Original Article

Primary Care Visit Use After Positive Fecal Immunochemical Test for Colorectal Cancer Screening

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BACKGROUND: For some patients, positive cancer screening test results can be a stressful experience that can affect future screening compliance and increase the use of health care services unrelated to medically indicated follow-up. **METHODS:** Among 483,216 individuals aged 50 to 75 years who completed a fecal immunochemical test to screen for colorectal cancer at a large integrated health care setting between 2007 and 2011, the authors evaluated whether a positive test was associated with a net change in outpatient primary care visit use within the year after screening. Multivariable regression models were used to evaluate the relationship between test result group and net changes in primary care visits after fecal immunochemical testing. **RESULTS:** In the year after the fecal immunochemical test, use increased by 0.60 clinic visits for patients with true-positive results. The absolute change in visits was largest (3.00) among individuals with positive test results who were diagnosed with colorectal cancer, but significant small increases also were found for patients treated with polypectomy and who had no neoplasia (0.36) and those with a normal examination and no polypectomy performed (0.17). Groups of patients who demonstrated an increase in net visit use compared with the true-negative group included patients with true-positive results (odds ratio [OR], 1.60; 95% confidence interval [95% CI], 1.54-1.66), and positive groups with a colorectal cancer diagnosis (OR, 7.19; 95% CI, 6.12-8.44), polypectomy/no neoplasia (OR, 1.37; 95% CI, 1.27-1.48), and normal examination/no polypectomy (OR, 1.24; 95% CI, 1.18-1.30). **CONCLUSIONS:** Given the large size of outreach programs, these small changes can cumulatively generate thousands of excess visits and have a substantial impact on total health care use. Therefore, these changes should be included in colorectal cancer screening cost models and their causes investigated further. ***Cancer* 2017;000:000-000**. © *2017 American Cancer Society.*

KEYWORDS: colorectal cancer, delivery of health care, early detection of cancer, primary health care.

INTRODUCTION

Colorectal cancer (CRC) is the third leading cause of cancer and cancer-related death in the United States.[1] Current screening guidelines offer endoscopic, radiologic, and fecal-based test options for the screening of average-risk adults aged ≥50 years;[2-4] of these, colonoscopy is the most commonly used CRC screening modality in the United States.[5] In comparison with breast and cervical cancer screening rates, CRC screening coverage in the United States remains relatively low (67.6% vs 72.8% for mammography and 82.6% for the Papanicolaou test).[6] To reach the unscreened percentage of the screening-eligible population, many large health care organizations have adopted organized population-based screening programs using high-sensitivity fecal occult blood testing (FOBT) (eg, the fecal immunochemical test [FIT]),[7] thus making FIT the second most commonly used CRC screening modality in the United States. Organized FIT screening is particularly well-suited to CRC screening for individuals who may be resistant to the use of colonoscopy, who are not good candidates for this procedure due to comorbidities, or who are unable to access endoscopic services. In addition, a recent study of the Centers for Disease Control and Prevention's Colorectal Cancer Control Program (CRCCP) found that the nonclinical costs associated with colonoscopy and FIT/FOBT-based programs are similar, but clinical costs differ considerably. Compared with $1150 per individual screened for colonoscopy programs in the CRCCP, the average annual clinical cost for screening and diagnostic testing for FIT/FOBT-based programs is $304, making stool-based programs very cost-effective as well.[8]

Undergoing cancer screening is a stressful experience for some individuals, and having an abnormal result can be especially distressing. Studies assessing the immediate psychological effect of breast cancer screening found that women with false-positive or abnormal results had statistically more symptoms of emotional distress,[9-12] anxiety,[13-16] and worry

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about future illness and breast cancer.[15,16] Similar reactions have been reported among patients with abnormal cervical cancer screening test results[17-19] and FOBT results for CRC screening.[20-23] Beyond the emotional stress and anxiety associated with abnormal cancer screening test findings, which constitute a large percentage of positive screening results, abnormal cancer screening results can affect future screening compliance[24,25] and increase the use of health care services unrelated to medically indicated follow-up of a positive screening test.[10]

Each year, millions of Americans undergo FIT screening. Nevertheless, to the best of our knowledge, no prior studies to date have examined the influence of a positive FIT result on outpatient primary care visit use. In a cohort of adults undergoing CRC screening with FIT at a large integrated health care organization in the United States, we conducted a study to evaluate changes in outpatient primary care visit use in the year after a positive FIT screening result versus the preceding 2 years compared with patients with true-negative (TN) FIT results. We hypothesized that, similar to other positive cancer screening tests, some patients may increase their health care use behavior (eg, seeking additional outpatient services[9,25,26]) following a positive FIT. Our hypothesis is based on the Transactional Model of Stress and Coping,[27-29] a theoretical framework that conceptualizes stressful experiences and coping as transactions between the patient and the environment. This model emphasizes personal appraisals of the perceived harm and threat presented by the stressor and the cultural and social resources at the individual's disposal with which to cope with the stressor.

