Fecal immunochemical test based colorectal cancer screening

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CHAPTER 1

Introduction
Imagine mister B, aged 65, who has just retired after a lifetime of hard work. Just when he is full of ideas about his newly acquired freedom, he notices some blood with his stool. He does not pay too much attention to the finding. Only after some time, when he starts losing weight and feeling tired, he decides to visit his general practitioner who then refers him to a gastroenterologist. Additional investigations then reveal a large colorectal cancer which has metastasized to the liver for which no curative options are available.

Now imagine the same mister B a few years earlier, at age 60. One morning before going to work he finds an envelope in his mailbox which contains an invitation to take part in a bowel cancer screening program. All mister B has to do is to take a sample of his stool using the small brush that he received by mail and to send it to the laboratory by return postal mail. He decides to accept the invitation and performs the stool test. Within two weeks he receives a letter stating that ‘the stool test result is unfavorable’ and he receives an invitation for the outpatient clinic within due time. During this appointment, he is told that small amounts of blood, invisible to the eye, have been detected in his stool and he is advised to undergo a follow-up investigation. This colonoscopy reveals a large polyp in the bowel which, luckily, can be immediately removed. After two weeks mister B is called by his doctor and is told that the polyp was non-cancerous and that it was radically removed. He receives the advice to undergo a surveillance colonoscopy in 6 years, which is one year after his retirement, which he can hopefully enjoy for many more years.

The two scenarios outlined above provide a background against which we can discuss the aim and outline of this thesis. Almost every person in the Netherlands knows about the existence of nationwide screening programs for breast and cervical cancer. The screening program for breast cancer, for example, exists for over 20 years and is attended by over 80% of all invited women. There is a continuing debate, however, about the reduction in mortality attributable to screening and the numbers of women overdiagnosed. Much less is known to the public about the potential beneficial effects of screening for colorectal cancer (CRC), which, with over 12,000 incident cases and a mortality rate of 5,000 persons annually, is the third most prevalent cancer in the Netherlands. In the United States, screening for CRC is recommended in persons over the age of 50 since the 1980s. Although several large randomized controlled trials have provided evidence of the effects of CRC screening, it was not until 2003 that the European Union officially recommended CRC screening using stool tests for the detection of occult blood.

At the start of the work reported in this thesis there was no consensus on CRC screening in the Netherlands. In June 2011 however, the minister of Health, Welfare and Sports decided to a phased introduction of a nationwide bowel cancer screening program starting in September 2013 using biennial fecal immunochemical testing (FIT). This decision was mainly based on two pilot screening trials that were carried out in 2006 in Amsterdam/Nijmegen and in Rotterdam. Besides, the Centre for Population Screening (CvB) and the National Institute for Public Health and the Environment (RIVM) had performed a feasibility analysis in 2010. It is expected that, in time, such a program could prevent around 2,400 deaths from CRC annually.

The studies presented in this thesis were carried out as a continuation of the pilot screening trial of 2006 that was performed in the Amsterdam region. In this region,
approximately 10,000 persons aged between 50 and 75 were invited for participation in a first round of bowel cancer screening with either a guaiac fecal occult blood test (gFOBT) or a FIT. Major lessons learned from the first screening round were that implementing a program in the Netherlands is feasible and that the FIT is to be preferred above the gFOBT both in terms of test characteristics as well as test acceptability. Of gFOBTs, 47% was returned compared to 60% of FITs (difference of 13%; P< .01). Differences in both intention-to-screen and per-protocol cancer detection rates favor FIT and were, respectively, 0.1% (95% CI 0.0 to 0.2) and 0.2% (95% CI 0.0 to 0.4).

Since FIT-screening has to be repeated every other year to ensure high program sensitivity, the same pilot cohort was invited for a second screening round in 2008. We were interested to evaluate the uptake and diagnostic yield of a second round of screening in the same pilot population. In addition, we wanted to look in more detail at ways in which the implementation of the screening program could be optimized. The work in this thesis focuses for a large part on exploring the screening program from an invitee/screenee perspective. A better understanding of this perspective may enable us to design a program that is tailored to the target group’s needs and expectations whilst trying to minimize the adverse effects as much as possible.

