Modifiable Failures in the Colorectal Cancer Screening Process and Their Association With Risk of Death

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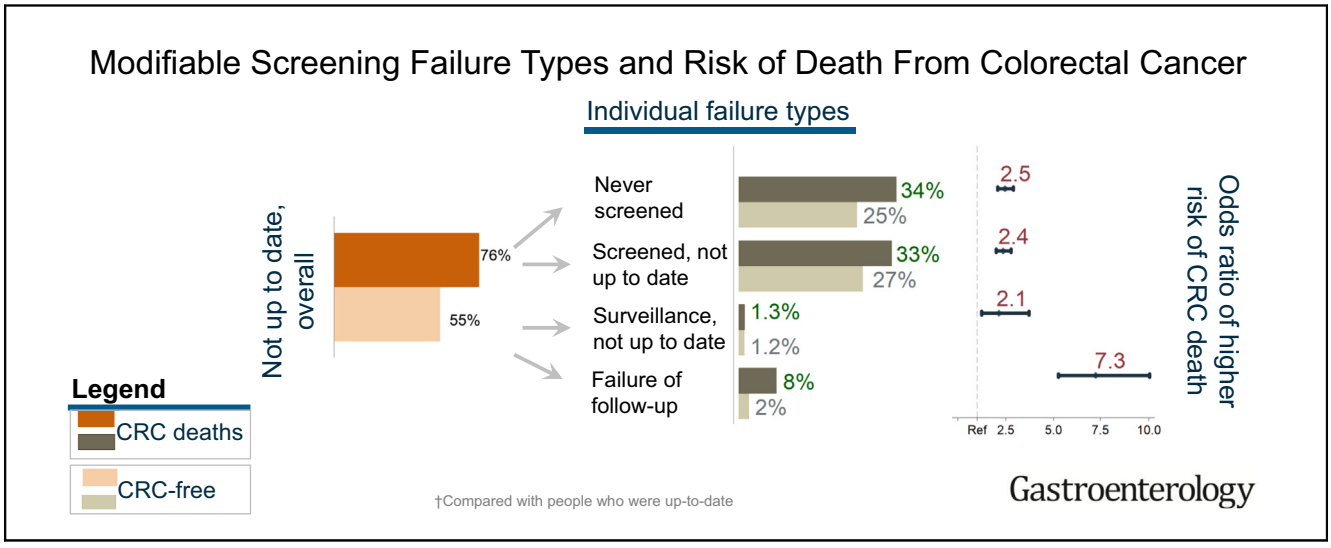

See Covering the Cover synopsis on page 1.

BACKGROUND & AIMS: Colorectal cancer (CRC) deaths occur when patients do not receive screening or have inadequate follow-up of abnormal results or when the screening test fails. We have few data on the contribution of each to CRC-associated deaths or factors associated with these events. **METHODS:** We performed a retrospective cohort study of patients in the Kaiser Permanente Northern and Southern California systems (55–90 years old) who died of CRC from 2006 through 2012 and had ≥5 years of enrollment before diagnosis. We compared data from patients with those from a matched cohort of cancer-free patients in the same system. Receipt, results, indications, and follow-up of CRC tests in the 10-year period before diagnosis were obtained from electronic databases and chart audits. **RESULTS:** Of 1750 CRC deaths, 75.9% (n = 1328) occurred in patients who were not up to date in screening and 24.1% (n = 422) occurred in patients who were up to date. Failure to screen was associated with fewer visits to primary care physicians. Of 3486 cancer-free patients, 44.6% were up to date in their screening. Patients who were up to date in their screening had a lower risk of CRC death (odds ratio, 0.38; 95% confidence interval, 0.33–0.44). Failure to screen, or failure to screen at appropriate intervals, occurred in a 67.8% of patients who died of CRC vs 53.2% of cancer-free patients; failure to follow-up on abnormal results occurred in 8.1% of patients who died of CRC vs 2.2% of cancer-free patients. CRC death was associated with higher odds of failure to screen or failure to screen at appropriate intervals (odds ratio, 2.40; 95% confidence interval, 2.07–2.77) and failure to follow-up on abnormal results (odds ratio, 7.26; 95% confidence interval, 5.26–10.03). **CONCLUSIONS:** Being up to date on screening substantially decreases the risk of CRC death. In 2 health care systems with high rates of screening, most people who died of CRC had failures in the screening process that could be rectified, such as failure to follow-up on abnormal findings; these significantly increased the risk for CRC death.

Keywords: Colon Cancer; Adenoma; Early Detection; Cancer Prevention.

WHAT YOU NEED TO KNOW

BACKGROUND AND CONTEXT

The main causes of colorectal cancer (CRC) deaths from potentially preventable failures of the screening process are not well described.

NEW FINDINGS

Among CRC deaths in this study, 76% had failures to screen or follow-up for abnormal screening; the latter increased CRC death risk by 10-fold. Being screening up-to-date reduced CRC death risk by 64%.

LIMITATIONS

The study was conducted in a setting with well-developed screening programs; the distribution of factors identified may vary by setting.

IMPACT

Even in settings with well-developed screening programs, the main methods for decreasing deaths from colorectal cancer were being up-to-date on screening and receiving appropriate timely follow-up for abnormal or incomplete screening exams; lack of appropriate surveillance was an uncommon cause of death from colorectal cancer.

Colorectal cancer (CRC) remains a leading cause of cancer death,[1] with approximately 881,000 deaths worldwide in 2018 and projected to increase to 1.1 million deaths by 2030.[2,3] Use of screening in average-risk persons beginning at 50 years of age with currently recommended strategies, including colonoscopy, sigmoidoscopy, and fecal testing, is effective at lowering the risk of death from CRC.[3–6] Thus, most deaths from CRC are believed to result from breakdowns in screening processes, particularly failures to undergo screening or stay current with screening.[7] However, deaths also can result from patients' failures to undergo surveillance endoscopy at recommended intervals after adenoma removal[4,6] or to not receive timely follow-up testing for positive screening results,[8] which has been shown to increase the risk of CRC diagnosis, including advanced-stage disease.[9,10] Deaths from CRC also occur in people whose screening is up to date, because of lesions missed during screening or interval cancers that develop before the next scheduled screening.[11] However, no studies to date have examined detailed screening histories and their relation to death from CRC.

Previous studies in cervical and breast cancer have helped to identify targets for decreasing screening failures for those cancers,[12–14] but similar information about CRC screening is lacking, particularly from settings with robust data systems and screening programs.[15] This study characterized failures in the screening process continuum over an extended period in patients who died of CRC in 2 large integrated health care systems with high screening rates to help identify targets for interventions to further decrease CRC mortality rates in diverse settings. This study also evaluated the screening histories of cancer-free patients and the association between up-to-date screening (by any test) and various types of failures in the screening process and risk of death from CRC.

Methods

Study Population and Setting

Data for this study were derived from screening-eligible members of Kaiser Permanente Northern California (KPNC) and Southern California (KPSC), 2 large integrated health care systems that provide care for approximately 7 million members. These health systems successfully implemented organized screening outreach programs that began in 2006–2008. The programs use fecal immunochemical testing (FIT) as the primary screening strategy or colonoscopy by patient or provider request.[16] CRC screening rates in these 2 health systems have increased over time, reaching more than 80% in 2012, exceeding the national average of 58% in 2012 or 61% in 2015.[16–19] This study was approved by the institutional review boards of KPNC, KPSC, and the University of Pennsylvania.

Data were collected as part of a large observational study that evaluated the effectiveness of screening in preventing CRC deaths, which has been fully described previously.[20,21] In that study, eligible patients were 55–90 years of age at the death date from CRC during 2006–2012 in KPNC or 2011–2012 in KPSC and were enrolled in their respective health plans for $\geq$5 years before their CRC diagnosis date.[21] The cohort was further restricted to those who died of adenocarcinomas because of strong evidence that detection of precancerous adenomas and early-stage cancers lowers the risk for death from these cancer types. We excluded those with a history of inflammatory bowel disease or a strong family history of CRC as defined previously.[18,19] We also excluded patients with missing medical charts.

We restricted this study to people diagnosed from 2002 through 2012 because screening was less common in the general US population before that period and Medicare began coverage for colonoscopy in mid-2001.[22] We included a CRC-free cohort of patients matched to those who died of CRC, using an incidence-density matching approach, on the diagnosis date on age, sex, study site, and years of enrollment in the health plan.[20,21] The diagnosis date was used as the reference date for ascertaining screening histories in the 2 groups of patients.

