

# Association Between Time to Colonoscopy After a Positive Fecal Test Result and Risk of Colorectal Cancer and Cancer Stage at Diagnosis

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**IMPORTANCE** The fecal immunochemical test (FIT) is commonly used for colorectal cancer screening and positive test results require follow-up colonoscopy. However, follow-up intervals vary, which may result in neoplastic progression.

**OBJECTIVE** To evaluate time to colonoscopy after a positive FIT result and its association with risk of colorectal cancer and advanced-stage disease at diagnosis.

**DESIGN, SETTING, AND PARTICIPANTS** Retrospective cohort study (January 1, 2010-December 31, 2014) within Kaiser Permanente Northern and Southern California. Participants were 70 124 patients aged 50 through 70 years eligible for colorectal cancer screening with a positive FIT result who had a follow-up colonoscopy.

**EXPOSURES** Time (days) to colonoscopy after a positive FIT result.

**MAIN OUTCOMES AND MEASURES** Risk of any colorectal cancer and advanced-stage disease (defined as stage III and IV cancer). Odds ratios (ORs) and 95% CIs were adjusted for patient demographics and baseline risk factors.

**RESULTS** Of the 70 124 patients with positive FIT results (median age, 61 years [IQR, 55-67 years]; men, 52.7%), there were 2191 cases of any colorectal cancer and 601 cases of advanced-stage disease diagnosed. Compared with colonoscopy follow-up within 8 to 30 days (n = 27 176), there were no significant differences between follow-up at 2 months (n = 24 644), 3 months (n = 8666), 4 to 6 months (n = 5251), or 7 to 9 months (n = 1335) for risk of any colorectal cancer (cases per 1000 patients: 8-30 days, 30; 2 months, 28; 3 months, 31; 4-6 months, 31; and 7-9 months, 43) or advanced-stage disease (cases per 1000 patients: 8-30 days, 8; 2 months, 7; 3 months, 7; 4-6 months, 9; and 7-9 months, 13). Risks were significantly higher for examinations at 10 to 12 months (n = 748) for any colorectal cancer (OR, 1.48 [95% CI, 1.05-2.08]; 49 cases per 1000 patients) and advanced-stage disease (OR, 1.97 [95% CI, 1.14-3.42]; 19 cases per 1000 patients) and more than 12 months (n = 747) for any colorectal cancer (OR, 2.25 [95% CI, 1.89-2.68]; 76 cases per 1000 patients) and advanced-stage disease (OR, 3.22 [95% CI, 2.44-4.25]; 31 cases per 1000 patients).

**CONCLUSIONS AND RELEVANCE** Among patients with a positive fecal immunochemical test result, compared with follow-up colonoscopy at 8 to 30 days, follow-up after 10 months was associated with a higher risk of colorectal cancer and more advanced-stage disease at the time of diagnosis. Further research is needed to assess whether this relationship is causal.

JAMA. 2017;317(16):1631-1641. doi:10.1001/jama.2017.3634

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Colorectal cancer is the second leading cause of cancer death in the United States.<sup>1</sup> Screening reduces mortality through removal of precancerous polyps and treatment of early-stage cancers.<sup>2</sup> The US Preventive Services Task Force endorses multiple screening approaches for early detection of colorectal cancer, including fecal immunochemical test (FIT) screening.<sup>2</sup> FIT screening is commonly used worldwide<sup>3,4</sup> and because of its sensitivity, effectiveness, low cost, and ability to be distributed by mail, it is an increasingly common method for meeting colorectal cancer screening goals in the United States.

A positive FIT result needs to be followed by a complete colon examination, typically with colonoscopy<sup>5</sup>; however, recommendations for how quickly to complete follow-up differ and lack a strong evidence base.<sup>6-8</sup> In practice, there is marked variation in time to follow-up after a positive stool test result, which may result in neoplastic progression. Few studies have evaluated colorectal cancer outcomes associated with variation in time to follow-up. Two studies of military veterans reported no association between longer intervals from a positive test result to colonoscopy and either cancer stage or survival, but small sample sizes limited power.<sup>9,10</sup> Because colorectal cancer screening theoretically affects every adult who reaches screening age and adoption of FIT screening worldwide is increasing, there is a need to provide evidence-based follow-up recommendations. The present study tested the hypothesis that longer time to colonoscopy after a positive FIT result is associated with an increased risk of any colorectal cancer and advanced-stage disease at diagnosis.

## Methods

### Study Population and Oversight

This study was approved by the local institutional review boards and a waiver was granted for obtaining written informed consent from study participants. This was a retrospective cohort study of Kaiser Permanente Northern California and Southern California health plan members. These integrated health care delivery organizations serve approximately 7.5 million members throughout California, and the diverse membership is similar to the region's census demographics.<sup>11-13</sup>

### Organized Colorectal Cancer Screening Programs

The health plans initiated organized FIT outreach in 2006.<sup>14</sup> Each year, health plan members aged 50 to 75 years who are eligible for screening and not up-to-date with screening by other methods are mailed a FIT kit (OC FIT-CHEK, Polymedco). Patients mail completed kits to regional laboratories where they are analyzed using OC-Sensor Diana (Polymedco; positive result,  $\geq 100$  ng/mL of hemoglobin [20  $\mu$ g of hemoglobin per gram of stool]). FIT kits are also distributed in-person to patients not up-to-date at office visits or when receiving a flu shot. Patients with a positive FIT result are referred by their physician or contacted by the gastroenterology department for colonoscopy scheduling.

## Key Points

**Question** Is time to colonoscopy after a positive fecal immunochemical test (FIT) result associated with an increased risk of colorectal cancer?

**Findings** In this cohort study of 70 124 patients with positive FIT results, there was no significant increase in risk of colorectal cancer or advanced-stage disease associated with colonoscopy follow-up within 10 months compared with 8 to 30 days. Follow-up after 10 months was associated with a higher risk of colorectal cancer and advanced-stage disease.

**Meaning** Follow-up colonoscopy more than 10 months after a positive FIT result was associated with greater risk of colorectal cancer and more advanced disease at time of diagnosis, but further research is needed to assess whether this relationship is causal.

### Study Eligibility Criteria

Members were eligible for the study if they were aged 50 to 75 years and had completed FIT screening between January 1, 2010, and October 31, 2012, for Kaiser Permanente Southern California members and January 1, 2010, and July 31, 2013, for Kaiser Permanente Northern California members. Among those with a positive FIT result, patients were excluded if they had a prior history of colorectal cancer, less than 1 year of membership after FIT screening and no record of a colonoscopy during that period, a more than 3-month gap in membership after screening, less than 1 year of membership prior to screening (to record prior out-of-system endoscopy procedures and diagnoses), a colonoscopy within 10 years or sigmoidoscopy within 5 years before FIT screening, or a colonoscopy or colorectal cancer diagnosis 1 to 7 days after their positive FIT result (because these FITs may represent diagnostic rather than screening tests).

