# Why do participants in the Flemish colorectal cancer screening program not undergo a diagnostic colonoscopy after a positive fecal immunochemical test?

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**Introduction**

Although initiatives have been largely spread throughout Europe, almost all population-based FIT screening programmes were implemented relatively recently, lowering possibilities to already observe ultimately desired colorectal cancer incidence or mortality effects [Gini, 2020] [1]. Yet, two Italian observational studies have reported the impact of FIT screening in reducing CRC incidence and mortality [Ventura, 2014; Rossi, 2015][2-3]. Screening practices including colonoscopy follow-up of positive FIT lead to a 15% relative risk reduction of CRC mortality [1]. In Flanders (Belgium) the CRC screening programme started in 2013 offering a free FIT (Eiken, Chemical Co. Ltd, OC Sensor) to people aged 56-74 years by mail. The target ages were extended gradually from 56-74 in 2013 to 55 in 2017, 53-54 in 2018, 51-52 in 2019 and to 50 in 2020 [4-5]. Both the participants and their GP (if GP filled in the participation form and/or known GP by a global medical dossier) receive the results of the FIT directly through the CCD. The GP is not asked to contact the patient about the result. In 2018 the uptake was 51.6% with a FIT positivity rate of 5.3%, corresponding with 16,905 participants (and their GP) who received the advice to undergo a diagnostic colonoscopy (DC) [6]. DC compliance after a positive FIT is crucial to achieve an overall reduction in CRC incidence and mortality.

In Flanders, 15.9 % (2,611) had no DC after the positive FIT in 2018 (data 2019 incomplete). 10.7% of them (1,755) had no follow-up whatsoever after a positive FIT in 2018, 2.5% (407) repeated the positive FIT with another stool test and 2.7% (449) had another (incorrect) follow-up [6].

Depending on the country, non-compliance rates vary from 7 to 42% [7-11]. Although a CRC screening program should aim at 100% DC completion, the EU Guidelines describe 85% as an acceptable level, and >90% as the desirable level of DC after a positive FIT [12]. Certain groups are at higher risk of non-DC-completion. As in other countries [7, 9-10] previous studies in Flanders indicated that FIT uptake [5] and DC compliance after a positive FIT are both associated with socio-demographic factors [13]. In Flanders men, older participants, lower socio-economic groups and nationalities other than Belgian are less likely to undergo a DC after a positive FIT [13]. Although the profile of the DC non-compliant group is well-documented, the knowledge regarding specific reasons for non-compliance to DC is lacking. The aim of this study was therefore to explore self-reported reasons for non-DC-compliance after a positive FIT in Flanders, by an online survey and telephonic interviews.

**Methods**

In a mixed-method design, by telephone (semi qualitative) and online surveys (quantitative research) the reasons of non-DC-compliance after a positive FIT were explored. Both surveys were piloted before performed in the eligible population. Eligible persons were limited to those with a positive FIT without a follow-up DC. All candidates were selected based on the administrative databases of the Centre for Cancer Detection (CCD).

*The semi-structured telephone interviews* were conducted from February until December, 2018. Between 01/01/2016 and 31/12/2017 a total of 6,678 persons had a positive FIT without a registered DC as follow-up (and without a virtual colonoscopy). A total of 135 invitees were selected by strategic sampling according to age (56-74) and gender to ensure maximal variation. *Online survey*: a total of 20,728 participants of the Flemish CRC screening program had a positive FIT in the period from 1 July 2015 until 30 June 2016. Of this group 11,398 had filled in a valid e-mail address on their participation form (with the stool sample) and received a link to the online survey in November 2016 (a reminder in December 2016). The aim of the online survey was to evaluate different processes of the entire screening program with a subset of questions for the non-DC-compliant group only.

Response to the telephone and online survey served as informed consent. No ethical approval was needed. The interviewees' and online survey respondents' anonymity was ensured throughout the study (ID coded before analyzing, and for the telephone interviewees recoded once to investigate DC follow-up 2 years later). No incentive was given.

