New approaches to the implementation of cardiovascular disease prevention
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CHAPTER 1

INTRODUCTION AND GENERAL OUTLINE
INTRODUCTION

Cardiovascular disease (CVD) is one of the biggest contemporary health problems worldwide. Mortality from CVD alone contributed to 17.3 million deaths in 2008, which represents 30% of all global deaths. Currently, 10% of the total global disease burden is attributed to CVD, and the World Health Organization predicts that both mortality and the total burden of CVD will increase dramatically in the near future.1

The major risk factors for CVD are well known, and evidence-based primary (in apparently healthy individuals) and secondary (in individuals with clinical manifestations of the disease) prevention has been shown to decrease cardiovascular mortality and morbidity. Clear targets have been defined for healthy lifestyles, risk factors, and medication use by the international societies in Europe and in the United States.2,3 However, the implementation of primary and secondary prevention is currently far from optimal. Therefore, new approaches to the implementation of cardiovascular disease prevention are needed.

Part 1: Risk assessment in primary prevention

The current approach to primary prevention of CVD is “case finding”, also known as the “high risk approach”. This approach focuses its efforts on identifying healthy individuals with the highest levels of CVD risk factors, and utilizes the established framework of medical services to reduce this risk.4 To aid this approach, several risk assessment tools have been developed. Using different algorithms based on different fatal and non-fatal outcomes, risk can be calculated for the very short term, 10-years, or lifetime. Decisions to initiate preventive measures are based on this risk. However, the so-called prevention paradox coined by Geoffrey Rose (1926-1993) points to the fact the majority of CVD comes from the population at low or moderate risk, and only a minority from the high-risk population.4 This is because the number of individuals at high risk is small as compared with the number of individuals at low to moderate risk. As an alternative to the high-risk approach, Rose suggested the “population strategy”. This approach is a public health-oriented approach, which aims to shift the population distribution of one or more risk factors to reduce the total burden of CVD, as opposed to reducing a single individuals’ risk. One such strategy is the polypill approach.5 The polypill includes a combination of low-dose preventive medication (i.e. statin, aspirin, blood-pressure lowering agents), which theoretically can lead to a drastic reduction in CVD if implemented on a population level. Disadvantages to such population strategies are that each individual only reaps a small benefit, and that major changes on a societal level are needed for effective implementation.

The European Society of Cardiology (ESC) guidelines on CVD prevention in clinical practice recommend treatment decisions to be made using the high risk approach, based on the predicted 10-year risk of CVD mortality.2,6 This risk can be calculated using the Systematic COronary Risk Evaluation (SCORE) algorithm, which is based on the pooling of several large, European population-based cohorts.7 The SCORE algorithm includes age, sex, smoking status, systolic blood pressure, and serum total cholesterol or total/HDL-cholesterol ratio, and can be rapidly calculated using SCORE risk charts and online calculators. Risk charts have been published for high-risk countries and low-risk countries, in addition to country-specific calibrated versions. Based on data from the World Health Organization,1 the most recent ESC guidelines have reclassified the United Kingdom (UK) as a low-risk country, with no country-specific calibrated version.2 However, the performance
of SCORE has not been studied in a large, population-based UK cohort. We therefore compared the predicted 10-year CVD mortality as calculated using the SCORE high-risk and low-risk algorithms with the observed 10-year CVD mortality in the European Prospective Investigation of Cancer-Norfolk (EPIC-Norfolk) prospective population study.\(^8\) (Chapter 2)

The most recent ESC guidelines on CVD prevention suggest that there is a fixed relationship between CVD mortality and the total burden of CVD events, defined as the composite of fatal plus non-fatal CVD.\(^2,6\) It is suggested that in high-risk individuals with a 10-year CVD mortality risk of \(\geq 5\%\), as estimated using SCORE, total CVD (mortality plus morbidity) is threefold higher, and possibly more in young men, and less in women and in older individuals.\(^2,6,9\) This has led to the suggestion of using a fixed multiplier (3×) for calculating total CVD based on CVD mortality only. From a patient’s perspective, total CVD risk is the most relevant parameter for initiating CVD prevention,\(^10\) and using CVD mortality only can result in underestimation of the total CVD burden.\(^10\) Although mortality is a more robust clinical outcome, CVD morbidity is equally relevant to providers of healthcare, policy makers and insurance companies. Currently, the relationship between total CVD and CVD mortality in the general population is unclear, and the proposed multiplier for conversion from CVD mortality to total CVD has not been validated. We therefore investigated the relationship between total CVD (fatal and non-fatal events) and CVD mortality in the EPIC-Norfolk prospective population study. (Chapter 3)

In the Netherlands, the current multidisciplinary guidelines on CVD risk management (CVRM) recommend using a modified version of the Systematic COronary Risk Evaluation (SCORE) to estimate 10-year risk of fatal and non-fatal CVD.\(^11\) The original SCORE chart and algorithm on which the modified, current version is based is the low-risk SCORE,\(^7\) which estimates 10-year risk of fatal CVD only. Using data from 2 different national cohorts,\(^7,11,12\) multipliers have been calculated to convert the risk of 10-year fatal CVD to the risk of 10-year fatal- and non-fatal CVD, including first non-fatal hospitalizations for myocardial infarction, cerebrovascular disease and congestive heart failure.\(^11,12\) These multipliers are 5x the SCORE predicted fatal CVD for individuals aged 35-45 years, 4x for individuals aged 45-65 years, and 3x for individuals aged \(\geq 65\) years. Overall risk is presented in the charts, and coded by colour.\(^11\) These multipliers have not been validated in other, large population-based studies, and include only 3 clinical manifestations of non-fatal CVD. Based on our findings in the EPIC-Norfolk study (Chapter 3), we applied the ratios of CVD mortality/morbidity to the original SCORE low-risk charts to design a new, updated risk chart, and compared the updated risk chart with the current risk chart. (Chapter 4)

