Community-based comprehensive lifestyle programs in patients with coronary artery disease: Objectives, design and expected results of Randomized Evaluation of Secondary Prevention by Outpatient Nurse SpEcialists 2 trial (RESPONSE 2)

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Patients with coronary artery disease (CAD) are at high risk of recurrent events. A healthy lifestyle can significantly reduce this risk. A previous trial, Randomized Evaluation of Secondary Prevention by Outpatient Nurse SpEcialists (RESPONSE), demonstrated that nurse-coordinated outpatient clinics improve drug treatment of cardiovascular risk factors. However, lifestyle-related risk factors, including smoking, overweight, and physical inactivity, were common and remained largely unchanged at follow-up in most patients (66%). The aim of the current study is to evaluate the impact of 3 community-based lifestyle programs in patients after hospitalization for CAD. We are conducting a multicenter (n = 15), randomized trial that will recruit 800 patients to test the efficacy of up to 3 widely available commercial lifestyle programs, aimed at patients and their partners, on top of usual care. These programs are aimed at smoking cessation (Luchtsignaal®), weight loss (Weight Watchers®), and improving physical activity (Philips DirectLife®).

Outcomes The primary outcome at 12 months is the proportion of patients in whom at least 1 lifestyle risk factor is improved without deterioration in any of the other 2, and a relative increase of at least 30% in this proportion is considered clinically relevant. (Am Heart J 2015;170:216-22.)

Patients with coronary artery disease (CAD) are at high risk of recurrent events and mortality.[1] This risk can be reduced by effective secondary prevention, which consists of appropriate medical therapy and improvement of lifestyle-related risk factors (LRRFs) including smoking, unhealthy diet, overweight or obesity, and a sedentary lifestyle.[2-4]

Physician compliance with guidelines for drug treatment of hypertension, diabetes mellitus, and dyslipidemia has improved substantially. This can be explained by accumulating evidence for the efficacy of these drugs, increased awareness among physicians, and implementation of dedicated outpatient support.[5] The health benefits from improving LRRFs are at least as great as the benefits of pharmacologic secondary prevention.[2,5-8] Therefore, current guidelines promote lifestyle risk management in patients with CAD.

However, implementation of lifestyle risk management has been challenging. The Prospective Urban Rural Epidemiology study found that the prevalence of healthy lifestyle behaviors was low in a worldwide sample of patients with CAD or stroke.[9] Data from 4 consecutive EUROASPIRE registries in Europe showed a trend of increasing overweight and obesity among patients with CAD.[5,10]

Nurse-coordinated outpatient clinics are now common, and nurses are engaged in cardiovascular risk management. However, their impact on lifestyle risk factors is limited.[11,12]

A medical approach may not be suitable to improve a patient's lifestyle long term. Home-based, long-term support involving patients' partners may potentially be more effective.[12-14] Since LRRFs tend to cluster, a

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comprehensive intervention may be expected to have a greater impact than interventions on a single risk factor.[3,11]

We aim to evaluate 3 community-based comprehensive lifestyle programs that have previously been validated[15-18] aimed at smoking cessation (Luchtsignaal®), weight reduction (Weight Watchers®), and promoting physical activity (Philips DirectLife®) with referral to these community-based programs coordinated by nurses at outpatient clinics.

Methods

Study design

A multicenter (n = 15) randomized trial was used to assess the efficacy of 3 widely available community-based lifestyle programs, on top of usual care, in patients who have recently been hospitalized for CAD in the Netherlands.

Timeline

Inclusion of patients has started in April 2013 and will be closed on June 30, 2015, with an expected overall number of 1000 patients.

Funding

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The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the manuscript, and its final contents.

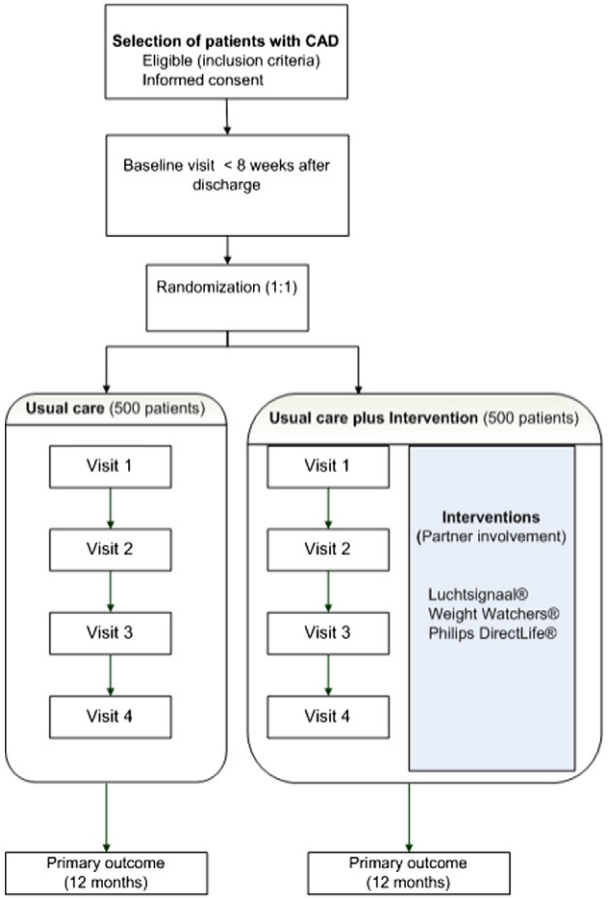
Patient population, recruitment, and randomization

Patients 18 years or older are recruited at outpatient clinics by treating cardiologists or nurses, within 8 weeks after hospitalization, which is defined as unstable angina and ST-elevation myocardial infarction and non–ST-elevation myocardial infarction, coronary artery bypass graft surgery, or percutaneous coronary intervention with at least 1 of the following 3 lifestyle risk factors: (1) current smoking, defined as smoking of any tobacco product in the 6 months preceding hospitalization; (2) body mass index (BMI) $\geq$27 kg/m^2; or/and (3) physical inactivity. Physical inactivity is defined as <30 minutes of physical activity of moderate intensity 5 times per week according to the current recommendation of the World Health Organization (WHO). Although guidelines recommend a BMI of $\leq$25 kg/m^2, the criterion of BMI $\geq$27 kg/m^2 was selected to ensure that there is a clear indication for weight reduction. A weight loss of $\geq$5%, as recommended by the current guideline,[2,3] is equivalent to a reduction from 27 to $\leq$25.65 kg/m^2.

Exclusion criteria include planned revascularization after hospital discharge, a limited life expectancy ($\leq$2 years), heart failure classified as New York Heart Association class III or IV, or inability to follow the program.

Patients with a Hospital Anxiety and Depression screening score >14 are excluded because they may not be able to address their lifestyle-related CAD risk factors before treatment of the mood disorder.[19]

Figure 1



Flowchart of the study design.

Written informed consent is obtained from patients and cardiologists. The study protocol has been approved by the local medical ethics committees (METC 2012_272) and is registered online (www.trialregister.nl, trial ID NTR3937).

Randomization is performed through an automated online protocol. Patients are randomized to either the lifestyle intervention program on top of usual care or to usual care alone in a 1:1 fashion. To ensure concealment of allocation, the automated online randomization protocol uses block randomization with randomly varying block sizes (4, 6, or 8 allocations). The flowchart of the trial is presented in Figure 1.

Usual care, nurse-coordinated outpatient clinic

Usual care includes outpatient clinic visits to physicians and nurses and referral to cardiovascular rehabilitation according to national guidelines.[2,3] Cardiologists are expected to adhere to current national and international guidelines for secondary prevention of cardiovascular