### Follow-up Time Intervals and Cancer Outcomes

The exposure was the time elapsed between a positive FIT result and subsequent colonoscopy. Time was examined as a continuous variable and in 7 intervals; the reference group was 8 to 30 days and comparison categories were 2 months (31-60 days), 3 months (61-90 days), 4-6 months (91-180 days), 7-9 months (181-272 days), 10-12 months (273-365 days), and more than 12 months (366-1751 days). The intervals were chosen to evaluate published follow-up recommendations (ie,  $\leq 31$  days [European recommendation<sup>15</sup>] and  $\leq 60$  days [Canadian<sup>3</sup> and Veterans Health Administration<sup>6</sup> recommendations]), to provide calendar month intervals as practical cutoffs (ie, 1, 2, 3, 4-6, 7-9, 10-12, and  $>12$  months), and to balance sample sizes based on outcome distributions.

The primary outcomes were any colorectal adenocarcinoma diagnosed at or within 6 months after the follow-up colonoscopy, cancer by stage, advanced-stage disease, and adenomas with advanced histology (ie, tubulovillous and villous adenomas). The window for the primary outcome was defined as diagnoses at or within 6 months to account for colonoscopies that were repeated due to variables such as poor bowel preparation, incomplete examination or excision, or patient intolerance, among others; however, 96% of diagnoses

were within 1 month after the colonoscopy. Adenoma size was not available electronically.

### Data Sources

FIT results and dates were obtained from laboratory databases. Colonoscopy procedures were identified using *Current Procedural Terminology* codes (44388-44394, 44397, 45355, 45378-45392), *International Classification of Diseases, Ninth Revision*, procedure codes (45.21-45.23, 45.25, 45.42, 45.43, 98.04), and Healthcare Common Procedure Coding System codes (G0105, G0121). Colorectal adenocarcinoma diagnoses and cancer stages were obtained from Kaiser Permanente cancer registries, which report to the Surveillance, Epidemiology, and End Results (SEER) Program and capture more than 99% of cancers diagnosed among members compared with manual review. Advanced-stage cancers were defined as stage III (regional lymph node involvement) or stage IV (distant metastasis) according to the American Joint Committee on Cancer staging system or, for those without such staging, as code 3 (disease in the regional lymph nodes), code 4 (regional disease with direct extension and spread to the regional lymph nodes), or code 7 (distant metastasis) according to the 2013 SEER Program Coding and Staging Manual.<sup>16</sup> Adenomas with advanced histology were identified using Systematized Nomenclature of Medicine codes in pathology databases linked to the date of the colonoscopy examination. Validation studies confirmed high levels (>95%) of sensitivity and accuracy for capture and classification of colonoscopy examinations, adenoma diagnoses, histology, and cancers.<sup>17</sup>

### Statistical Analyses

*P* values for differences in baseline characteristics were derived from  $\chi^2$  tests. Crude rates and 95% CIs were calculated as cases per 1000 patients who completed a colonoscopy. Risk analyses used multivariable logistic regression models. Odds ratios (ORs) and 95% CIs were adjusted for sex; age at FIT screening (50-54, 55-59, 60-64, 65-69, 70-75 years); self-reported race/ethnicity (non-Hispanic white, Hispanic, black, Asian/Pacific Islander, and other/unknown) because of racial/ethnic differences in colorectal cancer incidence; body mass index (BMI [calculated as weight in kilograms divided by height in meters squared]; <25.0, 25.0-29.9,  $\geq$ 30, unknown); region (Kaiser Permanente Northern California or Southern California); FIT screening year; completion of previous FIT screening (ever and in the prior year); and in the year before FIT screening, receipt of the flu or pneumonia vaccine, presence of gastrointestinal symptoms (bleeding or blood in stool, unexplained weight loss, abdominal pain, diarrhea, diverticulitis, inflammatory bowel disease, or Lynch syndrome), diagnosis of iron-deficiency anemia or diabetes, smoker status, number of primary care visits (0, 1, 2-3,  $\geq$ 4), and number of days hospitalized (0-1, 2-3,  $\geq$ 4). Hypothesis testing was 2-sided with an  $\alpha$  of .05. Sensitivity analyses included redefining the reference group to include patients whose examinations were performed after a positive FIT result within 1 to 30 days (to include the earliest examinations, though these have greater risk of being symptom-driven), 8 to 60 days, and 8 to 90 days; excluding follow-up colonoscopies more than 24 months after

a positive FIT result; including patients who had less than 1 year of membership prior to FIT screening, or who had a colonoscopy within 10 years or sigmoidoscopy within 5 years prior to FIT screening; and adding an exposure category of 1 to 7 days. To test for effect modification, interaction terms were added to the main model for each covariate and time was included as a continuous variable; likelihood ratio tests generated a *P* value for each time  $\times$  covariate interaction. Stratified models are presented when the *P* value for interaction was less than .10. Point estimates for ORs represent the overall risk estimate for each additional 30-day delay in follow-up compared with follow-up at 8 to 30 days. Analyses were performed with SAS (SAS Institute), version 9.3, and Stata (StataCorp), version 10.1.

## Results

Of 1 258 039 patients aged 50 to 75 years who completed FIT screening, 106 520 (8.5%) had a positive FIT result (Figure 1). Of these, 51 patients were excluded for history of colorectal cancer, 2873 for less than 1 year of membership after FIT screening and no record of a colonoscopy during that period, 17 for a membership gap of more than 3 months after screening, 9771 for less than 1 year of membership prior to FIT screening, 10 873 for a colonoscopy within less than 10 years or sigmoidoscopy within less than 5 years before FIT screening, and 1417 for colonoscopy or colorectal cancer diagnosis within 1 to 7 days after their positive FIT. Of the remaining 81 518 patients with a positive FIT result, 70 124 (86.0% and 65.8% of those with a positive FIT result [n = 106 520]) received a follow-up colonoscopy by the end of the study period.

