A Comparison of Fecal Immunochemical and High-Sensitivity Guaiac Tests for Colorectal Cancer Screening

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OBJECTIVES: **Annual testing using either a high-sensitivity guaiac fecal occult blood test (HS-gFOBT) or a fecal immunochemical test (FIT) is recommended for screening average-risk people for colorectal cancer. We compared the performance characteristics of the HS-gFOBT Hemoccult II SENSA and two FITs (InSure FIT and OC FIT-CHEK) for detecting advanced colorectal neoplasia.**

METHODS: **The study included 1,006 asymptomatic patients, aged 50–75 years, who were scheduled to receive a screening colonoscopy at gastroenterology practices in the Minneapolis and Indianapolis metropolitan areas. Each participant was asked to complete all three stool tests before their colonoscopy. Each test's performance characteristics were evaluated using the screening colonoscopic results as the reference standard.**

RESULTS: **Sensitivity for detecting advanced colorectal neoplasia was highest for InSure FIT (26.3%, 95% confidence interval (CI) 15.9–40.7), followed by OC FIT-CHEK (15.1%, 95% CI 6.7–26.1) and Hemoccult II SENSA (7.4%, 95% CI 1.9–17.0). InSure FIT was statistically significantly more sensitive than both OC FIT-CHEK (absolute difference in sensitivity=11.2%, 95% CI 0.4–24.2) and Hemoccult II SENSA (difference in sensitivity=18.9%, 95% CI 10.2–32.6). Specificities were relatively high for all tests (between 96.8% and 98.6%).**

CONCLUSIONS: **Our results suggest that some FITs are more sensitive than the HS-gFOBT Hemoccult II SENSA, but these results need to be confirmed in larger asymptomatic populations. Comparisons between the FITs examined in this study and other FITs are needed to determine the best tests for population screening.**

SUPPLEMENTARY MATERIAL is linked to the online version of the paper at http://www.nature.com/ajg

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INTRODUCTION

Colorectal cancer is a leading cause of cancer-related morbidity and mortality (1,2). There are several recommended screening options for the population aged ≥50 years at average risk for colorectal cancer, including colonoscopy every 10 years or annual fecal occult blood testing (FOBT) using either a high-sensitivity guaiac FOBT (HS-gFOBT) or a fecal immunochemical test (FIT) (3–5). Colonoscopy has higher sensitivity and specificity than FOBT for detecting advanced colorectal neoplasia; however, using colonoscopy to screen the average-risk population has several disadvantages, including higher cost, increased risk of complications, and limited capacity of the health-care system to perform colonoscopies. In addition, many patients prefer FOBT to colonoscopy; some patients may not be screened at all unless they are offered a stool blood test as an alternative to colonoscopy (6–10).

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Randomized trials have shown that annual or biennial testing using the traditional gFOBT reduces colorectal cancer incidence and mortality (11–15). However, the sensitivity and specificity of traditional gFOBTs is relatively low (16–19). Guaiac FOBTs detect the heme component of hemoglobin molecules because of the pseudoperoxidase activity of heme, which converts guaiac to a blue color when a developer is added. The newer version of the guaiac-based test (HS-gFOBT) added an enhancer to the developer to permit detection of lower levels of peroxidase activity and thereby increase sensitivity, although evidence for higher sensitivity is limited (16,20). A limitation of gFOBTs is that they can produce false-positive or false-negative results with certain foods, vitamins, or medications, so dietary restrictions are generally recommended before the test (3). In addition, three stool samples are recommended for gFOBTs, including the HS-gFOBT.

FIT is a newer type of FOBT that avoids some limitations of the gFOBT. FIT uses antibodies to detect the globin portion of human hemoglobin and does not require dietary restrictions (21). Additionally, some FITs require fewer samples. However, to our knowledge, only one study has directly compared the performance characteristics of a FIT available in the United States with the performance characteristics of the HS-gFOBT Hemoccult II SENSA in an asymptomatic screening population with endoscopic follow-up (16).

