Participation and ease of use in colorectal cancer screening: a comparison of two fecal immunochemical tests

C.M. de Klerk, E. Wieten, A. van der Steen, C.R. Ramakers, E.J. Kuipers, B.E. Hansen, I. Lansdorp-Vogelaar, P.M. Bossuyt, M.C.W. Spaander, E. Dekker

American Journal of Gastroenterology 2019

ABSTRACT

Introduction

The impact of fecal immunochemical test (FIT) based colorectal cancer (CRC) screening on disease incidence and mortality is affected by participation, which might be influenced by ease of use of the FIT. We compared participation rates and ease of use of two different FITs in a CRC screening program.

Methods

Two study designs within the Dutch CRC screening program. In a paired cohort study, all invitees received two FITs (OC-Sensor, Eiken, Japan and FOB-Gold, Sentinel, Italy) and were asked to sample both from the same stool. Ease of use of both FITs was evaluated by questionnaire. In a randomized controlled trial, invitees were randomly allocated to receive one of the two FITs to compare participation and analyzability.

Results

Of 42,179 invitees in the paired cohort study, 21,078 (50%) completed two tests and 20,727 (98%) returned the questionnaire. FOB-Gold was reported significantly easier to use. More participants preferred FOB-Gold (36%) than OC-Sensor (5%), yet most had no preference (59%, $p<0.001$). In the randomized trial, 936 of 1923 invitees (48.7%) returned the FOB-Gold and 940 (48.9%) the OC-Sensor, a difference of -0.2% (CI: -3.4% to 3.0%), well within the pre-specified 5% non-inferiority margin ($p=0.001$). Only one FOB-Gold (0.1%) and four OC-Sensors (0.4%) were not analyzable ($p=0.18$).

Discussion

While FOB-Gold was significantly but marginally considered easier to use than OC-Sensor, the number of analyzable tests and participation rates in organized CRC screening are not affected when either FIT is implemented as a primary screening test.

INTRODUCTION

Population-based screening using guaiac fecal occult blood testing (gFOBT) reduces colorectal cancer (CRC)-related mortality.[1] Since several years, gFOBT is being replaced by a quantitative and more sensitive FOBT, the fecal immunochemical test (FIT). Compared to gFOBT, FIT is a one sample test, that consists of a probe and a tube instead of a smear card, and does not require dietary restrictions.[2, 3] Consequently, participation rates are higher with FIT than gFOBT.[4, 5] FIT is currently recommended in European guidelines as the test of choice for CRC population screening.[2] Multiple FITs are however available for screening, varying in the sampling tube design, buffer volume and sampling instructions.[3] Despite the clear advantages of FIT over gFOBT, specific differences between FITs could also affect participation.

So far, comparative evidence on the effects on participation for the available FITs in organized population-based screening is limited. Little higher participation rates were observed with the OC-Sensor (Eiken, Japan) than with FOB-Gold (Sentinel, Italy) in Spanish, French and Latvian screening settings (62% vs 59%; 40% vs 38%; 47% vs 45%), but a Dutch pilot screening program observed no differences (63% vs 63%).[6-9]

Some previous studies used the preferences of screenees to assess differences in ease of use, but they either compared FIT versus gFOBT[4, 10, 11], single versus multiple FIT samples [12], or were performed in a small, non-screening setting [12]. Overall, these studies confirmed a preference for a one sample test, without dietary instructions, a sampling probe and a tube for fecal collection, over a card-based test.

Ease of use of FOB-Gold and OC-Sensor, two of the most frequently used FIT brands, has so far only been evaluated by comparing the number of returned non-analyzable tests. In those studies, results were in favor of OC-Sensor.[6, 8, 9] Since then, the FOB-Gold testing tube has been modified to facilitate opening the tube and to lower the number of non-analyzable tests due to a loss of buffer.[8]

We recently showed that the accuracy in detecting advanced neoplasia (AN) is comparable for OC-Sensor and FOB-Gold.[13] To facilitate further informed decision making about the choice of FIT in population-based screening programs, additional evidence on other aspects of FIT that could influence screening effectiveness, such as ease of use and participation, is needed. At request of the Dutch minister of Health, we performed a large cohort study in which screening invitees were asked to complete both OC-sensor and FOB-Gold and assess ease of use and preference of FIT brand by questionnaire. In parallel, a randomized trial compared participation rates and the proportions of non-analyzable tests between OC-sensor and FOB-Gold.

