Chapter 1 General Introduction
General Introduction

Health care has become increasingly expensive in recent years. The expenditures on healthcare in the Netherlands in 2000 amounted to around €50 billion (Fig. 1), whereas in 2008 the expenditures had increased to nearly €79 billion, which accounted for 13% of the gross domestic product (GDP) (Westert et al., 2010). Demographic changes (growth and ageing of the population) are responsible for an increase of 1% of the total health care expenditures per year. Further increase in expenditure is caused by inflation (1-2.5% increase of prices per year), new technical developments in healthcare, leading to more and more expensive treatment options, increased demand and the increase of prices above inflation. The CPB Netherlands Bureau for Policy Analysis has calculated that in 2009 there was a drop in GDP of 4% and health expenditure were estimated to increase by 6%, which corresponds to an increase of the health expenditures to 14% of the GDP (Westert, 2010).

Figure 1. Health care expenditure (€ billion), 1998-2008 (Source: Dutch healthcare performance report 2010)
In this time of scarce resources, it is increasingly important to control health care costs. Therefore it is necessary to make choices to optimally use the limited budget and to get most value for money. Choices in allocating the budget can, among others, be made based on political considerations, total budget impact, necessity (what does a new intervention add compared to existing alternatives?), own responsibility of people in terms of costs, pressure from society and the media and equity considerations. One other important element in decision-making may be the efficiency of the intervention, which is the relationship between effects and costs, or to put it differently, how much “bang” we get for the “buck”. All other circumstances being equal, society prefers to buy as much health as possible at the lowest cost possible.

Economic evaluation
To demonstrate the efficiency of an intervention, an economic evaluation has to be performed. Economic evaluation entails the comparison of two or more alternative courses of action in terms of both their costs and consequences (Drummond et al., 2005). Economic evaluation has been initiated and further developed during the last three decades of the past century. In the seventies the interest arose to involve economics in issues related to health care in both the United States and in England. In the Netherlands, the first cost-effectiveness analyses were performed because the Ministry of Health, the Dutch Health Care Insurance Board and the Health Council of the Netherlands wanted insight into the consequences of the introduction of new and expensive (therapeutic) interventions such as organ transplantations and in vitro fertilisation (Rutten-van Mölken et al., 2010). In 1988, the Ministry of Welfare, Health and Culture established, together with the Ministry of Education and Sciences and the Health Care Insurance Board, a special fund (‘Ontwikkelingsgeneeskunde’) for studies on the effectiveness and cost-effectiveness of new, expensive interventions (Van der Sande et al., 2003). Here, first experiences with economic evaluation in the Netherlands were achieved. At the same time, economic evaluation was used to inform decision makers on public health investments, such as breast cancer screening.
and cervical cancer screening programmes (van der Maas et al., 1989; Koopmanschap et al., 1990).

**Prevention**

Prevention is defined as the total of measures both within and outside health care aimed at protecting health, promotion of health and warding off of diseases (Mackenbach & Maas, 2002). *Health protection* interventions reduce health risks by changing the physical or social environment. It includes provisions such as sewer systems, safe drinking water supplies, and regulation of exposure to hazardous substances, flood defences, road and food safety provisions and building regulations. Regulating such matters is generally regarded as part of the collective responsibilities of governments and to a large extent falls outside the health care domain. *Health promotion* normally involves action to encourage healthy behaviour or to discourage unhealthy behaviours. This includes the establishment of a healthy social and physical environment that supports a healthy lifestyle. Health promotion interventions frequently take the form of public information campaigns focused on the general population or on certain groups within the population. *Disease prevention* concerns actions to prevent the occurrence of a specific disease (e.g. by vaccination) or to detect (a predisposition towards) a disease in an early stage (screening) (De Hollander et al., 2007; De Wit et al., 2007). The total societal costs spent on prevention in the Netherlands in 2007 were 13 billion euros (Fig.2). Of this amount, 10 billion euros (78%) were spent on health protection, 2.5 billion euros (19%) were spent on disease prevention and 450 million euros (3%) were spent on health promotion (Post et al., 2010).
Especially when large investments are needed for an intervention, e.g. to build an infrastructure for a cancer screening programme, a firm evidence base for its effectiveness and cost-effectiveness is needed prior to decision making (van den Berg et al., 2008). Besides, an increasing number of preventive interventions such as vaccinations and health promotion campaigns have been developed in the last decades. In relation to this, the number of economic evaluations has increased exponentially in the last decades as well. Over the 40 year period between 1970 and 2010, the annual number of entries in PubMed related to economic aspects of prevention has grown from 75 to 2639. Although not all of these publications describe full economic evaluations, the body of literature on the economic evaluation of prevention is becoming impressive.

*Guidelines for economic evaluation*
To develop a uniform approach to economic evaluations, several guidelines for economic evaluations and for decision-analytic modelling in economic evaluations have been developed (Drummond & Jefferson, 1996; Philips et al., 2004; Evers et al., 2005; ISPOR, 2009). In the Netherlands, the Dutch Health Care Insurance Board
published the first guidelines for pharmaco-economic research in 1999 (CVZ, 1999). In 2006 an updated version of these guidelines was launched (CVZ, 2006).

