (95%CI)	2013 (95%CI)	PD (95%CI)[a]	P-value
Total	60.4 (58.8,62.1)	63.3 (61.7,64.8)	2.9 (0.6,5 .3)	0.018
Race/Ethnicity				
Hispanic	47.9 (42.4,53.4)	54.4 (48.9,59.8)	6.5 (-1.3,14.3)	0.104
Non-Hispanic Black	57.2 (52.4,61.8)	61.6 (57.7,65.5)	4.5(-1.4,10.4)	0.139
Non-Hispanic White	62.1 (60.2,64.0)	64.3 (62.5,66.1)	2.2(-.05,4.9)	0.120
Non-Hispanic Other	53.6 (45.4,61.6)	58.8 (51.5,65.8)	5.3 (-5.9,16.5)	0.358
Insurance				
Private	58.1 (56.0,60.1)	59.6 (57.4,61.7)	1.5 (-1.4,4.4)	0.340
Medicare	56.5 (52.6,60.2)	63.8 (60.8,66.7)	7.4 (2.5,12.3)	0.003
Medicare + Private	71.2 (67.8,74.3)	73.9 (70.9,76.8)	2.8 (-1.5,7.1)	0.207
Income				
<$35,000	58.6 (54.7,62.5)	58.6 (54.7,62.5)	2.9 (-0.2,6.0)	0.077
$35,000-74,999	59.7 (57.3,62.2)	62.2 (59.7,64.6)	2.4 (-1.1,5.9)	0.176
≥$75,000	63.1 (60.4,65.7)	66.5 (64.3,68.7)	3.5 (0.0,7.0)	0.052
Education				
< High School	51.3 (46.7,55.9)	58.3 (53.7,62.8)	7.0 (0.3,13.7)	0.043
HS or GED	53.0 (49.9,56.1)	58.6 (55.7,61.4)	5.6 (1.3,9.9)	0.013
Some College	61.5 (58.6,64.4)	61.4 (58.5,64.2)	-0.1 (-4.2,4.0)	0.943
College Graduate	67.8 (64.7,70.8)	70.6 (68.0,73.1)	2.8 (-1.3,6.9)	0.183

a. Adjusted for insurance, income, race/ethnicity, education, sex (CRC only), age, immigration status, BMI and usual source of preventive care. Includes 12,678 respondents with non-missing data and 1,283 respondents with imputed income data

Chapter 5 Initiation of Colorectal Cancer Screening After Age 50 in a Coordinated Outreach/Inreach Program Using Population Health Management Approach (Aim 2)

Title: Colorectal Cancer Screening Initiation by Race/Ethnicity among New Screening-Eligible Adults in a Program using Population Health Management Approaches

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ABSTRACT

Introduction: Recent studies report racial disparities among individuals in organized colorectal cancer (CRC) programs; however, there is a paucity of information on CRC screening utilization by race/ethnicity among newly age-eligible adults in such programs.
Methods: This was a retrospective cohort study among Kaiser Permanente Northern California (KPNC) enrollees who turned 50 years of age between 2007-2012 (n=138,799) and were served by a system-wide outreach and facilitated in-reach screening program based primarily on mailed fecal immunochemical tests (FIT) to screening-eligible people. Kaplan Meier and Cox model analyses were conducted in 2015-2016 and used to estimate differences in receipt of CRC screening.
Results: The cumulative probabilities of CRC screening within one and two years of subjects' 50th birthday were 51% and 73%, respectively. Relative to non-Hispanic whites, the likelihood of completing any CRC screening was similar in blacks (hazard ratio (HR)=0.98, 95% confidence interval (CI) 0.96,1.00), 5% lower in Hispanics (HR=0.95, 95%CI 0.93,0.96) and 13% higher in Asians (HR=1.13, 95%CI 1.11,1.15) in adjusted analyses. FIT was the most common screening modality, representing 86% of all screening initiations. Blacks and Hispanics had lower receipt of FIT in adjusted analyses.
Conclusions: There was a high uptake of CRC screening among newly screening-eligible adults in an organized CRC screening program, but Hispanics were less likely to initiate screening near age 50 than non-Hispanic whites, suggesting that cultural and other individual-level barriers not addressed within the program likely contribute. Future studies examining the influences of culturally appropriate and targeted efforts for initiation of screening are needed.

Introduction

Colorectal cancer (CRC) is the third most common cancer and second leading cause of cancer death in the United States.[187] Despite its effectiveness, CRC screening remains underutilized. In 2013, only 58% of eligible adults were up-to-date with recommended CRC screening, a level well below nationwide screening goals.[18, 188] CRC screening is especially underutilized in racial/ethnic minorities including Asians and Hispanics where less than 45% of people in these groups are reported to be up-to-date with CRC screening compared to 60% in non-Hispanic whites.[20, 108] Blacks have also historically had lower CRC screening prevalence compared to whites, a disparity that has been the focus of several studies given the higher disease burden in this group.[20, 26, 27, 59, 80, 114] Factors contributing to lower CRC screening uptake in racial/ethnic minorities are complex but could be addressed through programs that improve awareness and access to healthcare, and mitigate cultural and logistical barriers to receiving needed services. [23, 101, 147, 189] Further, delay in screening initiation can contribute to disparities and may predict future cancer screening behaviors.[40] Thus, timely screening initiation can be an important target of intervention for boosting screening rates in diverse populations. However, the impact of such programs and screening initiation has not been widely studied.

In 2007, Kaiser Permanente Northern California (KPNC), an integrated health system that insures and provides healthcare, launched a CRC screening program using population health management approaches.[190] The program identifies screening-eligible average-risk adults and mails a fecal immunochemical tests (FIT) kits annually to their home address. An in-reach component reminds individuals and offers screening at

healthcare encounters. Despite rapid CRC screening uptake throughout the program, recent studies of the program reported lower odds of CRC screening in blacks and Hispanics relative to non-Hispanic whites, calling for increased understanding of these differences.[91, 190] Thus, the objective of the present study was to examine time to receipt of CRC screening from age 50 in a program with uniform population health approaches to delivery of screening according to race/ethnicity. We also examined detailed patterns of the type of test utilized to better understand potential racial differences in CRC screening within the organized screening program.

Methods

Study Population and Data Sources

Data on KPNC enrollees who turned 50 years of age between 2007 and 2012, after the program was in place, were used in this study. KPNC provides healthcare to over 3.8 million people annually or 22% of Northern California's adults aged 22-64 years[168] across 17 medical centers in the region. The CRC screening activities and the population health management approaches used[160]. Briefly, at the program's onset in 2007, FIT kits, along with instructions, were mailed to randomly selected adults who were not up-to-date with recommended CRC screening in weekly batches during the first 9-10 months of each calendar year with a goal to screen all eligible persons by the end of a person's 51st birth year, in accordance with the Healthcare Effectiveness Data and Information Set (HEDIS) measurement approach; compliance with screening is assessed beginning at age 51.[191] Several years into the program, FIT kits were mailed on or near their 50th birthday. Non-responders received phone or mailed reminders. Electronic medical record reminder alerts were used to offer screening during in-person healthcare visits, hereafter referred to

as in-reach screening. Approval for this study was obtained from institutional review boards at KPNC and Emory University.

Of the age-eligible adults, those who had prior CRC or inflammatory bowel disease diagnosis, or who had prior colorectal surgery, or a strong family history of heredity cancers were excluded to limit the study to average-risk adults. People who received a colonoscopy, FIT, or sigmoidoscopy before their 50th birthday were also excluded. We also excluded people who were enrolled in KPNC for less than 12 months, lived outside the KPNC service area, or had missing data on race/ethnicity or other key covariates.

Outcome

The outcome was time to the receipt of the first CRC screening test (FIT, colonoscopy, or sigmoidoscopy) after turning age of 50 years of age. Receipt of FIT testing and mailing dates were based on electronic laboratory and mailing records, respectively. Current Procedural Terminology (CPT) and International Disease Classification Codes (ICD-9) were used to identify colonoscopy and sigmoidoscopy.

Independent Variables

The primary independent variable was race/ethnicity categorized as non-Hispanic white (white), non-Hispanic black (black), Hispanic, Asian or Pacific Islanders (Asian), Native American and multiple races. To account for changes in screening initiation throughout the program, we included year of a person's 50th birthday (2007, 2008, 2009, 2010, 2011, 2012) as a covariate. Primary insurance payer (commercial, Medicaid, Medicare and

other) and census-tract poverty indices [low (0-3.9%), medium (4-7.9%) and high (≥8%)] were used as markers of socioeconomic status. Preferred language (English/non-English) was used as measure of acculturation. Additional covariates included family history of CRC according to electronic medical records, geographic region where a person received the majority of their health care (medical service area), gender, Charlson Comorbidity score (categorized as 0, 1, 2+) and body mass index (BMI) category, based on the World Health Organization's classification[175],

Statistical Analysis

Chi-square and Wilcoxin signed rank tests (with an α of 0.05 for significance) were used to examine differences in subjects' characteristics according to race/ethnicity. People were followed from their 50th birthday until the earliest of receipt of a CRC screening, date of death, date when no longer enrolled in KPNC, or the end of the follow-up period (December 31, 2013). Kaplan Meier product-limit estimator with log-rank statistics were used to derive the cumulative probability of receipt of CRC screening according to race/ethnicity. Among individuals receiving FIT, the time from their 50th birthday until they were mailed a FIT kit was calculated and used to represent "program" delays and the time from receiving a FIT and the lab date was used to represent "individual" delays. In order to determine potential racial differences in receipt of FIT in outreach versus inreach settings, we categorized FIT testing occurring before the first mailed kit as "in-reach" whereas FIT testing following a mailed kit was deemed to occur through "outreach".

Cox proportional hazard models were used to estimate hazard ratios (HR) and corresponding 95% confidence intervals (CI). A series of models were performed to determine if adjustment of variables attenuated the association between race/ethnicity and CRC screening initiation. Each model accounted for clustering of people within medical service areas using a sandwich covariance estimator. The proportional hazard assumption was tested using log-log survival curves along with log-time and covariate interaction terms. Insurance type and year of 50th birthday violated the proportional hazard assumption and were adjusted for in-strata. Interactions with race/ethnicity were examined with all other covariates.

Several sensitivity analyses were conducted. First, log binomial models were used to estimate prevalence ratios (PR) and 95% CI of initial CRC screening by the end of follow-up and within 2 years of the 50th birthday (in accordance with HEDIS measures) and were compared with Cox models to assess if differences in follow-up time might account for variations by race/ethnicity. Complementary log-log models, using 6-month interval censoring, were also used to estimate receipt of CRC screening before the end of follow-up to compare with models in the primary and sensitivity analyses to determine if the analytic approach altered our findings. We also examined receipt of FIT among people who were mailed FIT kits. Statistical analyses were performed with SAS version 9.4.

Results

There were 234,265 adults who turned 50 years of age between 2007 and 2013 in KPNC who were potentially eligible for this study. After exclusions, the final analytic sample contained 138,799 individuals (**Figure 5.1**). Among this sample, 56.7% were white, 8.2% were black, 17.4% were Hispanic, 16.8% were Asian, <1% were Native American and <1% were coded as multiracial **(Table 5.1)**. Blacks and Hispanics were more likely to be insured through Medicaid or reside in higher poverty areas, and tended to be more overweight/obese and have more comorbid conditions than whites and Asians. The average number of months enrolled in KPNC since a person's 50th birthday was shorter in Hispanics (44.7 months, p-value<0.001) and blacks (45.8 months, p-value=0.014) compared to whites (46.3 months).

Receipt of CRC Screening Overall

Among the analytic cohort, the cumulative probabilities of any CRC screening within 1, 2, 3, 4, 5, 6 and 7 years of a person's 50th birthday were 50.9%, 72.9%, 81.1%, 85.9%, 89.0%, 91.1% and 92.2%, respectively. By the end of follow-up, the cumulative probability of receiving any CRC screening modality, was highest in Asians (94.8%) followed by whites (91.9%), multiracial (91.9%), blacks (91.8%), Hispanics (90.9%), and Native Americans (90.9%) (p-value<0.001) (**Figure 5.2**). In our multivariable Cox models, relative to whites, the likelihood of initiating CRC screening was similar in blacks (HR=0.98, 95%CI 0.96,1.00), 5% lower in Hispanics (HR=0.95, 95%CI 0.93,0.96) and 13% higher in Asians (HR=1.13, 95%CI 1.11,1.15) (**Table 5.2**). Results from log binomial models were similar indicating that differences in follow-up did not account for the variations in CRC screening utilization by race/ethnicity **(Tables 5.3 and**

5.4). Additionally, complementary log-log model results were similar as were logistic regression model results, though point estimates in the former were further from the null. **(Table 5.5)** There was no significant interaction between race/ethnicity and other covariates (data not shown), including language preference where the likelihoods of CRC screening use among English-preferring Asians and Hispanics were similar to their non-English preferring counterparts.

Receipt of Mailed FIT Kits

The majority (86.4%) of people were mailed at least one FIT during follow-up. This proportion was slightly lower in blacks (84.9%) relative to whites (86.7%) (**Table 5.1**). Among participants who were not mailed a FIT, over 93% received CRC screening either through in-reach FIT testing (44%), colonoscopy (21%) or sigmoidoscopy (29%). The remaining 7% had not received testing before the end of follow-up and a substantial proportion (40%) of these individuals were in the most recent birth cohorts (i.e. turned 50 years of age in 2011 or 2012).

Receipt and Timing of FIT Testing

FIT was the most common form of completed CRC screening, representing 85.6% of all first completed CRC tests, and the cumulative probability of FIT testing ranged from 87.9% in Hispanics to 92.8% in Asians (**Figure 5.3**). In adjusted Cox models analyses compared to whites, receipt of FIT testing versus having no CRC tests was significantly lower in Hispanics (HR=0.94, 95%CI 0.93,0.96) and blacks (HR=0.95, 95%CI 0.93,0.98) but higher in Asians (HR=1.14, 95%CI 1.12, 1.16) (**Table 5.2**). In analyses restricted to individuals mailed at least one FIT, results were similar to the main findings (**Table 5.6**).

Among those completing FIT, in-reach FIT accounted for 22.6% of all tests and ranged from 21.5% in whites to 26.5% in Asians (p-value<0.001) (**Table 5.7**). The remaining 77.4% of adults receiving FIT did so through outreach where the median time from 50th birthday to FIT mailing (i.e., program delay) was 13 months regardless of race/ethnicity. The median time from FIT mailing to lab testing (i.e., individual delay) was 2 months and the distribution was left-skewed (**Figure 5.4**). Individual times to return varied by race/ethnicity and tended to be longer in Hispanic (p-value<0.001) and blacks (p-value<0.001) relative to whites.

Receipt of Colonoscopy and Sigmoidoscopy

Colonoscopy was significantly less common among Hispanics (HR=0.81, 95% CI 0.75,0.87) and Asians (HR=0.88, 95%CI 0.82,0.94) relative to whites. (**Table 5.2, Figure 5.5**) In contrast, sigmoidoscopy use was 41% and 22% greater in blacks and Asians compared to whites, respectively (**Table 5.2, Figure 5.6**).

Discussion

In our study in a screening program that used population health management approaches,[190] the cumulative probability of completing CRC screening within one and two years of becoming age-eligible was 51% and 73%, respectively, and approached 90% over the seven-year follow-up period. Hispanics had slightly lower CRC screening uptake compared to whites while Asians had higher uptake, a pattern that was consistent throughout the study period. FIT represented a large majority (86%) of all CRC tests as result of the system-wide outreach based primarily on mailed FITs and while most people

returned FIT kits in a timely fashion (within 2 months of being mailed a kit), Hispanics and blacks were less likely to return kits before the end of follow-up.

The overall high uptake of CRC screening and only modest differences by race/ethnicity diverge from nationwide patterns and those in California. [18, 192] For example, among people 50-54 years of age in the National Health Interview Survey and California Health Interview Survey, only 39% and 43% were screened, respectively.[108, 193] Greater CRC screening use among Asians and marginally lower screening in Hispanics relative to whites in the current study, within an integrated health care system with more equal access to care, differs from markedly lower CRC screening prevalence in Asians and Hispanics across the US, in the absence of organized screening programs.[18, 23, 28] Additionally, comparable CRC screening uptake in blacks relative to whites in our study is in contrast to historically lower screening in this group, but is more similar to contemporary data suggesting a narrowing in these differences.[91, 194]

The favorable patterns in our study were not likely to be due solely to having insurance as Asian, blacks and Hispanics in other insured populations have lower CRC screening adoption relative to whites.[114, 115, 194] The high screening rates in our study are likely due to a variety of mechanisms stemming from the population health management strategies used. [190] First, mailed introductory letters and FIT kits serve as a reminder and increase awareness of the need to be screened, which may account for higher CRC screening among Asians who tend to have positive attitudes toward screening when presented with

the opportunity.[124] Second, screening using outreach is not hampered by competing demands during a clinical encounter or the requirement for physicians to initiate recommendation for CRC screening, a prominent barrier among Hispanics and blacks.[111] Additionally, a mailed FIT is non-invasive, and does not require an individual to take time off work or incur opportunity costs, making it an easily accessible option for newly-eligible adults. This tactic may be particularly salient for Hispanics and blacks who tend to be employed in service and production related industries with limited paid-time off benefits. [195, 196]

Despite these encouraging results, blacks and Hispanics were still somewhat less likely to return FIT kits, which was not a result of differences in the presumed opportunity to be screened. The overall probabilities of being mailed a FIT kit and the average time from 50th birthday to mailing was 13 months, a timeframe reflecting the HEDIS measurement approach, were uniform across racial and ethnic groups. These results suggests that factors such as beliefs, attitudes and perceptions of CRC screening not addressed in the current organized screening program could play a role.[23, 197, 198] Specific barriers described among Hispanics include embarrassment and fear of tests as well as perceptions that screening is not needed in the absence of symptoms.[121 122, 123] Hispanics are also more likely than whites to report that they would delay stool-based testing if a doctor gave it to them. [124] Unlike previous investigations, [23, 198] language preference did not predict CRC screening or modify the association between Hispanic ethnicity and CRC screening in the current study, which may be a result of our insured population and language-specific outreach instructions. In other studies, blacks reported fear and

embarrassment as obstacles to screening in addition to mistrust in the medical system. [182] Some of these barriers may be addressed with more tailored and targeted approaches; [199, 200] however, the effectiveness and the cost-benefit of adjuvant program components has not been investigated and warrants future study.

