Comparison of a Brush-Sampling Fecal Immunochemical Test for Hemoglobin With a Sensitive Guaiac-Based Fecal Occult Blood Test in Detection of Colorectal Neoplasia

Alicia Smith[1,2]
Graeme P. Young, MB, BS, MD[2,3]
Stephen R. Cole[1,2]
Peter Bampton, MB, BS, MD[4]

[1] Bowel Health Service, Repatriation General Hospital Daw Park, South Australia, Australia.

[2] Department of Medicine, Flinders University of South Australia, Bedford Park, South Australia, Australia.

[3] Gastrointestinal Services, Flinders Medical Centre, Bedford Park, South Australia, Australia.

[4] Department of Endoscopy, Flinders Medical Centre, Bedford Park, Adelaide South Australia, Australia

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Address for reprints: Graeme P. Young, MB, BS, MD, Department of Gastroenterology and Hepatology, Flinders Medical Centre, Bedford Park, South Australia, Australia 5042; Fax: (011) 61 8 8204 3943; E-mail: graeme.young@flinders.edu.au

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BACKGROUND. Fecal immunochemical tests (FIT) are an advanced fecal occult blood test (FOBT) technology that reduces barriers to population screening by simplifying the logistics of stool-sampling. The current study was conducted to undertake a paired comparison of a sensitive guaiac FOBT (GFOBT; Hemoccult II Sensa, Beckman Coulter, Fullerton, CA) with a brush-sampling FIT (InSure; Enterix, North Ryde, NSW, Australia), to determine whether this FIT improves detection of significant neoplasia.

METHODS. Individuals sampled consecutive stools, at home, with both FIT and GFOBT sampling devices while following dietary restrictions appropriate for GFOBT. Study populations included a screening cohort (n = 2351) and a symptomatic diagnostic group (n = 161). Paired comparison of positivity rates was undertaken in those found to have cancer and/or significant adenoma (high-grade dysplasia, villous change, ≥10 mm, serrated histology or ≥3 polyps), benign pathology, or no pathology.

RESULTS. Combined results for both cohorts showed that the FIT returned a true-positive result significantly more often in cancer (n = 24; 87.5% vs. 54.2%) and in significant adenomas (n = 61; 42.6% vs. 23.0%). Of all UICC Stage I cancers, the FIT was positive in 12 of 13 compared with 4 of 13 with the GFOBT ($P = .002$). In analyses of just the screening cohort, the FIT remained significantly better at detecting cancers and significant adenomas; the false-positive rate for any neoplasia was marginally higher with the FIT than the GFOBT (3.4% vs. 2.5%; 95% CI of difference, 0–1.8%), whereas positive predictive values were 41.9% and 40.4%, respectively.

CONCLUSIONS. This brush-sampling FIT is more sensitive for cancers and significant adenomas than a sensitive GFOBT. As such, it should deliver greater reductions in colorectal cancer mortality and incidence than the GFOBT. ***Cancer* 2006;107:2152–9.** © *2006 American Cancer Society.*

KEYWORDS: colorectal cancer, screening, fecal occult blood test, immunochemical test, guaiac.

Colorectal cancer (CRC) screening is usually undertaken as a one-step or two-step process depending on whether colonoscopy is used as the only test or its use is preceded by a simpler test to determine who undergoes colonoscopy.[1] Fecal occult blood tests (FOBT) have been the traditional first-step test in the two-step process.[2] Their value is proven in randomized controlled trials at the population level.[3–6] FOBTs meet World Health Organization requirements[7] in that they are simple screening tests that serve to select

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those with a higher probability of having CRC.[1] FOBTs succeed because they are simple, inexpensive, convenient, and draw persons into the screening process, especially when they are reticent to undergo colonoscopy or where colonoscopic resources are inadequate for widespread population screening.[8]