METHODS

Study population

This study was embedded within the Dutch CRC screening program between May 2016 and March 2017. The Dutch CRC screening program started in 2014. It gradually invites 55 to 75-year old individuals for biennial FIT screening with the FOB-Gold test. Details have been described previously.[14] The target population for our study consisted of all individuals in the South-West region of The Netherlands that that were eligible for first-round screening in 2016. They were aged 59, 61, 63, 71 and 75. Exclusion criteria were identical to those in the Dutch CRC screening program: those with either a life expectancy of less than five years, a past proctocolectomy, current treatment for CRC and a history of inflammatory bowel disease, were not invited for colonoscopy at consultation after a positive FIT.[15] Organization and procedures were according to the Dutch CRC screening quality guidelines.[16]

Study design

We conducted a paired cohort study, in which invitees received two FITs (FOB-Gold and OC-Sensor) and a randomized trial, in which invitees received only one FIT, either FOB-Gold or OC-Sensor. To select invitees for both trials, random samples were taken from the same target population using a computer-generated algorithm (SPSS, IBM, version 23). Individuals selected for the randomized trial were not invited for the paired cohort study, and vice versa.

In the paired cohort study, invitees were instructed to sample each FIT from the same bowel movement. In the randomized trial, invitees received either a FOB-Gold or an OC-Sensor. All FITs were sent to the invitees with postal mail. This invitation package additionally included detailed sampling instructions for each test, as prescribed by the specific manufacturer, and an informed consent form. Invitees were asked to complete the consent and to fill in the stool sampling date.

Invitees for the paired cohort study additionally received a questionnaire about the ease of use for the two FITs (Supplementary Material 1). The questionnaire included seven factual questions focused on: 1. clarity of instructions on how to open the test, 2. ease of opening the test, 3. ease of using the stick, 4. ease of replacing the stick in the tube, 5. ease of closing the tube with the cap, 6. clarity of the sampling instructions and 7. the preferred test. Question 1-6 could be answered on a five-point scale, anchored at "1. Totally agree" to "5. Totally disagree". Question 7 invited a preference for either the "round test" (FOB-Gold), the "flat test" (OC-Sensor) or "no preference". In addition, we invited participants to clarify any reasons for their preference. A copy of the questionnaire is included in the supplementary material.

Consenting invitees were asked to return the FIT(s) and the consent form within three days after stool sampling to a specialized laboratory for analysis in a study specific sealed and pre-paid envelope. Invitees in the paired cohort study were asked to additionally return the questionnaire in the same envelope. Returned FITs and informed consent forms were checked by specialized laboratory staff. Questionnaires were scanned electronically; results were automatically uploaded to a database.

Characteristics of FOB-Gold and OC-Sensor tests

FOB-Gold and OC-Sensor have similar mechanisms for detecting blood in feces, based on antibodies to human globin. The difference in sampling tubes is illustrated in Figure 1.[3] The FOB-Gold is a round tube, containing 1.7 ml preservative buffer, with a wide opening and two screw caps at each end of the tube, one green cap to which the collection probe (stick) is attached and one transparent cap that is used for analysis in the laboratory. The probe ends in a serrated tip that should be inserted in the stool sample at four different places and replaced in the tube. The OC-Sensor is a flat tube, containing 2.0 ml preservative buffer, with a narrow opening and one green 'clicking' cap. The collection probe is attached to the cap, has a serrated tip and should be scraped through the stool sample in four different areas. After replacing the probe in the tube and closing the cap, participants are instructed to sway the tube to assure that the sample is fully suspended in the buffer.

Statistical analysis

Excluded from paired analysis were participants with incomplete tests: one or two non-analyzable tests (due to fecal overload, loss of 2/3 or more of the total buffer volume both from visual assess by laboratory staff and by automatic system), missing barcode or another technical problem) and participants with an unreliable test result (in case the return date was more than six days after sampling or if the sampling date was missing).[13] Differences between FITs in terms of ease of use were compared in the paired cohort study using the Wilcoxon signed-rank test statistic. To evaluate the existence of subgroup differences (sex, age or socioeconomic status) in the preference for either FOB-Gold, OC-Sensor, or neither, and to show the magnitude of any such differences we compared their reported FIT preference using chi-square statistics.

For each arm of the randomized trial, the participation rate was calculated by dividing the number of participants returning the FIT by the total number of invitees. We calculated an absolute and a relative difference in participation rate between FOB-Gold and OC-Sensor with corresponding 95% confidence intervals. We hypothesized there would be no substantial difference in participation rate between FOB-Gold and OC-Sensor, the test previously used in the Dutch pilot screening program. In testing this, we used a 5% non-inferiority margin. Proportions of non-analyzable tests were also assessed in the

randomized trial and compared using a chi-square test. Non-analyzability could be due to an unreadable barcode, a broken tube, missing buffer, a too large sample or too small sample, a missing sample or another reason that made analysis technically impossible.

For subgroup analyses, participants were categorized into two age groups: 55-64 years and 65-75 years, because the selected screening invitees in 2016 consisted of five specific birth years. Socioeconomic status was assessed by the area social status score (combining education, income and employment status) developed by the Netherlands Institute of Social Research[17], and grouped into quintiles, with 1 being the highest status and 5 being the lowest. In all tests except the non-inferiority test for participation, two-sided p-values of 0.05 were considered significant. For participation, a one-sided 0.025 significance level was used.