Two previous studies of KPNC enrollees aged 50-75 years noted lower CRC screening utilization among Hispanics and Blacks relative to whites, although these did not evaluate initial screening uptake as in the current study.[91, 190] We observed similar findings for newly screening-eligible Hispanics, though, black-white disparities in the current study were confined to FIT testing. [18] The lack of black-white differences in colonoscopy in our study could be related to lower frequency of use of colonoscopy among newly screening-eligible adults. We observed greater use of sigmoidoscopy in blacks and Asians compared to whites, a finding consistent with previous studies indicating slower transition to newer medical technologies in racial/ethnic minorities.[39 201] A previous study of newly screening-eligible enrollees in an integrated health system located in Washington state who received mailed and in-person clinic reminders reported similar CRC screening uptake in blacks and Hispanics. The discrepant findings with our study could result from differences in sample size and composition as well as programmatic factors. [116]

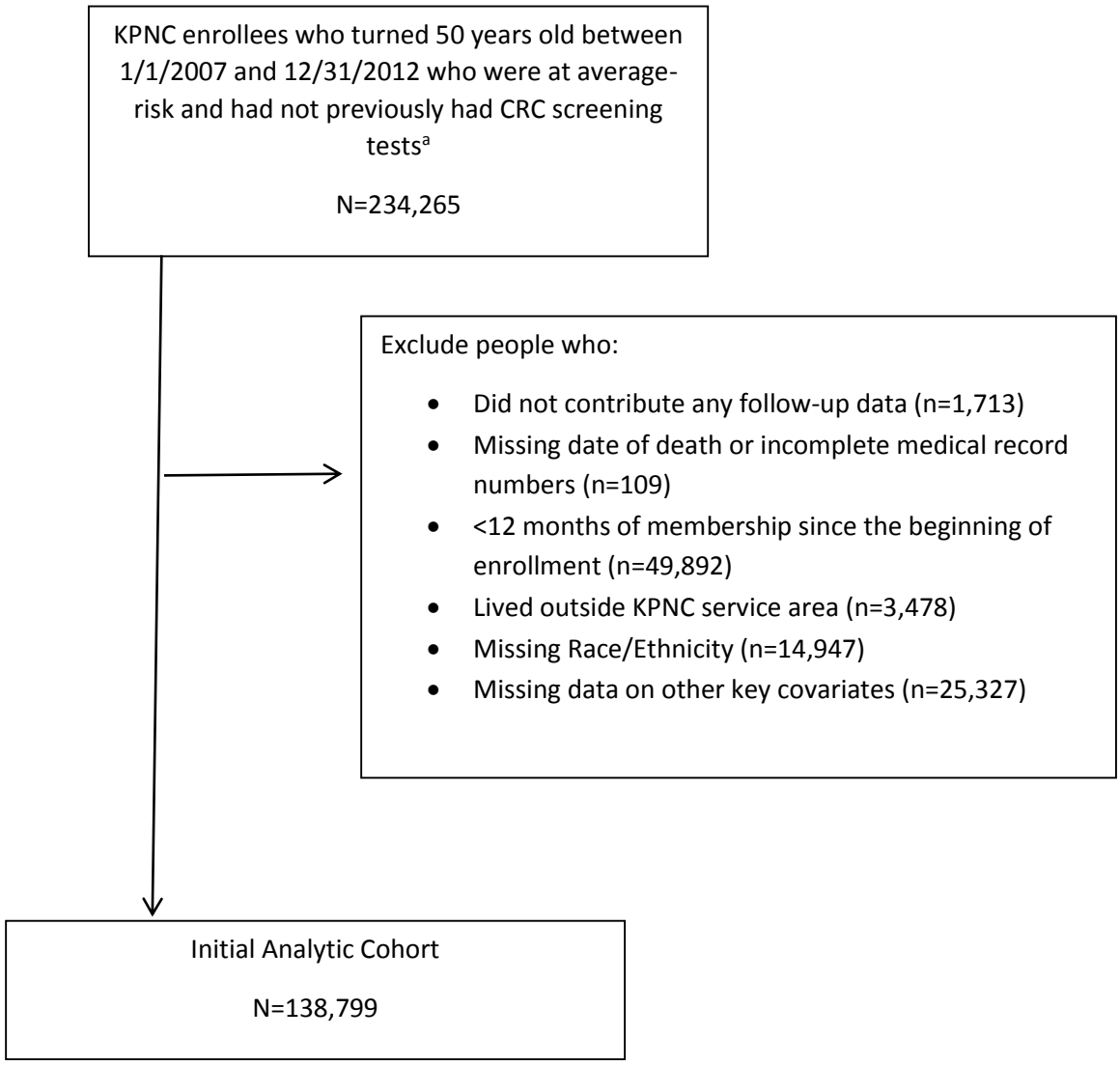
There are some limitations of this study. First, some tests may have been done for non-screening indications, although this would be less likely with broad-based outreach

programs. Second, people excluded because of missing race/ethnicity information (n=14,947) had lower CRC screening use (63%) compared to people with non-missing race/ethnicity (>90%). If racial/ethnic minorities were over-represented in those with missing race/ethnicity data, then disparities observed in our study are likely a conservative estimate. Additionally, incorporating individuals with missing race/ethnicity dampened the estimated overall receipt of CRC screening, marginally, to 89%. Additionally, among KPNC enrollees with known race/ethnicity, the concordance between race recorded in medical records and self-reported data was excellent for blacks and whites, high for Asians and good among Hispanics according to a previous validation study.[202] We also assumed that mailed FIT kits were delivered as we did not have information regarding delivery confirmation. Further, data on immigration status and specific ethnicity (e.g.: Korean for Asians) were not available.[28, 203] Additionally, we used area-based poverty measures, which may be discordant with individual level SES,[204] however, area-based indicators strongly correlated with health behaviors. Lastly, results from KPNC's integrated health system may not be generalizable to other healthcare settings, although programmatic approaches to cancer screening are widely used in different types of health care delivery systems.

In conclusion, among adults who newly became screening-eligible in KPNC's program, CRC screening uptake was considerably higher and differences by race/ethnicity were modest and narrower than previously reported in the overall US or California populations. However, Hispanics were still less likely to be screened compared to whites, which could be due to factors not addressed in the current population health management

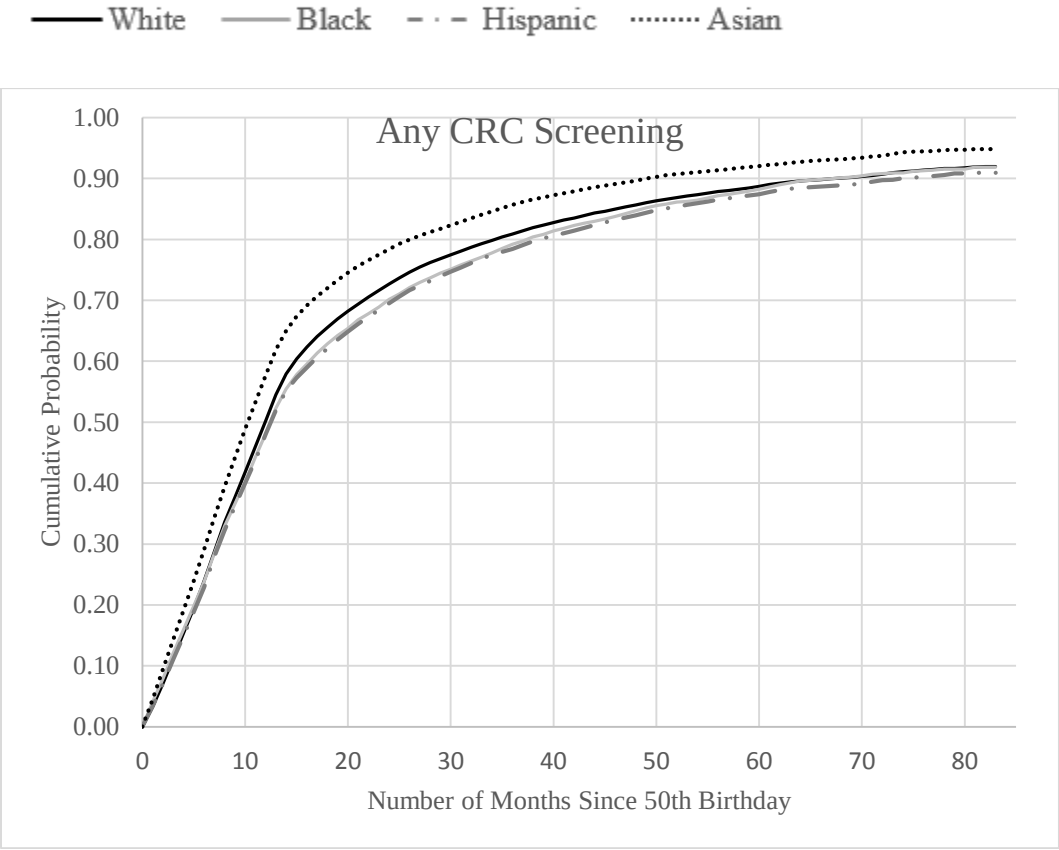
approach, but may be addressed using other methods such as tailored and targeted culturally-appropriate messaging. The effectiveness and the cost-benefit of adjuvant program components in the current study population have not been investigated and warrant future study.

Figure 5.1 Flow Diagram of Cohort Ascertainment, KPNC 2007-2012



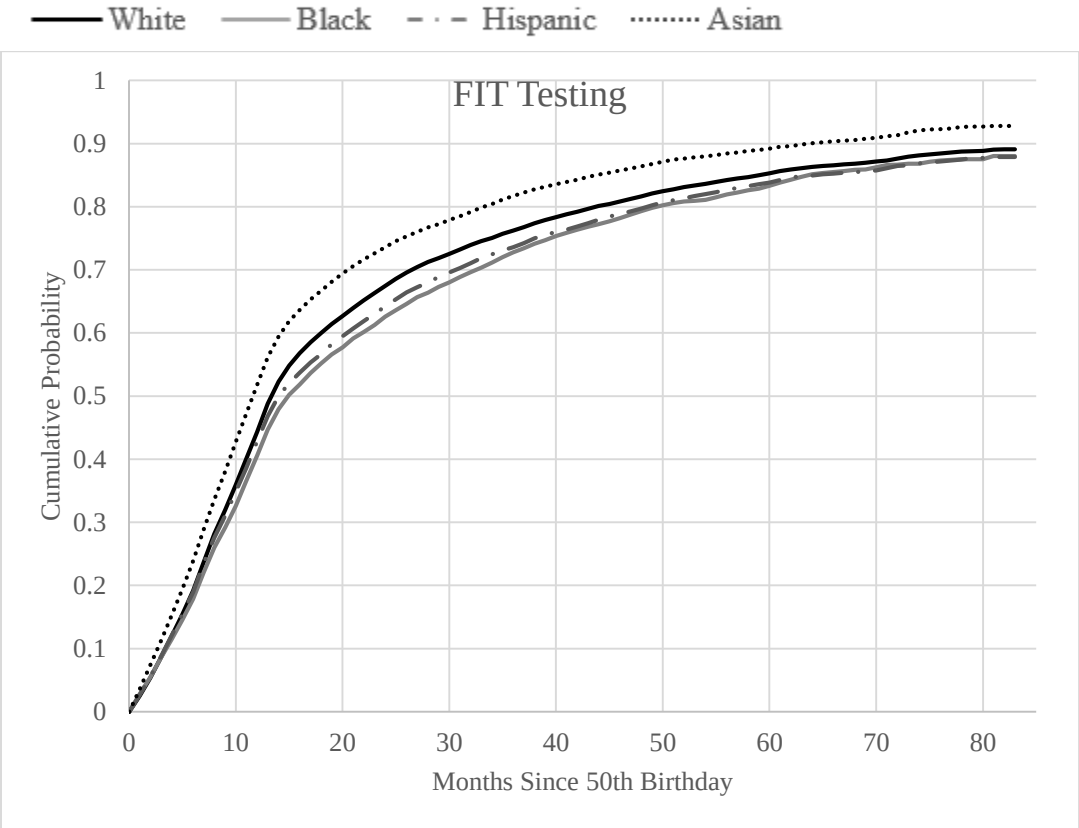
a. People with a strong family history, were diagnosed with inflammatory bowel disease, were diagnosed with CRC or had colorectal cancer surgery before their 50th birthday were considered non-average risk.

Figure 5.2 Cumulative Probability of CRC Screening by Race/Ethnicity among newly eligible enrollees, KPNC 2007-2012[a]



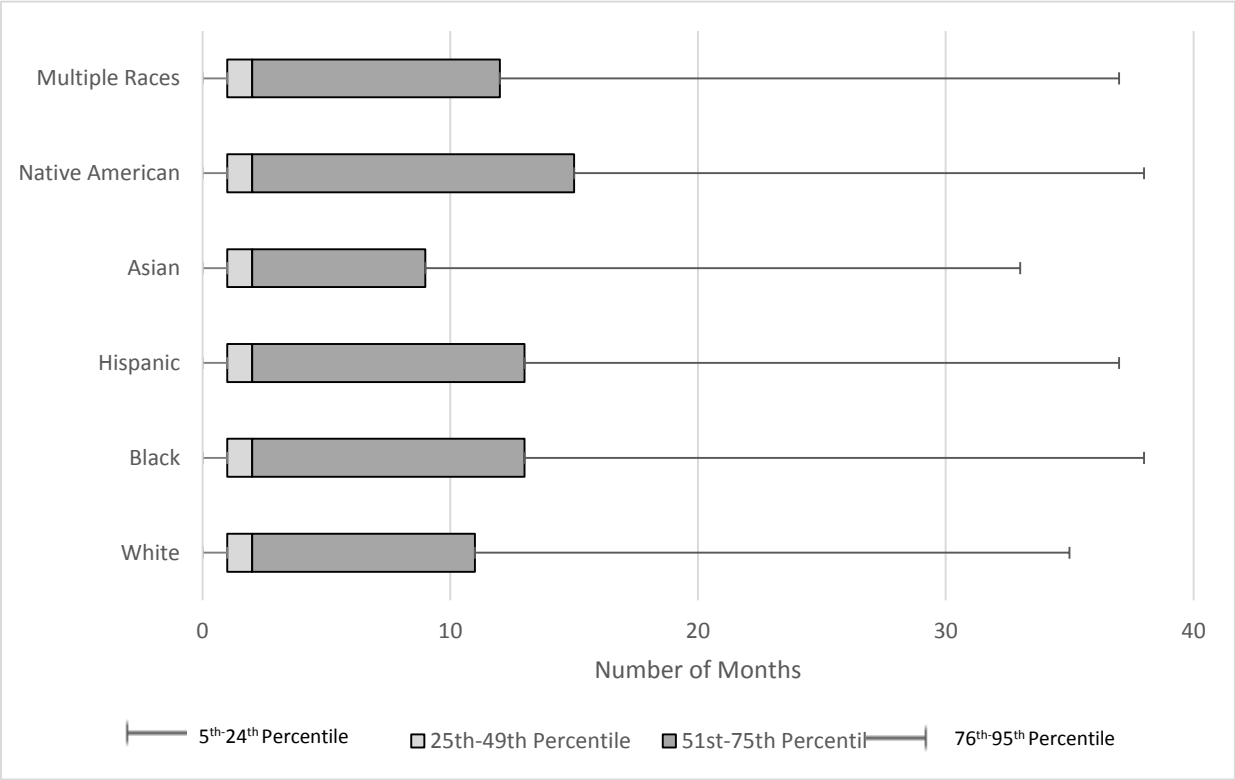
a. Data on White, black, Asian and Hispanics are only shown to improve visibility

Figure 5.3 Cumulative Probability of FIT Testing among newly eligible KPNC enrollees, KPNC 2007-2012[a]



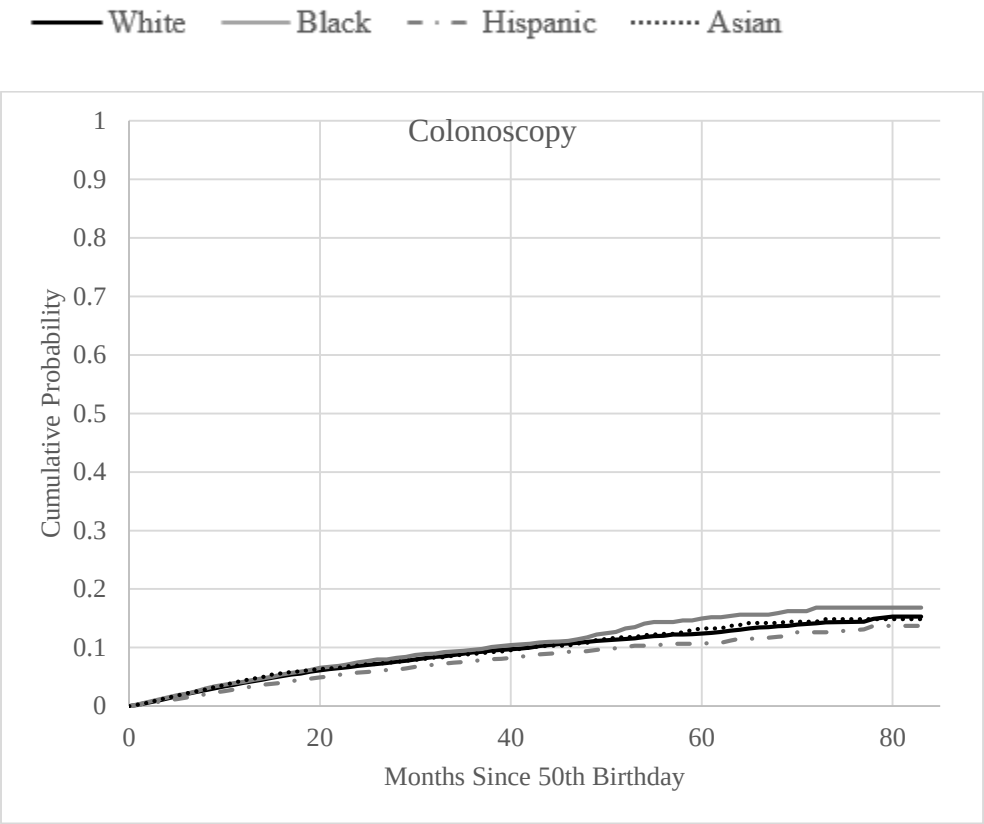
a. Data on White, black, Asian and Hispanics are only shown to improve visibility

Figure 5.4 Number of Months from FIT Mail Date to Return Date by Race/Ethnicity, KPNC 2007-2012[a]



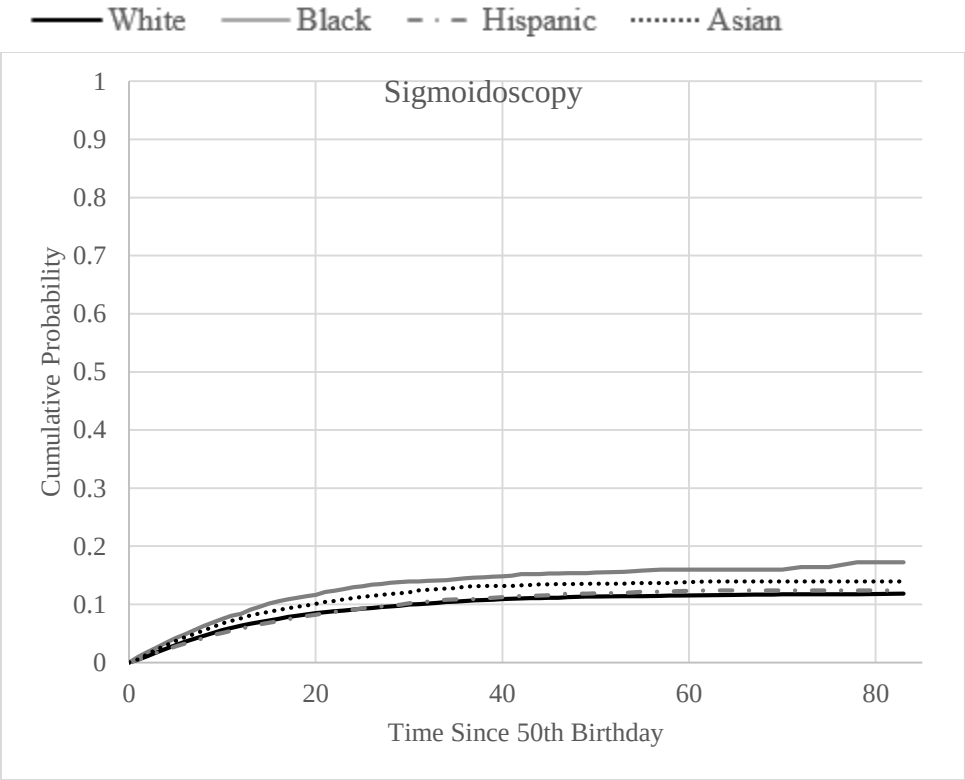
a. There were 119,925 individuals represented in this figure. The 5th, 25th, Median, 75th and 95th Percentiles of the number of months from FIT mail date to return date are presented. Wilcoxon Signed Rank Test P-values relative to White: Black (p<0.001), Hispanic (p<0.001), Asian (p<0.001), Native American (p=0.002), Multiple Races (p=0.714)

Figure 5.5 Cumulative Probability of Colonoscopy by Race/Ethnicity among newly eligible adults, KPNC 2007-2012[a]



a. Data on White, black, Asian and Hispanics are only shown to improve visibility

Figure 5.6 Cumulative Probability of Sigmoidoscopy by Race/Ethnicity among newly eligible adults, KPNC 2007-2012[a]



a. Data on White, black, Asian and Hispanics are only shown to improve visibility