In recent years, however, the adequacy of guaiac-based tests (GFOBT) relative to colonoscopy has been questioned,[9,10] even though they are included as options in guidelines for screening.[2,11] This has been reflected in a reduction in use of FOBT and an increase in use of colonoscopy, even though providers struggle to meet demand and many patients have no colorectal neoplasia.[8] A factor driving increased colonoscopic use is that advanced colonic neoplasms may be missed by a 1-time GFOBT screen. One-time sensitivity of the original GFOBT Hemoccult II (Beckman Coulter, Fullerton, California) for cancer appears to be less than 50%[13] and perhaps even lower.[14] Another study observed that 24% of advanced neoplasms are missed by 1-time GFOBT plus flexible sigmoidoscopy.[12] To improve sensitivity of GFOBT, rehydration has been used,[3] and newer GFOBT have been specifically designed to be more sensitive and readable.[13,15,16,17]

The logistics of performing GFOBTs also lead to questions concerning their usefulness.[1,16] GFOBTs detect peroxidase activity of heme in feces. Dietary peroxidases (found in a range of certain fruit and vegetables, especially if raw) can cause false-positive results with GFOBT. Antioxidants such as vitamin C may interfere with the chemistry of the reaction to cause false-negative results. Dietary heme from red meat also causes false-positives.[18] Nonsteroidal anti-inflammatory drugs (NSAIDs) can lead to microbleeding in the absence of colorectal pathology.[19] Screening by GFOBT is more accurate if these variables are controlled by proscription. This makes screening less convenient and reduces participation in screening.[20]

A newer immunochemical technology specifically detects human hemoglobin in stools.[1,8] This fecal immunochemical test (FIT) technology is not affected by any of the above variables. As globin is rapidly digested in stomach and small intestine, FITs are more selective than GFOBTs for occult bleeding of colorectal origin.[1,21] Early versions of FIT have been shown to be as sensitive for cancer but to have superior specificity compared with Hemoccult II Sensa and to be more sensitive, but with slightly lower specificity, compared with Hemoccult II.[13]

Stool-sampling processes have also evolved with the introduction of FIT. The original wooden spatula used with early GFOBT required multiple sampling from the surface of a stool kept clear of the toilet bowl water.[22] Sampling for some FITs requires a probe to be inserted into the stool, whereas others sample toilet bowl water from around the immersed stool.[23] These new sampling methods can result in substantially higher population participation rates when compared with GFOBT[24] and, if shown to have comparable or better performance, may be more appropriate for population screening.

FIT technology has not been subjected to the rigor of a randomized, controlled trial, but if it can be shown that FIT technology is more sensitive than GFOBT for advanced neoplasia, then a trial with mortality as the endpoint is unnecessary.[25] In this study, we undertook a head-to-head, paired comparison of relative performances of a sensitive GFOBT with a brush-sampling FIT to determine whether this FIT technology is a useful improvement in detection of neoplasia, especially of advanced adenomas, as adenoma removal reduces the incidence of colorectal cancer.[6]

MATERIALS AND METHODS

Study Populations

In the screening population, the decision to undertake colonoscopy was based first on the FOBT result and subsequently on identification of a high-risk setting when the FOBT was negative. The offer of screening occurred in either of two contexts. One, a community population comprised of persons at unknown risk for colorectal cancer was identified randomly from the general population in urban southern Adelaide. People aged 50–75 years were invited by mail to participate. Methods for selecting those from the Commonwealth Electoral Roll to be offered screening have been previously described in detail.[24] Many were participating in a screening test for the first time. All of those with a positive test were recommended to undergo colonoscopy. Participants were recruited during the period July 2002 to September 2004. The second was derived from a screening clinic based at Flinders Medical Centre and Repatriation General Hospital, where many patients go because of perceived risk for colorectal cancer based on family history or past colorectal adenoma.[26] Asymptomatic patients in the clinic database were offered screening by FOBT in the first instance, and, when a familial history or prior neoplasia was confirmed, colonoscopy was subsequently offered according to National Health and Medical Research Council of Australia guidelines[27] regardless of FOBT results. People were recruited over the period June 2000 to September 2004.

