Primary prevention of cardiovascular disease: evaluation of an individual-based strategy
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Chapter 1

General Introduction
Despite an impressive decline in incidence during the past four decades, cardiovascular diseases (CVD) are still the leading cause of death and disability in the world(1). In the Netherlands in 2010 CVD accounted for approximately 30 percent of all mortality and for more than 380,000 hospital admissions (2). Medical expenditure and loss of productivity due to CVD are estimated 5.5 billion Euro, approximately 8 percent of the total Dutch healthcare budget (3). The observed decline in CVD mortality between the 1970s and 1990s illustrates the potential for CVD prevention. The association between etiological factors and the development of CVD is well established. It has been demonstrated that common modifiable and intermediate risk factors explain over 90 percent of the global burden of CVD, and that adequate modification of these risk factors could potentially prevent two-thirds of heart disease incidence (4). Moreover, the same set of risk factors is associated with other chronic diseases including cancer, chronic respiratory diseases and diabetes (figure 1). Addressing these common risk factors therefore holds promise to prevent other chronic disease as well (5).

CARDIOVASCULAR PREVENTION

Prevention efforts are usually classified as either primary prevention, targeting the apparently healthy at high risk of developing a first cardiovascular event, or secondary prevention, targeting those with established CVD. A high risk of developing a first cardiovascular event can be defined by risk algorithms based on risk factors like age, sex, smoking, elevated blood pressure, dyslipidaemia or raised blood glucose. Assuming that atherosclerosis, the underlying disease process of CVD is a gradually progressive disease, approaches for primary prevention could also be used in secondary prevention.

In the 1980s, Sir Geoffrey Rose proposed two different approaches towards CVD prevention: the population strategy and the high-risk strategy (6). The population strategy aims at reducing the CVD incidence at the population level, usually through environmental changes targeted at the population at large. Examples include measures to ban smoking and reduce the salt content of food. The advantage is that it may bring large benefits to the population although
it may offer little to the individual. The impact of such an approach on the total number of cardiovascular events in the population may be large, because all subjects are targeted and a majority of events occur in the substantial group of people at only modest risk (6). In the high-risk approach, preventive measures are aimed at reducing risk factor levels in individuals at the highest risk, either individuals without CVD at the upper part of the total cardiovascular risk distribution or those with established CVD (1). The impact of this strategy at the population level is limited, since only a small proportion of the population will be at the highest risk. Therefore, at a population level, up to two-thirds of the burden may be unaltered as a consequence of the great numbers of individuals at low risk (7). However, since the widespread availability of low-cost lipid lowering and anti-hypertensive drugs the high-risk, or individual, strategy has regained interest. It is acknowledged that the largest preventive effect will be achieved when population and individual measures are combined (5;8).

CURRENT PRACTICE IN INDIVIDUAL PREVENTION

In current daily practice CVD prevention is mainly organised using a case finding strategy within the primary care setting. In The Netherlands this is based on the Cardiovascular Risk Management guideline (9). Consistent with the European Society of Cardiology prevention guideline [1], this guideline uses the Systematic Coronary Risk Evaluation (SCORE) risk algorithm to guide decision making. SCORE integrates multiple risk factors, including age, gender, smoking behaviour, systolic blood pressure and serum lipids, to calculate a 10-year CVD morbidity and mortality risk. SCORE $\geq 20\%$ is considered high risk, $10\%$ to $20\%$ intermediate risk, and $<10\%$ as low risk. The guidelines recommend lifestyle counselling in all individuals with modifiable levels of (behavioural) risk factors. Individuals at high risk, or at intermediate risk with one or more additional risk factors (e.g. a family history, kidney failure, a sedentary lifestyle, or overweight), are eligible for preventive drug intervention. The primary care physician plays a pivotal role in this strategy and is thus essential for its successful implementation. However, physicians find implementing even rudimentary preventive services challenging, due to a lack of time (10,11). They find it difficult to collect and process multiple risk factors in a single consultation (12). Furthermore, healthcare professionals have difficulties with explaining risk to individuals and motivating them to initiate preventive action (13). It is postulated that risk perception is key in motivation to behaviour change and failing to acknowledge individuals conceptions and preferences may lead to noncompliance with preventive interventions (14). Perhaps as a consequence of these challenges, it was found that 20% of the physicians do not use any prevention guideline and more than 40% do not use risk charts (15). CVD prevention using the case finding strategy therefore remains suboptimal.

