SIMPLE SCREENING INSTRUMENTS FOR CHRONIC DISEASE & PERSONALISED PREVENTION AT THE WORKPLACE

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Simple Screening Instruments for Chronic Disease & Personalised Prevention at the Workplace

Eenvoudige screeningsinstrumenten voor chronische ziekten & gepersonaliseerde preventie op het werk

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CHAPTER 1

General Introduction

BACKGROUND

Prevention refers to actions directed to preventing illness and promoting health. It includes the assessment of disease risk and early diagnosis. Preventive strategies are most commonly classified based on the level of selection being applied in the target group or the stage in the disease process where preventive measures are employed. The entire population is aimed at in universal prevention whereas other prevention strategies target specific groups in the general population. In selective prevention, individuals at high risk are identified through the presence of specific risk factors, such as smoking, age, and lack of physical activity. Indicated prevention is aimed at identifying individuals with minimal but detectable signs or symptoms e.g. high blood pressure and high cholesterol, but who are not diagnosed as having the disease of interest.[1]

Categorising by disease progression, primary prevention seeks to prevent the onset of disease by risk reduction in the community, whereas secondary prevention includes procedures that detect and treat pre-clinical pathological changes and thereby control disease progression. Once a disease has developed and has been treated in its acute clinical phase, tertiary prevention seeks to soften the impact caused by the disease on the patient's function, longevity, and quality of life.[2]

In this thesis we focus on screening, which is part of secondary preventive interventions and includes determining disease risk in apparently healthy individuals as well as detection of those at early stages of a disease or condition.[1,2] When used as a selective prevention strategy, screening is often a first step in controlling disease progression, as it selects individuals for early interventions and/or additional testing.[3]

SCREENING FOR CARDIOVASCULAR DISEASE RISK

Prevention of cardiovascular disease (CVD) is warranted as CVD is a major cause of premature death in Europe [4,5] and has a heavy impact on quality of life.[6] Furthermore, CVD is estimated to cost the EU economy 192 billion euros every year, of which110 billion euros represent direct health care costs and 82 billion lost productivity and the cost of informal care.[7] Next to population based elements (i.e. banning industrial trans fatty acids in food products, providing smoke free public and work places), early detection and management of individuals at high CVD risk is needed to prevent future health problems and its associated costs.[8]

Primary care plays an important role in CVD prevention and many European countries have large programmes to improve CVD prevention and risk management in primary care.[9] However, as health care usually emphasizes episodic treatment for acute symptoms, preventive care is a service not covered by insurance schemes and poorly reimbursed.[9] Not surprisingly, (primary care) physicians list a lack of financial incentives and time restraints

as barriers for implementing European CVD prevention guidelines.[10] These guidelines state that CVD risk should be assessed in all men over 40 and women over 50 years.[11]

CVD risk is determined by calculating a person's risk profile, which is based on several risk factors. A practical limitation of the current approach is that all validated risk profiles employed in the EU and USA include blood pressure and serum cholesterol levels in their calculations. To establish these risk factors, a consultation with a physician is needed. The evidence based SCORE (Systemic Coronary Risk Evaluation) risk profiling system for instance, estimates the 10-year mortality risk from CVD, based on 5-year age groups, gender, current smoking status, systolic blood pressure (mmHg), and serum cholesterol (mmol/L).[12] European guidelines state that individuals with a 10-year SCORE-estimated CVD mortality risk of ≥5% exceed the 'preventive care threshold', meaning that intensive health advice is warranted and drug treatment should be considered.

Potentially more cost-effective is implementing a stepped approach to CVD risk estimations with information collected outside the physician's office. The first step of a stepped approach entails the completion of a simple self-report screening questionnaire to preselect individuals with a high probability of exceeding a relevant threshold, for instance the preventive care threshold.

The selected group then qualifies for the second step; a 'full' risk estimation that includes blood pressure and cholesterol levels. In this digital age, a self-administered questionnaire could be made available relatively easy for high risk groups. A consequence of the preselecting process within the high risk age groups is that those referred to the primary care physician (second step) have a much higher likelihood of actually exceeding the preventive care threshold. Such a stepped approach could possibly be a cost-effective method of providing CVD prevention.

In the Netherlands, the effectiveness and cost-effectiveness of this new approach is topic of a large study starting in 2014.[8] In this study a self-administered CVD risk questionnaire will be utilised that is based on the FINDRISK score[13] and specified for the Dutch population.[6] Development and validation of a similar screening questionnaire based on the European guidelines is needed to facilitate (studies on the feasibility of) a stepped approach to CVD prevention in the EU.

A second strategy to facilitate an affordable screening for CVD risk focuses on blood pressure assessment. Blood pressure (BP) is not only an integral part of (a stepped approach to) multiple risk factor CVD risk profiling. In isolation, hypertension is a major risk factor for cardiovascular events.[14] An estimated 20% to 50% of hypertensive individuals are unaware of their condition.[15-19] For this reason, hypertension screening is an important addition towards the prevention of CVD. Barriers to implementing hypertension screening are similar to those described for overall CVD risk estimation.

Moreover, to establish an adequate BP estimation, multiple measurements are needed as BP is variable and influenced by many stressors, which include, amongst others, the white-coat effect when the measurements are conducted by a physician.[20] Therefore, British guidelines recommend ambulatory BP measurement (ABPM) in every patient with an elevated office blood pressure to confirm or rule out hypertension.[21] In ABPM, blood pressure is being measured continuously by a small digital blood pressure machine that is attached to a belt around the body and which is connected to a cuff around the upper arm. It is normally carried over 24 hours.

For the purpose of mass screening of BP, ABPM has several disadvantages. It is expensive, not widely available, and more discomfort is experienced during measurement compared with home BP measurement (HBPM).[21;22] In HBPM, individuals measure their own BP at home using a validated HBPM device. HBPM measurements have similar reproducibility as ABPM measurements,[23] are void of the white coat effect,[24] and show better correlation with target organ damage and CV events than conventional physician-based BP measurements.[25-30] Furthermore, utilising HBPM would have the additional advantage of moving hypertension screening outside the clinician's office, which could prove to be cost-effective in both the secondary and tertiary stage of prevention.

For screening purposes, limiting the number of HBPM from the 12 measurements that are currently recommended by the European Society of Hypertension[31] is highly recommended to increase feasibility. Thus far, however, no screening programmes have used HBPM as strategy to assess BP.

SCREENING FOR MENTAL HEALTH DISORDERS

Next to CVD, mental health disorders account for a large (27%) part of the burden of disease in the European Union.[32] Not surprisingly, the more prevalent mental health disorders, such as mood and anxiety disorders, have been targets of preventive efforts for many years. The staging of mental health disorders was already proposed two decades ago,[33] but in recent years has gotten increasingly topical, especially in the field of psychotic disorders.[34-37] With regard to psychotic disorders, evidence suggests that prodromal stages can be identified [38] and the duration of untreated psychosis is a modifiable prognostic factor.[39] Several outpatient early intervention programmes have shown positive results.[40;41]

A screening test aims to be sure that as few as possible with the disease get through undetected (high sensitivity) and as few as possible without the disease are subject to further diagnostic tests (high specificity). Given high sensitivity and specificity, the likelihood that a positive screening test will give a correct result (positive predictive value) strongly depends on the prevalence of the disease within the population. The positive predictive value of a screening test is low when the prevalence of the disease is low. Although psychosis-like experiences are common in the general population, the clinical diagnosis of psychosis is rare. The consensus

therefore is that population based screening for psychosis (risk) is not desirable as it would lead to overtreatment and stigmatization in individuals who will not develop illness.[42;43]

As studies have shown that the greatest contribution to the duration of untreated psychosis come from delays within mental health services,[44] improvements in the diagnostic process in the context of indicated prevention are required to timely detect (the prodromal phase of) psychosis. Like CVD risk estimation, a stepped approach that includes screening could facilitate a more effective and cost-effective diagnostic process. For this purpose, validated, simple tools are needed to preselect from a group of help seeking individuals those with acute psychosis and those at risk for developing psychosis.

PERSONALISED PREVENTION AT THE WORKPLACE

CVD risk assessment programmes are useful if they not only identify those at risk, but will also ensure that individuals are supported to reduce their risks and avoid the onset of disease.[7] Health promotion, which is the process of enabling people to increase control over and to improve their health,[45] therefore is an integral part of prevention.

Next to primary care, the workplace is considered to be an excellent setting for both screening and health promotion. It enables screening as it offers a controlled environment in which a large proportion of the population can be reached. By facilitating the creation of a health conscious environment, promoting healthy behaviour and providing a natural social support system needed to change behaviour, the workplace is also considered to be an choice setting to target risk factors for chronic disease.[46-48] One type of worksite health promotion programme (WHPP) frequently offered, is the health risk assessment (HRA). The traditional HRA will screen for risk factors to produce feedback that predominantly contains information on the assessed risk.[49] Reviews of the literature do not always support effectiveness of the traditional HRA.[49-50] Feedback merely containing risk information was suggested to be insufficient to initiate health-behaviour change.[51]

Modern HRAs are increasingly offered as ehealth applications; web-based tools to improve health.[52] These applications can be equipped with comprehensive decision-support systems that facilitate the tailoring of health recommendations, based on individual needs, risk factors and estimated disease risk. The process and outcome of this tailoring is coined personalised prevention. Personalised prevention could be viewed as bridging selective and indicated prevention strategies.[1] Whether health behaviour change is initiated among employees who use an HRA that delivers 'personalised prevention' by means of a web-based tool has yet to be determined.

In general, the lack of employee participation presents an important barrier to the impact of WHPPs.[49;53] Since most intervention studies on WHPPs randomize workers who have agreed to participate in the study, it is largely unknown whether those who could benefit most from

the intervention are as likely to participate as those who may have already been making more healthful choices.[54;55] Only few studies evaluated the influence of health, lifestyle, and work-related factors on participation, which hampers insight into the underlying determinants of participation in WHPPs, and, ultimately, the influence of selective participation on the effectiveness and cost-effectiveness of these programmes.[56] Furthermore, with regard to the web-based delivery aspect of health promotion programmes, it has been reported that women and older people are more likely to enroll, as they more often use the Internet to search for health-related information. It has also been postulated that individuals with a lower educational level are less likely to use web-based WHPPs, as those with less formal education are more likely to discontinue the adoption of innovations.[57] In short, there is a need for studies that analyse whether individual characteristics are associated with participation and non-participation in web-based WHPPs.

Deployment of sophisticated HRAs should be widespread among organizations in order to generate a sufficient impact in the population from a public health perspective. Currently, the prevalence of WHPPs is much higher in the US (77%) than in Europe (44%).[58] This is due, in part, to the fact that in the US, poor employee health comes at a direct cost to employers[49] who provide employer sponsored health insurance and make a substantial contribution to the cost of coverage. In Europe, independent health insurance companies and governmental provisions carry the burden of poor employee health in some form or the other. Also, in Europe, individual employee health is regarded as more of a personal issue and not a concern of the employer.[58]

Like their American counterparts, European employers need to be persuaded to invest in WHPPs. Although health risk factors have been associated with a loss of on the job productivity [59-63] no consistent reductions of absenteeism after participation in HRAs have been reported.[49] A recent review of seven studies in which HRAs were supplemented with additional interventions reported a slight decrease of on average 1 day of sickness absence per year in favour of the HRA from a baseline median of 5.6 sickness absence days.[49] Thus far, only one study evaluated a more sophisticated, web-based HRA that offered tailored feedback to its participants.[64] For this reason, studies that evaluate the impact of more sophisticated HRAs are highly needed.

OBJECTIVES OF THE THESIS

In screening programmes on chronic disease risk, simple, cost-effective measures are preferred as first step in the selection of those at increased risk. It is, therefore, important to investigate whether simple instruments, such as questionnaires and self-monitoring, can be developed and validated for use in screening programmes. Therefore, the first objective of this thesis is to investigate the role of self-administered tools in screening for risks of chronic disease.

The specific aims are:

1. To develop and validate screening questionnaires for cardiovascular disease risk and psychosis (risk);
2. To determine the feasibility of self-monitoring of blood pressure (BP) at home as a tool for hypertension screening by validating a single duplicate home BP measurement.

The effectiveness and cost-effectiveness of WHPPs strongly depend on adequate reach of those who could benefit most from the intervention. Since most intervention studies on WHPPs randomize workers who have agreed to participate in the study, this is largely unknown. For the same reason, the extent to which health behaviour change is initiated to reduce CVD risk after participation in a WHPP has to be determined. Also, the cost-effectiveness of implementing WHPPs from an employer's perspective needs to investigated. The second objective of the thesis is to investigate participation in WHPP and subsequent effects. The specific aims of the studies performed are:

3. To analyse how participation in a web-based WHPP is influenced by individual characteristics;
4. To assess the initiation of health behaviour change after participation in a web-based WHPP;
5. To evaluate the effect of participation in a web- based WHPP on absenteeism.

OUTLINE OF THIS THESIS

This thesis is divided into two parts. In Part 1 the role of self-administered tools in screening for chronic diseases risk is investigated. In part 2 participation in WHPP and subsequent effects are evaluated.

Part 1

Chapters 2, 3 and 4 focus on the first objective of this thesis. In chapter 2, a screening questionnaire that establishes CVD risk based on the European guidelines is developed and validated. To increase the feasibility of HBPM as a self-administered hypertension screening tool, chapter 3 investigates whether it is possible to reduce the number of measurements needed to diagnose or rule out hypertension. In chapter 4, the validity of a self-report questionnaire as a tool to identify individuals with psychosis (risk) is evaluated.

Part 2

Chapters 5, 6 and 7 focus on the second objective of this thesis. In chapter 5, the extent to which participation in a web-based WHPP is influenced by individual characteristics is investigated. Whether health behaviour change is initiated among employees who use a web-based HRA that delivers 'personalised prevention' is addressed in chapter 6. Finally, in chapter 7, the effect of participation in a web- based WHPP on absenteeism is evaluated.

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CHAPTER 2

A six question screen to identify persons at risk for developing cardiovascular diseases

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ABSTRACT

Background: European guidelines on primary prevention of cardiovascular diseases (CVD) recommend the use of SCORE risk charts, which include blood pressure and serum cholesterol as risk parameters. However, when applying SCORE to the general population, screening of many individuals is required to identify one subject at increased CVD risk. To facilitate cost-effective screening, we aimed to construct a web-based screening tool to identify subjects at increased CVD risk exclusively using non-invasive parameters.

Methods: We used data of Dutch employees from 25 organisations participating in a health risk assessment between August 2007 and January 2013. Participants were not being treated for CVD. Backward multivariate logistic regression analysis was use to predict the 10-year risk of fatal CVD of ≥5% based on the SCORE formula.

Results: Because there were only eight women with high CVD risk, we only used data of 6,189 male participants for the development and validation of the screening tool. Age, tobacco use, history of hypertension, alcohol consumption, BMI, and waist circumference were independent predictors of high CVD risk in men. Ten-fold cross-validation resulted in an area under the curve of 0.95 (SE 0.01, 95% confidence interval 0.94-0.96). A cut-off score ≥45 yielded the best performance on the developed questionnaire (sensitivity 92.9%, specificity 85.0%).

Conclusions: With a simple six-item questionnaire we were able to accurately identify subjects at high CVD risk in a population of working men. Our results provide an evidence-based stepwise approach for the use of SCORE as an instrument to identify subjects at increased CVD risk.

INTRODUCTION

Cardiovascular disease (CVD) is the major cause of premature death in Europe.[1;2] Despite the identification of modifiable risk factors such as smoking, blood pressure (BP) and dyslipidemia,[3] prevention of CVD remains challenging. One of the complicating factors is that treatable cardiovascular risk factors such as hypertension and dyslipidemia can be silently present for many years before detection by routine check-up, or worse, by the occurrence of a cardiovascular event.

Early detection of individuals at high CVD risk is the cornerstone of primary prevention. For estimation of CVD risk current guidelines from the joint task force of the European Association for Cardiovascular Prevention and Rehabilitation[4] recommend the use of the SCORE (Systemic COronary Risk Evaluation) risk estimation.[5] Based on age, gender, smoking status, cholesterol and BP an estimation of the 10-year risk of dying from CVD can be calculated, or derived from a risk chart. The risk estimation is used to offer the patient a tailored health care advice, which includes behavioural strategies to improve lifestyle and pharmacological interventions aimed at reducing BP and cholesterol. For practical reasons it is currently recommended to assess cardiovascular risk in all men over 40 and women over 50 years of age or post-menopausal without CVD.[6] Even when applying these criteria, screening of individuals at possible risk for CVD remains a huge effort[7] as it requires invasive blood sampling and a BP measurement. Simple non-invasive screening instruments have been developed to identify patients at increased risk for diabetes,[8-10] kidney disease,[11] or a combination of cardiometabolic endpoints.[12] These instruments allow a stepwise approach in the identification of high-risk individuals on a population level. However, for the identification of patients at high risk of CVD according to the SCORE risk estimation, such a simple prediction tool does not exist.

In the present study, our aim was to construct and validate a questionnaire based on simple, non-invasive parameters that identifies subjects at increased CVD risk based on the SCORE risk estimation. Therefore, we used the data of a large web-based health risk assessment (HRA) carried out in the Netherlands.

METHODS

Participants

The current study was performed as part of a worksite HRA implemented in Dutch organisations between August 2007 and January 2013. Study participants were employees aged 40-70 years that completed the HRA within this timeframe. Pregnant woman were excluded from enrolling in the HRA. Because the prediction tool was aimed at identifying previously undetected subjects at high CVD risk, employees with established CVD or on current treatment for hypertension, hypercholesterolemia, diabetes or chronic kidney disease

were excluded from analysis. Informed consent was obtained from all participants prior to the study in accordance with the requirements for identifiable data collection in the Dutch Code of Conduct for Observational Research (www.federa.org).

Health Risk Assessment

Details of the HRA have been described previously.[13] In brief, invitations to participate in the HRA were sent by the human resources department, management, or the safety, health, and welfare services of the organizations involved. The invitation email included a description of the HRA and informed employees that participation was voluntary and free of charge, that all personal data would be treated confidentially, and that no individual results would be shared with their employer or any other party.

Employees were classified as programme attendees when they activated their online account. Each attendee completed a web-based electronic health questionnaire which included approximately 100 questions covering socio-demographics, personal health history, family risk and the behavioural domain. This was followed by biometric measurements including length, weight and waist circumference conducted at the worksite by trained and certified staff. Two BP measurements were taken after 5 minutes of relaxation with a validated oscillometric device. If both systolic measurements were below 140 mmHg, the mean of both measurements was used for analyses. When at least one of the systolic BP readings was ≥140 mmHg, participants were instructed to relax for another 30 minutes in a secluded area after which a third BP measurement was taken. The mean of all three measurements was then used for analyses. At the same visit blood samples were collected for determination of total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides, glucose and HbA1C. A personalised web-based health report and health plan was automatically generated only after all health data were collected. At this point, the health promotion programme was completed.

Outcome measure

A predicted 10-year CVD mortality risk ≥5%, as calculated by the SCORE risk estimation[5] was the primary outcome measure for the development of the screening questionnaire.

This threshold was chosen because current guidelines state that above this threshold life style advices should be given, and treatment aimed at lowering BP or cholesterol should be considered.[1]

The SCORE risk estimation is based on 5-year age groups, gender, current smoking status, systolic BP (mmHg), and total cholesterol (mmol/L) or the total cholesterol/HDL ratio. In the current study we used total cholesterol to calculate SCORE. The Netherlands constitutes a low risk region in terms of CVD mortality, therefore the SCORE risk formula for low risk regions was used.[14]

Selection of potential predictor variables

For the development of the screening tool, non-invasively assessed variables that could have a possible pathophysiological association with CVD risk were selected from the HRA. This selection was independently carried out by two physicians (NvdH and DES). Disagreement between the two physicians was resolved through discussion moderated by a specialist in cardiovascular medicine (BJvdB), who gave the decisive vote. A total of 23 non-invasively assessed variables were selected as potential predictors for CVD.

Definition of predictor variables

From questions related to socio-economic status, date of birth, sex, marital status and ethnicity were selected. Education level was defined as the highest education level completed and was stratified in three categories, low (lower general secondary and lower vocational), middle (higher general secondary, pre-university and intermediate vocational), and high (higher vocational, university and doctorate) for analysis. For marital status, participants selected one of six categories. Ethnicity was defined according to parental background. As the majority of participants were of European descent, the non-European descent answer categories were merged into "other".

Self-rated health was assessed, as previously described, by the question "How do you rate your health in general?", and categorised in strata ranging from poor to very good. [15;16] Frequency of tobacco use was stratified in none, occasionally, weekly, or daily. Alcohol consumption was reported according to the questionnaire of the Dutch Municipal Health Service, which records the number of consumed alcohol units per week using a semi-quantitative scale given the weekly consumed number of units. Insufficient vegetable and fruit intake was defined as an average consumption of less than 3 tablespoons of vegetables or 2 pieces of fruit per day. Fat intake was estimated based on the daily consumption of butter, margarine, cheese and other sandwich fillings. Low fish consumption was defined as less than one fish meal per week. In accordance with the methods used in the INTERHEART study,[17] two items relating to stress at home and stress at work were combined into a general stress scale and graded as follows: 1) never experienced stress; 2) experienced some periods at home or at work; 3) experienced several periods at home or at work; 4) experienced permanent stress at home or at work. Physical activity was self-assessed by one item derived from the Dutch version of the International Physical Activity Questionnaire (IPAQ).[18] Participants were asked to enter the number of weekdays on which they spent at least 30 minutes on moderate to vigorous physical activity. Distress was self-assessed with the validated Dutch version of the Extended Kessler distress scale (EK-10), [19;20] ranging from 10 (no distress) to 50 (severe distress) with a cut-off score of ≥20. First degree family history of CVD (diagnosed before age 60), diabetes mellitus and hypertension was self-reported. History of diabetes mellitus, hypertension, hypercholesterolemia, renal insufficiency was assessed by asking participants whether they were ever treated for diabetes, blood pressure, high cholesterol or renal insufficiency. Subsequently, subjects were asked whether they were still using medication for the selected condition(s). Mental health problems were considered present if participants

received treatment for a mental health disorder, such as depression or anxiety. Length and weight were used to calculate body mass index (BMI) which was categorised into normal weight (BMI <25 kg/m^2), overweight (BMI ≥25 and <30 kg/m^2) and obese (BMI ≥30 kg/m^2). A waist circumference of ≥94 cm for men and ≥80 cm for women was considered as increased abdominal fat.

Statistical analysis

Descriptive statistics were used to present the baseline characteristics of the study population. Univariate logistic regression was performed to determine the single effects of the possible predictor variables on the outcome measure. Variables with a p-value <0.10 in the univariate logistic models were included in a multivariate model. A stepwise selection method was used with backward elimination of predictors. Variables with a p-value of <0.05 were retained in the final model. The total CVD risk score was calculated as the summed coefficients of the retained variables. Area under the curve (AUC) was used as a measure of overall test performance. An AUC of 0.80 or higher is typically considered as indicative of a useful screening instrument.[21] Sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio were calculated at various cut-off values on the total CVD risk score. The optimal cut-off value on the ROC was calculated using Youden's Index (J= sensitivity + specificity -1).[22] A test with J=0 has no diagnostic value whereas J=1 constitutes a perfect test. All analyses were performed using IBM SPSS version 19 (SPSS Inc., Chicago, Illinois, USA).

Internal validation

K-fold cross-validation was performed for the multivariate model with 10% of the data consecutively serving as a validation part (10-folds). Models were developed on one part of the data (90%) and validated on the independent part (10%). The advantage of K-fold cross validation is that all the cases in the dataset are eventually used for both model development and validation. The average performance was calculated over 10 repetitions using the AUC. The stepwise backward selection was applied in every training sample.[23;24]

RESULTS

There were 11,407 employees from 25 organisations who completed the HRA during the study period of which 1,653 participants (14.5%) met one or more exclusion criteria. Baseline characteristics of the 9,784 included study participants are described in Table 1. In total, 4.3% of men and 0.2% of women had a SCORE estimated CVD risk ≥5%. Because the number of women with a SCORE ≥5% was too low (*n*=8) to produce a model of valid statistical inference, we proceeded to develop a prediction model for men. [25]

Table 1 | Baseline characteristics of study sample (*n* = 9,784)

	Men (*n*= 6,189)		Women (*n*=3,565)	
Age (SD)	49.4	6.0	47.1	5.5
Education†				
Low (%)	973	15.7	1030	28.9
Midlevel (%)	1988	32.1	1430	40.1
High (%)	3228	52.2	1105	31
Etnicity				
European descent (%)	5821	94.12	3187	89.4
Other (%)	368	5.9	378	10.6
Tobacco use				
Not (%)	5294	85.5	2977	83.5
At least once a week (%)	469	7.6	251	7.0
At least 10 grams per day (%)	426	6.9	337	9.5
Body Mass Index (SD)	25.7	3.2	24.7	4.1
BMI <25 (%)	2738	44.2	2202	61.8
Overweight: BMI ≥25 - <30 (%)	2923	47.2	988	27.7
Obese: BMI ≥30 (%)	528	8.5	375	10.5
Serum total cholesterol (mmol/l)	5.8	1.0	5.5	1.0
History of hypercholesterolemia (%)	179	2.9	58	1.6
Systolic blood pressure (mmHg)	135.9	16.2	126.9	17.0
History of hypertension (%)	207	3.3	155	4.3
History of diabetes mellitus (%)	19	0.3	13	0.4
SCORE-low risk 5-10 (%)	235	3.8	7	0.1
SCORE-low risk >10 (%)	31	0.5	1	0.0
History of renal insufficiency (%)	72	1.2	29	0.8

†Education. Low: lower general secondary/lower vocational. Midlevel: higher general secondary/pre-university/ intermediate vocational. High: higher vocational/university.

Table 2 | Multivariate regression of high cardiovascular disease risk in men for sociodemographic, lifestyle and biometric variables (*n*=6,189)

		SCORE low risk region ≥5%				
		95.0% C.I.				
		Odds	Lower	Upper	B	Risk Score¶
Age	40-49 ¥					0
	50-54	15.517	4.644	51.844	2.742	19
	55-59	206.816	64.758	660.507	5.332	37
	60-70	1168.532	354.895	3847.520	7.064	49
Tobacco use	Not ¥					0
	At least once a week	14.232	9.977	20.300	2.655	19
Alcohol	<1 units per week ¥					0
consumption	1-7 units per week	1.142	.688	1.895	.132	1
	8-14 units per week	1.278	.753	2.170	.246	2
	15-21 units per week	2.035	1.135	3.648	.710	5
	≥22 units per week	2.376	1.295	4.360	.866	6
Body mass index	Normal weight: BMI <25 kg/m² ¥					0
(BMI)	Overweight: BMI ≥ 25 - <30 kg/m²	1.687	1.130	2.520	.523	4
	Obese: BMI ≥30 kg/m²	1.932	1.043	3.579	.659	5
Waist circumference	<94 cm					0
	≥94 cm	1.849	1.238	2.760	.615	4
History of hypertension	No					0
	Yes	6.158	3.551	10.680	1.818	13

¥ indicates reference category. ¶The risk score is produced by multiplying β's by 7 and rounding them to the nearest integer.

