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The Impact of Transitioning From Guaiac-Fecal Occult Blood Testing to Fecal Immunochemical Testing in a Canadian Colon Cancer Screening Program

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Abstract

Objectives: To determine the impact of transitioning from guaiac-based fecal occult blood testing (gFOBT) to fecal immunochemical testing (FIT) on the detection rate of adenomas, advanced adenomas (AA) and colorectal cancer (CRC).
Background: Recently, the health region in Edmonton, Alberta switched from gFOBT to FIT for CRC screening.
Study: A retrospective analysis of all patients, aged 50 to 74 years, referred for colonoscopy from January 1, 2013 to December 31, 2014 due to a positive gFOBT (at least one of three samples positively using the guaiac-based Hemoccult II SENSA in 2013) or FIT (≥75 μg/g of stool, using the Polymedco OC FIT-CHEK in 2014). The primary outcomes were the number of colon cancers, AA and adenomas detected in 2013 and 2014. A comparison between the two tests was also made for the composite outcome of detection of either AA or CRC.
Results: Six hundred and forty-nine patients underwent colonoscopy due to a positive gFOBT in 2013, and 2167 patients for a positive FIT in 2014. FIT compared with gFOBT detected more CRC (67 compared with 34), AA (770 compared with 147) and adenomas (1575 versus 320). By multivariable regression analysis adjusted for different demographics and endoscopic metrics, positive FIT was independently associated with higher adenoma detection rate (odds ratio [OR] 2.62; 95% confidence interval [CI] 2.13 to 3.21, $P < 0.001$), AA detection rate (OR 1.83, 95% CI 1.43 to 2.33, $P < 0.001$), and the composite outcome of AA and CRC (OR 2.04, 95% CI 1.60 to 2.59, $P < 0.001$).
Conclusions: Adoption of FIT compared with gFOBT led to higher detection of colon cancer, AA and adenomas.

Keywords: *Adenoma detection; Colorectal cancer; Colon cancer screening; Fecal immunochemical testing; Guaiac-based fecal occult blood testing; Polyp detection*

Colorectal Cancer Screening

Colorectal cancer (CRC) is the third most commonly diagnosed cancer worldwide (1), the second leading cause of cancer deaths in men and the third leading cause of cancer deaths in women (2). Since 2000, the incidence and mortality rates of CRC have declined, which can be largely attributed to increased prevention and earlier detection through population-based screening programs (3,4). Screening options vary by country and region, but options include stool-based tests, flexible sigmoidoscopy, colonoscopy and imaging-based

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modalities (5,6). The strongest evidence for a mortality benefit from CRC screening exists for annual or biannual guaiac-based fecal occult blood testing (gFOBT) (7–9). Despite being a strongly validated screening modality, there are several limitations to using gFOBT, namely false positives from dietary heme found in red meat or from peroxidases found in a number of foods. Furthermore, heme remains relatively stable throughout the gastrointestinal tract; therefore, a positive gFOBT may represent bleeding proximal to the colon (10). Finally, gFOBT testing is a slow process, requiring a technician to manually perform each test, with results subject to high inter-observer variability (11).

To address these limitations, fecal immunochemical testing (FIT) was developed, which uses labeled antibodies against the globin component of human hemoglobin and then calculates the concentration of the antibody-globin complex in a stool sample in an automated and reproducible fashion. Unlike heme, the globin moiety is vulnerable to enzymatic degradation in the stomach and small bowel, thus FIT is specific for blood loss from the lower gastrointestinal tract (10). Multiple studies have demonstrated the improved sensitivity, specificity and analytical practicality of FIT compared with gFOBT for the detection of advanced adenomas (AA) and CRC (10,12–14). Due to the significant advantages, many jurisdictions have started to utilize quantitative FIT as the first-line screening test for patients at average risk for CRC.