Another widely used strategy in primary prevention of CVD is the health risk assessment (HRA). In the UK, for example, the Diabetes, Heart Disease and Stroke pilot studies, citizens aged 40 to 74 years will be offered a cardiovascular HRA every five years. This includes a questionnaire on risk factors and measurement of weight, hip to waist ratio, blood pressure, and total cholesterol level. People at high risk for developing diabetes undergo measurement of glucose levels (16). In the United States, cardiovascular HRA is common practice as part of worksite wellness programmes (17). The traditional HRA screened for risk factors to produce feedback that
predominantly contained information on the assessed risk. However, reviews of the literature do not uniformly support the effectiveness of the traditional HRA (18;19). It was hypothesized that HRA with feedback that merely contains risk information would be insufficient to promote health (20). The impact of the traditional HRA also remains limited as a consequence of suboptimal delivery due to resource constraints, limited access to high risk populations and lack in uniformity (18;19). It is acknowledged that the impact of HRA programs could be enhanced by web-based delivery of the HRA, with incorporation of tailored health recommendations, aiming to reduce disease risk (20-23). To assure quality and safety, as well as proper medical follow-up, content should be evidence based and in line with local guidelines for treatment (17). The worksite has been proposed as a suitable platform for such programs, with the advantage of cost savings, the creation of a health-conscious environment and easier follow-up of high-risk individuals (17;24).

Perhaps the most rigorous strategy that has been suggested is the “polypill strategy”, proposed by Wald and Law in 2003 (25). In this strategy a combination of drugs with established efficacy in one pill (the “Polypill”), including a statin, three blood pressure lowering drugs at half standard dose (a thiazide diuretic, a beta blocker, and an angiotensin converting enzyme inhibitor), and aspirin, is administered to everyone above the age of 50 years. It was estimated that the strategy would yield an 80% reduction in CVD mortality against a few side effects. Recently the first clinical trials evaluating short term efficacy, feasibility, tolerability and safety were published (26-28). Although different formulations were used in these trials, the general impression was that approximately 60% reduction in CVD could be achieved with the polypill, with similar discontinuation rates between study arms. However, the polypill caused side effects sufficiently severe to stop treatment in about 1 in 20 and less severe side-effects in about 1 in 8 people. Moreover, it was estimated that there could be a 50% increase in risk for extracranial bleeding due to aspirin (27). Therefore, although promising in terms of efficacy, healthcare delivery, and compliance, there is still a concern in terms of safety, ethics, and formulation(29). Until more evidence is available, instead of a “fire and forget” approach, some sort of screening of risk should probably be applied to select the appropriate individuals for treatment (27;29;30).

**IMPROVEMENT OF INDIVIDUAL CVD PREVENTION**

Based on the above-mentioned limitations in current practice of primary prevention, further improvement in CVD prevention may be achieved by a strategy that includes the following characteristics:

1. A focus beyond the scope of a single disease or risk factor
2. Based on a HRA that conforms to guidelines
3. Provides individual health recommendations, that raise risk awareness and motivate to reduce risk
4. Is delivered efficiently to reach individuals of interest and limit professional workload
A possible strategy that could address these aspects is an HRA that utilizes health information technology to collect and integrate multiple risk factors, and process these data according to prevailing evidence into health recommendations. HRAs are increasingly offered as web-based applications. The use of web technology and email provides the opportunity to reach large groups of individuals, under circumstances that suits them (17;19). Also, utilizing information technology holds promise to reduce workload for the professional and improve guideline adherence (12). Moreover, there is an opportunity for tailoring, defined as “any combination of information or change strategies intended to reach one specific person, based on characteristics that are unique to that person, related to the outcome of interest, and have been derived from an individual assessment” (31). Although HRAs are becoming widely available, evaluations of strategies including web based HRA are scarce. To determine the effect and support policies for primary prevention an extensive evaluation of both the development of programmes using the web-based HRA strategy, as well as their delivery, is needed.

**OUTLINE OF THE THESIS**

In this thesis we evaluate an individual primary prevention strategy using web-based HRA with tailored feedback. We study aspects of this strategy in two parts.

In the first part we focus on the theoretical background of HRA content and risk estimation. In chapters 2, 3, and 4 we systematically review CVD guidelines to determine content of cardiovascular HRAs (chapter 2), for recommendations on the use of imaging of asymptomatic coronary artery disease in HRAs (chapter 3), and recommendations on abdominal aortic aneurysm screening (chapter 4). In chapter 5 we compared the impact of three major guidelines for the prevention of CVD in a large population based cohort in the UK. In chapter 6 we evaluated the performance of SCORE in predicting CVD mortality in the same cohort.