MATERIALS AND METHODS

Study Setting

The current retrospective cohort study was conducted among members of Kaiser Permanente Northern California (KPNC), an integrated health care organization with >3.5 million members in urban, suburban, and semirural regions within a large geographic area.[30] The study was conducted as part of the National Cancer Institute's Cancer Research Network and the Population-based Research Optimizing Screening through Personalized Regimens (PROSPR) consortium.[31] The PROSPR consortium conducts multisite, coordinated, transdisciplinary research to evaluate and improve cancer screening processes.[32]

FIT screening is a primary method of CRC screening at KPNC.[31] Each year, the program mails a FIT kit to average-risk health plan members aged 50 to 75 years who have no record of a colonoscopy within 10 years, sigmoidoscopy within 5 years, or fecal occult blood testing within the previous year. The completed FIT kits are returned by mail to a regional laboratory for analysis. Patients also can receive a FIT kit though in-reach, such as during a clinic visit. Those individuals with a positive FIT result are referred for follow-up colonoscopy. Patients with possible symptoms of CRC are referred for colonoscopy.

All data were extracted from KPNC electronic clinical databases. Diagnoses of CRC were confirmed through the KPNC cancer registry, which is part of the Surveillance, Epidemiology, and End Results registry. This research was approved by the Institutional Review Boards of Columbia University Medical Center and KPNC.

Eligibility Criteria

Records of all KPNC patients aged 50 to 75 years and who were enrolled between 2007 and 2011 were identified. Individuals were eligible for the study if they completed at least 1 FIT during the study period and were enrolled in KPNC continuously for at least 24 months before and for 12 months after their first FIT. Patients were ineligible if they had a history of CRC, inflammatory bowel disease, or colectomy before undergoing FIT screening.

FIT Result Groups and Covariates

Four major FIT result groups were created: 1) the true negative (TN) group included those patients with a negative FIT and no colonoscopy or CRC diagnosis within 12 months after the FIT; 2) the true-positive (TP) group was comprised of those patients who had a positive FIT and completed a diagnostic colonoscopy within 12 months of the FIT, which detected ≥1 adenomas or CRC; 3) the false-positive (FP) group were those patients who had a positive FIT result and a diagnostic colonoscopy within 12 months that did not detect adenomas or CRC; and 4) the "positive FIT/no colonoscopy" group were those patients who had a positive FIT result but did not complete a diagnostic colonoscopy within 12 months after the positive FIT.

Those individuals with a positive FIT result who completed a diagnostic colonoscopy were subcategorized based on colonoscopy findings. Patients with TP results were grouped as "CRC," "advanced adenoma (ie, tubulovillous and villous)," and "nonadvanced adenoma" and those with FP results were grouped as "polypectomy/no neoplasia (ie, no adenoma or CRC detected)" and "normal exam/no polypectomy."

Covariates of interest included age, sex, race/ethnicity, and Charlson comorbidity score[33] in the year before FIT screening.

Primary Outcome

The primary outcome of interest was net change in outpatient primary care visit use before and after the first FIT. If >1 FIT was completed during the study period, the first FIT was considered to be the "index FIT" and was used to determine outcomes. Outpatient primary care visit use was defined as ambulatory outpatient and urgent care visits with physicians, physician assistants, and nurse practitioners in the departments of internal medicine, family practice, obstetrics/gynecology, community health, gerontology/geriatrics, and primary care; excluded were visits to mental health and chemical dependency departments. Primary care visit counts were limited to a maximum of 1 visit per patient per day.

Outpatient primary care visit use in the period before the index FIT was the annualized mean of the number of primary care visits within the 2 years preceding the index FIT. For all major FIT groups (TN, TP, FP, and positive FIT/no colonoscopy) and positive FIT subgroups (CRC, advanced adenoma, nonadvanced adenoma, polypectomy/no neoplasia, and normal exam/no polypectomy), visit use after screening was examined in 2 ways: 1) the 12-month period beginning on the day after the index FIT result minus any primary care visits related to the follow-up diagnostic colonoscopy (eg, bowel preparation class and the colonoscopy visit) for those individuals who underwent this procedure; and 2) beginning on the day after the diagnostic colonoscopy for those patients with a positive index FIT result.