Table 3 | Case examples of the cardiovascular disease risk screening tool

Example nr.	Age	Tobacco use	Alcohol consumption	BMI	Waiste circumfrerence	History of hypertension	Risk Score	Estimated SCORE ≥5%?*
1	52	No	8-14	≥25- <30	<94cm	No	25	No
2	52	Yes	15-21	≥25- <30	≥94cm	No	51	Yes
3	57	No	8-14	≥25- <30	<94cm	No	43	No
4	57	Yes	<1	<25	<94cm	No	56	Yes
5	57	No	15-21	≥30	≥94cm	No	51	Yes
6	57	No	1-7	<25	<94cm	Yes	51	Yes
7	62	No	<1	<25	<94 cm	No	49	Yes

BMI; body mass index. *based on a cut-off of ≥45 points

Table 4 | Diagnostic classification accuracy of predicting high CVD risk at different cut-off values

	TP	FN	FP	TN	Sensitivity	Specificity	PPV	LR +	LR-
Cut-off ≥40	254	12	1181	4742	95.5%	80.1%	17.7%	4.8	0.1
Cut-off ≥45	247	19	888	5035	92.9%	85.0%	21.8%	6.2	0.1
Cut-off ≥50	198	68	438	5485	74.4%	92.6%	31.1%	10.1	0.3

CVD, cardiovascular disease; TP, true positive; FN, false negative; FP, false positive; TN, true negative; PPV, positive predictive value; LR+, positive likelihood ratio; LR-, negative likelihood ratio.

Model development

Of the 23 selected variables, 12 were predictive of the SCORE risk estimate in univariate analysis (Supplemental Table 1) and subsequently entered in the multivariate model. Table 2 shows the results of the multivariate regression analysis. Age, tobacco use, self-reported history of hypertension (without current treatment), alcohol consumption, BMI and abdominal obesity independently predicted a ≥5% SCORE risk. To facilitate practical use of the CVD risk score, β's of these 6 variables were multiplied and rounded to the nearest integer. A multiplication factor of 7 was chosen to sustain sufficient discriminative power between different predictor variables. This resulted in a total CVD risk score ranging from 0 to 96.

Model validation

Ten-fold cross-validation resulted in an AUC of 0.95 (95% CI [0.94- 0.95]), demonstrating good discriminatory power. At a cut-off value of ≥45 on the total CVD risk score, Youden's index reached its maximum, indicative of the optimal cut-off value. In Table 3 several case examples are depicted that illustrate the use of the screening questionnaire and the influence of individual parameters using a cut-off value of ≥45 on the total CVD risk score. Diagnostic classification accuracy at this cut-off value and two alternate cut-off points (≥40 and ≥50) is shown in Table 4.

DISCUSSION

We developed and validated a simple six-item screening questionnaire that accurately identifies male employees with high CVD risk based on the SCORE risk estimation. Because of the low prevalence of women with increased cardiovascular risk before age 65, screening for CVD in the context of a worksite HRA does not seem to be efficacious. Our screening tool limits the burden of taking BP and cholesterol measures in large numbers of employees at low CVD risk as our questionnaire preselects individuals who qualify for a SCORE risk estimation.

Our screening tool is the first non-invasive instrument in which the SCORE risk estimation is used as the endpoint. In addition, our screening tool is highly accurate (AUC =0.95) and performs better than other non-invasive screening instruments on CVD risk factors (AUCs varying between 0.70-0.85).[8-12] At the optimal cut-off value, 93% of the participants with a SCORE ≥5% were correctly identified, while 85% of those with a SCORE below the 5% threshold were correctly labelled negative. As the SCORE risk estimation is recommended for individual risk prediction in the current European guidelines on CVD prevention, our questionnaire can be applied in a screening programme based on these guidelines.[4] In such a programme, subjects are referred to the primary care physician for a BP and cholesterol measure to complete the SCORE risk estimation only if they test positive on the screening

questionnaire. As screen positives have a much higher likelihood of exceeding the ≥5% SCORE threshold, this stepped approach could possibly be a cost-effective method to identify individuals with high CVD risk.

When using the cut-off value of ≥45, the positive predictive value (PPV) of the screening questionnaire is 22%, meaning that about one in every five subjects identified as having a high CVD risk, truly has a SCORE ≥5%. In some screening settings a higher PPV may be desirable. This can be achieved by using a higher cut-off value on the total CVD risk score at the expense of sensitivity. However, if screening is repeated at regular intervals, subjects with initial false negative results will be correctly identified on the subsequent HRA. For example, when the ≥50 cut-off is used instead of ≥45, the PPV increases from 22% to 31%, but sensitivity drops from 93% to 74%. In our cohort, if screening is repeated after 3 years and all predictor variables except age are assumed equal, 49 of the 68 subjects (72%) falsely labelled negative during first screening are correctly identified as having high CVD risk at the second screening. After 5 years this number increases to 63 out of 68 (93%). This approach could be appealing but needs further investigation as risk factors do change over time and subjects who were initially labelled false negative are at higher CVD risk.

Of the predictors included in the screening questionnaire, age and tobacco conferred the largest predictive value, which is not surprising given the fact that they are both included in the SCORE risk assessment. Next to these variables, alcohol consumption, BMI, waist circumference and a history of hypertension (but currently untreated) independently predicted ≥5% SCORE risk. It is likely that they act as a surrogate for the remaining SCORE variables, systolic BP and total cholesterol. High BMI and a large waist circumference often coincide with a high BP or dyslipidemia as part of the metabolic syndrome.[26] A history of hypertension also indicates that the subject has or is prone to develop hypertension. Although alcohol consumption might even be protective for development of the metabolic syndrome,[27] there is a positive correlation between alcohol consumption and increased BP.[28] The contribution to the CVD risk score of these four variables is smaller than age and tobacco, but there are many situations in which they are decisive in determining the screening outcome. In addition, these variables can also be used for a tailored lifestyle advice.

The low prevalence of women that reached the ≥5% SCORE threshold in the current study population is in line with findings of a previous study comprising two Dutch population cohorts of similar age as the current population,[14] where 0.1% of the women and 3.1% of the men reached the ≥5% SCORE threshold. This low prevalence is not surprising given that the ≥5% threshold for low risk countries is not reached for non-smoking women until the age of 65, and for smoking women until the age of 60, irrespective of BP or cholesterol.[5] This suggests that development of a prediction model for women seems not useful from a worksite health care perspective in countries with a low SCORE risk.

There are a few limitations that should be addressed. First, the prediction model is developed and validated in a cohort of employees, which possibly limits the external validity of the questionnaire when used in the general population. Nonetheless, the workplace provides an ideal setting for CVD risk screening as most men in the targeted age range (40-70) are part of the working population, and because it can facilitate the creation of a health-conscious environment.[29] Second, our screening tool was based on the SCORE formula for low-risk countries, as the Netherlands are classified as a low-risk country with lower prevalence of cardiovascular risk factors and CVD as compared to high-risk countries. However, the methods described in the current study can also be used to develop a similar model for high-risk countries. Finally, the developed the questionnaire relies on self-reported length and weight to calculate BMI, which could lead to a slight underestimation.[30] We estimate that the influence on the developed CVD risk score is small, because the BMI used in our model is stratified into three categories.

In conclusion, we used the data of a health risk assessment conducted in 25 Dutch organisations to derive and validate a simple six-item screening tool to identify individuals at increased CVD risk as defined by the SCORE risk estimation. Our screening instrument can easily be presented as an online questionnaire, and therefore serves as a simple, quick and inexpensive tool to identify subjects at high cardiovascular risk in worksite related healthcare programmes in low CVD risk European countries. Future studies should investigate whether the newly developed screening tool can also be applied to the general population. Studies implementing our screening tool are warranted to evaluate the effectiveness and cost-effectiveness of a stepped approach to CVD risk estimation as part of the primary prevention of CVD.

Suppl. Table 1 | Univariate regression of high cardiovascular disease risk in men for sociodemographic, lifestyle and biometric variables

				SCORE low risk region ≥ 5				
						95.0% C.I.		
		n	%	B	Odds	Lower	Upper	Significant at p<0.10
Age	40-49 ¥	3232	52.2%					*
	50-54	1560	25.2%	2.864	17.530	5.285	58.149	
	55-59	1085	17.5%	5.022	151.660	48.191	477.282	
	60-70	312	5.0%	6.288	538.167	169.329	1710.414	
Education†	Low ¥	973	15.7%					*
	Midlevel	1988	32.1%	-.532	.588	.429	.805	
	High	3228	52.2%	-.981	.375	.275	.511	
Marital Status	Maried/registered partner ¥	4884	78.9%					*
	Divorced	332	5.4%	-.343	.710	.383	1.313	
	Cohabitant	628	10.1%	-.680	.507	.298	.860	
	Widowed	33	0.5%	1.718	5.575	2.394	12.981	
	Single	288	4.7%	-.662	.516	.241	1.105	
	Other	24	0.4%	-.105	.900	.121	6.696	
Etnicity	Caucasian ¥	5821						
	Other	368	5.9%	-.397	.673	.364	1.241	

Suppl. Table 1 | Continued

Self-rated health	Very good ¥	1277	20.6%					*
	Good	4161	67.2%	.403	1.496	1.058	2.116	
	Not good and not bad	711	11.5%	.377	1.457	.907	2.342	
	Poor or very poor	40	0.6%	.487	1.628	.379	6.983	
Tobacco use	Not ¥	5294	85.5%					*
	At least once a week	895	14.5%	1.731	5.644	4.384	7.268	
Alcohol consumption	<1 units per week ¥	1100	17.8%					*
	1-7 units per week	2577	41.6%	.255	1.290	.842	1.976	
	8-14 units per week	1433	23.2%	.655	1.925	1.241	2.987	
	15-21 units per week	664	10.7%	.914	2.494	1.538	4.044	
	≥22 units per week	415	6.7%	1.285	3.615	2.192	5.960	
Nutrition	Insufficient vegetable/fruits intake	5561	89.9%	-.238	.788	.542	1.146	
	High saturated fat intake	3980	64.3%	-.395	.674	.526	.863	*
	Fish consumption <1 x per week	2367	38.2%	-.217	.805	.620	1.043	
Stress at work or home	Never ¥	967	15.6%					*
	Some periods	3392	54.8%	-.579	.561	.416	.757	
	Several periods	1756	28.4%	-.869	.419	.291	.605	
	Permanent	74	1.2%	.154	1.167	.489	2.785	

Suppl. Table 1 | Continued

Distress		675	5.7%	.116	1.123	.769	1.639	
Current psychological treatment		175	1.5%	.194	1.215	.614	2.403	
1st degree family history	Diabetes Mellitus	1159	18.7%	-.021	.979	.713	1.344	
	Hypertension	2295	37.1%	-.131	.877	.677	1.137	
	Cardiovascular disease	656	10.6%	.112	1.118	.762	1.641	
History of	Diabetes Mellitus	19	0.3%	.213	1.238	.165	9.308	
	Hypertension	207	3.3%	1.282	3.604	2.357	5.512	*
	Hypercholesterolemia	179	2.9%	.955	2.598	1.570	4.297	*
	Renal insufficiency	72	1.2%	.515	1.674	.669	4.189	
Exercise, days per week ≥30 min.(0-7)				.000	1.000	.998	1.002	
Body Mass Index (BMI)	Normal weight:BMI <25 kg/m² ¥	2738	44.2%					*
	Overweight: BMI ≥25 - <30 kg/m²	2923	47.2%	.822	2.276	1.716	3.020	
	Obese: BMI ≥30 kg/m²	528	8.5%	.744	2.104	1.344	3.291	
Waist circumference	<94 cm ¥	2828	45.7%					*
	≥94 cm	3361	54.3%	.953	2.593	1.957	3.437	

¥ indicates reference category. †Education level. Low: lower general secondary/lower vocational. Mid level: higher general secondary/pre-university/ intermediate vocational. High: higher vocational/university.

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CHAPTER 3

Home blood pressure measurement as a screening tool for hypertension in a web-based worksite health promotion programme

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ABSTRACT

Background: Guidelines on home blood pressure measurement (HBPM) recommend taking at least 12 measurements. For screening purposes, however, it is preferred to reduce this number. We therefore derived and validated cut-off values to determine hypertension status after the first duplicate reading of a HBPM series in a web-based worksite health promotion programme .

Methods: 945 employees were included in the derivation and 528 in the validation cohort which was divided into a normal (*n*=297) and increased cardiometabolic risk subgroup (*n*=231), and a subgroup with a history of hypertension (*n*=98). Six duplicate home measurements were collected during three consecutive days. Systolic and diastolic readings at the first duplicate measurement were used as predictors for hypertension in a multivariate logistic model. Cut-off values were determined using receiver operating characteristics analysis.

Results: Upper (≥150 or ≥95 mmHg) and lower limit (<135 and <80 mmHg) cut-off values were derived to confirm or reject presence of hypertension after one duplicate reading. The area under the curve was 0.94 (SE 0.01, 95% confidence interval 0.93-0.95). In 62.5% of participants hypertension status was determined, with 1.1% false positive and 4.7% false negatives. Performance was similar in participants with high and low cardiometabolic risk, but worse in participants with a history of hypertension (10.4% false negatives).

Conclusion: One duplicate home reading is sufficient to accurately assess hypertension status in 62.5% of participants, leaving 37.5% in which the whole HBPM series needs to be completed. HBPM can thus be reliably used as screening tool for hypertension in a working population.

INTRODUCTION

Hypertension is a major risk factor for cardiovascular (CV) events,[1] and is estimated to affect up to one billion people worldwide.[2] Despite the importance of blood pressure (BP) lowering therapy in hypertensive patients, adequate BP control (office BP <140/90 mmHg) is achieved in merely half of hypertensive cases. In addition, 20% to 50% of hypertensive individuals are unaware of their condition.[3-7] These numbers indicate that there is still need to improve both awareness and control of hypertension. Potential tools to improve BP control and awareness are worksite health promotion programmes. Current health promotion programmes are often based on multiple risk factor interventions, in which BP is assessed as one of several CV risk factors. Although in general the benefit of these health promotion programmes in improving overall CV risk is limited,[8;9] previous uncontrolled studies have shown a positive effect on BP control.[10]

BP is variable and influenced by many stressors, which include, amongst others, the white-coat effect.[11] Therefore even for standardised office BP measurements the current European and Canadian guidelines recommend to take BP at least at two to three different visits before establishing the diagnosis of hypertension ,[12;13] The British guideline of the National Institute for Health and Clinical Excellence recommends ambulatory BP measurement (ABPM) in every patient with an elevated office BP to confirm or rule out hypertension.[14] For the purpose of mass screening of BP in health promotion programmes, however, ABPM has several disadvantages. It is expensive, not widely available, and patients experience more discomfort during measurement compared with home BP measurement (HBPM).[15;16] HBPM therefore seems more suitable for application in screening programmes to detect hypertension. HBPM measurements have similar reproducibility as ABPM measurements,[17] are void of the white coat effect,[18] and show better correlation with target organ damage and CV events than conventional office BP measurements.[19-24] Despite these advantages no health promotion programmes in which BP is assessed by HBPM have thus far been reported. Current recommendations on HBPM advocate to take at least 12 BP measurements.[25] For screening purposes, however, one or two duplicate BP measurements are preferred over a whole series to increase feasibility. Therefore, the aim of this study was to define and subsequently validate BP cut-off values to either confirm or reject the diagnosis of hypertension after one or two duplicate home BP measurements in persons at low and high CV risk. In addition, we examined whether these cut-off values could be applied to establish hypertension control in patients already known with hypertension.

METHODS

Participants

The web-based HBPM study was performed as part of a worksite health promotion programme (The Prevention Compass) as implemented at 16 Dutch companies during the period December 2010 – September 2011.

Initial assessment with a web-based electronic health questionnaire included questions about medical and family history, health complaints, psychological functioning and health behaviour. Participants aged ≥60, (aged ≥50 for male and ≥55 for female tobacco users), with a BMI ≥30, with a medical history of cardiovascular diseases (CVD), symptoms suggestive of CVD, or with a first degree relative diagnosed with CVD before age 60 years were considered to be at high cardiometabolic risk (CMR). Subjects with an estimated SCORE (Systemic Coronary Risk Evaluation)[26] risk of ≥5% based on age, gender, BMI, tobacco use and medical history were also classified as high CMR.

A subset of the participants with increased CMR was offered HBPM as part of additional biometric measurements. All other participants were offered HBPM irrespective of their CMR. Pregnant women were excluded. Informed consent was obtained before the study in accordance with the requirements for identifiable data collection in the Dutch Code of Conduct for Observational Research (www.federa.org).

Home blood pressure measurements

A validated HBPM device (Sensacare SAA-102, Sensacare Company, Hong Kong, China)[27] was sent to participants who accepted additional biometric measurements. They were instructed through an enclosed leaflet to take duplicate BP measurements every morning and evening for three consecutive days. Participants were advised to relax for five minutes before commencing each duplicate measurement. They were urged not to talk during the measurements and to breathe normally. They were instructed to place the cuff at heart level whilst resting their arm on a table. Participants noted down all readings on a chart enclosed with the measurement device. After all measurements were completed, participants entered the readings into a protected, personal webpage. Based on the average BP a tailored advice was reported back to the participants online.

Derivation cohort and validation cohorts

Participants who completed the HBPM before April 13th 2011 were assigned to the derivation cohort. The validation cohort consisted of all participants who completed the HBPM between April 13th 2011 and September 23rd 2011. From the total validation cohort, three predefined subgroups were selected. Those subgroups included participants with a normal CMR, participants with an increased CMR and participants with a history of diagnosed hypertension.

Outcome measure

The main outcome measure was the presence of hypertension defined as an average BP over six duplicate HBPM readings equal to or exceeding 135 mmHg systolic or 85 mmHg diastolic. For participants with a history of hypertension the same BP limits were used to determine whether their BP was adequately controlled.

Statistical analysis

Independent t-tests and χ^2 were used to determine differences in baseline variables. Repeated measures analysis of variance with Bonferroni posthoc correction for multiple testing was used to compare the average BP measurements of the first, second and third day. To determine the relevance of data derived from each increase of the number of duplicate BP measurements intraclass correlation coefficients (ICCs) were calculated. Using the ICCs, the average BP of six duplicate HBPM readings was compared with the first duplicate BP reading, the (average of) the first and second duplicate BP reading, and so on.

To determine cut-off values for normotension and hypertension two multivariate logistic models were built. In the first model, the average systolic and diastolic BP readings at the first duplicate HBPM were used as predictors. In the second model, the average systolic and diastolic BP readings of the first and second duplicate HBPM were used as predictors.

For each participant a logit score was calculated based on the unstandardised β's of systolic and diastolic BP (and the constant). The logit scores were subsequently entered into a Receiver Operating Characteristic (ROC) curve analysis.

Based on predefined limits for the maximum allowed percentages of participants incorrectly diagnosed as respectively normotensive (false negative) and hypertensive (false positive), cut-off points on the ROC curve were chosen. Corresponding BP readings were rounded to the nearest five mmHg (i.e. 122.5/84 was rounded to 125/85) to ensure that clinically useful cut-off values would be validated. An accuracy measures matrix with incremental five mmHg BP steps was computed to determine the accuracy of the first duplicate HBPM for predicting hypertension at various other cut-off values. The performance of the models was assessed by the ROC curve and the Area Under the Curve (AUC). The AUC of the model in the validation cohort(s) was tested for significant (one-tailed) differences with the AUC in the derivation cohort using Hanley and McNeil's formula.[28] The sensitivity, specificity, positive and negative predictive value, and the positive and negative likelihood ratio of the cut-off values were also calculated. All analyses were performed using SPSS 19.0 (SPSS inc., Chicago, Illinois, USA).

RESULTS

A total of 1,852 persons participated in the study. Of these participants, 378 (20.5%) did not complete or report their HBPM readings leaving 1,473 (79.5%) persons for analysis, including 52% with increased CMR. Persons who did not complete or report their HBPM readings were younger (48.0±10.0 versus 53±5.6 years, p< 0.01) and less highly educated (42.0% versus 51.8% higher education; p<0.01) than those who did. No sex differences were observed. A total of 945 participants (64.2%) completed the HBPM before April 13th 2011 and were assigned to the derivation cohort. The remaining 528 (35.8%) participants were assigned to the validation cohort. Table 1 summarises the baseline characteristics of the study cohorts. There were no differences between the derivation and the total validation cohort. Compared with the participants with a normal CMR , individuals with a high CMR were older (p<0.01) and more often male (p=0.01). Also, their mean systolic (p<0.01) and diastolic (p=0.04) BP was higher.

Derivation Cohort

Two hundred sixty-one (27.6%) subjects were diagnosed with (uncontrolled) hypertension based on their HBPM series. The average morning BP (123±14/78±10 mmHg) was lower than the average evening BP (126±14/78±10 mmHg, p<0.01 for systolic, p=0.01 for diastolic BP). Also, the average BP of the first, second and third measurement day were significantly different (p<0.01 for systolic, p<0.01 for diastolic BP). Systolic BP of the first day (125±14 mmHg) was higher than the systolic BP of the second (124±14 mmHg (p<0.01), but not of the third day (124±14 mmHg, p=0.11). The average diastolic BP of the first day (79±10 mmHg) was higher compared to the diastolic BP of the second (78±10 mmHg, p=0.01), and the third day (78±10mmHg, p<0.01).

The average of each consecutively included duplicate HBPM was compared with all six duplicate measurements using ICC. As shown in Figure 1, all ICCs were ≥0.9. The largest increase in ICC was observed between the average of the first (morning), and the average of the first and second (evening) duplicate HBPM. Addition of other duplicate measurements did not further increase ICC.

Two separate cut-off values were selected and subsequently rounded to their nearest five mmHg. The first cut-off BP value was set to discriminate normotensive from possible hypertensive persons. For the purpose of this study the false negative rate for hypertension was not allowed to exceed 5%. A reading of ≥135/80 mmHg at the first duplicate HBPM was chosen as the 'lower limit' cut-off value, indicating that participants with a first duplicate reading of ≥135 or ≥80 mmHg (sensitivity: 0.96, specificity: 0.71) were classified as having possible hypertension. Vice versa, those with a first duplicate HBPM reading of <135 mmHg and <80 mmHg were labelled as normotensive (sensitivity: 0.71, specificity: 0.96). Sensitivity and specificity of other cut-off values are shown in the Supplementary table S1.

Table 1 | Baseline characteristics of health risk assessment participants

	Derivation cohort (*n* =945)		Validation cohort I (*n*=528) Total		Validation cohort II (*n*=297) Normal CMR		Validation cohort III (*n* = 231) High CMR		Validation cohort IV (*n* = 98) Hypertension	
Male (%)	493	(52.2%)	299	(56.6%)	150	(50.5%)	149	(64.5%)	56	(57.1%)
Age (SD)	53.1	(5.2)	53.1	(6.2)	52.0	(5.3)	54.4	(7.0)	53.9	(4.9)
Education level*										
Low	177	(18.7%)	84	(15.9%)	45	(15.2%)	39	(16.9%)	21	(21.4%)
Mid level	253	(26.8%)	171	(32.4%)	82	(27.6%)	89	(38.5%)	35	(35.7%)
High	486	(51.4%)	254	(48.1%)	156	(52.5%)	98	(42.4%)	40	(40.8%)
Unknown	29	(3.1%)	19	(3.6%)	14	(4.7%)	5	(2.2%)	2	(2.0%)
Hypertension (%)	177	(18.7%)	98	(18.6%)	49	(16.5%)	49	(21.2%)	98	(100.0%)
SBP (SD)	124.5	(13.3)	126.0	(15.1)	123.9	(15.4)	128.6	(14.3)	130.1	(16.2)
DBP (SD)	78.3	(9.6)	79.3	(10.9)	78.4	(11.5)	80.4	(10.1)	83.0	(10.4)

Values are expressed as mean with standard deviation (SD) or total number with percentages.

Hypertension was defined as a history of diagnosed hypertension. For description of different cohorts see text. BP values are expressed in mmHg.

SPB, systolic blood pressure; DBP, diastolic blood pressure.

* Education level:

Low: lower general secondary/lower vocational

Intermediate: higher general secondary/pre-university/intermediate vocational

High: higher vocational/university

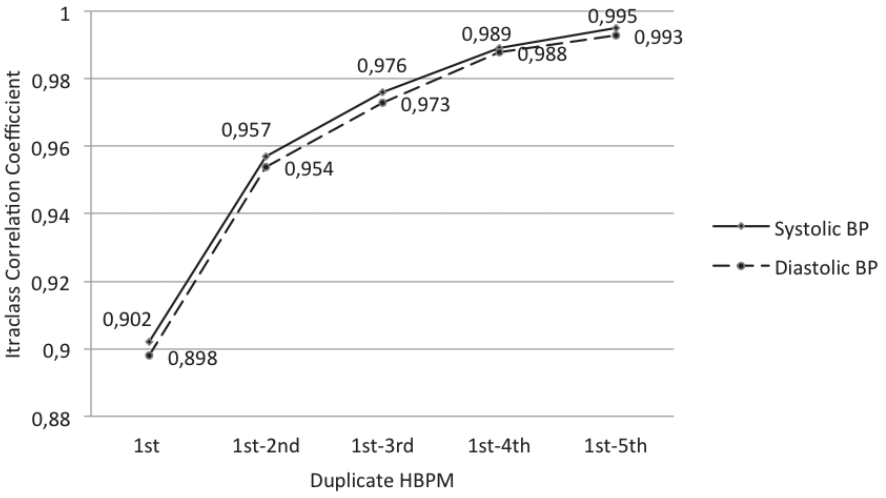

Figure 1 | Intraclass Correlation Coefficients from each increase in the number of duplicate home blood pressure measurements as compared with all six duplicate measurements.

The second cut-off BP value was set to positively diagnose hypertension. For the purpose of this study the false positive rate for hypertension were minimised at 1%. A value of ≥150/95 mmHg (sensitivity: 0.33, specificity: 1.00) was selected as the 'upper limit' cut-off value. Thus, participants with a first duplicate HBPM reading of ≥150 or ≥95 mmHg were classified as hypertensive. For those with a first duplicate HBPM between the lower and upper cut-off limits, no accurate diagnosis was possible based on the first duplicate HBPM.

The AUC of the second model, using the average readings of the first and second duplicate HBPM to predict hypertension, was 0.97 (standard error [SE] 0.01, 95% confidence interval [CI] 0.96-0.98), representing a marginal improvement on the first model [AUC 0.94, SE 0.01, 95% CI 0.93-0.95)]. We therefore proceeded to validate the cut-off scores based only on the first duplicate HBPM.

Validation cohorts

Figure 2 depicts the ROC curves of both the total validation and the derivation cohort. The AUC of the validation cohort (AUC 0.94, SE 0.01, 95% CI [0.92- 0.96]) was not different (p=.45) from the AUC in the derivation cohort. Table 2 shows the accuracy measures for the validation cohorts, using the cut-off values chosen in the derivation cohort.

There were 169 (32.0%) subjects diagnosed with (uncontrolled) hypertension in the total validation cohort. After the first duplicate measurement 62.5% of the total validation cohort could be classified. The classified group included 71.8% of the normotensive and 37.3% of the hypertensive participants, while 4 individuals (1.1%) with a normal BP were incorrectly labelled as hypertensive, and 8 persons with hypertension (4.7%) were incorrectly labelled as normotensive. The average BP of these 8 participants was 138/83 mmHg. The average BP of the uncategorised participants (37.5%) was 131/83 mmHg with 50% being hypertensive.

The AUC in the normal and high CMR subgroups were, respectively 0.95 (SE 0.01, 95% CI [0.92- 0.97]) and 0.92 (SE 0.02, 95% CI [0.89- 0.96]). The AUCs of the derivation cohort did not differ from the AUCs of both the normal (p=0.35) and high (p=0.23) CMR validation cohorts. After the first HBPM, 67.0% of the normal CMR and 56.7% of the high CMR subgroups were classified.

