Samenvatting van het proefschrift
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"Risk stratification and screening for colorectal cancer"

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The studies included in this thesis address a number of topics concerning risk stratification and differentiation in health care. As health care costs are increasing and the urge for prevention is rising, differentiating in the provision of health care may be one of the options for sustaining the health care system that we have now. Differentiation based on risks and needs can increase health care efficiency, by offering care to those individuals who need it most. The studies reported in this thesis evaluated differentiation in a number of ways: its use in colorectal cancer screening, regarding the use of aspirin for primary prevention, and with respect to the acceptability of differentiation in premiums and waiting times based on health behaviour.

Chapter Two describes integrated risk profiling as a primary prevention tool. With integrated risk profiling an individualized risk profile can be made in order to assess an individualized risk on disease. The place in Dutch health policy and the exact outcomes of risk profiling should still be studied in order to safely use this strategy. In Chapter Three we report a systematic review of risk models for breast, cervical and colorectal cancer. We distinguished three phases for model development: model derivation, validation and impact analyses. Many models for pre-selection in screening for the three assessed types of cancer have been developed. Most of these models have not been externally validated and no impact analyses have been performed. This gap in model development means that though many prediction models are developed, not many are used in screening. This leaves opportunities for new screening strategies and studies. We have assessed the effectiveness of pre-selection for colonoscopy by risk stratification in screening for colorectal cancer. FIT based colorectal cancer screening has low sensitivity and suboptimal specificity rates.[1] Risk evaluation could increase this sensitivity and specificity. We have evaluated this hypothesis by collecting data in a randomized colorectal screening cancer controlled trial in which colonoscopy was compared with colonography.[1] We asked individuals in the colonoscopy arm to answer a questionnaire, to study risk factors for colorectal cancer. In

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Chapter Four we report on these risk factors for colorectal cancer. We used the risk factors for the development of a multivariable risk algorithm, which we report in Chapter Five. Risk factors included in the algorithm are FIT result, square root FIT, calcium intake, number of family members, age, and smoking. The resulting model showed better accuracy than FIT-only screening. Screening for colorectal cancer based on risk, rather than on the FIT result only, could help in targeting efforts for early detection towards high risk individuals, thereby increasing the efficiency of screening. Practicalities of this method, such as its effect on participation, should be evaluated in further studies. Chapter Six describes the participation rates, yield and interval carcinomas of three rounds of FIT-based screening in the Netherlands. In the planned Dutch FIT-based colorectal cancer screening program, FIT will be repeated biannually. Over the years, the yield of screening will decline, and eventually a plateau will be reached. In the third round of screening the positive predictive value and FIT-positivity were lower than in previous rounds. FIT-based screening is imperfect, and we evaluated risk factors for false positive or false negative FIT results. The results are reported in Chapter Seven. In our study participants at higher age and smokers had a significantly higher risk of having a false negative FIT result. Males were at increased risk of having a false positive test result. This information could be used to develop more targeted screening strategies, for example by using different screening intervals in specific groups. In FIT based screening, colonoscopy is offered to participants with a positive FIT test result. Chapter Eight focuses on the accuracy of endoscopic - on site - assessment of screen detected lesions. If endoscopists were able to correctly identify polyps during colonoscopy, screening could be more efficient and more cost-effective. This would especially be useful in diminutive lesions. We assessed the accuracy of endoscopic diagnosis with histopathology as the clinical reference standard. We concluded that, at the moment, histopathology cannot yet be eliminated, since the accuracy of endoscopical diagnosis did not yet meet the standards. In Chapter Nine we focus on the acceptability of differentiation in health care, based on health behavior. Should individuals with an unhealthy behavior pay more for their treatment? Should they wait longer before there are treated? We offered these questions to participants in a Dutch screening pilot. We found that these Dutch screening participants were in favor of some form of financial differentiation between those who live healthy and those who do not. The acceptability of this type of differentiation differed between type and setting of the behavior. It seems that the extent to which individuals can be held responsible for their behavior guides the acceptability of differences in premiums or in waiting times. In the study reported in Chapter Ten we assessed the use of aspirin as a primary prevention tool for cardiovascular disease and cancer. At present, low dose aspirin is used for the primary prevention of cardiovascular disease and cancer. There are concerns about the harms of this form of treatment. We found that, on average, the harms of using aspirin are higher than the benefits, and concluded that the use of aspirin should be targeted towards those individuals at high risk of disease. ◄