

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Time to colonoscopy after a positive FIT and risks of CRC outcomes: impact of adjustment on risk estimates

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Time to colonoscopy ^a	Unadjusted		Model 1		Model 2	
	OR	(95% CI)	Adj OR ^b	(95% CI)	Adj OR ^c	(95% CI)
Advanced adenoma^d						
8-30 days	1.00	(reference)	1.00	(reference)	1.00	(reference)
2 months	1.13	(1.06, 1.20)	1.10	(1.03, 1.17)	1.09	(1.03, 1.17)
3 months	1.16	(1.06, 1.26)	1.09	(1.00, 1.19)	1.08	(0.99, 1.18)
4-6 months	1.05	(0.94, 1.17)	0.97	(0.87, 1.09)	0.97	(0.86, 1.08)
7-9 months	1.11	(0.91, 1.36)	1.01	(0.83, 1.23)	1.01	(0.82, 1.23)
10-12 months	1.34	(1.05, 1.71)	1.22	(0.95, 1.56)	1.20	(0.94, 1.53)
>12 months	1.49	(1.29, 1.71)	1.35	(1.17, 1.55)	1.32	(1.15, 1.52)
Any CRC						
8-30 days	1.00	(reference)	1.00	(reference)	1.00	(reference)
2 months	0.93	(0.84, 1.04)	0.88	(0.79, 0.98)	0.92	(0.83, 1.02)
3 months	1.03	(0.90, 1.19)	0.88	(0.76, 1.02)	0.95	(0.82, 1.10)
4-6 months	1.06	(0.89, 1.26)	0.84	(0.71, 1.01)	0.98	(0.82, 1.16)
7-9 months	1.48	(1.13, 1.95)	1.21	(0.91, 1.61)	1.30	(0.99, 1.72)
10-12 months	1.70	(1.21, 2.38)	1.41	(0.99, 2.01)	1.48	(1.05, 2.08)
>12 months	2.67	(2.25, 3.16)	2.22	(1.86, 2.67)	2.25	(1.89, 2.68)
Advanced-stage CRC^e						
8-30 days	1.00	(reference)	1.00	(reference)	1.00	(reference)
2 months	0.87	(0.71, 1.06)	0.82	(0.67, 1.00)	0.85	(0.69, 1.04)
3 months	0.86	(0.64, 1.14)	0.72	(0.54, 0.97)	0.78	(0.58, 1.04)
4-6 months	1.09	(0.79, 1.50)	0.85	(0.61, 1.18)	0.98	(0.71, 1.35)
7-9 months	1.59	(0.97, 2.61)	1.25	(0.75, 2.08)	1.32	(0.80, 2.18)
10-12 months	2.35	(1.36, 4.06)	1.90	(1.09, 3.33)	1.97	(1.14, 3.42)
>12 months	3.98	(3.04, 5.21)	3.21	(2.42, 4.26)	3.22	(2.44, 4.25)
CRC Stage 0						
8-30 days	1.00	(reference)	1.00	(reference)	1.00	(reference)
2 months	0.96	(0.75, 1.24)	0.95	(0.73, 1.22)	0.98	(0.75, 1.26)
3 months	0.95	(0.66, 1.36)	0.86	(0.60, 1.25)	0.91	(0.63, 1.32)
4-6 months	1.29	(0.87, 1.90)	1.11	(0.75, 1.66)	1.23	(0.83, 1.83)
7-9 months	1.12	(0.52, 2.40)	0.97	(0.45, 2.08)	1.06	(0.49, 2.28)
10-12 months	1.72	(0.76, 3.92)	1.45	(0.63, 3.32)	1.61	(0.70, 3.68)
>12 months	1.63	(0.98, 2.71)	1.34	(0.80, 2.23)	1.48	(0.89, 2.47)

eTable 1. (continued)