The Edmonton SCOPE Program

The Stop Colorectal Cancer through Prevention and Education (SCOPE) Program is the Edmonton, Alberta CRC screening program designed to improve access and the quality of screening for patients in this region of approximately 1 million inhabitants. The SCOPE Program was launched in late 2011 with a mandate to provide CRC screening via colonoscopy to high-risk patients. Patients at high risk were defined as those having a positive gFOBT (and subsequently FIT), a personal history of polyps or CRC, or a significant family history (at least one first-degree relative or two second-degree relatives) of polyps and/or CRC. Average-risk patients could only access screening colonoscopy after having a positive stool-based test, which from 2011 to 2013 consisted of gFOBT, and since 2014 has been FIT.

While there are several studies that demonstrate the superiority of FIT to gFOBT, currently, there are no Canadian studies assessing the performance characteristics of the Polymedco OC FIT-CHEK assay, which is the current assay being used for FIT in our region. The purpose of this study was to determine the impact of the replacement of gFOBT with FIT as the first-line screening test in a population-based CRC screening program on the detection of cancer and advanced neoplasia during subsequent colonoscopy.

MATERIALS AND METHODS

Study Design and Patient Population

This study is a retrospective analysis of a prospectively maintained database from the SCOPE Program, a regional CRC screening program in Edmonton, Alberta, Canada. To be eligible for the SCOPE program, patient needed to be between the age of 50 to 75 years, have no evidence of significant comorbidities (unstable coronary heart disease or heart failure, severe renal insufficiency, decompensated cirrhosis), have a BMI <40, and have no evidence of inflammatory bowel disease or overt gastrointestinal alarm symptoms. All patients, who underwent colonoscopy through the SCOPE program for a positive gFOBT from January 1, 2013 to December 31, 2013 or positive FIT from January 1, 2014 to December 31, 2014, were included. There were no patients in either group with a personal or family history of adenomatous polyps or CRC. The goal of the study was to compare colonoscopy outcomes among patients with a positive gFOBT in 2013 with patients who underwent colonoscopy after a positive FIT in 2014. The primary outcome was the number of detected colon cancers, AA and adenomas in 2013 and 2014. We also used the composite endpoint of the detection rate of CRC or AA (defined as adenomas with a diameter > 10 millimeters, villous histology, or high-grade dysplasia) in each group as a secondary outcome.

Fecal Testing

From January 2013 to December 2013, SCOPE patients were screened using Hemoccult II SENSA (Beckman Coulter Canada Inc.). For this gFOBT, patients were instructed to obtain stool specimens from three different bowel movements and to apply them to the test card windows. The test was considered positive if at least one window displayed a blue color within 60 seconds of application of the developer fluid to the card. A positive test from only one of three cards was required for referral to the SCOPE program. In January 2014, gFOBT was replaced with FIT using the OC FIT-CHEK assay (Polymedco, Cortlandt, NY). Using the supplied tube-based wet sampling kit, patients were instructed to collect a single sample from one bowel movement. Collection tubes for OC FIT-CHEK were loaded onto an automated OC device, which added an anti-globin reagent to the diluted stool samples and evaluated the amount of antibody-antigen complex formation. Based on the dilution methods and device calibration, test positivity was based on a threshold of 75 μg of hemoglobin per gram of stool. The choice of 75 μg of hemoglobin per gram of stool as a cut-off was legislated at a provincial level based on an estimated positivity rate of 10% of all appropriate FIT test in the hopes of not overwhelming the capacity of available endoscopy resources, while finding a significant proportion of adenomas and AA before the development of overt CRC.