Table 5.1 Characteristics of KPNC Enrollees who were newly eligible for CRC Screening, KPNC 2007-2012

Categories	Total	White	Black	Hispanic	Asian	Native American	Multiple Races	p-value
	N=138799	N=78728	N=11328	N=24160	N=23386	N=489	N=708	
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	
Year of 50th Birthday								
2007	23040 (16.6)	13594 (17.3)	1839 (16.2)	3735 (15.5)	3687 (15.8)	80 (16.4)	105 (14.8)	< 0.001
2008	23259 (16.8)	13391 (17)	1926 (17)	3976 (16.5)	3784 (16.2)	67 (13.7)	115 (16.2)	
2009	23567 (17)	13570 (17.2)	1928 (17)	4012 (16.6)	3836 (16.4)	76 (15.5)	145 (20.5)	
2010	23933 (17.2)	13535 (17.2)	2009 (17.7)	4161 (17.2)	4002 (17.1)	105 (21.5)	121 (17.1)	
2011	22770 (16.4)	12724 (16.2)	1861 (16.4)	4123 (17.1)	3870 (16.5)	75 (15.3)	117 (16.5)	
2012	22230 (16)	11914 (15.1)	1765 (15.6)	4153 (17.2)	4207 (18)	86 (17.6)	105 (14.8)	
Male	62055 (44.7)	35544 (45.1)	4842 (42.7)	11099 (45.9)	10023 (42.9)	232 (47.4)	315 (44.5)	< 0.001
Insurance Category								
Commercial	121841 (87.8)	68557 (87.1)	9964 (88)	21368 (88.4)	20911 (89.4)	417 (85.3)	624 (88.1)	< 0.001
High Deductible Commercial	7397 (5.3)	5117 (6.5)	158 (1.4)	971 (4)	1094 (4.7)	25 (5.1)	32 (4.5)	
Medicare+ Commercial	7187 (5.2)	3857 (4.9)	810 (7.2)	1377 (5.7)	1071 (4.6)	36 (7.4)	36 (5.1)	
Medicaid	1190 (0.9)	526 (0.7)	326 (2.9)	207 (0.9)	118 (0.5)	**	**	
Other	1184 (0.9)	671 (0.9)	70 (0.6)	237 (1)	192 (0.8)	**	**	
Language Preference								
Not English	11250 (8.1)	614 (0.8)	53 (0.5)	6879 (28.5)	3675 (15.7)	20 (4.1)	**	< 0.001
English	122162 (88)	75069 (95.4)	10635 (93.9)	16335 (67.6)	19012 (81.3)	451 (92.2)	660 (93.2)	
Missing	5387 (3.9)	3045 (3.9)	640 (5.6)	946 (3.9)	699 (3)	18 (3.7)	39 (5.5)	
BMI Category								

Underweight	958 (0.7)	529 (0.7)	35 (0.3)	57 (0.2)	333 (1.4)	**	**	< 0.001
Normal	37575 (27.1)	21514 (27.3)	1514 (13.4)	3811 (15.8)	10477 (44.8)	**	**	
Overweight	50253 (36.2)	27988 (35.6)	3610 (31.9)	9135 (37.8)	9097 (38.9)	155 (31.7)	268 (37.9)	
Obese	50013 (36)	28697 (36.5)	6169 (54.5)	11157 (46.2)	3479 (14.9)	246 (50.3)	265 (37.4)	
Charlson Comorbidity Score								
0	114375 (82.4)	66449 (84.4)	8793 (77.6)	19029 (78.8)	19168 (82)	389 (79.6)	547 (77.3)	< 0.001
1	17055 (12.3)	8714 (11.1)	1662 (14.7)	3547 (14.7)	2945 (12.6)	73 (14.9)	114 (16.1)	
≥2	7369 (5.3)	3565 (4.5)	873 (7.7)	1584 (6.6)	1273 (5.4)	27 (5.5)	47 (6.6)	
Family History Documented	7294 (5.3)	4463 (5.7)	692 (6.1)	981 (4.1)	1107 (4.7)	21 (4.3)	30 (4.2)	< 0.001
Area-Based Poverty								
Low 0-3.9%	51455 (37.1)	33111 (42.1)	2601 (23)	6419 (26.6)	8917 (38.1)	147 (30.1)	260 (36.7)	< 0.001
Med 4-7.9%	40627 (29.3)	23806 (30.2)	2549 (22.5)	6629 (27.4)	7291 (31.2)	141 (28.8)	211 (29.8)	
High ≥8%	46717 (33.7)	21811 (27.7)	6178 (54.5)	11112 (46)	7178 (30.7)	201 (41.1)	237 (33.5)	
Testing Characteristics								
Received CRC Screening before the End of Follow-Up	114949 (82.8)	65102 (82.7)	9220 (81.4)	19361 (80.1)	20296 (86.8)	383 (78.3)	587 (82.9)	< 0.001
Type of Test among Individuals who completed a CRC Screening Test								
FIT	98453 (85.6)	55911 (85.9)	7505 (81.4)	16724 (86.4)	17472 (86.1)	340 (88.8)	501 (85.3)	< 0.001
Sigmoidoscopy	6749 (5.9)	3953 (6.1)	638 (6.9)	1021 (5.3)	1086 (5.4)	14 (3.7)	37 (6.3)	
Colonoscopy	9747 (8.5)	5238 (8)	1077 (11.7)	1616 (8.3)	1738 (8.6)	29 (7.6)	49 (8.3)	
Mailed a FIT Kit at Least Once before Follow-Up	119925 (86.4)	68245 (86.7)	9621 (84.9)	21110 (87.4)	19906 (85.1)	419 (85.7)	624 (88.1)	< 0.001
Time Followed in Study	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	

Months followed until CRC screening or censoring	17.6 (16.57)	17.9 (16.71)	18.5 (17.07)	18.6 (16.99)	15.4 (15.16)	18.7 (16.72)	18 (16.91)	
Months followed from 50th Birthday until no longer enrolled in KPNC	45.8 (20.58)	46.3 (20.57)	45.8 (20.42)	44.7 (20.5)	45.1 (20.72)	44.2 (20.55)	46.7 (20.2)	

Abbreviations: Kaiser Permanente Northern California (KPNC), Colorectal Cancer (CRC), Fecal Immunochemical Test (FIT), Body Mass Index (BMI), High Deductible (HD)

Table 5.2 Proportional Hazard Models for Receipt of CRC Screening Overall and by Modality among newly eligible enrollees, KPNC 2007-2012

	Any CRC Screening			FIT			Colonoscopy			Sigmoidoscopy		
	HR	95%CI		HR	95% CI		HR	95%CI		HR	95% CI	
Unadjusted Models[a]												
White	1.00			1.00						1.00		
Black	0.96	0.94	0.98	0.91	0.88	0.93	1.09	1.00	1.19	1.41	1.32	1.50
Hispanic	0.94	0.92	0.95	0.94	0.93	0.96	0.82	0.76	0.87	0.98	0.93	1.04
Asian	1.19	1.17	1.21	1.20	1.18	1.22	1.05	0.98	1.11	1.22	1.16	1.29
Native American	0.90	0.82	1.00	0.93	0.84	1.03	0.55	0.32	0.92	0.86	0.60	1.24
Multiple Races	1.00	0.92	1.09	1.00	0.91	1.09	1.04	0.75	1.43	1.04	0.79	1.38
Partially Adjusted Models[b]												
White	1.00			1.00			1.00			1.00		
Black	0.97	0.95	0.99	0.94	0.92	0.97	0.99	0.90	1.08	1.19	1.11	1.28
Hispanic	0.94	0.92	0.95	0.94	0.93	0.96	0.77	0.72	0.83	1.06	1.05	1.11
Asian	1.13	1.11	1.14	1.14	1.12	1.16	0.87	0.81	0.93	1.18	1.18	1.25
Native American	0.91	0.82	1.01	0.93	0.84	1.04	0.58	0.35	0.99	0.92	0.92	1.32
Multiple Races	0.97	0.95	0.99	0.99	0.91	1.08	1.09	0.79	1.51	0.96	0.96	1.28
Fully Adjusted Models[c]												
White	1.00			1.00			1.00			1.00		
Black	0.98	0.96	1.00	0.95	0.93	0.98	1.03	0.95	1.13	1.21	1.13	1.30
Hispanic	0.95	0.93	0.96	0.94	0.93	0.96	0.81	0.75	0.87	1.06	1.00	1.13
Asian	1.13	1.11	1.15	1.14	1.12	1.16	0.88	0.82	0.94	1.18	1.12	1.25
Native American	0.91	0.82	1.01	0.93	0.84	1.04	0.60	0.35	1.01	0.93	0.64	1.33
Multiple Races	1.00	0.92	1.09	1.00	0.91	1.09	1.10	0.80	1.53	0.97	0.73	1.29

Abbreviations: Kaiser Permanente Northern California (KPNC), Colorectal Cancer (CRC), Fecal Immunochemical Test (FIT), Hazard Ratio (HR), Confidence Interval (CI), Body Mass Index (BMI)

a. Models only include race/ethnicity as a predictor
b. Models are adjusted for year of 50th birthday, gender, BMI category, Charlson Comorbidity, Family History, service area,
c. Models are adjusted for year of 50th birthday, gender, insurance, language preference, BMI category, Charlson Comorbidity, Family History, service area, census-tract poverty

Table 5.3 Log-Binomial Models Estimating Adjusted Prevalence Ratios and 95%CI of Receipt of CRC Screening Before the End of Follow-Up among newly eligible enrollees, KPNC 2007-2012

	Any CRC Screening[a]			FIT[b]			Colonoscopy[c]			Sigmoidoscopy[d]		
	PR	95%CI		PR	95%CI		PR	95%CI		PR	95%CI	
Race/Ethnicity												
White	1.00			1.00			1.00			1.00		
Black	0.99	0.99	1.00	0.97	0.95	0.98	1.05	0.97	1.14	1.23	1.15	1.31
Hispanic	0.99	0.98	0.99	0.98	0.97	0.99	0.83	0.78	0.89	1.08	1.03	1.14
Asian	1.03	1.02	1.04	1.04	1.03	1.05	0.82	0.77	0.88	1.12	1.07	1.19
Native American	0.97	0.93	1.01	0.98	0.93	1.04	0.63	0.37	1.05	0.95	0.67	1.33
Multiple Races	1.00	0.98	1.03	1.00	0.96	1.05	1.08	0.79	1.47	0.97	0.75	1.26

Abbreviations: Kaiser Permanente Northern California (KPNC), Colorectal Cancer (CRC), Fecal Immunochemical Test (FIT), Prevalence Ratio (PR), Confidence Interval (CI), Body Mass Index (BMI)

a. Model examines any type of CRC screening versus no screening and is adjusted for year of 50th birthday, gender, insurance, language preference, BMI category, Charlson Comorbidity, Family History, service area, census-tract poverty
b. Model examines FIT testing versus no testing and is adjusted for year of 50th birthday, gender, insurance, language preference, BMI category, Charlson Comorbidity, Family History, service area, census-tract poverty
c. Model examines colonoscopy versus no testing and is adjusted for year of 50th birthday, gender, insurance, language preference, BMI category, Charlson Comorbidity, Family History, service area, census-tract poverty
d. Model examines sigmoidoscopy versus no testing and is adjusted for year of 50th birthday, gender, insurance, language preference, BMI category, Charlson Comorbidity, Family History, service area, census-tract poverty

Table 5.4 Log-Binomial Models Estimating Adjusted Prevalence Ratios and 95%CI of Receipt of CRC Screening within 2 Year among Newly Eligible enrollees, KPNC 2007-2012

	Any CRC Screening[a]			FIT[b]			Colonoscopy[c]			Sigmoidoscopy[d]		
	PR	95%CI		PR	95%CI		PR	95%CI		PR	95%CI	
Race/Ethnicity												
White	1.00			1.00			1.00			1.00		
Black	0.97	0.96	0.99	0.96	0.94	0.97	0.98	0.87	1.11	1.09	1.03	1.16
Hispanic	0.96	0.95	0.97	0.96	0.95	0.97	0.79	0.71	0.87	0.97	0.92	1.02
Asian	1.05	1.04	1.05	1.05	1.04	1.06	0.96	0.88	1.05	1.20	1.15	1.26
Native American	0.94	0.88	1.00	0.94	0.88	1.01	0.61	0.30	1.26	0.85	0.61	1.20
Multiple Races	1.00	0.95	1.04	0.99	0.94	1.04	1.24	0.80	1.91	1.00	0.78	1.27

Abbreviations: Kaiser Permanente Northern California (KPNC), Colorectal Cancer (CRC), Fecal Immunochemical Test (FIT), Prevalence Ratio (PR), Confidence Interval (CI), Body Mass Index (BMI)

a. Model examines any type of CRC screening versus no screening and is adjusted for year of 50th birthday, gender, insurance, language preference, BMI category, Charlson Comorbidity, Family History, service area, census-tract poverty
b. Model examines FIT testing versus no testing and is adjusted for year of 50th birthday, gender, insurance, language preference, BMI category, Charlson Comorbidity, Family History, service area, census-tract poverty
c. Model examines colonoscopy versus no testing and is adjusted for year of 50th birthday, gender, insurance, language preference, BMI category, Charlson Comorbidity, Family History, service area, census-tract poverty
d. Model examines sigmoidoscopy versus no testing and is adjusted for year of 50th birthday, gender, insurance, language preference, BMI category, Charlson Comorbidity, Family History, service area, census-tract poverty

Table 5.5 Logit-Binomial Models Estimating Odds Ratios and Complementary Log-Log Models Estimating Hazard Ratios of Receipt of CRC Screening by the End of Follow-Up among Newly Eligible enrollees, KPNC 2007-2012

	Logistic Regression Model			Complementary Log-Log Model		
	OR	95%CI		HR	95%CI	
White	1.00			1.00		
Black	0.97	0.92	1.02	0.93	0.91	0.95
Hispanic	0.90	0.86	0.93	0.89	0.88	0.90
Asian	1.29	1.23	1.34	1.02	1.00	1.03

Abbreviations: Odds Ratio (OR), Hazard Ratio (HR),

a. Model examines sigmoidoscopy versus no testing and is adjusted for year of 50th birthday, gender, insurance, language preference, BMI category, Charlson Comorbidity, Family History, service area, census-tract poverty using logit-binomial regression.
b. Model examines sigmoidoscopy versus no testing and is adjusted for year of 50th birthday, gender, insurance, language preference, BMI category, Charlson Comorbidity, Family History, service area, census-tract poverty using complementary log-log models with interval censoring every 6-months.

Table 5.6 Multivariable Cox Proportional Hazard Models of Receipt of FIT Testing among newly eligible KPNC enrollees who were mailed a kit (2007-2012)

	Receipt of FIT Testing		
	HR	95%CI	
Race/Ethnicity			
White	1.00		
Black	0.95	0.92	0.97
Hispanic	0.94	0.92	0.96
Asian	1.14	1.12	1.16
Native American	0.93	0.83	1.04
Multiple Races	0.99	0.91	1.09

Abbreviations: Kaiser Permanente Northern California (KPNC), Hazard Ratio (HR), Confidence Interval (CI)

a. 119,925 respondents were included in the model. Adjusted for language, gender, insurance, BMI, family history, poverty, comorbidity, and service area

Table 5.7 Method of Testing (Outreach versus In-Reach) Among KPNC Enrollees Receiving FIT

Categories	Outreach	In-reach	p-value
	N (%)	N (%)	
TOTAL	69725 (77.4)	20416 (22.6)	
Race/Ethnicity			
White	40299 (78.5)	11048 (21.5)	$p < 0.0001$
Black	5359 (78.1)	1503 (21.9)	
Hispanic	11798 (77.2)	3489 (22.8)	
Asian	11662 (73.5)	4206 (26.5)	
Native American	239 (77.9)	68 (22.1)	
Multiple Races	368 (78.3)	102 (21.7)	

Abbreviations Kaiser Permanente Northern California (KPNC)

Chapter 6 Interval Colorectal Cancers, Race/Ethnicity and Physician Polyp Detection Rate in Medicare Enrollees (Aim 3)

Title: Racial and Ethnic Disparities in Interval Colorectal Cancer Incidence: A Matched Case-Control Study

Running Title: Interval Colorectal Cancer by Race/Ethnicity

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Abstract

Background: Interval colorectal cancers (CRC) accounts for 3-8% of all CRCs in the US. Data on interval CRC occurrence by race/ethnicity are scant.

Objective: To examine whether interval CRC incidence among elderly Medicare patients differs by race/ethnicity and whether this potential variation, could be accounted for by differences in quality of colonoscopy, as measured by physicians' polyp detection rate (PDR).

Design, Setting and Participants: Incidence density sampling-based matched case-control study of patients 66-75 years of age who received a colonoscopy between 2002-2011 in SEER-Medicare data.

Measurements: Adjusted conditional logistic regression was used to estimate incidence rate ratios (IRR) and 95% confidence interval (CI) for interval CRC, defined as a CRC diagnosis 6-59 months after colonoscopy.

Results: We analyzed 2,770 interval CRC patients and 11,080 matched controls. A higher proportion of blacks (29%) received a colonoscopy from lower-PDR physicians than whites (20%) (p-value<0.001). PDR was significantly associated with interval CRC incidence. Compared to whites, interval CRC incidence was significantly higher in blacks (IRR= 1.25, 95% CI 1.04, 1.51). Black-white disparities in interval CRC were more pronounced for rectal (IRR=1.65, 95% CI 1.13, 2.41) and distal cancer (IRR=1.55, 95% CI 1.01, 2.40) than for proximal (IRR=1.14, 95% CI 0.90, 1.44) colon cancer. Adjustment for PDR did not alter IRRs by race/ethnicity.

Limitations: Colonoscopy and polypectomy were identified using billing codes.

Conclusions: Among elderly Medicare enrollees, interval CRC incidence was higher in blacks than in whites, with the difference more pronounced for rectal and distal colon cancer than for proximal colon cancer. This association was not accounted for by differences in PDR.

Primary Funding Source: The American Cancer Society.

Introduction

Colorectal Cancer (CRC) is the third most common cancer and second leading cause of cancer-related death in the US.[1] CRC screening is effective in reducing CRC incidence and death risk by detecting pre-cancerous lesions or cancer at more curable stage.[16, 17, 67 9-11] However, some CRCs develop in screened populations, either because they were missed at the time of screening or developed during the interval between recommended screenings or surveillance.[205] Interval CRCs, cancers that develop after a negative colonoscopy but before the next recommended test, account for approximately 3-8% of all CRCs in the US, though estimates vary by study design and population.[32, 35, 205] Interval CRC risk and its associations with patient demographic and clinical factors as well as physician factors, including quality of colonoscopy metrics, has been examined in a few studies.[32, 35, 37, 87] However, interval CRC incidence by race/ethnicity are not well known as most previous studies were conducted in people of European decent.[32]

Black-white disparities in the occurrence of interval CRCs are of particular concern because blacks have the highest CRC incidence and mortality rates of any race or ethnicity in the US, with the incidence rates 22-27% higher than whites.[206] Approximately 40% of black-white disparities in CRC incidence are attributed to lower screening utilization in blacks.[26] The remaining proportion has not been fully explained though likely contributors include differences in socioeconomic status, lack of follow-up after a positive test, lifestyle and risk factors.[26, 80, 207-209] However, the disparity may partly be a reflection of the black-white difference in the quality of tests for CRC.[26] Whereas previous studies have noted poorer quality of mammography and higher risk of interval breast cancers in blacks compared with whites;[99, 100] similar detailed evidence

pertaining to quality of colonoscopy and interval CRCs by race/ethnicity is not available. In the present study, we examined whether the incidence of interval CRC varies by race/ethnicity in Medicare patients 66-75 years of age and whether physician's polyp detection rate (PDR) accounts for the potential differences in interval CRC between blacks and whites.