Time to colonoscopy ^a	Unadjusted		Model 1		Model 2	
	OR	(95% CI)	Adj OR ^b	(95% CI)	Adj OR ^c	(95% CI)
CRC Stage I						
8-30 days	1.00	(reference)	1.00	(reference)	1.00	(reference)
2 months	0.96	(0.82, 1.13)	0.90	(0.76, 1.07)	0.94	(0.80, 1.11)
3 months	1.22	(0.99, 1.51)	1.03	(0.83, 1.29)	1.12	(0.90, 1.39)
4-6 months	0.79	(0.58, 1.08)	0.62	(0.45, 0.84)	0.73	(0.54, 1.00)
7-9 months	1.25	(0.78, 1.99)	1.00	(0.62, 1.60)	1.12	(0.70, 1.79)
10-12 months	0.59	(0.24, 1.43)	0.45	(0.18, 1.09)	0.51	(0.21, 1.24)
>12 months	1.58	(1.13, 2.20)	1.18	(0.84, 1.66)	1.35	(0.96, 1.89)
CRC Stage II						
8-30 days	1.00	(reference)	1.00	(reference)	1.00	(reference)
2 months	0.95	(0.74, 1.21)	0.87	(0.68, 1.11)	0.92	(0.72, 1.17)
3 months	0.93	(0.66, 1.31)	0.76	(0.53, 1.08)	0.84	(0.59, 1.19)
4-6 months	1.35	(0.94, 1.94)	1.02	(0.70, 1.47)	1.22	(0.85, 1.77)
7-9 months	2.18	(1.28, 3.72)	1.69	(0.98, 2.93)	1.88	(1.09, 3.23)
10-12 months	2.87	(1.55, 5.33)	2.13	(1.13, 4.02)	2.39	(1.28, 4.46)
>12 months	3.57	(2.52, 5.07)	2.63	(1.83, 3.78)	2.94	(2.05, 4.20)
CRC Stage III						
8-30 days	1.00	(reference)	1.00	(reference)	1.00	(reference)
2 months	0.87	(0.69, 1.09)	0.81	(0.65, 1.03)	0.86	(0.68, 1.08)
3 months	1.04	(0.77, 1.41)	0.88	(0.64, 1.20)	0.96	(0.71, 1.31)
4-6 months	0.98	(0.67, 1.43)	0.76	(0.51, 1.11)	0.90	(0.61, 1.33)
7-9 months	1.47	(0.81, 2.64)	1.16	(0.64, 2.12)	1.26	(0.70, 2.29)
10-12 months	1.98	(1.01, 3.88)	1.51	(0.76, 3.01)	1.71	(0.87, 3.38)
>12 months	3.59	(2.60, 4.95)	2.79	(2.00, 3.90)	3.07	(2.21, 4.27)
CRC Stage IV						
8-30 days	1.00	(reference)	1.00	(reference)	1.00	(reference)
2 months	0.88	(0.58, 1.33)	0.80	(0.53, 1.23)	0.83	(0.54, 1.26)
3 months	0.25	(0.09, 0.70)	0.20	(0.07, 0.54)	0.21	(0.08, 0.59)
4-6 months	1.45	(0.80, 2.63)	1.02	(0.56, 1.88)	1.19	(0.65, 2.17)
7-9 months	2.06	(0.82, 5.19)	1.46	(0.57, 3.71)	1.57	(0.62, 4.00)
10-12 months	3.71	(1.47, 9.33)	2.50	(0.98, 6.38)	2.71	(1.06, 6.89)
>12 months	5.69	(3.47, 9.35)	3.71	(2.23, 6.19)	3.86	(2.32, 6.44)

Abbreviations: Adj, adjusted; CI, confidence interval; CRC, colorectal cancer; OR, odds ratio.

^a Time to colonoscopy intervals [months (days)]: 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 >12 months (366-1571 days).

^b Model 1 adjusted for adjusted for sex, age, race/ethnicity, body mass index, region, FIT screening year, completion of previous FIT screening (ever and in the prior year), and Charlson comorbidity score in the year before FIT screening. Models for any CRC include the entire population. Models for advanced adenoma exclude 2,191 patients diagnosed with CRC. Models for advanced-stage CRC exclude 14 patients with CRC of unknown stage. Models for stage-specific CRC exclude patients with CRC of any stage other than the specified stage. The adjusted advanced-stage CRC model dropped

244 patients with unknown BMI because no patient with unknown BMI had this outcome. The adjusted models for CRC stages 0, III, and IV dropped 242 patients with unknown BMI because no patient with unknown BMI had these outcomes. The adjusted CRC stage IV model dropped 2435 patients with unknown race/ethnicity because no patient with unknown race/ethnicity had this outcome.

^c Model 2 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 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. Models for any CRC include the entire population. Models for advanced adenoma exclude 2,191 patients diagnosed with CRC. Models for advanced-stage CRC exclude 14 patients with CRC of unknown stage. Models for stage-specific CRC exclude patients with CRC of any stage other than the specified stage. The adjusted advanced-stage CRC model dropped 244 patients with unknown BMI because no patient with unknown BMI had this outcome. The adjusted models for CRC stages 0, III, and IV dropped 242 patients with unknown BMI because no patient with unknown BMI had these outcomes. The adjusted CRC stage IV model dropped 2435 patients with unknown race/ethnicity because no patient with unknown race/ethnicity had this outcome. Note: model 2 was used in Figure 2.