Colonoscopy Procedure

All patients in this study followed a standard bowel preparation, which consisted of a low-residue diet for 5 days followed by clear fluids 24 hours before their colonoscopy, as well as a 4-L polyethethylene glycol-based split bowel preparation regimen prior to endoscopy. All endoscopists participating in the SCOPE Program performed a minimum of 200 colonoscopies per year. The endoscopists were not blinded to whether the patients were gFOBT or FIT positive. For all patients, a case report form was completed by the endoscopy nurse and by the endoscopist with documentation of all relevant endoscopic metrics including quality of bowel preparation, adequacy of patient sedation, total procedure time, cecal intubation, withdrawal time from the cecum and rectal retroflexion. Polyps detected and resected during colonoscopy were characterized based on number, size estimate (using a standard 7 mm open biopsy forceps as a reference), colonic location and endoscopic appearance. In addition, the case report form included details of any mass lesions identified and subsequently biopsied. All polyps were removed using standard endoscopic polypectomy techniques, and any tissue removed during endoscopy was sent for histologic analysis. Pathology results were automatically sent back to the SCOPE Program and entered into a centralized database. The study protocol was approved by the Health Research Ethics Board of the University of Alberta (Pro00058842).

Statistical Analysis

The data collected in this study were determined by single measurements related to the patient's colonoscopy with no other data points generated in follow-up. Data are presented as the mean ± standard deviation or frequencies and percentages. The Fisher exact probability was used to compare categorical variables, and the unpaired *t*-test was used to compare differences in means of continuous variables. Non-normally distributed variables were compared with the Mann–Whitney test, as appropriate. The main outcome measure was a comparison of the number of colon cancers, AA and adenomas detected between 2013 and 2014. The performance gFOBT and FIT for the detection of outcomes of interest (adenoma detection, AA detection, CRC detection and composite detection rate AA-CRC), and other well-established demographic and endoscopic quality metrics were analyzed by univariate and multivariate logistic regression analysis. Variables with a P value <0.1 in the univariate analysis were included in multivariate regression analysis. We were not able to calculate sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for gFOBT and FIT as all patients analyzed in this study had positive stool test results and information about the total number of individuals who underwent screening with stool tests was not available.

Sample Size

Our sample size was driven by the number of patients who were referred to the screening program with a positive gFOBT in 2013 and positive FIT in 2014. Introduction of the use of the FIT test in 2014 led to a marked increase in the number of individuals who underwent Colon Cancer screening and hence the number of cases that required colonoscopy. We calculated that for a comparison of ADR between FIT (assumed at 30%) and gFOBT (assumed at 20%) in patients who tested positive on stool testing, a sample size of at least 294 patients for each group was needed using a value of $Z\alpha = 1.96$ for two-sided test, $\alpha = 0.05$, and desired power of $Z\beta = 0.842$, $\beta = 0.2$ group (15).

RESULTS

Demographics and Endoscopic Metrics in Patients with Positive FOBT or FIT

We evaluated 2816 patients in this study. From January 1, 2013 to December 31, 2013, 649 patients underwent colonoscopy due to a positive gFOBT and from January 1, 2014 to December 31, 2014, 2167 patients underwent colonoscopy due to a positive FIT. Introduction of the use of the FIT test in 2014 was accompanied by strong efforts to raise awareness among patients and primary care physicians about the importance of colon cancer screening throughout the province of Alberta. This led to a marked increase in the number of individuals who participated in colon cancer screening and hence the number of cases that required colonoscopy.

Demographics and endoscopic metrics for these patients are summarized in Table 1. Patients who had a FIT positive had a higher frequency of reported cecal intubation (97 versus 94%, $P < 0.001$) and rectal retroflexion (98 versus 94%, $P < 0.001$), longer withdrawal time (14 ± 10 versus 12 ± 8 minutes, $P < 0.001$), and lower frequency of not reporting bowel preparation quality, compared to patients who had a positive gFOBT (Table 1).

Outcomes According to Patients with Positive FOBT or FIT

The primary outcomes of interest were the number of colon cancers, AA and adenomas detected in 2013 and 2014. As shown in Table 2, more CRC were detected in 2014 ($N = 67$) compared with 2013 ($N = 34$) and the same was true for AA (770 in 2014, 147 in 2013) and adenomas (1575 in 2014, 320 in 2013). The composite outcome of the detection of either AA or CRC was also significantly higher using FIT compared with gFOBT (837 in 2014, versus 181 in 2013).