Sample size calculations

The sample size for the paired trial was guided by the aim to evaluate differences in diagnostic yield, relative sensitivity, and relative specificity, as reported in detail elsewhere.[13]

Figure 1 FOB-Gold (left) and OC-Sensor (right) fecal immunochemical test

Modified from Schreuders et al. 2016 [3]

In the randomized trial, our objective was to yield estimates of the relative participation rate of both FITs in CRC screening with sufficient precision to allow national decision making on purchasing and implementing one of both tests. We assumed that 50% of invitees would participate in the randomized trial. Assuming no difference in participation between the two FITs, 2019 individuals were required in each arm of the randomized trial to have 90% power in excluding an absolute difference of 5% or more in participation, using a significance level of 0.025.

Ethical approval

The study protocol was evaluated by the Dutch National Health Council and approved by the Minister of Health (Population Screening Act; no. 769500-135716-PG; date 4 June 2015) and registered before its initiation at the Dutch Trial Registry as trail no. NTR5874.

RESULTS

Study participants

The study flow is summarized in Figure 2. Baseline characteristics of participants in the paired cohort study and the randomized trial are described in Table 1. Half of the participants were male and median age was 60 (IQR 59-61). There were significant differences between participants in the randomized trial and the paired cohort. The latter consisted of more elderly participants, and more participants with a higher socioeconomic status ($p<0.001$). There were no differences in between the two arms of the randomized trial.

Ease of use

Of 42,179 individuals invited to the paired cohort study, 21,078 participated and returned two completed FITs, of which 20,727 (98%) also returned the questionnaire (Figure 2). Reported answers on ease of use are shown in Table 2 and Figure 3.

Significant but small differences were found for almost all aspects of ease of use, in favor of FOB-Gold, except for the clarity of instructions for opening the test ($p=0.34$). The largest difference was found for replacing the stick in the tube, with 94% of participants 'totally agreeing' or 'agreeing' this was easy with FOB-Gold versus 79% indicating the same for OC-Sensor, resulting in an absolute difference of 15%. A difference of 5% was found for ease of closing the test with the cap: 98% said this was easy ('totally agree' and 'agree') for FOB-Gold compared to 93% for OC-Sensor. Smaller and sometimes tiny differences were observed for the other domains: ease of using the stick, ease of opening the test and clarity of the sampling instructions.

Figure 2 Flow of participants in the paired cohort study and in the randomized controlled trial.

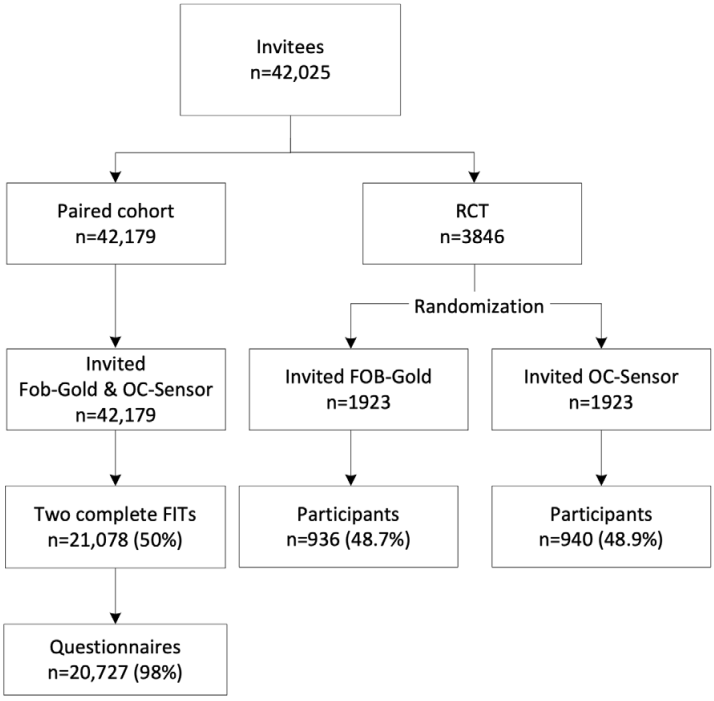


Table 1 Baseline characteristics per study arm

	Paired cohort	p-value**	RCT	
	Total n=20,727		FOB-Gold n=936	OC-Sensor n=940
Male sex, n (%)	10,425 (50%)	1.0	475 (51%)	472 (50%)
Female sex, n (%)	10,302 (50%)		461 (49%)	468 (50%)
Age in years median (IQR)*	60 (58-62)		60 (59-61)	60 (59-61)
55-64, n (%)	17,031 (82%)	<0.001	848 (91%)	841 (89%)
65-75, n (%)	3696 (18%)		88 (9%)	99 (11%)
SES, n (%)		<0.001		
Very high	4152 (20%)		46 (5%)	49 (5%)
High	4570 (22%)		117 (13%)	122 (13%)
Average	3819 (19%)		209 (22%)	217 (23%)
Low	4845 (23%)		376 (40%)	374 (40%)
Very low	3294 (16%)		181 (19%)	176 (19%)
Missing	47 (<1%)		7 (1%)	2 (<1%)

