Fecal immunochemical test based colorectal cancer screening

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Citation for published version (APA):
Denters, M. J. (2013). Fecal immunochemical test based colorectal cancer screening

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A feces collection paper does not enhance participation in a fecal immunochemical test based colorectal screening program: randomized clinical trial

M.J. Dinters, M. Deutekom, P.M. Bossuyt, P. Fockens, E. Dekker

Accepted for Publication in European Journal of Cancer Prevention
ABSTRACT

Discomfort with the collection of a stool sample is a frequently cited barrier for participation in fecal test-based colorectal cancer screening. The objective was to evaluate whether a feces collection paper enhances participation in a fecal immunochemical test (FIT)-based colorectal cancer screening program. Randomized clinical trial. Second round of a biennial Dutch FIT-based colorectal cancer screening program pilot. A random sample of 10,265 individuals from the general population, men and women aged 50-75 years at an average risk for colorectal cancer, was eligible for participation. Invitees were randomized to an FIT-only group (n=5,136) or an FIT in combination with a feces collection paper group (n=5,129). The main outcome measure was participation in screening. Overall, 5,367 tests of 10,265 were returned (52%). In the FIT-only group, 2,694 tests were returned (52%; 95% confidence interval (CI): 51-54%) versus 2,673 tests in the collection paper group (52%; 95% CI: 51% to 54%). This difference in participation rate was not significant (relative risk: 0.99; 95% CI: 0.97-1.04). A feces collection paper does not increase participation rates in FIT-based colorectal cancer screening. Future studies should explore other ways of facilitating participation in colorectal cancer screening programs.
INTRODUCTION
The effectiveness of colorectal cancer screening programs depends on the willingness of invitees to participate. Discomfort with the collection of a stool sample is a frequently cited barrier to participation in fecal test-based screening programs[1-4]. The results from our first screening round, in which participants were randomized to either a fecal immunochemical test (FIT) or a guaiac fecal occult blood test (FOBT), showed that 53% of nonparticipants found the fecal test to be disgusting versus 14% of participants[5]. Furthermore, participants who received the FIT rated the collection of stool less disgusting and easier than participants who received the guaiac FOBT. Similar results were found in a comparable screening study that randomized invitees between FIT, guaiac FOBT and flexible sigmoidoscopy[6]. Both screening studies described above found a higher uptake in invitees allocated to an FIT than in invitees allocated to a guaiac FOBT.

Advantages of the FIT over the guaiac FOBT are the number of stool samples required (one versus three), the collection procedure (brush versus smear) and the required diet restrictions (no diet versus diet). A better acceptability of the test could be one of the possible explanations for a higher uptake among invitees randomized to FIT. Other interventions that improve test acceptability may also have a positive effect on the participation rate. In Japan, for example, it is a practice to add a feces collection paper to the FIT. We hypothesized that the addition of such a feces collection paper would facilitate the collection of stool, improve the overall test acceptability, and lead to higher participation rates.

The aim of the study reported here was to evaluate whether a feces collection paper enhances the participation rate in an FIT based colorectal cancer screening program pilot.

METHODS
Study population and setting
The study was carried out within a second round of a colorectal cancer screening pilot program in the Netherlands. Screening was initially carried out with the FIT (OC-sensor, Eiken Chemical Co, Tokyo, Japan). The study protocol of the pilot is described in detail elsewhere[7]. Men and women at an average risk for colorectal cancer, aged between 50 and 74 years, living in the screening pilot target area were eligible for inclusion. Individuals who had tested positive in the first screening round and who had undergone a complete follow-up were excluded. The target area from which individuals were recruited for the second screening round was identical to that of the first round. It consisted of three municipalities within the surroundings of Amsterdam known to have an average uptake in the breast cancer screening program.

Recruitment
A file containing all eligible individuals was extracted from the municipality’s population database on the basis of date of birth and postal code provided by the municipalities.

Intervention
All individuals in the target area were randomized to receive either an IT only or an FIT with a feces collection paper. The rest of the invitation kit and the invitation procedure itself were completely identical in both groups.
**Invitation procedure**

A centralized invitation procedure was used. All invitation kits and reminders were sent out by the regional Comprehensive Cancer Centre Amsterdam, an institution also responsible for the organization of the breast and cervical cancer screening programs in the region. The regional Comprehensive Cancer Centre Amsterdam sent (a) an invitation kit including only an FIT or (b) an invitation kit including a feces collection paper and an FIT, on the basis of an externally developed computer-generated randomization procedure. Randomization was stratified by responder status in the first round (non-responder in first round, responder in first round, not invited in first round).

All invitation kits included an invitation letter, an information leaflet, detailed test instructions and an informed consent form. Invitees could perform the test at home and return the FIT with the signed informed consent form in a postage-free envelope to the specialized laboratory of our institution. A reminder was sent after 6 weeks and after 3 months.

**Collection paper**

The collection paper (Eiken Chemical Co.) was a biodegradable disposable paper float that can be placed in the toilet bowl to immobilize stool. The paper was designed for easy sampling (figure 1).