Data Collection

Electronic medical records and administrative, tumor, and vital status registry data were used to identify study patients and variables. Information on CRC diagnosis, tumor location, and receipt of initial treatment was ascertained from

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Abbreviations used in this paper: BE, barium enema; CI, confidence interval; CRC, colorectal cancer; FIT, fecal immunochemical test; FOBT, guaiac fecal occult blood test; KPNC, Kaiser Permanente Northern California; KPSC, Kaiser Permanente Southern California; OR, odds ratio; PCP, primary care physician; SES, socioeconomic status.

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tumor registries. We categorized tumors in the cecum, ascending colon, and transverse colon as right colon cancers, and those in the descending, sigmoid, and rectosigmoid colon as left colon cancers. Rectal tumors were categorized separately and others as unspecified. Cause-specific vital status was obtained from KPNC and KPSC mortality files, which were obtained from state and federal death registries that in turn were derived mostly from information in death certificates.[21]

Age, sex, race and ethnicity, health care usage, and clinical histories (to construct the Charlson comorbidity score at the 5-year point before the diagnosis date) were obtained from electronic databases and medical records.[20,21] The number of outpatient visits to primary care physicians (PCPs; family medicine, internal medicine, geriatrics, and obstetrics and gynecology) was enumerated in the 5-year period before CRC diagnosis, but excluded the 90-day period before diagnosis. Socioeconomic status (SES) was estimated using the percentage of people ≥25 years old with less than a high school diploma in each patient's census tract in the 2000 census.[23,24]

The date, type, reason, and results (number, size, types, and location of lesions, or positive or negative findings) of CRC tests (colonoscopy, sigmoidoscopy, barium enema [BE], and fecal tests) received in the 10-year period before diagnosis were collected from electronic data and chart audits performed by trained reviewers using standardized processes.[21] The results of fecal tests (FIT or guaiac fecal occult blood test [FOBT]) and other relevant laboratory abnormalities, such as iron-deficiency anemia, triggering diagnostic testing were extracted from laboratory databases.

Classification of CRC Test Indication and Screening History

The indication for each CRC test was assigned as screening, surveillance, or diagnostic using a multistep approach that included expert review of individual patients' data on selected tests as described previously.[21] Briefly, a test was considered surveillance if it followed an adenoma or a polyp finding from a previous endoscopic test, diagnostic if it was for the workup of relevant symptoms or a prior positive, abnormal, or incomplete test, and screening if it was indicated as such in the chart.[25]

We classified patients' testing histories by adapting the screening process framework of Zapka et al[12] for breast and cervical cancer with consideration for the multiplicity and different testing intervals for CRC screening and the potential for screening to detect cancers early and prevent disease through removal of precancerous lesions.[19] Patients were classified as failures to screen (and to screen at appropriate intervals), failure to follow-up an abnormal screening result, or failure of the screening test to prevent CRC death as defined below.

The classifications were based primarily on whether a patient was up to date by using the 2008 multi-society CRC screening guidelines,[26] defined as having received a colonoscopy within 10 years or sigmoidoscopy and/or BE within 5 years of CRC diagnosis. For FIT and FOBT, we used a 2-year interval because of evidence of effectiveness for this interval in clinical trials and its common use worldwide.[3] Patients who received CRC testing for workup of symptoms and had a

Table 1. Testing Categories, Definitions, and Implications for Patients Dying of CRC (n = 1750)[a]

Category	n (%)	Descriptions	Intervention
1. Failure to screen or screen at appropriate interval	1187 (67.8)		
1a. Failure to screen	591 (33.8)	No screening test during 10-y period	Improve access and uptake of screening
1b. Failure to screen at appropriate intervals	574 (32.8)	Received screening but had clinically important gaps; eg, initiated screening but not up to date on diagnosis date or did not initiate screening for several years after becoming age eligible and had cancer diagnosis by first screening test (had colonoscopy >10 y, sigmoidoscopy >5 y, or FOBT >2 y before diagnosis; or unscreened 5–10 y after becoming age eligible and cancer diagnosed by only screening test received	Close gaps in screening in screening eligible population; improve initiation of screening and regular rescreening; identify and target those who did not initiate screening or initiated but did not continue
1c. Failure to receive surveillance	22 (1.3)	Initiated screening (>1 y before diagnosis) and had adenoma but did not have follow-up surveillance as recommended or appropriate follow-up was not recommended for patient	Improve adherence to, or recommendations for, surveillance colonoscopy
2. Failure to follow-up for positive screening result	141 (8.1)	Had screening test with positive result but had no timely follow-up visit or diagnostic testing	Improve access to follow-up evaluation or targeting of screening to those who are candidates for colonoscopy to minimize misuse
3. Failure of screening test	422 (24.1)	Was up to date at cancer diagnosis date, including those who had positive test result and had diagnostic testing	Improve effectiveness of screening tests or of diagnostic testing after positive result

[a]Some patients classified as up to date with screening received a negative result for a diagnostic indication.

negative result were considered up to date in their screening for the testing interval of that modality; for example, a person with a negative colonoscopy result (that had adequate bowel preparation and was complete to the cecum) for a diagnostic indication of bleeding through the rectum would be considered up to date in screening for 10 years. Up-to-date status for surveillance was based on the performing physician's recommendation or relevant guidelines, if not specified.[11] When assigning follow-up intervals based on surveillance guidelines and, in part, because we did not have histology data, we used information on the number and size of polyps detected and used the shorter of recommended intervals such as 5 years for 1–2 polyps. Patients with incomplete tests (eg, inadequate bowel preparation for a colonoscopy) were considered up to date if the same or an appropriate alternative test was completed within 6 months of the original test date.

Thus, failures to screen (also referred to as "all failures to screen combined") was defined as not being up to date with screening on the CRC diagnosis date (or reference date for cancer-free patients), but excluded failure to follow-up on abnormal results. We further subdivided the failure-to-screen groups into (1) failure to ever screen, (2) failure to screen at appropriate intervals, and (3) failure to receive appropriate surveillance (Table 1 and Figure 1). The subcategories accounted for timely initiation of screening, rescreening at recommended intervals, and surveillance after polypectomy, respectively, as crucial processes in the screening continuum. Patients whose only relevant history was diagnostic testing in the 6-month period before CRC diagnosis (considered part of cancer workup) were classified as failure to ever screen. Failure to follow-up an abnormal screening result was defined as no follow-up diagnostic colonoscopy within 9 months after a positive fecal test result[9,10]; for sigmoidoscopy or BE, the 9-month interval or as recommended by the performing provider, whichever was longer, was used. Failure of the screening test was defined as being up to date with screening including timely follow-up and surveillance.

Patients with ≥2 types of failures were classified based on the type closest to the cancer diagnosis date. For example, a patient who delayed colonoscopy after a positive FIT result but who, at the delayed colonoscopy, had a polypectomy and subsequently failed to complete recommended surveillance was classified as a failure to receive surveillance.

Statistical Analysis

Differences in proportions of screening failure types were analyzed in patients who died of CRC and in matched cancer-free patients. Analyses also were performed according to diagnosis age (<55, 55–64, 65–74, 75–84, and ≥85 years), sex, race and ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, Asian or Pacific Islander, and other), number of PCP visits (0, 1, 2, and ≥3), diagnosis year, and tumor location (right, left, rectal, and unspecified) using χ^2 tests. Then, we used unconditional logistic regression models that simultaneously adjusted for these factors, comorbidity score, and SES to assess, separately, associations with failure to ever screen and all failures to screen combined; all test hypotheses were 2-sided. We repeated these analyses restricted to patients with documented receipt of initial cancer treatment in tumor registry data.

We fitted 3 separate conditional regression models to evaluate the association between being up to date in screening and failures in the screening process and risk of CRC deaths