^d Advanced adenomas were defined as adenomas with advanced histology (i.e., tubulovillous and villous adenomas).

^e 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 SEER Program Coding and Staging Manual 2013.

eTable 2. Time to colonoscopy after a positive FIT and risks of CRC outcomes: stratified analyses^a

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	CRC					Advanced-stage CRC ^b				
	Cases/Total ^c	Rate ^d	(95% CI)	Adj OR ^e	(95% CI)	Cases/Total ^c	Rate ^d	(95% CI)	Adj OR ^e	(95% CI)
Time overall (continuous)	2,191/70,124	31	(30, 33)	1.03	(1.03, 1.04)	601/70,110	9	(8, 9)	1.05	(1.04, 1.06)
Stratified by										
Age (years)										
50-60	931/34,413	27	(25, 29)	1.01	(1.00, 1.03)	251/34,408	7	(6, 8)	1.03	(1.01, 1.05)
61-75	1,260/35,711	35	(33, 37)	1.04	(1.03, 1.05)	350/35,702	10	(9, 11)	1.06	(1.04, 1.07)
Previously FIT screened										
No	907/18,064	50	(47, 53)	1.02	(1.01, 1.03)	263/18,060	15	(13, 16)	1.04	(1.02, 1.06)
Yes	1,284/52,060	25	(23, 26)	1.04	(1.03, 1.05)	338/52,050	6	(6, 7)	1.05	(1.04, 1.07)
Vaccinated in prior year^f										
No	1,109/31,984	35	(33, 37)	1.03	(1.02, 1.04)	305/31,975	10	(8, 11)	1.05	(1.03, 1.06)
Yes	1,082/38,140	28	(27, 30)	1.04	(1.03, 1.05)	296/38,135	8	(7, 9)	1.05	(1.03, 1.06)
Region										
KPSC	865/25,738	34	(31, 36)	1.05	(1.04, 1.06)	237/25,728	9	(8, 10)	1.06	(1.05, 1.08)
KPNC	1,326/44,386	30	(28, 31)	1.03	(1.02, 1.03)	364/44,382	8	(7, 9)	1.04	(1.03, 1.05)

Abbreviations: Adj, adjusted; CI, confidence interval; CRC, colorectal cancer; FIT, fecal immunochemical test; KPNC, Kaiser Permanente Northern California; KPSC, Kaiser Permanente Southern California; OR, odds ratio.

^a 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-by-covariate interaction. Stratified models are presented when interaction p<0.10; OR point estimates represent the overall risk estimate for each additional 30-day delay in follow-up compared to follow-up at 8-30 days. For any CRC, interaction p-values are p<0.001 for Age, p=0.001 for Previously FIT screened, p=0.06 for Vaccinated in prior year, and p=0.003 for Region. For advanced-stage disease, interaction p-values are p=0.01 for Age, p=0.08 for Previously FIT screened, p=0.72 for Vaccinated in prior year, and p=0.06 for Region.

^b 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 SEER Program Coding and Staging Manual 2013.

^c Cases / Total refers to the number of cases per the total number of patients who had a colonoscopy after a positive FIT.

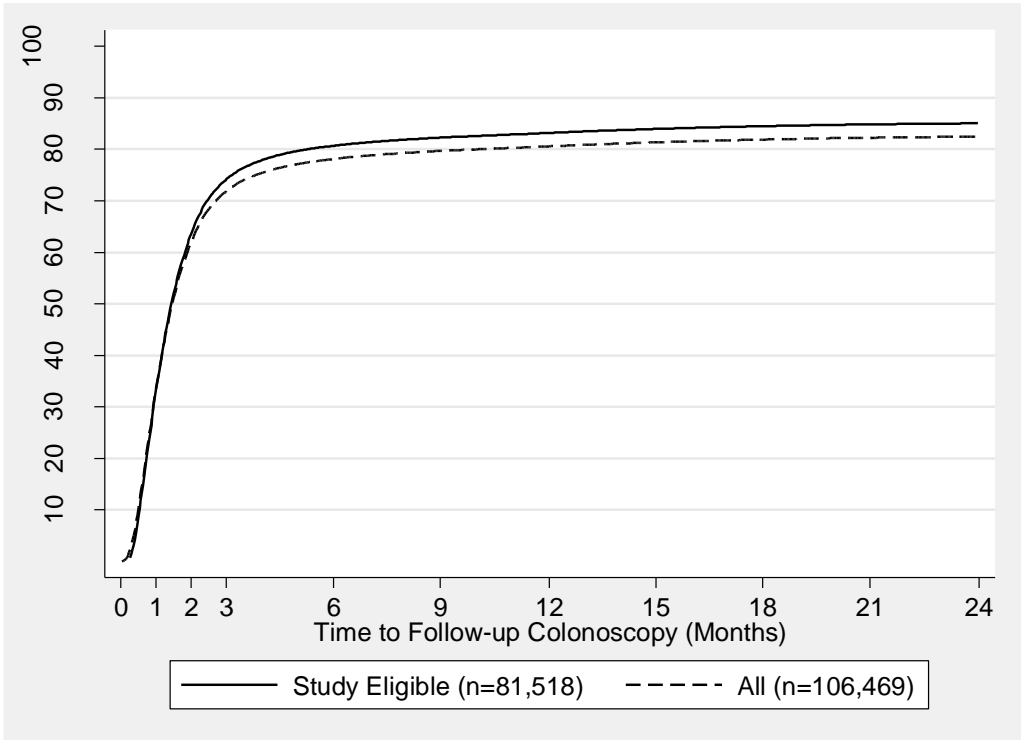
^d Rates (95% CIs) are per 1,000 patients who had a colonoscopy after a positive FIT.

