Chapter 10 Summary
SUMMARY
Health care costs have risen dramatically in recent years, making it increasingly necessary to control these costs. Cost control can be achieved by making choices, such that the available budget will be put to an optimal use. Next to the necessity of medical innovations and pressure from society, the cost-effectiveness of new interventions is an important factor in decision-making. To show the cost-effectiveness of interventions, an economic evaluation should be performed. In an economic evaluation the costs and effects of a new intervention are compared with current practice, or if no intervention exists, with 'doing nothing'. Several guidelines have been developed for performing economic evaluations. Their main focus, however, is on curative care rather than preventive care.

Prevention can be defined as the sum of healthcare and non-healthcare measures that aim at health protection, health promotion and disease prevention. An important difference between medical interventions and preventive interventions is that it may take years for preventive interventions to show any effect: for example, quitting smoking at a young age prevents chronic obstructive pulmonary disease (COPD) and lung cancer in old age. As a consequence the costs and effects of an intervention have to be calculated over a long period of time. This is done through modelling, which requires both empirical research data and making assumptions for parameters without empirical evidence. These assumptions may be uncertain because it is not (yet) known how the intervention will work out in practice. Thus, the willingness of a potential target group to participate in an intervention, the long term effects and possible negative side-effects are usually unknown or incompletely known. Still, the assumptions need to reflect as closely as possible the intervention as it would be actually implemented, to make a meaningful contribution to the decision about the (national or regional) implementation of an intervention.

At the Dutch National Institute for Public Health and the Environment (RIVM), cost-effectiveness research focuses on preventive public health interventions. In line with this focus, this thesis addresses the economic evaluation of preventive interventions. The aim of the research presented in this thesis was to critically describe the current
state of economic evaluations of preventive interventions, and to contribute to realistic economic evaluations in this field by performing original research. Chapters 2, 3, 4 and 5 investigate the current status of economic evaluations of preventive interventions in four reviews. Chapters 6 through 8 present several case studies. The results are discussed in Chapter 9.

**Economic evaluations in the field of prevention tend to be cost-effective**

In Chapter 2 we examined the economic evaluations in the field of prevention that were published in 2008. We also examined which of these studies used the ‘Life Years Gained’ (LYG) and ‘Quality Adjusted Life Years' (QALY) as outcome measures, the values of the incremental cost effectiveness ratios (ICER) reported, and how the target diseases and conditions of the preventive interventions that were the subjects of these economic evaluations relate to the global burden of disease. We found 232 original economic evaluations in the field of prevention published in 2008. In over a 100 studies, QALY was used as outcome measure and LYG in over 40 studies. Some 80% of the presented ICERs were below €50,000. The median ICER of all presented ICERs was €12,500. Most economic evaluations found focused on infectious diseases, and in particular on vaccinations. Vaccinations against infectious diseases that are relatively rare in the Western world make up a large proportion of the economic evaluations. Economic evaluations in the field of behavioral disorders and diseases of the respiratory tract were underrepresented, despite their relatively high burden. It is recommended to focus on the cost-effectiveness of interventions in areas where the future burden of disease is expected to be especially high, such as obesity and diabetes mellitus type 2.

**Economic evaluations of colon cancer screening by colonoscopy and colonography are based on an unrealistically high willingness to participate in the model calculations**

Chapter 3 investigates to what extent the assumptions regarding sensitivity and specificity and people’s willingness to participate correspond to reality in modelling
studies on the cost-effectiveness of colon cancer screening by colonoscopy and colonography. To this end, we performed a literature review on economic evaluations of colon cancer screening. The assumptions with respect to sensitivity and specificity found in the twelve modelling studies identified, correspond to the values reported in randomized studies. However, this does not apply to the assumptions made about the willingness to participate. These assumptions ranged from 50% to 100%, with an average of 78%, while trials show that the actual willingness to participate is about 30% and in countries where screening has already been implemented the turnout is below 20%. A low willingness to participate will affect the cost-effectiveness: there are fewer cases of colon cancer avoided, which reduces the number of life years gained and increases the costs of colon cancer treatment, altogether resulting in a less favourable ICER. Also, high program costs related to relatively few health benefits contribute to ICERs that are less favourable.

**Economic evaluations of screening for abdominal aortic aneurysms failed to include the possible complications of surgery**

In Chapter 4, the effectiveness and cost effectiveness of screening for abdominal aortic aneurysm (AAA) is investigated. The aim of the review was to provide an overview of the evidence of the effectiveness and cost effectiveness of screening for AAA. It showed that screening for AAA leads in the long term to a halving of AAA-related mortality and that overall mortality also seems to decline. The economic evaluations focusing on long-term trials in Australia, the UK and Denmark show the cost-effectiveness of screening: the ICERs are far below the threshold value for prevention of € 20,000 as used in the Netherlands. The literature mentions possible complications of AAA surgery. The economic evaluation models, however, rarely take these complications into account, although they lead to higher costs, higher mortality rates and lower quality of life. Again, the cost-effectiveness was presented as more favourable than it actually was. Economic evaluations are useful for decision makers only if all costs and benefits of all possible outcomes are included in the model.
Only part of the costs of preventive interventions for alcohol abuse was included in economic evaluations