![Image of collection paper use](image-url)

**Figure 1.** Use of collection paper. (1) Marking of the test bottle; (2) placement of the collection paper in the toilet bowl; (3) passage of stool on to the collection paper; (4) collection of the fecal sample; (5) placement of brush into the test bottle; (6) placement of test bottle into the sealed cover; (7) placement of test material into postage-free envelope; (8) return of test material by regular mail.
Questionnaire
All invitees were asked to complete a questionnaire 6 weeks after the invitation was sent. The burden of collecting the stool was assessed by two items that could be scored on a five-point scale [“how easy did you find it to collect the stool” (very easy/not at all easy); “how disgusted were you by collecting the stool” (very disgusted/not at all disgusted)].

Outcome measures
The primary outcome measure was the proportion of tests returned. The secondary outcome measure was the burden of collecting the stool sample as experienced by participants.

Data-analysis
We hypothesized that the addition of a feces collection paper would enhance the participation rate. Participation rate was measured as the number of test returned relative to the number of tests sent out. Differences between groups in the participation rate were tested for statistical significance using the Chi-square test statistic in an intention-to-treat analysis. Differences in the burden scores between groups were tested using the Mann-Whitney test statistic. Data were analysed using the statistical software SPSS 16.0 (SPSS Inc., Chicago, Illinois, USA).

Sample size
In the first round, 10,054 individuals were invited for screening. As we targeted screening on the same group, the number of individuals we intended to invite for the second round was also 10,000. With the invitation of 10,000 eligible persons and anticipating a 50% participation rate in the current study, the two-sided 95% confidence interval (CI) for the participation rate was expected to increase 1% from the observed proportion, using the large sample approximation to the binomial distribution. This sample size would give us 80% power to detect differences of ~ 3% in the participation rate between the trial arms, using the continuity corrected Chi-square test statistic and a 0.05 two-sided significance level.

RESULTS
Invites and procedure
A total of 10,265 individuals were invited between August 2008 and October 2009 (Figure 2). Two hundred invitations were sent out each week, except in July. One group of participants (n=5,129) received just the FIT, the remaining (n=5,136) received the collection paper in addition. The baseline characteristics of both groups are shown in Table 1.

Table 1. Baseline characteristics of invitees.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>FIT-only group (n=5,136)</th>
<th>Collection paper group (n=5,129)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean± SD) (years)</td>
<td>60 ±7</td>
<td>60 ±7</td>
</tr>
<tr>
<td>Males [n (%)]</td>
<td>2,508 (49)</td>
<td>2,501 (49)</td>
</tr>
</tbody>
</table>
Outcome

Participation

In the FIT-only group, 2,694 tests were returned (52.5%) versus 2,673 tests in the collection paper group (52.1%). The difference in the participation rate was small and not statistically significant, with a relative rate of 1.01 (95% CI: 0.97-1.04) (Table 2). Subgroup analyses according to sex and age did not show any significant differences in the participation rate (Table 2).

Table 2. Participation rate, invitees/participants (%).

<table>
<thead>
<tr>
<th></th>
<th>FIT-only group</th>
<th>Collection paper group</th>
<th>Relative risk for participation (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>2,694/5,136 (52)</td>
<td>2,673/5,129 (52)</td>
<td>0.99 (0.93-1.03)</td>
</tr>
<tr>
<td>Males</td>
<td>1,188/2,508 (47)</td>
<td>1,188/2,501 (48)</td>
<td>1.00 (0.95-1.06)</td>
</tr>
<tr>
<td>Females</td>
<td>1,506/2,628 (57)</td>
<td>1,485/2,628 (57)</td>
<td>0.98 (0.93-1.04)</td>
</tr>
<tr>
<td>&lt;55 years</td>
<td>674/1,399 (48)</td>
<td>703/1,398 (50)</td>
<td>1.04 (0.97-1.12)</td>
</tr>
<tr>
<td>55-59 years</td>
<td>689/1,286 (54)</td>
<td>682/1,276 (53)</td>
<td>1.00 (0.92-1.08)</td>
</tr>
<tr>
<td>60-64 years</td>
<td>587/1,051 (56)</td>
<td>567/1,051 (54)</td>
<td>0.96 (0.88-1.05)</td>
</tr>
<tr>
<td>65-69 years</td>
<td>398/726 (55)</td>
<td>402/736 (55)</td>
<td>1.00 (0.90-1.11)</td>
</tr>
<tr>
<td>&gt;69 years</td>
<td>330/614 (54)</td>
<td>302/601 (50)</td>
<td>0.93 (0.83-1.04)</td>
</tr>
</tbody>
</table>

Figure 2. Flowchart.
**Burden of collecting the stool sample**

In the FIT-only group, 1,787 participants completed both items assessing burden (66%) versus 1,756 participants in the collection paper group (74%). Responder characteristics are shown in Table 3. The item ‘collection of stool’ was rated as ‘very easy’ or ‘quite easy’ by 83% of participants in the FIT-only group versus 82% of participants in the collection paper group. In the FIT-only group, 76% of participants rated the item ‘disgusted by collecting the stool’ as ‘a little disgusting’ or ‘not at all disgusting’ versus 77% of participants in the collection paper group. There were no significant differences between the FIT-only group and the collection paper group in the distribution of scores over each of the two items ($P=0.614$ and $P=0.052$ respectively: Figure 3).