*Age at time of fecal immunochemical test (FIT) invitation

** Difference between study group in RCT and paired cohort

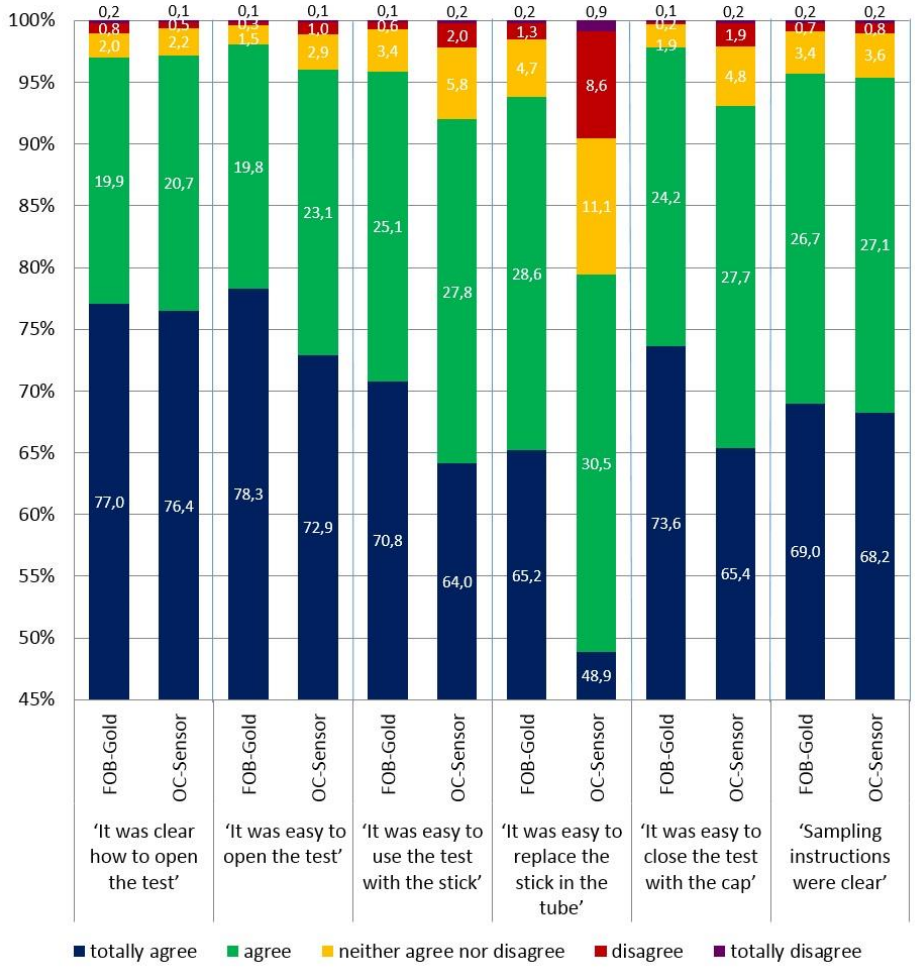
IQR: interquartile range; SES: socioeconomic status; RCT: randomised controlled trial

Table 2 Responses per aspect of ease of use for FOB-Gold and OC-Sensor

	FOB-Gold	OC-Sensor	p-value*
'It was clear how to open the test'	n=17,821	n=17,710	0.34
Totally agree	13,731 (77.0%)	13,524 (76.4%)	
Agree	3552 (19.9%)	3673 (20.7%)	
Neutral	362 (2.0%)	395 (2.2%)	
Disagree	146 (0.8%)	92 (0.5%)	
Totally disagree	40 (0.2%)	26 (0.1%)	
'It was easy to open the test'	n=17,794	n=17,688	<0.001
Totally agree	13,927 (78.3%)	12,896 (72.9%)	
Agree	3518 (19.8%)	4086 (23.1%)	
Neutral	275 (1.5%)	509 (2.9%)	
Disagree	55 (0.3%)	171 (1.0%)	
Totally disagree	19 (0.1%)	26 (0.1%)	
'It was easy to use the test with the stick'	n=17,760	n=17,644	<0.001
Totally agree	12,567 (70.8%)	11,298 (64.0%)	
Agree	4460 (25.1%)	4912 (27.8%)	
Neutral	600 (3.4%)	1,032 (5.8%)	
Disagree	110 (0.6%)	359 (2.0%)	
Totally disagree	23 (0.1%)	43 (0.2%)	
'It was easy to replace the stick in the tube'	n=17,783	n=17,681	<0.001
Totally agree	11,587 (65.2%)	8648 (48.9%)	
Agree	5084 (28.6%)	5392 (30.5%)	
Neutral	843 (4.7%)	1957 (11.1%)	
Disagree	236 (1.3%)	1520 (8.6%)	
Totally disagree	33 (0.2%)	164 (0.9%)	
'It was easy to close the test with the cap'	n=17,787	n=17,684	<0.001
Totally agree	13,095 (73.6%)	11,563 (65.4%)	
Agree	4304 (24.2%)	4907 (27.7%)	
Neutral	334 (1.9%)	841 (4.8%)	
Disagree	42 (0.2%)	330 (1.9%)	
Totally disagree	12 (0.1%)	43 (0.2%)	
'Sampling instructions were clear'	n=17,755	n=17,652	<0.001
Totally agree	12,248 (69.0%)	12,036 (68.2%)	
Agree	4749 (26.7%)	4787 (27.1%)	
Neutral	607 (3.4%)	641 (3.6%)	
Disagree	120 (0.7%)	148 (0.8%)	
Totally disagree	31 (0.2%)	40 (0.2%)	