In almost half (49.0%) of individuals in the subgroup with a history of hypertension BP was not optimally controlled. The AUC in this subgroup was 0.91 (SE 0.03, 95% CI [0.85-0.96]), which was not different from the AUC in the derivation cohort (p=.16). After the first duplicate HBPM, 44.9% of this subgroup was classified. The average BP of the uncontrolled hypertensive subjects who were mislabelled as having normal BP was 139/84 mmHg.

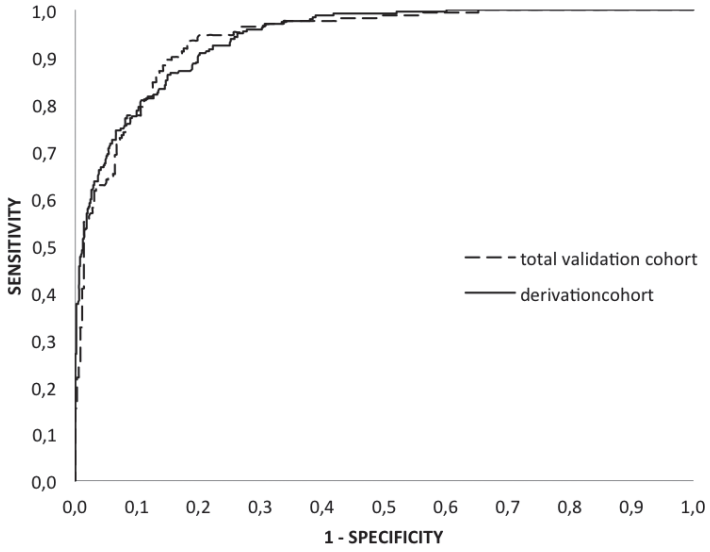

Figure 2 | Receiver Operating Characteristic curves for the prediction model of hypertension for the derivation and validation cohort.

Table 2 | Diagnostic Classification Accuracy by 1st duplicate HBPM Reading

	TP	FN	FP	TN	Sensitivity	Specificity	PPV	NPV	LR +	LR-
Total validation cohort (n=528)										
Cut-off for hypertensive (≥150 or ≥95 mmHg)	63	106	4	355	37.3%	98.9%	94.0%	77.0%	33.5	0.6
Cut-off for normotensive (<135 and <80 mmHg)	255	104	8	161	71.0%	95.3%	97.0%	60.8%	15.0	0.3
Normal CMR subgroup (n=297)										
Cut-off for hypertensive (≥150 or ≥95 mmHg)	33	48	2	214	40.7%	99.1%	94.3%	81.7%	44.0	0.6
Cut-off for normotensive (<135 and <80 mmHg)	161	55	3	78	74.5%	96.3%	98.2%	58.6%	20.1	0.3
High CMR subgroup (n= 231)										
Cut-off for hypertensive (≥150 or ≥95 mmHg)	30	58	2	141	34.1%	98.6%	93.8%	70.9%	24.4	0.7
Cut-off for normotensive (<135 and <80 mmHg)	94	49	5	83	65.7%	94.3%	94.9%	62.9%	11.6	0.4
History of hypertension subgroup (n=98)										
Cut-off for uncontrolled hypertensive (≥150 or ≥95 mmHg)	14	34	0	50	29.2%	100.0%	100.0%	59.5%	∞	0.7
Cut-off for controlled hypertensive (<135 and <80 mmHg)	25	25	5	43	50.0%	89.6%	83.3%	63.2%	4.8	0.6

TP, true positive; FN, false negative; FP, false positive; TN, true negative; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

DISCUSSION

The current study demonstrates that HBPM can be used as a reliable tool for diagnosing hypertension in a working population. One duplicate measurement was sufficient to classify 62.5% of the screened participants. Only 37.5% of the screened participants are required to complete the whole 3-day series of HBPM for a reliable classification. For participants with a history of hypertension, the proposed cut-off values classified merely 45% with > 10% false negatives, suggesting that one duplicate measurement at cut-off values derived from a general sample can not sufficiently discriminate BP control in these patients.

Although HBPM has made its way to routine medical practice, most current screening programmes still make use of a single, on-site BP measurement. Not only do we show that HBPM can be used as a reliable alternative, with the introduction of two simple cut-off values, we were also able to reduce the burden of HBPM to one duplicate reading for more than six out of every 10 participants. Lessening the burden of HBPM in a screening setting is important, as in our population 20% failed to completely record all requested measurements. In addition, the reduced number of readings required to accurately classify patients as either normotensive or hypertensive reduces measurement bias. We previously showed that many hypertensive patients do not follow the requested HBPM schedule resulting in over- or underestimation of BP.[29] The use of a single BP measurement for the majority of a screening population may therefore increase both feasibility and accuracy.

To apply current cut-off values in a screening programme it is required that participants report their first duplicate BP reading, for example on a protected personal webpage as in the current study, so that direct feedback can be given. If the first duplicate BP reading exceeds 150/95 mmHg or is below 135/80 mmHg, participants can be classified as hypertensive or normotensive, respectively, without performing further measurements. The remaining participants (whose BP values do not exceed the cut-off limits) are advised to complete the whole series of HBPM. Because the duplicate measurement from which the cut-off values were derived was taken in the morning, it is advised to apply the cut-off values on a duplicate measurement which is taken in the morning.

For participants with a history of hypertension, assessment of BP status after one duplicate measurement was considerably less accurate than in the other validation cohorts. This can most likely be explained by the fairly large amount of participants with uncontrolled hypertension (49%) within this subgroup combined with a higher average BP (139/84 mmHg). These findings underscore the importance of including participants with an established history of hypertension in health screening programmes as there is evidence that uncontrolled hypertension leads to excess CV mortality in treated hypertensive patients.[30] This also suggests that patients with a history of hypertension should always complete the minimally recommended number of 12 HBPM readings to assess BP control.[25]

The prevalence of hypertension in the current study population varied from 27.6% (derivation cohort) to 32.0% (validation cohort), which is similar to a previous report of a random Dutch population of subjects aged 35-60 years, showing a hypertension prevalence of 33% for men and 20% for women[31]. This indicates that the current population seems a good representation of the general population in terms of hypertension prevalence.

Because morning BP readings were significantly lower than evening readings, it could be argued that including them both would better reflect an individual's true BP. However, when predicting the binary outcome of hypertension status, the second model (first and second duplicate HBPM) showed only marginal improvement upon the first model (first duplicate HBPM), which would not be commensurate to the burden of taking a second duplicate HBPM.

This study has some limitations. First, although HBPM seems a useful tool for mass screening of hypertension, we did not investigate whether its use in a screening programme leads to better hypertension awareness and control. Second, we can not know whether the participants fully complied with the HBPM instructions. They could have, for example, taken BP outside the standardized condition or have uploaded a wrong BP. However, the same applies to regular HBPM. Third, in our population 20% failed to record all requested measurements. Because these subjects were different in education and age compared to those who completed the HBPM series, this might decrease the external validity of the proposed cut-off values. However, addition analysis showed no difference in the performance of the cut-off values between both education and age-categories within the validation cohort (data not shown). Finally, in the current health programme a web-based approach was used in which participants electronically uploaded their readings. Although 94% of the Dutch households have internet-access,[32] not all health programmes currently use this web-based approach. Perhaps future HBPM devices can be developed which are equipped with a build-in algorithm or a "screening mode" which can be used in health programmes.

Over the years HBPM has proven its value within medical clinics due to its reliable results and general acceptance by both patients and clinicians. This study shows that HBPM can be easily and reliably applied as a screening tool for hypertension. In a health screening programme, one duplicate measurement was sufficient to either diagnose or reject the presence of (uncontrolled) hypertension in more than six out of every ten participants. Future studies should elucidate whether HBPM can also be used as a screening tool in primary care and, ultimately, whether HBPM-based screening programmes lead to better hypertension awareness and control.

Supplementary Table 1 | Accuracy measures at different blood pressure cut-off values of the first duplicate measurement for predicting hypertension

Systolic → Diastolic ↓		120	125	130	135	140	145	150	155	160	165	170
70	se	1.000	1.000	1.000	1.000	1.000	0.996	0.996	0.996	0.996	0.996	0.996
	sp	0.251	0.263	0.278	0.282	0.284	0.284	0.284	0.284	0.284	0.284	0.284
75	se	1.000	1.000	1.000	1.000	0.992	0.981	0.977	0.977	0.977	0.977	0.977
	sp	0.415	0.463	0.496	0.504	0.506	0.507	0.507	0.507	0.507	0.507	0.507
80	se	0.985	0.973	0.962	0.962	0.935	0.916	0.904	0.904	0.900	0.900	0.900
	sp	0.513	0.624	0.684	0.709	0.724	0.728	0.732	0.732	0.732	0.732	0.732
85	se	0.969	0.935	0.874	0.824	0.762	0.709	0.690	0.686	0.682	0.682	0.682
	sp	0.541	0.715	0.819	0.883	0.906	0.911	0.917	0.917	0.917	0.917	0.917
90	se	0.958	0.912	0.820	0.693	0.602	0.513	0.471	0.460	0.448	0.444	0.441
	sp	0.544	0.732	0.855	0.942	0.977	0.984	0.990	0.990	0.990	0.990	0.990
95	se	0.954	0.908	0.805	0.648	0.521	0.395	0.326	0.295	0.257	0.249	0.241
	sp	0.545	0.734	0.858	0.944	0.981	0.991	0.999	0.999	0.999	0.999	0.999
100	se	0.954	0.908	0.793	0.625	0.475	0.310	0.222	0.180	0.138	0.123	0.111
	sp	0.545	0.734	0.858	0.944	0.981	0.991	0.999	0.999	0.999	0.999	0.999
105	se	0.954	0.908	0.789	0.621	0.460	0.287	0.188	0.138	0.084	0.065	0.054
	sp	0.545	0.734	0.858	0.944	0.981	0.991	0.999	0.999	0.999	0.999	0.999
110	se	0.954	0.908	0.789	0.621	0.460	0.287	0.188	0.138	0.077	0.057	0.042
	sp	0.547	0.735	0.860	0.946	0.982	0.993	1.000	1.000	1.000	1.000	1.000
115	se	0.954	0.908	0.789	0.621	0.456	0.284	0.180	0.130	0.069	0.050	0.034
	sp	0.547	0.735	0.860	0.946	0.982	0.993	1.000	1.000	1.000	1.000	1.000
120	se	0.954	0.908	0.789	0.621	0.452	0.276	0.169	0.119	0.057	0.038	0.023
	sp	0.547	0.735	0.860	0.946	0.982	0.993	1.000	1.000	1.000	1.000	1.000

Cut-off values above the black line indicates a BP level with a sensitivity of ≥95% in detecting hypertension defined as an average blood pressure of ≥135/90 mmHg on 12 home blood pressure measurements. Se, sensitivity; sp, specificity.

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CHAPTER 4

Diagnostic validity of the Eppendorf Schizophrenia Inventory (ESI): A self-report screen for ultrahigh risk and acute psychosis

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ABSTRACT

Providers of mental health services need tools to screen for acute psychosis and ultrahigh risk (UHR) for transition to psychosis in help-seeking individuals. In this study, the Eppendorf Schizophrenia Inventory (ESI) was examined as a screening tool and for its ability to correctly predict diagnostic group membership (e.g., help seeking, mild psychiatric complaints, highly symptomatic mood or anxiety disorder, UHR, acute psychosis). Diagnostic evaluation with established instruments was used for diagnosis in 3 research samples. UHR status was assessed with the Structured Interview for Prodromal Symptoms/Scale of Prodromal Symptoms[1] and the Bonn Scale for the Assessment of Basic Symptoms Prediction list.[2;3] This study showed that members of different diagnostic groups rate themselves significantly differently on the ESI and its subscales. A new subscale was constructed, the UHR–Psychosis scale, that showed good utility in detecting individuals with interview-diagnosed UHR status and acute psychosis. The scale is also sensitive to the threshold between UHR and acute psychosis. Practical applications of the ESI include use as a diagnostic tool within various settings.

INTRODUCTION

Most patients with schizophrenia spectrum diagnoses experience a lengthy period of nonspecific and specific psychotic symptoms, signs, and growing functional impairment before the emergence of frank psychosis. This prodromal period is considered highly important and has been a focal point of research for more than a decade, not in the least because a valid identification of the psychosis prodrome would make it possible to prevent, delay, or ameliorate the onset of psychotic disorders.[4-6] It was made clear early on that the retrospective term prodrome could not be appropriately applied to prospective studies because these clusters of symptoms failed to have predictive power in relation to subsequent psychosis in the general population.[6-8] Therefore, the terms at-risk mental state and ultrahigh risk (UHR) have been suggested, implying that a subthreshold syndrome can be regarded as a risk factor for subsequent psychosis in a help-seeking population and not with psychosis as an inevitable outcome.[7]

Traditional psychopathological assessment instruments were not sufficiently sensitive to this subthreshold condition of psychosis. Therefore, a number of new instruments were constructed.[9] The first influential instrument to be used was the Comprehensive Assessment of At-Risk Mental States (CAARMS).[6;8] The CAARMS defined three groups of UHR criteria on the basis of descriptions of the prodrome compiled from retrospective accounts of first-episode or remitted schizophrenia patients and their relatives, case studies, high-risk studies, and studies of the prodrome to psychotic relapse.[10] These CAARMS UHR criteria are (a) decline in functioning and familial risk of a psychotic spectrum disorder, (b) attenuated positive psychotic symptoms (APS), and (c) a brief psychotic episode (brief limited intermittent psychotic symptoms, or BLIPS). [6] Another instrument is the widely used Structured Interview for Prodromal Syndromes (SIPS) and its rating scale, the Scale of Prodromal Symptoms (SOPS).[1] The SIPS was developed using the Criteria of Prodromal States criteria, which present only minor modifications to the CAARMS criteria.

Whereas the aforementioned approach focuses on a one- to two-year time frame of transition to psychosis, the so-called late prodrome, the basic symptoms (or subjective experiences) approach focuses on an even earlier phase of the at-risk state: the period during which a person notices changes in perception and cognition.[2] In this phase, subtle alterations in perceptions occur, and derealization and transitory ideas of reference become noticeable. The basic symptoms approach was also operationalized in a structured interview, the Bonn Scale for the Assessment of Basic Symptoms (BSABS).[2]

Initial studies showed impressive transition to psychosis rates (40%–54%) in UHR cohorts as defined by the prediction list of the BSABS (BSABS-P) or SIPS/SOPS criteria.[3;6;11] Transition rates found in recent studies are much lower (16%).[12] Possible explanations for this decline include the earlier detection of UHR individuals in specialized clinics, resulting

in a reduced duration of symptoms prior to receiving help and subsequent avoidance of progression to psychosis.[13] Alternatively, it may be due to higher numbers of false positives being identified.[13]

Research further suggests that the use of subjective experiences in conjunction with attenuated symptoms may more narrowly define a group of patients to be at increased risk of developing psychosis.[14] A comprehensive list of early and late prodromal assessment instruments has been reviewed by Olsen and Rosenbaum.[9]

Administration of the UHR semistructured interviews requires specific training and several hours of clinicians' time.[10] Thus, research groups have engaged in recruitment strategies and screening procedures to increase the yield of valid referrals entering their UHR studies. However, as yet, there are no accepted standardized criteria for case.[3;6;11] This lack has resulted in the development of multiple prodromal screening questionnaires, two of which are the PROD-Screen[15] and the Prodromal Questionnaire.[10;16] For both instruments, concordant validity was established with prodromal syndromal diagnosis based on structured interviews. However, there was a lack of report on outcome, that is, information on what proportion of individuals labeled as being at UHR actually received a diagnosis of psychosis within a specified time frame. Also, the Prodromal Questionnaire is not sensitive to the threshold between UHR and psychosis. The PROD-Screen is not able to distinguish between highly symptomatic outpatients and SIPS-defined UHR status.

Reporting on two other instruments, the SIPS-Screen[17] and the Y-PARC Screen[18], has been very limited. The SIPS-Screen was tested on a sample of only 36 subjects referred for prodromal evaluation, but it showed promising results. The Y-PARC Screen has been validated on an isolated population in Micronesia with elevated rates of familial schizophrenia. Thus far this instrument is only reported on in relation to genetic high risk studies.[19]

Another (potential) screening questionnaire, the Eppendorf Schizophrenia Inventory (ESI), was developed by Mass.[20] He focused on subjective experiences, the self-perceived changes in cognition and perception that can precede more overt psychotic behavior. Items for the ESI are partly derived from the symptom descriptions of—among others—the BSABS, the Frankfurt Complaint Questionnaire [21], and the Schizotypal Personality.[22] Verbatim statements of early schizophrenia signs with emphasis on cognitive phenomena[19;23] were also used for item construction. Only symptoms predominant in both first episode and chronic psychotic patients were selected for the original ESI.[19] Preliminary ESI psychometrics were reported on by Mass[19;22] and were satisfactory. The ESI was found to discriminate well between schizophrenia inpatients and nonschizophrenia inpatients. However, the diagnostic validity of the ESI has not yet been investigated in a UHR cohort. Our main goal in the current study was to investigate the ESI's ability to correctly predict diagnostic group membership (e.g., help seeking, mild psychiatric complaints, highly symptomatic mood or anxiety disorder, UHR, acute psychosis) in three cohorts.

METHOD

Participants

First sample: High-risk referrals. Three samples were used for this study. The first sample consisted of individuals referred to the Ultrahigh Risk for Psychosis (VORS) Unit of the Academic Medical Centre because of suspicion that they were developing psychosis. The VORS Unit specializes in the assessment of UHR states for psychosis and first-episode psychosis. Help-seeking individuals were referred (during the period 2002–2006) from community mental health centers and psychiatrists in private practice. Eligible individuals, screened at the clinic, entered the Dutch Prediction of Psychosis Study (DUPS), a 24-month follow-along study, after informed consent was given. To be included in the DUPS study, participants had to be between 12 and 35 years old and belong to one of the following four groups: those with (a) familial risk or schizotypal personality disorder plus reduced functioning (drop of 30% in general assessment of functioning [GAF] score in the last year), (b) attenuated psychotic symptoms, (c) BLIPS of less than a week's duration, or (d) at least two basic symptoms.

Exclusion criteria for the DUPS study were a previous psychotic episode for more than a week, symptoms due to substance abuse, symptoms due to a known general medical disorder, or IQ below 85. The UHR status criteria used in the DUPS study are also used in its European counterpart, the European Prediction of Psychosis Study.[24;25]

For the current study (implemented in all samples), two additional exclusion criteria were used. First, the miminum age for inclusion was set at 16 years. This was done after several individuals younger then 16 years indicated that they did not comprehend a number of ESI items. Second, subjects who scored 0 on the ESI Frankness (FR) subscale were excluded from analyses (see the Instruments section).

The Dutch authorized translation of the ESI became available after the inclusion process for the DUPS study had started. As a result, of the 275 persons referred to the unit for UHR assessment, 192 completed the ESI. Those who completed the ESI did not differ from the individuals who did not complete the ESI with regard to age and sex.

Twenty-seven individuals were excluded as they were younger then 16 years at intake. Two persons were excluded on the basis of diagnosed organic mental disorder. Furthermore, data of three individuals were excluded from analysis because of a zero score on the ESI FR subscale (which indicated a socially desirable answer tendency).

Seventy-four of the 160 included subjects (45%) met the UHR criteria of having either APS, BLIPS of less then a week's duration, and/or basic symptoms. The UHR group consisted of 23% APS, 57% APS + BS, 9% APS + BS + BLIPS, and 11% other combinations.

Forty-three individuals (29%) were acutely psychotic at intake, 15 patients (9%) had experienced a psychotic episode in the recent past, 24 individuals (15%) did not meet UHR criteria and did not receive a diagnosis of any DSM–IV disorder, and four subjects (2%) received a diagnosis of bipolar disorder. The data of the latter were analysed together with the mood disorder group of the second research sample.

Second sample: Inpatients and highly symptomatic outpatients. The second sample consisted of 163 patients, referred to the Psychodiagnostic Unit of the Academic Medical Centre (during the period 2000–2008) for psychological evaluation. The referrals were both inpatients and highly symptomatic outpatients, most of whom attended a daily treatment program at the hospital. Data of five persons were excluded from analysis because of a zero score on the ESI FR subscale (which indicated a socially desirable answer tendency).

The referred patients were given a preliminary DSM–IV diagnosis based on a supervised psychiatric resident intake in which the longitudinal, expert, all data procedure (as described by Kranzler, Kadden, Babor, & Rounsaville was used.[26] These preliminary diagnoses were psychosis spectrum disorder (73 patients, 44%), mood disorder (50 patients + 4 bipolar from the first sample, 34%), anxiety disorder (17 patients, 11%), and hard drug dependence or abuse (18 patients, 11%).

Third sample: Mildly symptomatic outpatients. The third sample consisted of 32 outpatients who were undergoing outpatient treatment for mild psychiatric symptoms at Mediant mental health facility, located at Enschede in the eastern part of the Netherlands. These patients were routinely assessed with the Mini-International Neuropsychiatric Interview[27] for DSM–IV–TR Axis I disorders and the Structured Clinical Interview for DSM–IV–TR Axis II disorders (SCID–II; in a stepped procedure with the SCID–II screen and followed up with the SCID–II interview). Data of this sample were consecutively gathered during a 6-week period during early 2010. Two persons younger than 16 years old were excluded from analysis.

The main diagnosis for the 30 included patients were mood disorder (12 patients, 40%), anxiety disorder (six patients, 20%), personality disorder (four patients, 13%), adjustment disorder (two patients, 7%), eating disorder (two patients, 7%), dissociative disorder (two patients, 7%), abused as child (one patient, 3%), and somatoform disorder (one patient, 3%). Given the lack of variance in ESI scores across diagnostic groups in the third sample, data of this sample are analysed as one group (mildly symptomatic outpatients).

Instruments

ESI questionnaire. The ESI questionnaire consists of 40 items (statements), to be answered on a 4-point Likert-type subscale (rated on a scale of 3 = absolutely true to 0 = not true at all). A short instructional text asks subjects to take the current state (i.e., last 4 weeks) as a basis for the self-assessment. Mass[19] proposed four clinical subscales:

1. The Attention and Speech Impairment (AS) subscale (10 items) mainly describes impairments in the reception and interpretation of environmental stimuli, above all those affecting speech.
2. The Ideas of Reference (IR) subscale (seven items) represents a tendency to interpret trivial events in an excessively meaningful way and a delusional mood.
3. The Auditory Uncertainty (AU) subscale (eight items) describes an insecurity in discriminating between thoughts and words that actually have been heard as well as a vague impression of being influenced.
4. The Deviant Perception (DP) subscale (nine items) refers to aberrations of perceptual processes, especially involving disturbances of body image.

A five-item Frankness (FR) subscale was added as a control scale to assess the willingness and/or ability of respondents to admit to minor general personal flaws. A typical FR statement is "Sometimes I am offended if things do not go my way." As explained in the Participants section, we excluded the results of eight subjects (three people from the first sample, five people from the second sample) who answered not true at all to all five FR subscale items, as persons unwilling to admit to these common thoughts and behaviors would likely be even more reluctant to admit to thoughts that were out of the ordinary or experiences being asked about in the remainder of the ESI questionnaire. The FR subscale and its items were not subjected to analysis in this article.

SIPS/SOPS. The SIPS (1) is composed of Criteria of Prodromal States, Presence of Psychosis Scale, GAF, a checklist for schizotypal personality disorder, and a questionnaire of family history of mental illness.[9] Attenuated psychotic symptoms and BLIPS were assessed with the Criteria of Prodromal States section. It is composed of 19 items (five positive symptoms, six negative symptoms, four disorganization symptoms, and four general symptoms); each is given a score of 1 to 6 according to defined criteria. A score between 3 and 5 on the positive symptoms indicates attenuated psychotic symptoms and a score of 6 indicates a psychotic state. Positive symptoms with psychotic intensity that occurred for a total duration of less than 7 days before resolving spontaneously were considered BLIPS.

BSABS-P. The BSABS-P [2;3] assesses 17 selected self-perceived disturbances in cognition and perception that were found to be predictive for a transition to psychosis. Each basic symptom is given a score of 0 to 6 according to maximum frequency of occurrence during the preceding 3 months as the guiding criterion. An individual with a score between 3 and 6 on two out of a subset of nine basic symptoms met the basic symptom criterion for inclusion in the UHR group.

Procedure

First sample. The ESI was completed at home by referred persons before formal evaluation took place at the VORS Unit. Extensive diagnostic at the VORS Unit included a psychiatric interview (SCID–II [28]) with a psychiatrist and the SIPS and BSABS-P interviews, independently, with trained psychologists. Also, GAF was assessed (included in the SIPS interview). Parents or caretakers were interviewed by a social worker.

Follow-up assessments of clinical status (i.e., maintained UHR status or transitioned to psychosis) were carried out with the SIPS/SOPS, BSABS-P, and SCID at three time points: Time 1 (9 months), Time 2 (18 months), and Time 3 (24 months). A final follow-up assessment (standardized telephone interview) took place after 36 months. UHR patients were referred back to their referring mental health institution. Some received treatment, others were only monitored. However, it was stressed for patients, caretakers, and referring clinicians that if the participant's condition deteriorated in between follow-up assessments, the VORS Unit should be contacted for an additional assessment of clinical status. The deteriorating participant condition was then monitored monthly thereafter and patients were clinically reexamined (for transition) when this was decided by the project psychiatrist.

The follow-up for the referrals who did not attain UHR status at intake and did not receive a diagnosis of any disorder consisted of one assessment at Time 3. Individuals were asked about their condition by means of a standardized telephone interview.

Second sample. Patients from the second sample completed the ESI approximately 6–8 weeks after psychiatric admission at the Academic Medical Centre while participating in psychological evaluation for further treatment planning.

Third sample. Individuals from the third sample (outpatients with mild symptomatology from the Mediant outpatient clinic) completed the ESI as part of a prescheduled reevaluation of their status on DSM–IV–TR Axes I and II. Informed consent of all participants was obtained after the nature of the procedures had been fully explained.

Statistical Analysis

Correlations of ESI subscale scores with SOPS and BSABS-P scale scores were examined by calculating Spearman's rho coefficients. One-way analysis of variance (ANOVA), independent samples t tests, chi-square tests, and correlations were used to test for age, gender, and education effects on ESI scores. Stepwise logistic regression was used to select the ESI items with the highest predictive value in an optimum model/scale combination.

Overall prognostic accuracy of the newly derived scale was compared with the original ESI scales using a geometric approach: the area under the curve (AUC). With an AUC greater than 0.50, the scale predicts diagnosis at a rate better than chance.[29] An AUC of 0.80 or higher is typically considered indicative of a useful screening instrument.[29] Receiver-operating characteristic (ROC) curves were used to assess the screening accuracy of the new scale at various cutoff points because of the inverse relation between the varying sensitivity and specificity of measures.[30]

In addition to sensitivity and specificity ratios, positive likelihood ratios (LR+s) and negative likelihood ratios (LR-s) were calculated as accuracy measures. LR+ estimates how much the odds of the disease increase when a test is positive.[31] LR- estimates how much the odds of the disease decrease when a test is negative. LRs between 0.5 and 2 are not considered useful

and those less than 0.5 but greater than 0.2 or greater than 2 but less than 5 are suggestive and not conclusive. Values of LR+ that are greater than 5 argue strongly for psychosis and UHR whereas values of LR- that are less than 0.2 argue strongly against psychosis and UHR.