Factors Associated with Detection of Outcomes by Univariate Regression Analysis

By univariate regression analysis FIT was associated with higher detection rate of the composite outcome (AA and CRC detection rate) compared with gFOBT (odds ratio [OR] 2.04, 95% confidence interval [CI] 1.67 to 2.50, $P < 0.001$) (Table 3). As well, male gender (OR 1.90, 95% CI 1.61 to 2.23, $P < 0.001$)

Table 1. Baseline demographics and endoscopic quality metrics

Participant characteristics (%)	All patients ($n = 2816$)	g-FOBT Positive-2013 ($n = 649$)	FIT Positive-2014 ($n = 2167$)	*P* value
Male (%)	1658 (59)	369 (57)	1298 (59)	0.2
Endoscopist Specialty (%)				
Gastroenterology (GI)	2191 (78)	512 (79)	1679 (78)	0.5
Non-GI*	625 (22)	137 (21)	512 (22)	
Reported Cecal Intubation (%)	2722 (97)	611 (94)	2111 (97)	<0.001
Reported Rectal Retroflexion (%)	2730 (97)	609 (94)	2121 (98)	<0.001
Withdrawal Time (minutes)	13 ± 10	12 ± 8	14 ± 10	<0.001
Bowel Preparation Quality				
Excellent	834 (30)	182 (28)	652 (30)	0.3
Acceptable	1523 (54)	340 (52)	1183 (55)	0.3
Fair	220 (8)	58 (9)	162 (8)	0.2
Poor	27 (1)	5 (1)	22 (1)	0.8
Not Reported	212 (8)	64 (10)	148 (7)	0.01

FIT, Fecal immunochemical testing; gFOBT, Guaiac-based fecal occult blood testing.
*Internal Medicine, General Surgery, Nurse Practitioner.

Table 2. Primary outcomes according to patients with positive FOBT or FIT

Participant characteristics	All patients ($n = 2816$)	g-FOBT Positive-2013 ($n = 649$)	FIT Positive-2014 ($n = 2167$)
Adenoma Detection	1895	320	1575
Advanced Adenoma (AA) Detection	917	147	770
Colorectal Cancer Detection	101	34	67
AA or CC Detection	1018	181	837

and withdrawal time (OR 1.16, 95% CI 1.15 to 1.18, $P < 0.001$) were associated with higher composite outcome detection rates, whereas a poor preparation was associated with a lower composite outcome detection rate (OR 0.15, 95% CI 0.04 to 0.65, $P = 0.01$) (Table 3).

By univariate regression analysis, FIT was associated with higher ADR compared with gFOBT (OR 2.74, 95% CI 2.28 to 3.28, $P < 0.001$) (Table 3). In addition, male gender (OR 1.89, 95% CI 2.28 to 3.28, $P < 0.001$), reported cecal intubation (OR 3.64, 95% CI 2.38 to 5.57, $P < 0.001$), rectal retroflexion (OR 2.96, 95% CI 1.92 to 4.58, $P < 0.001$) and withdrawal time (OR 1.15, 95% CI 1.13 to 1.17, $P < 0.001$) were associated with higher ADR, whereas a poor preparation was associated with lower ADR (OR 0.33, 95% CI 1.53 to 0.72, $P = 0.005$) (Table 3).

Similarly, by univariate regression analysis, FIT was associated with higher AA detection rate compared with gFOBT (OR 1.88, 95% CI 1.54 to 2.31, $P < 0.001$) (Table 3). Likewise, male gender (OR 1.93, 95% CI 1.62 to 2.28, $P < 0.001$) and withdrawal time (OR 1.16, 95% CI 1.14 to 1.18, $P < 0.001$) were associated with higher AA detection rate, whereas a poor preparation was associated with lower AA detection rate (OR 0.16, 95% CI 0.04 to 0.69, $P = 0.01$) (Table 3).

