A 30-month worksite-based lifestyle program to promote cardiovascular health in middle-aged bank employees: Design of the TANSNIP-PESA randomized controlled trial

Jennifer K Coffeng, PhD,[a] Hidde P van der Ploeg, PhD,[a] José M Castellano, MD, PhD,[b,c] Juan M Fernández-Alvira, PhD,[b] Borja Ibáñez, MD, PhD,[b,d] Inés García-Lunar, MD,[b,e] Allard J van der Beek, PhD,[a] Antonio Fernández-Ortiz, MD, PhD,[b,f] Agustín Mocoroa, MD,[g] Laura García-Leal[b] Evelyn Cárdenas[b] Carolina Rojas[b] María I Martínez-Castro, PhD,[b] Silvia Santiago-Sacristán[b] Miriam Fernández-Gallardo[b] José M Mendiguren, MD,[g] Sameer Bansilal, MD,[h] Willem van Mechelen, MD, PhD,[a] and Valentín Fuster, MD, PhD[b,h] *Amsterdam, the Netherlands; Madrid, Spain; and New York, NY*

Background Cardiovascular disease (CVD) is the leading cause of death worldwide. With atherosclerosis as the underlying cause for many CVD events, prevention or reduction of subclinical atherosclerotic plaque burden (SAPB) through a healthier lifestyle may have substantial public health benefits.

Objective The objective was to describe the protocol of a randomized controlled trial investigating the effectiveness of a 30-month worksite-based lifestyle program aimed to promote cardiovascular health in participants having a high or a low degree of SAPB compared with standard care.

Methods We will conduct a randomized controlled trial including middle-aged bank employees from the Progression of Early Subclinical Atherosclerosis cohort, stratified by SAPB (high SAPB n = 260, low SAPB n = 590). Within each stratum, participants will be randomized 1:1 to receive a lifestyle program or standard care. The program consists of 3 elements: (*a*) 12 personalized lifestyle counseling sessions using Motivational Interviewing over a 30-month period, (*b*) a wrist-worn physical activity tracker, and (*c*) a sit-stand workstation. Primary outcome measure is a composite score of blood pressure, physical activity, sedentary time, body weight, diet, and smoking (ie, adapted Fuster-BEWAT score) measured at baseline and at 1-, 2-, and 3-year follow-up.

Conclusions The study will provide insights into the effectiveness of a 30-month worksite-based lifestyle program to promote cardiovascular health compared with standard care in participants with a high or low degree of SAPB. (Am Heart J 2017;184:121-32.)

Background

Cardiovascular disease (CVD) remains the leading cause for premature death and morbidity worldwide. Developed and developing countries spend most financial health care resources on CVD—more than all cancers combined.[1] In both the United States and Europe, the estimated annual costs for CVD are 282 and 169 billion euros, respectively, with direct health care costs accounting for approximately 60% of the costs (eg, hospital services, physicians, and prescribed medication). The surplus represents indirect costs from lost productivity and informal care.[2,3] With atherosclerosis as the underlying cause for the majority of clinical CVD events,[3] early detection of subclinical atherosclerotic plaque burden (SAPB) and consequent action may carry significant reductions in all costs. Atherosclerosis takes decades to develop symptoms, offering opportunities for early detection and customized lifestyle modifications to prevent CVD manifestations. Recently, the clinical significance of subclinical detection was emphasized in the High-Risk Plaque-US BioImage Study. This prospective study among approximately 6000 asymptomatic adults

From the [a]Department of Public and Occupational Health, and EMGO+ Institute for Health and Care Research, VU University Medical Center (VUmc), Amsterdam, the Netherlands, [b]Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC), Madrid, Spain, [c]HM Hospitales–Hospital Universitario HM Montepríncipe, [d]Instituto de Investigación Sanitaria-Fundación Jiménez Díaz, Madrid, Spain, [e]Hospital Universitario Quirónsalud–Universidad Europea de Madrid, Spain, [f]Hospital Clínico San Carlos, Universidad Complutense, Madrid, Spain, [g]Banco de Santander, Madrid, Spain, and [h]Icahn School of Medicine at Mount Sinai, New York, NY.

Trial registration: NCT02561065.

Submitted September 22, 2016; accepted November 8, 2016.

Reprint requests: Valentin Fuster, MD PhD. Physician-in-Chief, Mount Sinai Medical Center. Director, Mount Sinai Heart. Icahn School of Medicine at Mount Sinai. One Gustave L. Levy Place, Box 1030 New York City, NY 10029 + General Director, Centro Nacional de Investigaciones Cardiovasculares Carlos III (CNIC).

E-mail: valentin.fuster@mountsinai.org

0002-8703

http://dx.doi.org/10.1016/j.ahj.2016.11.002

has demonstrated an additional value of SAPB quantification with imaging techniques (coronary artery calcium score [CACS] and carotid 3D ultrasonography) to classical risk factors for CVD risk prediction.[4]

A healthy lifestyle that includes being physically active, not sitting too much, eating a healthy diet, and not smoking will contribute to improved cardiovascular health.[5-11]

WHO has identified the workplace as a key setting for promoting a healthy lifestyle for the prevention and control of noncommunicable diseases.[12] A number of reviews have indicated that worksite health promotion programs can be effective in promoting healthy lifestyle, including improving physical activity, sedentary and dietary behaviors, as well as smoking cessation.[13-19] Positive effects of such lifestyle interventions on work-related outcomes have also been reported and include improvements in sickness absenteeism, presenteeism, and work ability.[14,20-22]

The Progression and Early detection of Subclinical Atherosclerosis (PESA) cohort started in 2010 and consists of 4,184 asymptomatic adult bank employees of the *Banco de Santander* Headquarters in Madrid, Spain (PESA: NCT01410318). PESA evaluates the presence and progression of subclinical atherosclerotic lesions in the carotid, aortic, coronary, and iliofemoral territories using noninvasive advanced imaging techniques.[23] The value of SAPB identification and stratification driven by imaging data in a 30-month worksite-based lifestyle program will be assessed in the current TANSNIP-PESA study (Trans-Atlantic Network to study Stepwise Non-invasive Imaging as a tool for CVD Prognosis and prevention) nested within the cohort study. The network consists of experts in the fields of CVD imaging, diagnostics, worksite health promotion, and clinical trials who are carrying out several studies in the subclinical atherosclerosis field with the unifying purpose of enhancing SAPB stratification and enabling novel targeted therapies and SAPB reduction strategies. The current TANSNIP-PESA study is linked to the cohort study.