Statistical Analyses

Differences in demographic and clinical characteristics between the FIT result groups were evaluated using the chi-square test. For each patient, the net difference in the mean number of primary care visits within the 12 months after FIT screening minus the annualized mean number of primary care visits within the 2 years before FIT screening or after the diagnostic colonoscopy for individuals with a positive FIT result was calculated. The cumulative monthly primary care visit use before and after FIT was calculated and contrasted for the 4 major FIT screening result groups and FIT-positive subgroups using difference-in-difference analysis.[34]

Multivariable logistic regression models were used to evaluate the relationship between FIT result group (TN, TP, FP, and positive FIT/no colonoscopy) and positive FIT subgroups (CRC, advanced adenoma, nonadvanced adenoma, polypectomy/no neoplasia, and normal exam/no polypectomy) and the risk of a net increase in the number of primary care visits after FIT screening, with the TN group serving as the referent. These procedures then were repeated for the secondary analysis in which the post-FIT observation period for the FIT-positive groups was shifted from the 1-year interval after the FIT result to the year immediately after the diagnostic colonoscopy. The purpose of the sensitivity analysis was to determine whether additional primary care use occurred during the period between the positive FIT result and the date of the colonoscopy that may have been due to colonoscopy-related visits. For all models, odds ratios (ORs) and 95% confidence intervals (95% CIs) were adjusted for patient age, sex, and Charlson comorbidity score in the 12-month period before the index FIT. All analyses were performed using SAS statistical software (version 9.3; SAS Institute Inc, Cary, NC).

RESULTS

Demographic and Clinical Characteristics

A total of 483,216 individuals completed a FIT between 2007 and 2011 (Table 1). Overall, 456,324 patients (94.4%) had a TN result. Among the 26,892 individuals with a positive FIT result, 11,072 had a TP result (41.2%), 9701 had a FP result (36.1%), and 6119 had a positive FIT/no colonoscopy result (22.8%). Compared with those with a TN result, patients with a positive FIT result were more often older and male, had more comorbid conditions, and more often had ≥4 or more annual primary care visits within the 2 years before FIT screening. Among individuals with a positive FIT/no colonoscopy result, 9.2% had ≥10 or more outpatient primary care visits.

Net Change in Primary Care Visit Use Before and After the Index FIT

Major FIT result groups

Primary care visits for the 4 major FIT result groups (TN, TP, FP, and positive FIT/no colonoscopy) ranged overall between 0 and 16 visits before the index FIT and between 0 and 18 visits after FIT. In general, primary care visit use was lowest among the patients in the TN group (2.14 visits before and 2.17 visits after FIT) and highest among individuals with a positive FIT/no colonoscopy result (3.61 visits before and 4.22 visits after FIT) (Table 2). In the 12-month period after the index FIT, the net change in the use of primary care visits for those in the TN group was negligible (+0.02 visits), but was increased by 0.60 visits (OR, 1.60; 95% CI, 1.54-1.66) in the TP group, by

TABLE 1. Demographic Characteristics Among Individuals Aged 50 to 75 Years Who Completed FIT Screening at Kaiser Permanente Northern California Between 2007 and 2011

		Negative FIT	Positive FIT N = 26,892			
	Total N = 483,216	True Negative N = 456,324	True Positive N = 11,072	False Positive N = 9701	Positive, No Colonoscopy N = 6119	
	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)	*P*
Age, y						<.0001
50-64	351,693 (72.8)	334,783 (73.4)	6761 (61.1)	6569 (67.7)	3580 (58.5)	
65-75	131,523 (27.2)	121,541 (26.6)	4311 (38.9)	3132 (32.3)	2539 (41.5)	
Sex						<.0001
Female	257,232 (53.2)	245,175 (53.7)	4167 (37.6)	5081 (52.4)	2809 (45.9)	
Male	225,944 (46.8)	211,111 (46.3)	6904 (62.4)	4619 (47.6)	3310 (54.1)	
Data missing/unknown[a]	40 (0.0)	38 (0.0)	1 (0.0)	1 (0.0)	0 (0.0)	
Race						<.0001
White	291,252 (60.3)	275,059 (60.3)	6756 (61.0)	5891 (60.7)	3546 (58.0)	
Black	30,855 (6.4)	28,889 (6.3)	865 (7.8)	642 (6.6)	459 (7.5)	
Asian	75,736 (15.7)	71,784 (15.7)	1525 (13.8)	1536 (15.8)	891 (14.6)	
Other	29,204 (6.0)	27,281 (6.0)	758 (6.8)	678 (7.0)	487 (8.0)	
Data missing/unknown[a]	56,169 (11.6)	53,311 (11.7)	1168 (10.5)	954 (9.8)	736 (12.0)	
Ethnicity						<.0001
Hispanic	54,518 (11.3)	51,403 (11.3)	1292 (11.7)	1083 (11.2)	740 (12.1)	
Non-Hispanic	354,886 (73.4)	334,896 (73.4)	8252 (74.5)	7361 (75.9)	4377 (71.5)	
Data missing/unknown[a]	73,812 (15.3)	70,025 (15.3)	1528 (13.8)	1257 (13.0)	1002 (16.4)	
Charlson comorbidity score						<.0001
0	353,585 (73.2)	336,714 (73.8)	6971 (63.0)	6356 (65.5)	3544 (57.9)	
1	79,236 (16.4)	73,973 (16.2)	2157 (19.5)	1854 (19.1)	1252 (20.5)	
≥2	50,395 (10.4)	45,637 (10.0)	1944 (17.6)	1491 (15.4)	1323 (21.6)	
No. of primary care visits[b]						<.0001
0	88,870 (18.4)	84,721 (18.6)	1930 (17.4)	1353 (14.0)	866 (14.2)	
1-3	303,194 (62.8)	287,592 (63.0)	6719 (60.7)	5900 (60.8)	2983 (48.6)	
4-9	84,815 (17.6)	78,671(17.2)	2213 (20.0)	2226 (23.0)	1705 (27.9)	
≥10	6337 (1.3)	5340 (1.2)	210 (1.9)	222 (2.3)	565 (9.2)	