Factors Associated with Detection of Outcomes by Multivariable Regression Analysis

FIT was independently associated with higher composite detection rate (AA and CRC) compared with gFOBT (OR 2.04, 95% CI 1.60 to 2.59, $P < 0.001$), after adjusted for male gender, withdrawal time and poor bowel preparation (Table 4). In the multivariate analysis, FIT was independently associated with higher ADR compared with gFOBT (OR 2.61, 95% CI 2.13 to 3.21, $P < 0.001$), when adjusted for male gender, reported cecal intubation and rectal retroflexion, withdrawal time and acceptable and poor bowel preparation (Table 4). Also, FIT was independently associated with higher AA detection rate compared to gFOBT (OR 1.81, 95% CI 1.42 to 2.31, $P < 0.001$) when adjusted with male gender, withdrawal time and poor bowel preparation (Table 4).

DISCUSSION

The introduction of FIT as a CRC screening modality did have a significant impact in our health region. The uptake of FIT utilization at a primary care level was significantly higher than FOBT, subsequently resulting in a significantly higher rate of referral for colonoscopy to our colon cancer screening (SCOPE)

Table 3. Factors associated with primary outcomes by univariate logistic regression analysis

	Adenoma detection		**Odds ratio**	***P* value**
	Yes (*n* = 1895)	**No (*n* = 921)**	**(95% CI)**	
Male (%)	1212 (64)	446 (48)	1.89 (1.61–2.22)	<0.001
FIT: gFOBT (%)	1575 (83): 320 (17)	592 (64): 329 (36)	2.74 (2.28–3.28)	<0.001
Endoscopist Specialty (%)				
Gastroenterology (GI)	1459 (77)	732 (79.5)	0.86 (0.71–1.05)	0.1
No GI*	436 (23)	189 (20.5)		
Reported Cecal Intubation (%)	1860 (98)	862 (94)	3.64 (2.38–5.57)	<0.001
Reported Rectal Retroflexion (%)	1859 (98)	871 (95)	2.96 (1.92–4.58)	<0.001
Withdrawal Time (minutes)	15±10	9±6	1.15 (1.13–1.17)	<0.001
Bowel Preparation Quality (%)				
Excellent	549 (29)	285 (31)	0.91 (0.77–1.08)	0.3
Acceptable	1049 (55)	474 (52)	1.17 (0.99–1.37)	0.05
Fair	151 (8)	69 (8)	1.07 (0.80–1.44)	0.7
Poor	11 (1)	16 (2)	0.33 (1.53–0.72)	0.005
Not Reported	135 (7)	77 (8)	0.84 (0.63–1.13)	0.2
	Advanced adenoma detection		**Odds ratio**	***P* value**
	Yes (*n* = 917)	**No (*n* = 1899)**	**(95% CI)**	
Male (%)	635 (69)	1023 (54)	1.93 (1.62–2.28)	<0.001
FIT: gFOBT (%)	770 (84): 147 (16)	1397 (74): 502 (26)	1.88 (1.54–2.31)	<0.001
Endoscopist Specialty (%)				
Gastroenterology (GI)	697 (76)	1494 (79)	0.86 (0.71–1.04)	0.1
No GI*	220 (24)	405 (21)		
Reported Cecal Intubation (%)	894 (98)	1828 (96)	1.51 (0.94–2.43)	0.09
Reported Rectal Retroflexion (%)	896 (98)	1834 (97)	1.51 (0.92–2.45)	0.1
Withdrawal Time (minutes)	19 ± 12	10 ± 6	1.16 (1.14–1.18)	<0.001
Bowel Preparation Quality (%)				
Excellent	261 (28.5)	573 (30)	0.92 (0.77–1.10)	0.4
Acceptable	506 (55)	1017 (54)	1.07 (0.91–1.25)	0.4
Fair	73 (8)	147 (8)	1.03 (0.77–1.38)	0.8
Poor	2 (0.5)	25 (1)	0.16 (0.04–0.69)	0.01
Not Reported	75 (8)	137 (7)	1.15 (0.85–1.54)	0.4
	Colorectal cancer detection		**Odds ratio**	***P* value**
	Yes (*n* = 101)	**No (*n* = 2816)**	**(95% CI)**	
Male	69 (68)	1589 (59)	1.53 (1.00–2.34)	0.05
FIT: gFOBT (%)	67 (66): 34 (34)	2100 (77): 615 (23)	0.58 (0.38–0.88)	0.01
Endoscopist Specialty (%)				
Gastroenterology (GI)	76 (75)	2115 (78)	0.86 (0.54–1.37)	0.5
No GI*	25 (25)	600 (22)		
Reported Cecal Intubation (%)	87 (86)	2635 (97)	0.19 (0.10–0.35)	<0.001
Reported Rectal Retroflexion (%)	90 (89)	2640 (97)	0.23 (0.12–0.45)	<0.001
Withdrawal Time (minutes)	16 ± 11	13 ± 9	1.02 (1.01–1.04)	0.002
Bowel Preparation Quality (%)				
Excellent	26 (25.5)	808 (30)	0.82 (0.52–1.29)	0.4
Acceptable	55 (54.5)	1468 (54)	1.02 (0.68–1.51)	0.9
Fair	11 (11)	209 (7.5)	1.47 (0.77–2.78)	0.2
Poor	0	27 (1)	-	-
Not Reported	9 (9)	203 (7.5)	1.21 (0.60–2.44)	0.6