Study objectives

The primary objective of the TANSNIP-PESA study is to determine the effectiveness and cost-effectiveness of a comprehensive 30-month worksite-based lifestyle program in a population of asymptomatic bank employees from the PESA cohort who have either a high or a low degree of imaging-defined SAPB. The primary outcome measure is the adapted Fuster-BEWAT CVD risk and lifestyle composite score, and secondary outcome measures include physical activity, sedentary time, standing time, diet, smoking, anthropometric measures, blood biomarkers, self-rated health, work-related outcomes, health care consumption, program process measures, and cost measures.

The secondary objective is to determine whether the level of compliance with and effectiveness of the lifestyle program is different in those having a high degree of SAPB compared with those with a low degree of SAPB. Because of the higher urgency in the high-SAPB group, we hypothesize that this group will be more receptive to the intervention.

Methods

Trial design

A randomized controlled trial (RCT) stratified by SAPB will be conducted, nested within the PESA cohort.[23] Our target population will be 4,184 middle-aged (40-60 years) bank employees of the Banco de Santander Headquarters in Madrid (Spain) who are currently part of the PESA cohort. One arm (n = 260) will focus on a sample of bank employees drawn from the PESA cohort with a high degree of imaging-defined SAPB, and the second arm (n = 590) will be conducted on a sample of the PESA cohort drawn from the group with a low degree of imaging-defined SAPB (Figure 1). In both stratified SAPB arms, the participants will be randomized into a lifestyle program or into standard care for a 3-year period after completing the baseline assessments that will consist of completing several questionnaires, wearing for 7 consecutive days the activPAL activity monitor, and drawing a fasting blood sample. Primary follow-up assessments will be done at year 1, year 2, and year 3 for both standard-care and intervention group. Each participant in the standard-care group will receive care as usual, provided by their own occupational physician and other possible care providers. Participants in the intervention group will receive the intervention on top of standard care.

Primary follow-up assessments will be done at year 1, year 2, and year 3. The study protocol has been approved by the Ethics Committee of Instituto de Salud Carlos III in Madrid. All participants will provide written informed consent. The study will follow the Consolidated Standards of Reporting Trials guidelines.[24]

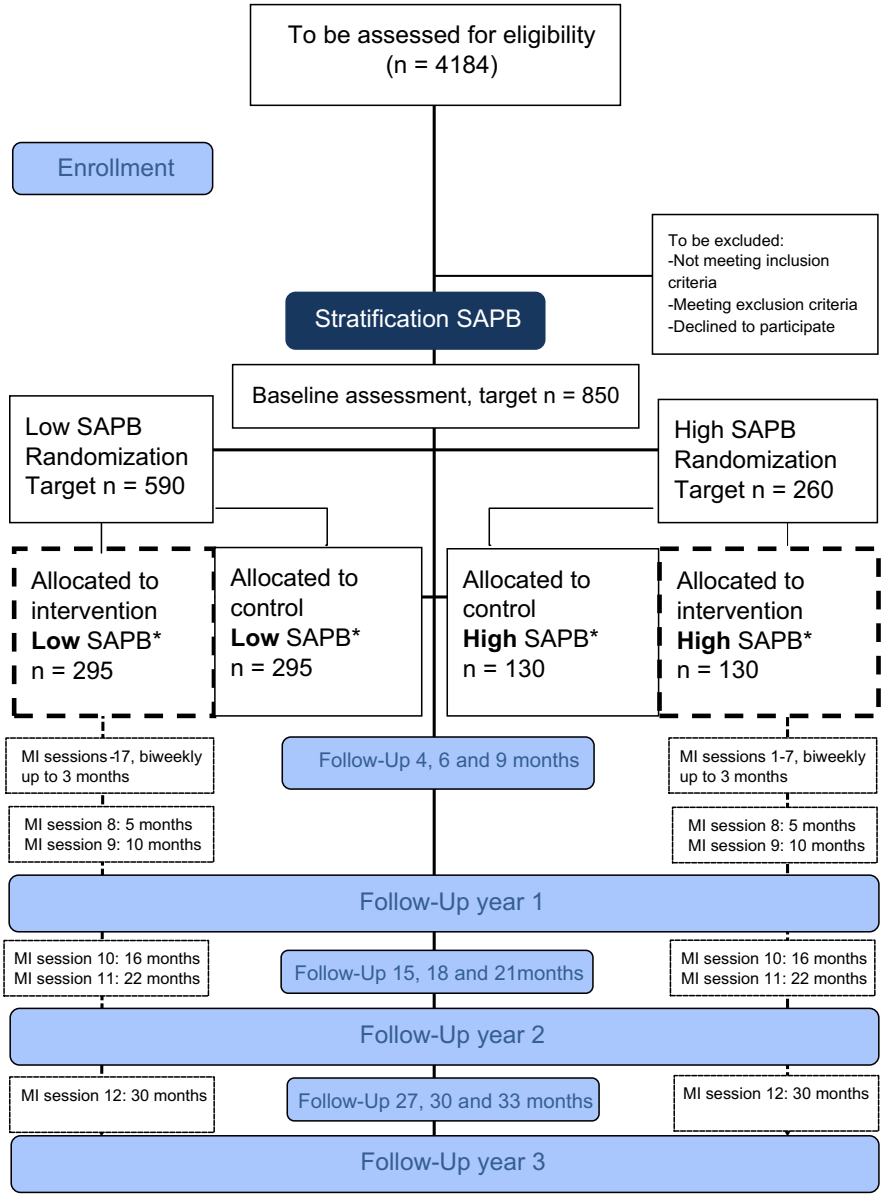
Participants

Participants who comply with the criteria stated in Table I will be eligible for participation in the RCT. High or low degree of imaging-defined SAPB will be determined based on noninvasive vascular imaging data from the PESA cohort study. *Subclinical atherosclerosis* is defined as the presence of atherosclerotic plaques by using 2D ultrasonography of the carotids, abdominal aorta, and iliofemoral arteries or by assessment of CACS by computed tomography (CT).[25]

Randomization and blinding

A stratified computerized fixed block randomization will take place at the individual level after collection of all baseline information. Participants will be stratified

Figure 1



SAPB= Subclinical Atherosclerotic Plaque Burden.

Study flowchart.

according to a high or low degree of imaging-defined SAPB. Group allocation will be concealed for research staff involved in data collection and cleaning.

Recruitment

The study will take place at Banco de Santander Headquarters in Madrid (Spain). Eligible participants will be recruited from May 2015 until the end of 2016. Information sessions will be organized for all participants of the PESA cohort study to introduce the RCT and to present the main aims and procedures of the study. Recruitment emails will be sent to all 4,184 PESA cohort participants with a link to express online interest in participation. Interested individuals will be invited to a visit with the research nurse to further explain the study, to answer remaining questions, to obtain written informed consent for participation in the study, and to complete the baseline assessment. At the time of submission of this article, 712 participants were included.