To add to the evidence on FOBT performance characteristics for detection of advanced colorectal neoplasia, we conducted a study in an asymptomatic screening population. Specifically, we compared the performance characteristics of the HS-gFOBT Hemoccult II SENSA with the performance characteristics of two FITs (OC FIT-CHEK and InSure FIT), using a screening colonoscopy completed after the stool tests were collected as the reference standard for determining the presence of advanced colorectal neoplasia.

METHODS

Participant recruitment

Participants in this study, the Study of In-home Tests for Colorectal Cancer (SIT), were recruited by two clinical sites: the University of Minnesota (UMN) and Indiana University (IU). UMN participants were recruited from clinics in the Minneapolis, Minnesota metropolitan area (Minnesota Gastroenterology and Park Nicollet Health Services). IU participants were recruited from Indiana University Health clinics in the Indianapolis, Indiana metropolitan area. Participants were enrolled between May 2011 and July 2014. All colonoscopies were performed not later than September 2014. The study protocol was approved by the Institutional Review Boards of the Centers for Disease Control and Prevention, Battelle Memorial Institute, UMN, and IU.

Participant eligibility criteria

Asymptomatic patients aged 50–75 years who were scheduled to have a colonoscopy for colorectal cancer screening were eligible. Patients were ineligible if they were having a colonoscopy because of bleeding or other symptoms or as a follow-up to a positive or abnormal flexible sigmoidoscopy, double-contrast barium enema, computed tomographic colonography, or FOBT. Patients were also ineligible if they had >1 episode of rectal bleeding in the past 6 months, a personal history of colorectal cancer or colorectal polyps, a positive FOBT in the past 12 months, a colonoscopy within the past 5 years, a prior colon resection or other colon/rectal surgery, a history of inflammatory bowel disease, a personal or family history of familial adenomatous polyposis or hereditary nonpolyposis colorectal cancer, were currently taking anticoagulant medication, or were not able to read English. To increase statistical power, most participants enrolled were aged 60–75, as older individuals are more likely to have colorectal neoplasia.

Fecal occult blood tests

Clinical site staff asked participants to complete sample collection for three types of FOBTs (one HS-gFOBT and two FITs) prior to their colonoscopy. The HS-gFOBT was the Hemoccult II SENSA test (manufactured by Beckman Coulter, Brea, CA), which required testing of three stool samples collected on different days. The FITs were the two-sample test InSure FIT (manufactured by Enterix, Edison, NJ), which required testing of two stool samples from different days, and the one-sample test OC FIT-CHEK (marketed by Polymedco, Cortlandt Manor, NY). For the two FITs, the cutoff values for positivity were the standard values used in the United States, as this study was designed to look at the performance characteristics of these tests in usual clinical practice. For InSure FIT, the cutoff value for positivity was 50 μg hemoglobin (Hb)/gram (g) of feces. For OC FIT-CHEK, the cutoff value was 20 μg Hb/g of feces. For each test, only one sample needed to be positive for the test to be considered positive.

Participants were randomly assigned to one of six equal-sized groups; each group completed the three FOBTs in a different order. After each FOBT was completed, the participant mailed it to a central laboratory for analysis (Hemoccult II SENSA to Emory University Hospital laboratory, Atlanta, GA; InSure FIT to Quest Diagnostics, Tucker, GA; and OC FIT-CHEK to Kaiser Permanente Regional Laboratory, Atlanta, GA). Participants were sent a monetary incentive of $100 for study participation.

Colonoscopy and pathology

A colonoscopy was performed by the clinic where the patient was recruited. Two pathologists at each clinic independently reviewed the pathology specimens from the colonoscopies. If the two pathologists did not agree, the pathology specimens were reviewed by a third pathologist.

Our primary definition of advanced colorectal neoplasia included any of the following colonoscopy findings confirmed by pathology: tubular adenoma with a size ≥10 mm, sessile serrated polyp with dysplasia, villous adenoma, tubulovillous adenoma, adenoma with high-grade dysplasia, or invasive carcinoma.