A diagnostic population was also recruited. Patients seen at either of the 2 institutions were considered for inclusion in the study if they were scheduled for diagnostic colonoscopy during the period April 2002 to September 2003. To be eligible, patients had to be capable of following instructions and be able to sample stools before performing bowel preparation for colonoscopy. Patients were ineligible if they had recent overt bleeding, a known benign colonic disorder likely to cause bleeding, or if they had previously undergone colorectal surgery.

Ethical approval for these studies was obtained from the Research and Ethics Committee, Repatriation General Hospital (RGH), Daw Park and the Flinders Clinical Research Ethics Committee, Flinders Medical Centre, Bedford Park. All persons participating in the study gave informed consent in compliance with Australia's National Health and Medical Research Council (NHMRC) guidelines.

Offer of Screening Test

Screening population

A letter offering screening was sent from the central screening service (Bowel Health Service, Repatriation General Hospital) accompanied by 1) an information sheet on screening for colorectal cancer, 2) stool sample collection kits for each of the 2 tests (InSure [Enterix Inc, North Ryde, NSW, Australia] and Hemoccult II Sensa [Beckman Coulter Inc., Fullerton, CA]) with instructions, 3) a brief questionnaire seeking personal details including risk status and preferred physician for follow-up, 4) a consent form, and 5) a reply-paid envelope for returning completed tests.

Invitees were asked to sample stools using the provided kits and to return samples by mail to the Bowel Health Service. They were asked to sample 2 consecutive stools by using the brush-sampling method characteristic of InSure[23] according to manufacturer's instructions. For Hemoccult II Sensa, they were asked to sample 3 consecutive stools by using the traditional spatula method[28] according to manufacturer's instructions. They were also asked to follow the manufacturer's instructions on diet and drug restrictions. Because the 2 tests use quite different stool sampling methods, sampling for each must be performed on separate stools.

Diagnostic population

Patients with symptoms that raise the possibility of a diagnosis of CRC were recruited before they proceeded to diagnostic colonoscopy or surgery. They were not recruited when they were found to have overt bleeding as a reason for colonoscopy. Instructions for stool sampling for these patients were the same as those for the screening populations.

The FIT

InSure uses immunochromatographic technology with a monoclonal capture antibody (raised against the beta subunit of human hemoglobin) and polyclonal antibodies (conjugated to colloidal gold) specifically to detect human globin.[23] The InSure test kit has 3 principal components: 2 brushes for sample collection; a test card for receiving, stabilizing, and transporting the samples to the test site; and an immunochromatographic test strip that is inserted into the test card at the laboratory for test development.

Each invitee was instructed to obtain a sample from each of 2 consecutive bowel actions by using the provided brushes to briefly brush the surface of the stool as it lay in the toilet bowl water. The brush is then applied to 1 of the 2 windows of the test card so that the water that is retained within the bristles of the brush is deposited. The second bowel action was to be similarly sampled.

At the laboratory, a test strip is inserted into the test card and a liquid reagent is added to the card. The reagent mobilizes the samples in the card and transfers them to the test strip. When blood is present in either sample (they cannot be read independently), 2 pink lines develop on the test strip. The appearance of only 1 line (the control line) indicates that the test is complete and that no blood was detected.

Within 5 days of receipt, test cards were developed by an automated process at the Enterix Australia P/L facilities in Sydney by operators unaware of an individual's details. Only test cards returned within the shelf life of the cards and within 14 days of sample application were developed. Test result was assessed visually and classified as positive or negative according to whether a pink line formed at the test position. Two observers independently read results and were unaware of the participant's clinical status.

The GFOBT

Hemoccult II Sensa is a well-described guaiac test.[28] Each invitee was instructed to commence the diet and drug restrictions and 3 days later to commence sampling from each of 3 consecutive bowel actions by using the spatulas provided. They were asked to keep the stool clear of the toilet bowl water using a paper saddle. Two samples were taken from separate points on the surface of each bowel movement, and each sample was smeared onto 1 of the 2 windows on the card for that stool. At the Bowel Health Ser-

vice and within 5 days of receipt, cards were developed by a trained technician with the Hemoccult II Sensa developer under tightly controlled conditions where each card window was examined carefully for 1 min for any appearance of a blue color, no matter how transient. Appearance of any blue color in any test card window was considered a positive result. Only test cards returned within the shelf life of the cards and within 14 days of sample application were developed. A second reader independently verified the result. Agreement between readers was at least 99%, and any disagreement was resolved by consensus. Both readers were unaware of the participant's clinical status.