Table I. Inclusion and exclusion criteria

Inclusion criteria	• Employees aged 40 to 60 y from the PESA cohort study; • Employees that will complete all 3 baseline assessment elements (ie, wearing an activPAL, drawing blood, and completing the questionnaire); • Employees that can be stratified into a high or low degree of imaging-defined SAPB. *High degree of imaging-defined SAPB* will be defined as a high burden of atherosclerotic disease detected either by 2D ultrasonography (upper tertile sum of maximum thickness of the plaques or CACS Agatston score by CT $\geq$ 1 point).[23] *Low degree of imaging-defined SAPB* will be defined as having a CACS Agatston score of zero and no plaque by 2D ultrasonography or being in the lowest 2 tertiles of plaque burden.[25] Participants without plaque burden but with a BMI $\geq$ 25 or reporting at least 1 unhealthy lifestyle behavior in their last PESA visit (ie, <150 min/wk of at least moderate-intensity physical activity assessed by accelerometer, sitting >7 h/d as assessed by accelerometer, not meeting Mediterranean diet guidelines as assessed by a computerized dietary history tool previously developed and validated in the EPIC-Spain study[26] and adapted by ENRICA investigators,[27] or smoking) will also be included in the low SAPB group.
Exclusion criteria	• Employees that have prior CVD history (myocardial infarction, angina pectoris, stroke, peripheral vascular disease, aortic aneurysm, angioplasty, heart surgery, atrial fibrillation, or any other heart disease); • Active treatment for cancer, history of transplant with active immunosuppressive or immunomodulator treatment; • Morbid obesity (body mass index $\geq$40 kg/m^2); • Any disease that decreases life expectancy to $\leq$3 y; • Employees will also be excluded if they are pregnant or lactating; • Or any condition that could affect adherence to the study procedures; • Employees without plaque burden, with a healthy BMI, and with a healthy lifestyle will be excluded from the RCT.

Lifestyle intervention program

The lifestyle program takes a socioecological approach.[28] The socioecological model of health promotion combines different approaches, focusing on making changes to the individual as well as to the social, physical, and/or organizational environment. This is in line with the WHO "healthy workplace model," which has emphasized that best practice interventions should involve individual, environmental, and organizational change components.[29]

The program has been developed in a systematic way using basics derived from the intervention mapping protocol,[30] such as a needs assessment, definition of program objectives, individual and environmental strategy selection, defining content program, and piloting. A blueprint for the program was developed in cooperation with employees from Banco de Santander in Madrid. End-user tailoring and involvement included (1) mapping lifestyle-related cardiovascular risk factors of the PESA cohort study participants, (2) mapping existing lifestyle policies of Banco de Santander and key determinants of lifestyle behaviors through focus group interviews with end-users, and (3) performing an environmental audit at Banco de Santander by investigating the presence of facilities for promoting a healthy lifestyle. After this, the following 3 program objectives were formulated: (1) increasing daily physical activity by reaching at least 10,000 steps per day, (2) reducing sedentary time by alternating sitting and standing throughout the day, and (3) promoting healthy eating with a strong focus on adopting a Mediterranean diet.

The program integrates 3 key components: (*a*) 12 motivational interviewing (MI) sessions that will be conducted by a trained psychologist over a 30-month period, (*b*) a wrist-worn physical activity tracker with smartphone connectivity, and (*c*) a sit-stand workstation to provide more opportunity to alternate between sitting and standing during work.

Participants randomized to the standard care group will not receive the lifestyle program but care as usual, at the discretion of their occupational physician (which could involve informing the employee about his CVD risk profile) and other possible care providers. Participants in the intervention group will receive the program on top of standard care.

A. *Personalized lifestyle counseling*

Trained psychologists will provide the participants 12 MI sessions over a period of 30 months. Well-established behavioral change strategies will be integrated in the MI sessions, including self-monitoring, goal setting, planning, reinforcement, relapse prevention, and overcoming barriers. The psychologist will tailor the intervention to the participant's specific needs and preferences. The MI sessions will also be aimed at raising awareness of the employees' PESA-assessed SAPB/cardiovascular health profile. The first 7 MI counseling sessions will take place biweekly over the first 3 months (0, 2, 4, 6, 8, 10, and 12 weeks) and will last for approximately 1 hour. The eighth counseling session will be at 5 months followed by

sessions at 10, 16, 22, and 30 months (all booster sessions), all lasting 30 minutes. Details on the content of the MI sessions can be found in the supplemental appendix.

The use of the physical activity tracker and sit-stand workstation is an integral part of all MI sessions and will be included in personal goals and action plans. Attention will be paid during all sessions to the social environment by incorporating possible social support from family, friends, and colleagues. The MI sessions will also use a workbook for the participant to refer back to, which summarizes the intervention content session by session. The workbook will also be used to record specific short- and longer-term behavioral change goals and action plans, which the participant will formulate with the assistance of the coach. The workbook will also provide helpful examples of behavior change, healthy lifestyles, and useful tools. Furthermore, participants can visit the specific Facebook page of the intervention group for extra information on lifestyle behaviors through appealing graphics, illustrations, and videos posted by the research team, as well as to share experiences with other intervention participants.

Personal progress will be registered in the intervention database for the psychologist to review and prepare future sessions. The psychologists will receive an initial 2-day training in MI by a Spanish MI expert and will have 3 coaching feedback sessions with the same MI expert over Skype. Adherence to MI techniques will be assessed by Motivational Interviewing Treatment Integrity (MITI)[31] scoring every 6 months. These scores will be used in the feedback session to improve further the skills of the psychologists. The MITI score that will be obtained on the second day of the initial MI training will serve as reference for future MITI scores.

B. *Physical activity tracker*

Participants in the current program will receive the Fitbit Flex at MI session 2. This is a next-generation activity tracker with wireless smartphone, tablet, and computer connectivity. The Fitbit allows participants to use common effective behavioral change techniques, such as self-monitoring, goal setting, real-time feedback, and simple rewards systems. A personalized dashboard on the Fitbit Web site provides summaries of the participant's physical activity, stimulating prompts and rewards, and allows for social media sharing. Within the Fitbit Web site, a separate group has been created for the intervention group. This allows participants to anonymously benchmark their personal scores against the average daily step score of the whole intervention group. The Fitbit use will be an integral part of the MI sessions.

C. *Sit-stand workstation*

Participants will receive an Ergotron sit-stand workstation (model Workfit P or T) in the first few weeks of the program (MI session 3). This can be integrated into a normal working desk. The sit-stand workstation use will be an integral part of the MI sessions.