RESULTS

Sociodemographics

Independent-samples t tests showed gender (p = .734) did not have an effect on the (total) ESI score (summed score of all 34 items from the original clinical subscales). Likewise, no correlation was found between age and ESI score (r = -.007). One-way ANOVAs showed education did have a significant effect on the total ESI score (p = .001). Scheffe's post hoc comparison tests indicated that individuals who completed lower to intermediate vocational training or lower general secondary education rated themselves significantly higher on the ESI compared with individuals who completed higher vocational training or had a (pre) university education. Therefore, education level was entered as a covariate in the logistic model of ESI items. The sociodemographics for all diagnostics groups are depicted in Table1.

Table 1 | Demographic Characteristics of the Diagnostic Groups

				Education level (%)		
Diagnostic Group	**Mean Age**	**Median**	**Male (%)**	**1**	**2**	**3**
Referrals to the UHR Unit						
No diagnosis / No UHR state	19	19	71	22	35	43
UHR for Psychosis	20	19	64	20	20	60
Remitted Psychosis	23	22	73	36	14	50
Acute Psychosis	21	20	88	25	19	56
Inpatients/highly symptomatic outpatients						
Anxiety /mood disorder	33	29	55	22	19	58
Psychosis (in treatment)	25	22	68	26	39	35
Substance dependence/abuse	29	28	83	56	44	0
Mildly symptomatic outpatients						
Anxiety/mood disorder	22	22	50	30	70	0

Note. UHR= UltraHigh Risk. For educational level, 1 = primary education or lower vocational training; 2 = lower general secondary education or intermediate vocational training; and 3 = higher general secondary education, higher vocational training, preuniversity education, or university education.

Table 2 | Spearman's rho correlation coefficients for ESI scales with SIPS/SOPS and BSABS

Scale	SIPS positive symptoms	SIPS negative symptoms	SIPS disorganisation symptoms	SIPS general symptoms	BSABS-P thought disturbances	BSABS-P perceptual disturbances	BSABS-P motoric disturbances	GAF current
AS	.268**	.278*	.199	.293**	.382**	.192	.155	-.326**
AU	.482**	.199	.214*	.300**	.343**	.219**	.112	-.330**
IR	.551**	.237**	.300**	.228**	.279**	.194	.041	-.263*
DP	.389**	.231**	.245**	.325**	.294**	.182	.079	-.298**
ESI	.469**	.275**	.270**	.332**	.380**	.226**	.118	-.352**

Note. SIPS/SOPS= Structured Interview for Prodromal Symptoms/Scale of Prodromal Symptoms; BSABS-P= Bonn Scale for the Assessment of Basic Symptoms Prediction list; GAF= General Assessment of Functioning; AS= Attention and Speech Impairment subscale of the ESI; AU= Auditory Uncertainty subscale of the ESI; IR= Ideas of Reference subscale of the ESI; DP= Deviant Perception subscale of the ESI. * p = .01, two-tailed. ** p = .001, two-tailed.

Correlations

Pearson product–moment correlations between ESI, SIP/SOPS, and BSABS-P scales were calculated for the first study sample. For this UHR referral group, Time 0 measurements of the SIPS/SOPS, BSABS-P, and GAF were correlated with scores on the ESI scales.

As can be seen in Table 2, the highest correlations were found between the ESI scales and the Positive Symptoms Scale of the SIPS/SOPS and the Thought Disturbances scale of the BSABS-P. Also, a strong negative correlation between ESI scales and GAF score was found.

Mean Scores

One-way ANOVAs indicated significant differences in mean ESI scale scores between the diagnostic groups ($p < .0001$). As can be seen in Table 3, acutely psychotic individuals show the highest overall ESI score and the mildly symptomatic outpatients from the third sample show the lowest. Individuals considered at UHR for developing psychosis showed an overall ESI score similar to the ESI scores of individuals with remitted psychosis from the same sample and psychotic inpatients from the second sample.

Table 3 | Mean Eppendorf Schizophrenia Inventory (ESI) Subscale Scores for all Diagnostic Groups

	ESI subscale					
Sample and Diagnostic Group	**AS**	**IR**	**AU**	**DP**	**Total**	**SE total**
Referrals to the UHR Unit						
No diagnosis / No UHR state	5.8	2.0	2.9	3.4	14.1	2.4
UHR for Psychosis	6.7	4.0	3.9	5.2	19.8	1.7
Remitted Psychosis	8.1	3.6	3.1	4.2	19.1	4.1
Acute Psychosis	11.1	8.2	8.4	8.3	36.0	3.1
Inpatients/highly symptomatic outpatients						
Anxiety /mood disorder	7.3	1.9	3.0	3.8	15.7	1.4
Psychosis (in treatment)	7.7	3.4	4.5	4.1	19.7	1.9
Substance dependence/abuse	10.2	5.3	5.7	5.6	26.7	4.8
Mildly symptomatic outpatients						
Anxiety/mood disorder	1.2	0.8	0.5	0.5	3.0	2.1

Note. AS= Attention and Speech Impairment subscale; IR= Ideas of Reference subscale; AU= Auditory Uncertainty subscale; DP= Deviant Perception subscale; UHR= ultrahigh risk.

Scheffe's post hoc test indicated the total ESI score was significantly elevated for the acute psychosis group compared with all groups except the remitted psychosis and drug abusing groups ($p < .0001$). Compared with the remitted psychosis group, the elevated score of the acutely psychosis group only approached significance ($p = .047$). Roughly the same scoring pattern was seen on the AU, IR, and DP subscales. On the AS subscale, the mean score of the acute psychosis group was only significantly elevated against the UHR group and the outpatient group from the third sample. Overall, Scheffe's tests indicated the AS scale was

the least able to distinguish between diagnostic groups. Although the mean scores of the substance abuse group were roughly equal to those of the acute psychosis group, because of the high standard error of measurement, elevated scores only reached significance compared with the mildly symptomatic outpatients from the third sample.

Individuals from the UHR group scored themselves significantly lower than did individuals from the acute psychosis group and significantly higher than did the outpatients from the third sample on the total ESI scale ($p < .0001$). Posttest comparisons on the other ESI (subscale) scores showed similar results.

ESI scores of psychotic inpatients from the second sample were found at levels comparable to those of the UHR group and much lower than those of the acutely psychotic group of the first sample. Differences in the timing of the diagnostic procedure and ESI completion are presumably responsible for this finding. Acutely psychotic individuals from the first sample completed the ESI before diagnostic evaluation at the VORS Unit. In contrast, individuals in the psychosis group from the second sample were referred for psychodiagnostic evaluation (including the ESI) 6–8 weeks after intake and prescription of antipsychotic medication, a period generally considered to be needed for clinical stabilization. Because subjects are asked to consider the last 4 weeks as the reference period when completing the ESI, acute psychotic symptoms would have remitted to a considerable extent at the moment of psychological evaluation and completion of the ESI questionnaire.

Accuracy Measures

Our focus in the current study is to evaluate the ESI's ability to accurately distinguish between help-seeking individuals who are acutely psychotic or at UHR for developing psychosis from individuals with other psychological or psychiatric complaints. For this reason, remitted psychotic subjects from the first sample and psychotic inpatients from the second sample are omitted from further analysis. Also, the drug abuse group was omitted from further analysis as hard drug/psychotropic abuse is a known confounder for accurate psychiatric diagnosis.

Two conditions are being evaluated. First is Condition A, ESI's ability to distinguish between individuals with no psychotic symptoms and those at UHR for psychosis or acute psychosis. For this purpose, data of referrals who did not attain UHR status at intake and did not receive a diagnosis of any disorder from the first sample, mood/anxiety patients from the second sample, and all outpatients of the third sample are analysed as one group against the data of the UHR subjects and acutely psychotic patients from the first sample. Second, for Condition B, to distinguish between persons with and without acute psychosis, we analysed the data of the no psychotic symptoms group and the UHR group as one group against the data of the acute psychosis group.

As can be seen in Table 4, for Condition A, the ESI scales produced AUCs between 0.63 and 0.76, with the IR scale producing the largest AUC (for IR, AUC = 0.76, SE = 0.03, 95% CI [.70, .82]).

Table 4 | Area Under the Curve Characteristics: Classification of UHR/Psychotic Versus Neither and Psychotic **versus** UHR/Neither.

			95% confidence interval	
ESI subscales	**Area under curve**	**SE**	**Lower bound**	**Upper bound**
UHR/Psychotic vs nonpsychotic (Condition A)				
AS	0.63	0.04	0.57	0.70
AU	0.69	0.03	0.62	0.75
IR	0.76	0.03	0.70	0.82
DP	0.72	0.03	0.66	0.79
Total	0.74	0.03	0.68	0.80
Psychotic vs UHR/nonpsychotic (Condition B)				
AS	0.72	0.04	0.65	0.80
AU	0.80	0.04	0.72	0.87
IR	0.82	0.04	0.74	0.90
DP	0.76	0.04	0.67	0.84
Total	0.81	0.03	0.75	0.88

Note. ESI = Eppendorf Schizophrenia Inventory; UHR = UltraHigh Risk; AS = Attention and Speech Impairment subscale; AU = Auditory Uncertainty subscale; IR = Ideas of Reference subscale; DP = Deviant Perception subscale.

ROC curves plotted for Condition B produced even better AUCs for all ESI scales (range = 0.72–0.82). Again, the IR scale produced the largest AUC (for IR, AUC = 0.82, SE = 0.04, 95% CI [.74, .90]).

To assess the possibility of selecting a subset of ESI items that would surpass the screening accuracy of the IR scale, we entered all clinical items in a stepwise logistic model. This resulted in the selection of three items for Condition A. Repeating this routine for Condition B resulted in the selection of two additional items above those selected in Condition A (one item was selected for Condition A but not for Condition B).

For Condition A, the summed, weighted items produced an AUC of 0.79 (SE = 0.03, 95% CI [0.73, 0.85]). For Condition B, the AUC was 0.87 (SE = 0.03, 95% CI [0.80, 0.93]).

The new scale was named the UHR–Psychosis scale and the selected ESI items are shown in the Appendix. Figures 1 and 2 depict the ROC curves for the UHR–Psychosis scale under Conditions A and B.

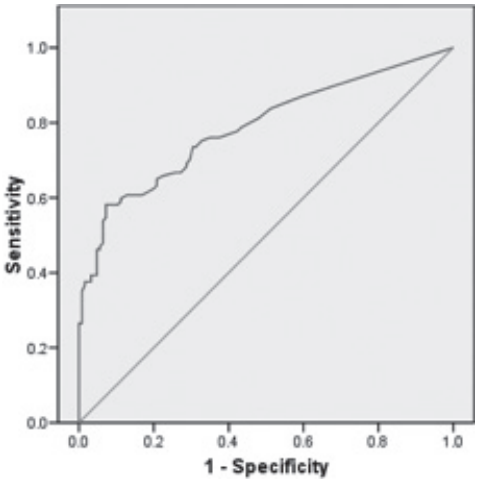

Figure 1 | Receiver operating characteristic curve: Eppedorf Schizophrenia Inventory UHR-Psychosis Scale predicting no psychotic symptoms versus ultrahigh risk/acute psychosis classification (condition A).

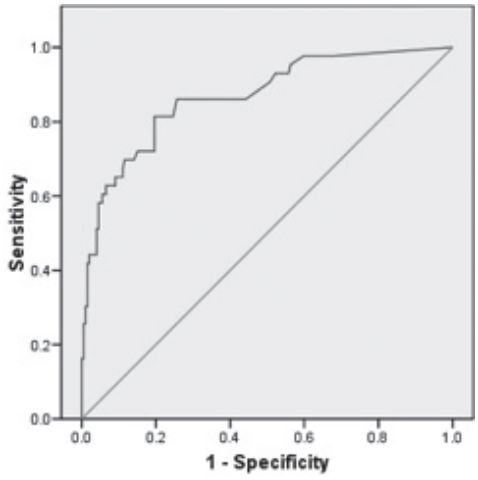

Figure 2 | Receiver operating characteristic curve: Eppedorf Schizophrenia Inventory UHR-Psychosis Scale predicting no psychotic symptoms/ ultrahigh risk versus acute psychosis classification (condition B).

We then proceeded with calculating accuracy measures at various cutoff points for the UHR–Psychosis scale (see Table 5): For example, at a cutoff score of >=0.30 in Condition A, the sensitivity is 0.81 and the specificity is 0.52, resulting in approximately half of the screened individuals correctly being classified as not having an acute psychosis or being at UHR (the other half incorrectly being labeled as at UHR or acutely psychotic) at the cost of excluding approximately two out of every 10 individuals at UHR or with acute psychosis.

Table 5 | Diagnostic classification accuracy by Eppendorf Schizophrenia Inventory Scores

UHR-scale cut-off	Sensitivity	Specificity	Positive LR	Negative LR
UHR/Psychotic vs nonpsychotic (Condition A)				
≥ 0.30	0.81	0.52	1.69	0.36
≥ 1.02	0.66	0.78	2.94	0.44
≥ 1.83	0.50	0.94	7.75	0.54
Psychotic vs UHR/nonpsychotic (Condition B)				
≥ 0.61	0.91	0.49	1.79	0.19
≥ 1.64	0.81	0.80	4.15	0.23
≥ 2.55	0.67	0.89	6.10	0.37

Note. LR = likelihood ratio; UHR = ultrahigh risk

For the second threshold between nonpsychotic individuals or individuals at UHR and individuals with acute psychosis (Condition B), a cutoff score of >=1.64 can be chosen. At this cutoff point, sensitivity is 0.81 and specificity is 0.80, meaning eight out of every 10 screened individuals would correctly be classified as not having an acute psychosis at the expense of two persons with acute psychosis being excluded.

Transition to Psychosis

From the UHR group, 19 individuals did not complete the 24-month follow-up measurements, although 11 persons could be reached for the 36-month standardized telephone interview (11% were lost to follow-up). A total of 15 individuals labeled as UHR during initial assessment made the transition to psychosis during the 36-month follow-up period (a transition rate of 20%). Of these 15 individuals, 73% rated themselves >=0.30 on the UHR–Psychosis scale (first threshold). Individuals who made the transition to psychosis did score themselves higher compared with the remainder of the UHR group on the UHR–Psychosis scale; however, this difference failed to reach significance.

Twenty-four individuals (4%) were screened at the VORS Unit for UHR and were considered not to have an increased risk for developing psychosis. One of this group (4%) did develop a psychosis within the 36-month time frame. Unfortunately, so far only 46% of this group could be reached for the follow-up telephone interview.

DISCUSSION

In this study, we evaluated the usefulness of the ESI as a screening tool in a clinical setting for detecting individuals with an increased risk for developing psychosis, the so-called UHR state. The results indicate the ESI is sensitive enough to differentiate between a nonpsychotic symptoms state and a UHR state. In addition, the ESI also differentiates adequately between a UHR state and frank psychosis, a finding not found in validation studies for other psychosis screening measures.[10]

Analysis of the mean ESI scores of the combined research groups indicated individuals from the UHR group rate themselves in between the mildly symptomatic outpatient group and the acute psychosis group of the first sample. The mean ESI scores of the UHR group actually resembled those of the remitted psychosis group and the psychosis group of the second sample, suggesting similarities between postpsychotic (or interepisodic) individuals and persons at UHR for psychosis. This makes sense on a conceptual level, as one would expect some patients with remitted psychosis to have residual psychotic(like) experiences and not fully return to premorbid levels of functioning. These residual symptoms could very well be similar to the subjective experiences encountered during a UHR state. However, the scoring range or variance of the remitted psychosis group turned out to be more than twice as large compared with the variance of the UHR group. This suggests that the remitted group tends to be more heterogenic than the UHR group.

Analysis of the AUCs showed that the seven-item IR subscale produced the largest AUC curves in both Condition A and Condition B. A new scale was created from a selection of the five strongest performing ESI items. The new UHR–Psychosis scale produced marginally larger AUCs in both test conditions.

An important finding of this study was that the self-rated ESI and its subscales are moderately to strongly correlated with established interview-based UHR instruments (i.e., SIPS/SOPS, BSABS-P). This makes it possible to use the ESI as a first step or a screener in the broader screening process for UHR for psychosis in mental health facilities. But in what way could the screener be best used in clinical practice? What would be its added value in detecting individuals at UHR for psychosis?

Boonstra, Wunderink, Sytema, and Wiersma[32] reported recently on their inquiry into the medical records of all patients between 18 and 45 years of age who had a first contact with mental health care services in the Dutch regions of Friesland and Twente during the year 2002. Medical records were screened for reported psychotic symptoms, initial DSM–IV diagnosis, and received treatment. In the 242 cases out of 5,585 in which one or more psychotic symptoms were reported, 73 persons (30%) were not treated for these symptoms. The Boonstra et al. study relied on reported psychotic symptoms as written in the medical files, so it is reasonable to assume that because of underdetection of psychotic symptoms, the actual percentage of patients with untreated psychotic symptoms may very well be at least 10% higher. These findings clearly underline the necessity of applying a two-step UHR assessment for psychosis: broad screening with measures such as the ESI and follow up with more elaborate clinical interviewing when positive screening occurs.

Set at a sensitivity of .81, the shortened ESI will detect 81% of the cases that would be given UHR status after clinical interviewing with the SIPS/SOPS and BSABS-P. Cases in which the ESI score exceeds the second threshold (indicative of acute psychosis) can be assessed with priority for psychosis spectrum disorders. If these criteria are not met, clinical interviewing to assess UHR status is the final step in the assessment of psychotic symptoms.

The accuracy for detecting acute psychosis (.81 sensitivity, .80 specificity) is substantially higher compared with screening for UHR. As a consequence, 48% of the screened individuals without relevant psychosis symptoms would also be referred for clinical interviewing (.81 sensitivity, .52 specificity). Because the transition rate of UHR to frank psychoses in recent studies, as in ours, fluctuates around 20% in a 3-year period, one could argue that the cost of screening outweighs the benefits. In this equation, one has to take into account that labeling an individual with UHR status reduces the time it takes to receive adequate help, and this could lead to a subsequent avoidance of progression to psychosis.

Screening for UHR and acute psychosis has its costs, both in training mental health workers to use the UHR clinical interview tools and in extra time allocated in the diagnostic process to assess ESI-positive individuals. However, in our experience, the time needed for structured clinical interviewing with the SIPS/SOPS and BSABS-P is directly related to symptom severity.

Of course, one could imagine circumstances in which an ESI cutoff would be chosen that would maximize specificity at the expense of sensitivity and vice versa. The purpose of this study was to validate the ESI test scores in a clinical setting; in our opinion, maximizing sensitivity to decrease the number of undetected UHR and acute psychosis cases gives the ESI its edge in the diagnostic process.

A shortcoming of the current study is that ESI test scores are validated in quite a mixed bag of study samples. This means the extent to which, for instance, cutoff scores can be generalized into other settings remains at least in part unknown. A study that describes actual implementation of the ESI in a stepped diagnostic process at the front door of a mental health facility is required to add to the robustness of the current findings.

Appendix

Paraphrased Item Content of the UHR–Psychosis Scale

Now and then events, broadcasts etc. seem to be related to me although it is actually impossible (IR)
I simply forgot many of my habits (AS)
Sometimes I hear my 'inner voice' as distinctly as if someone actually is talking to me (AU)
Often I have a feeling that something strange and unusual is happening around me (IR)
I have already felt being at the threshold of a significant revelation (IR)

Note. The Eppendorf Schizophrenia Inventory subscale each item was originally assigned to appears in parentheses. IR = Ideas of Reference subscale; AS = Attention and Speech Impairment subscale; AU = Auditory Uncertainty subscale.

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CHAPTER 5

Determinants of participation in a web-based health risk assessment and consequences for health promotion programs

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ABSTRACT

Background: The health risk assessment (HRA) is a type of health promotion program frequently offered at the workplace. Insight into the underlying determinants of participation is needed to evaluate and implement these interventions.

Objective: To analyse whether individual characteristics including demographics, health behavior, self-rated health, and work-related factors are associated with participation and nonparticipation in a Web-based HRA.

Methods: Determinants of participation and nonparticipation were investigated in a cross-sectional study among individuals employed at five Dutch organizations. Multivariate logistic regression was performed to identify determinants of participation and nonparticipation in the HRA after controlling for organization and all other variables.

Results: Of the 8431 employees who were invited, 31.9% (2686/8431) enrolled in the HRA. The online questionnaire was completed by 27.2% (1564/5745) of the nonparticipants. Determinants of participation were some periods of stress at home or work in the preceding year (OR=1.62, 95% CI=1.08-2.42), a decreasing number of weekdays on which at least 30 minutes were spent on moderate to vigorous physical activity ($OR_{dayPA=}$0.84, 95% CI=0.79-0.90), and increasing alcohol consumption. Determinants of nonparticipation were less-than-positive self-rated health (poor/very poor vs very good, OR= 0.25, 95% CI=0.08-0.81) and tobacco use (at least weekly vs none, OR=0.65, 95% CI=0.46-0.90).

Conclusions: This study showed that with regard to isolated health behaviors (insufficient physical activity, excess alcohol consumption, and stress), those who could benefit most from the HRA were more likely to participate. However, tobacco users and those who rated their overall health as less than positive were less likely to participate. A strong communication strategy, with recruitment messages that take reasons for nonparticipation into account, could prove to be an essential tool for organizations trying to reach employees who are less likely to participate.

INTRODUCTION

Seven modifiable risk factors account for more than half of the chronic disease burden: high blood pressure, tobacco use, excess alcohol consumption, high serum cholesterol, overweight, low fruit/vegetable intake, and physical inactivity.[1] The workplace is considered to be an excellent setting for health promotion programs that target these risk factors, not only because a large proportion of the population can be reached, but also because it makes use of a natural social network and can facilitate the creation of a health-conscious environment.[2-4] Web-based interventions serve as a feasible and acceptable delivery method for these programs, because they can provide scale at a relatively low cost per employee.[5;6] In addition, Internet access is available 24 hours a day, 7 days a week, which may serve both the employer and the employee, as program access is available across work shifts and into vacation and leisure time.[6]

Recent reviews of effectiveness studies concluded there is sufficient evidence that worksite health promotion programs (WHPPs) have meaningful effects on a number of risk factors.[7;8] The latter is directly beneficial for the employer: implementing a WHPP can lead to reductions in both absenteeism and productivity loss at work.[9;10] However, a lack of employee participation presents an important barrier to the impact of WHPPs.[7-11] Since most intervention studies on WHPPs randomize workers who have agreed to participate in the studies, it is largely unknown whether those who could benefit most from the intervention are as likely to participate as those who may have already been making more healthful choices.[12;13] The importance of studying determinants of participation in WHPPs was already emphasized 25 years ago, and has been underscored ever since.[14-16] Still, in 2009, the authors of a review concluded that few studies have evaluated the influence of health, lifestyle, and work-related factors on participation, which hampers insight into the underlying determinants of participation in WHPPs, and, ultimately, the influence of selective participation on the effectiveness of these WHPPs.[3] Except for the finding that women enroll more often than men, no consistent determinants of participation in WHPPs aimed at physical activity and nutrition were found.[3]

With regard to Web-based delivery of WHPPs, it has been reported that women and older people are more likely to enroll in these programs, as they more often use the Internet for searching for health-related information. It has also been postulated that individuals with a low educational level are less likely to use Web-based WHPPs, as those with less formal education are less likely to continue the adoption of innovations.[17]

One type of WHPP that is frequently offered is the health risk assessment (HRA), which screens for risk factors for chronic diseases[7;10] and delivers verbal or written feedback on one's personal risk profile along with subsequent recommendations for lifestyle improvements. While an HRA is often used as a gateway intervention to broader WHPPs, it can also be utilized as a tool for stimulating the initiation of health behavior change.[4;7]

In the current study, our aim was to analyse whether individual characteristics (including demographics, health behavior, self-rated health, and work-related factors) are associated with participation and nonparticipation in a Web-based HRA[9] implemented among employees in the Netherlands.

METHODS

Participating Organizations and Study Design

In this cross-sectional study, the HRA was implemented in five Dutch organizations, which included a university medical center, a large state-owned bank, a small bank, a financial institution, and the Dutch branch of an American multinational technology and consulting corporation. The HRA was applied in a pilot study among selected departments of the university medical center, which employed over 10,000 employees in 2009. The large state-owned bank was nationalized as a result of the global financial crises, and employed more than 27,000 employees in 2009. Starting in 2006, its employees were gradually invited to enroll in the HRA. Renewed enrollment in the HRA was offered to employees 3 years after the first HRA was completed. In the current study, we included all invitees from 2009 who had not previously participated in the HRA. All workers from the small bank (<1,000 employees) were invited, and from the financial institution (>3000 employees), all invitees from 2009 who had not previously participated in the HRA (renewed participation offered after 3 years) were included in this study. The Dutch branch of the American multinational technology and consulting corporation employed over 4500 employees in 2010. The HRA has been implemented in the organization since 2006. Two years after initial participation, renewed enrollment in the HRA is offered. In this study we included all employees who were invited during the first and second quarters of 2010 and had not previously participated in the HRA.

Procedures

Employees were invited to participate in the HRA during the period from January 2009 to August 2010. The university medical center imposed an age criterion, inviting employees who were at least 45 years old. Upper management encouraged managers of selected departments to stimulate enrollment in the HRA among their workers. The HRA was also highlighted in the in-house employee magazine.

During the study period, invitations to participate in the HRA were sent by the human resources department, management, or the safety, health, and welfare services of the organizations involved. The invitation email included a description of the HRA and informed employees that participation was voluntary and free of charge, that all personal data would be treated confidentially, and that no individual results would be shared with their employer or any other party. No incentives were offered.

The HRA is called "The Prevention Compass".[4;9] In the assessment phase, a Web-based health questionnaire is completed (in 30-45 minutes), biometric measurements (height, weight, waist circumference, blood pressure) are taken, and blood, urine, and feces samples are analysed. A personalised Web-based health report and health plan is automatically generated only after all health data are collected. At this point, the HRA is completed.

Employees were defined as enrollees when they enrolled in the program by activating their online account during the inclusion period. This period varied (3-12 months), as larger organizations chose to invite their employees gradually. Enrollees who completed all HRA measurements within 1 year after the inclusion period had ended were classified as participants. Those who enrolled but did not complete all measurements were labeled dropouts. Employees who had not enrolled in the program after the inclusion period had ended were labeled nonparticipants. The provider of the HRA sent nonparticipants an email inviting them to complete an online questionnaire. Those who responded to the online questionnaire were classified as responders, and those who did not respond were labeled nonresponders. Informed consent was obtained from all study participants prior to the study in accordance with the requirements for identifiable data collection in the Dutch Code of Conduct for Observational Research.

Measurements

For all study participants, gender and date of birth were available from the HRA invitation lists used by the organizations involved. Other individual characteristics (which included educational level, self-rated health, physical activity, body mass index (BMI), alcohol consumption, stress, work ability, and absenteeism during the previous year) were collected from the Web-based health questionnaire component of the HRA as part of a larger set of health data collected to generate a personal health report. As nonparticipants did not participate in the HRA and its Web-based health questionnaire, an online questionnaire was created that was made up almost entirely of the questions related to the above-mentioned individual characteristics of this study. Our goal was to lower the threshold and make it easier for nonparticipants to complete the questionnaire. Therefore, it was anonymous, no account had to be activated, and it took 10 minutes to complete. The questions relating to the individual characteristics were identical for participants and nonparticipants.

To determine educational level, respondents were asked to check 1 of 9 categories (ranging from no education to doctorate level) that indicated the highest level of education ever completed. Self-rated health[18;19] was measured by one question: "How do you rate your health in general?" The response options were "very good", "good", "moderate", "bad", or "very bad". Because of a lack of observations for the option "very bad," this category was merged with "bad" prior to the regression analysis.