**Data analyses** The *telephone interview*, conducted by three trained employees of the CCD, was guided by previously fixed key themes (Table 1). Additional non-fixed questions were formulated to gain more information. The average duration of the telephone interviews was approximately 10 minutes. All answers were typed and interviewers wrote contextualizing notes afterwards. The interviews were analyzed using open coding (Microsoft Word, 2016) The *online survey* data were analyzed using IBM

SPSS statistics software (version 24.0 for Windows). The Chi-square test was used to explore possible statistically significant associations (p-values <0.05) between socio-demographic variables and reasons for non-DC compliance.

**Table 1. Key questions of the telephonic interview**

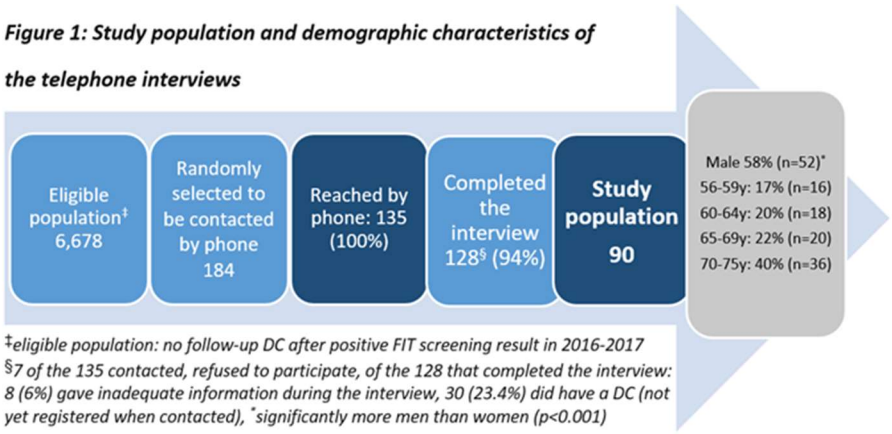
| | |
|---|---|
| Introductory question | *Q1: Do you remember the positive screening result letter, in which we advised you a diagnostic colonoscopy as follow-up? Did you receive this letter?* |
| Filtering question | *Q2: In our database no DC as follow-up was registered. Is it correct that you didn't have a DC? [if DC performed, interview stopped]* |
| Main questions | *Q3: Can you describe why you did not have a DC after the positive screening result?* |
| | *Q4: Did you discuss your positive screening result and a follow-up DC with your GP? What was his/her advice?* |
| | *Q5: Did you have another medical intervention instead of the DC? What kind of medical intervention?* |
| Closing question | *Q6: Would you like to add anything or do you have any further questions?* |

## Results

### Study population

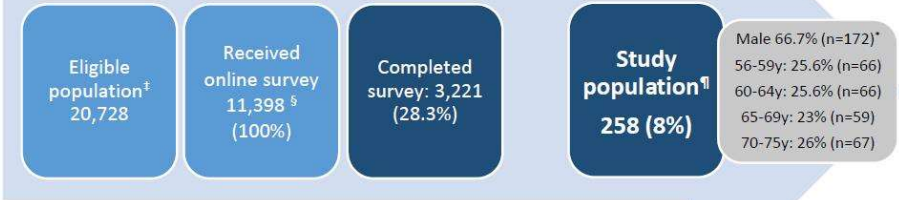
Of the 135 selected for the telephone interviews, only 90 interviewees met the inclusion criteria and completed the telephone interview. The other 45 gave incomplete answers, were not willing to participate or had undergone a DC (not yet registered in the database of CCD at the time of recruitment). Of the 90 interviewees, 10 stated not remembering the positive result letter with the advice to plan a DC and were therefore excluded from the analyses. In total 3,211 of the 11,398 invitees responded to the survey (28.2%), of which 2,953 with (92%) and 258 (8%) without a DC after the positive FIT. The final study population included 348 respondents without a DC (258 online survey participants and 90 interviewees). Participants characteristics are presented in Figures 1 (interviews) and 2 (online surveys). More elderly people responded to the telephone compared to the online survey.

