Primary prevention of cardiovascular disease: evaluation of an individual-based strategy
Çölkesen, B.E.

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Chapter 11

Summary and future perspectives
In this thesis we evaluated the individual-based strategy for primary prevention of cardiovascular disease. In chapter 1 we briefly outlined current practice in individual prevention and distillate aspects for further improvement. We discussed that individual-based prevention of CVD could be further improved 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 health risk assessment (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

We hypothesized that a web-based HRA with tailored feedback could meet these aspects. To study this hypothesis we first focussed on the theoretical background of HRA content and risk estimation. In chapter 2 we systematically reviewed CVD guidelines on cardiovascular risk assessment, to guide selection of screening interventions for a cardiovascular HRA. A total of 27 guidelines met our inclusion criteria. We performed a quality assessment of these guidelines, using the AGREE instrument and extracted their recommendations for cardiovascular risk assessment. Seventeen guidelines showed considerable quality of development and included recommendations on assessment of total cardiovascular risk, dyslipidemia, hypertension, and dysglycemia. Recommendations on total cardiovascular risk and dyslipidemia included prediction models integrating multiple risk factors. No consensus was found on recommended target populations, treatment thresholds, and screening tests. Our findings imply important variation in allocation of preventive interventions.

A screening modality for CVD that is gaining popularity is the imaging of asymptomatic coronary artery disease (CAD). In chapter 3 we systematically reviewed guidelines on imaging of asymptomatic CAD to evaluate the evidence on whether this modality has a place in CVD risk assessment. A total of 14 guidelines met our inclusion criteria, with great variation in quality. Of these, 8 guidelines recommended against or found insufficient evidence for testing of asymptomatic CAD. The other 6 guidelines recommended imaging individuals at intermediate or high CAD risk based on Framingham risk scores. Only 2 guidelines considered cost-effectiveness. We conclude that guidelines on risk assessment by imaging of asymptomatic CAD contain conflicting recommendations. More research, including RCTs, evaluating the impact of imaging on clinical outcomes and costs is needed before widespread dissemination in cardiovascular HRA.

Abdominal aortic aneurysm (AAA) is an important contributor to CVD mortality. Given the uncertainties regarding screening for this condition, systematically and transparently developed recommendations are needed. In chapter 4 we performed a systematic review of AAA screening guidelines to assist physicians in their choice of recommendations. A total of 7 guidelines met our inclusion criteria, of which 3 had quality scores below 40%. All selected guidelines contained a recommendation for one-time screening of elderly men by ultrasonography to select AAAs $\geq 5.5$ cm for elective surgical repair. There was no agreement on the management of smaller AAAs, as well as on screening of women and middle-aged men at elevated risk. Although consensus exists across guidelines on one-time screening of elderly men to detect
and treat AAAs ≥ 5.5 cm, for other target groups and management of small AAAs, prediction models and cost-effectiveness analyses are needed to provide guidance, before widespread dissemination in cardiovascular HRA can be undertaken.

**FUTURE PERSPECTIVES**

Critical appraisal of CVD guidelines can guide assurance of evidence based content of HRA and delivery of preventive interventions. Our systematic reviews on cardiovascular risk assessment and screening for subclinical CAD and aortic disease showed considerable variance among guideline recommendations as well as quality of their development. To guide choices for the content and scope of HRAs, future CVD guidelines should put more emphasis on rigour of development. In order to make informed decisions on preventive interventions delivered by HRAs, only the recommendations from rigorously developed guidelines can be used as a source. Furthermore, an agreement on the definition of global cardiovascular risk that is broadly applicable and identification of target populations are needed to make guidelines more helpful in the development of HRAs.