One item derived from the Dutch version of the International Physical Activity Questionnaire[20] was used to assess the number of weekdays on which at least 30 minutes were spent on

moderate to vigorous physical activity. BMI was based on height and weight as reported by respondents on the online questionnaire (nonparticipants) or measured by trained personnel (participants), and categorized into normal weight (BMI<25 kg/m^2), overweight (25≤BMI<30 kg/m^2), or obese (BMI≥30 kg/m^2).

Alcohol consumption was measured in units of alcohol per week based on a standard alcohol questionnaire of the Dutch Municipal Health Service ("GGD Monitor"). Because few participants reported high levels of alcohol consumption, answer categories "29–35 units", "36–42 units", "43–50 units", and "> 50 units" were merged with "22–28 units" into "≥22 units." One item measured the frequency of tobacco use (none, occasionally, weekly, or daily). Answer categories "daily" and "weekly" were merged into "daily/weekly" as a measure of frequent tobacco use.

Items from the INTERHEART study were used to measure general and financial stress.[21] In accordance with the methods used in that study, 2 items relating to stress at home and stress at work were combined into a general stress scale and graded as follows: (1) never experienced stress, (2) experienced some periods at home or at work, (3) experienced several periods at home or at work, or (4) experienced permanent stress at home or at work. Level of financial stress was defined as (1) little or none, (2) moderate, or (3) high or severe.

Work ability was measured with the single-item question on work ability from the Work Ability Index (WAI).[22] Both the WAI and the single-item question show similar patterns of associations with absenteeism, health, and symptoms.[23] On the single-item question, respondents were asked to assess their current work ability compared with their lifetime best, with a possible score of 0 ("completely unable to work") to 10 ("work ability at its best").

Absenteeism during the previous 12-month period was determined by a question that classified the number of absenteeism (calendar) days related to health problems into 1 of 5 categories (0, 1–9, 10–24, 25–99, 100–365).[24]

Statistical Analysis

Means and standard deviations were presented for the continuous variables of age, physical activity, and work ability. Percentages were presented for the dichotomous variable gender and the categorical variables of education, BMI, alcohol consumption, tobacco use, stress at home or work, financial stress, self-rated health, and absenteeism. Enrollees, participants, nonparticipants, questionnaire responders, and nonresponders were compared using the unpaired *t*-test for continuous variables and the chi-square test for dichotomous and categorical variables.

Spearman's rho correlation coefficients were computed to investigate interrelationships among individual characteristics. Using the Bonferroni approach to control for Type 1 errors across the 132 correlations of the 12 variables, a *P* value of less than .0004 (.05/132=.0004) was required for significance.[25] Correlations had to be at least 0.20 to be considered practically relevant.

Multivariate logistic regression analysis was performed to identify individual characteristics that contributed to participation in the HRA, after controlling for company and all other variables. This method presumes that all individual characteristics are measured for all cases and incomplete cases are discarded, which may result in biased estimates.[26] Therefore, multiple imputation of missing values of independent variables was employed. In multiple imputation, missing data are imputed based on variables correlated with the missing data and causes of missingness. In this study, ordinary least-squares regression models were applied to predict the missing values of continuous and ordinal variables, and discriminant prediction models were applied to the missing values of nominal variables. All individual characteristics as well as participant status (participant vs nonparticipant) were used as covariates in the predictive models. Uncertainty was accounted for by creating 10 imputed datasets.[27] Multivariate logistic regression analysis was carried out on each imputed dataset, producing multiple analysis results. These analysis results were combined using rules established by Rubin [27] to produce one overall analysis, which is reported and compared with the results of complete case analysis.

The SOLAS 4 statistical package was used for the multiple imputation of the missing values. All other analyses were performed using SPSS for Windows, version 19.

RESULTS

The study flow chart is presented in Figure 1. During the study period, 8431 employees were invited to participate in the HRA. Average participation was 31.9% (2686/8431) and ranged from 14.9% to 51.7% (university medical center: 51.7% (206/503), state-owned bank: 29.9% (1282/4284), small bank: 41.0% (213/520), financial institution: 34.3% (824/2404), Dutch branch of American multinational technology and consulting corporation: 14.9% (107/720)). The online questionnaire was completed by 27.2% (1564/5745) of the nonparticipants. Data on gender and age were available for 99.5% (8390/8431) of all HRA invitees from the invitation lists. Both enrollees ($P<.001$) and questionnaire responders ($P=.02$) were slightly older compared with nonparticipants and nonresponders. Also, enrollees were less often male ($P=.046$). Of those who enrolled in the HRA, 7.9% (213/2686) did not complete participation (dropouts). Compared with participants who completed the HRA, dropouts were younger ($P=.002$) and less often male ($P<.001$). Dropouts were excluded from further analysis, as no additional data beyond age and gender were available for this group. An example of a personal health risk profile page that was presented to those who completed the HRA is shown in Figure 2.

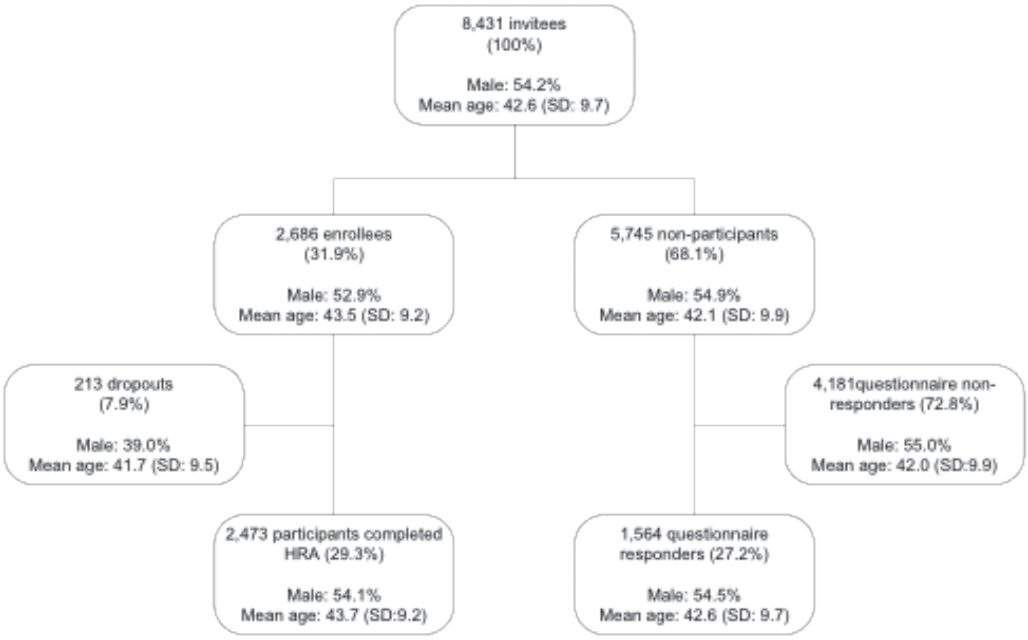

Figure 1 | Study flow chart

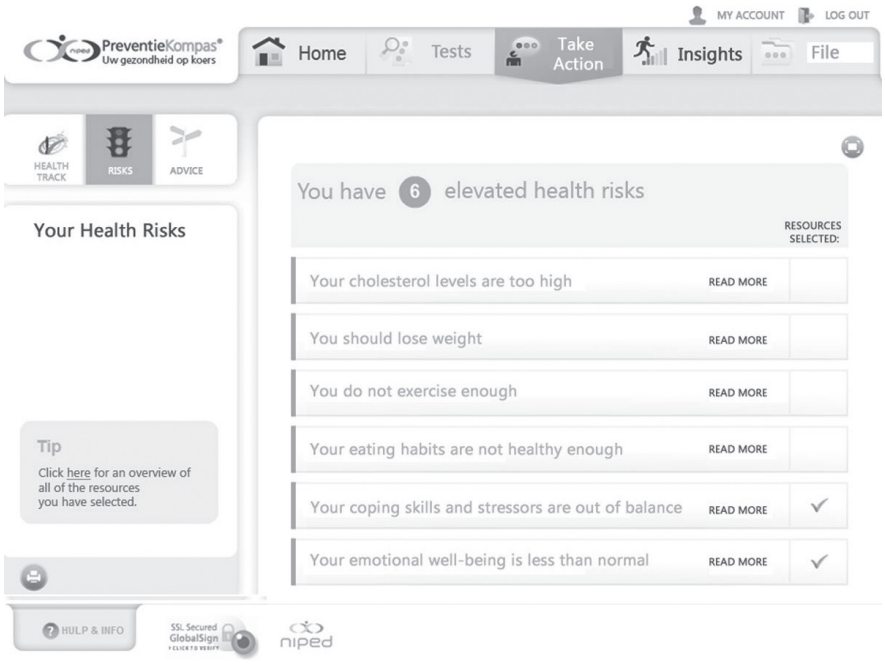

Figure 2 | Screenshot of the personal health risk profile page

Table 1 depicts the baseline characteristics of participants (those who completed the HRA) and nonparticipants who filled in the online questionnaire (hereafter described as nonparticipants). Participants were slightly older than nonparticipants. No differences in gender or education were found. Participants engaged in physical activity less frequently, had higher weekly alcohol consumption, and reported having had periods of stress at home or work during the previous year more often. Nonparticipants had lower self-rated health, used more tobacco, and reported slightly lower work ability, a higher level of financial stress, and more absenteeism in the preceding year.

A correlation matrix was computed to ascertain associations between the individual characteristics. Male gender was positively related with alcohol consumption (r=.33) and age was positively related with BMI (r=.21). A negative correlation (r=-.28) was found between the amount of stress at home or work and self-estimated work ability. Stress at home or work was positively correlated (r= .21) with financial stress. More positive self-rated health was correlated with higher work ability (r =.29) and negatively correlated with the amount of absenteeism during the previous 12-month period (r=-.22).

In table 2, the independent influence of demographics, health behavior, self-rated health, and work-related factors on HRA participation is shown for the imputed datasets (combined results), after controlling for organization (not shown) and all other independent variables. In the multivariate logistic regression analysis model, no effects were found for demographics. Less frequent physical activity, higher weekly alcohol consumption, and some periods of stress at home or work during the previous year remained statistically significantly associated with higher participation. It was also confirmed that less-than-positive self-rated health and tobacco use are significantly associated with lower participation. Higher levels of financial stress, more absenteeism, and lower work ability were no longer significantly related to lower participation.

Complete case analysis confirmed the direction of the reported results based on the imputed datasets. In addition, the following associations attained significance in the complete case analysis. Severe levels of financial stress, good self-rated health, and absenteeism (1-9 days and 100-365 days) were associated with lower participation. Having had several periods of stress at home or work and female gender were associated with higher participation. Also, in the complete case analysis, the association between occasional tobacco use and lower participation was marginally significant (P=.06).

Table 1 | Baseline characteristics of HRA participants, and nonparticipants who completed the online questionnaire.

		HRA participants *N*=2473	**HRA nonparticipants who completed questionnaire *N*=1564**	**P value**
Age		*n*=2473	*n*=1564	.001
	Mean (SD)	43.7 (9.2)	42.6 (9.7)	
Gender, n(%)		*n*=2472	*n*=1564	.81
	Male	1337 (54.1)	852 (54.5)	
	Female	1135 (45.9)	712 (45.5)	
Education[a], n(%)		*n*=2451	*n*=1549	.41
	Low	400 (16.3)	266 (17.2)	
	Intermediate	782 (31.9)	464 (30.0)	
	High	1269 (51.8)	819 (52.9)	
Physical activity		*n*=2473	*n*=1403	<.001
	Weekdays (0-7) ≥30 min. Mean (SD)	3.2 (2.1)	3.8 (2.2)	
Body mass index (BMI), n(%)		*n*=2473	*n*=1404	.42
	Normal weight: BMI <25kg/m²	1078 (43.6)	586 (41.6)	
	Overweight: BMI ≥25 - <30 kg/m²	1097 (44.4)	637 (45.3)	
	Obese: BMI ≥ 30 kg/m²	298 (12.1)	184 (13.1)	
Alcohol consumption, n(%)		*n*=2473	*n*=1403	<.001
	<1 units per week	702 (28.4)	552 (39.3)	
	1-7 units per week	1037 (41.9)	569 (40.6)	
	8-14 units per week	479 (19.4)	195 (13.9)	
	15-21 units per week	173 (7.0)	64 (4.6)	
	≥ 22 units per week	82 (3.3)	23 (1.6)	

Table 1 | Continued

Tobacco use, n(%)		*n*=2471	*n*=1251	<.001
	None	1961 (79.4)	889 (71.1)	
	Occasional	115 (4.7)	79 (6.3)	
	At least once a week	395 (16.0)	283 (22.6)	
Stress at home or work, n(%)		*n*=2436	*n*=1374	<.001
	Never	278 (11.4)	194 (14.1)	
	Some periods	1298 (53.3)	628 (45.7)	
	Several periods	822 (33.7)	522 (38.0)	
	Permanent	38 (1.6)	30 (2.2)	
Stress - financial, n(%)		*n*=2432	*n*=1374	<.001
	Little or none	1872 (77.0)	947 (68.9)	
	Moderate	490 (20.1)	352 (25.6)	
	High or severe	70 (2.9)	75 (5.5)	
Self-rated health, n(%)		*n*=2468)	(*n*=1564	<.001
	Very good	438 (17.7)	194 (12.4)	
	Good	1684 (68.2)	1055 (67.5)	
	Moderate	328 (13.3)	272 (17.4)	
	Bad or very bad	18 (0.7)	43 (2.7)	
Absenteeism, n(%)		*n*=2469	(*n*=1374	<.001
	0 days	975 (39.5)	462 (33.6)	
	1-9 days	1194 (48.4)	683 (49.7)	
	10-24 days	183 (7.4)	117 (8.5)	
	25-99 days	86 (3.5)	73 (5.3)	
	100-365 days	31 (1.3)	39 (2.8)	
Work ability		*n*=2466	*n*=1374	
	Mean (SD)	8.1 (1.4)	8.0 (1.5)	.007

[a] Education:
Low: lower general secondary/lower vocational
Intermediate: higher general secondary/pre-university/intermediate vocational
High: higher vocational/university

Table 2 | Influence of demographics, health and work-related factors on HRA participation.

		OR[a]	95% CI[b]
Age		1.127	0.961 - 1.322
	10 yr intervals		
Male gender		0.884	0.661 - 1.181
Education[c]	Low[d]		
	Intermediate	1.203	0.813 - 1.780
	High	0.919	0.618 - 1.365
Physical activity	Days per week ≥ 30 min.(0-7)	0.843	0.793 - 0.895
Body mass index (BMI)	Normal weight:BMI < 25 kg/m² [d]		
	Overweight: BMI ≥ 25 - < 30 kg/m²	0.893	0.674 - 1.185
	Obese: BMI ≥ 30 kg/m²	0.938	0.610 - 1.441
Alcohol consumption	<1 units per week[d]		
	1-7 units per week	1.447	1.074 - 1.949
	8-14 units per week	1.971	1.318 - 2.947
	15-21 units per week	2.224	1.210 - 4.088
	≥ 22 units per week	3.372	1.317 - 8.632
Tobacco use	None[d]		
	Occasional	0.303	0.186 - 0.494
	At least once a week	0.645	0.461 - 0.903
Stress at home or work	Never[d]		
	Some periods	1.618	1.081 - 2.421
	Several periods	1.467	0.950 - 2.226
	Permanent	1.505	0.534 - 4.240
Stress -financial	Little or none[d]		
	Moderate	0.777	0.571 - 1.056
	High or severe	0.650	0.329 - 1.282
Self-rated Health	Very good[d]		
	Good	0.711	0.489 - 1.035
	Moderate	0.567	0.344 - 0.935
	Bad or very bad	0.251	0.077 - 0.812

Table 2 | Continued

Absenteeism	0 days[d]		
	1-9 days	0.851	0.642 - 1.128
	10-24 days	0.719	0.442 - 1.172
	25-99 days	0.751	0.390 - 1.446
	100- 65 days	0.480	0.177 - 1.302
Work ability	(0-10)	1.014	0.919 - 1.120

[a] OR: Odds Ratio

[b] CI: Confidence Interval

[c] Education:

Low: lower general secondary/lower vocational

Intermediate: higher general secondary/pre-university/intermediate vocational

High: higher vocational/university

[d] Reference category

DISCUSSION

Principal Results and Comparison With Prior Work

In this study we evaluated the determinants of participation in a Web-based HRA by comparing participants and nonparticipants with regard to demographics, health behavior, self-rated health, and work-related factors. We found evidence of health-related participation, as workers who were more willing to participate in the HRA engaged in physical activity less frequently, consumed more alcohol, and more frequently experienced some periods of stress at home or work. Nonparticipants rated their overall health less positively and used more tobacco.

Participation in the HRA (31.9%) was similar to the response to the nonparticipant questionnaire (27.2%). The crude analysis pointed towards higher participation among older employees and females. These demographic differences were no longer present in the multivariate analysis. Therefore, the Web-based delivery of the WHPP did not result in selective participation by more highly educated, female, or older employees, which could be explained by the high Internet penetration (94%) in the Netherlands.[28] Although other studies have shown no consistent effect of age on participation[3;15], a meta-analysis performed by Robroek and colleagues (2009) found that women are more likely to participate in WHPPs than men.[3] Also, thus far a number of studies have shown fairly consistently that there is lower participation among employees of lower socioeconomic status.[14;15;29-33]

The current study found a strong association between physical activity and HRA participation. The likelihood of participating in the HRA increased as the number of weekdays an employee engaged in physical activity decreased. This result seems to indicate that employees who engage less in physical activity want to know about their state of health, and that those

already engaged in frequent physical activity find it less important to participate. However, reports on the influence of physical activity on participation have not been consistent, with some studies pointing towards higher participation in WHPPs among the less physically active,[30;34] and other studies indicating higher participation among those with low fitness risk[34] or above-average levels of both habitual activity and physical fitness.[35]

Participation in the HRA in our study was also associated with alcohol consumption. Higher weekly alcohol consumption increased the likelihood of participating in the HRA. This finding might be explained by the nonstigmatizing way of addressing alcohol consumption through the Internet. No association between excess alcohol consumption and participation was found in a recent study of a Web-based WHPP,[36] or other studies of WHPPs.[37]

In the current study, employees who experienced stress at home or at work during the prior year were more likely to participate in the HRA. Two other studies evaluated this association and found similar results.[38;39] These findings suggest that the HRA reaches an important group of workers, as workers under psychological strain are especially vulnerable to absenteeism and disability.[40]

We showed that individuals who rated their health as "moderate" or "bad/very bad" were less likely to participate in the HRA. Self-rated health is associated with physical and mental functioning.[18] In the long run, it is a robust predictor of all-cause mortality and morbidity, and mortality in a range of conditions including cardiovascular disease and cancer.[18] A more immediate association between self-rated health and self-reported absenteeism in the preceding year was found in the current study. Because of these associations, the lack of participation among employees with less-than-positive self-rated health could be interpreted as a general indication that less healthy employees are less likely to participate. One possible reason for this could be that these individuals are currently under treatment for a physical or mental condition. Receiving current medical treatment is an important reason for nonparticipation in WHPPs [38], and was found to be related to nonparticipation in this particular HRA.[41] One could argue that participating in a WHPP is less relevant for those receiving treatment. However, WHPPs and especially broad-based HRAs are designed to screen for a range of chronic diseases and health behaviors, and these programs are likely to benefit individuals who are already receiving medical treatment in other, potentially isolated, areas of health care. Moreover, not everyone with negative self-rated health is receiving medical care. Another reason for lower participation among employees with lower self-rated health could be less healthy employees' desire to keep their private life and their work life separate. One study found indications that employees with unhealthy lifestyles or who are in poor health are more likely to resist employer interference with employee health.[42] Lower participation among employees with negative self-rated health has been reported in an earlier study on this HRA[41] and other WHPPs,[14] but these reports are not consistent.[43]

Our study adds to the fairly consistent reports that tobacco users are less likely to participate in WHPPs.[30;33;37;38;44] Most tobacco users are well aware of their habit's adverse effects, and may find they can foresee the outcome and recommendations if they participate in a WHPP. They may find the prospect of such recommendations patronizing, and are probably already being confronted with the negative reactions of others in the workplace or at home as a result of their habit. In the HRA under investigation, tobacco users are not encouraged to feel "guilty" or otherwise "pressured" to quit. Intrinsic motivation is recognized as a necessary ingredient for lasting behavior change. Their freedom of choice is affirmed: he or she is respectfully informed of the health benefits of smoking less or quitting, and offered resources for bolstering resolve and self-confidence to become smoke-free. However, it is unlikely that the nonjudgmental aspect of this program was communicated to employees prior to their decision whether or not to participate in the HRA.

This is the second study to evaluate participant characteristics of the HRA, The Prevention Compass. Our study, conducted with a new cohort, addressed two major limitations of the earlier study, which was reported on in 2011.[41] First, in the 2011 study, only 14% of the nonparticipants completed the online questionnaire, which formed the basis for the comparison between nonparticipants and participants. As a result, selection bias could have influenced the findings reported in that study. This is hinted at by the substantial difference in reported age between questionnaire responders and nonresponders. Second, we used multivariate analysis in our study. This has the obvious advantage of being able to control for confounding by all other potential determinants. For example, in the 2011 study, it was reported that older employees were likely to participate in the HRA. Also, less self-reported absenteeism was found among participants. We found similar results in the crude analysis of our data. However, in the multivariate analysis, neither age nor absenteeism were still significant determinants. Two of the independent determinants of participation found in the current study—physical activity and alcohol consumption—were not evaluated in the earlier study.

In addition to individual characteristics, program and organizational factors have been linked to participation in WHPPs.[37] Offering financial incentives is one of these factors. Not surprisingly, these incentives increase participation, but one can wonder whether such an external motivator helps to bring about lasting health-behavior change.[45] One of the few studies that investigated the influence of other organizational factors reported a 13% increase in participation in companies with a strong communication strategy.[45] This refers to the extent to which a strategic, comprehensive, integrated communications plan with multiple communications pieces and delivery channels tailored to the employee population is used by companies that offer WHPPs to their work force. Differences in communications strategy during the process of invitation to and inclusion in the HRA could have accounted for some of the variety in participation among the 5 organizations in the current study. For instance, among the participating organizations in our study, the university medical

center had the highest participation (51.7%). In this organization, participation was actively encouraged by upper and middle management, and the HRA was highlighted in the in-house magazine.

By extension, the recruitment message used by organizations can result in selection among participants: whereas Organization A may emphasize one specific feature of the WHPP (eg, "increase your vitality by participating"), Organization B may emphasize another (eg, "screening for health risks"). Following this line of reasoning, the lack of consistent reports in the literature on most individual characteristics of participation may have been caused in part by the widely varying content of recruitment messages. Future research into the reach of WHPPs should consider these and other communication aspects. Based on the combined insight of individual and organizational characteristics of participation, framing the recruitment message could prove to be an essential tool for companies trying to reach employees with specific risk profiles.

Strengths and Limitations

A limitation of the current study is the low response of the nonparticipants to the nonparticipant questionnaire. Others have been confronted with comparable limitations.[36;41] Individuals who are unwilling to participate in a program are also less likely to respond when asked to participate in a derivative of that program, which in our study was the request to complete a nonparticipant questionnaire. However, in our study, questionnaire responders were of the same age and gender as those who did not respond. Therefore, it is less likely that the reported results have been influenced by selection bias. A strength of the current study is the large size of our study cohort.

No individual characteristics were available for dropouts other than age and gender. This is also a limitation of the current study. Although the number of dropouts (7.9%) was relatively low, their inevitable exclusion from the participant group could have had some influence on the reported findings.

Except for age and gender, which were available from the HRA invitation lists for nearly all (>99.5%) invitees, data on other individual characteristics were collected differently for participants and nonparticipants. For participants, data were collected from the Web-based health questionnaire component of the HRA as part of a larger set of health data collected to generate a personal health report. A separate, short online questionnaire was created to collect data on individual characteristics from the nonparticipants. Some might argue that this divergence in data collection threatens the reliability of the reported findings. However, we estimate this effect to be small, as both participants and nonparticipants completed a set of questions online that were identical with respect to the individual characteristics used in this study.

CONCLUSION

This study showed health-related participation in a Web-based HRA. With regard to isolated health behaviors (insufficient physical activity, excess alcohol consumption, and stress), those who could benefit most from the HRA were more likely to participate. Employees who rated their overall health as less than positive and tobacco users were less likely to participate. Web-based delivery of the WHPP did not result in selective participation by more highly educated, female, or older employees.

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CHAPTER 6

Initiation of health-behaviour change among employees participating in a web-based health risk assessment with tailored feedback

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ABSTRACT

Background: Primary prevention programs at the worksite can improve employee health and reduce the burden of cardiovascular disease. Programs that include a web-based health risk assessment (HRA) with tailored feedback hold the advantage of simultaneously increasing awareness of risk and enhancing initiation of health-behaviour change. In this study we evaluated initial health-behaviour change among employees who voluntarily participated in such a HRA program.

Methods: We conducted a questionnaire survey among 2289 employees who voluntarily participated in a HRA program at seven Dutch worksites between 2007 and 2009. The HRA included a web-based questionnaire, biometric measurements, laboratory evaluation, and tailored feedback. The survey questionnaire assessed initial selfreported health-behaviour change and satisfaction with the web-based HRA, and was e-mailed four weeks after employees completed the HRA.

Results: Response was received from 638 (28%) employees. Of all, 86% rated the program as positive, 74% recommended it to others, and 58% reported to have initiated overall health-behaviour change. 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 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). Being satisfied with the HRA program in general was associated with more frequent self-reported initiation of overall health-behaviour change (OR 2.77, 95% CI 1.73- 4.44), increased physical activity (OR 1.89, 95% CI 1.06-3.39), and improved diet (OR 2.89, 95% CI 1.61-5.17).

Conclusions: More than half of the employees who voluntarily participated in a web-based HRA with tailored feedback, reported to have initiated health-behaviour change. Self-reported initiation of health-behaviour change was more frequent among those at high CVD risk and BMI levels. In general employees reported to be satisfied with the HRA, which was also positively associated with initiation of health-behaviour change. These findings indicate that among voluntary participating employees a web-based HRA with tailored feedback may motivate those in greatest need of health-behaviour change and may be a valuable component of workplace health promotion programs.

INTRODUCTION

Cardiovascular diseases (CVD) are the leading cause of disability and death.[1] Much of the CVD burden could be eliminated by addressing preventable risk factors, including high blood pressure, hypercholesterolemia, hyperglycaemia, smoking, physical inactivity, high fat intake, and low fruit and vegetable intake.[2;3] The health risk assessment (HRA) is one of the most widely used strategies to stimulate changes in these factors.[4-6] The worksite has been proposed as a suitable platform for wide dissemination of prevention programs that utilize HRA, with the advantage of cost savings, the creation of a health-conscious environment and easier follow-up of high-risk individuals.[7;8]

The traditional HRA screened for risk factors to produce feedback that predominantly contained information on the assessed risk.[9] However, reviews of the literature did not always support effectiveness of the traditional HRA.[9;10] It was suggested that feedback merely containing risk information would be insufficient to initiate health-behaviour change.[11] It was acknowledged that improvements in affecting health-behaviour change could be achieved by web-based delivery of the HRA, with incorporation of tailored health recommendations.[11-14] These HRAs hold the advantage of simultaneously increasing awareness of risk and enhancing initiation of health-behaviour change.[11;15]

Despite this potential little has been documented regarding health-behaviour change after implementation of a web-based HRA with tailored feedback at the workplace. In the present study we evaluated initial health-behaviour change among employees who voluntarily participated in a web-based HRA including tailored feedback, offered to them by their employer as part of a worksite health management program. The HRA was designed to collect data that are necessary to screen for the risk of a number of preventable diseases, including CVD, and provide tailored feedback to educate, motivate and empower participants to engage in a better lifestyle and reduce CVD risk. The primary aim of this study was to assess self-reported initiation of health-behaviour change and associations with satisfaction with the HRA and baseline health status.