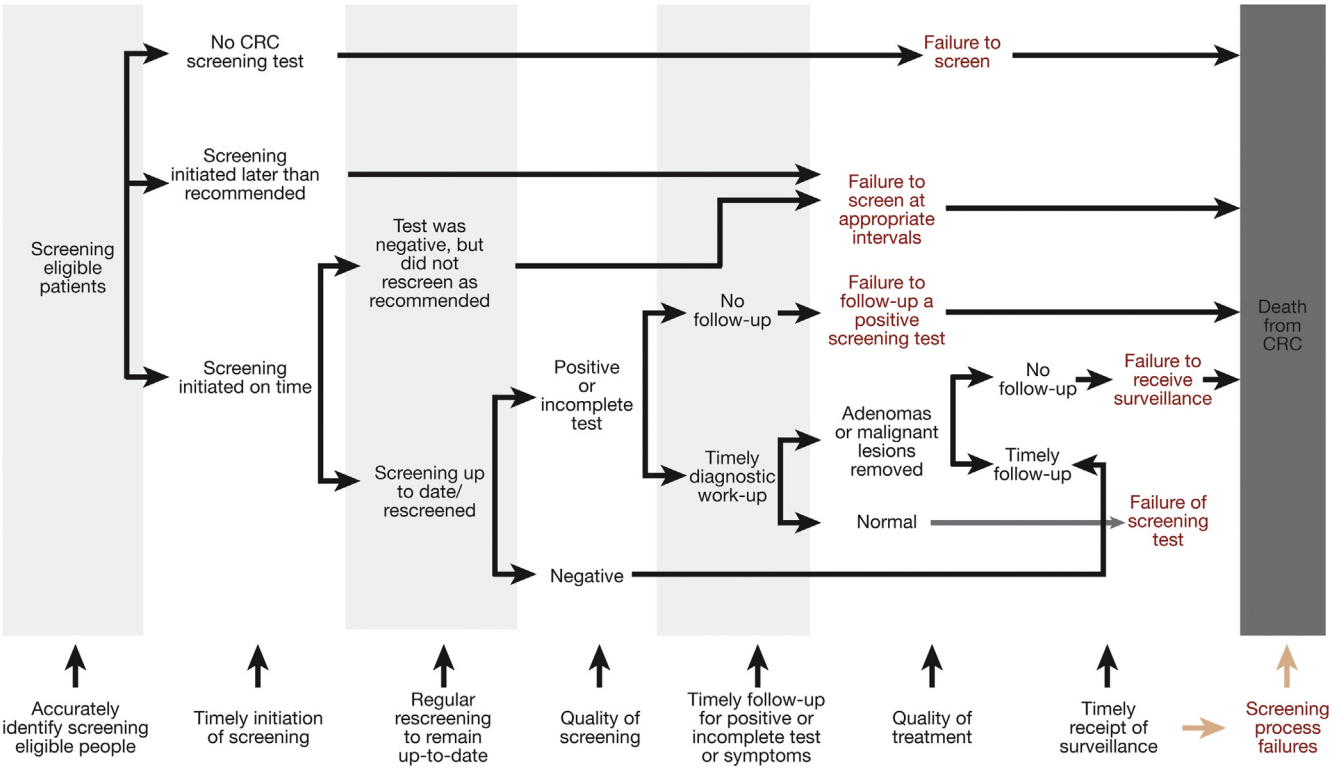

Figure 1. CRC test exposure trajectories and failures in people who died of CRC, KPNC and KPSC 2006–2012.

Table 2. Characteristics of Patients Who Died of CRC According to Testing Categories, KPSC and KPNC 2006–2012[a]

Characteristics	Failures to screen, n (%)			Failure to follow-up for positive result, n (%)	Failure of screening test, n (%)[b]	Total, n (%)
	Failure to screen	Failure to screen at appropriate intervals	Failure to receive surveillance			
Total	591 (33.8)	574 (32.8)	22 (1.3)	141 (8.1)	422 (24.1)	1750
Age at diagnosis (*y*)						
<55	10 (43.5)	9 (39.1)	1 (4.3)	0 (0.0)	3 (13)	23
55–64	211 (37.0)	193 (33.9)	1 (0.2)	25 (4.4)	140 (24.6)	570
65–74	145 (28.7)	172 (34.0)	10 (2.0)	57 (11.3)	122 (24.1)	506
75–84	185 (33.2)	172 (30.9)	9 (1.6)	54 (9.7)	137 (24.6)	557
≥85	40 (42.6)	28 (29.8)	1 (1.1)	5 (5.3)	20 (21.3)	94
Race and ethnicity						
NH white	388 (33.1)	388 (33.1)	19 (1.6)	90 (7.7)	287 (24.5)	1172
NH black	68 (32.4)	74 (35.2)	1 (0.5)	16 (7.6)	51 (24.3)	210
Hispanic	61 (37.2)	48 (29.3)	1 (0.6)	13 (7.9)	41 (25)	164
Asian or PI	61 (39.1)	52 (33.3)	0 (0.0)	15 (9.6)	28 (17.9)	156
Other	13 (27.1)	12 (25.0)	1 (2.1)	7 (14.6)	15 (31.3)	48
Sex						
Men	302 (34.2)	286 (32.4)	12 (1.4)	78 (8.8)	204 (23.1)	882
Women	289 (33.3)	288 (33.2)	10 (1.2)	63 (7.3)	218 (25.1)	868
Education less than HS education, % (*quartile*)[c]						
1	124 (33.0)	130 (34.6)	4 (1.1)	30 (8.0)	88 (23.4)	376
2	142 (33.7)	136 (32.3)	6 (1.4)	35 (8.3)	102 (24.2)	421
3	158 (36.2)	140 (32.0)	6 (1.4)	28 (6.4)	105 (24)	437
4	154 (32.2)	157 (32.8)	6 (1.3)	46 (9.6)	116 (24.2)	479
Missing	13 (35.1)	11 (29.7)	0 (0.0)	2 (5.4)	11 (29.7)	37
Health plan enrollment (*y*)						
5.0–7.4	100 (33.2)	97 (32.2)	3 (1.0)	21 (7.0)	80 (26.6)	301
7.5–9.9	108 (34.3)	116 (36.8)	4 (1.3)	24 (7.6)	63 (20)	315
≥10	383 (33.8)	361 (31.8)	15 (1.3)	96 (8.5)	279 (24.6)	1134
PCP visits, n[d]						
0	53 (65.4)	23 (28.4)	1 (1.2)	2 (2.5)	2 (2.5)	81
1	26 (57.8)	15 (33.3)	0 (0.0)	3 (6.7)	1 (2.2)	45
2	45 (46.9)	31 (32.3)	2 (2.1)	7 (7.3)	11 (11.5)	96
≥3	467 (30.6)	505 (33.0)	19 (1.2)	129 (8.4)	408 (26.7)	1528
Charlson score[e]						
0	426 (35.9)	400 (33.7)	13 (1.1)	79 (6.7)	268 (22.6)	1186
1	79 (26.8)	99 (33.6)	4 (1.4)	24 (8.1)	89 (30.2)	295
≥2	86 (32.0)	75 (27.9)	5 (1.9)	38 (14.1)	65 (24.2)	269
Diagnosis year						
2002–2005	96 (36.2)	90 (34.0)	3 (1.1)	15 (5.7)	61 (23)	265
2006–2008	233 (33.7)	273 (39.5)	9 (1.3)	39 (5.6)	137 (19.8)	691
2009–2012	262 (33.0)	211 (26.6)	10 (1.3)	87 (11.0)	224 (28.2)	794
Tumor location						
Rectal	146 (36.8)	143 (36.0)	4 (1.0)	22 (5.5)	82 (20.7)	420
Left	187 (44.5)	129 (30.7)	4 (1.0)	33 (7.9)	67 (16)	397
Right	232 (26.3)	292 (33.1)	14 (1.6)	83 (9.4)	261 (29.6)	882
Unspecified	26 (51.0)	10 (19.6)	0 (0.0)	3 (5.9)	12 (23.5)	51
Receipt of initial therapy						
Yes	463 (31.4)	516 (35.0)	18 (1.2)	115 (7.8)	362 (24.6)	1474
None	40 (42.6)	21 (22.3)	2 (2.1)	7 (7.4)	24 (25.5)	94
Unknown	10 (41.7)	5 (20.8)	0 (0.0)	2 (8.3)	7 (29.2)	24
Missing	78 (49.4)	32 (20.3)	2 (1.3)	17 (10.8)	29 (18.4)	158

HS, high school; NH, non-Hispanic; PI, Pacific Islander.
[a]Percentages might not add to 100% because of rounding.
[b]Includes 24 patients who had a negative BE result.
[c]Percentage of people at least 25 years old with less than a high school diploma in the census tract based on the 2000 decennial census.
[d]PCP (family medicine, internal medicine, geriatrics, and obstetrics and gynecology) outpatient encounters were enumerated in the 5-year period but excluded the 90-day period before the reference date.
[e]Charlson comorbidity score at baseline defined as 5 years before the reference date, which accounted for the minimum enrollment requirement for inclusion in the study.

adjusting for race and ethnicity, SES, comorbidity score, and PCP visits. In model 1, we estimated the association between being up to date in screening compared with a reference group composed of all screening process failures. For context, we provide the estimate for the association between not being up to date and risk of CRC death. In model 2, we used an indicator for all failures to screen combined plus an indicator for failure to follow-up; being up to date in screening was the reference group. In model 3, we used separate indicators for each of the screening process failures (failure to ever screen, screen at appropriate intervals, receive surveillance, and follow-up on abnormal result); being up to date was the reference group. In sensitivity analyses, we used 2 × 2 contingency tables and unadjusted regression models to evaluate the association between failure of follow-up and risk of death in those with abnormal or positive results. Analyses were performed using STATA 14.2 (StataCorp LP, College Station, TX).