* p-values based on Chi-square test statistics

Figure 3 Responses per aspect of ease of use for FOB-Gold and OC-Sensor



Preferred FIT

Most participants (59%) did not have a clear preference for either FIT brand, of those with a preference, more participants preferred FOB-Gold (36%) than OC-Sensor (5%) (p <0.001%; Table 3). Males preferred FOB-Gold slightly more often than females (37% versus 35%) and females preferred OC-Sensor more often (5.7% versus 4.5%) (p<0.001). Participants over 65 years of age were more frequently indifferent compared to younger participants (67% versus 57%; p<0.001), as were participants with a lower socioeconomic status, compared to those with a higher status (p<0.001).

Table 3 Preferred FIT brand as reported by participants, stratified by sex, age and socioeconomic status

	Total n=17,333	FOB-Gold n=6268 (36%)	OC-Sensor n=881 (5%)	No preference n=10,184 (59%)	p-value
Sex n=17,333					<0.001
- Males	8785	3244 (37%)	391 (4%)	5150 (59%)	
- Females	8548	3024 (35%)	490 (6%)	5043 (59%)	
Age* n=17,333					<0.001
- 55-64	14,365	5408 (38%)	761 (5%)	8196 (57%)	
- 65-75	2968	860 (29%)	120 (4%)	1988(67%)	
SES n= 17,295					
- Very high	3556	1345 (38%)	210 (6%)	2001 (56%)	<0.001
- High	3862	1466 (38%)	182 (5%)	2214 (57%)	
- Average	3225	1167 (36%)	166 (5%)	1892 (59%)	
- Low	3990	1364 (34%)	202 (5%)	2424 (61%)	
- Very low	2662	912 (34%)	120 (5%)	1630 (61%)	

FIT: fecal immunochemical test; SES: socioeconomic status
*Age at FIT invitation

Of the 6268 participants who preferred FOB-Gold, 1086 (17%) reported a reason for their preference. The most frequently reported reason was the wider opening of the tube, which made it easier to replace the sampling probe. In addition, the screw-cap was considered easier to open and easier and close. Taking a sample by sticking the probe in the stool, as with FOB-Gold, was reported easier than scraping, as prescribed for OC-Sensor. Moreover, some respondents indicated that less feces was sticking to the probe, making it easier to sample the right volume. The grip of the FOB-Gold was also frequently appreciated.

Of the 881 participants that preferred OC-Sensor 175 (20%) provided a reason for their preference. Some aspects of preference for OC-Sensor were similar to those reported for FOB-Gold, although in smaller proportions, for example the grip and easy closing of the cap. Especially appreciated in OC-Sensor was its single cap that avoids any confusion on which cap to open and prevents the loss of buffer. Its flat shape was also preferred to prevent the test from rolling away before and after sampling.

Participation

In the randomized trial, 936 out of 1923 invitees allocated to receive an FOB-Gold participated (48.7%) versus 940 out of 1923 (48.9%) allocated to OC-Sensor (RR = 1.00; 95% CI: 0.93 to 1.06) (Figure 2). The absolute difference was -0.2% (95% CI: -3.4% to 3.0%). The null hypothesis of a difference of 5% or more was rejected, demonstrating that FOB-Gold was non-inferior to OC-Sensor in terms of participation rate (p=0.001).

Non-analyzability

One out of 936 FOB-Gold tests (0.1%) could not be analyzed versus four out of 940 OC-Sensor tests (0.4%; p= 0.18).

DISCUSSION

This study found small, but statistically significant, differences in ease of use in favor of FOB-Gold compared with OC-Sensor. FOB-Gold was more often preferred than OC-Sensor, but most participants did not express a clear preference for either FIT. Despite these differences, our randomized trial showed that participation in the Dutch population based CRC screening program was not influenced by the type of FIT offered with the invitation sent by postal mail.