METHODS

Population and study procedure

We conducted a questionnaire survey among employees who completed a web-based HRA with tailored feedback. This HRA was applied as part of a worksite health management program at seven Dutch companies with mainly white-collar workers between 2007 and 2009. During this period 6790 employees were invited to complete the HRA. E-mail invitations were sent by the human resources department, with a single reminder after two weeks. The invitation e-mail included a description of the HRA and informed employees that participation was voluntary, at no cost, that all personal data would be treated confidentially,

and that no results would be shared with their employer or any other party. Employees who completed the HRA, were sent an electronic satisfaction and health-behaviour change questionnaire, four weeks after they had received their tailored feedback. The questionnaire measured overall satisfaction with the HRA and initiation of health-behaviour change. It was sent to the employees using an e-mail survey program, with a single reminder after one week, and took about 10 minutes to complete.

The web-based HRA with tailored feedback

The HRA consisted 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 approximately 100 questions covering socio-demographics, personal health history, family risk, and the behavioural domain. All questions are derived from validated questionnaires and health-behaviour constructs from the transtheoretical model,[16] protection motivation theory,[17] and social cognitive theory.[18] 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. An electronic firewall is placed between the servers and the Internet. Only users certified by ID and password are able to access the servers. By computer-based combination of the assessed risk with health-behaviour constructs, tailored health recommendations are generated. These are presented to the participant integrated within a web-based health action plan. Each health plan comprises: 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), self-efficacy, 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.[19;20] When seriously elevated risks are detected, 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.

Satisfaction and initiation of health-behaviour change questionnaire

The study questionnaire included seven questions examining satisfaction with the web-based HRA and initiation of health-behaviour change after receiving the tailored health advices. An outline of the items, questions, and scoring scales are shown in the Additional file 1. Satisfaction was measured with two questions, using evaluative statements on the program as a whole: 1) overall mark for the program, measured on a 5-point rating scale, and 2) recommending the program to others, measured on a 5-point agreement scale. Initiation of health-behaviour change was measured with one item that evaluated whether participants overall initiated health-behaviour change after receiving their health advices, followed by questions on which health-behaviour items change was initiated. Answer options were yes, no, and not applicable.

Analysis

All analyses included descriptive statistics to examine population characteristics, and questionnaire answers for satisfaction and initial health-behaviour change. Non-response bias was checked by comparing differences in baseline values between responders and non-responders to the study questionnaire, using chi-squared tests. To analyse the influence of demographic factors and health characteristics on satisfaction with the HRA, logistic regression analysis was performed, with dichotomized Likert scale responses in positive and negative evaluation as dependent variable and the variables of interest (age category, sex, education level, body mass index as a proxy for physical activity level and caloric intake, smoking status, and Framingham CVD risk score as a proxy for cardiovascular risk factor levels) as covariates. The Framingham score estimates 10-year CVD mortality and morbidity risk by combining age, sex, blood pressure, hypertension treatment status, total cholesterol, HDL-cholesterol, smoking and diabetes status[21]. CVD risk score was categorized in low, intermediate and high risk, defined as 10-year CVD risk of <10%, ≥10% to 20% and ≥20%. The influence of satisfaction with the HRA program and health characteristics on initial health-behaviour change was also examined using logistic regression. All analyses were adjusted for age, sex, and education level. Data were analysed using SPSS for Windows, version 17.

RESULTS

Of the 6790 invited employees, 2289 (34%) completed all HRA measurements and received tailored health advices. Approximately 30 days after receiving health advices all 2289 employees were sent the study questionnaire. The response rate was 28% (638/2289). There were no differences between employees who responded to the questionnaire and those who did not in sex, age category, education level, Framingham risk score, body mass index, and smoking status (see table 1). In tables 2 and 3 results of the questionnaire are summarized. Of all employees who responded to the questionnaire 86% gave a positive overall rating

and 74% recommended the program to others. Overall, 368 (58%) employees reported to have initiated health-behaviour change, 242 (38%) to have improved physical activity, 64 (10%) to have reduced alcohol intake, and 282 (44%) to have improved their diet. Twenty employees reported to have quit smoking, representing 14% (20/145) of all current smokers among the questionnaire responders.

Table 1 | Baseline characteristics of employees who completed the HRA and responded to the satisfaction and health-behaviour change questionnaire and those who completed the HRA but did not respond the questionnaire.

	questionnaire responders	**questionnaire non-responders**	**p**
	***n* = 638**	***n* = 1651**	
Sex			
Male	387(61%)	1017(62%)	0.679
Female	251(39%)	634(38%)	
Age Category			
<30 years	28(4%)	89(5%)	0.054
30-39 years	163(26%)	457(28%)	
40-49 years	233(37%)	646(39%)	
>50 years	214(34%)	459(28%)	
Education level			
Low	139(22%)	320(19%)	0.204
Midlevel	191(30%)	552(33%)	
High	308(48%)	779(47%)	
Framingham 10 year CVD risk score category			
Low CVD risk (Framingham score < 10%)	455(71%)	1213(73%)	0.578
Intermediate CVD risk (Framingham score ≥ 10% - < 20%)	132(21%)	318(19%)	
High CVD risk (Framingham score ≥ 20%)	51(8%)	120(7%)	
Body Mass Index category			
Normal weight: Body Mass Index < 25 kg/m2	349(55%)	885(54%)	0.248
Overweight: Body Mass Index ≥ 25 - < 30 kg/m2	221(35%)	620(38%)	
Obese: Body Mass Index ≥ 30 kg/m2	68(11%)	146(9%)	
Current smoking status			
non-smoker	493(77%)	1272(77%)	0.907
smoker	145(23%)	379(23%)	

Values are expressed as number (% of total)

Table 2 | Satisfaction scores of 638 employees who completed the HRA and responded to the satisfaction and health-behaviour change questionnaire.

	Satisfaction ratings	
	Positive	Negative
Overall mark	546(86%)	92(14%)
Recommend to others	473(74%)	165(26%)

Values are expressed as number (% of total). Positive for the satisfaction item "Overall mark" reflects the proportion rating the item as excellent, very good, or good, and negative reflects the proportion rating the item as average or poor. Positive for the satisfaction item "Recommend to others" reflects the proportion rating the item as certainly yes or probably yes, and negative reflects the proportion rating the item as maybe, probably no, and certainly no.

Table 3 | Self-reported initiation of health-behaviour-change of 638 employees who completed the HRA and responded to the satisfaction and health-behaviour change questionnaire.

	Initiation of health-behaviour-change after receiving health advices		
	Yes	No	na†
Initiated overall health-behaviour-change after receiving tailored health advices	368(58%)	243(38%)	27(4%)
More physical activity	242(38%)	212(33%)	184(29%)
Quit smoking	20(3%)	125(20%)	493(77%)
Reduced alcohol intake	64(10%)	198(31%)	376(59%)
Improved diet	282(44%)	158(25%)	198(31%)

Values are expressed as number of participants (%).
na†: Questionnaire responders who stated that health-behaviour change on item of interest was not applicable.

In table 4 the influence of demographic factors and health characteristics on self-reported health-behaviour change are summarized. Age category and sex did not influence self-reported health-behaviour change. Compared to those with a low education level, higher educated employees were less likely to reduce alcohol intake (OR 0.50, 95% CI 0.25-0.99). Compared with employees at low CVD risk, those at intermediate CVD risk more often reported to have started to change their health behaviour in general (OR 1.71, 95% CI 1.04-2.80), whereas those at high CVD risk more often reported to have increased physical activity (OR 3.36, 95% CI 1.52-7.45). Independently, overweight (OR 1.63, 95% CI 1.13-2.36) and obese (OR 1.76, 95% CI 1.00- 3.10) employees more frequently reported initiation of overall health-behaviour change, and to have increased their physical activity (OR 1.56, 95% CI 1.03-2.36 for overweight and OR 3.35, 95% CI 1.72-6.54 for obese). Obese employees also more often reported to have improved their diet (OR 3.38, 95% CI

1.50-7.60). No associations between smoking status and self-reported initiation of health-behaviour change were found. An overall positive satisfaction with the HRA was associated with more frequent self-reported initiation of overall health-behaviour change (OR 2.77, 95% CI 1.73-4.44), increased physical activity (OR 1.89, 95% CI 1.06-3.39), and improved diet (OR 2.89, 95% CI 1.61-5.17). Being positive on recommending the program to others was similarly associated with more frequent self-reported initiation of overall health-behaviour change (OR 2.27, 95% CI 1.57-3.29), increased physical activity (OR 1.65, 95% CI 1.06-2.59), and improved diet (OR 3.00, 95% CI 1.89-4.78). Reported satisfaction with the HRA was not related to demographic factors and health characteristics with (data not shown).

DISCUSSION

The present study evaluated self-reported initial health-behaviour change among employees who completed a web-based HRA with tailored feedback. More than half of the employees reported to have initiated overall health-behaviour change. Initiation of more physical activity and improved diet was more frequently reported among those at high CVD risk and BMI levels. In general, employees reported to be satisfied with the HRA, and this was also positively associated with initiation of health-behaviour change.

An important finding in the present study is that employees at higher risk of CVD and high BMI levels more frequently reported initiation of health-behaviour change in general, increase in physical activity and improved diet. These findings may imply that the program is capable of stimulating health-behaviour change among those at greatest need. A possible underlying mechanism may be the tailoring of health advices to individual health characteristics, stage of change,[16] motivation,[17] and self-efficacy.[18] The feedback provided in the program therefore might be less stigmatizing and better aligned with the intentions of the participants, allowing them to change in small steps. These are factors that were previously associated with poor satisfaction ratings of health services among those at higher risk levels.[9;12;14;22;23]

In the present study we found no influence of demographic factors and health characteristics on reported satisfaction with the HRA. These findings are not consistent with previous studies that evaluated satisfaction in the context of a health service. Studies usually associated higher age, female gender, and low educational level with higher levels of satisfaction.[22;24;25] However, previous satisfaction studies generally evaluated a service that was based on face-to-face encounters with health professionals. The web-based HRA program we studied is a highly automated health service that includes a face-to face encounter with professionals upon request or when medically necessary. These characteristics may be relevant in designing HRA programs to reach higher satisfaction, and consequently greater health-behaviour change.

Table 4 | Influences of demographic and health characteristics on self-reported initiation of health-behaviour change.

	Overall health-behaviour change	More physical activity	Quit smoking	Reduced alcohol intake	Improved diet
	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]	OR [95% CI]
Sex					
Male‡					
Female	0.88[0.63 - 1.23]	1.20[0.82 - 1.76]	2.00[0.76 - 5.24]	0.89[0.47 - 1.69]	1.25[0.84 - 1.88]
Age					
40-49 years‡					
<30 years	1.05[0.47 - 2.36]	1.44[0.57 - 3.66]	**	1.67[0.39 - 7.07]	2.04[0.72 - 5.81]
30-39 years	0.92[0.61 - 1.39]	1.14[0.71 - 1.85]	1.66[0.53 - 5.25]	1.54[0.70 - 3.36]	1.00[0.61 - 1.63]
>50 years	1.39[0.94 - 2.06]	0.90[0.58 - 1.39]	0.55[0.17 - 1.83]	1.33[0.68 - 2.59]	1.13[0.70 - 1.81]
Education level					
Low‡					
Midlevel	1.08[0.69 - 1.70]	1.07[0.63 - 1.81]	1.37[0.36 - 5.20]	0.64[0.30 - 1.37]	1.10[0.62 - 1.96]
High	0.99[0.65 - 1.49]	1.20[0.74 - 1.94]	1.10[0.31 - 3.93]	0.50[0.25 - 0.99]	0.64[0.38 - 1.07]
Framingham 10 year CVD risk score (%)					
Low CVD risk (Framingham score < 10%)‡					
Interm. CVD risk (Framingham score ≥ 10% - < 20%)	1.74[1.10 - 2.74]	1.40[0.84 - 2.32]	1.83[0.48 - 7.02]	1.29[0.63 - 2.63]	1.11[0.65 - 1.90]
High CVD risk (Framingham score ≥ 20%)	1.82[0.92 - 3.59]	2.76[1.29 - 5.90]	3.88[0.80 - 18.75]	1.83[0.72 - 4.63]	1.03[0.47 - 2.29]
Body Mass Index category					
Normal weight: Body Mass Index < 25 kg/m2 ‡					
Overweight: Body Mass Index ≥ 25 - < 30 kg/m2	1.63[1.13 - 2.36]	1.56[1.03 - 2.36]	0.89[0.29 - 2.68]	1.69[0.91 - 3.14]	1.44[0.93 - 2.23]
Obese: Body Mass Index ≥ 30 kg/m2	1.76[1.00 - 3.10]	3.35[1.72 - 6.54]	2.57[0.42 - 15.81]	1.20[0.45 - 3.19]	3.38[1.50 - 7.60]

Table 4 | Continued

Current smoking status					
non-smoker‡					
smoker	1.03[0.70 - 1.51]	0.89[0.58 - 1.38]	††	1.36[0.74 - 2.49]	0.93[0.59 - 1.47]
Satisfaction					
Negative overall mark‡					
Positive overall mark	2.77[1.73 - 4.44]	1.89[1.06 - 3.39]	0.70[0.17 - 2.85]	1.56[0.64 - 3.79]	2.89[1.61 - 5.17]
Negative recommend to others‡					
Positive recommend to others	2.27[1.57 - 3.29]	1.65[1.06 - 2.59]	0.53[0.19 - 1.46]	1.42[0.73 - 2.77]	3.00[1.89 - 4.78]

OR: Odds ratio. 95% CI: 95% confidence interval

‡: Reference category

*: OR could not be calculated because none of the responders at age <30 years reported quit smoking.

†: OR for reporting quit smoking between smokers and non-smokers is irrelevant.

ORs for Framingham score, Body Mass Index, and Smoking status were adjusted for age, sex, and education level.

The present study has several limitations. First, the response rate to the questionnaire was 28%, which is lower than the mean response rates of 60% to 67% in most satisfaction surveys.[26;27] However, our response rate is comparable with response rates of general e-mail health surveys, which are around 34%.[28] Moreover, we did not find any differences in demographic and health parameters between responders and non-responders to the questionnaire. Therefore we assume that the sample was representative for all participants of the HRA program. Second, participation in the HRA was voluntary, with a participation rate of 34%. Studies that evaluated HRA or health promotion programs reported participation rates from 20% to 76%,[29;30] with the general impression that females, older employees, and mainly the "worried well" are attracted.[31] Although the participation rate in this study is within the expected range, we cannot rule out that among non-participants in the HRA there were employees with less favourable health characteristics. Third, both satisfaction and health-behaviour change were self-reported and therefore may be due to a number of psychosocial artefacts, including social desirability bias and a novelty effect.[22;25] Finally, the high positive satisfaction rating for overall mark may be skewed, because an unbalanced Likert scale with 3 positive scores and 2 negative scores was used. However, a previous study using a comparable scale reported an overall positive rating of 84%, which is similar with our findings.[15] Furthermore, we found that the item "recommend to others", which was assessed on a balanced scale, was also rated positive by the majority of the participants and had similar influence on self-reported initiation of health-behaviour change. Therefore, we assume that the impact of the unbalanced scale was marginal.

CONCLUSION

More than half of the employees who voluntarily participated in a web-based HRA with tailored feedback, reported to have initiated health-behaviour change within four weeks after receiving their feedback. Self-reported initiation of health-behaviour change was more frequent among those at high CVD risk and with high BMI levels. In general, employees reported to be satisfied with the HRA, which was also positively associated with initiation of health-behaviour change. These findings indicate that among voluntary participating employees, a web-based HRA program with tailored feedback could motivate those in greatest need of health-behaviour change. A web-based HRA with tailored feedback could therefore be a valuable component of workplace health promotion programs.

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CHAPTER 7

Impact of a Web-based Worksite Health Promotion Program on Absenteeism

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ABSTRACT

Objective: To evaluate the effect of participation in a comprehensive, web-based worksite health promotion program on absenteeism.

Methods: Study population consists of Dutch workers employed at a large financial services company. Linear regression was used to assess the impact of program attendance on the difference between baseline and follow-up absenteeism rates, controlling for gender, age, job level, years of employment and non-completion of the program.

Results: Data from 20,797 individuals were analysed. 3,826 individuals enrolled in the program during the study period. A 20.3% reduction in absenteeism was shown amongst program attendees as compared to non participants during a median follow up period of 23.3 months.

Conclusions: Participating in the worksite health promotion program led to an immediate reduction in absenteeism. Improved psychological well-being, increased exercise and weight reduction are possible pathways toward this reduction.

INTRODUCTION

In Europe, 86% of deaths and 77% of the disease burden are caused by noncommunicable diseases that are linked by common risk factors with shared, underlying determinants and common opportunities for intervention and prevention. Almost 60% of the disease burden is accounted for by seven leading risk factors: high blood pressure (12.8%); tobacco (12.3%); alcohol (10.1%); cholesterol (8.7%); overweight (7.8%); low fruit and vegetable intake (4.4%) and physical inactivity (3.5%).[1] The workplace is considered to be an excellent setting to target these risk factors, because a large proportion of the population can be reached and workers spend about half their waking hours at work.[2] Health risk factors have been associated with a loss of on the job productivity.[3-8] The latter makes worksite health promotion programs especially interesting for employers. However, these programs should be effective enough to persuade employers to invest in them.[9]

Studies that evaluate the effectiveness of worksite health promotion programs have recently been reviewed by Soler and colleagues.[10] These programs include three elements: (1) collection of information on personal health behaviours and/or measurable health indicators; (2) translation of the collected information into individual risk scores; and (3) feedback to participants regarding their risk status. Health promotion programs that have been described in the literature vary considerably on these elements. The effectiveness of worksite health promotion programs is usually evaluated on behavioural aspects and physiological indicators.[4;11;12] For employers, changes related to productivity are particularly interesting. Thus far, no consistent reduction of absenteeism after participation in a worksite health promotion program has been reported, although moderate reductions in absenteeism are shown in studies evaluating worksite health promotion programs with additional interventions.[13;14]

In the current study, the effect on absenteeism of participation in a comprehensive, web-based worksite health promotion program is evaluated amongst workers in a Dutch multinational in the financial services industry. The health promotion program includes biometric measurements, laboratory testing, and assessment of lifestyle behaviour, mental health disorders (depression, anxiety), and psychological strain (stress, burnout). The latter is particularly important because in the Netherlands, about one in every three new recipients of work disability benefit is disabled for work because of mental health problems.[15] A central goal of the health promotion program is to change how people think and behave: it aims to raise awareness, educate, motivate, and empower individual healthcare users to take steps to promote their own health. The transtheoretical model of Prochaska and DiClemente[16] plays an important role as participants are guided through the stages of pre-contemplation, contemplation, preparation, action, and maintenance. The program offers individuals a personal action plan, which may include advice to visit a (mental) health professional for further diagnostic testing or evaluation, to change health-related lifestyle behaviour(s), or simply to maintain present healthful behaviours.

METHOD

Worksite health promotion program

The health promotion program is called The PreventionCompass. Its core is a computerized knowledge-based reasoning system. In the system, risk assessment algorithms, as well as test and treatment thresholds regarding disease processes with a major impact on quality of life, productivity, vitality, and disability adjusted life years (DALY's)[17] are kept up to date according to prevailing guidelines and best practices. To be included in the system, the 'medical benefit versus risk' balance of risk factors and disease processes must be positive in accordance with the criteria of Wilson and Jungner.[18] As a result, it integrates multiple evidence based disease risk algorithms focusing on (the risk profiles of) disease processes with proven prevention or early diagnostic options (including cardiometabolic diseases, common mental disorders, musculoskeletal problems and (colorectal) cancer), and (risk profiles for) decreased workability and work engagement. One of the main communication principles of the health promotion program is individual tailoring. Compared to generic information, tailored feedback is more effective in creating awareness and intention to change unhealthy behaviour.[19] Another general principle concerns the importance of supportive and nonjudgmental communication, regardless of the client's risk level or motivation for behaviour change. For example, smokers who express low or no motivation to quit are not encouraged to feel "guilty" or otherwise "pressured" to quit. It is recognized that intrinsic motivation is a necessary ingredient for lasting behavioural change. Instead the unmotivated smoker's freedom of choice is affirmed; he or she is respectfully informed of the health benefits of smoking less or quitting, and offered resources for bolstering resolve and self-confidence to become smoke-free. Furthermore, consistent with stepped care principles, the personal health management plan emphasizes low-intensity self-management and lifestyle change wherever possible. When lifestyle change is indicated, individual preferences – regarding for instance independent versus professionally supervised interventions – are taken into account.

Participants

The research sample consisted of individuals employed at a large Dutch financial services company during the period January 2007 – July 2009. Individuals whose employment ended during the baseline period, or who became employed during the follow up period were excluded from analyses. Data from persons employed on freelance basis as well as data from persons with missing socio-demographic variables were also excluded. Because the capacity for onsite collection of biometric measurements was limited, employees were invited gradually to ensure contained influx into the program. From August 1st , 2007 until June 30th , 2009 anonymous email invitations to participate in the worksite health promotion program were sent by the human resources department based on an at random selection within employee month of birth. For example, the 1st batch of invitees were an at random selection within all employees born in the month of January. A single reminder was sent after two weeks. The invitation e-mail included a description of the worksite health promotion program and informed employees that participation was voluntary and at no cost, that all

personal data would be treated confidentially, and that no individual results would be shared with their employer or any other party. All participated on a voluntary and informed basis.

Intervention

Employees were classified as program attendees when they activated their online account after which containers for the collection of laboratory (urine and faeces) samples were send to participants home address. Each attendee completed a web-based electronic health questionnaire, followed by biometric measurements (length, weight, waist circumference, blood pressure) conducted at the worksite by trained and certified staff. Participants handed the collected laboratory samples to the staff during this visit. At the same visit blood samples were collected for laboratory testing of total cholesterol, HDL, LDL, triglycerides, glucose and HbA1C. A personalised web-based health report and health plan was automatically generated only after all health data were collected. At this point, the health promotion program was completed. Each health plan comprised: 1) explanation of the assessed risk for each of the targeted preventable conditions, using a three-colour 'traffic light' 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), self-efficacy, and preferences with respect to interventions (e.g. guided vs. non-guided interventions). When seriously elevated cardiovascular risks were detected, the health plan included referral for further medical evaluation and treatment. A thirty minute health counselling session with the program physicians was also available upon request for all attendees.

On average, all measurements were collected within eight weeks after enrolment into the worksite health promotion program. With the exception of attendees registering in the final four months, data of attendees who had not completed all measurements by the end of the study period were analysed as a separate subgroup (enrolled but not completed participation).

Outcome measure

For all attendees of the worksite health promotion program, baseline and follow up periods were determined by the program enrolment date. Study participants who did not enrol in the worksite health promotion program during the study period were classified as nonparticipants. For them, the baseline period ended at August 1st 2007, the day invitation e-mails to participate in the worksite health promotion program were first sent.

For each study participant the absenteeism rates during baseline and follow up periods were determined as follows: first, the total number of workable days was calculated for both periods. If employment started during baseline or ended during follow up, workable days were adjusted proportionally. For part-time employees, workable days and absence episodes of ≥ 3 days were multiplied by the fraction of employment. In accordance with Dutch

practice, maternity leave was not recorded as absenteeism. Dividing the total number of absence days by the workable days resulted in the absenteeism rate. The difference between baseline and follow up absenteeism rates was used as the primary outcome measure and dependent variable in the regression equation.

$$\text{Absenteeism rate} = \frac{\text{Absence days}}{\text{Workable days}}$$

Workable days = days in period x A x B

A = proportion of time employed
B = fraction of employment

Statistical analysis

Linear regression was used to assess the impact of worksite health promotion program attendance on the difference between baseline and follow-up absenteeism rates, controlling for gender, age, job level, years of employment, and program completion. Job level explains at what education level an employee is functioning (source: Hay Group International). Subsequently, for all study participants, the observed absenteeism rate during baseline and the regression equation that resulted from the preceding step were used to estimate the expected absenteeism rates during follow-up under presumed participation and presumed non-participation in the program. The average difference in expected absenteeism rates during follow-up under presumed participation and presumed nonparticipation, was used as an estimate of the overall effect on absenteeism of the program. Data were analysed using SPSS for Windows, version 19.

RESULTS

A total of 23,258 individuals were employed during the study period. 1,297 individuals were excluded because their employment ended during the baseline period (n = 550), or started during the follow up period (n = 747). Data of 613 persons employed on freelance basis were excluded from analysis as were data from 551 persons with an unknown job level. Data from 20,797 individuals were analysed. Approximately 11,252 employees were invited to participate in the health promotion program during the study period. From this cohort, a total of 3,826 individuals enrolled in the worksite health promotion program.

Table 1 lists the baseline characteristics of the study participants. Program attendees were slightly older and were functioning at a higher job level. They worked more hours per week and more often longer than 10 years employed at the company. Also, more males were present amongst the program attendees. The fixed versus variable baseline/follow up periods for the nonparticipants and the worksite health promotion program attendees are reflected in the observed group differences in the duration of these periods.

Table 1 | Baseline characteristics study sample

	Total sample		Health promotion program attendees		Non participants	
	(*n* =20.797)		(*n* =3.826)		(*n* =16.971)	
Gender						
Male	10,395	(50,0%)	2,037	(53,2%)	8,358	(49,2%)
Female	10,402	(50,0%)	1,789	(46,8%)	8,613	(51,8%)
Age (years)						
Mean	41,4		42,2		41,2	
St.dev.	9,9		8,9		10,1	
Job Level						
Lower & secondary vocational	6,607	(31.8%)	776	(20,3%)	5,831	(34,4%)
Higher vocational	6,645	(32,0%)	1,412	(36,9%)	5,233	(30,8%)
University	7,545	(36,3%)	1,638	(42,8%)	5,907	(34,8%)
Years of Employment						
0 - 10	6,619	(31.8%)	919	(24,0%)	5,700	(33,6%)
11 - 20	5,405	(26,0%)	1,123	(29,4%)	4,282	(25,2%)
21- 30	4,632	(22,3%)	992	(25,9%)	3,640	(21,4%)
> 30	4,141	(19,9%)	792	(20,7%)	3,349	(19,7%)
Working hours						
36-40 hours per week	14,539	(69,9%)	2,715	(71,0%)	11,824	(69,7%)
32-35 hours per week	2,355	(11,3%)	466	(12,2%)	1,889	(11,1%)
24-31 hours per week	2,662	(12,8%)	486	(12,7%)	2,176	(12,8%)
< 24 hours per week	1,241	(6,0%)	159	(4,2%)	1,082	(6,4%)
Baseline absenteeism	3,23%		3,39%		3,20%	
Baseline period (months)						
Median	7.1		15.8		7.1	
Interquartile interval	5.7 - 7.1		10.7 - 21.8		5.7 - 7.1	
Follow Up period (months)						
Median	23.3		10.9		23.3	
Interquartile interval	14.0 - 23.3		4.6 - 16.1		17.5 - 23.3	
Enrolled but not completed health promotion program	204	(0,9%)	204	(5,3%)		

Table 2 presents the results of the linear regression analysis. Compared to nonparticipants, there is an absolute decline in absenteeism rate of 1.0% (95% CI: 0.6% to 1.4%) in the worksite health promotion program attendee group during follow-up. There was no statistically significant effect of attrition. The analysis also indicates that, in absolute terms, the absenteeism rate of females increased with 1.1% (95% CI: 0.7% to 1.4%) during follow up. An increase in absenteeism is observed for older employees (50-59 years). Although the effect was not statistically significant, results point towards an increase in absenteeism amongst employees functioning at lower and secondary vocational levels and a decease in absenteeism amongst employees functioning at university level. Also, a decrease in absenteeism is observed for employees with more than 10 years of employment. The absenteeism rate for employees working at the company for more than 30 years showed a decline of 1.7% (95% CI: 1,0% to 2,4%) during follow up. Based on the regression equation, the absenteeism rate at follow-up estimated for program attendance is 3.93%. For non-participation, the estimated absenteeism rate at follow up is 4.93%. The relative percentage gain of worksite health promotion program attendance, therefore, is calculated as follows:

$$\frac{3.93 - 4.93}{4.93} \times 100 = -20.28$$

Table 2 | Linear regression of the difference between baseline and follow up absenteeism on health program attendence

		95% confidence interval	
	ß	Lower	Upper
Health promotion program participation	-.010	-.014	-.006
Enrolled but not completed participation	.001	-.014	.017
Female sex	.011	.007	.014
Age			
18 - 29 ‡			
30 - 39	.000	-.006	.006
40 - 49	.006	.000	.013
50 - 59	.012	.004	.019
≥ 60	-.004	-.017	.009
Job Level			
Lower & secondary vocational	.003	-.001	.008
Higher vocational ‡			
University	-.003	-.007	.001
Years of Employment			
0 - 10 ‡			
11 - 20	-.010	-.014	-.005
21- 30	-.008	-.014	-.002
> 30	-.017	-.024	-.010

‡ Reference category

DISCUSSION

In this study a 20.3% reduction in absenteeism was shown amongst voluntary participants in a web-based worksite health promotion program, when comparing their absenteeism rates to those of non-participants. Absenteeism was also lower for males and employees working more than 10 years at the company . A trend towards a decrease in absenteeism was found for employees functioning at university level. Absenteeism was higher amongst employees aged 50 – 59 years and a trend towards an increase in absenteeism was found for employees functioning at lower and secondary vocational levels.