Study population

In total, 3,985 patients were screened for eligibility and invited to enroll; 1,382 patients met initial eligibility criteria and signed a

consent form. Of these, 1,095 (79.2%) participants completed the colonoscopy, the gFOBT, and at least one FIT. The test result for the gFOBT or FIT was considered invalid if the time from sample collection to laboratory analysis was greater than recommended by the manufacturer (>14 days for Hemoccult II SENSA or InSure FIT or >15 days for OC FIT-CHEK). Participants were excluded if they did not have a valid test result for the gFOBT and at least one of the two FITs, if the time from the first FOBT sample collection date to the colonoscopy was >100 days, or if tissue was removed during the colonoscopy but they did not have a second pathology review. In addition, unless advanced colorectal neoplasia was found, participants were excluded if bowel preparation was rated as inadequate or poor or if the cecum was not visualized. After these exclusions, 1,006 (72.8%) participants remained in the primary analysis. Because of the exclusion criteria, all these participants had completed the Hemoccult II SENSA test. A total of 947 also had a valid OC FIT-CHEK test result and 987 had a valid InSure FIT test result; 928 (67.1%) participants had valid results for all three stool tests.

Statistical analysis

Positivity rates and performance measures were calculated for each FOBT. Performance measures included sensitivity, specificity, positive predictive value, and likelihood ratios. To ensure that the correlated nature of the three FOBT tests was accounted for in the variability of the estimates and comparisons, bias-corrected estimates of performance measures were calculated from 2,000 bootstrap samples (22) drawn from the original sample using the bootstrap function in R (23). Point estimates and pairwise differences in sensitivity and specificity were calculated for each FOBT type and across covariate subgroups within each FOBT type. Ninety-five percent confidence intervals (CIs) were calculated using the adjusted bootstrap percentile method. Differences were considered statistically significant if the 95% CI for the difference estimate did not include zero. For subgroup analyses with <10 advanced colorectal neoplasia cases or with zero counts in a cell, CIs were not calculated for differences. Statistical analysis was performed with SAS software version 9.3 (SAS Institute, Cary, NC) and R version 3.2.5 (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Demographic and medical history characteristics of study participants are presented in **Table 1**. To increase statistical power, most participants enrolled were aged 60–75 years (61.5%). Participants were slightly more likely to be female (54.5%). Participant-reported race was primarily white (87.0%); 10.6% were black or African American, and few participants were Hispanic or Latino (2.5%). Most participants (86.8%) did not report a first-degree family history of colorectal cancer. Most participants (73.3%) had a prior colorectal cancer screening test (**Table 1**).

Advanced colorectal neoplasia was found on colonoscopy in 5.5% of participants (*N*=55), including two invasive cancers (**Table 2**). The other types of advanced findings are listed in

Table 1. Demographic and medical history characteristics of study participants (*N*=1006)

Characteristic	*N*[a] (%)
Gender	
Male	458 (45.5%)
Female	548 (54.5%)
Age at enrollment (years)	
50–54	160 (15.9%)
55–59	227 (22.6%)
60–75	619 (61.5%)
Race	
Black or African American	106 (10.6%)
White	871 (87.0%)
Other[b]	24 (2.4%)
Ethnicity	
Hispanic or Latino	25 (2.5%)
Not Hispanic or Latino	974 (97.5%)
Clinical site	
University of Minnesota	800 (79.5%)
Indiana University	206 (20.5%)
Family history of colorectal cancer reported	
Yes	133 (13.5%)
No	873 (86.8%)
Cancer screening history	
Any prior colorectal cancer screening[c]	
Yes	726 (73.3%)
No	265 (26.7%)
Prior FOBT (no positives in the past year)	
Yes	367 (36.8%)
No	629 (63.2%)
Prior colonoscopy	
Never	392 (39.6%)
>5–<10 years ago	292 (29.5%)
≥10 years ago	306 (30.9%)
Ever had a flexible sigmoidoscopy	
Yes	266 (26.8%)
No	726 (73.2%)
Ever had a CT colonography	
Yes	5 (0.5%)
No	994 (99.5%)
Ever had a double-contrast barium enema	
Yes	65 (6.7%)
No	909 (93.3%)

CT, computed tomography; FOBT, fecal occult blood test.
[a]Numbers may not sum to total due to missing data. Percentages were calculated after excluding participants with missing data.
[b]"Other" race includes American Indian or Alaska Native, Asian, Native Hawaiian or Other Pacific Islander, and mixed race.
[c]Reported prior FOBT, colonoscopy, flexible sigmoidoscopy, CT colonography, or double-contrast barium enema.