Results

We identified 1791 patients who died of adenocarcinoma of the colon and rectum from 2006 to 2012 and analyzed 1750 after exclusions for history of inflammatory bowel disease identified on chart audit (n = 1), family CRC history (n = 29), missing medical charts (n = 3), and CRC diagnosis before 2002 (n = 8). The average age at diagnosis of patients was 70 years and 49.5% were women, 67.0% were non-Hispanic white, 12.0% were non-Hispanic black, 9.4% were Hispanic, and 8.9% were Asian or Pacific Islander (Table 2). Most patients had a Charlson comorbidity score of 0. Approximately 84.2% (n = 1474) received initial cancer treatment, 5.4% (n = 94) did not receive treatment, 1.4% (n = 24) refused treatment, and 9.0% (n = 158) had unknown treatment status. The characteristics of patients with documented receipt of initial treatment (n = 1474) were similar to the overall study population (Supplementary Table 1). The characteristics of the cancer-free matched patients (n = 3486) are presented in Supplementary Table 2.

CRC Deaths by Testing History

Most patients (75.9%) who died of CRC in our study had an identifiable failure in the screening process (failure to screen, n = 591, 33.8%; screen at appropriate intervals, n = 574, 32.8%; receive surveillance, n = 22, 1.3%; or follow-up, n = 141, 8.1%) and 24.1% (n = 422) were up to date at the diagnosis date (Tables 1 and 2). Of those with failure of follow-up for an abnormal result, 103 had a positive FOBT result of whom 58 (57.3%) had a documented order for diagnostic colonoscopy (n = 42), sigmoidoscopy (n = 14), or BE (n = 2); 60 of them received FOBTs after the positive FOBT result, 6 had only BE, and 2 had only sigmoidoscopy (data are not shown).

Testing History and Tumor Location

Of the 1750 CRCs, 50.4%, 22.7%, 24.0%, and 2.9% were in the right colon, left colon, rectum, and unspecified location, respectively (Table 2). Right colon cancers composed 45.3% (n = 538) of all failures to screen combined and 58.9% (n = 83) of failures of follow-up. Most tumors in patients who were up to date in screening by any test or indication were located in the right colon overall (61.8%,

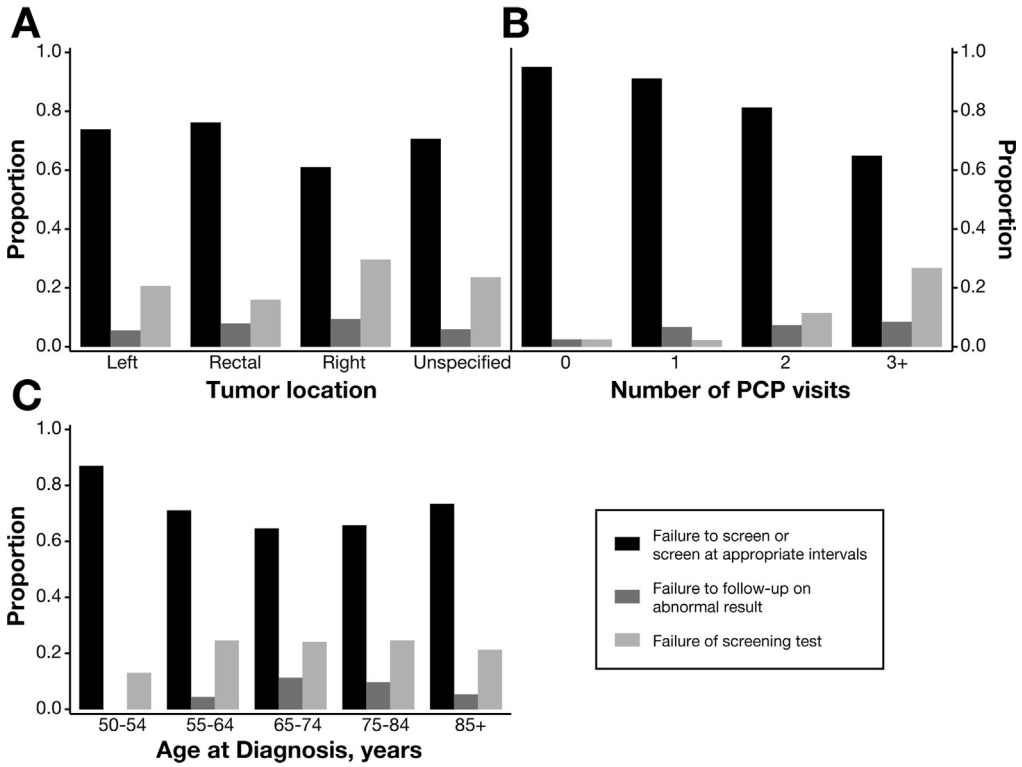

Figure 2. CRC testing history by (*A*) tumor location, (*B*) PCP visits, and (*C*) patient age in patients who died of CRC, KPNC and KPSC 2006–2012.

n = 261) and regardless of the type of test (colonoscopy, 58.6%, n = 41 of 70; sigmoidoscopy, 68.5%, n = 100 of 146; and fecal tests, 58.6%, n = 106 of 181; Supplementary Figure 1*A* and *B*). Failures to screen were more common for rectal or left colon cancers than for right colon cancers ($P < .01$; Figure 2*A* and Supplementary Figure 2*A*).

Associations With Testing History

Most patients had at least 1 PCP visit. The proportions with failures to screen increased with decreasing numbers of PCP encounters (Figure 2*B* and Supplementary Figure 2*B*). A larger proportion of younger patients (50–54 years) had failure to screen than patients ≥55 years (Figure 2*C* and Supplementary Figure 2*C*). The proportion of patients with combined failures to screen during 2002-2005 (71.3%) was similar to those diagnosed during 2006–2008 (74.5%; $P = .31$) but was smaller than those diagnosed in 2009–2012 (60.8%; $P < .01$).

In adjusted unconditional logistic regression analyses, compared with those who had ≥3 PCP encounters in the 5 years before CRC diagnosis, those who had 2 visits, 1 visit, or no visit had 2.32 (95% confidence interval [CI], 1.35–3.99), 6.41 (95% CI, 2.25–18.30), and 12.12 (95% CI, 4.35–33.76) times higher odds, respectively, to have had failures to screen (Table 3). Compared with those 65–74 years old, younger patients and those in the oldest group (≥85 years) were significantly more likely to have failures to screen. There was no statistically significant difference by race or sex. The likelihood of failures to screen was lower during 2009–2012 (odds ratio [OR], 0.45; 95% CI, 0.30–0.67) than during 2002–2005. Patterns were similar in analysis of failure to ever screen. Analyses restricted to those with documented treatment receipt did not change our findings (Supplementary Table 3).

Screening Histories of Cancer-Free Patients

A total of 3486 cancer-free patients were matched to the CRC deaths. We found similar associations between the selected characteristics and screening failures for matched cancer-free patients as patients who died of CRC (Supplementary Table 2). For instance, compared with those with ≥3 PCP encounters, those who had 2 visits, 1 visit, or no visit had 2.99 (95% CI, 1.91–4.70), 5.26 (95% CI, 2.39–11.56), and 7.29 (95% CI, 3.52–15.08) times higher odds, respectively, to have failures to screen.

Comparison of Screening Histories of Case and Cancer-Free Patients

A smaller proportion of patients dying of CRC than cancer-free patients were up to date in screening (24.1% vs 44.6%) at the diagnosis or reference date (Table 4). In multivariable conditional logistic analysis that also adjusted for race and ethnicity, SES, comorbidity score, and PCP visits, being up to date in screening was associated with a 62% (OR, 0.38; 95%, CI, 0.33–0.44) lower risk of death from CRC. Reciprocally, patients who were not up to date in screening had a 2.61 (95% CI, 2.26–3.01) higher risk of CRC death.