This paired design increased the power of the comparison. It was not possible to sample exactly the same stools as one test requires stool to be sampled while in the toilet bowl water, whereas the other test requires stool to be sampled while clear of water.

Case Categorization by Diagnosis

Diagnostic categories were allocated by the colonoscopist, according to preset criteria: cancer (or probable cancer), polyp, diverticular disease, hemorrhoids, other pathology, or normal. In some cases, the colonoscopist was aware of the positive FOBT result but was blinded to which test(s) was positive. Cancer and type of polyp were subsequently confirmed by histopathology. The final diagnosis was assigned by an individual blinded to the FOBT result. A person's adenoma status was subclassified as *significant* (size $\geq$10 mm, villous change, high-grade dysplasia, serrated histology, or 3 or more adenomas of any size or histopathology), or *small* (1 or 2 tubular adenomas all $<$10 mm). Cases found to have colitis or angiodysplasia were excluded from analyses, but all other pathologies were retained in the data set. Those who returned a positive test who chose not to proceed with colonoscopic follow-up were excluded from analysis.

Statistical Analyses

For each diagnosis of interest, test results were compared by paired 2x2 analysis with calculation of the 95% confidence interval (CI) of the difference.[29] True-positive rates were directly compared for the predetermined diagnoses of cancer, significant adenoma, or cancer plus significant adenoma (i.e., advanced neoplasia) to provide a relative measure of ability to detect neoplasia. False-positive rates were directly compared after cases with neoplasia were excluded (cases with benign pathology remained). Specificity in the screening population was deduced from the false-positive rate. In the first instance, results were compared with both cohorts combined because the goal was direct paired-comparison of tests for detection of lesions, and so case ascertainment should not be relevant. However, to gain a more direct measure of outcomes in the screening environment, comparisons were also undertaken in the screening cohort. True sensitivity for neoplasia was determined in those screening cases where colonoscopy was undertaken; where colonoscopy was subsequently undertaken in FOBT-negative subjects because of an identified high risk, any findings at colonoscopy were presumed to have been missed by the FOBT.

RESULTS

Study Populations

A total of 2547 people undertook the dual-FOBT screening-test procedure. Thirty-five were excluded. Of 18 without colonoscopic follow-up for a positive FOBT, 6 declined colonoscopy, and reports were incomplete in the remainder. The remaining 17 had colitis. Of the 2512 remaining, test positivity rates, neoplasms discovered, and test positive-predictive values are shown in Table 1. Overall, 4.7% were positive by Hemoccult Sensa and 6.7% by InSure (difference, 2.0%; 95% CI of difference, 1.0–3.0%). Test positive-predictive values were not significantly different. High risk factors were identified in 245 of the screening cohort with a negative FOBT, and these proceeded to colonoscopy within 2 years of the FOBT.

True-positive rates in those with neoplasia

Relative test positivity rates in cases with neoplasia, according to stage of neoplasia found at colonoscopy, are shown in Table 2 for all study populations. InSure was more sensitive than Hemoccult II Sensa in that it returned a positive result significantly more often in the 24 patients with cancer, the 61 patients with significant adenomas, and the 85 patients with advanced neoplasia (cancer or significant adenoma) but not the 86 patients with small adenoma (Table 2). InSure detected more of the UICC Stage I cancers compared with Hemoccult II Sensa (Table 2; Fisher exact test, $P = .002$).

Paired results for the screening population are shown in Table 3. InSure was significantly better at detecting neoplasia for all stages and/or categories of neoplasia except small adenomas.