Table 2. Findings in study participants with advanced colorectal neoplasia (*N*=55)

Type of advanced finding	Number with only this type of advanced finding (unless noted)[a,b]
Any advanced colorectal neoplasia[c]	55
Invasive carcinoma[a]	2
Tubular adenoma with size ≥10 mm	36
Sessile serrated polyp with dysplasia	4
Villous adenoma	0
Tubulovillous adenoma	7
Adenoma with high-grade dysplasia	0
Multiple advanced findings[b]	6

[a]One of the cases with invasive carcinoma also had a villous adenoma.
[b]Cases with multiple findings had:
(a) tubular adenoma with size ≥10 mm and adenoma with high-grade dysplasia (2 cases)
(b) tubular adenoma with size ≥10 mm and tubulovillous adenoma (1 case)
(c) tubular adenoma with size ≥10 mm and sessile serrated adenoma with cytological dysplasia (1 case)
(d) tubulovillous adenoma and adenoma with high-grade dysplasia (2 cases).
[c]Any of the following colonoscopic findings confirmed by pathology: tubular adenoma with a size of ≥10 mm, sessile serrated polyp with dysplasia, villous adenoma, tubulovillous adenoma, adenoma with high grade dysplasia, or invasive carcinoma.

Table 2. One of the cancer cases had positive Hemoccult II SENSA and InSure FIT tests but a negative OC FIT-CHEK test. The other cancer case was negative for all three stool tests. A total of 344 participants had one or more adenomas detected on colonoscopy for an adenoma detection rate (ADR) of 34.2%. The ADR was 40.4% for males and 29.0% for females. For the UMN site, the ADR was 38.5% for males and 26.5% for females. For the IU site, the ADR was 49.4% for males and 37.6% for females (data not shown).

Stool test performance characteristics for advanced colorectal neoplasia are presented in **Table 3**. Of the three stool tests, InSure FIT had the highest positivity (4.5%) and the highest sensitivity for advanced colorectal neoplasia (26.3%, 95% CI, 15.9–40.7) but also had the lowest specificity (96.8% (95% CI, 95.5–97.8)). In contrast, the Hemoccult II SENSA had the lowest positivity (1.7%) and the lowest sensitivity (7.4%, 95% CI, 1.9–17.0) but the highest specificity (98.6%, 95% CI, 97.7–99.2). Differences between Hemoccult II SENSA and InSure FIT were statistically significant for both sensitivity (difference=18.9%, 95% CI, 10.2, 32.6) and specificity (difference=−1.8%, 95% CI,−3.3, −0.7). For the OC FIT-CHEK, estimates for performance characteristics were between the values for InSure FIT and Hemoccult II SENSA (positivity of 3.0%, sensitivity of 15.1% (95% CI, 6.7–26.1), specificity of 97.8% (95% CI, 96.6–98.6)). The difference in sensitivity between OC FIT-CHEK and InSure FIT was statistically significant (difference=11.2%, 95% CI, 0.4, 24.2).

Stool test performance characteristics for serrated lesions of any size (sessile serrated polyps, sessile serrated polyps with dysplasia, or traditional serrated adenomas) are presented in **Table 4**. Sensitivity for serrated lesions was low for all three stool tests, ranging from 2.6% to 5.2%.

We also examined sensitivity and specificity among subgroups of participants, although statistical power was limited. Results were similar to the overall results when we excluded patients with a known family history of colorectal cancer in first-degree relatives or patients with a recent colorectal cancer screening test (colonoscopy within the past 10 years, double-contrast barium enema, computed tomographic colonography, or sigmoidoscopy within the past 5 years). Results were also similar when we performed analyses in the 928 patients with valid results for all three stool tests (see **Supplementary Table S1** online). There were no statistically significant differences in sensitivity or specificity when the population was stratified by age (50–59 vs. 60–75), gender, or race (African-American vs. white), although the comparisons of OC FIT-CHEK sensitivity and specificity by race, Hemoccult II SENSA sensitivity by age and race, and InSure FIT sensitivity by race were not possible due to small counts in some cells.