Methods

Study Design and Population

This study was an incidence density sampling-based matched case-control study among patients who received a colonoscopy in 2002-2011 between 66-75 years of age. Information on subjects were obtained from Medicare files linked to the data from the National Cancer Institute's Surveillance Epidemiology and End Results (SEER) program, which are described elsewhere.[172] Briefly, SEER is a collection of 18 population-based cancer registries, covering approximately 28% of the US population. Medicare is a federally-funded health insurance plan covering 97% of people ≥65 years. SEER data were used to identify cases and tumor information. Medicare carrier, outpatient and Medical Provider Analysis and Review (MEDPAR) data files were used to identify receipt and dates of colonoscopies and polypectomies (**Table 6.1**) as well as the physician that preformed these procedures. The SEER-Medicare database also maintains a 5% random sample of cancer-free Medicare beneficiaries residing in SEER registry areas. This study did not involve direct contacts with patients and was approved by Emory University's Institutional Review Board.

Case and Control Selection

We defined an interval CRC as a first primary invasive colorectal adenocarcinoma diagnosed 6 to 59 months after an index colonoscopy performed between 2002 and 2011. The lower bound of 6 months was used because most suspicious lesions found during a colonoscopy would have a diagnostic workup during this time frame. The upper bound of 59 months was used because claims were only available 6 years prior to CRC diagnosis and it is also in accordance with previous studies.[32 37] Claims data were only available for enrollees with fee-for-service (FFS) Parts A (inpatient) and B (outpatient) Medicare plans, therefore we restricted our analyses to cases who were continuously enrolled in these plans 12 months prior to and 6 months following their index colonoscopy to establish baseline comorbidities for non-cancer diagnoses in these patients and to allow time for the appropriate diagnostic workup of suspicious lesions found during colonoscopy. Further, cases missing key data elements were also excluded as outlined in **Figure 6. 1**. The same exclusion criteria were applied to controls selected from the 5% random sample of Medicare enrollees who received a colonoscopy between 2002 and 2011. Four controls were individually matched to each case of interval CRC on gender, exact age at, and year of colonoscopy and remaining at risk when the case occurred. In this sampling strategy a control may later become a case,[171] and the odds ratio estimates the incidence rate ratio (IRR).[166]

After exclusions the final study population included 2,770 cases and 11,080 controls. Interval CRCs were sub-classified into early (6 - 35 months after a colonoscopy) and late (36-59 months after a colonoscopy) cancers. The early interval represents the minimum amount of time that a patient would be recommended to have a surveillance colonoscopy

according to guidelines, with the exception of patients with >10 adenomas.[76] We also examined associations by SEER summary stage (localized, regional, and distant) and tumor location grouped as proximal, distal and rectal (including rectosigmoid junction).

Exposures

The primary exposures of interest in this study were race/ethnicity and physicians' polyp detection rate (PDR), a relative measure of colonoscopy quality. Race/ethnicity was based on Medicare enrollment data and categorized as non-Hispanic white, black, Hispanic, Asian, and Other. PDR was calculated for each physician by dividing the number of patients on whom polypectomy was performed by the total number of patients undergoing colonoscopy during a 5-year period and ranked into quartiles. A patient was assigned their physician's PDR in the 5-year period preceding the index colonoscopy; for example, a colonoscopy occurring in 2002 was assigned the physician's 1998-2002 average PDR. The abovementioned PDR measure was calculated using data from the 5% sample for 1,722 unique providers who performed at least 25 total colonoscopies (representing 500 colonoscopies based on the 5% sample) between 1998 and 2011 and 10 colonoscopies (representing 200 colonoscopies based on the 5% sample) within the corresponding 5-year period. The absolute PDR has been shown to be highly correlated ($r>0.90$) with adenoma detection rate (ADR) in the proximal colon [34, 95, 210, 211] and relative measures of PDR (eg: low, medium, high) are strongly associated with ADR.[34] While ADR is an established metric for colonoscopy quality[90], Medicare claims do not contain information on histopathology or tumor/polyp location thus leading to PDR as the exposure of choice.

Covariates

Region (Northeast, Midwest, South and West), metropolitan classification (urban, suburban and rural) and the percentage of persons in a zip code living below the federally designated poverty level [low (0-7.9%), medium (8-15.5%) and high (>15.5%)] were used to describe residence and socioeconomic status (SES). Diverticulitis diagnosis and Charlson comorbidity score prior to index colonoscopy were also considered as covariates. Provider's primary specialty was identified by Health Care Finance Administration specialty code in the carrier files and categorized as gastroenterology, CRC surgery, general surgery, general internal medicine or other/unknown. Polypectomy at index colonoscopy was also considered to determine if disparities in interval CRC might be possibly due to lack of surveillance. Further, to examine if results varied based on test indication, a validated algorithm to determine screening colonoscopy based on age and gastrointestinal symptoms and conditions (e.g.: abdominal pain, iron deficiency anemia) within 12 months of a colonoscopy was used. [212]

Statistical Analysis

Chi-Square tests were used to examine differences in covariates between cases and controls (two-sided p-value, α=0.05). Marginal conditional logistic regression models, with a sandwich covariance estimator accounting for clustering of patients within a physician, was used to estimate adjusted IRR and corresponding 95% confidence intervals (CIs). A series of models were performed to determine if adjustment of variables attenuated the association between race/ethnicity and interval CRCs. Two-way

interaction terms between race/ethnicity and each covariate were assessed and none were detected except for test indication. We also assessed the association between race/ethnicity and interval CRCs by the timing (early/late), tumor location, and stage of interval CRC. Sensitivity analyses stratified on screening and non-screening colonoscopy and polypectomy at index colonoscopy were also conducted. Additional models were based on subsets of cases and controls whose index colonoscopies were performed by gastroenterologists at varying levels of high colonoscopy volume (≥50 and ≥100). All analyses were performed using Statistical Analysis System version 9.2. Data analysis for this work was funded by the American Cancer Society.

Results

We identified 3,906 interval CRCs, representing 7.6% of all CRCs during the study period, of which 2,770 interval CRC cases (with 11,080 controls) met the inclusion criteria. Cases and controls were on average 71.0 years of age and 53% were males. There was a higher percentage of blacks among cases than in controls (**Table 6.2**). Approximately 64% of cases had proximal tumors and 66% were diagnosed with early interval CRC.

A higher proportion of blacks (29%) received their index colonoscopy from physicians in the lowest PDR quartile compared to whites (20%) (p-value<0.001) **(Table 6.3).** Most colonoscopies, regardless of race/ethnicity, were performed by physicians whose primary specialty was gastroenterology (**Table 6.3**), a group of physicians with greater colonoscopy volume than other physician specialties (**Table 6.4**). Receipt of a screening

colonoscopy was comparable in blacks (74%) and white (75%) (p-value=0.58) and polypectomy at index was similar (21% in blacks and 24% in white, p-value=0.120). Compared with patients who received a colonoscopy from a high-PDR physician, interval CRC incidence was higher in patients whose colonoscopy was performed by physicians with a low (IRR=1.97, 95% CI 1.68, 2.30), medium-low (IRR=1.56, 95%CI 1.35, 1.80), and medium-high PDR (IRR=1.20, 95%CI 1.04, 1.38) in dose-response pattern (Test for trend: p-value <0.001). **(Table 6.5)**

Interval CRC incidence was statistically significantly higher in blacks (IRR= 1.31, 95% CI 1.11, 1.55) compared to whites after accounting for matching factors (age, gender and year of colonoscopy) (**Table 6.5**) and did not substantially change with additional adjustment for demographic factors, and polypectomy at index colonoscopy. Further adjustment for PDR modestly attenuated black-white differences in interval CRC incidence rates (IRR=1.25, 95%CI 1.04, 1.51). Additional adjustment for test indication did not alter these results (data not shown).

In analyses stratified by tumor location, black patients had significantly elevated interval distal (IRR=1.55, 95% CI 1.01, 2.40) and rectal (IRR=1.65, 95%CI 1.13, 2.41) cancer incidence relative to white patients whereas no appreciable difference was observed for proximal CRCs (IRR=1.14, 95% CI 0.90, 1.44) **(Table 6.6).** Similar results were observed in models that only adjusted for matching factors (age, sex, and year of colonoscopy). **(Table 6.7)** When analyzed by stage, compared with white, blacks had significantly higher incidence of interval CRC diagnosed as distant disease (IRR=1.90,

95% CI 1.21, 2.97), but not regional or local disease **(Table 6.8).** Black-white differences were observed for early and late interval CRCs (**Table 6.9**).

Among patients with a polypectomy at their index colonoscopy, the black-white difference was more pronounced (IRR=1.60, 95% CI 1.19-2.15) than patients without a polypectomy at index (IRR=1.15, 95%CI 0.91, 1.46), but a test for interaction was not statistically significant (p-value for heterogeneity=0.33) (**Table 6.10**). In analyses considering test indication, black-white disparities were apparent both in patients with screening (IRR=1.30, 95%CI 1.02, 1.67) and non-screening colonoscopies (IRR=1.59, 95%CI 1.19, 2.12), with evidence of statistical interaction (p-value for heterogeneity <0.001) (**Table 6.11)**. Results of analyses restricted to patients receiving their index colonoscopy from a higher-volume gastroenterologist were similar to the main findings (**Tables 6.12 and 6.13**).

Compared to whites, Asians had statistically significantly lower interval CRC incidence in adjusted models (IRR=0.73, 95%CI 0.56, 0.97) (**Table 6.5**). There was no significant difference between interval CRC incidence in Hispanics, relative to whites, in the main analysis or by tumor location or stage.

Discussion

In this population-based study of elderly Medicare enrollees, interval CRC incidence was 25% higher in blacks compared to whites, while incidence among Asians was lower. Blacks were more likely than whites to have colonoscopies performed by physicians with

low PDR, a surrogate measure for the quality of colonoscopy. However, differences in PDR of the physician did not explain the observed black-white disparity. Black-white differences in interval CRC incidence was more pronounced for distal colon and rectal cancers than for proximal colon cancer and were largely due to high incidence of disease diagnosed at advance stage.

Missed lesions and PDR are especially important factors for proximal lesions because the proximal colon is harder to reach endoscopically and it is the most common location of difficult-to-detect sessile polyps.[77, 78, 213] A previous study reports that behavioral factors such as smoking and obesity account for a greater proportion of differences in proximal colon cancer incidence by measures of SES and raised the possibility that lower colonoscopy utilization could account for these differences.[208] Additionally, a SEER-Medicare study reporting a protective effect of ever receiving a colonoscopy, relative to not receiving a colonoscopy, was closer to the null in blacks compared to white, particularly for distal colon cancers after accounting for physician specialty but not PDR.[66] Our study observed greater differences in distal colon and rectal cancer incidence among blacks despite receiving a colonoscopy.

It is possible that quality factors other than PDR contribute to this pattern. Cecal intubation rates, withdrawal time and patient-related quality factors such as the adequacy of the bowel preparation may vary by race, and be correlated with PDR.[214] Data on incomplete resection of polyps, the second most common reason for interval CRCs,[32] by race ethnicity are not available in the published literature nor is it captured in SEER-

Medicare data. PDR is an indirect measure of lesions missed during a colonoscopy, the most commonly cited reason for interval CRCs, though other reasons include incomplete resection of polyps, or rapidly developing or "de-novo" tumors.[32, 205] A recent study estimated that 37% of interval rectal CRCs were attributable to incomplete polyp detection, compared to 10-16% of proximal tumors, which contribute to black-white differences in rectal interval cancer.[215] This factor may also contribute to our observation of higher incidence of advanced and early CRCs.

It is important to point out that some interval CRCs (13-24%) are believed to be "de novo" cancers and are thus unavoidable. It is not clear if incidence of such lesions differs by race.[32] Previous studies have suggested that blacks have more aggressive tumors, because they tend to be younger at diagnosis[84] and have higher prevalence of large polyps.[216] On the other hand the overall prevalence estimates for colorectal polyps and adenomas in blacks and whites are similar,[80 47] findings consistent with similar polypectomy prevalence observed in the current study. There is evidence that sessile serrated polyps are more aggressive and that interval CRCs are more likely to exhibit micro-satellite insatiability (MSI) and CpG island methylator phenotype (CIMP). [217] Whether or not these factors account for the higher incident interval CRCs among black patients in our study is not clear as studies on racial differences in MSI and CIMP are equivocal[85, 86, 218] and our study was not designed to directly answer this question. MSI tumors tend to be proximally located, and if this factor was driving racial disparities in interval CRCs, we would have expected especially elevated proximal interval CRC tumor incidence among blacks relative to whites. Our data provide little evidence that this may

be the case. Lower interval CRC incidence among Asians relative to whites observed in the current study is consistent with the previously reported lower overall CRC incidence in this group [219], a pattern commonly attributed to differences in risk factors, including obesity and diet. Our findings are in agreement with previous studies,[47, 220] reporting similar polyp and/or adenoma prevalence in Asians and whites. This raised the possibility that polyps may progress more slowly in Asians, though detailed information on tumor characteristics and biology (eg: MSI, CIMP status) in Asians is not available.

Polypectomy at index colonoscopy was similar between blacks and whites, though black-white differences were more apparent among patients with polypectomy than without polypectomy. Depending on the size and number of polyps detected, surveillance colonoscopy is recommended at intervals of up to 10 years of an index procedure in most instances.[76] We were not able to directly measure adherence to recommended follow-up interval due to a lack of information on histology and polyp size in Medicare claims. Black-white differences were observed within three years following a colonoscopy in our study and two previous SEER-Medicare-based studies noted that blacks were more likely to undergo a surveillance colonoscopy within three or five years of polyp removal.[221, 222] Taken together, this suggests that differences in recommended surveillance colonoscopy may only moderately contribute to higher incidence of interval CRC among blacks, though further study is needed to assess the utility of race-specific surveillance colonoscopy recommendations.

The majority of interval CRCs in our study were proximally located and occurred within 36 months of colonoscopy, this observation is generally consistent with the current literature.[32, 35, 37] We observed that 7.6% of CRCs diagnosed in Medicare patients within 5 years of an index colonoscopy, in line with previous studies with a similar definition.[32, 37] Our findings and those reported elsewhere [37] highlight the importance of attentive examination of the colon and rectum during a colonoscopy to achieve the optimal benefit of this test. A previous SEER-Medicare study covering the period from 1994 to 2005 noted higher odds of interval CRC relative to screen-detected CRCs for blacks relative to whites.[37] Our findings are consistent with this observation.

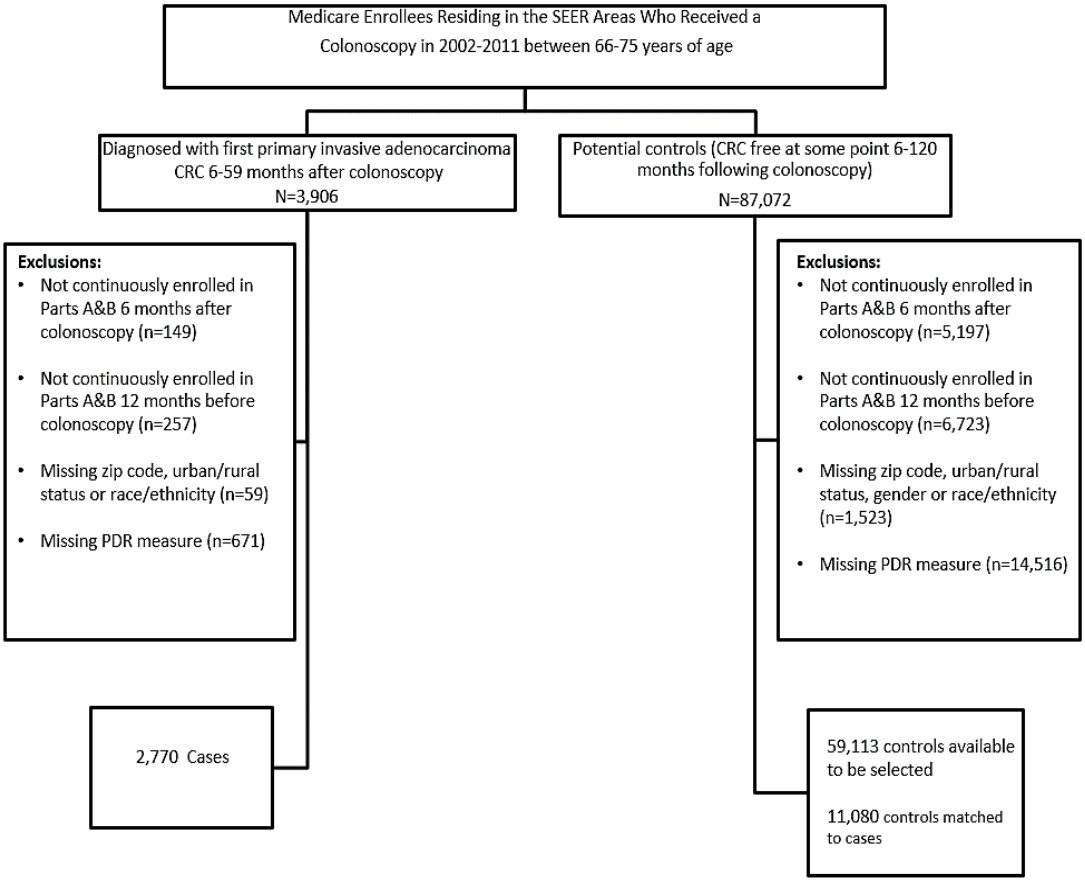
There are some limitations of this study. Colonoscopy and polypectomy were identified using billing codes. Compared to an endoscopic database, Medicare data have high sensitivity (>93%) and specificity (98%) for identifying colonoscopy and polypectomy.[223, 224] Although test indication was not directly available in claims data, results incorporating our algorithm-based screening indication did not alter our main findings. Additionally, we used PDR to approximate ADR, which are highly correlated. Although research supports the use of administrative data to estimate PDR, their correlation varies by tumor location[34, 95, 210, 211, 225]. Specifically, PDR is less strongly correlated with ADR in the distal colon and rectum [210, 211], likely as a result of a greater proportion of non-adenomatous polyps in these regions, however, physicians with high number of adenomas are also more likely to detect and remove non-adenomatous polyps[226] Further, the minimum number of colonoscopies required to adequately determine the PDR or ADR is uncertain. A recent study estimated that at least 500

examinations would be needed to determine ADR[227] and the study that served as the basis for establishing the American Gastroenterology Association's quality metrics included physicians with ≥300 colonoscopies[35], while other studies used a threshold of 50 colonoscopies.[34, 95] In the current study, we used a threshold of 500 colonoscopies, represented by 25 colonoscopies in the 5% Medicare sample for our study. Varying the threshold as well as restricting analyses to gastroenterologists did not alter our main results. Additionally, our PDR measures were based on Medicare FFS patients, which may not be representative of a physicians' patient population, though relative measures of procedural volume (e.g.: low, medium, high) in SEER-Medicare and Medicare have been shown to be similar[228] and there is also evidence that relative procedural volume in patients <65 and ≥65 years of age are also correlated.[229] In addition, we did not have information on the involvement of gastroenterology fellows, which has been shown to increase ADR[230] and could vary by practice setting and race/ethnicity. Information on tumor characteristics (eg: MSI) and polyp histopathology that presumably influence CRC risk[32] were not available in SEER-Medicare data. Data on behavioral factors, such as alcohol intake, smoking, obesity, low-fiber and folate intake, and physical inactivity, that clearly increase overall CRC risk were also not available, though the specific influence of these factors on interval CRCs is unexplored. Lastly, this study was conducted among an elderly population with health insurance and results may not be generalizable to younger populations.

In conclusion, we observed higher incidence of interval CRCs in blacks compared to whites in a population-based study of elderly Medicare enrollees. Proximal tumors

represented the majority of interval CRCs, and black-white differences were most pronounced for distal colon and rectal cancers. Quality of colonoscopy, as measured by PDR, was associated with interval CRC, but did not account for the racial disparities. Futures studies examining this issue are warranted given the particularly high overall incidence of interval CRC in black populations as well as larger disease burden in this group.