In the second part we evaluate the reach and the effectiveness of a Dutch prevention program including a web-based HRA with tailored feedback called the Prevention Compass. This programme was developed by the NDDO Institute for Prevention and Early Diagnostics (NIPED) in Amsterdam. We studied its implementation and initial effects in real-world work-site setting between 2007 and 2009. A detailed description of the program and its content is given in the Appendix to the introduction. Briefly, the HRA consists of four components: 1) a web-based electronic health questionnaire, 2) biometric measurements, 3) laboratory evaluation, and 4) tailored health recommendations, based on the results of the first three components. The electronic health questionnaire includes socio-demographics, personal health history, family risk, and the behavioural domain. All questions are derived from validated questionnaires. Biometric measurements (length, weight, waist circumference, blood pressure) are conducted at the worksite by trained and certified staff. Measurements are directly entered in the central HRA database. At the same visit blood samples are collected for laboratory testing of total cholesterol, HDL, LDL, triglycerides, glucose and HbA1C. Collected samples are shipped to a certified laboratory where analyses are completed and results are electronically transferred to the central HRA database. By computer-based combination of the assessed risk with health-
behaviour constructs, tailored health recommendations are generated and presented to the participant within a web-based health action plan. Each health plan includes: 1) explanation of the assessed risk for each of the targeted preventable conditions, using a three-colour system (green: normal risk profile; orange: moderately elevated risk profile; red: seriously elevated risk profile), 2) explanation of the threats associated with elevated risk and potential gains of taking preventive action, and 3) opportunities for taking preventive action based on the participant’s stated motivation for health-behaviour change (physical activity, smoking cessation, alcohol intake, dietary habits) and preferences with respect to interventions (e.g. guided vs. non-guided interventions). Where possible, recommendations are based on prevailing practice guidelines. For example, cardiovascular risk factor cut-off values are derived from the European and Dutch guidelines for cardiovascular risk management. When seriously elevated risks are detected, the health plan includes referral for further medical evaluation and treatment. A health counselling session with the program physician is also available upon request for all participants.

In chapter 7 we evaluate determinants of participation and non-participation. In chapter 8 the initiation of health-behaviour change among voluntary participants is studied. In chapter 9 we present the results of a follow-up study on the effects on CVD risk and in chapter 10 on lifestyle parameters. Finally, we provide a general summary and future perspectives.
REFERENCES


APPENDIX TO THE INTRODUCTION

Overview of the Prevention Compass web-based health risk assessment (HRA)
The HRA includes estimation of personal health risk by screening four domains associated
with preventable chronic disease, including CVD (see Appendix Table 1). The domains and
sub-domains are modular, meaning that they can be adjusted based on the characteristics of
the screened population.

<table>
<thead>
<tr>
<th>Lifestyle domain</th>
<th>Psychological domain</th>
<th>Social domain</th>
<th>Physical risk domain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical activity</td>
<td>Stress</td>
<td>Workability</td>
<td>Total cardiovascular risk</td>
</tr>
<tr>
<td>Smoking</td>
<td>Burn-out</td>
<td></td>
<td>Blood pressure</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>Depression</td>
<td></td>
<td>Lipids</td>
</tr>
<tr>
<td>Nutrition</td>
<td>Anxiety</td>
<td></td>
<td>Blood sugar</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Body weight and fat distribution</td>
</tr>
</tbody>
</table>

Risk assessment
The risk assessment component of the program includes a web-based electronic health
questionnaire, biometric measurements, and laboratory testing. The questionnaire includes
socio-demographics, personal health history, family risk, and the behavioural domain. All
questions are derived from validated questionnaires, including the International Physical
Activity Questionnaire (IPAQ), the standard nutrition and alcohol consumption questionnaire
of the Dutch Municipal Health Service, the Dutch Expert Centre on Tobacco Control
questionnaire, and constructs from the transtheoretical model. Biometric measurements
(length, weight, waist circumference, blood pressure) are conducted at the worksite by trained
and certified staff, usually staff of the occupational health services provider of the employer.
Measurements are directly entered in the central HRA database. At the same visit blood
samples are collected for laboratory testing of total cholesterol, HDL, LDL, triglycerides, glucose
and HbA1C. Collected samples are shipped to a certified laboratory where analyses are
completed and results are electronically transferred to the central HRA database. For system
security and data protection reasons personal identification data and risk assessment data are
stored on separate servers. A firewall is placed between the servers and the Internet. Only users
certified by ID and password are able to access the servers.