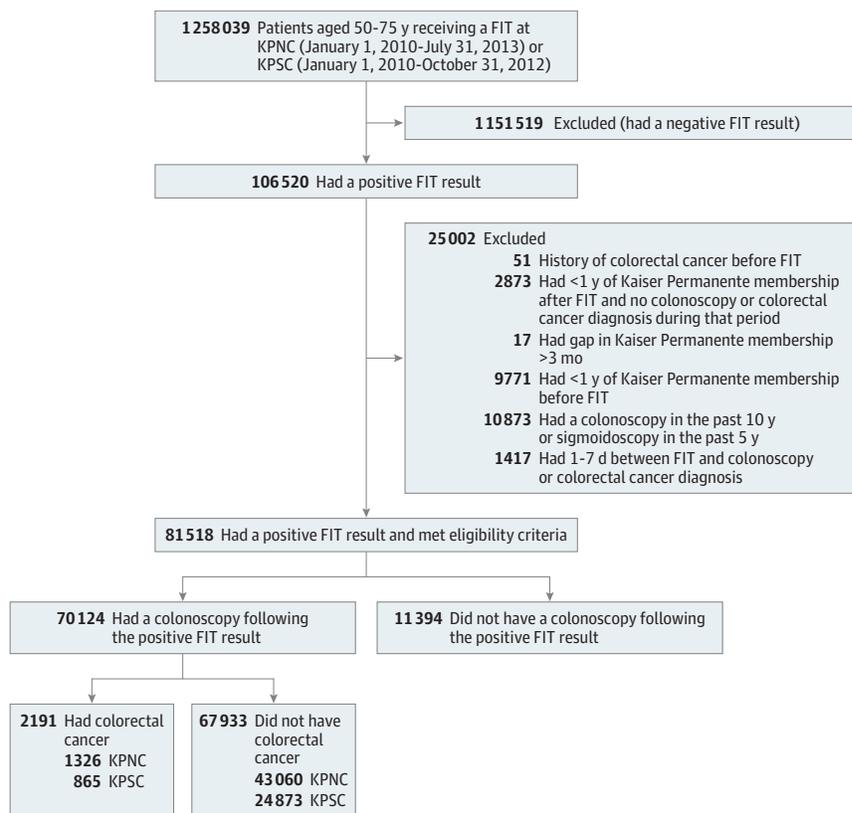
### Characteristics of the Cohort

Of the 81 518 eligible patients with a positive FIT result, 33.3% received a colonoscopy within 30 days, 63.6% within 2 months, 74.2% within 3 months, 80.6% within 6 months, and 83.2% within 12 months; completion rates were similar in the total group of 106 520 patients who had a positive FIT result (eFigure 1 in the Supplement). Among the 70 124 patients who received a follow-up colonoscopy (Table 1), the median age was 61 years (interquartile range [IQR], 55-67 years), 52.7% were men, 56.1% were non-Hispanic white, and 42.2% had a BMI of 30 or greater. The median time to colonoscopy was 37 days (IQR, 23-62 days). There were 2191 cases of any colorectal cancer and 601 cases of advanced-stage disease diagnosed (Table 2). Baseline covariates across time-to-colonoscopy exposure groups were typically within a few percentage points (Tables 1 and 2), although even small differences were significant given the large sample size.

### Time to Colonoscopy and Risk of Colorectal Cancer Outcomes

Compared with colonoscopy follow-up 8 to 30 days after a positive FIT result, each additional 30-day interval was associated with an average increased risk of approximately 3% for any colorectal cancer (OR, 1.03 [95% CI, 1.03-1.04]; 2191 cases of 70 124 patients = 31 cases per 1000 patients) and

Figure 1. Flow of Patients Through the Study



FIT indicates fecal immunochemical test; KPNC, Kaiser Permanente Northern California; KPSC, Kaiser Permanente Southern California.

advanced-stage disease of approximately 5% (OR, 1.05 [95% CI, 1.04-1.06]; 601 cases of 70 110 patients = 9 cases per 1000 patients); however, the relationships were not linear over time. Compared with patients who received follow-up within 8 to 30 days, there was no significant increase in risk of colorectal cancer outcomes for examinations within 6 months (Figure 2 and Figure 3 [Figures used model 2 from eTable 1 in the Supplement]; and eFigure 2 in the Supplement). For follow-up at 7 to 9 months, there was a higher risk of stage II colorectal cancer (OR, 1.88 [95% CI, 1.09-3.23]; 15 cases of 1292 patients = 12 cases per 1000 patients).

For colonoscopy follow-up at 10 to 12 months, the risk was higher for any colorectal cancer (OR, 1.48 [95% CI, 1.05-2.08]; 37 cases of 748 patients = 49 cases per 1000 patients), advanced-stage disease (OR, 1.97 [95% CI, 1.14-3.42]; 14 cases of 747 patients = 19 cases per 1000 patients), stage II colorectal cancer (OR, 2.39 [95% CI, 1.28-4.46]; 11 cases of 722 patients = 15 cases per 1000 patients), and stage IV colorectal cancer (OR, 2.71 [95% CI, 1.06-6.89]; 5 cases of 716 patients = 7 cases per 1000 patients).

For examinations at more than 12 months, the risk was higher for nearly all colorectal cancer outcomes: advanced adenomas (OR, 1.32 [95% CI, 1.15-1.52]; 247 cases of 2130 patients = 116 cases per 1000 patients), any colorectal cancer (OR, 2.25 [95% CI, 1.89-2.68]; 174 cases of 2304 patients = 76 cases per 1000 patients), advanced-stage disease (OR, 3.22 [95% CI, 2.44-4.25]; 72 cases of 2300 patients = 31 cases per 1000 pa-

tients), stage II colorectal cancer (OR, 2.94 [95% CI, 2.05-4.20]; 41 cases of 2171 patients = 19 cases per 1000 patients), stage III colorectal cancer (OR, 3.07 [95% CI, 2.21-4.27]; 49 cases of 2179 patients = 22 cases per 1000 patients), and stage IV colorectal cancer (OR, 3.86 [95% CI, 2.32-6.44]; 23 cases of 2153 patients = 11 cases per 1000 patients).

Compared with no adjustment, accounting for common baseline factors (eg, age, sex, race/ethnicity, comorbidity, and prior FIT screening) moderately reduced the strength of associations (eTable 1, model 1, in the Supplement), but did not change their direction; adjustment for additional factors related to health and health care utilization slightly strengthened the associations (eTable 1, model 2, in the Supplement).

In sensitivity analyses (Table 3), the pattern of increased OR estimates for any colorectal cancer, advanced-stage disease with examinations at 10 to 12 months and more than 12 months after FIT, or both persisted with different reference group definitions and when individuals were excluded if colonoscopy was performed more than 24 months after a positive FIT result (thereby excluding people unlikely to have a cancer, given they had not developed signs or symptoms after extended follow-up). When 20 644 originally excluded patients who had either less than 1 year of membership prior to FIT screening or were up-to-date with screening by prior endoscopy were included, risk was higher only for follow-up at more than 12 months. With 8 to 60 days and 8 to 90 days as the reference group, the risk of any colorectal cancer was also higher

Table 1. Characteristics Among Patients Who Received a Colonoscopy After a Positive FIT Result