Abbreviation: FIT, fecal immunochemical test.
[a] Excluded from univariable analysis.
[b] Annualized number of outpatient primary care visits within the 2 years before FIT screening.

0.22 visits (OR, 1.27; 95% CI, 1.22-1.33) in the FP group, and by 0.49 visits (OR, 1.50; 95% CI, 1.43-1.58) in the positive FIT/no colonoscopy group.

TP FIT result subgroups

In the TP subgroup, visits after the diagnostic colonoscopy increased by 3.00 visits among those who were diagnosed with CRC (OR, 7.19; 95% CI, 6.12-8.44) and by 0.44 visits among those with advanced adenoma (OR, 1.54; 95% CI, 1.42-1.67), whereas those patients diagnosed with a nonadvanced adenoma had an increase of 0.33 visits (OR, 1.36; 95% CI, 1.30-1.43) (Table 2).

FP FIT result subgroups

Net changes in primary care visits in the year after FIT screening for the FP group were greatest among those who underwent a polypectomy but had no pathological finding, with an increase of 0.36 visits (OR, 1.37; 95% CI, 1.27-1.48), whereas those for patients with examination results within normal limits only increased by 0.17 visits (OR, 1.24; 95% CI, 1.18-1.30).

Alternate observation period after positive FIT

When the observation period was shifted to a 12-month period beginning on the day after the diagnostic colonoscopy versus on the day after the positive FIT result for the FIT-positive groups, the net increase in visits was approximately one-half of that observed when the follow-up period commenced immediately after the FIT (Table 3). The exception was the case of the FP group, among whom visit use decreased by 0.10 visits (OR, 0.91; 95% CI, 0.86-0.95).

Monthly cumulative visits

Unadjusted monthly cumulative outpatient primary care visits before and after FIT screening are shown in Figure 1. Findings indicate that the timing of the initiation of increased use varied by major FIT result group: within 1

TABLE 2. Comparison of the Net Change in Outpatient Primary Care Visits Before and After Index FIT by Result Group Among Individuals Treated at Kaiser Permanente Northern California Between 2007 and 2011

		No. of Outpatient Primary Care Visits			
		Before Index FIT[a]	After Index FIT/ Diagnostic Colonoscopy[b]		
FIT Result Group	Total N = 483,216	Mean [SD]	Mean [SD]	Change in Visits, Absolute [SD]	OR (95% CI)[c]
True negative	456,324	2.14 [1.8]	2.17 [2.2]	0.02 [1.9]	Referent
True positive	11,072	2.30 [2.1]	3.05 [3.1]	0.60 [2.3]	1.60 (1.54-1.66)
CRC	1041	2.14 [2.0]	6.27 [4.5]	3.00 [2.7]	7.19 (6.12-8.44)
Advanced adenoma[d]	2500	2.20 [2.0]	2.69 [2.6]	0.44 [2.0]	1.54 (1.42-1.67)
Nonadvanced adenoma[e]	7531	2.36 [2.1]	2.73 [2.6]	0.33 [2.1]	1.36 (1.30-1.43)
False positive	9701	2.54 [2.2]	2.80 [2.7]	0.22 [2.1]	1.27 (1.22-1.33)
Polypectomy/no neoplasia[f]	2496	2.45 [2.1]	2.87 [2.7]	0.36 [2.1]	1.37 (1.27-1.48)
Within normal limits	7205	2.57 [2.2]	2.78 [2.6]	0.17 [2.1]	1.24 (1.18-1.30)
Positive FIT/no colonoscopy	6119	3.61 [3.5]	4.22 [4.2]	0.49 [2.7]	1.50 (1.43-1.58)

Abbreviations: 95% CI, 95% confidence interval; CRC, colorectal cancer; FIT, fecal immunochemical test; OR, odds ratio; SD, standard deviation.
[a] Annualized average of primary care visits within the 2 years before the index FIT.
[b] Annual average of primary care visits within the 1 year after the index FIT result.
[c] Multivariable analysis examining the relationship between the FIT result group and increased outpatient primary care visits after FIT screening, adjusted for age, sex, and Charlson comorbidity score.
[d] Villous and tubulovillous histology.
[e] Nonadvanced adenomas (eg, no villous or tubulovillous histology).
[f] No CRC or adenoma was detected.