Outcome assessments

Timing of assessments

Each participant will have 4 study visits: baseline and 1-, 2-, and 3-year follow-up (Figure 1). Each study visit includes anthropometric assessments, blood collection for cardiometabolic biomarkers, wearing an activPAL activity monitor for 7 consecutive days, and online completed questionnaires. Additional online questionnaires will be completed at 4 and 6 months after baseline to map intermediary behavior change. Furthermore, data for the economic evaluation on sickness absenteeism, presenteeism, and health care utilization will be collected each 3 months up to 36 months. Quantitative data for the process evaluation will be collected at 4, 12, 24, and 33 months. Information about translation of the questionnaires is given in the appendix. Qualitative data collection for process evaluation purposes will be completed with varying groups after the first 7 MI sessions, after MI session 9, and after MI session 12. All assessments and outcomes are summarized in Table II.

After providing written inform consent at the research center, a research nurse will perform the physical baseline assessments and provide participants with an activPAL activity monitor. After wearing the activPAL for 7 full days, it is returned by mail to the research center. The participant will receive the link to the online baseline questionnaire (to a secured database) by e-mail after the inclusion visit. At all follow-up measurements, the same order of assessments will be applied.

Primary outcome adapted Fuster-BEWAT score

The primary outcome measure is an adapted version of the Fuster-BEWAT score.[32] This is a CVD risk and lifestyle composite score, which consists of systolic and diastolic blood pressure (BP), physical activity, sedentary time, body mass index, fruit and vegetable consumption (as a proxy for overall diet), and smoking (Table III). The adapted Fuster-BEWAT will be assessed at baseline and at 1-, 2-, and 3-year follow-up. The initial Fuster-BEWAT score will also be calculated in addition as a secondary outcome for future testing of psychometric properties of the adapted Fuster-BEWAT score.

Secondary outcomes

Secondary outcomes are individual changes in mean scores of lifestyle behaviors (including physical activity, sedentary time, standing, diet, and smoking) as well as

Table II. Overview of outcomes used in the study

		Follow-up assessments (m)											
Outcome	Baseline	4	6	9	12	15	18	21	24	27	30	33	36
Adapted Fuster-BEWAT	X				X				**X**				**X**
Original Fuster-BEWAT	X				X				**X**				**X**
Objective physical activity/sedentary time													
activPAL activity monitor	X				X				**X**				**X**
Self-reported lifestyle behaviors													
Physical activity (IPAQ short)	X	X	X		X				**X**				**X**
Occupational activity (OSPAQ)	X	X	X		X				**X**				**X**
Sedentary behavior (WSQ)	X	X	X		X				**X**				**X**
Standing	X				X				**X**				**X**
Diet (MEDAS)	X	X			X				**X**				**X**
Smoking status	X				X				**X**				**X**
Sleeping (Sleep Habits Questionnaire)	X				X				**X**				**X**
Physical assessments													
Waist circumference	X				X				**X**				**X**
Body height	X												
Body weight	X				X				**X**				**X**
Blood pressure	X				X				**X**				**X**
Cardiometabolic biomarkers													
Complete blood count and chemistry panel	X				X				**X**				**X**
Specific biomarkers related to subclinical atherosclerosis	X				X								
Psychosocial assessments													
Depression (CES-D)	X				X				**X**				**X**
Perceived stress (PSS-14)	X				X				**X**				**X**
Social support (ESSI)	X				X				**X**				**X**
Job strain (JCQ)	X				X				**X**				**X**
Quality of life (EQ-5D-5L)	X				X				**X**				**X**
Relaxation and detachment (RECQ)	X				X				**X**				**X**
Self-rated Health (EQ VAS)	X				X				**X**				**X**
Vitality (VITA-16)	X				X				**X**				**X**
Personal characteristics													
Age	X												
Gender	X												
Marital status	X				X				**X**				**X**
Working h/wk	X				X				**X**				**X**
Employment status	X				X				**X**				**X**
Job type	X				X				**X**				**X**
Income	X				X				**X**				**X**
Education level	X				X				**X**				**X**
Economic evaluation													
Sickness absenteeism (WHO-HPQ)		X	X	X	X	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Presenteeism (WHO-HPQ)		X	X	X	X	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Health care consumption		X	X	X	X	**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Process evaluation													
Participant questionnaire		X			X				**X**		**X**		
Participant focus group interview		X			X						**X**		
Psychologist checklist			X		X		**X**		**X**		**X**		
Psychologist individual interview			X		X		**X**		**X**		**X**		
MITI scoring			X		X		**X**		**X**		**X**		
Stakeholder checklist					X				**X**				**X**
Stakeholder interview					X				**X**				**X**
Linkage to PESA													
Noninvasive imaging 2D/3D ultrasonography and CACS-CT					X								

IPAQ, International Physical Activity Questionnaire; *OSPAQ*, Occupational Sitting and Physical Activity Questionnaire; *WSQ*, Workforce Sitting Questionnaire; *MEDAS*, Mediterranean Diet Adherence Screener; *CES-D*, Center for Epidemiologic Studies Depression Scale; PSS, Perceived Stress Scale; *ESSI*, ENRICHD Social Support Instrument; *JCQ*, job content questionnaire; *EQ-5D-5L*, EuroQol five dimensions questionnaire; *RECQ*, recovery experience questionnaire; *EQ VAS*, EuroQol Visual Analogue Scale; *VITA-16*, Vitality 16-item questionnaire; *WHO-HPQ*, WHO Health and Work Performance Questionnaire; MITI, Motivational Integrity score; *PESA*, Progression of Early Subclinical Atherosclerosis' cohort; *CACS-CT*, Cardiac CT for Calcium Scoring.

Table III. Scoring of different elements of the adapted Fuster-BEWAT primary outcome measure.

Score	0	1	2	3	4
Systolic/diastolic blood pressure* (mm Hg)	≥140/90	134-139/87-89	128-133/84-86	121-127/81-83	≤120/80
Physical activity (steps/d)	<5500	5500-6999	7000-8499	8500-9999	≥10,000
Sitting (h/d)	≥12.5	11- < 12.5	9.5- < 11	8- < 9.5	<8
BMI (kg/m^2)†	≥32	30-31.9	27-29.9	25-26.9	<25
Fruit & vegetable consumption (servings/d)	≤1	2	3	4	≥5
Smoking (units/d)	>20	10-20	1-9	<1	0

Total score ranges from 0 to 24, with a higher score indicating a lower risk score.
* If systolic and diastolic blood pressures do not fall in the same group, then the participant is assigned to the group with the relatively highest blood pressure (ie, systolic or diastolic).
† At follow-up visits, a >5% decrease in BMI will add 1 extra point in the BMI score except for those participants who have changed BMI categories since baseline or are already in the normal-weight category (BMI <25). Similarly, a >5% increase in BMI at follow-up will mean 1 point less in the BMI score except for participants who have changed BMI categories since baseline or with BMI ≥32.

changes in anthropometric measures, blood biomarkers, self-rated health, work-related outcomes, health care consumption, program process measures, and cost measures at different measurement points.