Table 3. Continued

	Advanced adenoma and/or colorectal cancer detection		OR	*P* value
	Yes (*n* = 958)	**No (*n* = 1858)**	**(95% CI)**	
Male (%)	659 (69)	999 (54)	1.90 (1.61–2.23)	<0.001
FIT: gFOBT (%)	811 (85): 147 (15)	1356 (73): 502 (27)	2.04 (1.67–2.50)	<0.001
Endoscopist Specialty (%)				
Gastroenterology (GI)	728 (76)	1463 (79)	0.86 (0.71–1.03)	0.1
No GI*	230 (24)	395 (21)		
Reported Cecal Intubation (%)	931 (97)	1791 (96)	1.29 (0.82–2.03)	0.3
Reported Rectal Retroflexion (%)	936 (98)	1794 (97)	1.52 (0.93–2.48)	0.1
Withdrawal Time (minutes)	19 ± 12	10 ± 6	1.16 (1.15–1.18)	<0.001
Bowel Preparation Quality (%)				
Excellent	275 (28.5)	559 (30)	0.94 (0.79–1.11)	0.5
Acceptable	529 (55)	994 (54)	1.07 (0.92–1.25)	0.4
Fair	76 (8)	144 (8)	1.03 (0.77–1.37)	0.9
Poor	2 (0.5)	25 (1)	0.15 (0.04–0.65)	0.01
Not Reported	76 (8)	136 (7)	1.09 (0.82–1.46)	0.6

CI, Confidence interval; FIT, Fecal immunochemical testing; gFOBT, Guaiac-based fecal occult blood testing; OR, Odds ratio.
*Internal Medicine, General Surgery, Nurse Practitioner.

program. This trend of increasing number of individuals screened has continued in the years following 2014. The main reason was likely the fact that, at the time of the introduction of the FIT test, a strong and comprehensive provincial education campaign was launched which promoted the importance of colon cancer screening and was aimed at the general population and primary care physicians. Another reason may be an increased willingness of patients to complete one (for FIT) instead of three samples stool samples (for FOBT) without the need for any associated dietary modifications as well.

Our main outcome of interest was the detection of the number of patients with CRC, AA or adenomas. The results show that the introduction of the FIT test led to a marked increase in all three outcome measures compared with gFOBT. As mentioned above, this is in large part driven by the increase in number of patients screened but likely also by the known superiority of FIT compared with gFOBT (16–20). By significantly improving the detection of both premalignant and malignant lesions, FIT confers a very important advantage in a population-based cancer screening program.