TABLE 3. Comparison of Outpatient Primary Care Visits Before and After FIT For True-Negative and Positive FIT/No Colonoscopy and After Diagnostic Colonoscopy for FIT-Positive Groups and Subgroups at Kaiser Permanente Northern California Between 2007 and 2011

		No. of Outpatient Primary Care Visits			
		Before Index FIT[a]	After Index FIT/Diagnostic Colonoscopy[b]		
FIT Result Group	Total N = 483,216	Mean [SD]	Mean [SD]	Change in Visits, Absolute [SD]	OR (95% CI)[c]
True negative	456,324	2.14 [1.8]	2.17 [2.2]	0.02 [1.9]	Referent
True positive	11,072	2.33 [2.1]	2.81 [3.0]	0.34 [2.3]	1.23 (1.19-1.27)
CRC	1041	2.14 [2.0]	6.47 [3.0]	3.00 [2.7]	6.21 (5.33-7.24)
Advanced adenoma[d]	2500	2.20 [2.0]	2.47 [2.5]	0.24 [2.0]	1.21 (1.12-1.31)
Nonadvanced adenoma[e]	7531	2.36 [2.1]	2.47 [2.6]	0.07 [2.1]	1.05 (1.00-1.10)
False positive	9701	2.57 [2.2]	2.50 [2.6]	-0.10 [2.1]	0.91 (0.86-0.95)
Polypectomy/no neoplasia[f]	2496	2.45 [2.2]	65 [2.6]	0.15 [2.1]	1.11 (1.03-1.21)
Within normal limits	7205	2.57 [2.2]	2.50 [2.6]	-0.10 [2.1]	0.91 (0.86-0.95)
Positive FIT/no colonoscopy	6119	3.61 [3.5]	4.22 [4.2]	0.49 [2.7]	1.50 (1.43-1.58)

Abbreviations: 95% CI, 95% confidence interval; CRC, colorectal cancer; FIT, fecal immunochemical test; OR, odds ratio; SD, standard deviation.
[a] Annualized average of primary care visits within the 2 years before the index FIT.
[b] Annual average of primary care visits within the 1 year after the index FIT result for the true-negative and true-positive FIT result/no colonoscopy groups and after the diagnostic colonoscopy for the true-positive and false-positive FIT result groups and subgroups.
[c] Multivariable analysis examining the relationship between FIT result group and increased outpatient primary care visits after FIT screening, adjusted for age, sex, and Charlson comorbidity score.
[d] Villous and tubulovillous histology.
[e] Nonadvanced adenomas (eg, no villous or tubulovillous histology).
[f] No CRC or adenoma was detected.

month to 2 months for the positive FIT/no colonoscopy group; within 2 months to 3 months for the TP group; and within approximately 4 months to 5 months for the FP group. Among the FIT-positive subgroups, an increase in the use of primary care visits among the subgroups of the TP FIT groups (CRC, advanced adenoma, and