Theoretical framework
The tailored feedback provided as part of the intervention is based on Prochaska’s transtheoretical
model (32). According to this model, behavioural change is a process consisting of five subsequent
phases: precontemplation (no intention of behaviour change between one and six months),
contemplation (considering behaviour change between one and six months), preparation
(getting ready to change behaviour in the next month), action (performing the change in
behaviour), and maintenance (steady stage of behaviour change reached). In the feedback,
individuals receive recommendations that fit their current stage of change. Participants in
earlier stages receive information to motivate them to change their lifestyle, whereas
participants in later stages receive concrete action plans on how to change their lifestyle.
Tailored feedback: web-based health action plans

Feedback to participants consists of tailored health action plans that are automatically generated by computer algorithms. Each health plan comprises:

1. Explanation of the assessed risk for each of the HRA domains, using a three-colour system (green: normal risk profile; orange: moderately elevated risk profile; red: seriously elevated risk profile)
2. Explanation of the threats associated with elevated risk (orange and red categories) and potential gains of taking preventive action
3. Opportunities for taking preventive action based on the participant’s stated motivation for lifestyle behaviour change, self-efficacy, and preferences with respect to lifestyle interventions (e.g. guided vs. non-guided interventions).

Where possible, risk profile thresholds are based on prevailing local practice guidelines. For example, the cardiovascular risk factor cut-off values are derived from the European and Dutch guidelines for cardiovascular risk management. Appendix figure 1 shows the algorithm by which the HRA data are processed by the knowledge system. When seriously elevated risks are detected (red categories), the health plan includes referral for further medical evaluation and treatment. A 30 minute health counselling session with the program physician is also available upon request for all participants.

Example

Participant: 42-year old man, total moderate intensity physical activity 60 minutes on 4 days of the week, eats one portion of fruit and 100 grams of vegetables a day, and has a mean blood pressure of 132/85 mmHg. Is highly motivated for health improvement, is in the preparation stage for physical activity, has a low self-efficacy, and has a preference for non-guided improvement of physical activity.

In Appendix figure 2 a screenshot is shown of the risk profiles page of the web-based feedback for this participant. An orange bar is shown for physical activity, because he does not meet local guideline recommendations for physical activity. Also an orange bar is shown for nutrition, because his intake of fruit and vegetables is under the recommended level according to healthy nutrition guidelines. Finally an orange bar is shown for blood pressure, because he has a slightly elevated systolic and diastolic blood pressure according to cardiovascular disease risk management guidelines. The participant can get further information on the risk profile by clicking on the button next to the colour bars. This information is tailored to his motivation and stage of change (i.e. highly motivated and in the preparation stage).

In Appendix table 2 an example is given of the feedback on the physical activity profile of this participant. When the button at the right bottom is clicked, the participant goes to the health feedback page of his health plan. For this participant feedback includes:
1. A physical activity improvement schedule to reach recommended levels of physical activity, which he can implement himself (i.e. non-guided physical activity improvement)
2. A nutrition scheme for implementation of daily fruit and vegetable intake
3. Advice to schedule an appointment with the program staff to re-measure his blood pressure three months after he implemented advised lifestyle changes.

Appendix figure 1.

GKC = the amount of previously diagnosed cerebrovascular, peripheral vascular or cardiac diseases. Determinant type A = a family member below 65 years with heart disease OR physical inactivity OR obesity OR moderately reduced kidney function. Determinant type B = a family member below 65 years with heart disease OR a seriously reduced kidney function OR obesity (＞35kg/m2) OR intima-media thickness of the artery walls ＞1 OR both high blood pressure and left ventricular hypertrophy.
Appendix figure 2
Example of the risk profiles page of the web-based feedback.

Appendix Table 2. Example of tailored feedback for physical activity.

<table>
<thead>
<tr>
<th>Your lifestyle profile</th>
<th>Green</th>
<th>Orange</th>
<th>Red</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exercise</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diet and nutrition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motivation for a healthy lifestyle</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Your psychological profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coping skills and stressors</td>
</tr>
<tr>
<td>State of mind</td>
</tr>
<tr>
<td>Personal characteristics</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Your physical profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure</td>
</tr>
<tr>
<td>Cholesterol</td>
</tr>
</tbody>
</table>

What does this mean for me?
Your current moderate intensity physical activity is 60 minutes on four days a week. An activity level under 30 minutes of moderate intensity level physical activity on five days a week is considered insufficient.

Regular physical activity helps improve your overall health and fitness, and reduces your risk for many chronic diseases, including heart attack, colorectal cancer, and diabetes as well as improving your overall vitality and quality of life. For you it is also important to know that improving your physical activity will help you to control your slightly elevated blood pressure.

What can I do?
It is very positive that you already realize the benefits of regular physical activity and have been trying to make exercise a part of your life. You are not always confident that you can maintain your exercise routine. Identifying problem situations and barriers to exercise is the first step in figuring out how to overcome them.

In your health recommendations section you can find out how you can improve your physical activity to recommended levels.