Study protocol

# BOOSTSITLESS

Remote 3-week Booster Intervention to Reduce Sedentary Time in Patients With Coronary Artery Disease: A randomized controlled trial

Radboudumc, Nijmegen, the Netherlands
Trial registration number: NCT06038188
Version: 1.0. Date: 28-02-2023

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## 2. Trial Summary

Official Title: Remote 3-week Booster Intervention to Reduce Sedentary Time in Patients With Coronary Artery Disease: A randomized controlled trial

Brief title: BOOSTSITLESS

ClinicalTrials.gov ID: NCT06038188

Study ID: NL72604.091.20

Brief Summary: The BOOSTSITLESS is a randomized controlled trial designed to examine the effects of a 3-week remote Booster intervention on changes in sedentary time among cardiac rehabilitation graduates.

Keywords: Cardiac rehabilitation; e-Health; prevention; sitting; physical activity; cardiovascular disease.

Detailed summary:
Introduction: Previous studies revealed that sedentary time (ST) can effectively be targeted in patients with coronary artery disease (CAD) participating in cardiac rehabilitation (CR). However, only transient effects were observed, as patients relapsed to a sedentary lifestyle in subsequent months. We examined the effectiveness of a 3-week remote Booster intervention on changes in ST among CR graduates.
Methods: CAD patients previously completing CR with a ST reduction program (1.5-2.5 years ago) were included in this randomized controlled trial (1:1, stratified for gender). All participants received usual care, whereas Booster participants additionally received a 3-week remote behavioral change intervention consisting of education, goal-setting, motivational interviewing, and telemonitoring. The primary outcome was the change in accelerometer-derived ST from baseline to post-intervention and secondary outcomes included changes in ST and physical activity characteristics. A baseline constrained linear mixed-model was performed.
Expected conclusions: We hypothesized that the Booster intervention would result in a greater replacement of ST for physical activity compared to control. The results of the study will have important clinical implications as it can show the potential of eHealth to improve activity behavior of patients beyond completion of traditional CR programs.

## 3. Scientific background – Trial rationale

Cardiovascular disease is the leading global cause of death and the prevalence of coronary artery disease (CAD) increased by 74.7% from 1990 to 2016.[1] In developed countries survival rates following myocardial infarction (MI) improved over the past decades[2], which has largely been due to the

development of reperfusion techniques and modern drug therapies[3]. Despite this progress, rates of recurrent MI or fatal CAD within 5 years after MI are high in both males (17%) and females (21%).[1] Therefore, the current focus has to be on further improvements of secondary prevention.

The beneficial effects of physical activity (PA) in secondary prevention after MI are well known. A physically active lifestyle is related to a reduction of cardiovascular mortality and morbidity in patients with CAD[4,5] and because of survival benefits and lower recurrence risk, referral to an exercise rehabilitation program is strongly recommended for cardiac patients.[6] Importantly, emerging evidence from epidemiological studies reveal that, independent of engagement in PA, high levels of sedentary behaviour (SB; defined as any waking behaviour characterized by an energy expenditure ≤1.5 metabolic equivalents (MET) while in a seated, reclined or lying posture[7,8]) are associated with increased risks for cardiovascular mortality and morbidity in the general population.[9-11] Patients with cardiovascular disease show higher levels of SB compared to the general population[12], and in these patients SB is associated with lower cardiorespiratory fitness.[13] This suggests that SB may play an important role in the prognosis of patients with CAD.

Cardiac rehabilitation (CR) is a comprehensive program in which supervised exercise training is the cornerstone, complemented with risk factor management and psychosocial support.[14] The efficacy of CR in secondary prevention of CAD is well established.[15] CR participation is therefore a class I recommendation in guidelines of European and American cardiovascular societies.[16,17] Although current CR programs go beyond exercise training with a multidisciplinary approach, including psychosocial management, smoking cessation, nutrition counselling and management of blood pressure, lipid spectrum and weight, most programs do not specifically target SB.[14] Yet, increasingly evidence is available that SB in patients with CAD remains high after following CR programs.[13,18-20] Reducing SB might have cumulative and clinically relevant effects on the secondary prevention of CAD[21,22]. Additionally, breaking up SB by taking active breaks may counteract the detrimental effects of prolonged SB regardless of reducing total SB or increasing time spent in moderate- to vigorous intensity physical activity (MVPA).[23] Given these highly relevant benefits, reducing SB in patients with CAD is a very promising new area of focus among CR programs and probably more feasible and sustainable in this predominantly inactive population.[24]