***Figure 1: Study population and demographic characteristics of the telephone interviews***




*‡eligible population: no follow-up DC after positive FIT screening result in 2016-2017*
*§7 of the 135 contacted, refused to participate, of the 128 that completed the interview: 8 (6%) gave inadequate information during the interview, 30 (23.4%) did have a DC (not yet registered when contacted), *significantly more men than women (p<0.001)*

***Figure 2: Study population and demographic characteristics of the online survey respondents***




*‡Positive FIT result in 01/06/2015 until 30/06/2016, §part of eligible population who have given the CCD a valid e-mail address, ¶of the 3,221 that filled in the survey, 258 respondents did not have a DC after their positive screening result, *significantly more men than women (p<0.001)*

***Telephone interview*** Although delivered both to the participants and their GP, 10 interviewees did not remember the positive result letter (*Q1*). Among the 80 respondents who did remember the positive result, different reasons of not having a DC emerged (*Q3*). The most common reasons were having haemorrhoids (and the perception that the positive FIT was a false positive one) (n=13), a negative advice of a GP to plan a DC (n=12), lack of complaints (n=12), suffering from another serious illness and/or other medical priorities (n=11), having (temporarily) postponed the DC (n=7) and fear of the DC (n=6). Few interviewees also mentioned a lack of time (n=3) or had no particular reason (n=3). Additional arguments given were: no visible blood in the stool (n=2), no familial risk of CRC (n=2), had a colonoscopy in the past (before the stool test) (n=1), had a negative FIT from the pharmacy after the positive FIT in the screening program (n=1), having other non-medical priorities (n=2), the willingness to wait for the next screening invitation, and only when that second stool test is positive willing to plan a DC (n=1). Some interviewees indicated never undergoing a colonoscopy and let nature take its course

(not intervene if it is cancer) (n=2) and some thought the test was false positive, as it was with people they knew that participated and where the DC after the positive FIT was negative (n=2).

The majority of the interviewees (54 out of 80; 67.5%) discussed the positive FIT with their GP (*Q4*). In 23/54 (42.6%), the GP correctly advised a DC, however the patient did not follow this advice. The other 31 interviewees (57.4%) mentioned that the GP even discouraged a DC due to suspicion of haemorrhoids (n=7), not taking the positive FIT seriously (n=4), waiting for the next screening invitation after 2 years (only in case the second FIT would be positive the GP would recommend a DC) (n=2), GP performed a second stool test which was negative (n=2), GP performed a blood test which was reassuring (n=2), GP thought the positive FIT was false due to (blood thinning) medication use (n=3), other health issues that had priority (n=5) and Crohn disease (n=2).

17/80 interviewees (21%) had another follow-up instead of the DC (*Q5*), such as a blood test (n=5), a second stool test via the GP (n=5) and a self-test bought in a pharmacy (n=1). After the telephonic interview, 38.8% (n=31) had some questions or remarks: 9 interviewees indicated that they would still participate in the CRC screening program and would plan a DC when tested positive a second time (n=9), 7 interviewees indicated that they would still schedule a DC, two interviewees were considering it and two interviewees would discuss a DC again with their GP. Four interviewees asked when they would receive their next invitation with FIT. Most interviewees explicitly thanked the interviewer for highlighting the importance of a correct follow-up after their positive FIT.

Two years after the telephone surveys (12/2020) only 8 of the 90 interviewees had a DC (9%). 36 out of 90 did not receive a new invitation (no more in target population due to age) and 46 received a new invitation with FIT. 30 out of 46 interviewees who received a new FIT participated again (66%) of which 13 tested positive once again. Only 7 of those 13 went for a DC after the second test, indicating that 6 of them, even after a second positive FIT, did not undergo a DC.

**Online survey**

In Table 2 the questions only added in the online survey for the positive FIT participants without a DC are given.