Our study stands out by the large sample size and the availability of employee records of study participants (recorded absenteeism, start/end and fraction of employment, job level, years of employment) as well as health promotion program enrollment dates of attendees. This resulted in an accurate calculation of absenteeism rates and baseline periods. Furthermore, potential confounding by age, sex, job level, years of employment and health program completion was corrected for in the statistical analysis.

An important limitation of our study is the fact that we were unable to distinguish between employees who did not enrol in the program because they were not invited, and employees who did not enrol because they were not interested. Both types of employee were classified as non participants. Based on a participation rate of 34% that was found in another evaluation study of the same worksite health promotion program,[20] we estimate that approximately 11,252 of the 20,797 study participants were invited during the study period, from which 3,826 chose to enrol in the program. Another limitation is the fact that the study period was artificially split up into baseline and follow-up periods for non participants at the fixed date of August 1st, 2007. This way, no invitation bias could have influenced baseline absenteeism of the non participants, because August 1st 2007 is the date invitation e-mails to participate in the worksite health promotion program were first send out to employees. On the downside, seasonal fluctuations in absenteeism may have introduced some bias in the results. With regard to the participation rate it is important to note that the expected company wide absenteeism decline as a result of implementing this program is of course greatly affected by the participation of employees in the program.

Thus far, the only Dutch effectiveness study reporting on worksite health promotion in relation with absenteeism is the so called 'Brabantia Project'.[21] After the program, a decrease in absenteeism of 51% was shown in the intervention group compared to a decrease of 34% in the control group. However, in that particular study, the 14.3 – 15.8% baseline absenteeism rates were more then double the national average for workers in the light metal industry at that time, leaving much room for these rates to decline. Also, differences in absenteeism rates at follow up were not adjusted for confounding variables and baseline absenteeism. Feedback to the participants regarding their risk status was limited to the biomedical measures of the assessment and interventions were not tailored at the individual

level. For example, all participants from the experimental group received health education on alcohol use, regardless of individual alcohol intake. The worksite health promotion program evaluated in current study has a more sophisticated approach. Collected health data is translated into a personalised health report and advice, which is then used to drive behavioural change. The premise that lasting behavioural change can only be achieved when an individual is intrinsically motivated to change his or her behaviour is a key underlying principle in this program. Therefore, the advice is tailored even further based on the participant's readiness to change health related behaviours. Recently, Mills and colleagues[8] reported on the effectiveness of a similar worksite health promotion program. In addition to a reduction in the cumulative count of health risk factors and an increase in on-the-job productivity, a significant reduction in absenteeism was found in the intervention group. An interesting future study would be to examine differences in effectiveness between 'relatively simple' and 'more sophisticated' health promotion programs.

It is postulated that changes toward a healthier lifestyle will reduce the risk for future chronic disease. In this study however, an immediate impact of attending a worksite health promotion program on absenteeism was shown. The question is which pathway or underlying mechanism is responsible for this decline. Burton and colleagues reported that both alcohol use and smoking are relatively stable over a short period of time (2 years), whereas physical activity, weight, life dissatisfaction and stress have the greatest amount of churn in a working population that is not participating in any particular health promotion program.[4] For the worksite health promotion program in the current study, 58% of the attendees initiate health behaviour change after participation.[20] It is plausible to assume that the initiated health behaviour change has positively affected psychological wellbeing, either in isolation or combination with increased exercise and weight reduction. Obviously, these health risk factors are related, since physical activity not only contributes to weight loss but is also inversely related to depressive symptoms.[22] Overweight has been associated with increased absenteeism[23] and recently it was reported that for overweight individuals, a lack of physical activity increases absenteeism even further.[24] Furthermore, by engaging the psychological self-help modules that are available in the worksite health promotion program, or by seeking counselling, a number of attendees probably have successfully addressed their mental health problems, whereas others could have diminished their stress levels, all of which resulted in an immediate effect on the absenteeism rate.

This study showed that participating in a worksite health promotion program can lead to a immediate reduction in absenteeism. Future research is necessary to identify the mechanisms responsible for this short term effect.

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CHAPTER 8

General discussion

MAIN FINDINGS

Objective 1 To investigate the role of self-administered tools in screening for risks of chronic disease

The first specific aim of developing and validating screening questionnaires for cardiovascular disease (CVD) risk and psychotic disorders was addressed in chapters 2 and 4. In the study described in chapter 2, it was found that adequate screening of CVD risk in men over 40 years old does not require taking blood pressure measures or determining blood serum cholesterol levels. European guidelines state that individuals with a 10-year SCORE-estimated CVD mortality risk of ≥ 5% exceed the 'preventive care threshold', meaning that intensive health advice is warranted and drug treatment should be considered. Our study showed that the ≥ 5% SCORE threshold can be predicted with high accuracy by a model that adds questions about weight, height, waist circumference, alcohol use and history of hypertension to questions about age and tobacco use which are already used in the SCORE risk estimation. Performance of the newly developed model in a cohort of middle aged male employees (40-70 years) was strong (AUC of 0.95; 95% CI 0.95- 0.96).

In conclusion, a simple six-item questionnaire is able to accurately identify subjects at high CVD risk as measured by the SCORE risk estimation in a population of working men.

The study described in chapter 4 showed that by deploying the Eppendorfer Schizophrenia Inventory (ESI), a self-report questionnaire developed in 2000,[1] individuals with overt psychosis can be distinguished from those at so-called ultra-high risk (UHR) of conversion to psychosis and both can be discerned from patients with other common mental health disorders. Performance was best in the subscale of seven items relating to delusional mood and ideas of reference, which is the tendency to interpret trivial events in an excessively meaningful way (UHR/acute psychosis vs neither: AUC 0.76; 95% CI 0.70- 0.82, acute psychosis vs UHR/nonpsychotic: AUC 0.82; 95% CI 0.74- 0.90). We also created a new scale (UHR-Psychosis scale) based on a selection of five items from the ESI whose performance has yet to be validated in a separate cohort.

In conclusion, the ESI questionnaire can be used within secondary mental health care services to detect individuals at ultra-high risk of conversion to psychosis as well as those with acute psychosis.

The second specific aim was determine the feasibility of self-monitoring of blood pressure at home as a tool for hypertension screening by validating a single duplicate home BP measurement (HBPM). The study described in chapter 3 showed that if upper (≥150 or ≥95 mmHg) and lower limit (<135 and <80 mmHg) cut-off values for systolic and diastolic blood pressure were used, one duplicate HBPM is sufficiently discriminative (AUC 0.94; 95% CI 0.93-0.95) to confirm or reject the presence of hypertension in 62.5% of employees participating in a HRA, leaving only 37.5% that have to complete the three day HBPM

series of six duplicate measurements, as recommended by European guidelines. Using these cut-off values resulted in 1.1% being falsely identified as hypertensive and 4.7% falsely labelled as normotensive (false negatives). Performance was similar in participants with high and low cardio metabolic risk, but worse in participants with a history of hypertension (10.4% false negatives).

In conclusion, home blood pressure measurement is a feasible tool for hypertension screening in a working population.

Objective 2 To investigate participation in worksite health promotion programs (WHPPs) and subsequent effects

The third specific aim, to analyse how participation in a web-based workplace health promotion program (WHPP) is influenced by individual characteristics, was addressed in chapter 5. Determinants of participation were some periods of stress at home or work in the preceding year (OR 1.62), a decreasing number of weekdays on which at least 30 minutes were spent on moderate to vigorous physical activity (OR dayPA 0.84) and increasing alcohol consumption (none vs 15-21 units, OR 2.22). Determinants of nonparticipation were less-than-positive self-rated health (poor/very poor vs very good, OR 0.25) and tobacco use (at least weekly vs none, OR 0.65).

In conclusion, with regard to some isolated health behaviors (insufficient physical activity, excess alcohol consumption, and stress), those who could benefit most from a WHPP were more likely to participate. Those who rated their overall health as less than positive and tobacco users were less likely to participate.

The fourth specific aim was to assess the initiation of health behaviour change after participation in a web-based WHPP. The study described in chapter 6 showed that 58% of participants initiated health-behaviour change after completing a WHPP. With regard to isolated health behaviors, 38% increased their physical activity, 10% reduced their alcohol intake, 44% improved their diet and 14% of the tobacco users quitted smoking. Compared to employees at low CVD risk, those at intermediate CVD risk more often reported changes in their general health behaviour (OR 1.71), whereas those at high CVD risk more often reported to have increased physical activity (OR 3.36). Independently, overweight (OR 1.63) and obese (OR 1.76) employees more frequently reported initiation of overall health behaviour change, and to have increased their physical activity (OR 1.56 for overweight and OR 3.35 for obese). Obese employees also more often reported to have improved their diet (OR 3.38). No associations between smoking status and self-reported initiation of health behaviour change were found.

In conclusion, more than half of the employees who participated in a web-based workplace health promotion program reported to have initiated health-behaviour change. Self-reported initiation of health-behaviour change was more frequent among those at high CVD risk and high BMI levels.

To evaluate the effect of participation in a web-based WHPP on absenteeism was the final specific aim of this thesis. In the study described in chapter 7 the impact of programme attendance on the difference between baseline and follow-up absenteeism rates was assessed, controlling for gender, age, job level, years of employment, and noncompletion of the programme. A 20% reduction in absenteeism was shown among participants compared with non-participants during a median follow-up period of 23 months.

In conclusion, participating in a web-based workplace health promotion program was associated with a reduction in absenteeism.

METHODOLOGICAL LIMITATIONS

Study population

The findings in two studies with respect to objective 2 will be sensitive to selection bias. Self-selection may have occurred in the study in chapter 5, where it was analysed whether selective participation had occurred among the 32% of employees who enrolled in the WHPP after being invited to participate. In order to compare individual characteristics of participants with non-participants, the latter were invited to complete an online questionnaire. Self-selection may have been introduced as only 27% of the non-participants completed the online questionnaire. Non-participants who completed the online questionnaire and those who did not were of similar age and gender. As these were the only variables available for those who did not complete the questionnaire, we are unable to rule out self-selection on the health, lifestyle and work-related variables used as outcome measures in the study. Selection bias may therefore have affected the generalizability of the findings presented in chapter 5.

A similar potential bias was present in the study described in chapter 6. An online questionnaire was sent out to WHPP participants after completion of the programme to assess the initiation of health behaviour change. However, in this case, questionnaire responders were comparable to non-responders with regard to all demographics (age, sex, education level) and health indicators (CVD risk, BMI, smoking status) that were used in the study which minimizes the chance of selection bias to have occurred.

Study design

In the study described in chapter 7, the relation between participating in a WHPP and absenteeism was investigated. The study did not have a randomised control design, which limits our ability to attribute the found 20% reduction in absenteeism to program participation. However, it is likely that the association between program attendance and absenteeism in this retrospective study is caused by the WHPP as the analysis on absenteeism between participants and non-participants was corrected for a range of relevant variables that are known to influence such as baseline absenteeism, age, gender, and functioning level.

In chapter 6, it was reported that 58% of WHPP participants indicated to have initiated changes in health behavior after participation in the program. In this cohort study no control group was used which represents a weakness in the design. As a result it was not possible to ascertain the extent to which the reported health behavior change was solely due to participation in the WHPP.

Measurement methods

Chapters 2, 5, and 6 were based upon studies in which health behavior was self-reported. Research into the extent in which self-reported health behaviours reflect objective measures has shown mixed results. Smoking status for instance can be objectively assessed by the measurement of urinary cotinine, which is a biomarker of the exposure to tobacco smoke. It was reported that smoking prevalence based on self-report was only 0.3% lower when compared to urinary cotinine measurements in a general population sample, which seems to indicate self-reports on smoking behavior can be used as a valid measure of tobacco use.[2] In case of alcohol consumption however, self-reports on frequency are reported to be more accurate than self-reports on quantity.[3;4] The relation between self-reports and direct measures of physical activity is even less clear. A review showed correlations between self-reports and direct measures varied between -0.71 and 0.96.[5] Trends differed by measure of physical activity employed, level of physical activity measured and the gender of participants. This lack of an agreement in findings poses a serious problem for both reliance on self-report measures of physical activity and for attempts to correct for systematic differences between self-reports and direct measures.[5]

We do not expect deviations between self-reports and objective outcome measures to have influenced the findings described in chapters 5 and 6, as those findings exclusively relate to self-reports. In chapter 2, however, we show that BMI category, based on direct measurement of height and weight by professionals, is one of the six variables that predict CVD risk in our newly developed CVD risk screening tool. When the tool is used in practice however, self reported measures of height and weight are used to calculate BMI.

The findings of a review published in 2007 suggest there is a trend for BMI to be underestimated when based on self-reports on height and weight as compared to direct measures of these variables.[6] That same year, it was reported that measured BMI was on average 0.6 kg/m² (CI, 0.5;0.7) higher in men and 0.8 kg/m² higher (0.7;0.9) in women when compared with self-rated BMI in a general population sample.[7] Older age and increasing (measured) overweight were found to be associated with an increasing underestimation of body weight. The authors proposed a simple formula to correct self-reported BMI based on these variables. Although the main predictor variables of our newly developed CVD risk screening tool are age and tobacco use, we advise to add this correction to the calculation of self-reported BMI to avoid that its underestimation leads to an underestimation of CVD risk when using the tool.

Self-reporting of health behavior may also be biased as a result of socially desirable response tendencies, which is the tendency to present a favourable image of oneself in questionnaires. For instance, Adams[8] reported an overestimation of self-reported physical activity in a paper-and-pencil questionnaire among individuals with this tendency. With regard to web-based questionnaires, however, it was recently reported that there is no association between social desirability and self-reported health risk behaviors[9] and these findings were confirmed in a study that focussed on web-based self-reports on physical activity.[10] It is postulated that the social distance and impersonal nature of the internet make socially desirable response tendencies less likely to occur.[9]

In chapter 3, home blood pressure measurement (HBPM) was investigated for its use as a screening tool for hypertension. As a reference for hypertension, the averaged BP of six HBPMs was used (≥ 135 mmHg systolic or ≥ 85 mmHg diastolic). HBPM have similar reproducibility as ambulatory blood pressure monitoring (ABPM)[11;12] which is considered the gold standard for BP. To optimize comparability to ABPM, it is proposed to discard the HBPM readings collected on the first day which are typically the highest of a series.[13] We chose not to follow this advice, since the main goal of our study was to increase the feasibility of using HBPM for screening purposes by reducing as much as possible the number of HBPMs necessary to confirm or rule out hypertension. Our study did confirm that average HBPMs of the first day are the highest of a three day series, but the differences with measurements on other days were small. The average systolic HBPM of the first day was only 0.7 mmHg higher than the average HBPM of the second day. For the prediction of two binary outcomes (rule out or confirm hypertension) this difference was not meaningful. Therefore, small differences in average BP between the first and second day were considered not to have affected the reliability of the study described in chapter 3.

Imputation of missing data

In chapter 4, on the determinants of participation in a worksite health promotion program, imputation of missing values of independent variables was employed. Missing values in the dataset were likely to in part be missing due to unobserved variables (so-called 'missing not at random'), which potentially undercuts the reliability of the imputed values, as the imputation method uses patterns found in the values of observed variables to estimate missing values. It has, however, been noted that the negative effects on the reliability are often minimal with multiple imputation.[14-16] The latter was used in the study described in chapter 4. Complete case analysis also confirmed the direction of the reported results in this chapter.

NEW INSIGHTS

Simple self-administered tools can be used to screen for cardiovascular disease risk and hypertension

Although several screening instruments have been developed which include only simple, readily available, and non-invasively assessed parameters to identify persons at high risk for developing diabetes[17-19] kidney disease,[20] or a combination of cardio metabolic end points,[21] we are the first to report on the development and validation of a simple six item self-report screening tool for the assessment of CVD risk in men based on European CVD prevention guidelines (chapter 2).

Among the largest barriers in implementing the guidelines in clinical practice are requirements of both time and finances to meet all individuals for a risk assessment which includes blood sampling and blood pressure measurements to complete the recommended SCORE risk estimation.[17] Our tool can be applied in a web-based screening programme in which subjects are referred to the primary care physician to obtain these measures only if they test positive on the screening questionnaire. As referred screen positives have a much higher likelihood of exceeding the ≥5% SCORE 'preventive care' threshold, this stepped approach could possibly be a cost-effective method of identifying individuals with high CVD risk.

In chapter 3, we describe the first study in which home blood pressure measurements (HBPM) are used as a tool for hypertension screening. Our study shows that the number of 12 HBPM currently recommended by European guidelines to establish blood pressure within the context of hypertension management can be reduced to one duplicate measurement for six out of every ten individuals in a screening setting. Reducing the number of measurements is likely to increase the feasibility of HBPM as a screening tool and could potentially lower attrition in hypertension screening programmes.

A self-report questionnaire can be used to screen for psychosis (risk) within mental health services

We showed that the ESI screening questionnaire can be utilized to identify individuals at ultra high risk (UHR) for conversion to psychosis and distinguish them from patients with acute psychosis and those with other DSM diagnoses. Although several UHR screening questionnaires have been developed in the past decades,[22] most are not sensitive to the threshold between UHR, acute psychosis and other diagnostic categories. Also, some were either validated in very small or non-representative samples and most lacked adequate reporting, for instance on what proportion of individuals labeled UHR made the conversion to psychosis within a specified timeframe.[23-25]

The ESI questionnaire can be used to facilitate the diagnosis of patients with acute psychosis and those at UHR who are referred to mental health facilities. This is needed as evidence suggests that delays within mental health services are the greatest contribution to the duration

of untreated psychosis (DUP)[26] which is associated with, among others, higher scores for overall psychopathology, disease related symptoms, and lower level of functioning.[27;28] Also, determining UHR status is an expensive process. A structured clinical interview is administered that requires several hours of a clinician's time. Therefore, a stepped approach in which trained staff is only deployed if patients screen positive on the ESI questionnaire is warranted to increase the effectiveness as well as cost-effectiveness of confirming or ruling out UHR or acute psychosis. To decrease DUP, priority can be given to individuals whose ESI score suggest acute psychosis. To maximize efficiency, the ESI questionnaire can be offered as a web-based screen during the referral process, before intake at the mental health facility.

Employee groups with a 'mixed bag' of health and work-related risks participate in worksite health promotion programmes

Our study in chapter 5 shows that participants in the WHPP represent a 'mixed bag' among the employee population with regard to isolated health behaviours, general health, and work-related factors. For some factors (alcohol use, physical activity, stress), employees who could benefit from these programmes were more likely to participate, whereas in other areas (tobacco use, self-rating of general health) employees that one wants to reach with WHPPs participated less. Our study adds to the fairly consistent reports of lower participation among tobacco users.[29-33] With regard to other health and work related factors, it is plausible to assume that, based on our results and the inconsistent findings in available literature to date, WHPPs do not only attract employees who are already making healthful choices.

Implementing health promotion programmes is cost effective for employers

In chapter 7 a 20% reduction in absenteeism was shown within a group of employees in the 23 month period following their participation in a WHPP compared to non-participants of the same company. The effectiveness of worksite health promotion programmes is usually evaluated for its impact on behavioural aspects and physiologic indicators that will reduce the risk for future chronic disease. For employers, however, additional short-term changes related to productivity are particularly interesting. Although reports on the effectiveness of WHPP in relation with absenteeism have not been consistent, our study adds evidence to the modest reductions in absenteeism found in other studies.[34;35]

RECOMMENDATIONS FOR POLICY AND PRACTICE

Deploy simple instruments, such as questionnaires and self-monitoring, as screening tools to increase effectiveness and cost-effectiveness of selective and indicated prevention

Prevention of chronic disease is warranted, not only to increase quality of life for the individual but also to battle associated costs for society. We believe that utilizing simple and accurate self-administered screening instruments (first part of this thesis) to asses risk in the context of selective prevention and to facilitate timely diagnosis in the context of indicated prevention

could increase both the effectiveness and cost-effectiveness of prevention. We recommend to offer these tools online and in case of CVD prevention, as part of comprehensive web-based e-health promotion programmes. These programmes provide tailored feedback on how to reduce risk and offer free access to self-help programs and low-cost evidence-based risk reduction interventions specifically selected to match the individual participants' preferences and motivation. To obtain a full CVD risk estimation for those who test positive at the first screening step, a blood pressure (BP) measurement and a blood sample is needed. As we showed, at this second step of screening, involvement of health care professionals can still be limited as participants can measure their BP at home with a validated BP device (first part of this thesis). We also showed that when screening for hypertension, it is possible to confirm or rule out diagnosis after a single double home BP measurement for six out of every ten screened individuals. Once again, embedding hypertension screening by home BP measurements in an e-health programme facilitates its use as participants can upload their first readings and automatically receive feedback on whether or not to complete the full BP measurement series.

With regard to diagnosis of mental disorders, we recommend to use self-report screens like the validated ESI questionnaire (first part of this thesis) in secondary mental health care services as a first step to select individuals for interview by a health care professional.

Incentivise employers to pay for health promotion programmes

The monetary cost of prevention and who should pay is topic of debate. We recommend that employers should be incentivised to offer their employees comprehensive evidence-based health promotion programmes. As participation in these programmes seems to have an immediate, modest effect on absenteeism (second part of this thesis), employers gain directly from its implementation. Only widespread deployment of sophisticated WHPP among organisations can generate sufficient impact in the population.

RECOMMENDATIONS FOR FUTURE RESEARCH

Optimise the implementation and performance of personalised prevention e-health applications

In the second part of this thesis we focused on Prevention Compass, an e-health application that is offered as a worksite health promotion programme. The investigated application delivers personalised prevention which means that health recommendations are tailored to individual needs, risk factors, and estimated disease risks. For its developers, it is obvious that Prevention Compass is the prototype of a personal prevention application with good potential for future research and development.

For instance, in this thesis the effects of individual characteristics on participation in a WHPP were studied. During the last year, we have seen participation in this particular programme rise substantially (participation range 40-60%). We suspect this rise to be the result of structured marketing and communication efforts offered to participating organisations. This suggests that tailoring should not only apply to changes in behaviours, but also to motives and reasons of prospective participants to become engaged in a WHPP. This needs further investigation.

Also, with regard to both participation and effectiveness, the classic construct of locus of control of reinforcement, which is part of social learning theory,[36;37] seems relevant. It refers to the extent to which an individual believes that his behaviour is causally related to particular health aspects or other outcomes (internal) or determined by external factors such as luck, powerful others or fate (external).[37] Although some have argued that health locus of control has limited use for predicting health behaviour change,[38] others have demonstrated its relationship to a variety of health related behaviours.[37] To date however, few studies have evaluated locus of control in relation to personalised prevention delivered by e-health applications. One study found it to be one of the characteristics that explained the variance in the use of an online weight-management diary.[39] Another study showed that 'internals' have more favorable cognitive responses to tailored health education materials whereas 'externals' respond more favorable to non-tailored materials. These findings suggest that the effectiveness of personalised prevention by e-health apps at least in part could be explained by the construct of locus of control, but this needs to be investigated more extensively.

Use A/B testing as a research strategy to optimize the performance of personalised prevention e-health applications

With regard to research methods, it is recommended to employ so-called A/B testing, which is used in the field of e-commerce, to optimize web-based personalised prevention tools. In A/B testing, users are randomly exposed to one of two variants (of a website); either the control (A) or intervention (B). The intervention variant is usually a "new" modified version of the "existing" control variant.[40] For the optimization of personalised prevention tools and its implementation, variants may for instance differ in communication of the purpose of the tool, risk communication, standard integration of biometric measurements or mode of health behaviour measurement. The random allocation of users to variant A and B guarantees that no other factor can influence a difference on the key performance indicator. In other words, A/B testing can be viewed as a modern RCT.[40] Based on the results of the experiments either the "new" version of the e-health tool is implemented, or the original version is maintained. If the new version of the tool is implemented, it will act as control variant during the next optimization iteration.[40]

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SUMMARY

SAMENVATTING

SUMMARY

Screening is part of secondary preventive interventions and includes determining disease risk in apparently healthy individuals as well as detection of those at early stages of a disease or condition. In this era of rising health care costs, the value of prevention of chronic diseases is recognized, but cost-effectiveness of preventive measures is crucial for its deployment. A practical limitation of the current approach to cardiovascular disease (CVD) prevention is that a consultation with a physician is needed to determine CVD risk in high risk groups (all men over 40 and women over 50 years old). A similar limitation exists within the context of indicated prevention of mental disorders. Determining psychosis risk is an expensive process as it requires several hours of a clinician's time. Also, more timely detection of patients with first episode psychosis by health care professionals is needed in order to reduce the duration of untreated psychosis.

Potentially more effective and cost-effective is a stepped approach to chronic disease risk estimations. In this approach information collected outside the health care professionals office is used as the first step in the screening proces. It is, therefore, important to investigate whether simple instruments, such as questionnaires and self-monitoring, can be developed and validated for use in screening programmes. Therefore, the first objective of this thesis is to investigate the role of self-administered tools in screening for risks of chronic disease. The specific aims are:

1. To develop and validate screening questionnaires for cardiovascular disease risk and psychosis (risk);
2. To determine the feasibility of self-monitoring of blood pressure (BP) at home as a tool for hypertension screening by validating a single duplicate home BP measurement.

CVD risk assessment programmes are useful if they not only identify those at risk, but will also ensure that individuals are supported to reduce their risks and avoid the onset of disease. The workplace is considered to be an excellent setting for both screening and health promotion. One type of worksite health promotion programme (WHPP) frequently offered, is the health risk assessment (HRA). Modern web-based health HRAs can be equipped with comprehensive decision-support systems that generate tailored health recommendations, based on individual needs, risk factors and estimated disease risk. The process and outcome of this tailoring is coined personalised prevention.