Characteristics <sup>a</sup>	Time to Colonoscopy, No. of Patients (%) <sup>b</sup>							Total
	8-30 Days	2 Months	3 Months	4-6 Months	7-9 Months	10-12 Months	>12 Months	
Total patients	27 176	24 644	8666	5251	1335	748	2304	70 124
Region								
KPNC	14 473 (53.3)	17 102 (69.4)	6233 (71.9)	3781 (72.0)	978 (73.3)	501 (67.0)	1318 (57.2)	44 386 (63.3)
KPSC	12 703 (46.7)	7542 (30.6)	2433 (28.1)	1470 (28.0)	357 (26.7)	247 (33.0)	986 (42.8)	25 738 (36.7)
Sex								
Women	12 772 (47.0)	11 678 (47.4)	4111 (47.4)	2527 (48.1)	631 (47.3)	353 (47.2)	1076 (46.7)	33 148 (47.3)
Men	14 404 (53.0)	12 966 (52.6)	4555 (52.6)	2724 (51.9)	704 (52.7)	395 (52.8)	1228 (53.3)	36 976 (52.7)
Age, y								
50-54	6755 (24.9)	5787 (23.5)	1975 (22.8)	1273 (24.2)	319 (23.9)	166 (22.2)	526 (22.8)	16 801 (24.0)
55-59	5655 (20.8)	5132 (20.8)	1784 (20.6)	1098 (20.9)	289 (21.6)	145 (19.4)	478 (20.7)	14 581 (20.8)
60-64	5685 (20.9)	5167 (21.0)	1899 (21.9)	1161 (22.1)	272 (20.4)	182 (24.3)	487 (21.1)	14 853 (21.2)
65-69	4818 (17.7)	4501 (18.3)	1556 (18.0)	844 (16.1)	226 (16.9)	124 (16.6)	414 (18.0)	12 483 (17.8)
70-75	4263 (15.7)	4057 (16.5)	1452 (16.8)	875 (16.7)	229 (17.2)	131 (17.5)	399 (17.3)	11 406 (16.3)
Median (IQR)	61 (55-67)	61 (55-67)	61 (55-67)	60 (55-67)	61 (55-67)	61 (55-67)	61 (55-67)	61 (55-67)
Race/ethnicity								
Non-Hispanic white	15 178 (55.9)	14 123 (57.3)	4929 (56.9)	2828 (53.9)	708 (53.0)	387 (51.7)	1197 (52.0)	39 350 (56.1)
Hispanic	5103 (18.8)	3923 (15.9)	1357 (15.7)	837 (15.9)	234 (17.5)	138 (18.4)	435 (18.9)	12 027 (17.2)
Black	2178 (8.0)	1938 (7.9)	677 (7.8)	499 (9.5)	122 (9.1)	64 (8.6)	255 (11.1)	5733 (8.2)
Asian/ Pacific Islander	3745 (13.8)	3805 (15.4)	1407 (16.2)	905 (17.2)	224 (16.8)	136 (18.2)	340 (14.8)	10 562 (15.1)
Other	972 (3.6)	855 (3.5)	296 (3.4)	182 (3.5)	47 (3.5)	23 (3.1)	77 (3.3)	2452 (3.5)
Year FIT screened								
2010	6246 (23.0)	6210 (25.2)	2726 (31.5)	1747 (33.3)	518 (38.8)	292 (39.0)	956 (41.5)	18 695 (26.7)
2011	7827 (28.8)	7122 (28.9)	3200 (36.9)	2053 (39.1)	460 (34.5)	246 (32.9)	791 (34.3)	21 699 (30.9)
2012	9018 (33.2)	7792 (31.6)	2010 (23.2)	1076 (20.5)	250 (18.7)	157 (21.0)	463 (20.1)	20 766 (29.6)
2013	4085 (15.0)	3520 (14.3)	730 (8.4)	375 (7.1)	107 (8.0)	53 (7.1)	94 (4.1)	8964 (12.8)
BMI								
<25.0	6007 (22.1)	5514 (22.4)	2020 (23.3)	1150 (21.9)	313 (23.4)	158 (21.1)	504 (21.9)	15 666 (22.3)
25.0-29.9	9754 (35.9)	8590 (34.9)	2951 (34.1)	1795 (34.2)	453 (33.9)	253 (33.8)	817 (35.5)	24 613 (35.1)
≥30.0	11 349 (41.8)	10 448 (42.4)	3649 (42.1)	2283 (43.5)	564 (42.2)	337 (45.1)	971 (42.1)	29 601 (42.2)
Unknown	66 (0.2)	92 (0.4)	46 (0.5)	23 (0.4)	5 (0.4)	0	12 (0.5)	244 (0.3)
Distribution of FIT to patient								
In-person	7472 (27.5)	5768 (23.4)	1991 (23.0)	1300 (24.8)	385 (28.8)	227 (30.3)	773 (33.6)	17 916 (25.5)
FIT mailed	19 704 (72.5)	18 876 (76.6)	6675 (77.0)	3951 (75.2)	950 (71.2)	521 (69.7)	1531 (66.4)	52 208 (74.5)
Previously FIT screened								
FIT screened in prior year	7400 (27.2)	7249 (29.4)	2454 (28.3)	1423 (27.1)	317 (23.7)	162 (21.7)	508 (22.0)	19 513 (27.8)
Vaccinated in prior year <sup>c</sup>	15 170 (55.8)	13 478 (54.7)	4635 (53.5)	2738 (52.1)	657 (49.2)	363 (48.5)	1099 (47.7)	38 140 (54.4)
Gastrointestinal symptoms in prior year <sup>d</sup>	3190 (11.7)	2654 (10.8)	915 (10.6)	602 (11.5)	194 (14.5)	100 (13.4)	313 (13.6)	7968 (11.4)
Anemia in prior year <sup>e</sup>	912 (3.4)	823 (3.3)	325 (3.8)	238 (4.5)	88 (6.6)	42 (5.6)	134 (5.8)	2562 (3.7)
Diabetes in prior year	5831 (21.5)	5797 (23.5)	2145 (24.8)	1300 (24.8)	338 (25.3)	183 (24.5)	642 (27.9)	16 236 (23.2)
Smoking in prior year	4147 (15.3)	3724 (15.1)	1274 (14.7)	842 (16.0)	220 (16.5)	140 (18.7)	466 (20.2)	10 813 (15.4)
Primary care visits in prior year, No.								
0	2945 (10.8)	2967 (12.0)	1064 (12.3)	641 (12.2)	164 (12.3)	103 (13.8)	307 (13.3)	8191 (11.7)
1	5401 (19.9)	4963 (20.1)	1706 (19.7)	996 (19.0)	230 (17.2)	144 (19.3)	441 (19.1)	13 881 (19.8)
2-3	9339 (34.4)	8234 (33.4)	2882 (33.3)	1653 (31.5)	448 (33.6)	214 (28.6)	724 (31.4)	23 494 (33.5)
≥4	9491 (34.9)	8480 (34.4)	3014 (34.8)	1961 (37.3)	493 (36.9)	287 (38.4)	832 (36.1)	24 558 (35.0)

(continued)

Table 1. Characteristics Among Patients Who Received a Colonoscopy After a Positive FIT Result (continued)

Characteristics <sup>a</sup>	Time to Colonoscopy, No. of Patients (%) <sup>b</sup>							Total
	8-30 Days	2 Months	3 Months	4-6 Months	7-9 Months	10-12 Months	>12 Months	
Inpatient days in prior year								
0-1	25 255 (92.9)	22 870 (92.8)	7997 (92.3)	4696 (89.4)	1171 (87.7)	654 (87.4)	2042 (88.6)	64 685 (92.2)
2-3	867 (3.2)	720 (2.9)	242 (2.8)	186 (3.5)	52 (3.9)	44 (5.9)	89 (3.9)	2200 (3.1)
≥4	1054 (3.9)	1054 (4.3)	427 (4.9)	369 (7.0)	112 (8.4)	50 (6.7)	173 (7.5)	3239 (4.6)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); FIT, fecal immunochemical test; IQR, interquartile range; KPNC, Kaiser Permanente Northern California; KPSC, Kaiser Permanente Southern California.

<sup>a</sup>  $P < .001$  for differences in proportions across time intervals for all variables except sex ( $P = .82$ ).

<sup>b</sup> Time to colonoscopy intervals: 2 months (31-60 days), 3 months (61-90 days), 4 to 6 months (91-180 days), 7 to 9 months (181-272 days), 10 to 12 months (273-365 days), and more than 12 months (366-1571 days).

<sup>c</sup> Vaccinated in prior year refers to receipt of the flu or pneumonia vaccine in the year before FIT screening.

<sup>d</sup> Gastrointestinal symptoms include bleeding or blood in stool, unexplained weight loss, abdominal pain, diarrhea, or diverticulitis diagnosed in the year before FIT and inflammatory bowel disease or Lynch syndrome diagnosis any time before FIT.

<sup>e</sup> Anemia refers to iron-deficiency anemia.