This study was conducted within the logistics of the Dutch CRC screening program and included a large and representative sample of the screening population. Because the study population was screening-naive, their expressed preferences were not influenced by a previous experience with one of the tests. With the large study group, we had enough power to detect small differences in preferred aspects of use. Nevertheless, some limitations have also to be acknowledged. Due to a limited number of screening-naive individuals in our study population in 2016, fewer were invited in each arm of the randomized controlled trial than we anticipated in our sample size calculations (1923 instead of 2019). Despite this failure to reach the targeted number, we could reject inferiority of FOB-Gold in terms of participation. Ease of use and preferences were evaluated in a large study with paired design and the effects on participation in a randomized trial, in which invitees were randomly allocated to one of both tests. These were two different groups, but both groups were randomly selected from the same target screening population, facilitating generalizability. Participants in our paired cohort, in which ease of use was assessed, were somewhat older and more had a higher socioeconomic status than in the randomized trial. Since the two arms in the randomized trial were balanced, we feel confident to conclude that any of the differences in ease of use have not affected participation. Our questionnaire had been tested in a previous study [18], but was not validated for this comparative evaluation. We do not expect any selection bias in the responding participants because the participation rate in the paired cohort was similar to that in the RCT, and 98% of participants also returned the questionnaire. The specific aim of this study was to compare FOB-Gold and OC-Sensor because these FITs were implemented in the Dutch CRC screening programme. Although these FIT brands are among all available FITs widely used ones, our results cannot be generalized to possible differences between other FIT-brands. Although our screening naive study population had no experience with one of the FITs, we cannot exclude that participant's responses might have been influenced by the fact that FOB-Gold is the test that is currently used in the national Dutch screening program.

The ease of use was appreciated differently for each FIT for almost all aspects, favoring FOB-Gold. Most differences were small and might be considered clinically irrelevant, though the higher reported ease of replacing the sampled probe into the FOB-Gold tube was evident. Earlier studies comparing FOB-Gold and OC-Sensor, did not rely on a survey with paired design to assess ease of use, but instead evaluated the number of non-analyzable tests and found higher error rates for FOB-Gold.[6, 8, 9] We found very few non-analyzable tests, and no difference in proportions by FIT. The main reasons for non-analyzability of FOB-Gold in former studies were fecal overload[8], wrong opening of the tube and loss of buffer [9] or 'incorrect sample manipulation'[6]. In our study the only non-analyzable FOB-Gold tube was missing its buffer, despite adaptations of the FOB-Gold's caps, designed to avoid opening of the wrong side of the tube.

Combining analyzability and appreciated ease of use, suggestions for optimal test design can be derived. Loss of buffer with FOB-Gold is probably due to the presence of two caps, one at each end of tube; this was reported to be more impractical by some of the participants. The wide opening of the FOB-Gold tube is appreciated but may lead, in rare cases, to over-sampling. On the other hand, a small opening in OC-Sensor can lead to under-sampling and appears to be less well appreciated in our study. Considering the other reported evaluations of participants on FIT shape, sampling instruction, cap opening and closure of these two FITs, the ultimate design could be envisioned. An ideal FIT would then be square shaped, have a wide opening, one screw cap, and sampling is instructed by sticking the probe in the stool. Possibly, the ideal FIT would positively affect the proportion of analyzable FITs.

It is known that participation in CRC screening is generally lower for persons with lower socioeconomic status and for ethnic minorities, while CRC incidence and mortality are higher in these groups.[19-21] To avoid any increase in health inequities within the population through screening, any difference in FITs that influences participation by socioeconomic or ethnic subgroup is of relevance. Our results show differences in preferences between subgroups by sex, age and socioeconomic status, but these were small and inconsequential for the screening uptake rate. Hence, we would currently not endorse using different tests for different sexes, ages or socioeconomic status. Our results are however based on the preferences of those participating in screening and did not include information on participant's ethnic background. Evidence on culturally, ethnically or racially related barriers to engage in FOBT- screening is limited, but a disgust of stool handling was included in the top five barriers in an ethnically and racial diverse population.[22] Although future study initiatives that specifically address culturally or ethnically derived barriers to engage in FIT screening could be valuable to optimize CRC screening participation, we do however not expect big differences in preference between FITs for different ethnic groups.

The absence of a difference in participation rate for OC-Sensor or FOB-Gold within an organized CRC screening program confirms the results of a previous study in the pilot program in the Netherlands, in which the uptake was 63% with both tests.[8] At time of the pilot program, no alternative screening option existed in the Netherlands, while invitees in our study had the option to participate in the national screening without participating in this study. This probably explains a slightly lower participation rate in our evaluation compared with the former study. Other studies have shown significant though small differences in favor of OC-Sensor: 59% compared with 62%[6] and 45% versus 47%.[9] Whether participation rates in successive screening rounds is influenced by the FIT that was distributed in the first round is not yet known, but may be relevant for the evaluation of ongoing screening programs.