**Figure 3a - Ease of collecting stool sample as reported by participants.** There was no significant difference in distribution of scores between groups ($P=0.614$).

**Figure 3b - Disgust with collecting stool a sample as reported by participants.** There was no significant difference in distribution of scores between groups ($P=0.052$).
DISCUSSION

This study is the first to investigate the effects of a feces collection paper on participation in an FIT-based colorectal cancer screening program. We did not observe any difference in the uptake of screening between invitees who were supplied with a collection paper and invitees who received an FIT only. We also asked participants about their experience with collecting the stool. To our surprise, participants supplied with a collection paper rated the collection of stool equally easy and equally disgusting as participants who had not received a collection paper.

When designing the study we hypothesized that a collection paper would enhance participation through facilitation of the stool-collection process. However, we failed to find any differences either in uptake of screening or in experienced burden. In contrast to our expectations, the collection paper did not alter participant’s perception of the stool-collection process and therefore probably did not result in a higher uptake.

Unfortunately, we do not have data to confirm whether invitees who were randomized to the collection paper group actually used the paper. Therefore, we can only conclude that supplying invitees to an FIT screening program with a collection paper does not influence participants’ perception of the test and does not make them more willing to participate. We cannot draw any conclusions on the effects of the actual use of the collection paper.

Previous studies have investigated various other interventions aimed at increasing participation rates in colorectal cancer screening such as tailored interventions[8;9], educational video-based strategies[10], advance notification letters[11], varying recruitment methods[12;13], psycho-educational interventions[14], reminders[15;16] and automated telephone outreach[17]. Of the strategies mentioned above, tailored behavioral interventions proved effective methods for increasing screening adherence directly[8] or for moving persons forward in their stage of adoption for colorectal cancer screening[9]. Also, a video-based intervention significantly reduced barriers to screening and improved compliance with colorectal cancer screening with FOBT [10]. A study by Cole et al., which investigated the effect of different invitation strategies on participation in FIT-based screening, found that an advance notification letter significantly increased participation in screening[11]. Furthermore, an intervention strategy that involved high rates of face-to-face contact with the study participants was shown to result in a higher enrollment yield in older African American men[13]. Similarly, a Spanish colorectal cancer screening program also found higher participation rates in invitees who were randomized to a visit by a trained nonhealth professional compared with those that received an invitation letter signed

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>FIT-only group (n=1,788)</th>
<th>Collection paper group (n=1,760)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (men ± SD) (years)</td>
<td>61 ±7</td>
<td>60 ±7</td>
</tr>
<tr>
<td>Males [n (%)]</td>
<td>781 (44)</td>
<td>785 (45)</td>
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</table>
by a physician by postal mail[12]. Thompson et al. also studied different intervention methods and found that an interactive talk by a physician or nurse increased adherence by 12-13%[16]. In addition, individuals invited for sigmoidoscopy screening randomly allocated to a psycho-educational intervention that specifically addressed barriers towards screening had a higher level of attendance compared to controls allocated to a standard invitation[14]. A reminder postcard was found to be the most effective single intervention in the study by Thompson and colleagues described earlier; it increased participation by 24-25%. Sequist et al. also found that screening rates were higher for patients who received a reminder by postal mail compared with those who did not[15]. Finally, a study examining the effect of a single interactive outreach call to engage participants in conversation about the importance of colorectal cancer screening and options for and barriers to screening failed to change participation rates of colorectal cancer screening[17]. On the basis of the studies described above, recruitment strategies with a high rate of personalized contact seem to influence the participation rate positively. These strategies, however, are also expensive and time-consuming. More simple and low-cost interventions, such as mailed notification letters and reminders, have also proven to be effective in increasing uptake. These low-cost interventions are probably more suitable in mass-screening programs.

It is important to stress that, apart from high participation rates, high rates of informed choice are increasingly becoming recognized as mandatory in any mass screening program. Rather than coercing individuals into participation, invitees should be provided with all relevant information, enabling them to make an informed decision to participate or not. Therefore, screening programs should not be evaluated only on the basis of participation rates. Patient autonomy requires that individuals should be able to choose whether they wish to participate in screening[18]. In this process, it is important that barriers are removed, so that invitees can exercise informed choice about screening. The interventions described above could be used as ways to lower these barriers.

**Conclusion**

The addition of a collection paper did not result in a higher uptake in an FIT-based cancer screening pilot program. Future studies should explore other interventions aimed at removing barriers and facilitating participation in colorectal cancer screening.
REFERENCE LIST