Table 2. Colorectal Cancer Outcomes in Patients Who Received a Colonoscopy After a Positive FIT Result

Characteristics	Time to Colonoscopy, No. of Patients (%) <sup>a</sup>							Total
	8-30 Days	2 Months	3 Months	4-6 Months	7-9 Months	10-12 Months	>12 Months	
Advanced adenoma <sup>b</sup>	2135 (8.1)	2168 (9.0)	779 (9.3)	429 (8.4)	114 (8.9)	75 (10.5)	247 (11.6)	5947 (8.8)
Any colorectal cancer	807 (3.0)	685 (2.8)	265 (3.1)	165 (3.1)	58 (4.3)	37 (4.9)	174 (7.6)	2191 (3.1)
Advanced-stage colorectal cancer <sup>c</sup>								
Present	219 (0.8)	173 (0.7)	60 (0.7)	46 (0.9)	17 (1.3)	14 (1.9)	72 (3.1)	601 (0.9)
Unknown	3 (<1)	2 (<1)	2 (<1)	2 (<1)	0	1 (0.1)	4 (0.2)	14 (<1)
Colorectal cancer stage								
0	129 (0.5)	113 (0.5)	39 (0.5)	32 (0.6)	7 (0.5)	6 (0.8)	17 (0.7)	343 (0.5)
I	314 (1.2)	275 (1.1)	122 (1.4)	48 (0.9)	19 (1.4)	5 (0.7)	40 (1.7)	823 (1.2)
II	142 (0.5)	122 (0.5)	42 (0.5)	37 (0.7)	15 (1.1)	11 (1.5)	41 (1.8)	410 (0.6)
III	169 (0.6)	133 (0.5)	56 (0.6)	32 (0.6)	12 (0.9)	9 (1.2)	49 (2.1)	460 (0.7)
IV	50 (0.2)	40 (0.2)	4 (<1)	14 (0.3)	5 (0.4)	5 (0.7)	23 (1.0)	141 (0.2)
Unknown	3 (<1)	2 (<1)	2 (<1)	2 (<1)	0	1 (0.1)	4 (0.2)	14 (<1)
No colorectal cancer	26 369 (97.0)	23 959 (97.2)	8401 (96.9)	5086 (96.9)	1277 (95.7)	711 (95.1)	2130 (92.4)	67 933 (96.9)

Abbreviation: FIT, fecal immunochemical test.

<sup>a</sup>  $P < .001$  for differences in proportions across time intervals for all variables. Time to colonoscopy intervals: 2 months (31-60 days), 3 months (61-90 days), 4 to 6 months (91-180 days), 7 to 9 months (181-272 days), 10 to 12 months (273-365 days), and more than 12 months (366-1571 days).

<sup>b</sup> Advanced adenoma refers to adenomas with advanced histology (ie, tubulovillous and villous adenomas).

<sup>c</sup> Advanced-stage cancers were defined as stage III (regional lymph node involvement) or stage IV (distant metastasis) according to the American Joint Committee on Cancer staging system or, for those without such staging, as code 3 (disease in the regional lymph nodes), code 4 (regional disease with direct extension and spread to the regional lymph nodes), or code 7 (distant metastasis) according to the 2013 Surveillance, Epidemiology, and End Results Program Coding and Staging Manual.

in the 7 to 9 months exposure group. The 1 to 7 days exposure group had a higher risk of colorectal cancer outcomes, suggesting that extremely rapid follow-up (within a week) likely represents a high-risk group.

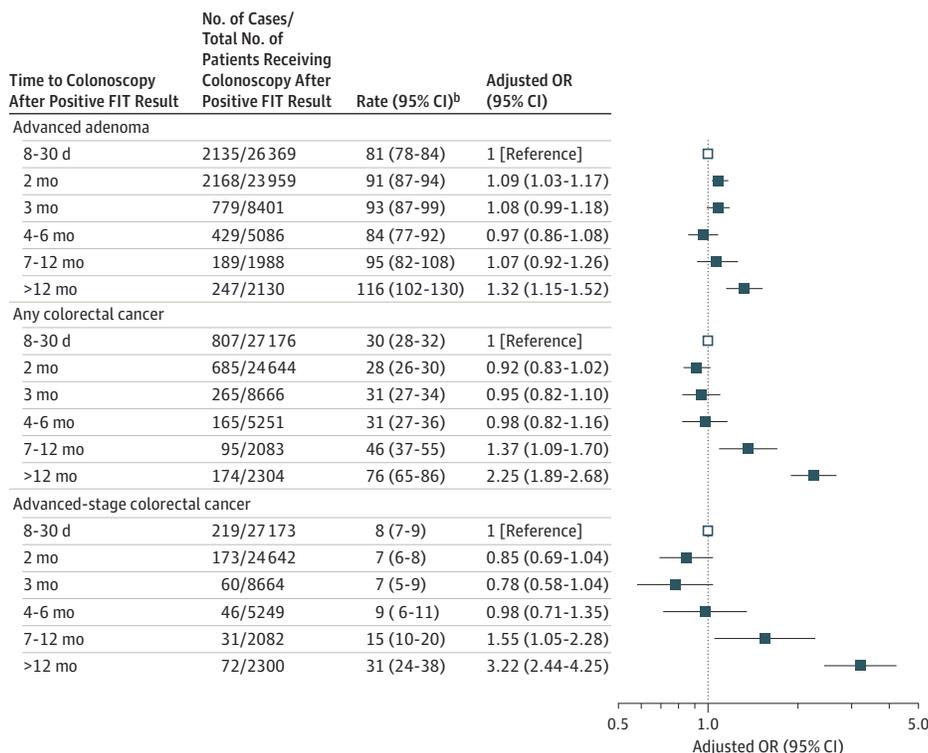
The associations between time to colonoscopy and risk of any colorectal cancer and advanced-stage disease differed somewhat across strata of age, prior FIT screening, and no preventive vaccinations in the year before FIT screening (eTable 2 in Supplement); region was also an effect modifier for advanced-stage disease. However, the differences were small, with the exception of age, and significant associations persisted across all strata. For example, similar increases in risk for advanced-stage disease were found for patients with and

without prior FIT screening (OR, 1.05 [95% CI 1.04-1.07] with prior FIT screening vs OR, 1.04 [95% CI 1.02-1.06] without prior FIT screening). Also, stronger associations for both any colorectal cancer and advanced-stage disease were found among older patients rather than younger patients, although significant associations were found for both groups.

## Discussion

Among patients in a community-based setting with positive FIT results, there was no significant increase in risk of overall colorectal cancer or advanced colorectal cancer associated with

**Figure 2. Time to Colonoscopy After a Positive FIT and Adjusted Risk<sup>a</sup> of Advanced Adenoma, Any Colorectal Cancer, and Advanced-Stage Colorectal Cancer**



BMI indicates body mass index (calculated as weight in kilograms divided by height in meters squared); FIT, fecal immunochemical test; OR, odds ratio. Models for any colorectal cancer include the entire population. Advanced adenoma was defined as adenomas with advanced histology (ie, tubulovillous and villous adenomas). Models for advanced adenoma exclude 2191 patients diagnosed with colorectal cancer. Advanced-stage cancers were defined as stage III (regional lymph node involvement) or stage IV (distant metastasis) according to the American Joint Committee on Cancer staging system or, for those without such staging, as code 3 (disease in the regional lymph nodes), code 4 (regional disease with direct extension and spread to the regional lymph nodes), or code 7 (distant metastasis) according to the 2013 Surveillance, Epidemiology, and End Results Program Coding and Staging Manual. Models for advanced-stage colorectal cancer exclude 14 patients with

colorectal cancer of unknown stage. The adjusted advanced-stage colorectal cancer model dropped 244 patients with unknown BMI because no patient with unknown BMI had this outcome.