Figure 6.1 Study Population Derivation, SEER-Medicare 2002-2011



Abbreviations: Colorectal Cancer (CRC), Surveillance Epidemiology End Results (SEER), and Polyp Detection Rate (PDR)

*Table 6.1 International Classification-9 and Current Procedural Terminology Codes to Identify Colonoscopy and Polypectomy**

	CPT codes	ICD-9 Procedure Codes
Colonoscopy	G0105, G0120, 45378, 45379, 45380, 45381, 45382, 45383, 45384, 45385,	45.23, 45.25, 45.42, 45.43
Polypectomy	45383,45384, 45385	45.42, 45.43, 48.36

Abbreviations: Current Procedural Terminology (CPT), International Classification of Diseases (ICD), Clinical Modification (CM)
*CPT and ICD-9 CM codes were identified using outpatient, carrier/physician and Medical Provider Analysis and Review (MEDPAR) files.

Table 6.2 Characteristics of Cases and Controls, SEER-Medicare 2002-2011

	Controls N (%)	**Cases N (%)**	**P-value**
Total	11,080	2,770	
Race/Ethnicity			<0.001
White	9368 (84.5)	2351 (84.9)	
Black	693 (6.3)	228 (8.2)	
Hispanic	195 (1.8)	39 (1.4)	
Asian	465 (4.2)	81 (2.9)	
Other	359 (3.2)	71 (2.6)	
Physicians' PDR			<0.001
Q1 Low	2308 (20.8)	670 (24.2)	
Q2 Medium Low	2999 (27.1)	779 (28.1)	
Q3 Medium High	3092 (27.9)	709 (25.6)	
Q4 High	2681 (24.2)	612 (22.1)	
Provider Specialty			<0.001
GI	8467 (76.4)	1925 (69.5)	
CRC Surgery	462 (4.2)	132 (4.8)	
General Internal	977 (8.8)	252 (9.1)	
General Surgery	951 (8.6)	286 (10.3)	
Other	223 (2)	175 (6.3)	
Diagnosed with Diverticulitis	6832 (61.7)	1814 (65.5)	<0.001
Charlson Comorbidity Score			<0.080
0	9274 (83.7)	2280 (82.3)	
1	1370 (12.4)	386 (13.9)	
2+	436 (3.9)	104 (3.8)	
Geographic Region			
Northwest	2053 (18.5)	658 (23.8)	<0.001
Midwest	1275 (11.5)	413 (14.9)	
South	3048 (27.5)	636 (23)	
West	4704 (42.5)	1063 (38.4)	
Zip-Code Level Poverty			0.080
Low	3451 (31.1)	903 (32.6)	
Medium	3581 (32.3)	836 (30.2)	
High	4048 (36.5)	1031 (37.2)	
Urban/Rural Status			0.33
Urban	9286 (83.8)	2298 (83)	
Suburban	1599 (14.4)	413 (14.9)	
Rural	195 (1.8)	59 (2.1)	
Index Colonoscopy Information			
Polypectomy at Index	2614 (23.6)	1254 (45.3)	<0.001
Screening Colonoscopy*	8312 (75)	1562 (56.4)	<0.001
Matching Factor†			
Colonoscopy Age			---
66-69	3580 (32.3)	895 (32.3)	
70-75	7500 (67.7)	1875 (67.7)	
Year of Colonoscopy			---

2002-2003	3772 (34)	943 (34)	
2004-2005	1916 (17.3)	479 (17.3)	
2006-2007	3284 (29.6)	821 (29.6)	
2008-2009	1796 (16.2)	449 (16.2)	
2010-2011	312 (2.8)	78 (2.8)	
Gender			---
Male	5816 (52.5)	1454 (52.5)	
Female	5264 (47.5)	1316 (47.5)	
Case Characteristics			
Stage			---
Localized		1389 (50.1)	
Regional		931 (33.6)	
Distant		391 (14.1)	
Unknown		59 (2.1)	
Tumor Location			---
Proximal		1785 (64.4)	
Distal		396 (14.3)	
Rectum		521 (18.8)	
Unknown/NOS		68 (2.5)	
Interval CRC Timing			---
Early (6-35 months)		1837 (66.3)	
Intermediate (36-59 months)		933 3.7)	

Abbreviations: Surveillance Epidemiology and End Result (SEER), Colorectal Cancer (CRC), Quartile (Q), Gastroenterology (GI), Polyp Detection Rate (PDR) Not Otherwise Specified (NOS)

*Screening colonoscopy was determined using an algorithm

† No p-value displayed for colonoscopy age, year or gender as these were matching factors. Exact age and year of colonoscopy were matched on.

Table 6.3 Characteristics by Race/Ethnicity among Controls, SEER-Medicare

Categories	Total	White	Black	Hispanic	Asian	Other	p-value all race/ethnicities	p-value black vs white
	N=11080 N (%)	N=9368 N (%)	N=693 N (%)	N=195 N (%)	N=465 N (%)	N=359 N (%)		
PDR Quartile							< 0.001	< 0.001
Q1 Low	2308 (20.8)	1851 (19.8)	199 (28.7)	54 (27.7)	113 (24.3)	91 (25.3)		
Q2 Medium Low	2999 (27.1)	2564 (27.4)	196 (28.3)	54 (27.7)	101 (21.7)	84 (23.4)		
Q3 Medium High	3092 (27.9)	2694 (28.8)	139 (20.1)	52 (26.7)	115 (24.7)	92 (25.6)		
Q4 High	2681 (24.2)	2259 (24.1)	159 (22.9)	35 (17.9)	136 (29.2)	92 (25.6)		
Provider Specialty							< 0.001	0.051
GI	8467 (76.4)	7126 (76.1)	542 (78.2)	155 (79.5)	356 (76.6)	288 (80.2)		
CRC Surgery	462 (4.2)	413 (4.4)	33 (4.8)	*	*	*		
General Internal	977 (8.8)	763 (8.1)	53 (7.6)	25 (12.8)	89 (19.1)	47 (13.1)		
General Surgery	951 (8.6)	882 (9.4)	45 (6.5)	*	*	*		
Other/Missing	223 (2)	184 (2)	20 (2.9)	*	*	*		
Poverty Level							< 0.001	< 0.001
Low	3451 (31.1)	3107 (33.2)	67 (9.7)	19 (9.7)	110 (23.7)	148 (41.2)		
Medium	3581 (32.3)	3102 (33.1)	139 (20.1)	45 (23.1)	180 (38.7)	115 (32)		
High	4048 (36.5)	3159 (33.7)	487 (70.3)	131 (67.2)	175 (37.6)	96 (26.7)		
Urban/Rural Status							< 0.001	< 0.001
Metro	1794 (16.2)	1692 (18.1)	66 (9.5)	15 (4.2)	*	*		
Suburban/Rural	9286 (83.8)	7676 (81.9)	627 (90.5)	344 (95.8)	*	*		
Polyp Removed at Index Colonoscopy	2614 (23.6)	2246 (24)	148 (21.4)	28 (14.4)	112 (24.1)	80 (22.3)	0.015	0.120
Screening Colonoscopy	8312 (75)	7050 (75.3)	515 (74.3)	125 (64.1)	321 (69)	301 (83.8)	< 0.001	0.58
Diverticulitis Diagnosis	6832 (61.7)	5777 (61.7)	421 (60.8)	124 (63.6)	294 (63.2)	216 (60.2)	0.72	0.63

Charlson Comorbidity Score							0.25	0.56
0	9274 (83.7)	7867 (84)	573 (82.7)	155 (79.5)	377 (81.1)	302 (84.1)		
1	1370 (12.4)	1137 (12.1)	88 (12.7)	*	66 (14.2)	*		
2+	436 (3.9)	364 (3.9)	32 (4.6)	*	22 (4.7)	*		
Gender							< 0.001	< 0.001
Female	5816 (52.5)	4850 (51.8)	419 (60.5)	113 (57.9)	247 (53.1)	187 (52.1)		
Male	5264 (47.5)	4518 (48.2)	274 (39.5)	82 (42.1)	218 (46.9)	172 (47.9)		
Age at Colonoscopy							0.100	0.47
66-69	3580 (32.3)	3045 (32.5)	216 (31.2)	131 (36.5)	132 (28.4)	56 (28.7)		
70-75	7500 (67.7)	6323 (67.5)	477 (68.8)	228 (63.5)	333 (71.6)	139 (71.3)		
Colonoscopy Year							< 0.001	0.080
2002-2003	3772 (34)	3230 (34.5)	218 (31.5)	83 (42.6)	162 (34.8)	79 (22)		
2004-2005	1916 (17.3)	1622 (17.3)	128 (18.5)	34 (17.4)	*	69 (19.2)		
2006-2007	3284 (29.6)	2792 (29.8)	202 (29.1)	45 (23.1)	131 (28.2)	114 (31.8)		
2008-2009	1796 (16.2)	1460 (15.6)	131 (18.9)	*	96 (20.6)	*		
2010-2011	312 (2.8)	264 (2.8)	14 (2)	*	*	*		
Region							< 0.001	< 0.001
Northeast	2053 (18.5)	1827 (19.5)	147 (21.2)	*	29 (6.2)	38 (10.6)		
Midwest	1275 (11.5)	1126 (12)	128 (18.5)	*	*	*		
South	3048 (27.5)	2710 (28.9)	297 (42.9)	*	*	*		
West	4704 (42.5)	3705 (39.5)	121 (17.5)	177 (90.8)	413 (88.8)	288 (80.2)		

Abbreviations: Surveillance Epidemiology and End Results (SEER), Polyp Detection Rate (PDR), Quartile (Q), Gastroenterology (GI), Colorectal Cancer (CRC)
*Data suppressed to protect patient confidentiality

Table 6.4 Summary of Polyp Detection Rates, Physician Characteristics and Colonoscopy Volume, SEER-Medicare 1998-2011[, †]*

	Quartile 1 (Low)	Quartile 2 (Medium Low)	Quartile 3 (Medium High)	Quartile 4 (High)		
Year of Colonoscopy (Range)			**Median PDR**			
1998-2002	12.0 (0-17.6)	23.6 (17.7-28.6)	34.6 (28.7-41.7)	51.2 (41.8-100)		
1999-2003	12.1 (0-17.7)	23.3 (17.8-28.9)	35.0 (29.0-41.7)	50.6 (41.8-100)		
2000-2004	11.9 (0-17.0)	22.5 (17.1-27.5)	33.3 (27.6-40.0)	48.7 (40.1-100)		
2001-2005	11.3 (0-16.7)	21.9 (16.9-26.7)	32.1 (26.7-38.5)	46.4 (38.6-100)		
2002-2006	10.2 (0-15.7)	20.9 (15.8-25.6)	30.1 (25.8-37.3)	45.7 (37.4-100)		
2003-2007	8.8 (0-13.7)	19.2 (13.6-23.9)	29.4 (24.0-35.6)	44.4 (35.7-100)		
2004-2008	7.7 (0-12.0)	17.7 (12.1-22.7)	28.6 (22.8-34.9)	43.3 (35.000)		
2005-2009	6.5 (0-11.1)	16.7 (11.2-21.6)	27.8 (21.7-34.1)	42.9 (34.2100)		
2006-2010	5.7 (0-10.7)	16.0 (10.8-21.0)	27.3 (21.1-33.3)	42.9 (33.4100)		
2007-2011	4.6 (0-9.1)	15.5 (9.2-20.0)	26.5 (20.1-33.3)	43.8 (33.5100)		
Total 1998-2011	11.0 (0-15.0)	20.0 (15.124.4)	29.3 (24.4-34.6)	42.3 (34.6-90)		
Colonoscopy Volume			**Median (Range)[‡]**			
Total 1998-2011	77 (25-493)	95 (25-424)	99.5 (26-424)	103 (25-500)		
Physician Specialty[§]				**Number of Physicians (%)**	**Median PDR (range)**	**Median Colonoscopy Volume (IQR)**
GI	252 (21.9)	352 (30.6)	291 (25.3)	255 (22.2)	25.8 (16.7-37.0)	106 (68-154)
CRC Surgery	11 (13.6)	18 (22.2)	27 (33.3)	25 (30.9)	33.3 (23.5-41.4)	80 (52-114)
General Internal	48 (30.6)	38 (24.2)	32 (20.4)	39 (24.8)	25.0 (13.2-37.9)	77 (49-117)
General Surgery	49 (26.3)	47 (25.3)	55 (29.6)	35 (18.8)	25.9 (15.2-35.7)	62 (43-84)
Other	54 (36.5)	33 (22.3)	35 (23.6)	26 (17.6)	19.4 (6.6-32.8)	81 (48.5-153)

Abbreviations: Surveillance Epidemiology and End Results (SEER), Polyp Detection Rate (PDR), Quartile (Q), Gastroenterology (GI), Colorectal Cancer (CRC), Interquartile Range (IQR)

*PDR was calculated for each of the corresponding time periods: 1998-2002, 1999-2003, 2000-2004, 2001-2005, 2002-2006, 2003-2007, 2004-2008, 2005-2009, 2006-2010, 2007-2011. A patient was assigned the PDR of their physician's PDR ranking in the 5 years preceding the index colonoscopy. For example, a person with a colonoscopy in 2002 was assigned their physicians' PDR from 1998-2002.

† PDR was calculated using outpatient, carrier and MEDPAR 5% random sample of Medicare patients residing in SEER registry areas. Colorectal cancer cases that were originally in the 5% sample were included.

‡ The correlation between median colonoscopy and PDR (r=0.13)

§ P-value comparing PDR ranking by physician specialty based on Chi-Square Tests: <0.001. Mean PDR (standard deviation) for the following physician specialties: GI 27.6 (15.4), CRC Surgery 33.4 (16.2), General Internal 27.1 (17.8), General Surgery 26.8 (16.3), Other 21.4 (17.6), p-value examining differences by physician specialty based on F-test<0.001. Mean colonoscopy volume (standard deviation) for the following physician specialties: GI 119.9 (70.0), CRC Surgery 93.2 (56.0), General Internal 95.7 (67.6), General Surgery 68.4 (35.4), Other 116.9 (98.6), p-value examining differences by physician specialty <0.001.

Table 6.5 Association between Race/Ethnicity and Interval Colorectal Cancers, SEER-Medicare 2002-2011

	Model 1 Adjusted for matching factors*			*Model 2* Model 1+ geographic factors, poverty, and comorbidity †			*Model 3* Model 2+ PDR and Physician Specialty ‡		
	IRR	95%CI		IRR	95%CI		IRR	95%CI	
Race/Ethnicity									
White	1.00			1.00			1.00		
Black	1.31	1.11	1.55	1.32	1.10	1.57	1.25	1.04	1.51
Hispanic	0.80	0.56	1.14	0.89	0.62	1.29	0.86	0.59	1.25
Asian	0.69	0.53	0.91	0.71	0.53	0.94	0.73	0.56	0.97
Other	0.79	0.60	1.03	0.82	0.63	1.08	0.83	0.63	1.10
Physicians' PDR									
Q1 Low							1.97	1.68	2.30
Q2 Medium Low							1.56	1.35	1.80
Q3 Medium High							1.20	1.04	1.38
Q4 High							1.00		
Provider Specialty									
GI							1.00		
CRC Surgeon							1.27	0.99	1.64
General Internal Medicine							1.11	0.93	1.31
General Surgery							1.37	1.15	1.64
Other/Unknown							3.51	2.75	4.47
Polypectomy at Index Colonoscopy				2.68	2.44	2.94	3.18	2.88	3.51
Diagnosed with Diverticulitis				1.19	1.09	1.3	1.19	1.09	1.30

Abbreviations: Surveillance Epidemiology and End Results (SEER), Quartile (Q), Polyp Detection Rate (PDR), Colorectal Cancer (CRC), Gastroenterologist (GI)

*Model 1 adjusts for matching factors (exact year and age of colonoscopy and gender) through the study design and race/ethnicity (white, black, Hispanic, Asian and other) as a covariate. Model also accounts for patients clustered within a physician and includes 2770 cases and 11,080 controls.

† Model 2 adjusts for matching factors (exact year and age of colonoscopy and gender) through the study design as well as race/ethnicity (white, black, Hispanic, Asian and other), geographic region (Northeast, Midwest, South and West), poverty level (Low, Medium High), urban/rural status (urban, non-urban), Charlson comorbidity score (0,1,2+), diverticulitis (yes/no), and polyp removal at index colonoscopy (yes/no) as covariates. Model also accounts for patients clustered within a physician. Includes 2770 cases and 11,080 controls.

‡ Includes 2770 cases and 11,080 controls. Model 3 adjusts for matching factors (exact year and age of colonoscopy and gender) through the study design geographic region (Northeast, Midwest, South and West), poverty level (Low, Medium High), urban/rural status (urban, non-urban), Charlson comorbidity score (0,1,2+), diverticulitis (yes/no), polyp removal at index colonoscopy (yes/no), physician specialty (GI, CRC Surgeon, General Internal Medicine, General Surgery and Other) and PDR (Q1, Q2, Q3, Q4) as covariates. Model also accounts for patients clustered within a physician. Includes 2770 cases and 11,080 controls.

Table 6.6 Association Between Race/Ethnicity and Colorectal Cancers by Tumor Location, SEER-Medicare 2002-2011

	Proximal [*, †]			Distal [*, ‡]			Rectal [*, §]		
	IRR	95%CI		IRR	95%CI		IRR	95%CI	
Race/Ethnicity									
White	1.00			1.00			1.00		
Black	1.14	0.90	1.44	1.55	1.01	2.40	1.65	1.13	2.41
Hispanic	0.74	0.47	1.18	1.25	0.51	3.03	0.78	0.37	1.63
Asian	0.50	0.34	0.73	0.90	0.48	1.69	1.48	0.91	2.41
Other	0.71	0.49	1.03	1.25	0.66	2.38	0.82	0.46	1.46
Physicians' PDR									
Q1 Low	2.04	1.70	2.46	1.79	1.24	2.58	2.26	1.66	3.08
Q2 Medium Low	1.59	1.34	1.88	1.30	0.92	1.84	1.59	1.17	2.17
Q3 Medium High	1.15	0.98	1.36	1.13	0.81	1.58	1.17	0.86	1.58
Q4 High	1.00			1.00			1.00		

Abbreviations: Surveillance Epidemiology and End Results (SEER), Quartile (Q), Polyp Detection Rate (PDR)

*Model is adjusted for age and year of colonoscopy, gender, urban/rural status, zip-code poverty, comorbidity, diverticulitis, index polypectomy, physician polyp detection rate, physician specialty and accounts for clustering of patients within a physician.