In chapter 5 we compared three widely used guidelines by applying them to data from the population-based European Prospective Investigation of Cancer- Norfolk (EPIC-Norfolk) cohort. We examined the potential implications of applying the guidelines in terms of subjects classified as high-risk and recommended statin therapy, and we estimated numbers of first CVD events that could have been prevented and number-needed-to-treat (NNT) with statin therapy for each guideline. 21,263 men and women aged 39-79 years from the EPIC-Norfolk cohort were retrospectively classified at baseline by statin therapy recommendations according to the NICE, ESC and ATPIII CVD prevention guidelines. Recommendations based on baseline data were related to 10 year follow-up to calculate number of new CVD events that could be prevented by statins, NNT and CVD incidence decrease. Statin therapy was recommended to 34% by the NICE guideline, 29% by ESC and 32% by ATPIII. A total of 263 events could potentially have been prevented by application of the NICE guideline, 219 by ESC and 199 by ATPIII. The NNT with statins over 10 years was 27 with the NICE guideline, 28 with ESC and 34 with ATPIII. Application of the NICE guideline could have decreased CVD incidence by 13%; using ESC guidelines the figure is 11% and with ATPIII it is 10%. The NICE guideline selected greater percentages of elderly and subjects with prevalent CVD risk factors. It performed best in recommending statins and could have prevented the greatest number of CVD events. With all guidelines, nearly half the subjects who developed a CVD event were not considered eligible for statins at baseline. According to these findings we concluded that less selective prevention strategies need to be explored.

The European Society of Cardiology endorses CVD risk stratification using the Systematic COronary Risk Evaluation (SCORE) algorithm, with separate algorithms for high-risk and low-risk countries. In chapter 6 we evaluated the performance of the SCORE in predicting CVD mortality in the EPIC-Norfolk cohort. We compared the SCORE predicted mortality with the observed mortality in this cohort. We included individuals without known CVD or diabetes aged 39-65 years at baseline and with a follow-up of at least 10 years in our analysis. CVD mortality was defined
as death due to ischemic heart disease, cardiac failure, cerebrovascular disease, peripheral artery disease and aortic aneurysm. Predicted CVD mortality was calculated using the SCORE high-risk and low-risk algorithms. Among 15,171 included participants (57.1% female; mean age of 53.9 years) predicted CVD mortality was 2.85% (95%-CI 2.80-2.90) with the SCORE high-risk algorithm and 1.55% (95%-CI 1.52-1.58) with the low-risk algorithm. The observed 10-year CVD mortality was 1.25% (95%-CI 1.08-1.44). Similar results were observed across all sex and age subgroups. Thus, the SCORE low-risk algorithm performed better in predicting 10-year CVD mortality in The UK, compared with the high-risk algorithm. Our findings indicate that The UK has correctly been reclassified as a low-risk country in recent European guidelines (1). Our findings are consistent with recent literature showing that several countries classified as high-risk in the 1980s and 1990s, including the UK and the Netherlands, now have similar CVD mortality rates with countries previously classified as low-risk, induced by both acute and chronic cardiovascular treatments, as well as improvements in prevention.

FUTURE PERSPECTIVES

Adequate prediction of future CVD risk forms the mainstay of cardiovascular HRA and allocation of preventive interventions. Due to advances in treatment and prevention of CVD, regions formerly classified as high-risk might now need reclassification. For allocation of preventive interventions resulting from an HRA, we observed that the less selective guidelines performed better in CVD prevention. To ensure that those at greatest risk will be considered for further preventive interventions, it is desirable to align risk assessment and guideline recommendations with risk characteristics in the population in which the guidelines will be applied. A possible next step in refining the process of risk assessment and intervention allocation could be to consider lifetime risk of CVD. This is the risk of CVD developing in an individual at some point during his or her lifetime (2). Recently the Cardiovascular Lifetime Risk Pooling Project, representing a combined analysis of data from more than 250,000 individuals derived from 18 cohorts during a period of more than 50 years, found that the presence of elevated levels of traditional risk factors (i.e. sex, blood pressure, cholesterol level, smoking status, and diabetes status) at all ages translated into markedly higher lifetime risks of CVD (3). It was estimated that 56% of the US population are considered to be at low CVD risk in the short term, but actually are at high risk across their remaining lifespan (4). Adding lifetime risk to HRAs for further risk stratification, communication, as well as motivation for lifestyle change and intervention compliance should be explored.