There were no statistically significant differences in sensitivity or specificity when the population was stratified by the time from stool collection to laboratory analysis (≤7 days vs. ≥8 days) or by season of stool collection (May–September vs. October–April). Positivity rates were lower for each stool test for the hotter months of May–September compared with October–April, but this difference was only statistically significant for InSure FIT.

When we expanded the definition of advanced colorectal neoplasia to include sessile serrated polyps with a size ≥10 mm (*N*=15), the sensitivity for each stool test was reduced (5.8% for Hemoccult II SENSA, 11.8% for OC FIT-CHEK, 20.5% for InSure FIT). The sensitivity for each stool test was further reduced when we also added ≥3 conventional adenomas of any size (*N*=33) to this definition of advanced colorectal neoplasia (3.9% for Hemoccult II SENSA, 11.0% for OC FIT-CHEK, 16.1% for InSure FIT).

DISCUSSION

In this study, we compared the test performance characteristics of the HS-gFOBT Hemoccult II SENSA with the performance characteristics of two FITs in an asymptomatic population undergoing screening colonoscopy. Specificities were relatively high for all of the tests (between 96.8% and 98.6%). Sensitivity for advanced colorectal neoplasia was higher for the two FITs than for the HS-gFOBT Hemoccult II SENSA, although none of the stool tests had a sensitivity for advanced colorectal neoplasia >30%. InSure FIT had the highest sensitivity (26.3%), followed by OC FIT-CHEK (15.1%) and Hemoccult II SENSA (7.4%).

We could only find one previous study of InSure FIT that compared FIT results, whether positive or negative, with colonoscopic results. In a small study of 304 patients, of whom approximately one-third had a personal history of colorectal neoplasia, the sensitivity for advanced colorectal neoplasia was 36% (95% CI, 18–53), slightly higher than we found, although within our 95% confidence bounds (24). The specificity was 92% (95% CI, 89–96), lower than we found and outside our 95% confidence bounds.

Table 3. Performance characteristics of immunochemical and guaiac fecal occult blood tests for detection of advanced colorectal neoplasia (*N*=1006)

	Advanced colorectal neoplasia on colonoscopy		Positivity (%)	Sensitivity[a]		Specificity[a]		PPV[a]		Likelihood ratio[a]	
	Yes	No		(%)	(95% CI)[b]	(%)	(95% CI)[b]	(%)	(95% CI)[b]		(95% CI)[b]
Stool test result											
InSure FIT											
Positive	14	30	4.5	26.3	(15.9–40.7)	96.8	(95.5–97.8)	31.8	(19.0–47.1)	8.5	(4.4–14.3)
Negative	39	904									
OC FIT-CHEK											
Positive	8	20	3.0	15.1	(6.7–26.1)	97.8	(96.6–98.6)	28.7	(12.5–46.4)	7.2	(2.6–14.3)
Negative	45	874									
Hemoccult II SENSA											
Positive	4	13	1.7	7.4	(1.9–17.0)	98.6	(97.7–99.2)	23.6	(6.3–50.0)	5.8	(1.1–16.0)
Negative	51	938									
Difference between test results[c]											
InSure FIT–OC FIT-CHEK				11.2	(0.4, 24.2)	–1.0	(–2.4, 0.5)				
InSure FIT–Hemoccult II SENSA				18.9	(10.2, 32.6)	–1.8	(–3.3, –0.7)				
OC FIT-CHEK–Hemoccult II SENSA				7.8	(–1.4, 19.1)	–0.9	(–2.2, 0.3)				

CI, confidence interval; PPV, positive predictive value.
[a]Point estimates were based on bias-corrected estimates from 2,000 bootstrap samples drawn from the original sample.
[b]Ninety-five percent confidence intervals were calculated using the adjusted bootstrap percentile method (bias-corrected and accelerated).
[c]Difference in sensitivity or specificity between the stool tests.