Lifestyle behaviors assessments

Physical activity and sedentary time will be objectively assessed with an activPAL activity monitor (PAL Technologies Limited, Glasgow, UK) attached to the front of the participant's thigh for at least 7 consecutive full days. Research has shown that this activPAL activity monitor is valid and responsive.[33,34] Participants will also daily complete a short diary reporting the exact wearing times (ie, the time at which the activPAL was put on and off) and the times of starting and finishing work (ie, to determine the exact wearing time at work). The physical activity and sedentary behavior data from the activPAL will also be used for the primary outcome, the adapted Fuster-BEWAT score. The following questionnaires regarding physical activity and sedentary behavior will be administered: the International Physical Activity Questionnaire short form (7 items)[35]; the Occupational Sitting and Physical Activity Questionnaire to assess time spent sitting, standing, and activity at work[36]; the Workforce Sitting Questionnaire measuring total and domain-specific sitting time based on working and nonworking days[37]; and single questions to assess average daily standing.

Data on dietary habits will be collected with the Mediterranean Diet Adherence Screener (MEDAS).[38] MEDAS is a short 14-item questionnaire aimed to assess adherence to a Mediterranean Diet. MEDAS has 2 items asking about fruit and vegetable consumption. Smoking status will be a self-reported measure, as well as the average number of cigarettes or other tobacco products consumed daily. Furthermore, sleeping will be measured using the Sleep Habits Questionnaire consisting of 21 items developed by the Sleep Heart Health Study.[39]

Physical assessments

Waist circumference, body height, body weight, and BP will be measured at the research center and will all be registered in the database. Waist circumference will be measured twice with a tape measure to the nearest 0.1 cm at the midpoint between the lower border of the ribs and the iliac crest. Body height will be measured on bare feet using a stadiometer (Asimed Height Rod HM-200M) to the nearest 0.1 cm. Body weight will be measured using the Asimed HM-200M scale on bare feet and wearing only light garments. Body mass index (BMI; kg/m^2) will be calculated from the body height and weight obtained from the above measurements. BP (in mm Hg) will be assessed 3 times with a fully automated BP monitor (OMRON HBP 1300), and all measurement points are to be registered in the database. The cuff will be placed on the right upper arm while the arm is rested on a table.

Cardiometabolic biomarkers

Complete blood count and chemistry panel will be obtained at baseline and at every follow-up visit. Specific biomarkers related to subclinical atherosclerosis will be analyzed at baseline and at follow-up year 1. A preliminary list of the planned biomarkers to measure is provided in the Appendix. Approximately 40 mL will be drawn during the baseline visit. Baseline blood samples will also be stored at −80°C for future omics (proteomics and metabolomics) analysis. Each aliquot will have a unique identifier by using a laboratory information management system to guarantee an accurate tracking of all procedures. The sample will be analyzed by an accredited laboratory.

Psychosocial assessment

Participants will complete validated psychosocial questionnaires. Depression will be measured using the 20-item Center for Epidemiologic Studies Depression Scale.[40] Perceived stress will be measured using the 14-item Perceived Stress Scale.[41] Social support will be measured using the official Spanish-translated ENRICHD Social Support Instrument, which is a 7-item self-report survey to test emotional, informational, instrumental, and appraisal support.[42] Job strain will be measured with an

adapted version of the official Spanish translation of the Job Content Questionnaire (JCQ) from the job content center using 17 items of the original 35 JCQ items.[43] The JCQ assesses skill discretion (eg, learning new things, developing own abilities), decision authority (eg, allows own decisions), psychological job demands (eg, work fast, conflicting demands), and job insecurity (eg, steady work). Quality of life will be self-reported using the EuroQol (EQ-5D-5L),[44] which consists of 5 dimensions (ie, mobility, self-care, usual activities, pain/discomfort, anxiety/depression) and 5 report levels (ie, no problems, slight problems, moderate problems, severe problems, and extreme problems). Self-rated health will be assessed with the EuroQol Visual Analogue Scale. Relaxation and detachment after work will be measured using 8 items from the Recovery Experience Questionnaire.[45] Vitality will be measured using the Vitality 16-item questionnaire, which assesses energy, motivation, and resilience.[46]

Personal characteristics

Sociodemographic information, including age, gender, marital status, working hours per week, job status, job type, income and education level, will be assessed.

Economic evaluation

To evaluate the cost-effectiveness of the lifestyle program, sickness absenteeism, presenteeism (ie, working while feeling ill), and health care consumption (eg, general practitioner, allied health professionals, complementary medicine consumption) will be assessed every 3 months until 36 months after baseline. Sickness absenteeism and presenteeism will be assessed with items from the WHO Health and Work Performance Questionnaire (WHO-HPQ).[47] Presenteeism is conceptualized in the WHO-HPQ as a measure of actual work performance in relation to best performance, irrespective of the presence or absence of health complaints. Sickness absenteeism will be self-reported using the WHO-HPQ in hours per month.

Process evaluation

The RCT also include a process evaluation, which is based on the framework of evaluating complex interventions.[48] The feasibility of the program will be investigated using quantitative and qualitative methods on 3 levels: the participant, the psychologist, and the stakeholder. Further details are given in the Appendix.

Linkage to data collected in PESA

The RCT is linked to the PESA cohort study. In PESA, a wealth of data is collected, including behavioral lifestyle, anthropometric, blood biomarker, and imaging outcomes, which have been described in detail elsewhere.[23] Within the PESA cohort, participants are assessed at the PESA baseline and 3 and 6 years after baseline. Participants of the current RCT have all completed their PESA baseline assessment and at time of inclusion in the RCT are due in 1 year's time for either their 3-year or their 6-year PESA assessment. The noninvasive imaging techniques that are performed in PESA include: 2D ultrasonography (2D-US) of carotids, abdominal aorta and iliofemoral arteries, 3D ultrasonography (3D-US) of carotid and femoral arteries, and CACS by CT scanning. Participants with a high degree of SAPB will additionally receive advanced imaging consisting of fludeoxyglucose positron emission tomography–magnetic resonance imaging of carotid and iliofemoral territories.