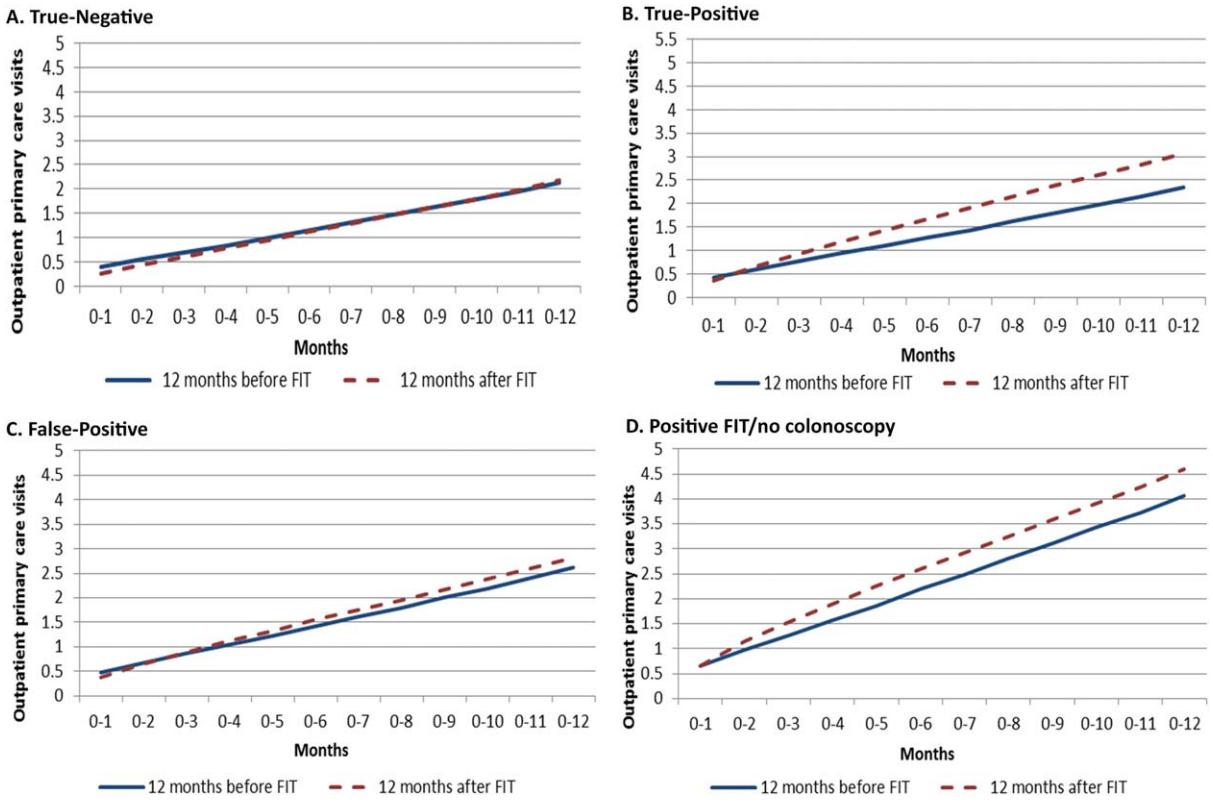

Figure 1. Unadjusted change in cumulative monthly health care use among fecal immunochemical test (FIT) screening result groups comparing the 12-month period before FIT (solid line) with the 12-month period after (dashed line) at Kaiser Permanente Northern California between 2007 and 2011.

nonadvanced adenoma) began 1 month to 2 months after FIT, whereas the increase occurred a little later (2-3 months after FIT) for the polypectomy/no neoplasia subgroup (Fig. 2).

DISCUSSION

We found that, among individuals undergoing CRC screening in a large integrated health care setting, outpatient primary care use after FIT screening increased for all major FIT result groups (TN, FP, and positive FIT/no colonoscopy), but was greatest among those in the TP group (+0.60 visits). This effect was due in part to the subgroup of FIT-positive patients diagnosed with CRC who had a net increase of 3.00 primary care visits in the year after screening. Patients with TP FIT results and diagnosed with an adenoma, with and without advanced histology, also were found to have significant net increases in primary care visits in the year after FIT screening (+0.44 and +0.33 additional visits, respectively). Those with a positive FIT result but who did not complete a diagnostic colonoscopy increased their use by approximately one-half of a visit; among the FP group, those who underwent a polypectomy with no adenoma or CRC detected increased their use by 0.36 visits. Shifting the follow-up time interval for the positive FIT groups from the day after the FIT to the day after the diagnostic colonoscopy resulted in small decreases in primary care visit use. This suggests that little change in primary care use occurs in the period between the positive FIT result and the diagnostic colonoscopy and that the observed increases in use occurred after the definitive diagnosis with colonoscopy for FIT-positive results. That the direction of use reversed for those with a polypectomy with no neoplasia from an increase of 0.17 visits to -0.10 likely reflects the large sample size and potential outliers but requires further investigation.

The findings of the current study support our hypothesis that a positive FIT result may result in an increase in outpatient primary care visit use and are consistent with studies of breast and lung cancer screening, in which health care use was found to increase after an abnormal screening test, even after excluding medically required diagnostic visits.[9,10,25,26] Our hypothesis was framed by the Transactional Model of Stress and