Table 3. Logistic Regression Model Predicting Testing History According to Sociodemographic and Health Care Factors for Patients Dying of CRC, KPNC and KPSC 2006-2012[a]

Characteristics	Adjusted OR (95% CI)	
	Failure to ever screen[b]	All failures to screen combined[c]
Race and ethnicity		
Non-Hispanic white	1.0 (ref)	1.0 (ref)
Non-Hispanic black	0.92 (0.66–1.27)	0.96 (0.69–1.34)
Hispanic	1.13 (0.79–1.60)	0.90 (0.63–1.30)
Asian or Pacific Islander	1.25 (0.87–1.79)	1.20 (0.81–1.77)
Other	0.68 (0.35–1.33)	0.54 (0.29–1.00)
Age at diagnosis (*y*)		
50–54	1.61 (0.67–3.90)	3.00 (0.86–10.5)
55–64	1.44 (1.11–1.88)	1.28 (0.98–1.67)
65–74	1.0 (ref)	1.0 (ref)
75–84	1.36 (1.04–1.78)	1.24 (0.95–1.62)
≥85	2.15 (1.34–3.46)	2.24 (1.33–3.74)
Women (vs men)	0.99 (0.81–1.22)	1.01 (0.82–1.24)
PCP visits, n		
0	4.32 (2.65–7.04)	12.12 (4.35–33.76)
1	3.30 (1.78–6.13)	6.41 (2.25–18.30)
2	2.01 (1.31–3.09)	2.32 (1.35–3.99)
≥3	1.0 (ref)	1.0 (ref)
Year of diagnosis		
2002–2005	1.0 (ref)	1.0 (ref)
2006–2008	0.76 (0.53–1.09)	0.96 (0.65–1.40)
2009–2012	0.66 (0.45–0.97)	0.45 (0.30–0.67)

ref, reference
[a]Simultaneously adjusted for all variables in the table, years of enrollment in health plan, Charlson comorbidity score, and percentage with less than high school education.
[b]Patients who failed to receive any testing were compared with patients who failed to rescreen at appropriate intervals, failed to receive appropriate surveillance, failed to follow-up a positive result, or were up to date with CRC screening.
[c]Patients who failed to screen or screen at appropriate intervals were compared with patients who failed to follow-up a positive result or were up to date with CRC screening.

A larger proportion of patients who died of CRC than cancer-free patients had a failure to ever screen (33.8% vs 25.4%), screen at appropriate intervals (32.8% vs 26.6%), or follow-up on abnormal results (8.1% vs 2.2%). Similar proportions of CRC deaths and cancer-free patients had failure to receive surveillance (1.3% vs 1.2%). Compared with cancer-free matched controls, patients who died of CRC had 2.40 (95% CI, 2.07–2.77) higher odds of all failures to screen (combined) and 7.26 (95% CI, 5.26–10.03) higher odds of failure to receive follow-up for abnormal results compared with those who were up to date in screening (Figure 3 and Supplementary Table 4). That estimate was similar to the estimate from sensitivity analyses in the subgroup of patients at risk for failure of follow-up, comparing those who had failure of follow-up with those who received follow-up (OR, 7.06; 95% CI, 4.30–11.58, Supplementary Table 5).

Table 4. Screening Histories of CRC Deaths and Cancer-Free Patients, KPSC and KPNC 2006–2012

Failure type	Total		No screening		Colonoscopy		Sigmoidoscopy		BE		FOBT	
	Cases (n = 1750)	Controls (n = 3486)	Cases (n = 591)	Controls (n = 884)	Cases (n = 119)	Controls (n = 409)	Cases (n = 341)	Controls (n = 832)	Cases (n = 68)	Controls (n = 69)	Cases (n = 631)	Controls (n = 1292)
Failure to screen or screen at appropriate intervals												
Failure to ever screen	591 (33.8)	884 (25.4)	591 (100)	884 (100)	—	—	—	—	—	—	—	—
Failure to screen at appropriate intervals	574 (32.8)	929 (26.6)	—	—	17 (14.3)	11 (2.7)	170 (49.9)	348 (41.8)	40 (58.8)	53 (76.8)	347 (55.0)	517 (40.0)
Failure to receive surveillance	22 (1.3)	41 (1.2)	—	—	21 (17.6)	38 (9.3)	1 (0.3)	2 (0.2)	—	—	—	1 (0.1)
Failure to follow-up for abnormal finding	141 (8.1)	76 (2.2)	—	—	11 (9.2)	19 (4.6)	24 (7.0)	15 (1.8)	3 (4.4)	—	103 (16.3)	42 (3.3)
Up to date on screening	422 (24.1)	1556 (44.6)	—	—	70 (58.8)	341 (83.4)	146 (42.8)	467 (56.1)	25 (36.8)	16 (23.2)	181 (28.7)	732 (56.7)

Figure 3. Association between screening patterns and death from CRC, KPNC and KPSC 2006–2012. Estimates derived from 3 separate conditional logistic regression analyses of screening histories on risk of CRC death were adjusted for race and ethnicity, SES, Charlson score, and PCP visits. Supplementary Table 4 presents sample sizes. *This estimate is for all failures to screen combined. The model included a separate indicator for failure to follow-up; being up to date in screening was the reference group. †This estimated the association between being up to date with screening compared with a reference that consisted of all screening process failures.

In analysis of the individual screening failures, CRC death was associated with 2.46 (95% CI, 2.08–2.91) higher odds of failure to ever screen, 2.36 (95% CI, 2.00–2.78) higher odds of failure to screen at appropriate intervals, and 2.15 (95% CI, 1.24–3.73) higher odds of failure to receive surveillance.

Discussion

In this study of 1750 patients who died of CRC, approximately 76% had identifiable failures in the screening process and 24% died of CRC despite being up to date with screening. We found that being up to date in screening significantly lowered (by 62%) the risk of death from CRC. Conversely, failure to screen or screen at appropriate intervals or failure to receive follow-up for abnormal results significantly increased the risk for CRC death.

In this study, not being up to date in screening increased the risk of CRC death by nearly 3-fold. The most common type of screening process failure was a failure to ever screen or to screen at appropriate intervals and approximately 8% did not receive follow-up after an abnormal result. We found that most patients had visits with PCPs, but a larger proportion of patients with no or few PCP encounters had a failure to screen or screen at appropriate intervals compared with those with more frequent encounters. Most patients who died of CRC despite being up to date in screening had right colon cancer, irrespective of the type of test received. Despite accounting for nearly 1 in 5 colonoscopies nationally,[27] failure to receive adequate surveillance

was observed in a relatively small proportion of patients dying of CRC (1.3%) and cancer-free individuals (1.2%).

Several randomized trials and observational studies have found screening to be effective in lowering the risk of CRC death.[3,20,28–31] A modeling study suggested that a substantial proportion of US CRC deaths are in unscreened patients.[15] In this study, we evaluated the entire CRC screening continuum to provide deeper insights into opportunities for interventions to minimize CRC deaths. For example, our finding that 34% of patients had no prior testing (failure to ever screen) suggests that improving access to and uptake of screening remains important in decreasing CRC mortality (Table 1), even in populations with relatively high rates of screening. Multicomponent interventions such as eliminating access-related barriers and enhancing the ability of providers to deliver screening have been shown to improve uptake.[32] In the present study, those with fewer PCP contacts had a higher likelihood of failures to screen than those with more contacts, suggesting that interventions to increase health care provider–patient engagement might help increase screening uptake. These findings also are supported by studies suggesting that physician recommendation is one of the strongest predictors of CRC screening uptake.[33]

We previously reported that 84% of screening exposures in people who died of CRC occurred within 1 year of diagnosis compared with 3% in matched cancer-free patients.[21] This suggests that screening was received too late in the disease course to be protective and reinforces the potential benefits of timely initiation of screening. In this study, approximately one-third of patients who died of CRC had not screened at appropriate intervals, pointing to the need for improvements in identifying those who might delay initiating screening and improving long-term adherence to screening. Evidence on interventions to improve repeat screening is scant,[34] although reminders have been shown to improve adherence to fecal testing,[32] which has a more frequent testing interval (annually or biennially) than non-stool tests (sigmoidoscopy every 5 years and colonoscopy every 10 years).

Lack of follow-up after a positive fecal test result is relatively common in many settings,[8] including in clinical trials,[35] and has been attributed to multiple barriers, including lack of physician referral (by PCPs or endoscopists) and nonadherence to referrals or non-receipt of colonoscopy owing to structural or financial barriers.[22,36–38] In our study, the sizable proportion of patients (8%) dying of CRC who had an abnormal screening result without appropriate follow-up and its strong association (OR, 7.26) with the risk of death from CRC suggests that interventions to improve timely follow-up after an abnormal result are important for optimizing the effectiveness of screening in preventing deaths from CRC. A recent systematic review suggested that patient navigation and provider reminders might improve follow-up after a positive fecal test result, but evidence for other interventions is lacking and requires more research.[39]

Patients who were up to date on screening had an approximately 62% lower risk of death from CRC compared with those who were not up to date, which has not been reported previously. In our study, 24% of CRC deaths were up to date on screening, which could be due initiating screening too late in the disease course, "de novo" interval cancers that developed between screening tests, or false negative test results (ie, undetected cancers) that might be due to variations in test quality as measured by adenoma or polyp detection rate[9,11,40,41] or influences on the sensitivity of fecal tests such as excessive ambient temperature exposure.[42] The published literature shows that all current screening modalities are less effective in the right colon than in the more accessible left colon and rectum.[20,28,43,44] Compared with other testing groups, patients who were up to date in screening were disproportionately represented among right colon cancers (62%). Thus, technologic advances to improve the sensitivity of screening tests for right colon cancers remains an important target for decreasing CRC deaths.