<sup>a</sup> Adjusted for sex; age; race/ethnicity; BMI; region; FIT screening year; completion of previous FIT screening (ever and in the prior year); and in the year prior to FIT screening, receipt of the flu or pneumonia vaccine, presence of gastrointestinal symptoms (bleeding or blood in stool, unexplained weight loss, abdominal pain, diarrhea, diverticulitis, inflammatory bowel disease, or Lynch syndrome), diagnosis of iron-deficiency anemia or diabetes, current smoker, number of primary care visits, and number of days hospitalized.

<sup>b</sup> Rates (95% CIs) were per 1000 patients who had a colonoscopy after a positive FIT.

colonoscopy follow-up within 10 months compared with 8 to 30 days. There was a higher risk of stage II colorectal cancer at 7 to 9 months; of any colorectal cancer, advanced-stage disease, and stage II and IV colorectal cancer at 10 to 12 months; and of advanced adenomas, any colorectal cancer, advanced-stage disease, and stages II-IV colorectal cancer at more than 12 months.

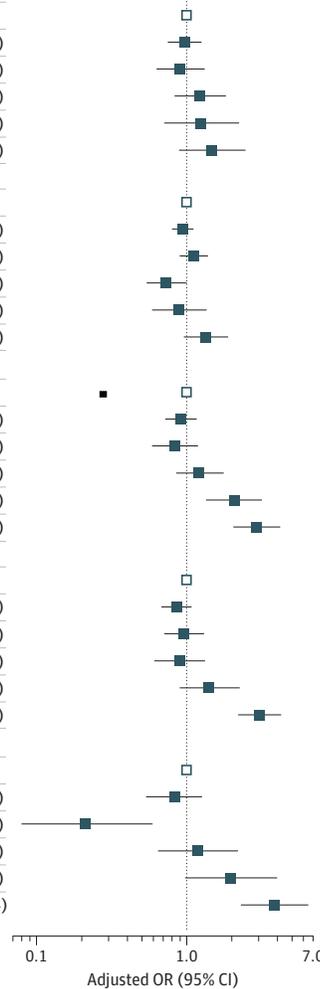
Time intervals between a positive FIT result and colonoscopy follow-up vary widely in practice.<sup>18-34</sup> In studies among veterans and within a public health care system, for example, the average and median times to colonoscopy were 103 days among veterans and 174 days within a public health care system.<sup>26,34</sup> Longer intervals could increase the chance of neoplastic progression, whereas short intervals may substantially increase patient and clinician burdens without benefiting cancer outcomes. In the current study, nearly 75% of patients with a positive FIT result received a colonoscopy

within 90 days. This required rapid communication of positive results to patients and physicians, sufficient colonoscopy access, rapid scheduling, and tracking of examination completion.<sup>14</sup> However, even with one of the most rapid follow-up rates reported to date,<sup>34</sup> only one-third of patients with a positive FIT result received a follow-up colonoscopy within 30 days.

Guidelines for colonoscopy follow-up vary and lack supporting data. In 2006, a Canadian consensus group recommended colonoscopy follow-up within 2 months of a positive FIT result, although no rationale was provided.<sup>7</sup> In 2007, the Veterans Health Administration issued a directive that a colonoscopy be performed within 60 days of a positive FIT result,<sup>6</sup> however, a subsequent report found insufficient evidence to support the recommendation.<sup>8</sup> Similarly, in 2012, European guidelines recommended colonoscopy within 31 days after referral for a positive FIT result, despite a lack

Figure 3. Time to Colonoscopy After a Positive FIT and Adjusted Risk<sup>a</sup> of Colorectal Cancer Stages 0-IV

Time to Colonoscopy After Positive FIT Result	No. of Cases/ Total No. of Patients Receiving Colonoscopy After Positive FIT Result	Rate (95% CI) <sup>b</sup>	Adjusted OR (95% CI)
<b>Stage 0 colorectal cancer</b>			
8-30 d	129/26498	5 (4-6)	1 [Reference]
2 mo	113/24072	5 (4-6)	0.98 (0.75-1.26)
3 mo	39/8440	5 (3-6)	0.91 (0.63-1.32)
4-6 mo	32/5118	6 (4-8)	1.23 (0.83-1.83)
7-12 mo	13/2001	6 (3-10)	1.26 (0.71-2.24)
>12 mo	17/2147	8 (4-12)	1.48 (0.89-2.47)
<b>Stage I colorectal cancer</b>			
8-30 d	314/26683	12 (10-13)	1 [Reference]
2 mo	275/24234	11 (10-13)	0.94 (0.80-1.11)
3 mo	122/8523	14 (12-17)	1.12 (0.90-1.39)
4-6 mo	48/5134	9 (7-12)	0.73 (0.54-1.00)
7-12 mo	24/2012	12 (7-17)	0.89 (0.59-1.36)
>12 mo	40/2170	18 (13-24)	1.35 (0.96-1.89)
<b>Stage II colorectal cancer</b>			
8-30 d	142/26511	5 (4-6)	1 [Reference]
2 mo	122/24081	5 (4-6)	0.92 (0.72-1.17)
3 mo	42/8443	5 (3-6)	0.84 (0.59-1.19)
4-6 mo	37/5123	7 (5-10)	1.22 (0.85-1.77)
7-12 mo	26/2014	13 (8-18)	2.07 (1.35-3.17)
>12 mo	41/2171	19 (13-25)	2.94 (2.05-4.20)
<b>Stage III colorectal cancer</b>			
8-30 d	169/26538	6 (5-7)	1 [Reference]
2 mo	133/24092	6 (5-6)	0.86 (0.68-1.08)
3 mo	56/8457	7 (5-8)	0.96 (0.71-1.31)
4-6 mo	32/5118	6 (4-8)	0.90 (0.61-1.33)
7-12 mo	21/2009	10 (6-15)	1.42 (0.90-2.26)
>12 mo	49/2179	22 (16-29)	3.07 (2.21-4.27)
<b>Stage IV colorectal cancer</b>			
8-30 d	50/26419	2 (1-2)	1 [Reference]
2 mo	40/23999	2 (1-2)	0.83 (0.54-1.26)
3 mo	4/8405	0 (0-1)	0.21 (0.08-0.59)
4-6 mo	14/5100	3 (1-4)	1.19 (0.65-2.18)
7-12 mo	10/1998	5 (2-8)	1.99 (0.99-3.98)
>12 mo	23/2153	11 (6-15)	3.86 (2.32- 6.44)



BMI indicates body mass index (calculated as weight in kilograms divided by height in meters squared); FIT, fecal immunochemical test; OR, odds ratio. Models for stage-specific colorectal cancer exclude patients with colorectal cancer of any stage other than the specified stage. The adjusted models for colorectal cancer stages 0, III, and IV dropped 242 patients with unknown BMI because no patient with unknown BMI had these outcomes. The adjusted colorectal cancer stage IV model dropped 2435 patients with unknown race/ethnicity because no patient with unknown race/ethnicity had this outcome.