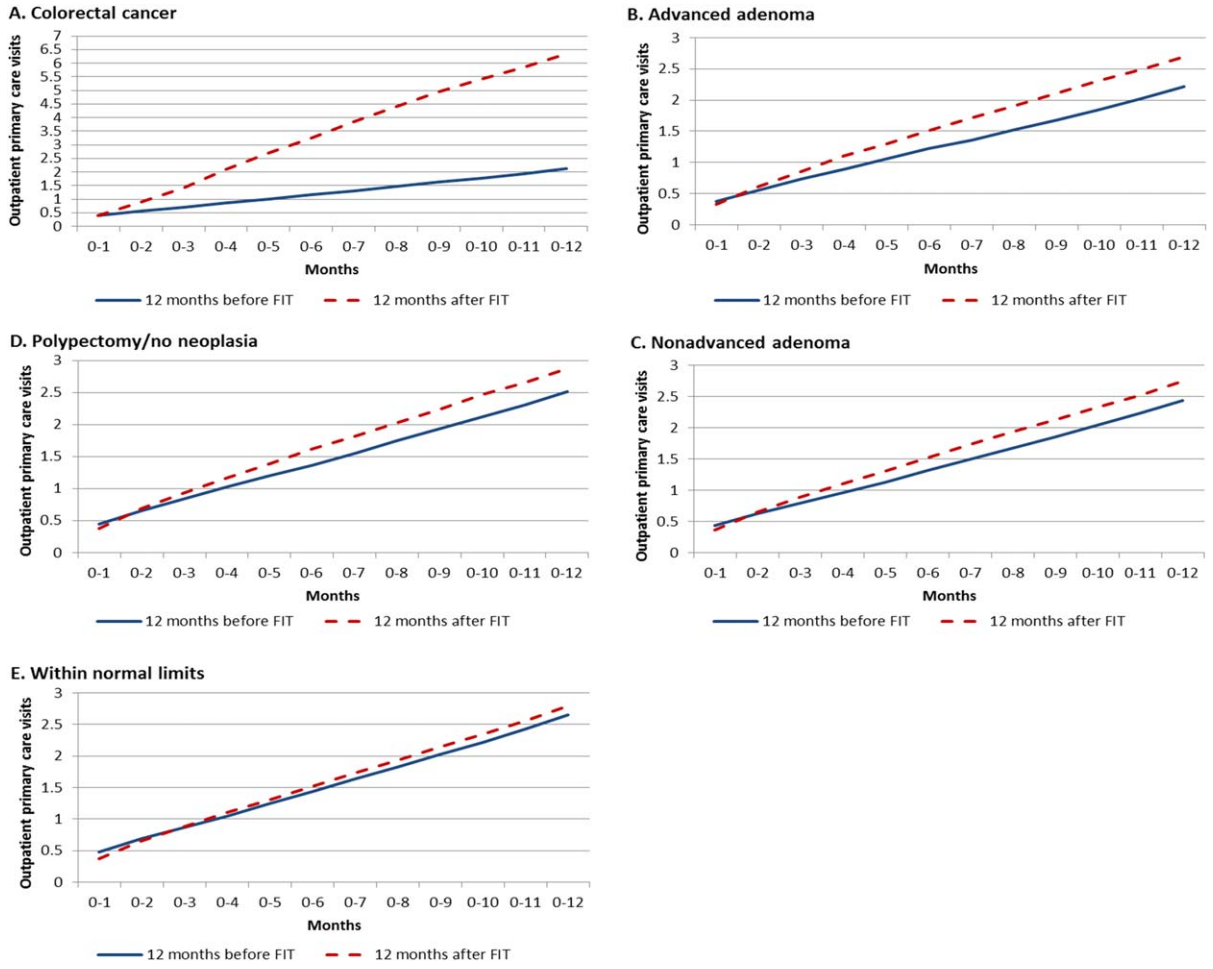

Figure 2. Unadjusted change in cumulative monthly health care use among fecal immunochemical test (FIT)-positive screening result subgroups comparing the 12-month period before FIT with the 12-month period after at Kaiser Permanente Northern California between 2007 and 2011.

Coping,[27-29] which offers a possible explanation as to how the stress of a positive FIT result may upset an individual's psychological well-being such that poor coping efforts drive them toward health care use to restore balance.

Barton et al found that, among enrollees of a large New England health maintenance organization, having positive mammography results that did not yield a cancer diagnosis (FP result) was a significant and independent predictor of a 14% increase (incidence ratio, 1.14; 95% CI, 1.03-1.25) in non-breast-related health care use in the form of breast-related and non-breast-related ambulatory visits and mental health professional visits.[9] Byrne et al[26] examined health care use after screening for lung cancer and found that health care use increased in all result groups but was greatest among those with a suspicious result. A single study conducted among a subsample of participants in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial from a single Midwestern site between 1993 and 1999 evaluated health care expenses after a flexible sigmoidoscopy.[35] Excluding the cost of the diagnostic colonoscopy, medical expenses in the 12 months after a false positive sigmoidoscopy result were found to be nearly double ($P<.0001$) that in the 12-month period before the test. The false positive test was considered to be the primary driver of the increased expenditures.

Another notable finding in the current study was that 22.8% of patients who had a positive FIT result did not undergo a diagnostic colonoscopy within 12 months after their screening test. This group was older, had more comorbid conditions, and had more annual primary care visits both before and after screening compared with the other 3 major FIT result groups; thus, this group likely included some individuals who were not ideal candidates

for CRC screening with FIT. Within KPNC, the monitoring and tracking of diagnostic colonoscopy follow-up is conducted at the local level.[30] Common reasons for patients failing to follow up abnormal results include breadth of services at or distance to specialty clinics, poor communication (eg, no patient reminders), and limited insurance coverage.[36] Investigating factors associated with failure to receive a follow-up diagnostic colonoscopy after a positive FIT result may inform efforts to increase CRC screening adherence and avoid inappropriate FIT screening and the attendant costs among those likely to decline or who cannot complete subsequent diagnostic testing with colonoscopy.

