Risk profiling and screening for colorectal cancer
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General introduction
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"Better to prevent than to cure." An often heard Dutch saying. But how far should prevention go? What should we do to prevent disease? Can this urge for prevention do more harm than good? Is prevention still as important, in a society in which the costs of health care keep rising? Should the provision of health care be more differentiated? To investigate these prospects we looked at screening for colorectal cancer, aspirin use for primary prevention of cardiovascular disease and cancer and policy aspects of differentiation in screening.

Colorectal cancer (CRC) is one of the leading causes of cancer related death. Colorectal cancer has a long latency period, in with precursors of cancer (adenomas) can be removed by polypectomy. The high incidence of CRC, the high burden of disease, the availability of screening tests and of effective pre-clinical treatment of adenomas and early stage cancers are reasons why population screening for CRC is deemed appropriate.1 2

Several methods for colorectal cancer screening are available. Colonoscopy, in which the entire colon is inspected, is the reference standard for the detection of colorectal neoplasia. Colonoscopy is a burdensome and costly procedure and should therefore only be considered in individuals with an increased risk on CRC and adenomas. For this reason pre-selection with Fecal Immunochemical Blood testing (FIT) has been introduced. In the Netherlands in 2013 a screening program will be introduced in which all men and women between 55 and 75 years of age are invited to participate in biennial FIT-based colorectal cancer screening.

FIT-based screening is not flawless; its sensitivity is low and specificity is suboptimal.3 Pre-selection for screening could probably be optimized further. One of the ways to do this is with the use of CRC risk factors. The use of risk algorithms can improve the sensitivity effectiveness of pre-selection in FIT-based screening.

The studies included in this thesis were performed to improve our understanding of the effectiveness screening for colorectal cancer, the harms and benefits of screening, prevention and differentiation in health care.

Outline of this thesis

Chapter two focuses on integrated risk profiling. It discusses the use of integrated risk
profiling in screening and its place in the Dutch health care system. Chapter three reviews the literature available for several types of pre-selection with risk algorithms for colorectal, breast and cervix cancer. This review focuses on risk algorithms that can be easily clinically implemented. Risk algorithms like those described in chapter three use risk factors in order to calculate the risk of disease.

Chapter four focuses on those risk factors for colorectal cancer. We have collected information on these risk factors in a primary colonoscopy screening setting in Amsterdam, and estimated the strength of the association with advanced adenoma, detected at colonoscopy. In the study reported in Chapter five the risk factors discussed in chapter four were used to develop a multivariable risk model that calculates the chances of having colorectal neoplasia. We compared the accuracy of this risk model with that of FIT only.

In Chapter six we describe the outcomes of a third round of FIT-based screening pilot program in the Netherlands. Primary outcomes were yield, participation and interval cancers.

FIT used in screening has a low sensitivity and suboptimal specificity. For this reason we have assessed the risk factors for having a false positive or false negative test, and report our findings in Chapter seven.

In everyday practice, lesions detected during colonoscopy are retrieved and evaluated by a pathologist. To make screening more cost- and time-efficient, this histopathologic assessment could be replaced by visual inspection by the endoscopist. This is only feasible if the endoscopist is able to correctly diagnose colorectal lesions during colonoscopy. We evaluated the accuracy of “optical diagnosis” by the endoscopist in chapter eight.

In Chapter nine we report a questionnaire study with vignettes, which was designed to document the ideas of the Dutch screening public about differentiation in health care. Should individuals who live less healthy pay more or wait longer for their health care?

Several forms of active prevention also has its downsides. Aspirin is increasingly used to lower the risk of cardiovascular disease and cancer. In Chapter ten we report on the harms and benefits of taking aspirin as a primary prevention measure.

The thesis closes with a summary of the findings presented in this thesis in Chapter eleven.
References