Sample size

Based on baseline information (n = 4,149) from the PESA cohort study on the adapted Fuster-BEWAT score (low degree of SAPB mean score [SD] = 14.53 [3.49]; high degree of SAPB mean score [SD] = 13.28 [3.79]), 2 separate statistical power calculations were performed. For both power calculations a power of 80% and an α of 5% is used, with an anticipated dropout of no more than 20% over 3 years. The 2 power calculations revealed that the following sample sizes would be able to detect clinically relevant changes in the primary outcome:

I. If the *low degree of SAPB arm* would recruit 590 participants: a change of 0.89 in the adapted Fuster-BEWAT score would be detectable. On the PESA baseline score, this would translate in a detectable relative change of 6.13%.
II. If the *high degree of SAPB arm* would recruit 260 participants: a change of 1.45 in the adapted Fuster-BEWAT score would be detectable. On the PESA baseline score, this would translate in a detectable relative change of 10.92%.

Given our previous experience with lifestyle intervention studies using outcomes such as the BEWAT score, we are well powered to detect change that would be clinically relevant and thus meaningful for the respective cohorts.[32] Furthermore, a larger effect is anticipated in the high degree of SAPB arm, as there is more room for improvement. Finally, the sample sizes for both arms are limited by the boundaries of the sampling pool size of the PESA cohort.

Statistical analyses

Effectiveness analyses

Linear mixed effect models with outcome as the dependent variable will be performed on an intention-to-treat basis; the group (intervention vs standard care) will be modeled as independent variable and time of follow-up measurements (T1, T2, and T3) as fixed factor, while we will adjust for the baseline value of the primary outcome. Per-protocol analyses will be performed to investigate the effects of the intervention in participants with high compliance to the lifestyle

program. For all analyses, a 2-tailed significance level of $P < .05$ will be considered statistically significant. All analyses will be performed with SPSS 20.0 (SPSS Inc, Chicago, IL).

Cost-effectiveness analyses

The cost-effectiveness analyses will take a societal and employer's perspective. Analyses will be performed according to the intention-to-treat principle. In the main analysis, missing economic data will be imputed using multiple imputation techniques.[49] Sensitivity analyses will be done to assess the robustness of the results. Total societal and employer's costs will be estimated and compared between the intervention and control group. The 95% confidence intervals will be estimated using approximate bootstrap confidence intervals.[50] Societal costs will include all cost measures described above in the outcome section. For the employer's perspective, only costs relevant to the employer will be included (ie, intervention and productivity-related costs: consisting of sickness absenteeism and presenteeism). For the cost-effectiveness analysis, incremental cost-effectiveness ratios will be calculated by dividing the difference in costs between groups to their difference in effects on the primary outcome measure (societal perspective), and outcome measures relevant to the company (employer's perspective). Bootstrapped cost-effect pairs will be graphically presented on cost-effectiveness planes.[51] Cost-effectiveness acceptability curves will be generated showing the probability for cost-effectiveness of the intervention at different ceiling ratios.

Discussion

This article describes the study protocol of an RCT whose primary objective will be to determine the effectiveness of a 30-month worksite-based program that aims to promote cardiovascular health through improving lifestyle behaviors in participating middle-aged bank employees with a high or low degree of SAPB. The RCT will also determine whether participant's awareness of their degree of SAPB will influence their compliance with the lifestyle program as well as its effectiveness.

The trial will include a comprehensive evaluation with state-of-the-art assessment tools including objective assessments of physical activity and sedentary behavior, anthropometrics and blood biomarkers, psychosocial and work-related outcomes, as well as an economic and a process evaluation. The current program is theory driven and systematically designed to improve cardiovascular health. The participants will receive 12 MI sessions. MI is a collaborative, goal-oriented counseling style that can be translated into 4 generic principles, namely, expressing empathy by reflective listening, identifying discrepancies between participant's goals and current behavior, rolling with resistance by adjusting to participant's resistance rather than opposing it, and supporting self-efficacy.[52] Previous systematic reviews and meta-analyses have revealed that MI is effective in facilitating behavioral change across a range of lifestyle domains.[53-55] Furthermore, the participants will receive a physical activity tracker. The Lancet special issue on physical activity showed that pedometers were the most effective intervention tool to improve physical activity.[56] The last intervention program component involves a sit-stand workstation. Recent literature reviews have shown that lifestyle programs can reduce sedentary time.[16] For the workplace setting, especially sit-stand workstations have been shown to be effective in reducing occupational sitting time, albeit longer-term studies are needed to determine maintenance and long-term impact on behavioral, work, and health outcomes.[17] Sit-stand workstations allow employees to adjust the height of their workstation, including the computer screen, keyboard, and mouse, and allows them to easily switch between sitting and standing throughout the working day. Reductions in sedentary time are most successfully achieved by incorporating environmental modifications (such as a sit-stand workstation) and self-regulatory skills training (such as MI).[57] The current study will be one of the first to evaluate longer-term effectiveness of sit-stand workstations, as well as their impact on health and work-related outcomes.

Another strength is that the study is closely linked to the existing PESA cohort study, which has the advantage that more and better data will be available on the lifestyle behaviors and health of the participants in the RCT. This will allow for studying natural temporal changes in lifestyle behaviors and SAPB pre-, during, and post- RCT over a 6- to 8-year period within the control group and, more importantly, how the lifestyle program impacted on these changes in the intervention group. The link to the PESA cohort also makes state-of-the-art SAPB imaging data available for the RCT participants as well as longitudinal blood biomarker data.

The focus of the lifestyle program to achieve long-term behavior change and the integration of MI maintenance sessions starting at 5 months up to 30 months after baseline are also a strength of the TANSNIP-PESA study. Most lifestyle programs are often focused on short-term behavioral change, and few studies have a follow-up assessment beyond 1 year postbaseline. As only longer-term behavioral lifestyle changes can have a lasting impact on cardiovascular health, the current study also includes assessments at 2- and 3-year follow-up.

If shown to be (cost-)effective, the lifestyle program has the potential to be implemented and evaluated in other work settings. The role of SAPB imaging in identifying at-risk populations and its possible role in motivating people through SAPB communication integrated in lifestyle programs could be crucial in achieving better

compliance and higher effectiveness in lifestyle programs. Nevertheless, implementation of structural SAPB screening might also be challenging because of cost implications. However, advances in technology make noninvasive testing of SAPB more widely available, and this is likely to provide new windows for opportunities at community and worksite level to prevent or detect atherosclerosis at an early stage. This is in line with other screening examples such as the early detection and prevention of breast cancer and colon cancer. Implementation of screening for SAPB needs to be founded on strong evidence and requires extensive study on health benefits and cost efficiency.