^e 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 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. Models for any CRC include the entire population. Models for advanced adenoma exclude 2,191 patients diagnosed with CRC. Models for advanced-stage CRC exclude 14 patients with CRC of unknown stage. Models for stage-specific CRC exclude patients with CRC of any stage other than the specified stage. The adjusted advanced-stage CRC model dropped 244 patients with unknown BMI because no patient with unknown BMI had this outcome. The adjusted models for CRC stages 0, III, and IV dropped 242 patients with unknown BMI because no patient with unknown BMI had these outcomes. The adjusted CRC stage IV model dropped 2435 patients with unknown race/ethnicity because no patient with unknown race/ethnicity had this outcome.

^f Vaccinated in prior year refers to receipt of the flu or pneumonia vaccine in the year before FIT screening.

eFigure 1. Distribution of times to colonoscopy after a positive FIT^a

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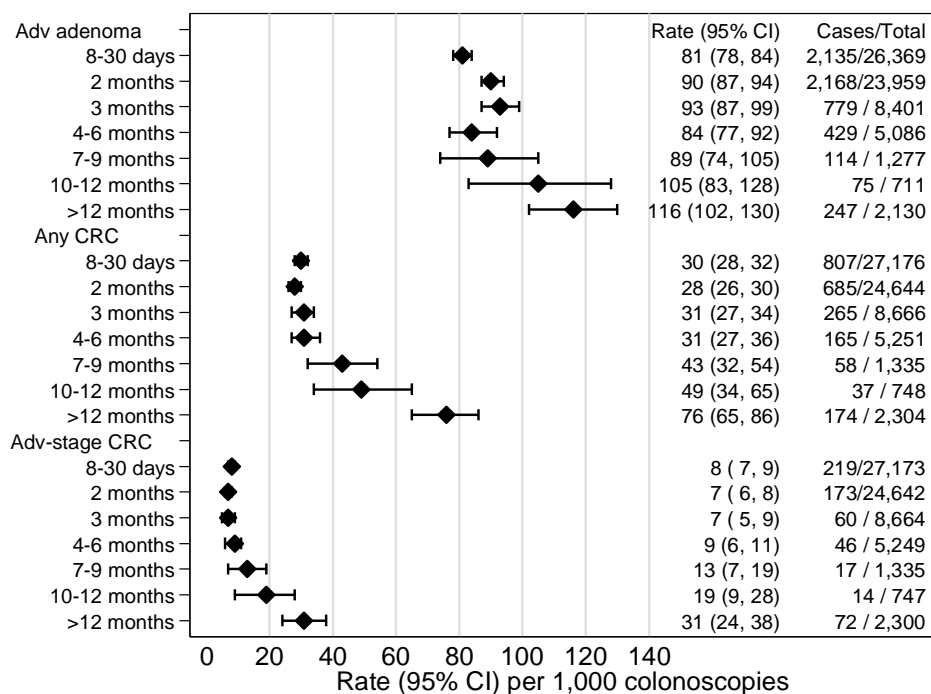


Abbreviations: FIT, fecal immunochemical test.

“All” includes the 106,520 patients with a positive FIT noted in Figure 1 minus 51 patients with a prior history of colorectal cancer.