Many (e-Health) initiatives arose focussing on physical activity in CVD patients, but in general it sorted only into small-to-medium effects that are not sustained over time and the more effective interventions are complex and therefore difficult to implement in routine care.[25-27] Intervention studies targeting SB in CVD patients are scarce. To address this gap, we developed an in-person delivered intervention integrated in routine care with an add-on e-health component to prompt and monitor behaviour change. This intervention was co-created together with both patients and health care professionals (HCPs) and adapted to fit with restrictions and opportunities in routine care. In this study we investigated the effect of the *'**S**itting **I**nterruption **T**reatment as a persona**L**iz**E**d **S**econdary prevention **S**trategy'* (SIT LESS) intervention on SB in patients with coronary artery disease directly after CR and after 6 months of follow-up. This study showed that enrichment of CR with a tailored sedentary behavior intervention induces greater reductions in ST compared to usual care[28]. However, these beneficial lifestyle adaptations were only temporary[28] as sustainable PA habits after CR remain challenging[29,30].

E-Health programs could support patients to maintain beneficial PA levels following CR[29]. Moreover, short, remote Booster programs may already nudge CR graduates towards a more physically active lifestyle[31]. Such Booster programs should include continued support to allow self-monitoring of behavior, goal-setting and associated feedback[29]. However, the effect of a remote eHealth-based Booster program aiming to reducing ST in patients with CAD is currently unknown. Therefore, the

effects of SIT LESS Booster sessions on SB will be examined among patients who participated in the SIT LESS group ~2 years ago.

## 4. Objectives

The primary objective is to examine the effectiveness of a remote 3-week Booster behavior intervention compared to usual care on reducing ST.

Secondary objectives are:

a) To examine the effectiveness of a remote 3-week Booster behavior intervention compared to usual care on improving sedentary behavior defined as number of prolonged sedentary bouts and prevalence of a ST ≥9.5 h/day.
b) To examine the effectiveness of a remote 3-week Booster behavior intervention compared to usual care on improving physical activity characteristics.

## 5. Trial design

A parallel-group randomized controlled trial will be conducted to determine the effectiveness of a 3-week, fully-remote and personalized behavior change intervention (Booster intervention) with a primary focus on reducing and interrupting ST in patients with CAD. The Booster is a compressed version of the SIT LESS intervention, which has previously been described in detail[32]. Participants who received the original SIT LESS intervention during their CR program (1.5 to 2.5 years ago) and of which accelerometry-based ST and PA characteristics were derived will be approached for this study at the end of August 2023. After inclusion, baseline characteristics are gathered including the same assessment of ST and PA characteristics by an accelerometer send by mail (**Figure 1**). Following baseline measurements, participants are randomly assigned into the control or Booster group. The control groups received usual care, where the Booster group additionally receives the Booster intervention. Finally, the accelerometry measurement are repeated in both groups at the end of the Booster intervention (post-intervention). Our trial is approved by the Medical Ethics Committee of the Radboud university medical center (NL72604.091.20), is in accordance with the principles of the Declaration of Helsinki and all participants will give written informed consent.

Randomization will occur after the completion of all baseline assessments using a computerized algorithm (Castor Electronic Data Capture 2021, Ciwit B.V., Amsterdam, The Netherlands).