Continuous evaluation of new strategies to optimize screening program effectiveness and reduce possible harms is crucial to guarantee screening quality, and should be performed on a routine basis.[23] The absence of a difference in participation rates between FOB-Gold and OC-Sensor in this study, despite a preference for one particular test in a minority of participants and differences in reported ease of use, shows that these small differences do not affect the willingness to engage in CRC screening. This result, in combination with the evidence that both FITs have an equivalent accuracy to detect AN [13], implies that other considerations can guide the selection of a test in population-based screening programs for CRC. Cost-effectiveness analyses, efficiency in logistics and efficiency in laboratory analyses are other considerations that should be taken into account.

Acknowledgements

The authors would like to thank the Netherlands Organisation for Health Research and Development of the Dutch Ministry of Health (ZonMw) for funding, and all participants for their efforts to perform two tests and a questionnaire. The authors thank all involved coworkers of the Foundation of Population Screening South-West (Bevolkingsonderzoek Zuid-West), and all involved co-workers at Daklapack packaging for their contributions to the study. Finally, the authors thank Star lab (Rotterdam, The Netherlands), for their efforts in analyzing twice as many FITs compared to the nationwide Dutch screening program during the study period.

REFERENCES

1. Kronborg O, Fenger C, Olsen J, Jorgensen OD, Sondergaard O. Randomised study of screening for colorectal cancer with faecal-occult-blood test. Lancet. 1996;348(9040):1467-71.
2. Halloran SP, Launoy G, Zappa M, International Agency for Research on C. European guidelines for quality assurance in colorectal cancer screening and diagnosis. First Edition--Faecal occult blood testing. Endoscopy. 2012;44 Suppl 3:SE65-87.
3. Schreuders EH, Grobbee EJ, Spaander MCW, Kuipers EJ. Advances in Fecal Tests for Colorectal Cancer Screening. Current Treatment Options in Gastroenterology. 2016;14(1):152-62.
4. Deutekom M, van Rossum LG, van Rijn AF, Laheij RJ, Fockens P, Bossuyt PM, et al. Comparison of guaiac and immunological fecal occult blood tests in colorectal cancer screening: the patient perspective. Scand J Gastroenterol. 2010;45(11):1345-9.
5. Moss S, Mathews C, Day TJ, Smith S, Seaman HE, Snowball J, et al. Increased uptake and improved outcomes of bowel cancer screening with a faecal immunochemical test: results from a pilot study within the national screening programme in England. Gut. 2017;66(9):1631-44.
6. Zubero MB, Arana-Arri E, Pijoan JI, Portillo I, Idigoras I, Lopez-Urrutia A, et al. Population-based colorectal cancer screening: comparison of two fecal occult blood test. Front Pharmacol. 2014;4:175.
7. Faivre J, Dancourt V, Denis B, Dorval E, Piette C, Perrin P, et al. Comparison between a guaiac and three immunochemical faecal occult blood tests in screening for colorectal cancer. Eur J Cancer. 2012;48(16):2969-76.
8. Grobbee EJ, van der Vlugt M, van Vuuren AJ, Stroobants AK, Mundt MW, Spijker WJ, et al. A randomised comparison of two faecal immunochemical tests in population-based colorectal cancer screening. Gut. 2016;66(11):1975-82.
9. Santare D, Kojalo I, Huttunen T, Rikacovs S, Rucevskis P, Boka V, et al. Improving uptake of screening for colorectal cancer: a study on invitation strategies and different test kit use. Eur J Gastroenterol Hepatol. 2015;27(5):536-43.
10. Cole SR, Young GP, Esterman A, Cadd B, Morcom J. A randomised trial of the impact of new faecal haemoglobin test technologies on population participation in screening for colorectal cancer. J Med Screen. 2003;10(3):117-22.
11. Ellis RJ, Wilson S, Holder RL, McManus RJ. Different faecal sampling methods alter the acceptability of faecal occult blood testing: a cross sectional community survey. Eur J Cancer. 2007;43(9):1437-44.
12. Pham R, Cross S, Fernandez B, Corson K, Dillon K, Yackley C, et al. "Finding the Right FIT": Rural Patient Preferences for Fecal Immunochemical Test (FIT) Characteristics. J Am Board Fam Med. 2017;30(5):632-44.
13. Wieten E, de Klerk CM, van der Steen A, Ramakers CR, Kuipers EJ, Hansen BE, et al. Equivalent Accuracy of 2 Quantitative Fecal Immunochemical Tests in Detecting Advanced Neoplasia in an Organized Colorectal Cancer Screening Program. Gastroenterology. 2018;155(5):1392-9 e5.
14. Toes-Zoutendijk E, van Leerdam ME, Dekker E, van Hees F, Penning C, Nagtegaal I, et al. Real-Time Monitoring of Results During First Year of Dutch Colorectal Cancer Screening Program and Optimization by Altering Fecal Immunochemical Test Cut-off Levels. Gastroenterology. 2017;152(4):767-75.e2.
15. National Institute for Public Health and the Environment (RIVM). Exclusion criteria colonoscopy (Dutch)http://www.rivm.nl/Documenten_en_publicaties/Professioneel_Praktisch/Richtlijnen/Preventie_Ziekte_Zorg/Darmkanker/Exclusiecriteria_coloscopie (date accessed 20th June 2017); 2013.