A limitation of our study is the fact that we only included patients who tested positive on gFOBT or FIT in our study. For interpretation of the univariate and multivariate analyses, it is important to point out that in the results it was only possible to look at findings in patients who were referred because of a positive stool test. The more important data would be comparisons of outcomes in all patients who underwent colon cancer screening, that is, it also include all the patients who had negative stool test results. Unfortunately, these data were not available for the authors to assess.

Results of other studies confirm that FIT is superior to FOBT. Brenner et al. found that three different quantitative FIT assays out-performed gFOBT for detection of both adenomas and AA based on sensitivity, specificity, PPV and NPV (21). Similarly, a comparison of FIT to gFOBT by Oort et al. (22) found that FIT has a significant higher sensitivity for AA compared with gFOBT (35.6 versus 18.0; $P < 0.001$). Taken together, our results and previous studies indicate that the improved detection rate for adenomas and AA conferred by FIT offers a significant improvement in the primary prevention of CRC.

Screening for CRC serves the important dual purposes of both primary prevention to identify premalignant adenomas that have yet to undergo malignant transformation, as well as early detection of CRC that can still be treated with curative intent. Previous studies have demonstrated a reduction in CRC-related mortality with annual or biannual population-based screening with guaiac-based fecal occult blood testing (7,9,23–27). However, gFOBT has been widely criticized for its poor sensitivity and specificity for CRC, with an estimated sensitivity for cancer with once-only testing using traditional gFOBT of only 50% (28). In contrast, fecal immunochemical test has greatly improved diagnostic characteristics for CRC screening. A recent meta-analysis of nineteen studies examining the detection of CRC by FIT demonstrates a pooled sensitivity of 79% (95% CI 0.69 to 0.96), specificity of 94% (95% CI 0.92 to 0.95), positive likelihood ratio of 13.10 (95% CI 10.49 to 16.35), negative likelihood ratio of 0.23 (95% CI 0.15 to 0.33) and diagnostic accuracy of 95% (95% CI 93 to 97%) (29). These data further support that FIT is a superior test when compared with FOBT.

Table 4. Factors associated with primary outcomes by multivariable logistic regression analysis

	Adenoma detection		**OR**	***P* value**
	Yes (*n* = 1895)	**No (*n* = 921)**	**(95% CI)**	
Male (%)	1212 (64)	446 (48)	1.62 (1.35–1.93)	<0.001
FIT: gFOBT (%)	1575 (83): 320 (17)	592 (64): 329 (36)	2.61 (2.13- 3.21)	<0.001
Reported Cecal Intubation (%)	1860 (98)	862 (94)	3.99(2.10–7.57)	<0.001
Reported Rectal Retroflexion (%)	1859 (98)	871 (95)	2.16 (1.11–4.20)	0.02
Withdrawal Time (minutes)	15 ± 10	9 ± 6	1.15 (1.13–1.17)	<0.001
Bowel Preparation Quality (%)				
Acceptable	1049 (55)	474 (52)	0.95 (0.79–1.13)	0.6
Poor	11 (1)	16 (2)	0.41 (0.17–0.97)	0.04
	Advanced adenoma detection		**OR**	***P* value**
	Yes (*n* = 917)	**No (*n* = 1899)**	**(95% CI)**	
Male (%)	635 (69)	1023 (54)	1.71(1.41–2.08)	<0.001
FIT: gFOBT (%)	770 (84): 147 (16)	1397 (74): 502 (26)	1.81 (1.42–2.31)	<0.001
Reported Cecal Intubation (%)	894 (98)	1828 (96)	1.49 (0.73–3.01)	0.3
Withdrawal Time (minutes)	19 ± 12	10 ± 6	1.16 (1.14–1.17)	<0.001
Bowel Preparation Quality (%)				
Poor	2 (0.5)	25 (1)	0.26 (0.06–1.12)	0.07
	Colorectal cancer detection		**OR**	***P* value**
	Yes (*n* = 101)	**No (*n* = 2816)**	**(95% CI)**	
Male (%)	69 (68)	1589 (59)	1.67 (1.06–2.64)	0.03
FIT: gFOBT (%)	67 (66): 34 (34)	2100 (77): 615 (23)	0.63 (0.40–1.00)	0.05
Reported Cecal Intubation (%)	87 (86)	2635 (97)	0.26 (0.11–0.59)	0.001
Reported Rectal Retroflexion (%)	90 (89)	2640 (97)	0.41 (0.16–1.02)	0.06
Withdrawal Time (minutes)	16 ± 11	13 ± 9	1.02 (1.01–1.04)	0.005
	Advanced adenoma and/or colorectal cancer detection		**OR**	***P* value**
	Yes (*n* = 958)	**No (*n* = 1858)**	**(95% CI)**	
Male (%)	659 (69)	999 (54)	1.69 (1.39–2.04)	<0.001
FIT: gFOBT (%)	811 (85): 147 (15)	1356 (73): 502 (27)	2.04 (1.60–2.59)	<0.001
Withdrawal Time (minutes)	19 ± 12	10 ± 6	1.16 (1.14–1.18)	<0.001
Bowel Preparation Quality (%)				
Poor	2 (0.5)	25 (1)	0.23 (0.05–1.02)	0.06