<sup>a</sup> Adjusted for sex; age; race/ethnicity; BMI; region; FIT screening year; completion of previous FIT screening (ever and in the prior year); and in the year prior to FIT screening, receipt of the flu or pneumonia vaccine, presence of gastrointestinal symptoms (bleeding or blood in stool, unexplained weight loss, abdominal pain, diarrhea, diverticulitis, inflammatory bowel disease, or Lynch syndrome), diagnosis of iron-deficiency anemia or diabetes, current smoker, number of primary care visits, and number of days hospitalized.

<sup>b</sup> Rates (95% CIs) were per 1000 patients who had a colonoscopy after a positive FIT.

of evidence for effectiveness. Given the lack of supporting evidence for recommendations, and the substantial difficulties for patients and clinicians to rapidly schedule and complete sedated examinations (which require time off from work, a person to accompany the patient home, and skilled personnel),<sup>15</sup> current US consensus guidelines offer no recommendation regarding the time interval between a positive FIT result and follow-up colonoscopy.<sup>2,5</sup>

Prior studies have mainly explored risk factors for different times to follow-up colonoscopy<sup>18-25,27,29-32</sup> and methods for improving follow-up,<sup>26,33,35-37</sup> rather than the actual consequences of different times to follow-up on cancer outcomes. An analysis of 100 veterans referred for colonoscopy after a positive FIT result reported no association between follow-up time and colorectal cancer stage.<sup>10</sup> A study of 231 veterans—which, due to sample-size limitations, primarily evaluated trends rather than specific time intervals—reported

that each additional 30-day wait for colonoscopy after a positive FIT result was associated with an increased risk of any adenoma (OR, 1.10 [95% CI, 1.02-1.19]), but did not achieve statistical significance for advanced neoplasia (advanced adenomas or intramucosal carcinoma) or invasive cancers.<sup>9</sup> Both studies included single sites with predominantly male populations. A Canadian study of 246 patients with colorectal cancer reported no association between wait-time and node positivity or presence of distant metastases at diagnosis.<sup>38</sup> A modeling study reported that, compared with colonoscopy within 2 weeks of a positive FIT result, waiting 12 months might reduce the total years of life gained from screening by an estimated 9%.<sup>39</sup> Although the modeling study reported a steady increase in risk between the duration of the delay and screening benefits lost, the current study only found evidence for a higher risk of overall colorectal cancer and advanced disease for colonoscopies performed

Table 3. Time to Colonoscopy Among Patients Receiving a Positive FIT Result

Time to Colonoscopy <sup>a</sup>	Any Colorectal Cancer			Advanced-Stage Colorectal Cancer <sup>b</sup>		
	No. of Cases/ Total No.	Rate per 1000 Patients (95% CI)	Adjusted OR (95% CI) <sup>c</sup>	No. of Cases/ Total No.	Rate per 1000 Patients (95% CI)	Adjusted OR (95% CI) <sup>c</sup>
<b>Comparison Group, 1-30 d</b>						
1-30 d	871/28 567	30 (28-32)	1 [Reference]	248/28 564	9 (8-10)	1 [Reference]
2 mo	685/24 644	28 (26-30)	0.90 (0.81-0.99)	173/24 642	7 (6-8)	0.79 (0.65-0.97)
3 mo	265/8666	31 (27-34)	0.93 (0.80-1.07)	60/8664	7 (5-9)	0.73 (0.54-0.97)
4-6 mo	165/5251	31 (27-36)	0.95 (0.80-1.13)	46/5249	9 (6-11)	0.91 (0.66-1.25)
7-9 mo	58/1335	43 (32-54)	1.27 (0.96-1.67)	17/1335	13 (7-19)	1.22 (0.74-2.01)
10-12 mo	37/748	49 (34-65)	1.44 (1.02-2.02)	14/747	19 (9-28)	1.83 (1.06-3.17)
>12 mo	174/2304	76 (65-86)	2.19 (1.84-2.60)	72/2300	31 (24-38)	2.99 (2.27-3.93)
<b>Comparison Group, 8-60 d</b>						
8-60 d	1492/51 820	29 (27-30)	1 [Reference]	392/51 815	8 (7-8)	1 [Reference]
3 mo	265/8666	31 (27-34)	0.99 (0.87-1.14)	60/8664	7 (5-9)	0.84 (0.64-1.11)
4-6 mo	165/5251	31 (27-36)	1.02 (0.86-1.20)	46/5249	9 (6-11)	1.06 (0.78-1.44)
7-9 mo	58/1335	43 (32-54)	1.36 (1.04-1.79)	17/1335	13 (7-19)	1.43 (0.87-2.33)
10-12 mo	37/748	49 (34-65)	1.54 (1.10-2.16)	14/747	19 (9-28)	2.13 (1.24-3.67)
>12 mo	174/2304	76 (65-86)	2.34 (1.98-2.77)	72/2300	31 (24-38)	3.48 (2.68-4.52)
<b>Comparison Group, 8-90 d</b>						
8-90 d	1757/60 486	29 (28-30)	1 [Reference]	452/60 479	7 (7-8)	1 [Reference]
4-6 mo	165/5251	31 (27-36)	1.02 (0.87-1.20)	46/5249	9 (6-11)	1.09 (0.80-1.48)
7-9 mo	58/1335	43 (32-54)	1.36 (1.04-1.79)	17/1335	13 (7-19)	1.47 (0.90-2.40)
10-12 mo	37/748	49 (34-65)	1.54 (1.10-2.16)	14/747	19 (9-28)	2.19 (1.28-3.77)
>12 mo	174/2304	76 (65-86)	2.35 (1.99-2.77)	72/2300	31 (24-38)	3.58 (2.76-4.63)
<b>Excluding Colonoscopies &gt;24 mo After FIT</b>						
8-30 d	807/27 176	30 (28-32)	1 [Reference]	219/27 173	8 (7-9)	1 [Reference]
2 mo	685/24 644	28 (26-30)	0.92 (0.82-1.02)	173/24 642	7 (6-8)	0.85 (0.69-1.04)
3 mo	265/8666	31 (27-34)	0.95 (0.82-1.10)	60/8664	7 (5-9)	0.78 (0.58-1.04)
4-6 mo	165/5251	31 (27-36)	0.98 (0.82-1.16)	46/5249	9 (6-11)	0.98 (0.70-1.35)
7-9 mo	58/1335	43 (32-54)	1.30 (0.99-1.71)	17/1335	13 (7-19)	1.31 (0.79-2.16)
10-12 mo	37/748	49 (34-65)	1.47 (1.04-2.07)	14/747	19 (9-28)	1.97 (1.14-3.42)
>12 mo	105/1521	69 (56-82)	2.13 (1.72-2.64)	42/1520	28 (19-36)	2.98 (2.12-4.18)
<b>Including &lt;1-y Kaiser Permanente Membership Before FIT or Prior Endoscopy</b>						
8-30 d	999/33 924	29 (28-31)	1 [Reference]	283/33 920	8 (7-9)	1 [Reference]
2 mo	837/30 124	28 (26-30)	0.92 (0.84-1.01)	210/30 121	7 (6-8)	0.81 (0.67-0.97)
3 mo	313/10 604	30 (26-33)	0.94 (0.82-1.07)	72/10 600	7 (5-8)	0.74 (0.57-0.97)
4-6 mo	199/6539	30 (26-35)	0.95 (0.81-1.11)	55/6537	8 (6-11)	0.89 (0.66-1.20)
7-9 mo	72/1700	42 (33-52)	1.29 (1.00-1.65)	21/1700	12 (7-18)	1.23 (0.79-1.94)
10-12 mo	42/963	44 (31-57)	1.29 (0.94-1.77)	14/962	15 (7-22)	1.42 (0.82-2.44)
>12 mo	205/3072	67 (58-76)	2.03 (1.73-2.38)	82/3066	27 (21-32)	2.67 (2.07-3.44)