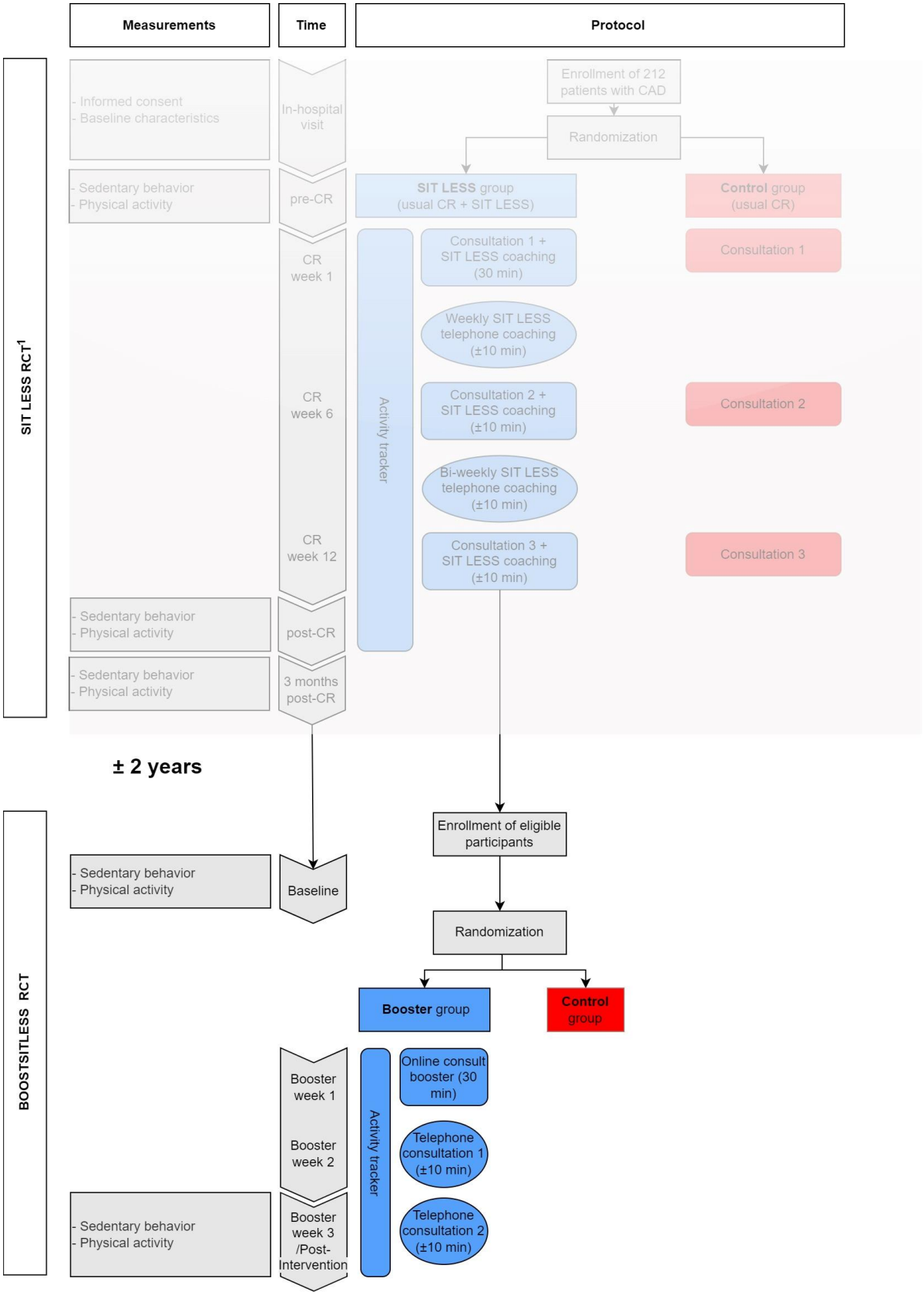


**Figure 1**. SIT LESS (transparent) and BOOSTSITLESS randomized controlled trial flowchart.
CR: Cardiac Rehabilitation; SIT LESS, Sedentary Behavior Intervention as a Personalized Secondary Prevention Strategy

## 6. Disease condition and selection of patients

Eligible patients are defined on the inclusion and exclusion criteria. In general, patients with coronary artery disease who followed cardiac rehabilitation with a special sedentary reduction program (SIT LESS). Specific inclusion and exclusion criteria are:

Inclusion Criteria:

1. Participation in the SIT LESS intervention group of the original SIT LESS study. Inclusion criteria of the SIT LESS study were:
    a. Patients aged ≥ 18 years old
    b. Referred to CR because of stable CAD, an acute coronary syndrome, and/or after coronary revascularization.