Strengths of this study include the comprehensive evaluation of all eligible CRC deaths, the ability to evaluate the entire screening continuum, and the use of manual review of patient medical records to construct screening histories. However, we could not determine whether individual failures in the CRC screening process were due to patient-, provider-, health system-, or test-related factors. Our findings were unchanged in analyses restricted to those with documented receipt of initial treatment, but we could not determine the quality or completeness of treatments after CRC diagnosis, which also influences mortality risk.[45–47] Some patients might have received testing outside KPSC and KPNC, although incomplete data capture is rare in our population.[20,21] Also, we did not have information on the histology of polyps detected at endoscopy, which might result in misclassification of testing histories.

The proportions due to each of the screening failures likely vary across populations and settings, depending on the level of exposure to screening, approaches used for screening delivery, and the primary screening modality used. In KPNC, screening uptake increased from approximately 40% to more than 80% during the interval studied compared with nearly 60% nationally toward the end of the study period.[17,48,49] Thus, the proportion due to non-screening would likely be larger in settings and communities with lower screening uptake. Thus, our results might have limited generalizability to systems with low screening rates. However, our findings have broad applicability beyond the present setting. For example, the proportion due to non-screening in the present study was largest among those without regular PCP contacts and thus is the likely predominant failure in settings with low exposure to screening. The distribution of failure types can vary over time as screening technology, quality, and delivery improve, which could lead to fewer failures of screening tests. In our study, the proportion due to nonadherence to screening or failure of the screening test decreased over time (from 71%–74% before 2008 to 61% in 2009–2012), with implementation of organized screening in the health care systems suggesting a positive impact of system-wide outreach.

In conclusion, compared with those who were not up to date, being up to date on screening lowered the risk of dying of CRC by more than 60%. Relative to those who were up to date, the risk of death from CRC was more than 2-fold higher in people who had failed to screen and about 7-fold higher in those with failure of follow-up. In 2 health systems with high rates of screening, we observed that most patients dying of CRC had potentially modifiable failures of the screening process. Compared with cancer-free patients, those who died of CRC were more likely to have failed to ever screen, to screen at appropriate intervals, and to not follow-up an abnormal result. This study suggests that, even in settings with high screening uptake, access to and timely uptake of screening, regular rescreening, appropriate use of testing given patient characteristics, completion of timely diagnostic testing when screening is positive, and improving the effectiveness of screening tests, particularly for right colon cancer, remain important areas of focus for further decreasing CRC deaths.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2018.09.040.

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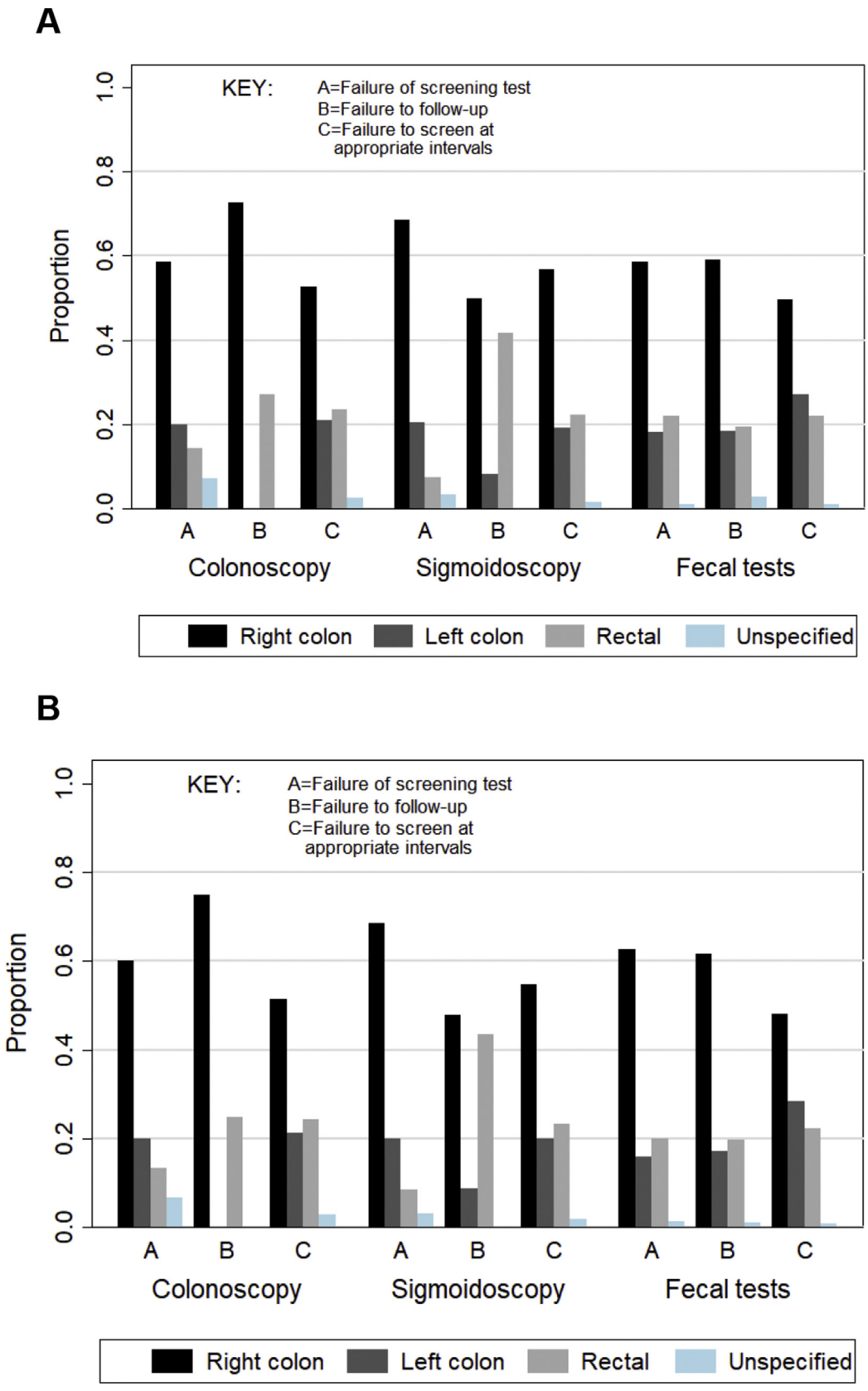
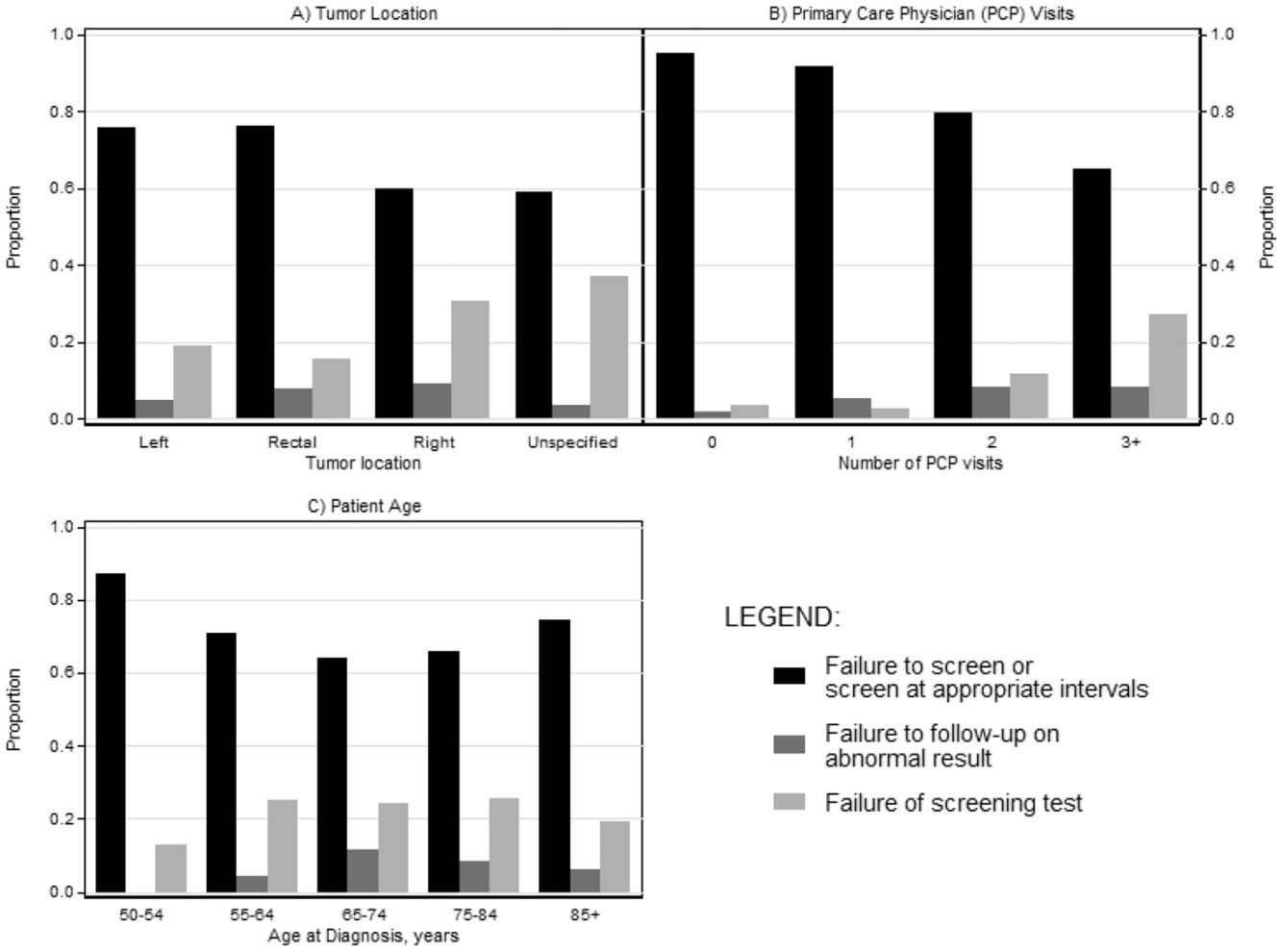