***Table 2: Online survey questions***

| **Questions** |
| --- |
| *Q1: Who contacted who after receiving the positive result letter?*<br><br>*I contacted my GP - My GP contacted me - I did not have any contact with my GP about the positive result letter* |

| |
|---|
| *Q2: Can you describe why you did not have a DC after the positive screening result? (=Q3 in the telephone survey)* |
| *Q3: Who mainly took the decision not to have a DC after the positive screening result?*<br>*I did, my GP, my specialist, someone else* |
| *Q4: Did you have another medical intervention instead of the DC? If yes, what kind of medical intervention? (=Q5 in the telephone survey)*<br>*(if yes different kind of medical interventions popped up to choose)* |
| *Q6: Would you like to add anything or do you have any further questions? (=Q6 in the telephone survey)* |

The majority (54.3%, n=140) of the respondents contacted the GP themselves after receiving the result, in 17.4% (n=45) the GP contacted the respondent. In 28.3% (n=73) there was no GP contact whatsoever concerning the positive FIT (*Q1)*. The main question 'Why did you not undergo a DC? (*Q2*)' was answered by 66.7% (n=172). 7.4% (n=19) gave an irrelevant or evasive answer (nothing to do with the question asked) and 26% (n=67) did not fill in the question. The open answers were categorized into 15 groups (see Table 3). If more reasons were given, the first or most highlighted reason was categorized. Almost 15% indicated they would still schedule a DC, 5.8% indicated that they kept postponing it or did not have time at that moment and another 2.3% were still doubting about planning a DC (in total 22.6% of the respondents). These 22.6% respondents might not reveal the actual reason for not planning a DC. Postponing a DC follow-up could be the result of other reasons of not having a DC. 14% had a second FIT after the first positive one (mainly delivered by the GP) and 6.4% had another follow-up than DC. 14% of the respondents believed the FIT was falsely positive, and more than 5% stated that the GP thought a DC was not necessary, without giving more background information why the GP advised not to plan a DC . One fifth gave a medical reason for not having a DC, including previous colonoscopy or polyps (9.3%), complaints not linked to CRC (8.7%) and complaints linked to CRC (1.7%). More than 6% did not undergo a DC due to fear of the colonoscopy and more than 5% were just not willing to undergo a DC (reason not given in detail) (*Q2*). On the question 'Who mainly took the decision not to have a DC after the positive screening result?' the majority (65.9% or 170 respondents) indicated that they had made the decision themselves not to have a DC, in 22.5% (n=58) the GP took the decision, in 8.1% (n=21) the gastroenterologist and in 3.5% (n=9) someone else mainly pushed the decision not to plan a DC. The percentage that made the decision themselves increased with age (for example 54.5% in the 56-59 year olds versus 77.8% in the oldest group), and vice versa, the older, the less often that decision was made by the GP (*Q3*). The majority of respondents (69.4%, n=179) did not have another

follow-up after the positive FIT. 14.7% (n=38) had another FIT (in line with the results of *Q2*), 7% (n=18) had a blood test, 3.9% (n=10) had a virtual colonoscopy, 2.7% (n=7) had a PET scan and 2.3% (n=6) had another follow-up (*Q4*).

**Table 3: Reasons of not having undergone a DC after the positive FIT**

| **Reasons no DC (172 respondents out of 258) in 15 categories** | **Number of respondents (%)** |
|---|---|
| DC will be scheduled | 25 (14.5%) |
| keep postponing DC | 10 (5.8%) |
| still doubting to plan a DC | 4 (2.3%) |
| second FIT after positive FIT in CRC screening program (including one self-test of pharmacy) | 24 (14.0%) |
| other follow-up completed (PET, CT) | 11 (6.4%) |
| assuming the positive FIT result is a false positive one (due to haemorrhoids, medication use, diverticulitis, no trust in the FIT result in general) | 24 (14.0%) |
| advice GP not to plan a DC / GP thinks a DC is not necessary | 9 (5.2%) |
| previous colonoscopy before the screening test / previously removed polyps | 16 (9.3%) |
| medical complaints not linked to CRC or recent surgery | 15 (8.7%) |
| medical complaints linked to CRC (abdominal complaints, constipation and/or diarrhea) | 3 (1.7%) |
| fear of colonoscopy | 11 (6.4%) |
| not willing to undergo a DC in general / not willing to undergo a DC due to the bowel preparation | 9 (5.2%) |
| personal reason | 4 (2.3%) |
| no family history of CRC / no complaints | 4 (2.3%) |
| others (fear of the hospital, lack of knowledge colonoscopy, financial issues) | 3(1.7%) |
| **Total** | **172 (100%)** |