Commissioned by the Health Care Insurance Board the first manual for costing research was published in 2000 (Oostenbrink et al., 2000). In 2004 and in 2010 updated versions of this manual were released (Oostenbrink et al., 2004; Hakkaart-van Roijen et al., 2010). Despite the availability of these guidelines, the literature still shows major differences in both methodology and outcomes even when the same preventive intervention in one particular situation is evaluated (Bilcke & Beutels, 2009; Turner et al., 2011). For example, two Dutch economic evaluations investigating the cost-effectiveness of a rotavirus vaccination for 0-4 years old children presented cost-utility ratio’s as wide apart as €21,900 and €119,000 per DALY respectively (Zomer et al., 2008; Goossens et al., 2008). Hence, the availability of guidelines does not guarantee the results of economic evaluations to be informative for decision makers.

Guidelines have been developed mainly for the evaluation of therapeutic interventions, such as new drugs. No specific guidelines for the economic evaluation of preventive interventions are available. Although it is generally acknowledged that the economic evaluation of preventive interventions holds some specific problems (Weatherly et al., 2009; Cohen & Patel, 2009; Kelly et al., 2005), there is a tendency to simply use the guidelines that are available in performing such evaluations. Economic evaluations of preventive interventions differ from economic evaluations of curative health care in several respects. One of these differences is related to the fact that health gains through preventive measures do not appear immediately, but arise many years after the intervention. For example, the detection and treatment of (at that time still innocent) polyps at the age of 55, may prevent the development of colorectal cancer 15 years later. Preventing smoking among young people may lead to a reduction in the incidence and prevalence of chronic obstructive pulmonary disease and lung cancer decades later. Different from the evaluation of therapeutic interventions, where clinical trials and economic evaluations are often organised concurrently and with a
limited follow-up time, economic evaluation of preventive interventions in generally requires modelling of future costs and effects. In the context of economic evaluation, a decision analytic model uses mathematical relations to define a series of possible effects that would flow from a set of alternative options being evaluated (Briggs et al., 2006). Based on the inputs into the model, the outcome of each effect is expressed in terms of probabilities and every effect has a cost and an outcome. When clinical trials yield intermediate outcomes (i.e. a reduction of blood pressure), these intermediate outcomes are ‘translated’ by modelling to clinical endpoints like life years gained or quality adjusted life years gained (Brennan & Akehurst, 2000; Sun & Faunce, 2008). If a clinical trial shows that an intervention leads to a decrease in blood pressure, this result has to be ‘translated’ into a future decrease in the incidence of acute myocardial infarctions and strokes and an associated increase in life years gained.

**Participation is essential**

One other issue related to economic evaluation of prevention in the long term is the limited availability of good quality data on future developments with regards to effects and costs. Also, limited information on (future) human behaviour adds to the uncertainty of outcomes of economic evaluations. When it is impossible to obtain solid data, e.g. on adherence and compliance rates of an intervention, assumptions are made and a sensitivity analysis of the various assumptions is required (Buxton et al., 1997; Brennan & Akehurst, 2000).

Participation in preventive programs, such as lifestyle improvement programs, vaccination, and screening programs, is essential to make such programs cost-effective. Lifestyle interventions can be beneficial in terms of reduction of risk factors, like elevated blood pressure, cholesterol, and high body weight (Toobert et al., 2007; Pi-Sunyer et al., 2007; Davies et al., 2008), but only if participants comply with and adhere to the lifestyle changes in the longer term. Similarly, screening programs need a certain level of participation in order to contribute to individual and population health. In practice, however, the willingness to participate is in general low (lifestyle
programs) or declining (e.g. vaccination programs). It is therefore important to adequately estimate the expected level of participation and, in addition, to know which factors potentially increase the participation rate. The higher the participation rate the more favourable the ICER generally will be. Often, we have limited knowledge on willingness to participate in preventive programs. This makes it difficult to underpin the assumptions necessary for decision analytic model studies.

**Aim of this thesis**
The Dutch National Institute for Public Health and the Environment (RIVM) mainly focuses on preventive public health interventions. As researcher at the institute the author is involved in the economic evaluations of preventive interventions. The aim of the research presented in this thesis is to critically describe the current status quo of economic evaluations of preventive interventions, and to contribute to realistic economic evaluations in this field by performing original research.

**Outline of this thesis**
This thesis is organised into two parts. The first part addresses the current status of economic evaluations of preventive interventions, based on reviews of the literature. In the second part of the thesis, original work is presented. Chapter 2 of this thesis gives insight in the number of economic evaluations of prevention published in one particular year (2008), and the diseases they focus on in relation to the global burden of disease. Chapters 3, 4, and 5 describe literature reviews on specific public health interventions, namely colorectal cancer screening (Chapter 3), screening for aneurysma of the abdominal aorta (Chapter 4), and prevention of alcohol abuse (Chapter 5). In the second part of the thesis, first an economic modelling study is presented on an opportunistic screening programme followed by one on preventive medication for cardiovascular diseases (Chapter 6). In Chapter 7, a resource allocation study of different interventions directed at COPD prevention is described. Finally, Chapter 8 shows the importance of the investigation of participants’
preferences in a conjoint analysis of a lifestyle program for diabetes patients. The thesis concludes with a general discussion in **Chapter 9**.

**References**