As the hypothetical scenarios of the introduction illustrate, the aim of a screening program for CRC is to detect CRC at an earlier stage than would have been the case in the absence of screening. This aims for less invasive cancer treatments to cure a patient, but also enables early detection and removal of precancerous lesions, advanced adenomas, to prevent cancer, both resulting in a lower morbidity and mortality from CRC. Based on this rationale we were interested to see whether most of the cancers in persons that had participated in the first round were indeed detected in this round. We hypothesized that, had this been the case, the yield in the second round would be significantly lower in terms of both number and stage of detected lesions. In chapter 2 of this thesis we compare the yield of the second round of screening with that of the first round in terms of number of positive FITs and subsequent findings at colonoscopy.

As the term population screening suggests, a screening program is most effective when many persons in a population decide to participate. A program with a screening test that has excellent test characteristics but that nobody is willing to undergo will not be effective. Since FIT-screening should be performed at regular intervals (e.g. two yearly) to have an optimal program-sensitivity, invitees should be willing to undergo the test repeatedly. In chapter 3 we describe the participation rates in the second round of FIT-screening and compare these to the first round. To provide more insight, we were able to evaluate first-round participants and non-participants and also new invitees separately.

To obtain optimal participation in a FIT-screening program, strategies to facilitate participation could be developed. We hypothesized that supplying persons with a floating feces collection paper could alleviate the burden of collecting the stool in the toilet, possibly resulting in increased participation rates. In chapter 4 we describe the results of a randomized controlled trial in which all second round invitees were randomly allocated to receive either a collection paper with the FIT or not. Primary outcome measure was the participation rate.
Besides aversion from handling stool, there could be a multitude of other reasons why persons decide to engage in screening or not. Understanding these reasons might facilitate the development of interventions aimed at the most prevalent obstacles. In chapter 5 we describe the results of a questionnaire survey eliciting reasons for (non-)participation. The development of this questionnaire was based on the Health Belief Model\(^1\) and on previous research\(^2\).

A concept related to participation is Informed Decision Making (IDM)\(^3\). It is widely recognized that persons invited to screening should be provided with enough and well-balanced information about the pros and cons of participation, enabling decision-making based on a personal view. In chapter 6 we evaluated the proportion of participants who had adequate knowledge and a positive attitude towards the screening program.

Persons that are invited for a FIT-screening program will experience emotional and cognitive consequences from this invitation. Since a FIT-screening test does not have a 100% specificity, a proportion of persons will experience distress that, in retrospect, was unnecessary. In chapter 7, we report on the results of a questionnaire survey on the psychological consequences of being invited for FIT-screening using the Psychological Consequences of Screening questionnaire (PCQ)\(^4\).

In FIT-screening, all persons with a positive FIT-result are advised to undergo a colonoscopy. This is an invasive procedure with a considerable burden. With appropriate knowledge of patients’ perceptions of the procedure, efforts can be made to improve the acceptability of colonoscopy. Chapters 8, 9 and 10, report on patients’ experiences with the colonoscopy procedure.

Since we were interested to learn if endoscopists anticipate well on patients’ experiences with the colonoscopy, we performed a study that is described in chapter 8. Here we explored the level of agreement between endoscopists and patients undergoing colonoscopy on several aspects of the colonoscopy procedure, using a questionnaire that was based on focus group sessions with patients that underwent a colonoscopy. The results of this study were used to develop the questionnaires that were eventually applied in chapters 9 and 10.

In chapter 9, the experience of FIT positives with the colonoscopy procedure is described as well as possible interventions to make the procedure more acceptable.

In chapter 10 we explore how the colonoscopy is perceived by patients undergoing colonoscopy for other reasons than a positive FIT-result in screening. We compare the experiences with colonoscopy between patients with five different indications for colonoscopy: symptoms suggestive of cancer, adenoma or carcinoma surveillance, inflammatory bowel disease, familial predisposition for bowel cancer and irritable bowel syndrome.

In the final chapter 11 we present an overview of the main findings presented in this thesis. We also discuss the implications of these findings in terms of optimizing implementation of a CRC screening program using FIT, as well as recommendations for future research.
GENERAL INTRODUCTION

REFERENCE LIST