**Discussion**

In this retrospective study we used two research methods (online survey and telephone interviews) among participants in the Flemish CRC screening program with a positive FIT, but without a DC as follow-up to obtain first insights into motivation for the lack of a DC after a positive FIT. The profile of participants without a DC after the positive FIT was already explored [13], therefore this study focusses entirely on self-reported reasons for the lack of DC after a positive FIT.The study has several limitations. In the online survey only people of which the CCD had a valid e-mail address were included. Theoretically, the results of this group could differ from a group of which no valid e-mail address was provided. The online survey has an underrepresentation of the elderly people, whereas in the telephone interviews the 72-74 years are overrepresented, possibly due to the research method that

was used. Selection bias could also occur in the people who participate in the survey versus the people who do not participate. People who filled in the survey might be more motivated to express their experiences.

A timely DC after a positive FIT is a critical step on the CRC screening continuum. Modeling studies suggest that longer time to DC after a positive FIT might lead to clinically relevant increases in the risks of CRC, advanced-stage CRC and CRC mortality [14]. In Flanders (2013-2017), the detected CRCs in participants with a DC within 12 months after the positive FIT have a significantly more favorable distribution compared to CRCs detected in participants without a DC within 12 months [BCR, personal communication]. Of the 812 CRCs detected in FIT positive participants without a DC within 12 months, 19.7% was registered as stage III and 12.2% as stage IV, compared to 9.4% and 2.0%, respectively of the 8,939 CRCs in positive FIT participants with a DC within 12 months [BCR, personal communication]. The five-year relative survival rate for CRC (period 2014-2018) is quite high in Flanders, namely 74.9% [15], and for stage I 97.6% compared to 18.7% when diagnosed in Stage IV [BCR, personal communication]. These results again highlight the clinical importance of early detection by a timely DC after a positive FIT.

The online survey (a more quantitative approach) and the telephonic interviews (a more qualitative approach) reveal similar reasons of lack of DC: the perception that the positive FIT was a false positive one (possibly due to haemorrhoids or second negative stool test by GP), still postponing or still planning the DC, medical reasons and fear of the colonoscopy. The perception of a false positive result, fear of colonoscopy, other health issues and repeating the FIT were described by others as well [7, 16]. More than half of the telephone interviewees mentioned that the GP discouraged a DC. One fifth of the survey respondents indicate that mainly the GP took the decision not to undergo a DC. Main reasons of not advising the patient a DC are the suspicion of hemorrhoids or a false positive FIT. Some GPs perform a blood test or second stool test instead. A previous evaluation revealed that some GPs were not fully aware of the screening programme procedures. Despite the availability of the organised Flemish programme, some GPs still prescribed non-organised FITs to patients in the target population. Some GPs repeated the positive FIT, hoping for a second positive one, to convince patients to undergo a DC [17]. Non-organised FITs are not free-of-charge, results and follow-up information are not systematically registered and quality indicators (such as detection rates and interval cancers) are not systematically monitored by the CCD, the BCR or any other authorities. The literature also indicates that GPs sometimes fail to act on positive FIT results; either because they never received the result or choose to repeat the FIT [18-20]. In Flanders, in only a minority of cases a GP is not filled in the participation form (not known by a global medical dossier or not filled in by the participant) and does not receive the result letter. Some GPs have a too low perception of the risk associated with a positive

FIT, which might influence their patients' decision making. In a Dutch study an underestimation of CRC and advanced adenoma probabilities after a positive FIT among GPs was noted. When told the actual probabilities, some GPs stated that this knowledge might change the way they would inform patients [21].