In the review in Chapter 5 we mapped out the differences between the costs included in cost of illness studies on alcohol abuse and the costs included in economic evaluations of such preventive interventions directed at alcohol abuse that were performed from a societal perspective. Not one of the five economic evaluations found had included all the societal costs as included in cost-of-illness studies. It is remarkable that all of the studies failed to include costs resulting from alcohol-related traffic accidents. In the cost-of-illness studies, health care costs due to alcohol abuse amounted to 18% of the total costs (the sum of health care costs and societal costs), whereas in the economic evaluations they amounted to 57% of the total costs. Because not all relevant societal costs due to alcohol abuse were included in the economic evaluations of preventive interventions, the total costs and effects of preventive interventions were underestimated. Likewise, because not all costs are included that can be avoided by an intervention, it is predicted that the ICER was also underestimated

Taking a polypill by Dutch people of 40 years and older with a 10-year risk of cardiovascular death above 5% seems to be cost-effective

In Chapter 6 we calculated the effect of three different polypills and separate medications aimed at reducing risk factors in all people over 40 years old with a 10-year risk of cardiovascular death of 5%, 7.5% and 10%. The polypill is a combination drug. In our study, we used different combinations of three antihypertensives, a cholesterol lowering drug and an antiplatelet agent. The aim of the study was to calculate the costs of the polypill in the primary prevention of cardiovascular disease. Three polypills were examined: 1) the Indian polycap, containing three different types of antihypertensive drugs, a low dose statin (20 mg) and aspirin, 2) like 1) but without aspirin, 3) like 2) but with a double dose of statin (40 mg). In addition, scenario studies of separate antihypertensive and / or statin medications were simulated. All scenarios were compared with ‘usual care’ as described in the Dutch guideline cardiovascular
risk management. All scenarios appeared cost-effective compared with usual care, with the ICER ranging from € 8,200 to € 12,300 per QALY. The polypill containing three antihypertensive drugs and a double dose of cholesterol lowering drug daily resulted in most health benefits. Using this polypill will lead to a decrease of 3.5% of cardiovascular diseases with a 10-year risk threshold of 7.5%. Leaving out aspirin prevents the development of unwanted side effects such as gastrointestinal bleedings and brain hemorrhage. The most uncertain factor in the scenarios was the assumption regarding of willingness to participate, as relevant research data are lacking.

**To stop smoking remains the most effective and cost-effective management of COPD for both smokers with complaints and for smokers without symptoms**

The aim of the study described in Chapter 7 was to determine the most cost-effective approach for the prevention and treatment of COPD with a budget allocation model. We examined the effect of quitting smoking and of continuous therapy with inhaled corticosteroids and long-acting medication consisting of β2-agonists and long-acting parasympathicolytica. In a meta-analysis we investigated the most effective drug treatment. This meta-analysis showed no difference between the various drug treatments. Compared with placebo, inhaled corticosteroids in combination with long-acting β2-agonists appeared to be the most effective treatment. This therapy was used in the model. To calculate the effects of stop-smoking programs we used the results from several randomized controlled trials (RCT). We also looked at the consequences if quitting smoking was postponed. The results showed that to stop smoking as of now both by the whole population and the smokers with COPD was the most cost effective approach. The ICER of all stop smoking approaches ranged between € 2300 and €5600 per QALY. Smoking cessation by 25% of the non diseased smoking population, based on available figures regarding willingness to participate, costs 0.4 billion euros. The investigation showed that for any given budget the disease burden of COPD can be minimized by investing in stop-smoking interventions instead of the much more expensive medication treatment of COPD.
The willingness to participate and the limited impact of financial incentives

The international literature showed the willingness to participate in and compliance with lifestyle interventions to be low. Before implementing an intervention it is necessary to have insight into the willingness of the target group to participate. Chapter 8 presents a study that we conducted in order to gain knowledge about the influence of both positive and negative financial incentives and the influence of other factors on the willingness to participate in lifestyle interventions. Other factors included time required for participation in an intervention, group composition, available resources and type of instructor. We used the technique of conjoint analysis to investigate the associations between various factors and thus to understand the preferences of participants. Of all the factors considered, money appeared to be the only significant factor significantly affecting the willingness to participate. The study found that receiving money does not motivate participants and that having to pay money discourages from participation in lifestyle interventions.

Economic evaluations of preventive interventions should sketch a picture representing everyday reality

Economic evaluations that examine cost-effectiveness have to be performed with the highest accuracy. This applies not only to methodological issues, but also to the connection with everyday practice in terms of effectiveness and costs. Policymakers should take into account that the assumptions regarding effectiveness are generally based on short-term efficacy studies while in fact reliable insight in long-term effectiveness is needed. This thesis concludes that guidelines specifically geared towards economic evaluations of preventive interventions should be developed to obtain a large degree of uniformity and transparency. It is important that prior to the implementation of a preventive intervention reliable statements about the costs can be made, to avoid unpleasant surprises after the fact. In this respect, knowledge about the preferences of participants is indispensable. It is advisable that more behavioral research should be carried out to increase the understanding of these preferences. New interventions can then be tailored to the needs and preferences of specific target
groups. The implementation of an intervention should be a continuous process in which evaluation allows for adjusting the intervention in an appropriate manner.