^a The number of FIT-positive patients at risk at each follow-up time interval is as follows for study eligible and all patients, respectively: 0 months: 81,518 and 106,469; 1 month: 54,342 and 70,113; 2 months: 29,698 and 39,587; 3 months: 21,032 and 28,690; 6 months: 15,781 and 21,493; 9 months: 14,446 and 19,144; 12 months: 13,698 and 17,598; 15 months: 12,433 and 16,029; 18 months: 11,110 and 14,308; 21 months: 9,630 and 12,431; and 24 months: 8,293 and 10,681. The median (quartile 1, quartile 3) times to colonoscopy were 43 (25, 95) days for screening eligible FIT-positive patients and 43 (25, 103) days for all FIT-positive patients.

eFigure 2A. Time to colonoscopy after a positive FIT and crude rates of advanced adenoma,^a any CRC, and advanced-stage CRC^b



Abbreviations: Adv-stage, advanced-stage; CI, confidence interval; CRC, colorectal cancer; FIT, fecal immunochemical test.

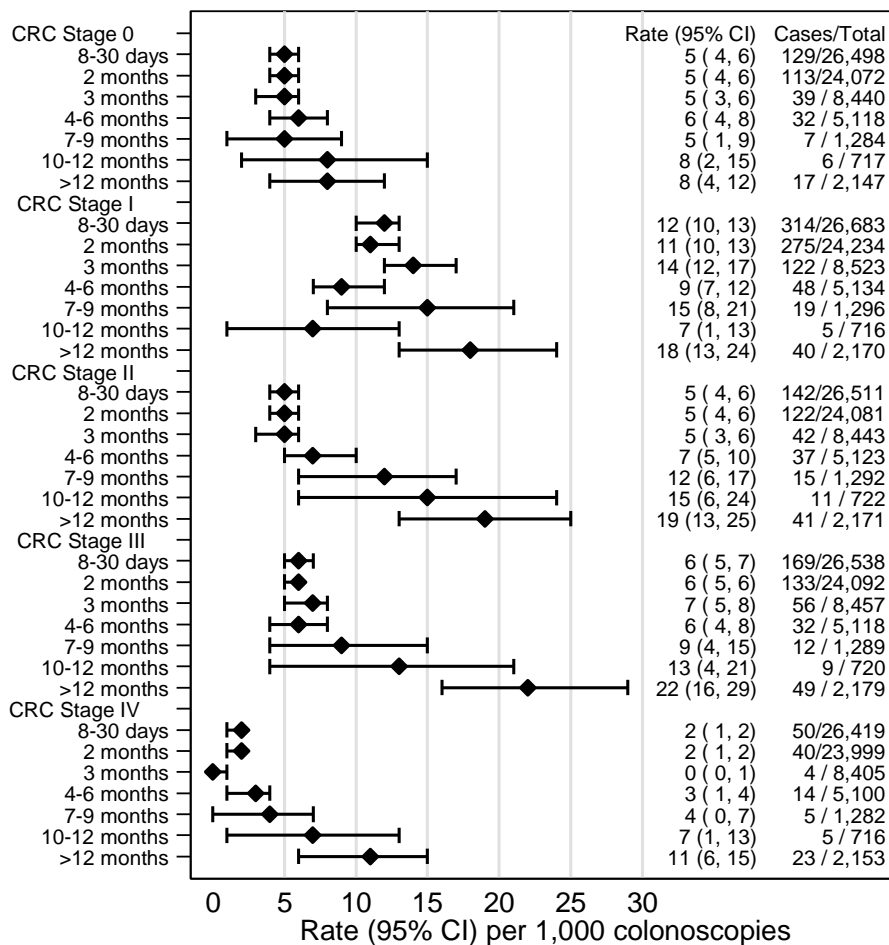
^aAdvanced adenoma refers to adenomas with advanced histology (i.e., tubulovillous and villous adenomas).

^bAdvanced-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 SEER Program Coding and Staging Manual 2013.

Rates (95% CIs) are per 1,000 patients who had a colonoscopy after a positive FIT.

Cases/Total refers to the number of cases per the total number of patients who had a colonoscopy after a positive FIT. Denominators for advanced adenoma exclude 2,191 patients diagnosed with CRC. Denominators for advanced-stage CRC exclude 14 patients with CRC of unknown stage.

eFigure 2B. Time to colonoscopy after a positive FIT and crude rates of CRC stages 0-IV



Abbreviations: Adv-stage, advanced-stage; CI, confidence interval; CRC, colorectal cancer; FIT, fecal immunochemical test.

Rates (95% CIs) are per 1,000 patients who had a colonoscopy after a positive FIT.

Cases/Total refers to the number of cases per the total number of patients who had a colonoscopy after a positive FIT. Denominators for stage-specific CRC exclude patients with CRC of any stage other than the specified stage.