In the second part of the thesis we evaluate the reach and effectiveness of a Dutch program including a web-based HRA with tailored feedback (see Appendix to chapter 1 for a detailed description of the programme). We studied these parameters in a work-site setting. In chapter 7 we evaluated determinants of participation and reasons for non-participation among 5125 employees at four Dutch financial and information technology services companies. We found a participation rate of 37% in the programme. There were no differences between participants and non-participants in sex, education level, tobacco use, and current work ability. However, compared to non-participants, participants were older (44 versus 41 years, p<0.001), and had better self-rated health
(85% “good” or “very good”, compared to 78% among non-participants (p<0.001)). Participants also seemed to have a better absenteeism profile (with 88% reporting <10 days sickness absence in the previous year, compared to 86% of the non-participants (p<0.05)). These differences could imply that employees at high risk are not reached. A non-participant survey was conducted among the non-participants, with a 14% response (423/3102). In this survey we found that the major reasons for non-participation included lack of time (39%) and not being aware of the opportunity to participate (11%). Therefore, implementing a less time consuming HRA process and providing adequate information to employees prior to inviting them may be necessary to reach larger proportions of employees, including those with less favourable health and work characteristics.

In chapter 8 we evaluated initial health-behaviour change among 2289 employees who voluntarily participated in a web-based HRA with tailored feedback at seven Dutch worksites between 2007 and 2009, using a questionnaire survey. Response was received from 638 (28%) employees. Compared with employees at low CVD risk, those at high risk more often reported to have increased physical activity (OR 3.36, 95% CI 1.52-7.45). Obese employees (body mass index (BMI) > 30 kg/m²) more frequently reported to have increased physical activity (OR 3.35, 95% CI 1.72-6.54) and improved diet (OR 3.38, 95% CI 1.50-7.60). Initiation of health-behaviour change was thus more frequently reported among those at high CVD risk and BMI levels, what could indicate that among voluntary participating employees a web-based HRA with tailored feedback may motivate those at greatest risk.

In chapter 9 we evaluated the effect on CVD risk of the web-based HRA with tailored feedback by conducting a prospective follow-up study among 368 voluntary participating employees at a single Dutch worksite in 2008. Follow-up data on CVD risk were collected one year after initial participation. The primary outcome was the change in Framingham CVD risk score at 6 months relative to baseline. We checked for a possible background effect of an increased health consciousness as a consequence of program introduction at the worksite. Therefore, we compared baseline measurements of early program participants with baseline measurements of participants who completed the program six months later. A total of 176 employees completed study follow-up measurements after mean 7 months. There was a graded relation between CVD risk changes and baseline risk, with a relative reduction of 17.9% (p=0.001) in the high-risk category (baseline CVD risk ≥ 20%). This was 5% among all participants. Changes were not explained by additional health counselling, medication or an increase in health consciousness within the company. Our results could indicate that web-based HRA could improve CVD risk in similar populations.

In chapter 10 we evaluated the effects on lifestyle of the web-based HRA with tailored feedback with a prospective follow-up study, with changes relative to baseline in proportions meeting recommendations for physical activity, fruit and vegetable intake, smoking and alcohol consumption as primary outcomes. We checked for a possible background effect of an increased health consciousness as a consequence of program introduction at the worksite by comparing baseline measurements of early program participants with baseline measurements of participants who completed the program a year later. A total of 142 employees completed follow-up measurements after mean 15 months. The proportion with a total physical activity amount of ≥150 minutes/week (a sum of the total recommended amount by the guideline;
i.e. at least 30 minutes of moderate intensity physical activity on at least five days a week) increased from 46% to 71% (p<0.001). The proportion with a physical activity pattern according to local recommendation was not increased. No differences were found in the proportions meeting recommendations for daily intake of fruit and vegetables, of moderate alcohol consumption, and smoking cessation. Changes were not explained by additional health counselling or increased health consciousness within the company. Our findings indicate a 25% increase in total physical activity, however not on the recommended frequency of five times a week, in program participants.

FUTURE PERSPECTIVES

In our studies we evaluated the reach and effect of a web-based HRA with tailored feedback. Our studies were conducted at the worksite after the programme was implemented as part of usual workplace health management. Because of this real-world setting we were unable to randomize or construct a control group. However, the design of our study enabled us to check for a possible background effect of an increased health consciousness as a consequence of program introduction at the worksite. The lack of such a background effect could imply that differences after follow-up may be attributed to the web-based HRA. Although our effect studies showed promising results on CVD risk reduction and total physical activity levels, further evaluations with rigorous control groups and longer follow-up should provide further evidence.
REFERENCES