†Model includes 1785 cases and 7140 controls

‡Model includes 396 cases and 1584 controls

§Model includes 521 cases and 2084 controls

Table 6.7 Association between Race/Ethnicity and Interval CRC by Tumor Location in Minimally Adjusted Models, SEER-Medicare 2002-2011

	Proximal [*, †]			Distal [*, ‡]			Rectal [*, §]		
	IRR	95%CI		IRR	95%CI		IRR	95%CI	
White	1.00			1.00			1.00		
Asian	0.43	0.30	0.62	0.76	0.42	1.38	1.58	0.98	2.55
Black	1.16	0.94	1.44	1.49	0.98	2.25	1.77	1.27	2.48
Hispanic	0.68	0.44	1.05	1.02	0.44	2.36	0.79	0.36	1.71
Other	0.69	0.49	0.97	1.09	0.59	2.00	0.78	0.44	1.38

*Model adjusts for matching factors (exact year and age of colonoscopy and gender) through the study design and race/ethnicity (white, black, Hispanic, Asian and other) as a covariate

†Model includes 1785 cases and 7140 controls

‡Model includes 396 cases and 1584 controls

§Model includes 521 cases and 2084 controls

Table 6.8 Association between Race/Ethnicity and Interval Colorectal Cancer by SEER Summary Stage, SEER-Medicare 2002-2011

	Localized *,†			Regional *,‡			Distant *,§		
	IRR	95%CI		IRR	95%CI		IRR	95%CI	
Race/Ethnicity									
White	1.00			1.00			1.00		
Black	1.27	0.98	1.64	1.21	0.88	1.67	1.90	1.21	2.97
Hispanic	0.98	0.57	1.69	0.80	0.43	1.48	0.76	0.25	2.33
Asian	0.86	0.58	1.28	0.74	0.49	1.12	0.51	0.24	1.05
Other	1.05	0.70	1.56	0.82	0.51	1.31	0.53	0.23	1.21
Physicians' PDR									
Q1 Low	2.03	1.66	2.49	2.34	1.82	3.01	1.59	1.09	2.33
Q2 Medium Low	1.73	1.43	2.10	1.54	1.21	1.95	1.36	0.96	1.94
Q3 Medium High	1.23	1.01	1.48	1.37	1.09	1.72	1.20	0.85	1.68
Q4 High	1.00			1.00			1.00		

Abbreviations: Surveillance Epidemiology and End Results (SEER), Quartile (Q), Polyp Detection Rate (PDR)

* Model is adjusted for age and year of colonoscopy, gender, urban/rural status, zip-code poverty, comorbidity, diverticulitis, index polypectomy, physician polyp detection rate, physician specialty and accounts for clustering of patients within a physician.
† Model includes 1389 cases and 5556 controls
‡ Model includes 931 cases and 3724 controls
§ Model includes 391 cases and 1564 controls

Table 6.9 Association between Race/Ethnicity and Interval Colorectal Cancer Timing, SEER-Medicare 2002-2011

	Early (6-35 months)*, †			Late (36-59 months)*, ‡		
	IRR	95%CI		IRR	95%CI	
Race/Ethnicity						
White	1.00			1.00		
Black	1.39	1.11	1.73	1.31	0.98	1.76
Hispanic	0.80	0.48	1.34	0.71	0.37	1.36
Asian	0.87	0.63	1.20	0.65	0.41	1.01
Other	0.82	0.58	1.17	0.88	0.56	1.37
Physicians' PDR						
Q1 Low	2.02	1.67	2.44	1.81	1.44	2.29
Q2 Medium Low	1.74	1.46	2.08	1.41	1.13	1.75
Q3 Medium High	1.30	1.09	1.55	1.05	0.85	1.30
Q4 High	1.00			1.00		

Abbreviations: Surveillance Epidemiology and End Results (SEER), Incidence Rate Ratio (IRR), Confidence Interval (CI), Polyp Detection Rate (PDR), Quartile (Q)

*Adjusted for age and year of colonoscopy, gender, urban/rural status, zip-code poverty, comorbidity, diverticulitis, index polypectomy, physician polyp detection rate, physician specialty and accounts for clustering of patients within a physician.
† Model includes 1837 cases and 7348 controls
‡ Model includes 933 cases and 3732 controls

Table 6.10 Association between Race/Ethnicity and Interval Colorectal Cancer by Index Polypectomy, SEER-Medicare 2002-2011

	No Polypectomy*, †			Polypectomy*, ‡		
	IRR	95%CI		IRR	95%CI	
Race/Ethnicity						
White	1.00			1.00		
Black	1.15	0.91	1.46	1.60	1.19	2.15
Hispanic	1.13	0.74	1.72	0.52	0.22	1.20
Asian	0.66	0.47	0.93	0.82	0.56	1.21
Other	0.84	0.58	1.21	0.96	0.63	1.46
Physicians' PDR						
Q1 Low	1.57	1.30	1.91	2.90	2.26	3.72
Q2 Medium Low	1.25	1.04	1.51	2.03	1.68	2.47
Q3 Medium High	1.04	0.86	1.25	1.34	1.12	1.61
Q4 High	1.00			1.00		

Abbreviations: Surveillance Epidemiology and End Results (SEER), Incidence Rate Ratio (IRR), Confidence Interval (CI), Polyp Detection Rate (PDR), Quartile (Q)

*Adjusted for age and year of colonoscopy, gender, urban/rural status, zip-code poverty, comorbidity, diverticulitis, index polypectomy, physician polyp detection rate, physician specialty

† Model includes 1516 cases and 6064 controls

‡ Model includes 1254 cases and 5016 controls

Table 6.11 Association between Race/Ethnicity and Interval Colorectal Cancer, SEER-Medicare 2002-2011

	Non- Screening*, †			Screening*, ‡		
	IRR	95%CI		IRR	95%CI	
Race/Ethnicity						
White	1.00			1.00		
Black	1.59	1.19	2.12	1.30	1.02	1.67
Hispanic	0.83	0.50	1.39	0.75	0.41	1.4
Asian	0.79	0.53	1.17	0.60	0.41	0.88
Other	1.23	0.76	2.00	0.79	0.56	1.12
Physicians' PDR						
Q1 Low	1.77	1.40	2.25	1.95	1.60	2.38
Q2 Medium Low	1.39	1.11	1.74	1.65	1.37	1.99
Q3 Medium High	1.10	0.88	1.37	1.27	1.05	1.52
Q4 High	1.00			1.00		

Abbreviations: Surveillance Epidemiology and End Results (SEER), Incidence Rate Ratio (IRR), Confidence Interval (CI), Polyp Detection Rate (PDR), Quartile (Q)

*Adjusted for age and year of colonoscopy, gender, urban/rural status, zip-code poverty, comorbidity, diverticulitis, index polypectomy, physician polyp detection rate, physician specialty and accounts for clustering of patients within a physician.
† Model includes 1208 cases and 4832 controls
‡ Model includes 1562 cases and 6248 controls

Table 6.12 Association between Race/Ethnicity and Interval Colorectal Cancer among Adults Receiving a Colonoscopy from Gastroenterologist Who Performed ≥50 Colonoscopies, SEER-Medicare 2002-2011

	All Interval CRCs*†			Proximal*‡			Distal*§			Rectal *‖		
	IRR	95%CI		IRR	95%CI		IRR	95%CI		IRR	95%CI	
Race/Ethnicity												
White	1.00			1.00			1.00			1.00		
Black	1.36	1.09	1.69	1.21	0.91	1.61	1.76	1.05	2.94	1.71	1.09	2.69
Hispanic	0.70	0.44	1.14	0.72	0.42	1.21	0.71	0.20	2.53	0.33	0.11	1.03
Asian	0.66	0.47	0.93	0.44	0.28	0.70	1.03	0.49	2.17	1.36	0.72	2.56
Other	0.70	0.50	0.99	0.81	0.53	1.25	1.49	0.69	3.24	0.42	0.15	1.18
Physicians' PDR												
Q1 Low	1.89	1.55	2.31	2.05	1.63	2.59	1.62	1.02	2.56	1.68	1.13	2.49
Q2 Medium Low	1.54	1.29	1.84	1.55	1.25	1.92	1.31	0.87	1.97	1.51	1.04	2.20
Q3 Medium High	1.22	1.03	1.45	1.22	0.99	1.50	1.12	0.75	1.69	1.06	0.73	1.53
Q4 High	1.00			1.00			1.00			1.00		

Abbreviations: Surveillance Epidemiology and End Results (SEER), Colorectal Cancer (CRC), Incidence Rate Ratio (IRR), Confidence Interval (CI), Polyp Detection Rate (PDR), Quartile (Q)

*Models are restricted to cases and controls who received a colonoscopy from a gastroenterologist that performed at least 50 colonoscopies. Models are adjusted for age and year of colonoscopy, gender, urban/rural status, zip-code poverty, comorbidity, diverticulitis, index polypectomy, physician polyp detection rate, physician specialty and accounts for clustering of patients within a physician.

† Model includes 1768 cases and 9488 controls

‡ Model includes 1139 cases and 6196 controls

§ Model includes 252 cases and 1359 controls

|| Model includes 331 cases and 1763 controls

Table 6.13 Association between Race/Ethnicity and Interval Colorectal Cancer among Adults Receiving a Colonoscopy from Gastroenterologist Who Performed ≥100 Colonoscopies, SEER-Medicare 2002-2011

	All Interval CRCs*†			Proximal*‡			Distal*§			Rectal*‖		
	IRR	95%CI		IRR	95%CI		IRR	95%CI		IRR	95%CI	
Race/Ethnicity												
White	1.00			1.00			1.00			1.00		
Black	1.54	1.19	1.99	1.28	0.89	1.82	2.50	1.42	4.37	1.38	0.78	2.45
Hispanic	0.89	0.51	1.56	0.90	0.50	1.61	2.08	0.56	7.78	0.18	0.03	1.10
Asian	0.62	0.41	0.95	0.40	0.21	0.77	1.40	0.60	3.26	1.17	0.54	2.55
Other	0.67	0.43	1.05	0.69	0.39	1.23	2.43	0.96	6.15	0.30	0.07	1.26
Physicians' PDR												
Q1 Low	1.64	1.27	2.11	1.72	1.28	2.31	1.28	0.72	2.25	1.94	1.20	3.12
Q2 Medium Low	1.45	1.17	1.80	1.57	1.22	2.03	1.08	0.67	1.72	1.17	0.75	1.84
Q3 Medium High	1.17	0.95	1.43	1.17	0.92	1.50	1.03	0.64	1.65	0.97	0.63	1.49
Q4 High	1.00			1.00			1.00			1.00		

Abbreviations: Surveillance Epidemiology and End Results (SEER), Colorectal Cancer (CRC), Incidence Rate Ratio (IRR), Confidence Interval (CI), Polyp Detection Rate (PDR), Quartile (Q)

*Models are restricted to cases and controls who received a colonoscopy from a gastroenterologist that performed at least 100 colonoscopies. Models are adjusted for age and year of colonoscopy, gender, urban/rural status, zip-code poverty, comorbidity, diverticulitis, index polypectomy, physician polyp detection rate, physician specialty and accounts for clustering of patients within a physician.

† Model includes 1210 cases and 6554 controls
‡ Model includes 768 cases and 4302 controls
§ Model includes 182 cases and 962 controls
|| Model includes 223 cases and 1207 controls

Chapter 7 Conclusions and Future Directions

Summary of Findings

Screening is an important aspect of both primary and secondary CRC prevention. However, CRC screening utilization is suboptimal, particularly in racial and ethnic minorities and in individuals of lower SES.[19, 20, 23, 59] There are numerous initiatives and efforts aimed at improving CRC screening utilization at the national, regional, health-system and local level. These programs are expected to mitigate sociodemographic disparities in CRC screening; however, data on results of these programs in different population groups are limited. These knowledge gaps are addressed in the first two studies of this dissertation. The third aim addresses racial/ethnic differences in the incidence for interval cancers among people who are screened for CRC. The third study also examined the quality of the last colonoscopy as another determinant of interval cancer. To-date few studies have examined the relationship between race/ethnicity and interval cancers, as well as quality of colonoscopy in different racial and ethnic groups.[32]

In the first study, we examined changes in CRC screening by race/ethnicity and SES following implementation of the 2011 ACA provision that removed cost-sharing. In this study of a nationally representative sample of Medicare and privately insured people, there were modest gains (5.9-7.2%) in CRC screening between years 2008 (pre-ACA) and 2013 (post-ACA). There were increases in CRC screening among adults with low income, an observation that may, in part, reflect the removal of financial barriers to cancer screening.[113, 147] In the analyses by race/ethnicity, increases in CRC screening were observed in whites and especially in blacks. However, there were no significant increases in Hispanics, a group with especially low CRC screening utilization, in

unadjusted or adjusted analyses. These findings underscore that financial barriers represent only a part of the constellation of factors, which include inconsistent physician recommendations, logistical obstacles, fear, insufficient awareness and beliefs that CRC screening is not necessary or important,[183, 186]

In the second study, we examined the association between race/ethnicity and time to CRC screening among adult KPNC members who just turned 50 and became eligible for the organized screening program. We observed that CRC screening uptake was considerably higher and differences by race/ethnicity were modest and narrower than those previously reported elsewhere in California and in the US. The less pronounced racial/ethnic differences in our study were not attributable solely to having insurance because Asian, blacks and Hispanics in other studies of insured populations had lower CRC screening uptake relative to whites.[114, 115, 194] The high screening rates in our study are likely due to the specific population health management strategies used at Kaiser Permanente.[190] Although we found little evidence of racial/ethnic disparities , Hispanics were less likely to receive CRC screening compared to other groups. These results suggest that factors such as beliefs, attitudes and perceptions of CRC screening not addressed in the current organized screening program could play a role.[23, 197, 198] Some of these barriers may be addressed with tailored and targeted approaches to CRC screening, however, the effectiveness and the cost-benefit of adjuvant program components in the current study population has not been investigated.

The third study examined whether the incidence of interval CRC varies by race/ethnicity in Medicare patients 66-75 years of age and whether this variability is attributable to differences in colonoscopy quality as measured by physician's polyp detection rate (PDR). In this population-based case-control study, interval CRC incidence was 25% higher in blacks compared to whites, while incidence among Asians was lower. Blacks were more likely than whites to have colonoscopies performed by physicians with low PDR. However, differences in PDR did not explain the observed black-white disparity. PDR is an indirect measure of lesions missed during a colonoscopy. Although missed lesions are viewed as the most common reason for interval CRCs, other reasons may include incomplete resection of polyps, or rapidly developing or "de-novo" tumors.[32] Missed lesions and PDR are especially important factors for proximal lesions because the proximal colon is harder to reach endoscopically and it is the most common location of difficult-to-detect sessile polyps.[77, 78, 213] However, black-white differences in proximal interval CRC incidence were not as pronounced as those observed for distal and rectal tumors in the current study. It is possible that quality factors other than PDR contribute to this pattern, however, data on other measures, including incomplete resection of polyps, the second most common reason for interval CRCs,[32] by race ethnicity are not available in the published literature nor is it captured in SEER-Medicare. It is possible that incidence of "de novo" CRCs differs by race; however, our study was not designed to answer this question.[32] Previous studies have suggested that blacks have more aggressive tumors[84 216], though the overall prevalence estimates for colorectal polyps and adenomas in blacks and whites are similar[80 47]. Depending on the size and number of polyps detected, surveillance colonoscopy is recommended at intervals of up to 10 years of an

index procedure in most instances.[76] Black-white differences were observed within three years following a colonoscopy in our study and two previous SEER-Medicare-based studies noted that blacks were more likely to undergo a surveillance colonoscopy within three or five years of polyp removal.[221, 222] Taken together, this suggests that differences in recommended surveillance colonoscopy may only moderately contribute to higher incidence of interval CRC among blacks, though these findings warrant further investigation.

Study Strengths and Limitations

Each study included in this dissertation has its own set of notable strengths and limitations. The most important strength of the first study is the use of a nationally-representative sample that allowed evaluating a broad national policy with limited missing data. On the other hand, the cross-sectional nature of the study and limited 2-year time frame following the ACS are key limitations. The second study was based on an integrated health system with the unique ability to follow people over relatively long-periods of time, however, a sizeable number of adults in this study were missing data on race/ethnicity. The third study is notable for its sound nested case-control design, which used robust administrative data with good information on colonoscopy procedures. A significant limitation of this study is the need to rely on PDR as an imperfect proxy measure of quality of colonoscopy.

Public Health Impact and Future Directions

In summary, this dissertation provides information on racial/ethnic disparities in relation to current policies and programs aimed at improving CRC screening. Findings from this

dissertation, along with other contemporary reports[231, 232], indicate that removing cost will likely not eliminate all racial/ethnic disparities in CRC screening and will not lead to substantial increases in CRC screening in the short term. It is encouraging, however, that gains in CRC screening were observed among low-income adults, a group that may benefit the most from such policies. Less tangible aspects of removing costs, such as placing public-value on preventive health could lead to longer-term benefits. Questions regarding the negative consequences of the loop-hole of Medicare's policy regarding payment for the removal of polyps during a colonoscopy or colonoscopies that are a result of a positive stool-based test have yet to be answered.

Moving beyond cost, outreach programs, such as those in KPNC have achieved unparalleled CRC screening rates, exceeding the Healthy People 2020 goal of 70.5%[233] and approaching the 80% goal set by the National Colorectal Cancer Roundtable.[188] Yet, there are some subgroups, most notably Hispanics, who remain less likely to initiate CRC screening. These findings, as well as reports by others,[189, 190] suggest that culturally appropriate targeted interventions may be needed in order to close the existing gaps. Such interventions are currently being tested within the Kaiser Permanente System, but their effectiveness at reducing racial/ethnic disparities in clinical outcomes, including incidence and mortality has yet to be evaluated.

Although CRC screening uptake is clearly improving among blacks, this group may still face higher incidence of interval cancers. The reasons for higher incidence of interval CRCs among blacks are not fully understood, however it appears that quality of

colonoscopy does not account for the observed differences. Our finding that black-white disparities are particularly evident in terms of incidence of distal and rectal interval cancers is unexpected and requires further investigation. Additional studies with more comprehensive quality metrics along with more detailed information regarding tumor characteristics are needed to help understand higher interval CRCs in blacks. These studies will inform surveillance recommendations, clinical guidelines and other forms of public health action.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin. 2016;66: 7-30.

2. Nagy R, Sweet K, Eng C. Highly penetrant hereditary cancer syndromes. Oncogene. 2004;23: 6445-6470.

3. 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: e20456.

4. Fedirko V, Tramacere I, Bagnardi V, et al. Alcohol drinking and colorectal cancer risk: an overall and dose-response meta-analysis of published studies. Ann Oncol. 2011;22: 1958-1972.

5. Aune D, Lau R, Chan DS, et al. Nonlinear reduction in risk for colorectal cancer by fruit and vegetable intake based on meta-analysis of prospective studies. Gastroenterology. 2011;141: 106-118.

6. Grosso G, Buscemi S, Galvano F, et al. Mediterranean diet and cancer: epidemiological evidence and mechanism of selected aspects. BMC Surg. 2013;13 Suppl 2: S14.

7. Park Y, Hunter DJ, Spiegelman D, et al. Dietary fiber intake and risk of colorectal cancer: a pooled analysis of prospective cohort studies. JAMA. 2005;294: 2849-2857.

8. Huncharek M, Muscat J, Kupelnick B. Colorectal cancer risk and dietary intake of calcium, vitamin D, and dairy products: a meta-analysis of 26,335 cases from 60 observational studies. Nutr Cancer. 2009;61: 47-69.

9. Mandel JS, Church TR, Bond JH, et al. The effect of fecal occult-blood screening on the incidence of colorectal cancer. N Engl J Med. 2000;343: 1603-1607.

10. Hardcastle JD, Chamberlain JO, Robinson MH, et al. Randomised controlled trial of faecal-occult-blood screening for colorectal cancer. Lancet. 1996;348: 1472-1477.

11. Kronborg O, Fenger C, Olsen J, Jorgensen OD, Sondergaard O. Randomised study of screening for colorectal cancer with faecal-occult-blood test. Lancet. 1996;348: 1467-1471.

12. Atkin WS, Edwards R, Kralj-Hans I, et al. Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial. Lancet. 2010;375: 1624-1633.

13. Segnan N, Armaroli P, Bonelli L, et al. Once-only sigmoidoscopy in colorectal cancer screening: follow-up findings of the Italian Randomized Controlled Trial--SCORE. J Natl Cancer Inst. 2011;103: 1310-1322.

14. Schoen RE, Pinsky PF, Weissfeld JL, et al. Colorectal-cancer incidence and mortality with screening flexible sigmoidoscopy. N Engl J Med. 2012;366: 2345-2357.

15. Holme O, Loberg M, Kalager M, et al. Effect of flexible sigmoidoscopy screening on colorectal cancer incidence and mortality: a randomized clinical trial. JAMA. 2014;312: 606-615.

16. Doubeni CA, Weinmann S, Adams K, et al. Screening colonoscopy and risk for incident late-stage colorectal cancer diagnosis in average-risk adults: a nested case-control study. Ann Intern Med. 2013;158: 312-320.

17. U. S. Preventive Services Task Force. Screening for colorectal cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2008;149: 627-637.

18. Fedewa SA GSA, 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: 637-652.

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

20. Shapiro JA, Klabunde CN, Thompson TD, Nadel MR, Seeff LC, White A. Patterns of colorectal cancer test use, including CT colonography, in the 2010 National Health Interview Survey. Cancer Epidemiol Biomarkers Prev. 2012;21: 895-904.

21. Intstitute of Medicine. Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care. Washington DC: Intstitute of Medicine, 2003.