16. National Institute for Public Health and the Environment (RIVM). Uitvoeringskader Bevolkingsonderzoek Darmkanker (Dutch). www.bevolkingsonderzoekdarmkanker.nl/downloads (date accessed 20th June 2017); 2017.
17. Netherlands Institute of Social Research. Socioeconomic status scores The Netherlands. https://www.scp.nl/Onderzoek/Lopend_onderzoek/A_Z_alle_lopende_onderzoeken/Statusscores (date accessed 20 March 2017); 2016.
18. de Wijkerslooth TR, de Haan MC, Stoop EM, Bossuyt PM, Thomeer M, Essink-Bot ML, et al. Burden of colonoscopy compared to non-cathartic CT-colonography in a colorectal cancer screening programme: randomised controlled trial. Gut. 2012;61(11):1552-9.
19. de Klerk CM, Gupta S, Dekker E, Essink-Bot ML. Socioeconomic and ethnic inequities within organised colorectal cancer screening programmes worldwide. Gut. 2017.
20. Doubeni CA, Laiyemo AO, Major JM, Schootman M, Lian M, Park Y, et al. Socioeconomic status and the risk of colorectal cancer: an analysis of more than a half million adults in the National Institutes of Health-AARP Diet and Health Study. Cancer. 2012;118(14):3636-44.
21. Williams R, White P, Nieto J, Vieira D, Francois F, Hamilton F. Colorectal Cancer in African Americans: An Update. Clin Transl Gastroenterol. 2016;7(7):e185.
22. Jones RM, Woolf SH, Cunningham TD, Johnson RE, Krist AH, Rothemich SF, et al. The relative importance of patient-reported barriers to colorectal cancer screening. Am J Prev Med. 2010;38(5):499-507.
23. Bell KJ, Bossuyt P, Glasziou P, Irwig L. Assessment of changes to screening programmes: why randomisation is important. BMJ. 2015;350:h1566.

Supplementary Material 1 Questionnaire

Vragen testbuisjes.

Wij vragen u voor beide testbuisjes onderstaande vragen in te vullen.

	Rond testbuisje	**Plat testbuisje**
1. Het was duidelijk hoe het testbuisje te openen	☐ helemaal mee eens ☐ mee eens ☐ neutraal ☐ mee oneens ☐ helemaal mee oneens	☐ helemaal mee eens ☐ mee eens ☐ neutraal ☐ mee oneens ☐ helemaal mee oneens
2. Het was makkelijk om het testbuisje te openen	☐ helemaal mee eens ☐ mee eens ☐ neutraal ☐ mee oneens ☐ helemaal mee oneens	☐ helemaal mee eens ☐ mee eens ☐ neutraal ☐ mee oneens ☐ helemaal mee oneens
3. Het was makkelijk om de test uit te voeren met het staafje	☐ helemaal mee eens ☐ mee eens ☐ neutraal ☐ mee oneens ☐ helemaal mee oneens	☐ helemaal mee eens ☐ mee eens ☐ neutraal ☐ mee oneens ☐ helemaal mee oneens
4. Het was makkelijk om het staafje met de ontlasting in het testbuisje te doen	☐ helemaal mee eens ☐ mee eens ☐ neutraal ☐ mee oneens ☐ helemaal mee oneens	☐ helemaal mee eens ☐ mee eens ☐ neutraal ☐ mee oneens ☐ helemaal mee oneens
5. Het was makkelijk om het dopje weer op het testbuisje te doen	☐ helemaal mee eens ☐ mee eens ☐ neutraal ☐ mee oneens ☐ helemaal mee oneens	☐ helemaal mee eens ☐ mee eens ☐ neutraal ☐ mee oneens ☐ helemaal mee oneens
6. Het instructieboekje bij de test was duidelijk	☐ helemaal mee eens ☐ mee eens ☐ neutraal ☐ mee oneens ☐ helemaal mee oneens	☐ helemaal mee eens ☐ mee eens ☐ neutraal ☐ mee oneens ☐ helemaal mee oneens

7. Welk testbuisje heeft uw voorkeur om te gebruiken?

☐ Rond testbuisje
☐ Plat testbuisje
☐ Geen voorkeur