Positivity rates in those without neoplasia

False-positive rates were compared in the screening population after excluding cases found to have neoplastic pathology (leaving n = 2218); patients in the diagnostic population were excluded as there was a

TABLE 1
Characteristics of the Study Populations and Basic Screening Outcomes

Population	Median age, y	Gender (F:M)	No. positive		Any test positive	No. underwent colonoscopy	Nos. found with neoplasia	Positive predictive value for Ca and Sig Ad		Positive predictive value for all neoplasia	
			FIT	GFOBT				FIT	GFOBT	FIT	GFOBT
Screening (n = 2351)	64.0	52.2:47.8	131 (5.6%)	94 (4.0%)	186 (7.9%)	431	Ca: 17 Sig Ad: 45 Small Ad: 71	26.0%	20.2%	41.9%	40.4%
Diagnostic (n = 161)	66.2	53.5:46.5	37 (23.0%)	24 (14.9%)	46 (28.6%)	161	Ca: 7 Sig Ad: 16 Small Ad: 15	35.1%	33.3%	43.2%	45.9%

FIT, fecal immunochemical test for hemoglobin; GFOBT, guaiac-based fecal occult blood test; Ca, cancer; Sig Ad, significant adenoma; Small Ad, small adenoma (see Methods).

TABLE 2
True Positivity Rate for Each FOBT According to Stage of Neoplasia and Cohort

	Screening cohort			Diagnostic cohort			Screening and diagnostic cohorts combined		
	No.	InSure positive (%)	HOS positive (%)	No.	InSure positive (%)	HOS positive (%)	No.	InSure positive (%)	HOS positive (%)
Cancer stage*									
I	10	9 (90)	3 (27.3)	3	3 (100)	1 (33.3)	13	12 (92.3)	4 (30.8)
II	4	3 (75)	3 (75)	1	1 (100)	1 (100)	5	4 (80)	4 (80)
III	3	2 (66.7)	2 (66.7)	3	3 (100)	3 (100)	6	5 (83.3)	5 (83.3)
Total cancer	17	14 (82.4)	8 (47.1)	7	7 (100)	5 (71.4)	24	21 (87.5)	13 (54.2)†
Adenoma status									
Multiple	16	8 (50)	2 (12.5)	5	1 (20)	0	21	9 (42.9)	2 (9.5)
HGD	8	2 (25)	2 (25)	2	1 (50)	1 (50)	10	3 (30)	3 (30)
Villous	11	6 (54.5)	4 (36.4)	2	1 (50)	1 (50)	13	7 (53.8)	5 (38.5)
Serrated	1	0	0	0	0	0	1	0	0
≥10 mm	9	4 (44.4)	3 (33.3)	7	3 (42.9)	1 (14.3)	16	7 (43.8)	4 (25)
Total significant adenoma	45	20 44.4)	11 (24.2)	16	6 (37.5)	3 (18.8)	61	26 (42.6)	14 (23.0)‡
Small adenoma	71	21 (29.6)	19 (26.8)	15	3 (20)	3 (20)	86	24 (27.9)	22 (25.6)

FOBT, fecal occult blood test; HOS , Hemoccult II Sensa; HGD, high grade dysplasia.

* Respective TNM classification for UICC Stage: I – T1 or T2, N0, M0; II – T3, N0, M0; III – Any T, N1-3, M0.[30]

† Paired difference for combined results, 33.3%; 95% confidence interval (CI) of difference, 11.2–55.4%.

‡ Paired difference for combined results, 19.7%; 95% CI of difference, 7.0–32.4%.

bias to higher overall positivity rates (Table 1). InSure had a marginally higher relative false-positive rate at 3.4% versus Hemoccult II Sensa at 2.5% (difference, 0.9%; CI of difference, 0.0–1.8%). This difference was due to differential detection of nonneoplastic pathologies, because if all cases found to have such pathology were excluded, then there was no significant difference in the remaining 2070; respective positivity rates were 1.2% and 1.3% (difference, 0.1%; CI of difference, −0.5–0.8%).