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

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

24. Diaz JA, Roberts MB, Goldman RE, Weitzen S, Eaton CB. Effect of language on colorectal cancer screening among Latinos and non-Latinos. Cancer Epidemiol Biomarkers Prev. 2008;17: 2169-2173.

25. Jones RM, Devers KJ, Kuzel AJ, Woolf SH. Patient-reported barriers to colorectal cancer screening: a mixed-methods analysis. Am J Prev Med. 2010;38: 508-516.

26. 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: 728-736.

27. Siegel R, Desantis C, Jemal A. Colorectal cancer statistics, 2014. CA Cancer J Clin. 2014;64: 104-117.

28. Fedewa SA, Sauer AG, Siegel RL, Smith RA, Torre LA, Jemal A. Temporal Trends in Colorectal Cancer Screening among Asian Americans. Cancer Epidemiol Biomarkers Prev. 2016.

29. Gomez SL, Noone AM, Lichtensztajn DY, et al. Cancer incidence trends among Asian American populations in the United States, 1990-2008. J Natl Cancer Inst. 2013;105: 1096-1110.

30. Pinheiro PS, Sherman RL, Trapido EJ, et al. Cancer incidence in first generation U.S. Hispanics: Cubans, Mexicans, Puerto Ricans, and new Latinos. Cancer Epidemiol Biomarkers Prev. 2009;18: 2162-2169.

31. Haenszel W, Kurihara M. Studies of Japanese migrants. I. Mortality from cancer and other diseases among Japanese in the United States. J Natl Cancer Inst. 1968;40: 43-68.

32. Singh S, Singh PP, Murad MH, Singh H, Samadder NJ. Prevalence, risk factors, and outcomes of interval colorectal cancers: a systematic review and meta-analysis. Am J Gastroenterol. 2014;109: 1375-1389.

33. Anderson JC, Butterly LF. Colonoscopy: quality indicators. Clin Transl Gastroenterol. 2015;6: e77.

34. Williams JE, Holub JL, Faigel DO. Polypectomy rate is a valid quality measure for colonoscopy: results from a national endoscopy database. Gastrointest Endosc. 2012;75: 576-582.

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

36. Jensen CD, Doubeni CA, Quinn VP, et al. Adjusting for patient demographics has minimal effects on rates of adenoma detection in a large, community-based setting. Clin Gastroenterol Hepatol. 2015;13: 739-746.

37. Cooper GS, Xu F, Barnholtz Sloan JS, Schluchter MD, Koroukian SM. Prevalence and predictors of interval colorectal cancers in medicare beneficiaries. Cancer. 2012;118: 3044-3052.

38. Baker DW, Brown T, Buchanan DR, et al. Comparative effectiveness of a multifaceted intervention to improve adherence to annual colorectal cancer screening in community health centers: a randomized clinical trial. JAMA Intern Med. 2014;174: 1235-1241.

39. Mehta SJ, Jensen CD, Quinn VP, et al. Race/Ethnicity and Adoption of a Population Health Management Approach to Colorectal Cancer Screening in a Community-Based Healthcare System. J Gen Intern Med. 2016.

40. Rauscher GH, Hawley ST, Earp JA. Baseline predictors of initiation vs. maintenance of regular mammography use among rural women. Prev Med. 2005;40: 822-830.

41. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin. 2015;65: 87-108.

42. Howlader N NA, Krapcho M, Garshell J, Miller D, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z,Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2012. Bethesda, MD: National Cancer Institute, 2015.

43. Jemal A, Siegel RL, Ma J, et al. Inequalities in premature death from colorectal cancer by state. J Clin Oncol. 2015;33: 829-835.

44. Fleming M, Ravula S, Tatishchev SF, Wang HL. Colorectal carcinoma: Pathologic aspects. J Gastrointest Oncol. 2012;3: 153-173.

45. Fearon ER. Molecular genetics of colorectal cancer. Annu Rev Pathol. 2011;6: 479-507.

46. 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: 1315-1329; quiz 1314, 1330.

47. 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: 172-180.

48. Jass JR. Classification of colorectal cancer based on correlation of clinical, morphological and molecular features. Histopathology. 2007;50: 113-130.

49. Gryfe R, Kim H, Hsieh ET, et al. Tumor microsatellite instability and clinical outcome in young patients with colorectal cancer. N Engl J Med. 2000;342: 69-77.

50. Campbell PT, Jacobs ET, Ulrich CM, et al. Case-control study of overweight, obesity, and colorectal cancer risk, overall and by tumor microsatellite instability status. J Natl Cancer Inst. 2010;102: 391-400.

51. Haggar FA, Boushey RP. Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors. Clin Colon Rectal Surg. 2009;22: 191-197.

52. Gatto NM, Frucht H, Sundararajan V, Jacobson JS, Grann VR, Neugut AI. Risk of perforation after colonoscopy and sigmoidoscopy: a population-based study. J Natl Cancer Inst. 2003;95: 230-236.

53. Levin TR, Conell C, Shapiro JA, Chazan SG, Nadel MR, Selby JV. Complications of screening flexible sigmoidoscopy. Gastroenterology. 2002;123: 1786-1792.

54. Levin TR, Zhao W, Conell C, et al. Complications of colonoscopy in an integrated health care delivery system. Ann Intern Med. 2006;145: 880-886.

55. Geiger TM, Ricciardi R. Screening options and recommendations for colorectal cancer. Clin Colon Rectal Surg. 2009;22: 209-217.

56. Allison JE, Fraser CG, Halloran SP, Young GP. Population screening for colorectal cancer means getting FIT: the past, present, and future of colorectal cancer screening using the fecal immunochemical test for hemoglobin (FIT). Gut Liver. 2014;8: 117-130.

57. US Food and Drug Administration. FDA approves first non-invasive DNA screening test for colorectal cancer. Available from URL: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm409021.htm.

58. Berrington de Gonzalez A, Kim KP, Yee J. CT colonography: perforation rates and potential radiation risks. Gastrointest Endosc Clin N Am. 2010;20: 279-291.

59. Shapiro JA, Seeff LC, Thompson TD, Nadel MR, Klabunde CN, Vernon SW. Colorectal cancer test use from the 2005 National Health Interview Survey. Cancer Epidemiol Biomarkers Prev. 2008;17: 1623-1630.

60. Morikawa T, Kato J, Yamaji Y, Wada R, Mitsushima T, Shiratori Y. A comparison of the immunochemical fecal occult blood test and total colonoscopy in the asymptomatic population. Gastroenterology. 2005;129: 422-428.

61. Halligan S, Wooldrage K, Dadswell E, et al. Computed tomographic colonography versus barium enema for diagnosis of colorectal cancer or large polyps in symptomatic patients (SIGGAR): a multicentre randomised trial. Lancet. 2013;381: 1185-1193.

62. Kaminski MF, Bretthauer M, Zauber AG, et al. The NordICC Study: rationale and design of a randomized trial on colonoscopy screening for colorectal cancer. Endoscopy. 2012;44: 695-702.

63. Manser CN, Bachmann LM, Brunner J, Hunold F, Bauerfeind P, Marbet UA. Colonoscopy screening markedly reduces the occurrence of colon carcinomas and carcinoma-related death: a closed cohort study. Gastrointest Endosc. 2012;76: 110-117.

64. Brenner H, Chang-Claude J, Jansen L, Knebel P, Stock C, Hoffmeister M. Reduced risk of colorectal cancer up to 10 years after screening, surveillance, or diagnostic colonoscopy. Gastroenterology. 2014;146: 709-717.

65. Baxter NN, Goldwasser MA, Paszat LF, Saskin R, Urbach DR, Rabeneck L. Association of colonoscopy and death from colorectal cancer. Ann Intern Med. 2009;150: 1-8.

66. Baxter NN, Warren JL, Barrett MJ, Stukel TA, Doria-Rose VP. Association between colonoscopy and colorectal cancer mortality in a US cohort according to site of cancer and colonoscopist specialty. J Clin Oncol. 2012;30: 2664-2669.

67. Nishihara R, Wu K, Lochhead P, et al. Long-term colorectal-cancer incidence and mortality after lower endoscopy. N Engl J Med. 2013;369: 1095-1105.

68. Weiss NS. Commentary: cohort studies of the efficacy of screening for cancer. Epidemiology. 2015;26: 362-364.

69. Goodman M, Fletcher RH, Doria-Rose VP, et al. Observational methods to assess the effectiveness of screening colonoscopy in reducing right colon cancer mortality risk: SCOLAR. J Comp Eff Res. 2015: 1-11.

70. 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: 2564-2575.

71. Newcomb PA, Storer BE, Morimoto LM, Templeton A, Potter JD. Long-term efficacy of sigmoidoscopy in the reduction of colorectal cancer incidence. J Natl Cancer Inst. 2003;95: 622-625.

72. Winawer SJ. Natural history of colorectal cancer. Am J Med. 1999;106: 3S-6S; discussion 50S-51S.

73. Brenner H, Altenhofen L, Katalinic A, Lansdorp-Vogelaar I, Hoffmeister M. Sojourn time of preclinical colorectal cancer by sex and age: estimates from the German national screening colonoscopy database. Am J Epidemiol. 2011;174: 1140-1146.

74. 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: 130-160.

75. Short MW, Layton MC, Teer BN, Domagalski JE. Colorectal cancer screening and surveillance. Am Fam Physician. 2015;91: 93-100.

76. Lieberman DA, Rex DK, Winawer SJ, et al. Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology. 2012;143: 844-857.

77. Robertson DJ, Lieberman DA, Winawer SJ, et al. Colorectal cancers soon after colonoscopy: a pooled multicohort analysis. Gut. 2014;63: 949-956.

78. le Clercq CM, Bouwens MW, Rondagh EJ, et al. Postcolonoscopy colorectal cancers are preventable: a population-based study. Gut. 2014;63: 957-963.

79. Baxter NN, Sutradhar R, Forbes SS, Paszat LF, Saskin R, Rabeneck L. Analysis of administrative data finds endoscopist quality measures associated with postcolonoscopy colorectal cancer. Gastroenterology. 2011;140: 65-72.

80. 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: 538-546.

81. Polite BN, Dignam JJ, Olopade OI. Colorectal cancer model of health disparities: understanding mortality differences in minority populations. J Clin Oncol. 2006;24: 2179-2187.

82. Shavers VL. Racial/ethnic variation in the anatomic subsite location of in situ and invasive cancers of the colon. J Natl Med Assoc. 2007;99: 733-748.

83. Yoon HH, Shi Q, Alberts SR, et al. Racial Differences in BRAF/KRAS Mutation Rates and Survival in Stage III Colon Cancer Patients. J Natl Cancer Inst. 2015;107.

84. Dimou A, Syrigos KN, Saif MW. Disparities in colorectal cancer in African-Americans vs Whites: before and after diagnosis. World J Gastroenterol. 2009;15: 3734-3743.

85. Carethers JM, Murali B, Yang B, et al. Influence of race on microsatellite instability and CD8+ T cell infiltration in colon cancer. PLoS One. 2014;9: e100461.

86. Ashktorab H, Smoot DT, Carethers JM, et al. High incidence of microsatellite instability in colorectal cancer from African Americans. Clin Cancer Res. 2003;9: 1112-1117.

87. Singh H, Turner D, Xue L, Targownik LE, Bernstein CN. Risk of developing colorectal cancer following a negative colonoscopy examination: evidence for a 10-year interval between colonoscopies. JAMA. 2006;295: 2366-2373.

88. Rex DK, Bond JH, Winawer S, et al. Quality in the technical performance of colonoscopy and the continuous quality improvement process for colonoscopy: recommendations of the U.S. Multi-Society Task Force on Colorectal Cancer. Am J Gastroenterol. 2002;97: 1296-1308.

89. Rex DK, Petrini JL, Baron TH, et al. Quality indicators for colonoscopy. Am J Gastroenterol. 2006;101: 873-885.

90. Rex DK, Schoenfeld PS, Cohen J, et al. Quality indicators for colonoscopy. Am J Gastroenterol. 2015;110: 72-90.

91. Burnett-Hartman AN, Mehta SJ, Zheng Y, et al. Racial/Ethnic Disparities in Colorectal Cancer Screening Across Healthcare Systems. Am J Prev Med. 2016.

92. Chen SC, Rex DK. Endoscopist can be more powerful than age and male gender in predicting adenoma detection at colonoscopy. Am J Gastroenterol. 2007;102: 856-861.

93. Coe SG, Wallace MB. Assessment of adenoma detection rate benchmarks in women versus men. Gastrointest Endosc. 2013;77: 631-635.

94. Sanaka MR, Rai T, Navaneethan U, et al. Adenoma detection rate in high-risk patients differs from that in average-risk patients. Gastrointest Endosc. 2015.

95. Patel NC, Islam RS, Wu Q, et al. Measurement of polypectomy rate by using administrative claims data with validation against the adenoma detection rate. Gastrointest Endosc. 2013;77: 390-394.

96. Sanduleanu S, le Clercq CM, Dekker E, et al. Definition and taxonomy of interval colorectal cancers: a proposal for standardising nomenclature. Gut. 2015;64: 1257-1267.

97. Diamond SJ, Enestvedt BK, Jiang Z, et al. Adenoma detection rate increases with each decade of life after 50 years of age. Gastrointest Endosc. 2011;74: 135-140.

98. Shaukat A, Oancea C, Bond JH, Church TR, Allen JI. Variation in detection of adenomas and polyps by colonoscopy and change over time with a performance improvement program. Clin Gastroenterol Hepatol. 2009;7: 1335-1340.

99. Rauscher GH, Allgood KL, Whitman S, Conant E. Disparities in screening mammography services by race/ethnicity and health insurance. J Womens Health (Larchmt). 2012;21: 154-160.

100. Rauscher GH, Conant EF, Khan JA, Berbaum ML. Mammogram image quality as a potential contributor to disparities in breast cancer stage at diagnosis: an observational study. BMC Cancer. 2013;13: 208.

101. Liss DT, Baker DW. Understanding current racial/ethnic disparities in colorectal cancer screening in the United States: the contribution of socioeconomic status and access to care. Am J Prev Med. 2014;46: 228-236.

102. Centers for Disease Control and Prevention. Questionnaires, Datasets, and Related Documentation 1997 to the Present. Available from URL: http://www.cdc.gov/nchs/nhis/quest_data_related_1997_forward.htm.

103. Anderson LM, May DS. Has the use of cervical, breast, and colorectal cancer screening increased in the United States? Am J Public Health. 1995;85: 840-842.

104. Meissner HI, Breen N, Klabunde CN, Vernon SW. Patterns of colorectal cancer screening uptake among men and women in the United States. Cancer Epidemiol Biomarkers Prev. 2006;15: 389-394.

105. Seeff LC, Manninen DL, Dong FB, et al. Is there endoscopic capacity to provide colorectal cancer screening to the unscreened population in the United States? Gastroenterology. 2004;127: 1661-1669.

106. De-Navas-Walt C PB. Income, Poverty, and Health Insurance Coverage in the United States. Washington DC: US Census Bureau, 2012.

107. Klabunde CN, Cronin KA, Breen N, Waldron WR, Ambs AH, Nadel MR. Trends in colorectal cancer test use among vulnerable populations in the United States. Cancer Epidemiol Biomarkers Prev. 2011;20: 1611-1621.

108. US Department of Health and Human Services. 2013 National Health Interview Survey (NHIS) Public Use Data Release. Hyattsville, Maryland: US Department of Health and Human Services, 2014.

109. Halpern MT, Pavluck AL, Ko CY, Ward EM. Factors associated with colon cancer stage at diagnosis. Dig Dis Sci. 2009;54: 2680-2693.

110. Valeri L, Chen JT, Garcia-Albeniz X, Krieger N, VanderWeele TJ, Coull BA. The role of stage at diagnosis in colorectal cancer black-white survival disparities: a counterfactual causal inference approach. Cancer Epidemiol Biomarkers Prev. 2015.

111. Ahmed NU, Pelletier V, Winter K, Albatineh AN. Factors explaining racial/ethnic disparities in rates of physician recommendation for colorectal cancer screening. Am J Public Health. 2013;103: e91-99.

112. Fedewa SA, Ma J, Sauer AG, et al. How many individuals will need to be screened to increase colorectal cancer screening prevalence to 80% by 2018? Cancer. 2015;121: 4258-4265.

113. O'Malley AS, Forrest CB, Feng S, Mandelblatt J. Disparities despite coverage: gaps in colorectal cancer screening among Medicare beneficiaries. Arch Intern Med. 2005;165: 2129-2135.

114. Doubeni CA, Laiyemo AO, Klabunde CN, Young AC, Field TS, Fletcher RH. Racial and ethnic trends of colorectal cancer screening among Medicare enrollees. Am J Prev Med. 2010;38: 184-191.

115. White A, Vernon SW, Franzini L, Du XL. Racial and ethnic disparities in colorectal cancer screening persisted despite expansion of Medicare's screening reimbursement. Cancer Epidemiol Biomarkers Prev. 2011;20: 811-817.

116. Wernli KJ, Hubbard RA, Johnson E, et al. Patterns of colorectal cancer screening uptake in newly eligible men and women. Cancer Epidemiol Biomarkers Prev. 2014;23: 1230-1237.

117. McAlearney AS, Reeves KW, Dickinson SL, et al. Racial differences in colorectal cancer screening practices and knowledge within a low-income population. Cancer. 2008;112: 391-398.

118. Maxwell AE, Crespi CM, Antonio CM, Lu P. Explaining disparities in colorectal cancer screening among five Asian ethnic groups: a population-based study in California. BMC Cancer. 2010;10: 214.

119. Kandula NR, Wen M, Jacobs EA, Lauderdale DS. Low rates of colorectal, cervical, and breast cancer screening in Asian Americans compared with non-Hispanic whites: Cultural influences or access to care? Cancer. 2006;107: 184-192.

120. Baron RC, Melillo S, Rimer BK, et al. Intervention to increase recommendation and delivery of screening for breast, cervical, and colorectal cancers by healthcare providers a systematic review of provider reminders. Am J Prev Med. 2010;38: 110-117.

121. Getrich CM, Sussman AL, Helitzer DL, et al. Expressions of machismo in colorectal cancer screening among New Mexico Hispanic subpopulations. Qual Health Res. 2012;22: 546-559.

122. Coronado GD, Farias A, Thompson B, Godina R, Oderkirk W. Attitudes and beliefs about colorectal cancer among Mexican Americans in communities along the US-Mexico border. Ethn Dis. 2006;16: 421-427.

123. Fernandez ME, Wippold R, Torres-Vigil I, et al. Colorectal cancer screening among Latinos from U.S. cities along the Texas-Mexico border. Cancer Causes Control. 2008;19: 195-206.

124. Walsh JM, Kaplan CP, Nguyen B, Gildengorin G, McPhee SJ, Perez-Stable EJ. Barriers to colorectal cancer screening in Latino and Vietnamese Americans. Compared with non-Latino white Americans. J Gen Intern Med. 2004;19: 156-166.

125. Gancayco J, Soulos PR, Khiani V, et al. Age-based and sex-based disparities in screening colonoscopy use among medicare beneficiaries. J Clin Gastroenterol. 2013;47: 630-636.

126. Surveillance E, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 9 Regs Research Data, Nov 2014 Sub (1973-2012) <Katrina/Rita Population Adjustment> - Linked To County Attributes - Total U.S., 1969-2013 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2015, based on the November 2014 submission.

127. Heitman SJ, Au F, Manns BJ, McGregor SE, Hilsden RJ. Nonmedical costs of colorectal cancer screening with the fecal occult blood test and colonoscopy. Clin Gastroenterol Hepatol. 2008;6: 912-917 e911.

128. Farmer MM, Bastani R, Kwan L, Belman M, Ganz PA. Predictors of colorectal cancer screening from patients enrolled in a managed care health plan. Cancer. 2008;112: 1230-1238.

129. Zapka JG, Puleo E, Vickers-Lahti M, Luckmann R. Healthcare system factors and colorectal cancer screening. Am J Prev Med. 2002;23: 28-35.

130. Ford JS, Coups EJ, Hay JL. Knowledge of colon cancer screening in a national probability sample in the United States. J Health Commun. 2006;11 Suppl 1: 19-35.