Part 2: Nurse coordinated secondary prevention after an acute coronary syndrome

Patients with established coronary artery disease (CAD) are at particularly high risk of subsequent coronary events and death. Effective secondary prevention can reduce this risk. Modification of cardiovascular risk factors can reduce the risk of recurrent myocardial infarction, decrease the need for interventional procedures, improve quality of life, and effectively extend survival.\(^13\)

Comprehensive guidelines for the long-term management of patients with CAD have been issued by the American Heart Association/American College of Cardiology (AHA/ACC)\(^14\) and the European Society of Cardiology (ESC).\(^2,15\) Effective secondary prevention includes interventions to change behavior and modify lifestyle (smoking cessation, regular exercise, weight control, and healthy food choices) and pharmaceutical interventions (antiplatelet agents, statins, β-blockers,
angiotensin converting enzyme inhibitors, and angiotensin receptor blockers). In a systematic review of lifestyle interventions in patients with CAD, a marked reduction in mortality risk was associated with smoking cessation (35-50%), physical activity (20-30%), moderate alcohol consumption (15-20%) and healthy dietary choices (15-45%). Risk reductions were seen in both CAD patients and in general population cohorts. Furthermore, pharmacological interventions reduce the mortality risk in CAD patients: low-dose aspirin (18%), statins (21%), β-blockers (23%), and ACE inhibitors (26%). Combined, these interventions could potentially reduce the risk of recurrent events by more than two thirds.

Unhealthy lifestyles (i.e. smoking, an unhealthy diet, overweight and insufficient physical activity) are among the most important of the modifiable risk factors for CVD. Ideally, an intervention in secondary prevention of CVD should be able to successfully improve these risk factors, as several other risk factors (i.e. hypertension, diabetes mellitus, dyslipidemia) improve along with healthier lifestyles. However, the results of the EUROASPIRE surveys (European Action on Secondary Prevention by Intervention to Reduce Events) show that the implementation of secondary prevention, including successful lifestyle modification, is disappointing.

There are several reasons why successful lifestyle modification in patients with CVD is difficult. First, individuals with clinically manifest CVD are generally middle-aged or older, and have spent decades developing their unhealthy lifestyles as individuals, part of their families, and within social networks. While an acute CVD event might motivate patients to improve their lifestyles, existing unhealthy lifestyle may be challenging to successfully modify in the short and long term. Second, physicians lack the time, motivation, and incentives to invest in strategies to improve patients’ lifestyles. In short, at present a considerable gap exists between guidelines on secondary prevention and the actual implementation of these measures.

One approach to improve secondary prevention may be to involve other allied professionals, with new initiatives such as nurse coordinated prevention programs. Potentially, nurses participating in such programs are motivated to follow guidelines, have more time for advising and counseling patients, and can monitor and assist attempts to improve unhealthy lifestyles. We therefore designed the Randomised Evaluation of Secondary Prevention by Outpatient Nurse Specialists (RESPONSE) trial to quantify the impact of a practical, hospital-based nurse coordinated prevention programme integrated into the routine clinical care of patients who have sustained an acute coronary syndrome. (Chapters 5-9)

Aims of this thesis:

1. To investigate the performance of the Systematic COronary Risk Evaluation (SCORE) in a contemporary, UK population based cohort, after the reclassification of the UK as a low-risk country; to investigate the relationship between CVD mortality and CVD morbidity in this cohort; to evaluate the consequences of this for the risk stratification in the Netherlands

2. To evaluate the effect of a nurse coordinated prevention programme on cardiovascular risk and quality of life in patients that have suffered from an acute coronary event
Outline of this thesis

**Part I (chapters 2-4) Risk assessment in primary prevention**

The first part of the thesis concerns risk assessment in primary prevention, in particular regarding the use of SCORE, and the consequences of including non-fatal outcomes in risk-assessment. In *chapter 2*, we investigate whether the SCORE low-risk algorithm provides a more accurate risk prediction of 10-year CVD mortality in a UK population than the high-risk algorithm, as the UK has recently been reclassified as a low-risk country. In *chapter 3*, we investigate the relationship between 10-year CVD mortality and 10-year CVD morbidity, and whether using mortality risk to calculate morbidity risk leads to an underestimation of the overall cardiovascular risk. In *chapter 4*, we evaluate the current Dutch SCORE-charts recommended by the national guidelines. Using the findings as presented in *chapter 3*, we evaluate whether the Dutch SCORE-charts underestimate an individuals’ risk of clinically relevant fatal- and non-fatal CVD.

**Part II (chapters 5-9) Nurse coordinated secondary prevention after an acute coronary syndrome**

The second part of this thesis concerns the findings of the Randomised Evaluation of Secondary Prevention by Outpatient Nurse SpEcialists (RESPONSE) trial, a trial designed to quantify the impact of a practical, hospital-based nurse coordinated prevention programme integrated into the routine clinical care of patients who have sustained an acute coronary syndrome. In *chapter 5*, we present the study design, objectives and expected results of our randomized trial. In *chapter 6*, we present the main findings of our trial. In *chapter 7*, we present the effects of this programme on quality of life and depression. In *chapter 8*, we address the fact that patients participating in this trial received incomplete trial information to minimize contamination and a so-called “Hawthorne-effect”, and present patients’ perspectives in participating in a trial with such a design. Finally, in *chapter 9*, nurses’ perspectives on participating in such programs are presented.
REFERENCES