(continued)

Table 3. Time to Colonoscopy Among Patients Receiving a Positive FIT Result (continued)

Time to Colonoscopy <sup>a</sup>	Any Colorectal Cancer			Advanced-Stage Colorectal Cancer <sup>b</sup>		
	No. of Cases/ Total No.	Rate per 1000 Patients (95% CI)	Adjusted OR (95% CI) <sup>c</sup>	No. of Cases/ Total No.	Rate per 1000 Patients (95% CI)	Adjusted OR (95% CI) <sup>c</sup>
Including 1-7 d Exposure Category <sup>d</sup>						
1-7 d	64/1391	46 (35-57)	1.45 (1.11-1.89)	29/1391	21 (13-28)	2.38 (1.60-3.55)
8-30 d	807/27 176	30 (28-32)	1 [Reference]	219/27 173	8 (7-9)	1 [Reference]
2 mo	685/24 644	28 (26-30)	0.91 (0.82-1.02)	173/24 642	7 (6-8)	0.84 (0.69-1.03)
3 mo	265/8666	31 (27-34)	0.95 (0.82-1.09)	60/8664	7 (5-9)	0.77 (0.58-1.03)
4-6 mo	165/5251	31 (27-36)	0.97 (0.82-1.16)	46/5249	9 (6-11)	0.97 (0.70-1.34)
7-9 mo	58/1335	43 (32-54)	1.30 (0.98-1.71)	17/1335	13 (7-19)	1.30 (0.79-2.15)
10-12 mo	37/748	49 (34-65)	1.47 (1.04-2.07)	14/747	19 (9-28)	1.95 (1.12-3.39)
>12 mo	174/2304	76 (65-86)	2.24 (1.88-2.67)	72/2300	31 (24-38)	3.20 (2.43-4.22)

Abbreviations: FIT, fecal immunochemical test; OR, odds ratio.

<sup>a</sup> Time to colonoscopy intervals: 2 months (31-60 days), 3 months (61-90 days), 4 to 6 months (91-180 days), 7 to 9 months (181-272 days), 10 to 12 months (273-365 days), and more than 12 months (366-1571 days).

<sup>b</sup> Advanced-stage cancers were defined as stage III (regional lymph node involvement) or stage IV (distant metastasis) according to the American Joint Committee on Cancer staging system or, for those without such staging, as code 3 (disease in the regional lymph nodes), code 4 (regional disease with direct extension and spread to the regional lymph nodes), or code 7 (distant metastasis) according to the 2013 Surveillance, Epidemiology, and End Results Program Coding and Staging Manual.

<sup>c</sup> Adjusted for sex; age; race/ethnicity; body mass index (BMI); region; FIT screening

year; completion of previous FIT screening (ever and in the prior year); and in the year prior to FIT screening, receipt of the flu/pneumonia vaccine, presence of gastrointestinal symptoms (bleeding or blood in stool, unexplained weight loss, abdominal pain, diarrhea, diverticulitis, inflammatory bowel disease, or Lynch syndrome), diagnosis of iron-deficiency anemia or diabetes, current smoker, number of primary care visits, and number of days hospitalized. Models for any colorectal cancer include the entire population. Models for advanced-stage colorectal cancer exclude 14 patients with colorectal cancer of unknown stage. The adjusted advanced-stage colorectal cancer model dropped 244 patients with unknown BMI because no patient with unknown BMI had this outcome.

<sup>d</sup> The 1 to 7 days exposure category refers to patients receiving colonoscopy or colorectal cancer diagnosis within 1 to 7 days after their positive FIT.

more than 10 months after a positive FIT result. Therefore, although the time interval from colorectal polyp initiation to colorectal cancer is believed to span years, our study findings raise the possibility that by the time a lesion is detectable by FIT, further lesion progression might occur as soon as 6 to 12 months after a positive FIT result, although confounding remains a possible explanation for these findings.

Study strengths include its large size and number of colorectal cancer outcomes; comprehensive capture of FIT and cancer results; a multi-medical center, community-based, diverse population; validated approaches for capturing pathology data and colonoscopy examinations; histological confirmation of adenomas; validated SEER cancer registries; evaluation of a large number of possible confounding factors; and evaluation of assumptions through sensitivity analyses.

Limitations include the observational design and potential influence of unmeasured confounders, although the large number of patients allowed well-powered evaluations of a large number of possible confounding factors. Increases

in risk over time were seen across all strata of assessed potential confounders, including among patients with and without prior screening, comorbidities, and health care-seeking behaviors. Measures of colonoscopy quality were not available for all patients; however, a large-scale chart review in the study population demonstrated cecal intubation rates of 97.7% and adequate to excellent bowel preparations in 92.0% of examinations.<sup>40</sup> In addition, adenoma size was not available; thus, advanced adenomas were defined only by advanced histology.

## Conclusions

Among patients with a positive fecal immunochemical test result, compared with follow-up colonoscopy at 8 to 30 days, follow-up after 10 months was associated with a higher risk of colorectal cancer and more advanced-stage disease at the time of diagnosis. Further research is needed to assess whether this relationship is causal.

### ARTICLE INFORMATION

**Author Contributions:** Dr Corley had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Concept and design:** Corley, Jensen, Doubeni, Zauber, J.K. Lee, A.T. Lee.

**Acquisition, analysis, or interpretation of data:** All authors.

**Drafting of the manuscript:** Corley, Jensen, Marks.

**Critical revision of the manuscript for important intellectual content:** Corley, Jensen, Quinn, Doubeni, Zauber, J.K. Lee, Schottinger, Zhao, Ghai, A.T. Lee, Contreras, Quesenberry, Fireman, Levin.

**Statistical analysis:** Jensen, J.K. Lee, Marks, Zhao, Quesenberry, Fireman.

**Obtained funding:** Corley, Jensen, Quinn, Doubeni, Zauber, A.T. Lee, Levin.

**Administrative, technical, or material support:**

Quinn, Schottinger, Marks, Ghai, A.T. Lee.

**Supervision:** Corley, Quinn, A.T. Lee, Levin.

**Other:** Contreras.

**Conflict of Interest Disclosures:** All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Corley reports receiving grant support from Wyeth/Pfizer. No other disclosures were reported.

**Funding/Support:** This study was conducted within the National Cancer Institute–funded (grant U54 CA163262) Population-based Research Optimizing Screening Through Personalized Regimens consortium, which conducts multisite, coordinated, transdisciplinary research to evaluate and improve cancer-screening processes, and by grant K07 CA212057 from the National Cancer Institute (Dr J.K. Lee).

**Role of the Funder/Sponsor:** The National Cancer Institute had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit for publication.

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