Supplementary Figure 1. Distribution of tumor location according to test type and testing history for (*A*) all cases overall and (*B*) restricted to those with documented receipt of first treatment.



Supplementary Figure 2. Detailed CRC testing history by (*A*) tumor location, (*B*) PCP visits, and (*C*) patient age in patients who died of CRC and initiated treatment, KPNC and KPSC 2002–2012.

Supplementary Table 1. Characteristics of Patients Who Died of CRC According to Testing Categories Restricted to Those Known to Have Initiated Treatment, KPSC and KPNC 2006–2012[a]

	Failure to screen or screen adequately, n (%)					
Characteristics	Failure to screen	Failure to screen at appropriate intervals	Failure to receive surveillance	Failure to follow-up for positive result, n (%)	Failure of screening test[b]	Total
Total	463 (31.4)	516 (35.0)	18 (1.2)	115 (7.8)	362 (24.6)	1474
Age at diagnosis (*y*)						
<55	10 (43.5)	9 (39.1)	1 (4.3)	0 (0.0)	3 (13.0)	23
55–64	172 (34.7)	177 (35.8)	1 (0.2)	21 (4.2)	124 (25.1)	495
65–74	117 (26.2)	162 (36.2)	8 (1.8)	52 (11.6)	108 (24.2)	447
75–84	136 (30.5)	150 (33.6)	7 (1.6)	38 (8.5)	115 (25.8)	446
≥85	28 (44.4)	18 (28.6)	1 (1.6)	4 (6.3)	12 (19.0)	63
Race and ethnicity						
NH white	303 (30.7)	351 (35.6)	15 (1.5)	71 (7.2)	247 (25.0)	987
NH black	53 (29.8)	65 (36.5)	1 (0.6)	13 (7.3)	46 (25.8)	178
Hispanic	50 (35.0)	44 (30.8)	1 (0.7)	13 (9.1)	35 (24.5)	143
Asian or PI	50 (37.3)	46 (34.3)	0 (0.0)	14 (10.4)	24 (17.9)	134
Other	7 (21.9)	10 (31.3)	1 (3.1)	4 (12.5)	10 (31.3)	32
Sex						
Men	242 (32.3)	263 (35.1)	10 (1.3)	64 (8.5)	171 (22.8)	750
Women	221 (30.5)	253 (34.9)	8 (1.1)	51 (7.0)	191 (26.4)	724
Education less than HS, % (*quartile*)[c]						
1	100 (30.5)	120 (36.6)	3 (0.9)	25 (7.6)	80 (24.4)	328
2	104 (30.4)	123 (36.0)	5 (1.5)	28 (8.2)	82 (24.0)	342
3	123 (33.8)	122 (33.5)	5 (1.4)	23 (6.3)	91 (25.0)	364
4	124 (30.5)	142 (35.0)	5 (1.2)	37 (9.1)	98 (24.1)	406
Missing	12 (35.3)	9 (26.5)	0 (0.0)	2 (5.9)	11 (32.4)	34
Health plan enrollment (*y*)						
5.0–7.4	95 (33.9)	92 (32.9)	2 (0.7)	19 (6.8)	72 (25.7)	280
7.5–9.9	92 (32.6)	112 (39.7)	4 (1.4)	21 (7.4)	53 (18.8)	282
≥10	276 (30.3)	312 (34.2)	12 (1.3)	75 (8.2)	237 (26)	912
PCP visits, n[d]						
0	38 (63.3)	18 (30.0)	1 (1.7)	1 (1.7)	2 (3.3)	60
1	19 (51.4)	15 (40.5)	0 (0.0)	2 (5.4)	1 (2.7)	37
2	36 (42.9)	29 (34.5)	2 (2.4)	7 (8.3)	10 (11.9)	84
≥3	370 (28.6)	454 (35.1)	15 (1.2)	105 (8.1)	349 (27.0)	1293
Charlson score[e]						
0	341 (33.5)	367 (36.0)	12 (1.2)	67 (6.6)	232 (22.8)	1019
1	66 (26.3)	86 (34.3)	2 (0.8)	20 (8.0)	77 (30.7)	251
≥2	56 (27.5)	63 (30.9)	4 (2.0)	28 (13.7)	53 (26.0)	204
Diagnosis year						
2002–2005	91 (35.1)	90 (34.7)	3 (1.2)	14 (5.4)	61 (23.6)	259
2006–2008	191 (31.7)	249 (41.3)	8 (1.3)	35 (5.8)	120 (19.9)	603
2009–2012	181 (29.6)	177 (28.9)	7 (1.1)	66 (10.8)	181 (29.6)	612

HS, high school; NH, non-Hispanic; PI, Pacific Islander.
[a]Percentages might not add to 100% because of rounding
[b]Includes 9 patients who had a negative BE result.
[c]Percentage of people at least 25 years old with less than a high school diploma in the census tract based on the 2000 decennial census.
[d]Charlson comorbidity score at baseline defined as 5 years before diagnosis, which accounted for the minimum enrollment requirement for inclusion in the study.
[e]PCP (family medicine, internal medicine, geriatrics, and obstetrics and gynecology) encounters were enumerated in the 5-year period before diagnosis, excluding the 90-day period before diagnosis.

Supplementary Table 2. Characteristics of Matched Cancer-Free Patients According to Testing Categories, KPSC and KPNC 2006–2012[a]