Exclusion Criteria:

1. Unable to give informed consent
2. Wheelchair-bounded / not physically able to stand or walk.
3. Dutch Language barrier
4. Coronary arterial bypass graft surgery expected within 8 weeks after inclusion
5. New York Heart Association class III or IV heart failure
6. Participation in another interventional study targeting sedentary behavior or physical activity

## 7. Screening and recruitment

No screening was needed as participants randomized to the intervention group during the original SIT LESS study were eligible for inclusion.

Participants meeting the eligibility criteria will be recruited by email and telephone call. Recruitment starts at the end of August 2023 and may extend until November 2023 (~2 years after the pre-CR measurement of the SIT LESS study). Information necessary for the CONSORT flow diagram will be collected. For the enrollment phase, we will note the number of patients that were assessed for eligibility by the research team, the number of excluded patients (plus reason for exclusion), and the number of randomized participants. For the allocation, the number of participants allocated to the BOOSTSITLESS intervention, and the number of participants who received or did not receive the intervention (plus reasons) will be noted. For follow-up, the number of participants who were lost to follow-up and the number who discontinued the intervention (plus reasons) were counted. Finally, the number of participants that were included in the analyses using the intention-to-treat will be described together with the reasons for exclusion.

## 8. Outcome Measures

Primary outcome

Change in daily ST (h/day; baseline and post-intervention).

ST is objectively assessed using a validated accelerometer (ActivPAL3$^{TM}$micro, PAL Technologies Ltd., Glasgow, United Kingdom)[3]. The ActivPAL is a small device (25x45x5 mm), waterproof attached to the participant's thigh using hypoallergenic tape. The ActivPAL combines a tri-axial accelerometer with an inclinometer which accurately distinguishes between sitting, standing and walking[3]. Participants are instructed to wear the ActivPAL 24 h/day for 8 consecutive days and to fill in a diary with sleep times and moment of attachment and detachment. Raw data is analyzed by a modified version of the script of Winkler et al.[4]. Total ST (Metabolic Equivalent of Task score (METs) ≤1.5 while awake in a sitting, lying or reclining posture)[5] is expressed in h/day.

Secondary outcomes

- Change in number of prolonged sedentary (bouts/day; baseline and post-intervention). Prolonged sedentary bouts are defined as an accumulation of ST (≥30 min) and based on ActivPAL data.
- Prevalence of an average ST >9.5 h/day (number, (%); baseline and post-intervention). Daily ST will be dichotomized using 9.5 h/day as cut-off as it was previously shown that exceeding this upper limit of normal was associated with an increased risk of morbidity and mortality[6]. ActivPAL data will be used for this outcome.
- Change in the prevalence of a sitting time ≥9.5 h/day.
- Change in daily time spent in light-intensity physical activity (LIPA in h/day; baseline and post-intervention). The ActivPAL data will be used and LIPA is categorized as physical activity with MET levels < 3.
- Change in daily time spent in moderate-to-vigorous intensity physical activity (MVPA in h/day; baseline and post-intervention). The ActivPAL data will be used and MVPA is categorized as physical activity with MET levels ≥ 3.
- Change in step count (steps/day; baseline and post-intervention). The ActivPAL data will be used for this outcome.

## 9. Sample calculations and statistical analysis

Sample size.

As our study has an explorative character, no formal sample size calculation was performed prior to trial initialization. Before the original SIT LESS study, a sample size calculation was performed and described[32]. Based on that calculation, 106 patients were needed in the SIT LESS arm of the trial. Participants in this study arm will be eligible for participation in the BOOSTSITLESS.

In the original SIT LESS study, we found an effect size Cohen D of 0.3[28] with an alpha of 0.05 and beta of 0.2 (power 0.8). The estimated sample size, based on previously mentioned parameters and repeated-measures ANOVA, needed for this study was 24 participants (12 in each study arm)(**Figure 2**).