The strengths of the current study include its large size and the ability to adjust for potential confounders such as age and sex and the comprehensive capture of FIT results in a large community-based, diverse population that is similar with regard to socioeconomic characteristics to the region's census demographics. Furthermore, we used validated approaches for capturing pathology data and follow-up colonoscopy examinations, as well as CRC case ascertainment through cancer registries that report to the Surveillance, Epidemiology, and End Results program. Limitations of the current study were that we used an observational study design that precludes assigning and the possible influence of unmeasured confounders, for example, baseline interindividual differences in the use of outpatient visits within the 2 years before FIT, specific socioeconomic factors, family history of adenomas, alcohol and tobacco use, obesity, and sedentary lifestyle. In particular, mental health and substance abuse diagnoses are not included in the Charlson comorbidity index; prior studies have reported that these diagnoses are associated with CRC screening, follow-up testing, and outpatient visit use, and therefore could potentially confound the association between FIT result group and changes in primary care visit use after FIT screening. In addition, the Charlson comorbidity index, which was developed to assess inpatient comorbidity, is less effective in identifying outpatient comorbidities and therefore our comorbidity scores actually may underestimate existing chronic conditions among this patient population, although between 10.0% (TN group) and 21.6% (positive FIT/no colonoscopy group) of individuals were found to have $\geq$2 comorbidities using this measure, which may suggest that this group could be "sicker" at baseline. However, a comparison of mean baseline outpatient visit use between the groups demonstrated that visit use was comparable (overlapping standard deviations), suggesting that, although the positive FIT group has more comorbidity, they do not appear to be using more outpatient visits before FIT. Some of the additional visits observed among patients who underwent a colonoscopy after a positive FIT result may be related to treatment planning for the CRC cases diagnosed or possibly to complications from the colonoscopy procedure (eg, pain or bleeding), particularly among those individuals who underwent a polypectomy. However, because such events are relatively rare, are a direct result of the screening process, and would not be expected in the absence of screening, these visits were not excluded. In addition, although the population studied was similar with regard to characteristics to the region's census demographics, the findings of the current study may not be generalizable to CRC screening in other populations or health care settings.

We observed increases in outpatient primary care visits (albeit the increase was small in some groups) after FIT screening, with usage patterns dependent on test results. We also demonstrated that changes in visit use take place in close proximity to the FIT result. Given the large size of outreach programs, which include the majority of the screening-eligible adult population, even small increases in primary care visit cumulatively can generate large numbers of visits and can have substantial impacts on total health care use. For example, if 1 of every 2 to 3 positive FIT tests results in a single additional visit, the result could be thousands of excess visits, thereby exerting strain on systems and staff. This is of particular interest for a CRC screening test that is assumed to be inexpensive (in cost models, FIT is estimated to be $<$\$20 per test), in which even a modest increase in more costly primary care visits may impact cost-effectiveness assumptions and outcomes. In programs such as the Centers for Disease Control and Prevention's CRCCP, in which resources are limited, additional unaccounted for costs may restrict the allocation of services to those in need.[8] In either case, the management of unexpected costs associated with increased primary care use as a result of FIT requires further modeling and investigation.

Furthermore, the question of whether the observed increase in health care use is beneficial to the patient and is evoked by a negative psychological reaction to the positive test and an ensuing coping behavior is of great interest. Thus, a closer examination of the additional visits and the psychological drivers motivating behavior after a positive FIT screening result represent the next steps in this inquiry. The findings of the current study also underscore the need to account for changes in primary care visit use in the calculation of health care costs associated with screening effectiveness. Further investigation of the specific changes in visit use, the effect of repeated annual FIT

testing on primary care visit use, and the impact of increased primary care visits among those who do not comply with diagnostic colonoscopy and whether this group attends CRC screening in the future and the influence that behavior has on CRC morbidity and mortality in this group is indicated.

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CONFLICT OF INTEREST DISCLOSURES

Alfred Neugut has acted as a paid consultant for Pfizer, Teva Pharmaceuticals, Otsuka Pharmaceuticals, Eisai Pharmaceuticals, and United BioSource Corporation, and has acted as a member of the Medical Advisory Board of EHE International for work performed outside of the current study.

AUTHOR CONTRIBUTIONS

Grace Clarke Hillyer: Study concept and design, analysis and interpretation of the data, drafting of the article, and critical revision. **Christopher D. Jensen**: Analysis and interpretation of the data and critical revision. **Wei K. Zhao**: Analysis and interpretation of the data. **Alfred I. Neugut**: Study concept and design, analysis and interpretation of the data, and critical revision. **Benjamin Lebwohl**: Study concept and design, analysis and interpretation of the data, and critical revision. **Jasmin A. Tiro**: Analysis and interpretation of the data and critical revision. **Lawrence H. Kushi**: Analysis and interpretation of the data and critical revision. **Douglas A. Corley**: Study concept and design, acquisition of the data, analysis and interpretation of the data, and critical revision.

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