A limitation of the study is that the sample is not truly population based but rather a convenience sample. Although this may limit generalizability to the general population, our study results will be broadly applicable to worksite wellness programs involving middle-aged professionals. Like other lifestyle program RCTs, our study may suffer from selection bias related to the level of motivation with regard to willingness to adopt a healthier lifestyle. To address this limitation, we will compare data for those who participate in the RCT and those who do not using the rich data available for the target population (ie, participants in PESA). The link between the current RCT and PESA not only is a strength but also comes with some challenges. Especially, the coordination between the RCT, PESA, and the bank's occupational health service will require coordination efforts. Furthermore, participation in both the RCT and PESA might also influence the results of both studies, as the assessments and participation in the SAPB imaging might influence participant's lifestyle behaviors. It is, for example, possible that those in the control group who are aware of their high SAPB will attempt to improve their lifestyle, which would make the SAPB screening an intervention in itself. Nevertheless, long-term behavior lifestyle change is challenging, and if the extensive lifestyle program offered to the intervention group cannot do better than a possibly self-motivated control group, it is probably not worth pursuing further, and the SAPB screening in itself might be sufficient.

In conclusion, the TANSNIP-PESA study will provide insights into the effectiveness of a worksite-based lifestyle program to promote cardiovascular health compared with standard care in participants with a high or low degree of imaging-defined SAPB.

Financial support

TANSNIP-PESA is funded by Fundación Centro Nacional de Investigaciones Cardiovasculares Carlos III with support from an Investigator Sponsor Study grant to Icahn School of Medicine from AstraZeneca. PESA is funded by Fundación Centro Nacional de Investigaciones Cardiovasculares Carlos III and Grupo Santander. The CNIC is supported by the Spanish Ministry of Economy and Competitiveness (MINECO) and the Pro-CNIC Foundation, and is a Severo Ochoa Center of Excellence (MINECO award SEV-2015-0505). The funders have not been involved in the design and conduct of the study, nor were they involved in the drafting of the manuscript and its final content.

Author contributions

The TANSNIP-PESA consortium led by V. F. obtained funding for the research. All authors have contributed to the design of the study. The first draft of this manuscript was produced by JC and HvdP. All authors have read and approved the final manuscript.

Acknowledgements

We thank the participants in the study and gratefully acknowledge the collaboration and technical assistance of the medical services staff at Banco de Santander in Madrid. Special thanks to Magdalena García Lopez and Emilio Marín Manzano from Banco de Santander for their tremendous help in making the RCT possible. We would also like to thank Sergio Cárdenas Melero and Jesús Molina Carretero for their excellent ICT support. Finally, we are extremely grateful to the PESA team for their support in integrating the RCT with PESA.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ahj.2016.11.002.

References

1. Bloom DE, Cafiero ET, Jané-Llopis, et al. *The global economic burden of non-communicable diseases. Geneva: World Economic Forum, Harvard school of Public Health. 2011.*
2. Leal J, Luengo-Fernandez R, Gray A, et al. Economic burden of cardiovascular diseases in the enlarged European Union. Eur J Heart 2006;27:1610-9.
3. Mozaffarian D, Benjamin EJ, Go AS, et al, On behalf of the American Heart Association Statistics committee and Stroke Statistics Subcommittee. Executive summary: Heart Disease and Stroke Statistics—2015 update: a report from the American Heart Association. Circulation 2015;131:e29-322.
4. Baber U, Mehran R, Sartori S, et al. Prevalence, impact, and predictive value of detecting subclincial coronary and carotid atherosclerosis in asymptomatic adults: the BioImage study. J Am Coll Cardiol 2015;24:1065-74.
5. Proper KI, Singh AS, van Mechelen W, et al. Sedentary behaviors and health outcomes among adults: a systematic review of prospective studies. Am J Prev Med 2011;40:174-82.
6. Thorp AA, Owen N, Neuhaus M, et al. Sedentary behaviors and subsequent health outcomes in adults: a systematic review of longitudinal studies, 1996-2011. Am J Prev Med 2011;41:207-15.