Specificity for neoplasia can be deduced (from 1 minus false-positive rate) from these false-positive rates as 96.6% for InSure compared with 97.5% for Hemoccult II Sensa. Specificity for any pathology was 98.8% and 98.7%, respectively.

Test comparisons in cases screened by colonoscopy

An estimate of true sensitivity can be obtained from results in those screening cases where colonoscopy was performed (Table 4). Although numbers were relatively small, InSure was significantly more sensitive for cancer (75% vs. 37.5%) and significant adenomas (27% vs. 15%). The positivity rate for those with a normal colonoscopy appears high at 11.5% for InSure and 15.8% for Hemoccult, but these are bi-

TABLE 3
Results of Paired Comparisons of InSure and Hemoccult II Sensa (HOSensa) in the Screening Cohort in Cases Found to Have Neoplasia

		InSure +	InSure −	
Cancer*				
HOSensa	+	7	1	8 (47.1%)
	−	7	2	9
		14 (82.4%)	3	N = 17
Significant adenoma†				
HOSensa	+	9	2	11 (24.4%)
	−	11	23	34
		20 (44.4%)	25	N = 45
Advanced neoplasia (Cancer or significant adenoma)‡				
HOSensa	+	16	3	19(30.7%)
	−	18	25	43
		34 (54.8%)	28	N = 62
Small Adenoma§				
HOSensa	+	8	11	19 (26.8%)
	−	13	39	52
		21 (29.6%)	50	N = 71

Data are shown according to whether both or just 1 test was positive. Differences in detection rates between the 2 tests and confidence intervals (CI) are provided in these footnotes.

* Difference, 35.3%; 95% CI of difference, 7.3–63.3%.

† Difference, 20.0%; 95% CI of difference, 5.4–34.6%.

‡ Difference, 24.2%; 95% CI of difference, 11.0–37.4%.

§ Difference, 2.8%; 95% CI of difference, −10.7–16.3%.

TABLE 4
Results of Paired Comparisons of InSure and Hemoccult II Sensa (HOSensa) in the Screening Cohort in All Cases That Had Undergone Colonoscopy

		InSure +	InSure −	
Cancer*				
HOSensa	+	3	0	3 (37.5%)
	−	3	2	5
		6 (75%)	2	N = 8
Significant adenoma†				
HOSensa	+	4	1	5 (15.2%)
	−	5	23	28
		9 (27.3%)	24	N = 33
Cancer or significant adenoma‡				
HOSensa	+	7	1	8 (19.5%)
	−	8	25	33
		15 (36.6%)	26	N = 41
Normal colonoscopy§				
HOSensa	+	2	20	22 (15.8%)
	−	14	103	117
		16 (11.5%)	123	N = 139
Normal or nonneoplastic pathology at colonoscopy‖				
HOSensa	+	10	33	43 (16.8%)
	−	32	181	213
		42 (16.4%)	214	N = 256

* Difference, 37.5%; 95% CI of difference 4.0–71.0%.

† Difference, 12.1%; 95% CI of difference, −1.8–26.1%.

‡ Difference, 17.1%; 95% CI of difference, 3.7–30.4%.

§ Difference, 4.3%; 95% CI of difference, −3.9–12.5%.

‖ Difference, 0.4%; 95% CI of difference, −5.8–6.6%.

ased because some patients had a colonoscopy because they had had a positive FOBT.

DISCUSSION

The results of this study show that an FIT (specifically the brush-sampling FIT, InSure, applied as a 1-time test, is significantly better at detecting colorectal neoplasia than a sensitive GFOBT (i.e., spatula-sampling Hemoccult II Sensa). The relevance to benefit in screening is born out by differential results for early stage cancer and for advanced adenomas, important target lesions when screening. InSure was positive in 12 of 13 patients with Stage-A cancer (which included 7 of the 8 polypoid cancers with invasive features), whereas Hemoccult II Sensa detected only 4 of 13. InSure also returned a significantly higher true-positive rate than Hemoccult II Sensa for patients in whom significant adenomas were detected. This shows that FITs are more capable of distinguishing pathologic bleeding in early stage lesions.