The effectiveness and cost-effectiveness of WHPPs strongly depend on adequate reach of those who could benefit most from the intervention. Since most intervention studies on WHPPs randomize workers who have agreed to participate in the study, this is largely unknown. The extent to which health behaviour change is initiated to reduce CVD risk after participation in a WHPP also has to be determined. Furthermore, the cost-effectiveness of implementing WHPPs from an employer's perspective needs to be investigated. The second objective of the thesis is to investigate participation in WHPPs and subsequent effects. The specific aims of the studies performed are:

3. To analyse how participation in a web-based WHPP is influenced by individual characteristics;
4. To assess the initiation of health behaviour change after participation in a web-based WHPP;
5. To evaluate the effect of participation in a web- based WHPP on absenteeism.

The role of self-administered tools in screening for risks of chronic disease

Chapter 2 presents a cross-sectional study on the development and validation of a six item self report screen to identify workers at risk for cardiovascular disease using WHPP information of 6,189 male employees from 25 organisations. It was found that adequate screening of CVD risk in men over 40 years old does not require taking blood pressure measures or determining blood serum cholesterol levels. Our study showed that the ≥5% SCORE 'preventive care threshold', as outlined in the current European guidelines, can be predicted with high accuracy by a model that adds questions about weight, height, waist circumference, alcohol use and history of hypertension to questions about age and tobacco use which are already used in the SCORE risk estimation (AUC of 0.95; 95% CI 0.95- 0.96).

Chapter 4 presents a cross-sectional study in which an existing self-administered questionnaire, the Eppendorf Schizophrenia Inventory (ESI), was examined for its ability to correctly identify individuals with psychosis (risk) in a combined cohort of three samples (*n*=348) of individuals referred to or under current treatment at two mental health care facilities. The ESI adequately distighuishes patients with overt psychosis from those at so-called ultra-high risk (UHR) of conversion to psychosis and both can be discerned from patients with other common mental health disorders. Performance was best in the subscale of seven items relating to delusional mood and ideas of reference, which is the tendency to interpret trivial events in an excessively meaningful way (UHR/acute psychosis vs neither: AUC 0.76 (95% CI 0.70- 0.82), acute psychosis vs UHR/nonpsychotic: AUC 0.82 (95% CI 0.74- 0.90).

Chapter 3 presents a cross-sectional study in which self-monitoring of blood pressure at home (HBPM) was examined as a tool for hypertension screening among 1,473 employees (derivation cohort *n* =945, validation cohort *n* = 528) who participated in a web-based WHPP. The study showed that if upper (≥150 or ≥95 mmHg) and lower limit (<135 and <80 mmHg) cut-off values for systolic and diastolic blood pressure were used, one duplicate HBPM is sufficiently discriminative (AUC 0.94; 95% CI 0.93-0.95) to confirm or rule out the presence of hypertension in 62.5% of the screened individuals, leaving only 37.5% that have to complete the three day HBPM series of six duplicate measurements, as currently recommended by European guidelines. Using these cut-off values resulted in 1.1% being falsely identified as hypertensive and 4.7% falsely labelled as normotensive. Performance of these cut-off values was similar in participants with high and low cardiometabolic risks, but worse in participants with a history of hypertension (10.4% false negatives).

Participation in worksite health promotion programs and subsequent effects

Chapter 5 presents a cross-sectional study investigating the influence of individual characteristics on participation in a web-based WHPP among 2,473 participants and 1,564 non-participants. Determinants of participation were some periods of stress at home or work in the preceding year (OR 1.62), a decreasing number of weekdays on which at least 30 minutes were spent on moderate to vigorous physical activity (OR dayPA 0.84) and increased weekly alcohol consumption (none vs 15-21 units, OR 2.22). Determinants of non-participation were less-than-good self-rated health (poor/very poor vs very good, OR 0.25) and tobacco use (at least weekly vs none, OR 0.65).

Chapter 6 presents a cohort study among WHPP participants (*n*= 638) examining the initiation of health behaviour change after completion of the web-based programme. The study showed that 58% of participants did in fact initiated health-behaviour change. With regard to isolated health behaviours, 38% increased their physical activity, 10% reduced their alcohol intake, 44% improved their diet and 14% of the tobacco users quitted smoking. Compared to employees at low cardiovascular disease (CVD) risk, those at intermediate CVD risk more often reported changes in their general health behaviour (OR 1.71), whereas those at high CVD risk more often reported to have increased physical activity (OR 3.36). Independently, overweight (OR 1.63) and obese (OR 1.76) employees more frequently reported initiation of overall health behaviour change, and to have increased their physical activity (OR 1.56 for overweight and OR 3.35 for obese). Obese employees also more often reported to have improved their diet (OR 3.38). No associations between smoking status and self-reported initiation of health behaviour change were found.

Chapter 7 presents a retrospective cohort study assessing the impact of WHPP completion on absenteeism among 20,797 employees of a large financial institution of which 3,826 participated in the programme. After controlling for gender, age, job level, years of employment, and noncompletion of the programme, a 20% reduction in absenteeism was shown among participants compared with non-participants during a median follow-up period of 23 months.

In **chapter 8** the main findings of this thesis are presented. In addition, methodological limitations pertaining to study population, study design, measurement methods and data preparation are discussed. In conclusion, the following recommendations are presented based on new insights from this thesis. Simple, accurate self-administered tools can be developed to screen for chronic disease. It is recommended to deploy these instruments to increase the effectiveness and cost-effectiveness of selective and indicated prevention. Participation in WHPPs may lead to reduced absenteeism among relevant employee groups, which makes implementing these programmes cost effective for employers. As only widespread deployment of sophisticated WHPPs among organisations can generate sufficient impact in the population, it is recommended to incentivise employers to pay for WHPPs.

SAMENVATTING

Screening maakt onderdeel uit van secondaire preventieve interventies en bestaat zowel uit het vaststellen van ziekterisico in (schijnbaar) gezonde individuen als uit het detecteren van (degenen met) vroege stadia van een ziekte of aandoening. In dit tijdperk van stijgende zorgkosten wordt de waarde van preventie van chronische ziekten onderkend, maar is de kosten-effectiviteit bepalend voor de inzet van preventieve maatregelen. Een praktische beperking bij de huidige preventie aanpak van cardiovasculaire aandoeningen (CVA) is dat er een consult met een arts nodig is om het CVA risico vast te stellen in hoog risico groepen (alle mannen boven de 40 en vrouwen boven de 50 jaar). In de context van geindiceerde preventie van psychische aandoeningen bestaat een vergelijkbare beperking. Het vaststellen van psychose risico is een kostbaar proces omdat een clinicus hier een aantal uren mee bezig is. Verder is het nodig dat patienten met een eerste psychose eerder door zorgverleners worden herkend om de duur van onbehandelde psychose te verminderen.

Een getrapte aanpak zou zowel effectiever als kosteneffectiever kunnen zijn bij het vaststellen van (chronisch) ziekterisico. Bij deze aanpak wordt in de eerste stap van het screeningproces gebruik gemaakt van informatie die niet via de gezondheidszorgprofessional is verzameld. Het is daarom belangrijk om te onderzoeken of eenvoudige instrumenten zoals vragenlijsten en zelfmonitoring ontwikkeld en gevalideerd kunnen worden om gebruikt te worden in screeningsprogramma's. Daarmee is het eerste doel van dit proefschrift te onderzoeken wat de rol is van door individuen zelf te gebruiken instrumenten bij screening op (het risico op) chronische ziekten. De specifieke doelen zijn:

1. Het ontwikkelen en valideren van screenings vragenlijsten voor cardiovasculair risico en psychose(risico)
2. Het bepalen van de bruikbaarheid van het zelf thuis monitoren van bloeddruk als een hypertensiescreening tool door een enkele dubbele thuismeting te valideren.

Programma's gericht op het bepalen van CVA risico zijn pas nuttig wanneer zij naast de risicoschatting individuen in staat stellen om hun risico's te verminderen en ziekte te voorkomen. De werkplek wordt als een uitstekende setting beschouwd voor zowel screening als gezondheidsbevordering. Een veelvuldig aangeboden (bedrijfs)gezondheids bevorderend programma is het gezondheidsrisico onderzoek. Moderne online gezondheidsrisico onderzoeken kunnen worden uitgerust met uitgebreide beslisondersteuning die op maat gemaakte gezondheidsadviezen genereren op basis van individuele behoeften, risicofactoren en ziekterisico. Het proces en de uitkomst van dit 'op maat maken' wordt ook wel gepersonaliseerde preventie genoemd.

Het adequaat bereiken van degenen die er het meeste baat bij hebben bepaalt in belangrijke mate de effectiviteit en kosten-effectiviteit van gezondheidsbevorderende programma's. Het is tot nu toe grotendeels onbekend in hoeverre dit het geval is, aangezien in de meeste gerandomiseerde onderzoeken op dit gebied het al dan niet toewijzen aan een

gezondheidsbevorderend programma gebeurd onder werknemers die al hebben toegezegd mee te zullen werken aan het onderzoek. Eveneens dient te worden bepaald in hoeverre deelname aan een gezondheidsbevorderende programma resulteert in het initieren van leefstijlveranderingen om het CVA risico te verminderen. Daarnaast dient de kosten-effectiviteit vanuit het perspectief van de werkgever onderzocht te worden. Het tweede hoofddoel van dit proefschrift is dan ook het onderzoeken van participatie aan gezondheidsbevorderende programma's en de hieruit voortvloeiende effecten. De specifieke doelen van de uitgevoerde onderzoeken zijn:

3. Analyseren hoe individuele kenmerken de participatie aan een online aangeboden gezondheidsbevorderende programma beinvloeden;
4. Het beoordelen van leefstijlverandering na deelname aan een online aangeboden gezondheidsbevorderende programma;
5. Het evalueren van het effect van deelname aan een online aangeboden gezondheidsbevorderende programma op verzuim.

De rol van door individuen zelf te gebruiken instrumenten bij screening op chronische ziekte risico

Hoofdstuk 2 presenteert cross-sectioneel onderzoek over de ontwikkeling en validatie van een uit zes items bestaande, door het individu zelf te gebruiken screeningsinstrument, waarmee werknemers met verhoogd risico op cardiometabole aandoeningen geidentificeerd kunnen worden. In deze studie werd gebruik gemaakt van informatie van 6.189 mannelijke werknemers afkomstig van 25 organisaties. Er werd gevonden dat het niet nodig is bloeddrukmetingen te verrichten of het bloedserum cholesterol niveau vast te stellen om adequaat te screenen op verhoogd cardiometabool risico onder mannen boven de 40 jaar. Onze studie toont aan de ≥5% SCORE 'preventieve drempelwaarde' zoals beschreven in de huidige Europese richtlijn met grote nauwkeurigheid kan worden voorspeld door een model dat vragen over gewicht, lengte, buikomtrek, alcoholgebruik en bekendheid met hypertensie toevoegt aan de reeds in de SCORE risicoschatting gebruikte vragen over leeftijd en tabakgebruik (AUC of 0.95; 95% CI 0.95- 0.96).

Hoofdstuk 4 presenteert een cross-sectionele studie waarin een bestaande zelfinvul vragenlijst, de Eppendorf Schizophrenia Inventory (ESI), wordt beoordeeld op het vermogen om individuen met psychose(risico) te identificeren in een gecombineerd cohort bestaande uit drie steekproeven (*n*=348) van individuen die verwezen werden of onder behandeling waren bij twee ggz instellingen. De ESI maakt adequaat onderscheid tussen patienten met acute psychose en degenen met een zogenaamd ultra-hoog risico (UHR) op transitie naar psychose. Beiden kunnen worden onderscheiden van patienten met andere, veelvoorkomende, mentale stoornissen. De best presterende subschaal bestond uit items die verband houden met waanachtige stemming en betrekkingsideeen, dit laatste is de tendens om overmatige betekenis toe te kennen aan triviale gebeurtenissen (UHR/acute psychose vs geen van beide: AUC 0.76 (95% CI 0.70- 0.82), acute psychose vs UHR/nonpsychotische stoornis: AUC 0.82 (95% CI[0.74- 0.90).

Hoofdstuk 3 presenteert een cross-sectionele studie waarin bij 1.473 werknemers (derivatie cohort *n* =945, validatie cohort *n* = 528) die mee hadden gedaan aan een web-based gezondheidsbevorderend programma werd onderzocht of het zelf thuis monitoren van bloeddruk gebruikt kan worden als een tool voor hypertensiescreening. Het onderzoek toonde aan dat wanneer 'hoog' (≥150 or ≥95 mmHg) en 'laag' (<135 and <80 mmHg) afkapwaarden voor systolische and diastolische bloeddruk gebruikt worden, een enkele dubbele thuismeting voldoende onderscheidend (AUC 0.94; 95% CI 0.93-0.95) was om hypertensie uit te sluiten of te bevestigen bij 62,5% van de gescreende individuen. Hierdoor hoeft slechts 37,5% de gehele driedaagse serie van zes dubbele metingen te verrichten zoals aanbevolen in de huidige Europese richtlijnen. Het gebruik deze afkapwaarden had tot gevolg dat 1,1% onterecht geidentificeerd werd als hypertensief en 4,7% onterecht gelabeld werd als normotensief. De prestatie van deze afkapwaarden was hetzelfde bij participanten met hoog en laag cardiometabool risico, maar minder goed bij participanten die bekend waren met hypertensie (10.4% fout negatief).

Participatie aan gezondheidsbevorderende programma's en de hieruit voortvloeiende effecten

Hoofdstuk 5 presenteert een cross-sectionele studie waarin bij 2.473 deelnemers en 1.564 niet-deelnemers wordt onderzocht hoe individuele kenmerken deelname aan een online aangeboden gezondheidsbevorderend programma beinvloeden.. Determinanten van deelname waren perioden van stress in de thuis of werksituatie gedurende het afgelopen jaar (OR 1.62), een verminderd aantal weekdagen waarop tenminste 30 minuten aan matig tot sterk inspannende fysieke activiteit (FA) gedaan wordt (OR dagFA 0.84), en verhoogd wekelijks alcoholgebruik (geen vs 15-21 units, OR 2.22). Determinanten van niet-deelname waren het beoordelen van de eigen gezondheid als minder dan goed (slecht/heel slecht vs heel goed, OR 0.25), en tabakgebruik (ten minste wekelijks vs niet, OR 0.65).

Hoofdstuk 6 presenteert een cohort studie waar onder deelnemers (*n*= 638) aan een gezondheidsbevorderend programma het initieren van leefstijlverbetering na voltooing van het web-based programma in kaart gebracht wordt. Het onderzoek toont aan dat 58% van de deelnemers start met het verbeteren van de leefstijl. Met betrekking tot de geisoleerde leefstijlgedragingen; 38% ging meer bewegen, 10% verminderde alcohol-inname, 44% ging gezonder eten en 14% van de tabakgebruikers stopte met roken. Werknemers met een gemiddeld cardiovasculair risico rapporteerden vaker algemene leefstijlverbeteringen (OR 1.71) in vergelijking met werknemers met laag cardiovasculair risico. Werknemers met een hoog cardiovasculair risico rapporteerden vaker meer te zijn gaan bewegen (OR 3.36). Onafhankelijk van dit effect rapporteerden werknemers met overgewicht (OR 1.63) en obesitas (OR 1.76) vaker algemene leefstijlverbeteringen en meer te zijn gaan bewegen (overgewicht OR 1.56 en obesitas OR 3.35). Daarnaast rapporteerden werknemers met obesitas vaker gezonder te zijn gaan eten (OR 3.38). Er werden geen verbanden gevonden tussen tabaksgebruik en zelf gerapporeerde leefstijlveranderingen.

Hoofdstuk 7 presenteert een retrospectieve cohort studie waarin de impact van deelname aan een gezondheidsbevorderend programma op verzuim wordt onderzocht bij 20.797 werknemers van een grote financiele organisatie, waarvan er 3.826 deelnamen aan het programma. Rekening houdend met geslacht, leeftijd, functieniveau, dienstjaren en uitval uit het programma, werd er een 20% afname in het verzuim waargenomen onder deelnemers in vergelijking met niet-deelnemers gedurende een follow-up periode waarvan de mediaan 23 maanden was.

In **hoofdstuk 8** worden de belangrijkste bevindingen van dit proefschrift gepresenteerd. In aanvulling hierop worden de methodologische beperkingen met betrekking tot onderzoekspopulatie, onderzoeksdesign, meetmethoden en datapreparatie besproken. Ten slotte worden de volgende aanbevelingen gedaan gebaseerd op nieuwe inzichten voortkomend uit dit proefschrift. Het is mogelijk om eenvoudige, accurate, door individuen zelf te gebruiken instrumenten te ontwikkelen ten behoeve van screening op chronische ziekten. Het wordt aanbevolen deze instrumenten in te zetten om de effectiviteit en kosteneffectiviteit van selectieve en geindiceerde preventie te vergroten. Deelname aan gezondheidsbevorderende programma's leidt mogelijk tot verzuimreductie bij relevante werknemersgroepen, waardoor inzet van deze programma's kosteneffectief is voor werkgevers. Omdat alleen met brede inzet van doorwrochten gezondheidsbevorderende programma's voldoende impact op populatieniveau bereikt wordt, is het de aanbeveling werkgevers te stimuleren de implementatiekosten van deze programma's te dragen.

DANKWOORD

ABOUT THE AUTHOR

LIST OF PUBLICATIONS

PhD PORTFOLIO

DANKWOORD

Dit proefschrift was niet tot stand gekomen zonder de steun van collega's, vrienden en familie.

Beste Roderik, jij gaf mij de mogelijkheid te promoveren binnen het NIPED en je was betrokken bij de conceptualisatie van een belangrijk deel van de studies uit dit proefschrift. Zonder uitzondering was je gedurende het hele traject beschikbaar om mee te denken. Ik heb enorm veel van je geleerd. Dank je voor je inspirerende begeleiding van de afgelopen jaren.

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Dank ook aan alle collega's van het NIPED, dankzij jullie inzet is er überhaupt data beschikbaar voor onderzoekers om onderzoek mee te doen.

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Niels P., dank voor alles wat je mij geleerd hebt over methoden van onderzoek en analysetechnieken. Het ga je goed in Manchester.

Beste Niels (vd H.), als mede-promovendus hebben we samen twee studies opgezet en uitgevoerd. We vulden elkaar goed aan. Ik hoop dat we in de toekomst nog eens samen onderzoek kunnen doen. Veel succes met jouw opleiding tot internist.

Beste Peter, dank je voor de kans die je mij gaf onderzoek te doen binnen het VORS project van de adolescentenkliniek van het AMC.

Vrienden en familie, jullie waren voor mij een onmisbare steun tijdens dit traject.

Bart, NY is niet om de hoek, maar je hebt voorzichtige plannen om in 2015 terug naar Nederland te komen, dat geeft ons de kans elkaar weer wat vaker te zien.

Beste Dimitri, wat is het hard gegaan de afgelopen 10 jaar, als jonge vaders zien ook wij elkaar momenteel te weinig. Goed om te weten dat je er bent.

Lieve mama en zus, dank voor jullie onaflatende interesse en steun tijdens alle academische stappen sinds de middelbare school en het bijzonder tijdens dit traject. Veel dank ook lieve Jeannine en Mariejan voor jullie betrokkenheid en support.

Raoul, communist, coole dude en wereldberoemd onderzoeker. En nu dan ook mijn paranimf. Ik geniet tijdens de etentjes in Amsterdam-West. Wat heb ik het getroffen met jou als schoonbroer.

Mijn allerliefste Mirthe, ineens was je er, met al je warmte op een kille winterdag in 2007. Vanaf dat moment heb je de zon doen schijnen in mijn leven. Je bent het mooiste, zuiverste, liefste, slimste en creatiefste mens die ik ken. Dank je voor al jouw steun en liefde van de afgelopen jaren. Ik hou van je.

Lieve Max, iedere dag met jou is een feest. Levenslustig stap je op de wereld af met je blonde krullen en je danst en zingt en maakt zelfs al grapjes. Je bent fantastisch in alles wat je doet.

ABOUT THE AUTHOR

Maurice Antoine Jacques Niessen was born on the 30th of March 1973 and raised in Nieuwegein, the Netherlands. In 1990 he graduated from lower secondary school at the Randdijk public school community in Nieuwegein and in 1993 he graduated from higher secundary school at Niels Stensen College in Utrecht. After briefly studying social-pedagogical care he started studying psychology at the University of Amsterdam in 1995. In 2001 he obtained his Master of Arts degree in clinical psychology. From 2004 to 2007 he worked as a research assistant at the Academic Medical Centre (AMC) in Amsterdam were he was involved in research into the early diagnosis of psychosis. From 2009 to 2012 he did research into risk profiling and personalised prevention at the NDDO Institute for Prevention and Early Diagnostics (NIPED). From 2011 to 2014 he was an external PdD candidate at the Department of Public Health at the Erasmus Medical Centre in Rotterdam, where he carried out the research presented in this thesis. From 2012 to 2014 he coordinated research into ehealth at the NIPED Research Foundation. He currently works at Minddistrict were he continuous to work towards sustainable mental healthcare through ehealth innovation.

He lives together with his beloved Mirthe and their son Max.

Maurice Antoine Jacques Niessen is geboren op 30 maart 1973 en groeide op in Nieuwegein. In 1990 behaalde hij zijn MAVO diploma aan Openbare Scholengemeenschap de Randdijk te Nieuwegein en in 1993 behaalde hij zijn HAVO diploma aan het Niels Stensen College te Utrecht. Na kort pedagogische hulpverlening te hebben gestudeerd startte hij in 1995 met de studie Psychologie aan de Universiteit van Amsterdam. In 2001 behaalde hij de master Klinische Psychologie. Vanaf 2004 tot 2007 was hij als onderzoeksassistent in het Academisch Medisch Centrum betrokken bij onderzoek naar vroegdiagnostiek van psychose. Van 2009 tot 2012 deed hij onderzoek naar risicoprofilering en persoonlijke preventie bij het NDDO Institute for Prevention and Early Diagnostics (NIPED). Vanaf 2011 tot 2014 was hij als buitenpromovendus verbonden aan de afdeling Maatschappelijke Gezondheidszorg van het Erasmus MC in Rotterdam en voerde het promotieonderzoek uit dat resulteerde in dit proefschrift. Vanaf 2012 tot 2014 coördineerde hij als programmamanager bij de Stichting NIPED Research wetenschappelijk onderzoek op het gebied van ehealth. Momenteel werkt hij bij Minddistrict verder aan duurzame geestelijke gezondheidszorg door middel van ehealth innovatie.

Hij woont samen met zijn geliefde Mirthe en hun zoon Max (2012).

LIST OF PUBLICATIONS

This thesis

2014

Van der Hoeven NV, Niessen MA, Kraaijenhagen RA, Burdorf A, van den Born BJ. A six question screen to identify persons at risk for developing cardiovascular disease. Submitted.

2013

Niessen MA, van der Hoeven NV, van den Born BJ, van Kalken CK, Kraaijenhagen RA. Home blood pressure measurement as a screening tool for hypertension in a web-based worksite health promotion programme. Eur J Public Health 2013 Oct 1. [Epub ahead of print]

Niessen MA, Laan EL, Robroek SJ, Essink-Bot ML, Peek N, Kraaijenhagen RA, Van Kalken CK, Burdorf A. Determinants of participation in a web-based health risk assessment and consequences for health promotion programs. J Med Internet Res. 2013;15(8):e151.

2012

Niessen MA, Kraaijenhagen RA, Dijkgraaf MG, Van Pelt D, Van Kalken CK, Peek N. Impact of a Web-based worksite health promotion program on absenteeism. J Occup Environ Med. 2012; 54(4):404-8.

2011

Colkesen EB, Niessen MA, Peek N, Vosbergen S, Kraaijenhagen RA, van Kalken CK, Tijssen JG, Peters RJ. Initiation of health-behaviour change among employees participating in a web-based health risk assessment with tailored feedback. J Occup Med Toxicol. 2011; 9:6.

2010

Niessen MA, Dingemans PM, van de Fliert R, Becker HE, Nieman DH, Linszen D.Diagnostic validity of the Eppendorf Schizophrenia Inventory (ESI): a self-report screen for ultrahigh risk and acute psychosis. Psychol Assess. 2010; 22(4):935-44.

Other publications

Vosbergen S, Laan EK, Colkesen EB, Niessen MA, Kraaijenhagen RA, Essink-Bot ML, Peek N. Evaluation of end-user satisfaction among employees participating in a web-based health risk assessment with tailored feedback. J Med Internet Res. 2012;14(5):e140.

Peek N, Niessen MAJ, Kraaijenhagen RA. Prevalentie van leefstijl- en risicofactoren voor hart- en vaatziekten in Nederland onder Nederlandse werknemers. In: I. Vaartjes et al. (eds.), Hart- en vaatziekten in Nederland, 2010. Den Haag: Nederlandse Hartstichting;2010.

Nieman D, Becker H, van de Fliert R, Plat N, Bour L, Koelman H, Klaassen M, Dingemans P, Niessen M, Linszen D. Antisaccade task performance in patients at ultra high risk for developing psychosis. Schizophr Res. 2007;95(1-3):54-60.

PhD PORTFOLIO SUMMARY

Summary of PhD training
PhD student: Maurice AJ Niessen
Period: 2011 -2014
Promotor: Prof.dr.ir. A. Burdorf

	Year	Workload (ECTS)
Presentations		
Europrevent, Dublin – Ireland		
-Home blood pressure measurement as a screening tool for hypertension in healthy employees	2012	0.4 ECT
Europrevent, Prague - Czech Republic		
-Reduction in absenteeism with a web-based integrated risk profiling and health management service	2010	0.4 ECT
Expert meeting on the feasability of collecting family history data for disease risk assessment VU, EMGO, Amsterdam	2011	0.5 ECT
Inspiratiesessie Impact meten binnen de gezondheidzorg, Noaber Foundation, Terschuur	2013	0.5 ECT
Seminars and symposia		
Item response theory in health measurement, Hoofddorp	2013	0.4 ECT
Item response theory in health measurement, Hoofddorp	2011	0.4 ECT
Masterclass Stan Newman Stichting Zorg binnen bereik E-Vita, Utrecht	2013	0.4 ECT
Research funding		
Workshop subsidie aanvragen formuleren, ZonMW, Den Haag	2013	0.4 ECT
Inventarisatie van familiaire ziektegeschiedenis voor vroegdiagnostiek en preventie van kanker, Stichting Mitialto	2012	1.5 ECT
Angst en depressiescreening op de werkvloer, Fonds Psychische Gezondheid	2013	1.5 ECT
Review of papers		
Workplace Self-Management Program: Impact on Health Behavior Frequency and Self-Efficacy	2012	0.2 ECT
Application of the RE-AIM Framework to Evaluate the Impact of a Worksite-Based Financial		
Incentive Intervention for Smoking Cessation	2011	0.2 ECT
A Review and Analysis of the Clinical and Cost Effectiveness Studies of Comprehensive Health Promotion and Disease Management Programs at the Worksite: Update VIII 2008-2010	2011	0.2 ECT

Review of abstracts, Medicine 2.0 World Congress on Social Media, Mobile Apps, Web 2.0		
The Patient-Therapist Relationship as an Indicator for Treatment Success in E-Health Treatments for Patients with Chronic Somatic Conditions	2013	0.1 ECT
Health-Related Behavior on the Online Social Networking Site Facebook – a Content Analysis of Communication on Facebook	2013	0.1 ECT
Evidence Based Medical Diagnostics via Statistical and Clinical Analytics of Ultrasound Images	2013	0.1 ECT
Social Media Guidelines for Communication in Health Settings in Germany	2014	0.1 ECT