Characteristics	Failures to screen, n (%)					
	Failure to screen	Failure to screen at appropriate intervals	Failure to receive surveillance	Failure to follow-up for positive result, n (%)	Failure of screening test, n (%)[b]	Total, n (%)
Total	884 (25.4)	929 (26.6)	41 (1.2)	76 (2.2)	1556 (44.6)	3486
Age at diagnosis (*y*)						
<55	28 (43.1)	6 (9.2)	0 (0.0)	0 (0.0)	31 (47.7)	65
55–64	336 (30.1)	274 (24.6)	9 (0.8)	14 (1.3)	482 (43.2)	1115
65–74	184 (18.5)	274 (27.6)	10 (1.0)	23 (2.3)	502 (50.6)	993
75–84	258 (23.2)	315 (28.4)	18 (1.6)	38 (3.4)	482 (43.4)	1111
≥85	78 (38.6)	60 (29.7)	4 (2.0)	1 (0.5)	59 (29.2)	202
Race and ethnicity						
NH white	576 (24.7)	619 (26.6)	30 (1.3)	61 (2.6)	1045 (44.8)	2331
NH black	66 (26.6)	65 (26.2)	3 (1.2)	5 (2.0)	109 (44)	248
Hispanic	96 (25.4)	101 (26.7)	3 (0.8)	4 (1.1)	174 (46)	378
Asian or PI	86 (21.4)	119 (29.7)	4 (1.0)	5 (1.2)	187 (46.6)	401
Other	60 (46.9)	25 (19.5)	1 (0.8)	1 (0.8)	41 (32)	128
Sex						
Men	427 (24.2)	440 (25.0)	31 (1.8)	41 (2.3)	823 (46.7)	1762
Women	457 (26.5)	489 (28.4)	10 (0.6)	35 (2.0)	733 (42.5)	1724
Education less than HS, % (*quartile*)[c]						
1	215 (24.4)	216 (24.5)	15 (1.7)	14 (1.6)	420 (47.7)	880
2	209 (23.6)	249 (28.2)	11 (1.2)	16 (1.8)	399 (45.1)	884
3	211 (25.2)	234 (27.9)	7 (0.8)	22 (2.6)	364 (43.4)	838
4	230 (27.8)	223 (27.0)	8 (1.0)	24 (2.9)	341 (41.3)	826
Missing	19 (32.8)	7 (12.1)	0 (0.0)	0 (0.0)	32 (55.2)	58
Health plan enrollment (*y*)						
5.0–7.4	204 (34.2)	160 (26.8)	2 (0.3)	10 (1.7)	221 (37)	597
7.5–9.9	207 (32.4)	172 (27.0)	10 (1.6)	12 (1.9)	237 (37.1)	638
≥10	473 (21.0)	597 (26.5)	29 (1.3)	54 (2.4)	1098 (48.8)	2251
PCP visits, n[d]						
0	48 (69.6)	12 (17.4)	0 (0.0)	1 (1.4)	8 (11.6)	69
1	32 (66.7)	8 (16.7)	0 (0.0)	0 (0.0)	8 (16.7)	48
2	60 (54.1)	22 (19.8)	1 (0.9)	1 (0.9)	27 (24.3)	111
≥3	744 (22.8)	887 (27.2)	40 (1.2)	74 (2.3)	1512 (46.4)	3257
Charlson score[e]						
0	704 (26.6)	681 (25.7)	26 (1.0)	55 (2.1)	1183 (44.7)	2649
1	92 (19.7)	137 (29.4)	5 (1.1)	14 (3.0)	218 (46.8)	466
2+	88 (23.7)	111 (29.9)	10 (2.7)	7 (1.9)	155 (41.8)	371
Reference year						
2002–2005	212 (39.6)	143 (26.7)	4 (0.7)	7 (1.3)	170 (31.7)	536
2006–2008	378 (27.5)	435 (31.6)	17 (1.2)	27 (2.0)	518 (37.7)	1375
2009–2012	294 (18.7)	351 (22.3)	20 (1.3)	42 (2.7)	868 (55.1)	1575

HS, high school; NH, non-Hispanic; PI, Pacific Islander.
[a]Percentages might not add to 100% because of rounding.
[b]Includes 24 patients who had a negative BE result.
[c]Percentage of people at least 25 years old with less than a high school diploma in the census tract based on the 2000 decennial census.
[d]PCP (family medicine, internal medicine, geriatrics, and obstetrics and gynecology) outpatient encounters were enumerated in the 5-year period excluding the 90-day period before the reference date.
[e]Charlson comorbidity score at baseline defined as 5 years before the reference date, which accounted for the minimum enrollment requirement for inclusion in the study.

Supplementary Table 3. Associations With Testing Histories for Patients Dying of CRC Who Initiated Therapy and in Cancer-Free Matched Control Patients, KPNC and KPSC 2006–2012

	Adjusted OR[a] (95% CI)			
	Cases who initiated cancer treatment		Cancer-free matched control patients	
	Failure to ever screen[b]	All failures to screen combined[c]	Failure to ever screen[b]	All failures to screen combined[c]
Race and ethnicity				
NH white	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
NH black	0.92 (0.66–1.27)	0.96 (0.69–1.34)	1.04 (0.76–1.43)	1.02 (0.77–1.34)
Hispanic	1.13 (0.79–1.60)	0.90 (0.63–1.30)	1.01 (0.77–1.31)	1.03 (0.82–1.30)
Asian or PI	1.25 (0.87–1.79)	1.20 (0.81–1.77)	0.83 (0.64–1.10)	1.03 (0.82–1.29)
Other	0.68 (0.35–1.33)	0.54 (0.29–1)	1.82 (1.21–2.73)	1.49 (0.99–2.25)
Age at diagnosis (*y*)				
50–54	1.61 (0.67–3.90)	3.00 (0.86–10.5)	2.38 (1.36–4.14)	0.85 (0.50–1.45)
55–64	1.44 (1.11–1.88)	1.28 (0.98–1.67)	1.73 (1.4–2.15)	1.26 (1.05–1.51)
65–74	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
75–84	1.36 (1.04–1.78)	1.24 (0.95–1.62)	1.66 (1.32–2.08)	1.51 (1.26–1.81)
≥85	2.15 (1.34–3.46)	2.24 (1.33–3.74)	4.22 (2.97–5.98)	3.86 (2.74–5.43)
Sex				
Male	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Female	0.99 (0.81–1.22)	1.01 (0.82–1.24)	1.23 (1.05–1.45)	1.28 (1.11–1.47)
PCP visits, n				
0	4.32 (2.65–7.04)	12.12 (4.35–33.76)	7.94 (4.56–13.81)	7.29 (3.52–15.08)
1	3.30 (1.78–6.13)	6.41 (2.25–18.30)	5.99 (3.19–11.23)	5.26 (2.39–11.56)
2	2.01 (1.31–3.09)	2.32 (1.35–3.99)	3.78 (2.53–5.65)	2.99 (1.91–4.70)
≥3	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
Year of diagnosis				
2002–2005	1.0 (ref)	1.0 (ref)	1.0 (ref)	1.0 (ref)
2006–2008	0.76 (0.53–1.09)	0.96 (0.65–1.40)	0.67 (0.52–0.87)	0.95 (0.65–1.39)
2009–2012	0.66 (0.45–0.97)	0.45 (0.30–0.67)	0.39 (0.29–0.52)	0.45 (0.30–0.67)

NH, non-Hispanic; PI, Pacific Islander; ref, reference.

[a]Simultaneously adjusted for all variables in the table, years of enrollment in health plan, Charlson comorbidity score, and percentage with less than high school education.

[b]Patients who failed to receive any testing were compared with patients who failed to rescreen at appropriate intervals, failed to receive appropriate surveillance, failed to follow-up a positive result, or were up to date with CRC screening (n = 1011).

[c]Patients who failed to screen or screen adequately were compared with patients who failed to follow-up a positive result or were up to date with CRC screening.

Supplementary Table 4. Association Between Screening Patterns and Death of CRC, KPNC and KPSC 2006–2012[a]

Models and screening histories analyzed	Cases, n	Controls, n	OR (95% CI)
Model 1			
Not up to date	1328	1930	1.0 (ref)
Up to date	422	1556	0.38 (0.33–0.44)
Model 2			
All failures to screen combined	1187	1854	2.40 (2.07–2.77)
Up to date on screening	422	1556	1.0 (ref)
Model 3			
Failure to ever screen	591	884	2.46 (2.08–2.91)
Failure to screen at appropriate intervals	574	929	2.36 (2.00–2.78)
Failure to receive surveillance	22	41	2.15 (1.24–3.73)
Failure to follow-up for abnormal result	141	76	7.26 (5.26–10.03)
Up to date on screening	422	1556	1.0 (ref)

[a]Estimates were derived from 3 separate conditional logistic regression analyses of screening histories on risk of CRC death. Each model adjusted for race and ethnicity, SES, Charlson score, and PCP visits. Not up to date included failures to screen and failure to follow-up an abnormal result. Failures to screen combined included failure to ever screen, screen at appropriate intervals, and receive surveillance.

Supplementary Table 5. Sensitivity Analysis of Crude Associations Between Failures of Follow-Up and Risk of CRC Death in the Strata at Risk for Failure of Follow-Up or Surveillance[a]

Failure type	Cases	Colorectal cancer-free patients	Unadjusted OR (95% CI) computed from 2 × 2 table
Surveillance failure			
Yes	22	41	
No	13	77	3.17 (1.41–7.14)
Positive FOBT result			
Yes	103	42	
No	29	77	6.51 (3.50–12.10)
Any abnormal or positive result			
Yes	141	76	
No[b]	41[b]	156[b]	7.06 (4.30–11.58)
Any abnormal or positive result			
Yes	141	76	
No[c]	36	121	6.70 (4.90–9.19)
Failure of follow-up or surveillance[d]			
Yes	163	117	
No	49	198	5.63 (3.67–8.63)

[a]Crude or unadjusted ORs and 95% CIs from the respective 2 × 2 contingency table cells were determined using the STATA tabodds procedure.
[b]This analysis included patients who were up to date and were at risk for failure of diagnostic testing and surveillance (n = 40; 5 cases and 35 controls).
[c]This analysis excluded patients who were up to date at the diagnosis date but at risk for failure of diagnostic testing and surveillance.
[d]Analysis included all patients flagged as being at risk for follow-up surveillance testing, including those who also were at risk for diagnostic testing.