A strong case can be made for CRC screening where an FOBT is used as the first step.[3–6,8] Woolf[31] and Fletcher[32] draw out many of these reasons. Acceptability of a test is as important to achieving successful screening outcomes as is performance. Colonoscopy may reduce the miss rate for significant lesions, but only if it is performed. An alternative strategy proven to reduce death rate at lower cost and risk at the population level remains appropriate.[31,32]

Two-step screening, where the FOBT result determines who proceeds to colonoscopy, is a classic example of the World Health Organization concept of screening.[7] The detection of blood is not intended to be the definitive diagnostic finding, but it determines who is more likely to have colorectal neoplasia at the time of testing.[33] This selection process has several advantages when dealing with a healthy population. It is a simple, convenient, and noninvasive way to draw healthy persons into screening,[17] especially those reticent to undergo any form of screening, including colonoscopy. It more effectively addresses feasibility and acceptability than does 1-step screening.[1,31,32] It focuses colonoscopic resources onto those more likely to have neoplasia, an important issue given that resources are limited.[1] With colonoscopic screening, many undergo screening for no

gain, because they do not have or never will develop colorectal cancer in their lifetime. They are subject to harm that may counterbalance the benefit, an issue never tested by randomized trial.

The true-positive rates observed in this study for those found to have cancer in either population are likely to overestimate the true sensitivity of screen-detected cancers in the general population because the diagnostic cohort was included. The design is powerful for determining relative sensitivity, as results are paired for these tests. Better estimates of true sensitivity come from the screening population (Tables 3 and 4), although because not everyone had a colonoscopy, results shown in Table 4 represent the upper limit of actual sensitivity within the limitation of the number of detected cases. InSure is consistently significantly better at detection and achieves a once-only sensitivity of 75% for cancer in the colonoscopy group (Table 4). It can be anticipated that the better relative detection rate for InSure, through its better sensitivity for adenomas, would have a greater impact on mortality and incidence rates.

The study design did not allow a direct estimate of specificity for neoplasia or pathology of any type, but it did provide relative false-positive rates, and specificity could be deduced from these. The significantly better detection rate by the brush-sampling FIT was achieved at a slightly higher false-positive rate (for neoplasia) than with the sensitive GFOBT. The higher rate with the FIT proved to be because of concomitant benign pathology as positivity rates were almost identically low (at 1.2 and 1.3%, respectively) after removal of all cases found to have pathology in the screening population. This shows that false-positive rates with any FOBT will vary with the prevalence of benign pathology in the screened population. Several studies have previously shown that the Hemoccult II Sensa test can give unexpectedly high positive rates in certain populations, probably because of failure to follow dietary recommendations.[13,34] FITs are not subject to such an effect in those populations.[13,34]

Although this study has been directed toward examining relative effectiveness for detection of neoplasia, the FIT technology also has distinct behavioral advantages. Patients are more likely to participate, i.e., complete and return the test sampling kit, when diet and drug restrictions are removed[20] and when a simpler sampling procedure, such as the brush method combined with reduced number of samples, is used.[24] As detection of neoplasia at the population level is a product of sensitivity and participation, brush-sampling FIT will achieve better detection than spatula-sampling GFOBT.

Two-step screening with FIT has a real place in practice. It provides a way to confront the reality of limited colonoscopic resources and to engage a broad range of the population beyond those willing to have a screening colonoscopy. This brush-sampling FIT is significantly better at detecting advanced colorectal neoplasia than a sensitive GFOBT. Combined with behavioral advantages, such as where screening with FIT lead to a better participation rate,[24] brush-sampling FIT can be predicted to deliver better reductions in colorectal cancer mortality and incidence than will GFOBT. This can be achieved without a large increase in the false-positive rate. In any case, where colonoscopic screening is seen as the alternative, a higher false-positive rate is of little consequence in terms of resource utilization. FIT will provide superior outcomes compared with GFOBT in 2-step screening for colorectal cancer.

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