There have been several studies of the OC FIT-CHEK family of FITs. This family of FITs includes tests with different names (such as OC-Micro, OC-Sensor, and OC-SENSA Micro) manufactured by Eiken Chemical Company (Tokyo, Japan) and marketed in the United States by Polymedco. In our study, we tested one stool sample using OC FIT-CHEK with a cutoff value for positivity of 20 μg Hb/g of feces, the cutoff value used in the United States. Other studies that have examined the one-sample OC FIT-CHEK (or comparable FIT tests with different names) at this cutoff value, and that used colonoscopy follow-up for all patients, have reported sensitivities for advanced colorectal neoplasia ranging from 24% to 33%, somewhat higher than in our study and some exceeding our 95% confidence bounds (25–29). The specificity for FIT in these studies ranged from 95 to 97%, similar to the specificity in our study (25–29).

To our knowledge, only one previous study of asymptomatic patients has reported Hemoccult SENSA performance characteristics for advanced colorectal neoplasia with colonoscopy follow-up for all patients (20). In this study, the sensitivity for Hemoccult SENSA was 21% for advanced colorectal neoplasia, higher than our upper confidence bound, with a specificity of 97%, consistent with our confidence bounds. Another study followed up positive Hemoccult SENSA tests with colonoscopy and negative Hemoccult SENSA tests with sigmoidoscopy (16). They found an even higher sensitivity of 41% for large distal adenomas, with a much lower specificity than we found (91%).

For all three stool tests, we found that the sensitivity for serrated lesions was low. Our results are consistent with previous studies of serrated lesions (27,30,31). The low single-test sensitivity for serrated lesions may be due to the fact that serrated lesions are less likely to bleed (32). We were unable to examine the performance characteristics for large or advanced serrated lesions separately because of the small number of these lesions.

Results for a specific type of FIT cannot be generalized to other types of FIT. In our study, the two FITs appeared to differ in their performance characteristics, although only the difference in sensitivity was statistically significant. It should be noted that in our study the performance characteristics of each FIT were measured at different cutoff values for positivity and required different numbers of stool samples, as recommended by each FIT's manufacturer and as used in standard clinical practice in the United States. However, even with the same cutoff value and number of samples, the performance characteristics of different FITs can vary (33,34). Factors that can affect performance characteristics, other than cutoff concentration, include use of different antibodies that detect different epitopes and different immunoassay methods (21,33,35). Also, the buffers used in FITs can contain different preservatives, which can affect performance characteristics (34–36).

Table 4. Performance characteristics of immunochemical and guaiac fecal occult blood tests for detection of serrated lesions (*N*=1006)

	Serrated lesions on colonoscopy		Sensitivity[a]		Specificity[a]		PPV[a]		Likelihood ratio[a]	
	Yes	No	(%)	(95% CI)[b]	(%)	(95% CI)[b]	(%)	(95% CI)[b]		(95% CI)[b]
Stool test result										
InSure FIT										
Positive	4	40	5.2	(1.4–12.9)	95.6	(94.1–96.8)	9.1	(2.3–22.5)	1.2	(0.3–3.3)
Negative	72	871								
OC FIT-CHEK										
Positive	3	25	4.2	(1.2–11.4)	97.1	(95.9–98.1)	10.9	(0.0–27.8)	1.5	(0.3–4.8)
Negative	69	850								
Hemoccult II SENSA										
Positive	2	15	2.6	(0.0–8.7)	98.4	(97.4–99.0)	11.9	(0.0–33.9)	1.7	(0.0–6.2)
Negative	76	913								
Difference between test results[c]										
InSure FIT–OC FIT-CHEK			1.0	(–3.0, 7.1)	–1.5	(–3.2, 0.1)				
InSure FIT–Hemoccult II SENSA			2.6	(–1.4, 9.3)	–2.8	(–4.2, –1.4)				
OC FIT-CHEK–Hemoccult II SENSA			1.6	(–2.3, 7.1)	–1.2	(–2.6, 0.1)				

CI, confidence interval; PPV, positive predictive value.
[a]Point estimates were based on bias-corrected estimates from 2,000 bootstrap samples drawn from the original sample.
[b]Ninety-five percent confidence intervals were calculated using the adjusted bootstrap percentile method (bias-corrected and accelerated).
[c]Difference in sensitivity or specificity between the stool tests.