131. Hudson SV, Ferrante JM, Ohman-Strickland P, et al. Physician recommendation and patient adherence for colorectal cancer screening. J Am Board Fam Med. 2012;25: 782-791.

132. Maruthur NM, Bolen S, Gudzune K, Brancati FL, Clark JM. Body mass index and colon cancer screening: a systematic review and meta-analysis. Cancer Epidemiol Biomarkers Prev. 2012;21: 737-746.

133. Oluyemi AO, Welch AR, Yoo LJ, Lehman EB, McGarrity TJ, Chuang CH. Colorectal cancer screening in high-risk groups is increasing, although current smokers fall behind. Cancer. 2014;120: 2106-2113.

134. Bell RA, Shelton BJ, Paskett ED. Colorectal cancer screening in North Carolina: associations with diabetes mellitus and demographic and health characteristics. Prev Med. 2001;32: 163-167.

135. Tsai MH, Xirasagar S, Li YJ, de Groen PC. Colonoscopy Screening Among US Adults Aged 40 or Older With a Family History of Colorectal Cancer. Prev Chronic Dis. 2015;12: E80.

136. Trask PC, Rabin C, Rogers ML, et al. Cancer screening practices among cancer survivors. Am J Prev Med. 2005;28: 351-356.

137. Mayer DK, Terrin NC, Menon U, et al. Screening practices in cancer survivors. J Cancer Surviv. 2007;1: 17-26.

138. Yaghjyan L, Wolin K, Chang SH, Colditz G. Racial disparities in healthy behaviors and cancer screening among breast cancer survivors and women without cancer: National Health Interview Survey 2005. Cancer Causes Control. 2014;25: 605-614.

139. Hudson SV, Hahn KA, Ohman-Strickland P, Cunningham RS, Miller SM, Crabtree BF. Breast, colorectal and prostate cancer screening for cancer survivors and non-cancer patients in community practices. J Gen Intern Med. 2009;24 Suppl 2: S487-490.

140. Bishop MM, Lee SJ, Beaumont JL, et al. The preventive health behaviors of long-term survivors of cancer and hematopoietic stem cell transplantation compared with matched controls. Biol Blood Marrow Transplant. 2010;16: 207-214.

141. Snyder CF, Frick KD, Peairs KS, et al. Comparing care for breast cancer survivors to non-cancer controls: a five-year longitudinal study. J Gen Intern Med. 2009;24: 469-474.

142. Jones RM, Woolf SH, Cunningham TD, et al. The relative importance of patient-reported barriers to colorectal cancer screening. Am J Prev Med. 2010;38: 499-507.

143. Percac-Lima S, Lopez L, Ashburner JM, Green AR, Atlas SJ. The longitudinal impact of patient navigation on equity in colorectal cancer screening in a large primary care network. Cancer. 2014;120: 2025-2031.

144. Lasser KE, Murillo J, Lisboa S, et al. Colorectal cancer screening among ethnically diverse, low-income patients: a randomized controlled trial. Arch Intern Med. 2011;171: 906-912.

145. Gross CP, Andersen MS, Krumholz HM, McAvay GJ, Proctor D, Tinetti ME. Relation between Medicare screening reimbursement and stage at diagnosis for older patients with colon cancer. JAMA. 2006;296: 2815-2822.

146. Zauber AG KA, Rutter CM, Lansdorp-Vogelaar I, Savarion J, van Ballegooijen M, Kuntz KM. Cost-Effectiveness of CT Colonography to Screen for Colorectal Cancer. Rockville, Maryland: Agency for Healthcare Research and Quality, 2009.

147. 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: 299-307.

148. Reschovsky JD WC. Location, Location, Location: Hospital Outpatient Prices Much Higher than Community Settings for Identical Services. Detroit, MI: National Institute for Health Care Reform, 2014.

149. von Wagner C, Good A, Whitaker KL, Wardle J. Psychosocial determinants of socioeconomic inequalities in cancer screening participation: a conceptual framework. Epidemiol Rev. 2011;33: 135-147.

150. Koh HK, Sebelius KG. Promoting prevention through the Affordable Care Act. N Engl J Med. 2010;363: 1296-1299.

151. Centers for Medicare & Medicaid Services. The Affordable Care Act

and Medicare. . Available from URL: http://www.medicare.gov/about-us/ [accessed 09/24/2014, 2014].

152. Halpern MT, Romaire MA, Haber SG, Tangka FK, Sabatino SA, Howard DH. Impact of state-specific Medicaid reimbursement and eligibility policies on receipt of cancer screening. Cancer. 2014;120: 3016-3024.

153. Choi SK, Adams SA, Eberth JM, et al. Medicaid Coverage Expansion and Implications for Cancer Disparities. Am J Public Health. 2015;105 Suppl 5: S706-712.

154. Grubbs SS, Polite BN, Carney J, Jr., et al. Eliminating racial disparities in colorectal cancer in the real world: it took a village. J Clin Oncol. 2013;31: 1928-1930.

155. Maxwell AE, Hannon PA, Escoffery C, et al. Promotion and provision of colorectal cancer screening: a comparison of colorectal cancer control program grantees and nongrantees, 2011-2012. Prev Chronic Dis. 2014;11: E170.

156. Itzkowitz SH, Winawer SJ, Krauskopf M, et al. New York Citywide Colon Cancer Control Coalition: A public health effort to increase colon cancer screening and address health disparities. Cancer. 2016;122: 269-277.

157. Tiro JA, Kamineni A, Levin TR, et al. The colorectal cancer screening process in community settings: a conceptual model for the population-based research optimizing screening through personalized regimens consortium. Cancer Epidemiol Biomarkers Prev. 2014;23: 1147-1158.

158. Taplin SH, Rodgers AB. Toward improving the quality of cancer care: addressing the interfaces of primary and oncology-related subspecialty care. J Natl Cancer Inst Monogr. 2010;2010: 3-10.

159. Anhang Price R, Zapka J, Edwards H, Taplin SH. Organizational factors and the cancer screening process. J Natl Cancer Inst Monogr. 2010;2010: 38-57.

160. Steenkamer BM, Drewes HW, Heijink R, Baan CA, Struijs JN. Defining Population Health Management: A Scoping Review of the Literature. Popul Health Manag. 2016.

161. 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: 364-371.

162. Guerra CE, Schwartz JS, Armstrong K, Brown JS, Halbert CH, Shea JA. Barriers of and facilitators to physician recommendation of colorectal cancer screening. J Gen Intern Med. 2007;22: 1681-1688.

163. Armour BS, Friedman C, Pitts MM, Wike J, Alley L, Etchason J. The influence of year-end bonuses on colorectal cancer screening. Am J Manag Care. 2004;10: 617-624.

164. Artiga S F, J, Cornachione E, Garfield R. . Key Facts on Health and Health Care by Race and Ethnicity. Menlo Park, CA: The Henry J Kaiser Family Foundation, 2016.

165. Lee JK, Levin TR, Corley DA. The road ahead: what if gastroenterologists were accountable for preventing colorectal cancer? Clin Gastroenterol Hepatol. 2013;11: 204-207.

166. Rothman K GS, Lash T. Modern Epidemiology. Philadelphia, PA: Lippincott Williams and Wilkins, 2008.

167. Dahlhamer JM SC. Subunit Nonresponse in the National Health Interview Survey (NHIS): An Exploration Using Paradata. JSM Proceedings. 2009: 262-276.

168. Gordon NP. Similarity of the Adult Kaiser Permanente Membership in Northern California to the Insured and General Population in Northern California: Statistics from the 2007 California Health Interview Survey. Internal Division of Research report. Oakland, CA: Kaiser Permanente Northern California Division of Research, 2012.

169. Garcia-Closas M, Lubin JH. Power and sample size calculations in case-control studies of gene-environment interactions: comments on different approaches. Am J Epidemiol. 1999;149: 689-692.

170. National Cancer Institute. Surveillance, Epidemiology and End Results Program. About the Program. Available from URL: http://seer.cancer.gov/about/ [accessed 08/01/2015.

171. Engels EA, Pfeiffer RM, Ricker W, Wheeler W, Parsons R, Warren JL. Use of surveillance, epidemiology, and end results-medicare data to conduct case-control studies of cancer among the US elderly. Am J Epidemiol. 2011;174: 860-870.

172. Warren JL, Klabunde CN, Schrag D, Bach PB, Riley GF. Overview of the SEER-Medicare data: content, research applications, and generalizability to the United States elderly population. Med Care. 2002;40: IV-3-18.

173. The Henry J Kaiser Family Foundation. Medicare Advantage. Available from URL: http://kff.org/medicare/fact-sheet/medicare-advantage/ [accessed 10/11/2015.

174. Vernon SW. Participation in colorectal cancer screening: a review. J Natl Cancer Inst. 1997;89: 1406-1422.

175. World Health Organization. BMI Classification. Available from URL: http://apps.who.int/bmi/index.jsp?introPage=intro_3.html [accessed 05/16/2016.

176. Bieler GS, Brown GG, Williams RL, Brogan DJ. Estimating model-adjusted risks, risk differences, and risk ratios from complex survey data. Am J Epidemiol. 2010;171: 618-623.

177. Division of Health Interview Statistics NCfHS. Multiple Imputation of Family Income and Personal Earnings in the National Health Interview Survey: Methods and Examples Hyattsville, MD: National Center for Health Statistics, 2014.

178. Bandi P, Cokkinides V, Smith RA, Jemal A. Trends in colorectal cancer screening with home-based fecal occult blood tests in adults ages 50 to 64 years, 2000-2008. Cancer. 2012;118: 5092-5099.

179. Zauber AG. Cost-effectiveness of colonoscopy. Gastrointest Endosc Clin N Am. 2010;20: 751-770.

180. McAlearney AS, Reeves KW, Tatum C, Paskett ED. Perceptions of insurance coverage for screening mammography among women in need of screening. Cancer. 2005;103: 2473-2480.

181. Flowers L MC, Okrent D,. Colonoscopy Screening after the Affordable Care Act: Cost Barriers Persist for Medicare Beneficiaries Washington DC: AARP Public Policy Institute, 2013.

182. James AS, Campbell MK, Hudson MA. Perceived barriers and benefits to colon cancer screening among African Americans in North Carolina: how does perception relate to screening behavior? Cancer Epidemiol Biomarkers Prev. 2002;11: 529-534.

183. Guessous I, Dash C, Lapin P, et al. Colorectal cancer screening barriers and facilitators in older persons. Prev Med. 2010;50: 3-10.

184. Trivedi AN, Rakowski W, Ayanian JZ. Effect of cost sharing on screening mammography in Medicare health plans. N Engl J Med. 2008;358: 375-383.

185. Rauscher GH, Johnson TP, Cho YI, Walk JA. Accuracy of self-reported cancer-screening histories: a meta-analysis. Cancer Epidemiol Biomarkers Prev. 2008;17: 748-757.

186. Klabunde CN, Schenck AP, Davis WW. Barriers to colorectal cancer screening among Medicare consumers. Am J Prev Med. 2006;30: 313-319.

187. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin. 2015;65: 5-29.

188. National Colorectal Cancer Roundtable. National Colorectal Cancer Roundtable. Available from URL: http://nccrt.org/about/.

189. Gupta S, Sussman DA, Doubeni CA, et al. Challenges and possible solutions to colorectal cancer screening for the underserved. J Natl Cancer Inst. 2014;106: dju032.

190. Mehta SJ JC, Quinn VP, Schottinger JE, Zauber AG, Meester R, Laiyemo AO, Fedewa SA, Goodman M, Fletcher RH, Levin TR, Corley DA, Doubeni CA. Race/Ethnicity and Adoption of a Population Health Management Approach to Colorectal Cancer Screening in a Community-Based Healthcare System. J Gen Intern Med. 2016;In Press.

191. National Committee on Quality Assurance. NQF-Endorsed Measures Specifications. Available from URL: http://www.ncqa.org/LinkClick.aspx?fileticket=POLoMIAi3Mo%3d&tabid=59&mid=1604&forcedownload=true.

192. Maxwell AE, Crespi CM. Trends in colorectal cancer screening utilization among ethnic groups in California: are we closing the gap? Cancer Epidemiol Biomarkers Prev. 2009;18: 752-759.

193. 2009 California Health Interview Survey. Public Use File Release 1 [computer file]. Los Angeles, CA: UCLA: Center for Health Policy Research 2011.

194. Fedewa SA, Goodman M, Flanders WD, et al. Elimination of cost-sharing and receipt of screening for colorectal and breast cancer. Cancer. 2015;121: 3272-3280.

195. Peipins LA, Soman A, Berkowitz Z, White MC. The lack of paid sick leave as a barrier to cancer screening and medical care-seeking: results from the National Health Interview Survey. BMC Public Health. 2012;12: 520.

196. US Bureau of Labor Statistics. Labor Force Characteristics by Race and Ethnicity, 2014. Available from URL: http://www.bls.gov/opub/reports/race-and-ethnicity/archive/labor-force-characteristics-by-race-and-ethnicity-2014.pdf.

197. Stimpson JP, Pagan JA, Chen LW. Reducing racial and ethnic disparities in colorectal cancer screening is likely to require more than access to care. Health Aff (Millwood). 2012;31: 2747-2754.

198. Jerant AF, Arellanes RE, Franks P. Factors associated with Hispanic/non-Hispanic white colorectal cancer screening disparities. J Gen Intern Med. 2008;23: 1241-1245.

199. Freeman KL JL, Thompson H, DuHamel KN. Colorectal Cancer Brochure Development for African Americans. Journal of Health Disparities Research and Practice. 2010;3: 43-56.

200. Cooperman JL, Efuni E, Villagra C, DuHamel K, Jandorf L. Colorectal cancer screening brochure for Latinos: focus group evaluation. J Cancer Educ. 2013;28: 582-590.

201. Groeneveld PW, Sonnad SS, Lee AK, Asch DA, Shea JE. Racial differences in attitudes toward innovative medical technology. J Gen Intern Med. 2006;21: 559-563.

202. Gomez SL, Kelsey JL, Glaser SL, Lee MM, Sidney S. Inconsistencies between self-reported ethnicity and ethnicity recorded in a health maintenance organization. Ann Epidemiol. 2005;15: 71-79.

203. Siegel RL, Fedewa SA, Miller KD, et al. Cancer statistics for Hispanics/Latinos, 2015. CA Cancer J Clin. 2015;65: 457-480.

204. Diez-Roux AV, Kiefe CI, Jacobs DR, Jr., et al. Area characteristics and individual-level socioeconomic position indicators in three population-based epidemiologic studies. Ann Epidemiol. 2001;11: 395-405.

205. Adler J, Robertson DJ. Interval Colorectal Cancer After Colonoscopy: Exploring Explanations and Solutions. Am J Gastroenterol. 2015;110: 1657-1664.

206. DeSantis CE, Siegel RL, Sauer AG, et al. Cancer statistics for African Americans, 2016: Progress and opportunities in reducing racial disparities. CA Cancer J Clin. 2016;66: 290-308.

207. 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: 792-797.

208. 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: 1353-1362.

209. Samadder NJ, Curtin K, Tuohy TM, et al. Characteristics of missed or interval colorectal cancer and patient survival: a population-based study. Gastroenterology. 2014;146: 950-960.

210. Gohel TD, Burke CA, Lankaala P, et al. Polypectomy rate: a surrogate for adenoma detection rate varies by colon segment, gender, and endoscopist. Clin Gastroenterol Hepatol. 2014;12: 1137-1142.

211. Boroff ES, Gurudu SR, Hentz JG, Leighton JA, Ramirez FC. Polyp and adenoma detection rates in the proximal and distal colon. Am J Gastroenterol. 2013;108: 993-999.

212. Adams KF, Johnson EA, Chubak J, et al. Development of an Algorithm to Classify Colonoscopy Indication from Coded Health Care Data. EGEMS (Wash DC). 2015;3: 1171.

213. Farrar WD, Sawhney MS, Nelson DB, Lederle FA, Bond JH. Colorectal cancers found after a complete colonoscopy. Clin Gastroenterol Hepatol. 2006;4: 1259-1264.

214. Butterly L, Robinson CM, Anderson JC, et al. Serrated and adenomatous polyp detection increases with longer withdrawal time: results from the New Hampshire Colonoscopy Registry. Am J Gastroenterol. 2014;109: 417-426.

215. Brenner H, Chang-Claude J, Jansen L, Seiler CM, Hoffmeister M. Colorectal cancers occurring after colonoscopy with polyp detection: sites of polyps and sites of cancers. Int J Cancer. 2013;133: 1672-1679.

216. Lieberman DA, Holub JL, Moravec MD, Eisen GM, Peters D, Morris CD. Prevalence of colon polyps detected by colonoscopy screening in asymptomatic black and white patients. JAMA. 2008;300: 1417-1422.

217. Jass JR. Serrated route to colorectal cancer: back street or super highway? J Pathol. 2001;193: 283-285.

218. Xicola RM, Gagnon M, Clark JR, et al. Excess of proximal microsatellite-stable colorectal cancer in African Americans from a multiethnic study. Clin Cancer Res. 2014;20: 4962-4970.

219. 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: 182-202.

220. Sung JJ, Lau JY, Young GP, et al. Asia Pacific consensus recommendations for colorectal cancer screening. Gut. 2008;57: 1166-1176.

221. Lansdorp-Vogelaar I, Fedewa S, Lin CC, Virgo KS, Jemal A. Utilization of surveillance after polypectomy in the medicare population--a cohort study. PLoS One. 2014;9: e110937.

222. Cooper GS, Kou TD, Barnholtz Sloan JS, Koroukian SM, Schluchter MD. Use of colonoscopy for polyp surveillance in Medicare beneficiaries. Cancer. 2013;119: 1800-1807.

223. Schenck AP, Klabunde CN, Warren JL, et al. Data sources for measuring colorectal endoscopy use among Medicare enrollees. Cancer Epidemiol Biomarkers Prev. 2007;16: 2118-2127.

224. Ko CW, Dominitz JA, Green P, Kreuter W, Baldwin LM. Accuracy of Medicare claims for identifying findings and procedures performed during colonoscopy. Gastrointest Endosc. 2011;73: 447-453 e441.

225. Francis DL, Rodriguez-Correa DT, Buchner A, Harewood GC, Wallace M. Application of a conversion factor to estimate the adenoma detection rate from the polyp detection rate. Gastrointest Endosc. 2011;73: 493-497.

226. Chen SC, Rex DK. Variable detection of nonadenomatous polyps by individual endoscopists at colonoscopy and correlation with adenoma detection. J Clin Gastroenterol. 2008;42: 704-707.

227. Do A, Weinberg J, Kakkar A, Jacobson BC. Reliability of adenoma detection rate is based on procedural volume. Gastrointest Endosc. 2013;77: 376-380.

228. Baldwin LM, Adamache W, Klabunde CN, Kenward K, Dahlman C, J LW. Linking physician characteristics and medicare claims data: issues in data availability, quality, and measurement. Med Care. 2002;40: IV-82-95.

229. Begg CB, Cramer LD, Hoskins WJ, Brennan MF. Impact of hospital volume on operative mortality for major cancer surgery. JAMA. 1998;280: 1747-1751.

230. Rogart JN, Siddiqui UD, Jamidar PA, Aslanian HR. Fellow involvement may increase adenoma detection rates during colonoscopy. Am J Gastroenterol. 2008;103: 2841-2846.

231. Han X, Robin Yabroff K, Guy GP, Jr., Zheng Z, Jemal A. Has recommended preventive service use increased after elimination of cost-sharing as part of the Affordable Care Act in the United States? Prev Med. 2015;78: 85-91.

232. Cooper GS, Kou TD, Schluchter MD, Dor A, Koroukian SM. Changes in Receipt of Cancer Screening in Medicare Beneficiaries Following the Affordable Care Act. J Natl Cancer Inst. 2016;108.

233. U.S. Department of Health and Human Services. Healthy People 2020 Available from URL: https://www.healthypeople.gov/2020/topics-objectives/topic/cancer/objectives [accessed 05/01/2016.