7. van Uffelen JG, Wong J, Chau JY, et al. Occupational sitting and health risks: a systematic review. Am J Prev Med 2010;39:379-88.
8. WHO. *Global recommendations on physical activity for health. Geneva: World Health Organization. 2010.*
9. Wilmot EG, Edwarson CL, Achana FA, et al. Sedentary time in adults and the association with diabetes, cardiovascular disease and death: systematic review and meta-analysis. Diabetologia 2012;55: 2895-905.
10. Wolf PA, D'Agostino RB, Kannel WB, et al. Cigarette smoking as a risk factor for stroke. The Framingham Study. JAMA 1988;259:1025-9.
11. World Health Organization. *WHO global strategy on diet, physcial activity, and health. 2002. [Geneva].*
12. World Health Organization Europe. *Action plan for implementation of the European Strategy for the Prevention and Control of Noncommunicable Diseases 2012-2016. 2012. [Copenhagen, Denmark].*
13. Hutchinson AD, Wilson D. Improving nutrition and physical activity in the workplace: a meta analysis of intervention studies. Health Promot Int 2012;27:238-49.
14. Conn VS, Hafdahl AR, Cooper PS, et al. Meta-analysis of workplace physical activity interventions. Am J Prev Med 2009;37: 330-9.
15. Proper KI, Koning M, Van der Beek AJ, et al. The effectiveness of worksite physical activity programs on physical activity, physical fitness, and health. Clin J Sport Med 2003;13:106-17.
16. Martin A, Fitzsimons C, Jepson R, et al. Interventions with potential to reduce sedentary time in adults: systematic review and meta-analysis. Br J Sports Med 2015:1056-63.
17. Neuhaus M, Eakin EG, Straker L, et al. Reducing occupational sedentary time: a systematic review and meta-analysis of evidence on activity-permissive workstations. Obes Rev 2014;15:822-38.
18. Cahill K. Workplace interventions for smoking cessation. Cochrane Database Syst Rev 2008;4:1-126.
19. KD L. Worksite-based incentives and competitions to reduce tobacco use. A systematic review. Am J Prev Med 2010;38:S263-74.
20. Cancelliere C, Cassidy JD, Ammendolia C, et al. Are workplace health promotion programs effective at improving presenteeism in workers? A systematic review and best evidence synthesis of the literature. BMC Public Health 2011;11:1-11.
21. Kuopalla J, Lamminpaa A, Husman P. Work health promotion, job well-being, and sickness absenses—a systematic review and meta-analysis. J Occup Environ Med 2009;50:1216-27.
22. Rongen A, Robroek SJW, Van Lenthe FJ, et al. Workplace health promotion: a meta-analysis of effectiveness. Am J Prev Med 2013;44: 406-15.
23. Fernández-Ortiz A, Jiménez-Borrreguero LJ, Penalvo JL, et al. The Progression and Early Detection of Subclinical Atherosclerotic (PESA) study: rationale and design. Am Heart J 2013;166:990-8.
24. Moher D, Hopwell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. J Clin Epidemiol 2010;63:e1-37.
25. Fernández-Friera L, Peñalvo JL, Fernández-Ortiz A, et al. Prevalence vascular distribution, and multiterritorial extent of subclinical atherosclerosis in a middle-aged cohort: the PESA (Progression of Early Subclinical Atherosclerosis) study. Circulation 2015;131:2104-13.
26. Guallar-Castillón P, Rodríguez-Artalejo F, Tormo MJ, et al. Major dietary patterns and risk of coronary heart disease in middle-aged persons from a Mediterranean country: the EPIC-Spain Cohort study. Nutr Metab Cardiovasc Dis 2012;22:192-9.
27. Rodríguez-Artalejo F, Graciani A, Guallar-Castillón P, et al. Rationale and methods of the study on nutrition and cardiovascular risk in Spain (ENRICA). Rev Esp Cardiol 2011;64:876-82.
28. McLaren L, Hawe P. Ecological perspectives in health research. J Epidemiol Community Health 2005;59:6-14.
29. WHO. *Healthy workplaces a model for action for employers, workers, policy-makers and practitioners. Geneva: World Health Organization. 2010.*
30. Bartholomew LK, Parcel GS, Kok G, et al. *Planning health promotion programs: an intervention mapping approach. San Francisco, CA: Jossey- Bass. 2006.*
31. Moyers TB, Martin T, Manual JK, et al. *Revised global scales: motivation interviewing treatment integrity 3.0 (MITI 3.0). University of New Mexico, Center on Alcoholism,Substance Abuse and Addictions (CASAA). 2007.*
32. Goméz E, Fernández-Alvira JM, Vilanova M, et al. A comprehensive lifestyle peer-group-based intervention on cardiovascular risk factors: the randomized controlled Fifty-Fifty Program. JACC 2016;67: 476-85.
33. Kozey-Keadle S, Libertine A, Lyden K, et al. Validation of wearable monitors for assessing sedentary behavior. Med Sci Sports Exerc 2011;43:1561-7.
34. Ryan CG, Grant PM, Tigbe WW, et al. The validity and reliability of a novel activity monitor as a measure of walking. Br J Sports Med 2006;40:779-84.
35. Craig CL, Marschall AL, Sjostrom M. International Physical Activity Questionnaire: A 12 country reliability and validity. Med Sci Sports Exerc 2015;35:1381-95.
36. Chau J, van der Ploeg HP, Dunn S, et al. Validity of the occupational and sitting questionnaire. Med Sci Sports Exerc 2012;44:118-25.
37. Chau J, van der Ploeg HP, Dunn S, et al. A tool for measuring worker's sitting time by domain: the workforce sitting questionnaire. Br J Sports Med 2011;45:1216-22.
38. Martinez-Gonzales MAM, Garcia-Arellano A, Toledo E, et al. A 14-item Mediterranean diet assessment tool and obesity indexes among high-risk subjects: the PREDIMED trial. PLoS One 2012;7:1-10.
39. Unruh ML, Redline S, An MW, et al. Subjective and objective sleep quality and aging in the sleep heart health study. J Am Geriatr Soc 2008;56:1218-27.
40. Radloff LS. A self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385-401.
41. Cohen S, Spacapan S, Oskamp S, eds. The social psychology of health Journal of Occupational Health Psychology; 1988. p. 31-67. Thousand Oaks, CA, US: Sage Publications, Inc.
42. Vaglio J, Conard M, Poston WS, et al. Testing the performance of the ENRICHD social support instrument in cardiac patients. Health Qual Life Outcomes 2004;2:1-5.
43. Karasek R, Brisson C, Kawakami N, et al. The Job Content Questionnaire (JCQ): an instrument for internationally comparative assessments of psychosocial job characteristics. J Occup Health Psychol 1998;3:322-55.
44. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res 2011;20:1726-36.
45. Sonnentag S, Fritz C, eds. The Recovery Experience Questionnaire: development and validation of a measure for assessing recuperation and unwinding from work, 12. Journal of Occupational Health Psychology; 2007. p. 204-21.
46. Strijk JE, Wendel-Vos GCW, Picavet HSJ, et al. What is vitality and how to measure it? (in Dutch: Wat is vitaliteit en hoe is het te meten?). Tijdschrift voor Gezondheidswetenschappen 2015;1: 32-40.
47. Kessler RC, Barber C, Beck A, et al. The World Health Organization Health and Work Performance Questionnaire (HPQ). J Occup Environ Med 2003;45:156-74.

48. Moore GF, Audrey S, Barker M, et al. Process evaluation of complex interventions: Medical Research Council guidance. BMJ 2015;350:1-7.
49. Van Buuren S. Multiple imputation of discrete and continuous data by fully conditional specification. Stat Methods Med Res 2007;16:219-42.
50. Burton A, Billingham LJ, Bryan S. Cost-effectiveness in clinical trials: using multiple imputations to deal with incomplete cost data. Clin Trials 2007;4:154-61.
51. Stinnet AA, Mullay J. Net health benefits: a new framework for the analysis of uncertainty in cost-effectiveness analysis. Med Decis Mak 1998;18:S68-80.
52. Miller WR, Zweben A, DiClemente CC, et al. *Motivational enhancement therapy manual: a clinical reasearch guide for therapists treating individuals with alcohol abuse and dependence. Rockville: MD National Institute on Alcohol Abuse and Alcoholism. 1992.*
53. Lundahl B, Moleni T, Burke BL, et al. Motivational interviewing in medical care settings: a systematic review and meta-analysis of randomized controlled trials. Patient Educ Couns 2013;93:157-68.
54. Lundahl BW, Kunz C, Brownell C, et al. A meta-analysis of motivational interviewing: twenty-five years of empirical studies. Res Soc Work Pract 2010;20:137-60.
55. Rubak S, Sandbaek A, Lauritzen T, et al. Motivational interviewing: a systematic review and meta-analysis. Br J Gen Pract 2005;55:305-12.
56. Heath GW, Parra DC, Sarmiento OL, et al. Evidence-based intervention in physical activity: lessons from around the world. Lancet 2012;380:272-81.
57. Gardner B, Smith L, Lorencatto F, et al. How to reduce sitting time? A review of behavior change strategies used in sedentary behaviour reduction interventions among adults. Health Psychol Rev 2015;10: 90-112.

Further Reading

58. Bullinger M, Alonso J, Apolone G, et al. Translating health status questionnaires and evaluating their quality: the IQOLA project approach. International Quality of Life Assessment. J Clin Epidemiol 1998;51:913-23.
59. Geisinger KF. Cross-cultural normative assessment: translation and adaptation issues influencing the normative interpretation of assessment instruments. Psychol Assess 1994;6:304-12.
60. Markland D, Tobin VJ. Need support and behavioural regulations for exercise among exercise referral sheme clients: the mediating role of psychological need satisfaction. Psychol Sport Exerc 2010;11:91-9.