For any FOBT, including FITs, hemoglobin concentration may degrade during the time from sample collection to analysis, particularly at higher temperatures (33,35,37). Buffers are used to stabilize the hemoglobin during this time but can differ in their ability to stabilize hemoglobin (35). Some manufacturers have changed or are considering changing the buffer to improve stability. Some, but not all, studies have found that time or temperature affects sensitivity or positivity rates (35,38–40). We excluded patients whose time from sample collection to laboratory analysis was greater than 14 or 15 days, as recommended by the manufacturer. We found no statistically significant differences in sensitivity or specificity by season when the stool was collected (May–September vs. October–April) or time from stool collection to laboratory analysis (≤7 days vs. ≥8 days), but our power was limited. We did find that positivity rates were lower for each stool test for the hotter months of May–September, but the differences were only statistically significant for InSure FIT.

In our study, unlike many prior studies, the tests were conducted under conditions similar to those encountered in "real-world" clinical practice, including mailing of the tests to the laboratory without refrigeration during the mailing process. Some of the small number of previous studies found test sensitivities higher than we found. We do not know the reason for these differences, but these differences may have been due to chance or due to the conditions under which the tests were conducted.

Our study had several limitations. We did not have enough colorectal cancer cases to assess the sensitivity and specificity for cancer. Sensitivity for cancer would be expected to be higher than sensitivity for advanced colorectal neoplasia. We also had limited power to examine sensitivity for advanced colorectal neoplasia, particularly within subgroups. In addition, as in prior studies, we were only able to look at one-time screening instead of a program of annual stool test screening over multiple years. The one-time sensitivity for advanced colorectal neoplasia for the stool tests was relatively low, but sensitivity should be higher if the tests are performed annually as recommended by guidelines (5,41).

The 2016 US Preventive Services Task Force recommendations for colorectal cancer screening include either annual FIT or HS-gFOBT (5). In our study, one of the two FITs we examined, the InSure FIT, had significantly higher sensitivity than the other FIT (OC FIT-CHEK) and the HS-gFOBT (Hemoccult II SENSA). The OC FIT-CHEK also had higher sensitivity than the Hemoccult II SENSA, although the difference was not statistically significant. Our results suggest that some FITs are more sensitive than the HS-gFOBT Hemoccult II SENSA, but these results need to be confirmed in larger asymptomatic study populations. Some FITs that are currently on the market do not have published literature to support their use. Comparisons between the two FITs examined in this study and other brands of FITs on the market are needed to determine which tests are most suitable for population screening for asymptomatic individuals.

CONFLICT OF INTEREST

Guarantor of the article: Jean A. Shapiro, PhD.

Specific author contributions: Planning the study: Shapiro, Bobo, Church, Rex, Chovnick, Zauber, Lieberman, Levin, Nadel; conducting the study: Shapiro, Bobo, Church, Rex, Chovnick; collecting data: Shapiro, Bobo, Church, Rex, Chovnick; interpreting data and drafting the manuscript: Shapiro, Bobo, Church, Rex, Chovnick, Thompson, Zauber, Lieberman, Levin, Joseph, Nadel. All authors have approved the submitted manuscript.

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DISCLAIMER

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. Use of trade names in this report is for identification only and does not imply endorsement by the US Department of Health and Human Services.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Recommended colorectal cancer screening options include a high-sensitivity guaiac fecal occult blood test (HS-gFOBT) or a fecal immunochemical test (FIT).
- ✓ FITs vary in their performance characteristics.
- ✓ There is limited data comparing the performance characteristics of FITs to the HS-gFOBT.

WHAT IS NEW HERE

- ✓ One of the FITs studied (InSure FIT) had significantly higher sensitivity for advanced colorectal neoplasia than the other FIT (OC FIT-CHEK) and the HS-gFOBT (Hemoccult II SENSA).
- ✓ Our results suggest that some FITs are more sensitive than the HS-gFOBT Hemoccult II SENSA.

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