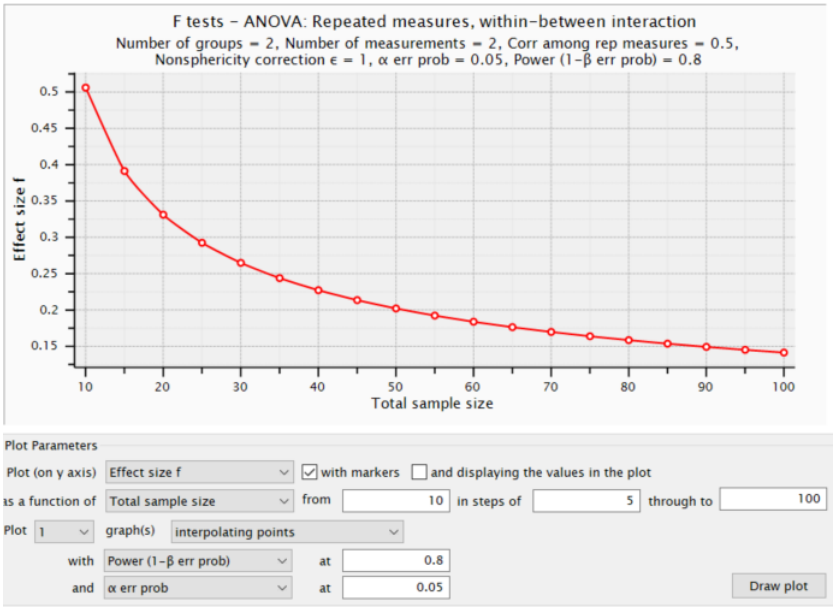


**Figure 2.** Sample size calculation using G*power (version 3.1)

Statistical analyses.
The treatment effects will be tested using baseline constrained mixed models (i.e. adjusting for baseline of the outcome studied) for the study outcomes using an intention-to-treat approach as primary analysis. A detailed Statistical Analysis Plan has been developed in a separate document that will be available.

## 10. Treatments/Interventions

Control group: The control group (as well as the Booster group) will be treated with usual care, which includes periodic medical revisions and medication control of the cardiologist.

Booster group: 3-week duration. Participants will use a pocket-worn, commercially available, small (30x32x10 mm) and lightweight (20 g), activity tracker (Activ8sit, 2M Engineering, Valkenswaard, The Netherlands, **Figure 3**). The activity tracker consists of an inclinometer and a tri-axial accelerometer, which allows for recognizing prolonged periods of sedentary behavior and physical activity patterns. Upon recording prolonged, uninterrupted sitting (i.e. 30 minutes), vibrotactile feedback will be provided by the activity tracker to remind patients to replace sedentary behavior by low-intensity physical activity (e.g. standing or walking). Patients can review their sedentary behaviour and physical activity patterns in a web-based environment.

**A** **B**

**Figure 3:** Activity tracker. For the SIT LESS intervention the Activ8sit (A) will be used. The activity tracker can easily be worn in the trouser pocket (B).

During the first online Booster consult, the researcher and participant will reactivate knowledge on the detrimental health effects of SB, discuss patients' personal goals and motivation, and collaboratively set action plans for reducing SB in the upcoming week (±30 minutes). Thereafter, the Booster group will be contacted on a weekly basis by phone to evaluate SB of the preceding week. The Booster sessions will be delivered completely remote, so all devices will be sent home to the participants by mail, and participants do not have to visit the hospital for this study. (**Figure 1**)

## 11. Adherence, attendance and compliance

For participants randomized to the Booster-arm, the adherence will be assessed by counting the number of valid wear days of the activity tracker (≥ 10 h/day), and by dividing the number of valid days by the total number of days of the intervention period x 100%.

The adherence to the daily use of the activity tracker will be reported as the mean ± standard deviation (when normally distributed) or as median [interquartile range] (when not-normally distributed).

All protocol deviations made to the protocol (e.g. change in pre-defined inclusion/exclusion criteria, baseline and post-intervention, data cleaning/processing) will be reported and described.

## 12. Safety and adverse events

We assess the risks regarding this study as negligible. Nevertheless, the number and reasons of adverse events (e.g. falls, injuries, musculoskeletal problems, major cardiovascular disease events, and any other events potentially related to the implementation of the trial protocol) at each time point will be collected, reported, and described separately for each study arm. No formal statistical testing will be undertaken.

## 13. Ethics and legal issues

Our trial is approved by the Medical Ethics Committee of the Radboud university medical center (NL72604.091.20), is in accordance with the principles of the Declaration of Helsinki and all participants will give written informed consent.

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