CI, Confidence interval; FIT, Fecal immunochemical testing; gFOBT, Guaiac-based fecal occult blood testing; OR, Odds ratio.

The strength of this study is that it reflects the performance characteristics of a new screening modality in a real-life screening program, not in highly controlled and regulated clinical trial setting. Monitoring the impact of FIT on our screening program and its patients is very important as we have the ability to alter the cut-off for a positive FIT, thereby changing the sensitivity and specificity of the test to reach a desired target of CRC and AA detection. If our FIT positivity threshold is too low, the test may become too sensitive and results in an unmanageable increase in referral volume with a decrease in the significance of screening findings. Conversely, if our threshold for positive results is too high, the specificity of the test may result in lower referral volumes and patients with an unacceptable high rate of CRC and AA. Conducting studies of this nature will help fine tune the performance characteristics of FIT, thereby optimizing early detection and prevention of AA and CRC without overwhelming limited access to endoscopic surveillance.

Another limitation of our study is that it compared patient cohorts in different years and was not a head to head comparison of results of both tests performed in the same patients. As a result, it is not possible to calculate sensitivity, specificity, or PPV and NPV of FIT and gFOBT. Although not a weakness, there was improvement in the quality of the procedure in 2014

compared with 2013, reflected by higher cecal intubation rates, withdrawal time and rectal retroflexion rates. These differences may result in a greater than expected increase in ADR and AA detection that are not a direct result of using the FIT test. Our program does have ongoing quality improvement initiatives to further improve the delivery of CRC screening.

Our study is the first report on the impact of transitioning from gFOBT to FIT in a Canadian colon cancer screening program. The increased volume of FIT-positive referrals, combined with the fact that over 70% of these patients have an adenoma and 35% have an advanced lesion, has led to a considerable increase in the resources needed for CRC screening in Edmonton. The number of colonoscopies performed by the SCOPE program has increased from approximately 3000 per year in 2013 to over 9000 per year in 2016 to accommodate the additional referrals, and current projections indicate that this number will need to increase further to meet ongoing demand for CRC screening and to ensure the colonoscopy is completed in a timely fashion. Additionally, due to the complexity of findings in FIT-positive patients, we have needed to increase the allotted time per procedure to accommodate thorough mucosal assessment and polypectomy. The downstream impact of utilizing FIT for CRC screening has also led to increased referrals for therapeutic removal of large advanced polyps, surgical intervention for nonresectable polyps and malignancy, and a significant increase in the volume of tissue samples requiring histologic assessment. Understanding the impact of implementing FIT into our CRC screening program will hopefully help other jurisdictions in planning appropriate resource allocation to optimize their own CRC screening strategies.

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