GPs clearly have a motivating role towards their patients to plan a DC by correctly informing them. Our study indicated that about 70% (67,5% of the telephone interviewees and 71,7% of the survey respondents) discussed the positive FIT with their GP. In that discussion, GPs have a potential crucial impact on the decision to plan an DC after a positive FIT. The current study highlights the importance of continuously providing GPs with sufficient and accurate information about the screening programme.

Although the lack of DC after a positive FIT is often linked to a negative advice of the GP in our study, this partly might be the result of social desirable answering. Of note, some patients persevere in not willing a DC although they were correctly advised by their GP (especially when they dismissed the FIT positive as a false positive and/or were afraid of the DC) [16]. Most interviewees stated they would certainly participate at the following FIT invitation, and in case of a subsequent positive FIT they would plan a DC. The telephone interview persuaded some interviewees to discuss a DC with their GP or to schedule a DC after all. However, indicating to plan a DC after the interview or online survey may also be subject to socially desirable answering. The results indicated that 29 survey respondents (17%) and nine interviewees (10%) were thinking about planning a DC. Eight interviewees did perform a DC within two years after the interview. Thirteen other interviewees tested positive in a following screening round (2 years later), and only half of them went for a DC, the other did not, even after a second positive FIT. For the survey respondents these data is lacking due to anonymity.

Based on the literature, several interventions were implemented in the Flemish CRC screening program to improve DC compliance after a positive FIT. Since some years the CCD tries to increase GP awareness not to repeat the positive FIT by another FIT by information leaflets, the website and by adding information in the positive result letter so GPs can correctly advice patients with a positive FIT.

A review with 23 studies about interventions to improve DC after positive FIT showed moderate evidence of sending reminders to the participant [22]. Since March 2019 a fail-safe mechanism was developed. A reminder letter – shortly after the positive FIT result – is not possible due to administrative delay of registered colonoscopies (due to the lack of a central colonoscopy register) in Flanders. Instead, if a positive FIT is not followed by a DC (or virtual colonoscopy) the participant and GP receive – 24 months after the positive FIT- a reminder recommendation to undergo a DC (instead of a new FIT invitation).

Azulay et al. [23] found an association between comprehension of a positive FIT result and a DC. The improvement of patient understanding of the positive FIT result was a stronger predictor of DC follow-up than all other socio-demographic variables, including age, gender, education, and ethnicity. FIT positive participants should receive a clear explanation of the need for DC follow-up [23]. Since 2020, more information about the importance and possible results of a DC (by an infographic and website link for more information) was added in the positive FIT letter (to participant and GP). Currently a third intervention is developed: the GPs will receive a yearly feedback report with aggregated DC compliance rate after positive FIT for their patients that participated in the Flemish CRC screening program, supplemented with the regional DC rate and the Flemish average. This feedback allows GPs to monitor their DC rate compared to other practices in the region, which possibly motivates GPs to improve the DC compliance among their patients. Feedback reports only are not sufficient for improving DC compliance [24], but they might have an additive effect to the other installed interventions in Flanders, such as the mailed reminders for the patients and the added information about the DC in the positive result letter. In 2021/2022 an online survey will be launched in cooperation with the GPs organisation to further investigate why some GPs discourage a DC after a positive FIT. Based on the results of this survey the need of other interventions will be discussed with the GPs organisation.

**Conclusions**

The effectiveness of a CRC screening programme based on FIT depends on high DC compliance after a positive FIT. The investigation of self-reported reasons for not planning a DC after a positive FIT in Flanders provides evidence for tailored interventions to improve DC compliance. Such interventions should mainly focus on a better information of both participants and GPs about the clinical importance of a DC after a positive FIT. Ultimately, an enhanced DC compliance should increase CRC detection and survival rates in Flanders.

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