

# A secondary analysis of data from the OPTICARE randomized controlled trial investigating the effects of extended cardiac rehabilitation on functional capacity, fatigue, and participation in society

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## Abstract

**Objective:** In this secondary analysis of data from the OPTICARE trial, we compared the effects of two behavioral interventions integrated into cardiac rehabilitation to standard rehabilitation with regard to functional capacity, fatigue, and participation in society.

**Design:** This is a randomized controlled trial.

**Setting:** This study was conducted in a cardiac rehabilitation setting.

**Subjects:** A total of 740 patients with acute coronary syndrome were recruited for this study.

**Interventions:** Patients were randomized to (1) three months of standard rehabilitation; (2) cardiac rehabilitation plus nine months after-care with face-to-face group lifestyle counseling; or (3) cardiac rehabilitation plus nine months after-care with individual lifestyle telephone counseling.

**Main measures:** Functional capacity (6-minute walk test), fatigue (Fatigue Severity Scale), and participation in society (Utrecht Scale for Evaluation of Rehabilitation-Participation) were measured at randomization, 3, 12, and 18 months.

**Results:** Additional face-to-face sessions resulted at 12 months in 12.49 m more on the 6-minute walk test compared to standard rehabilitation ( $P = .041$ ). This difference was no longer present at 18 months. Prevalence of fatigue decreased from 30.2% at baseline to 11.9% at 18 months compared to an improvement from 37.3% to 24.9% after standard rehabilitation (between-group difference: odds ratio = 0.47;  $P = .010$ ). The additional improvements in functional capacity seemed to be mediated by increases in

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daily physical activity. No mediating effects were found for fatigue. No additional improvements were seen for participation in society. Additional telephonic sessions did not result in additional intervention effects.

**Conclusion:** Extending cardiac rehabilitation with a face-to-face behavioral intervention resulted in additional long-term improvements in fatigue and small improvements in functional capacity up to 12 months. A telephonic behavioral intervention provided no additional benefits.

### Keywords

Participation (WHO ICF), physical fitness, lifestyle change, acute coronary syndrome, behavioral

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## Introduction

Cardiac rehabilitation programs focus on the adoption of a healthy lifestyle and optimization of cardiovascular risk factors and are known to decrease the risks of death and re-hospitalization.<sup>1-5</sup> Other important gauges of cardiac rehabilitation success are improvements in aerobic capacity, fatigue, and participation in society. Aerobic capacity is known to be related to re-hospitalization and mortality,<sup>6,7</sup> and fatigue and participation in society are known to affect quality of life.<sup>8,9</sup> To date, cardiac rehabilitation results for these outcomes have been suboptimal in patients with acute coronary syndrome.<sup>8,10,11</sup>

In the OPTICARE (OPTimal CARDiac REhabilitation) randomized controlled trial, two novel cardiac rehabilitation interventions based on behavioral techniques (one offered face-to-face in groups and one offered individually by phone) were evaluated in patients with acute coronary syndrome.<sup>12</sup> The primary aim of these interventions was to further improve cardiovascular health and physical activity.<sup>12</sup> Although the novel interventions did not lead to additional improvements in cardiovascular health,<sup>13</sup> additional improvements in physical activity were observed.<sup>14</sup> Because the novel interventions addressed a wide range of health behaviors and psychosocial problems, the interventions may more broadly affect (functional) aerobic capacity, fatigue, and participation in society. Previous studies have shown that behavioral lifestyle interventions can lead to improvements in these outcomes.<sup>15-17</sup> We hypothesized that, in addition to direct effects of the novel interventions, improvements may also be mediated by improvements in moderate-to-vigorous physical

activity (e.g. brisk walking or biking) and sedentary behavior (behaviors requiring very low energy expenditure, mainly sitting or lying during waking hours).<sup>18-20</sup>

The objective of the current study was to evaluate the effects of the two novel behavioral lifestyle interventions in comparison with standard cardiac rehabilitation on the secondary outcomes of functional capacity, fatigue, and participation in society. Secondary, in case significant intervention effects were found, we explored whether these effects were mediated by changes in physical activity and sedentary behavior.

## Methods

This study concerns a secondary analysis of data from the OPTICARE randomized controlled trial. The trial was carried out between November 2011 and August 2014 at Capri Cardiac Rehabilitation in the Netherlands. The study, which has been described in detail previously,<sup>12-14</sup> was prospectively registered at ClinicalTrials.gov (NCT01395095) and was approved by the Medical Ethics Committee of the Erasmus Medical Centre in Rotterdam, the Netherlands (MEC-2010-391). Patients referred for cardiac rehabilitation were invited to participate. Inclusion criteria were acute coronary syndrome diagnosis, age greater than 18 years, and Dutch language proficiency. The exclusion criterion was the presence of severe physical or cognitive impairment that could limit cardiac rehabilitation participation.<sup>12</sup>

Randomization was performed with opaque sealed envelopes, which were prepared and sequentially numbered by an independent statistician who

used a computer random number generator. Patients were randomized (1:1:1) to standard cardiac rehabilitation or to one of the two novel interventions:

1. *Standard cardiac rehabilitation*: Standard cardiac rehabilitation<sup>2,5</sup> lasted three months. In this period, patients completed two 75-minute exercise sessions per week. In addition, patients could participate in a three-session educational program about a heart-healthy diet, coping with emotions, and cardiovascular risk factors. Based on motivation and indication, patients could also participate in group counseling sessions addressing stress management, healthy diet, or smoking cessation. If clinically indicated, patients were referred to a dietician, psychiatrist, psychologist, or social worker for individual treatment. At the end of the three-month cardiac rehabilitation program (initial phase), no after-care was offered.
2. *Cardiac rehabilitation plus face-to-face counseling*: During the initial phase, patients participated in the standard three-month cardiac rehabilitation program plus three 75-minute counseling sessions (at four-week intervals) designed to increase physical activity level. During these sessions, information was also provided about the benefits of frequently interrupting sedentary time. All sessions were conducted face-to-face in small groups of four to eight patients. During the sessions, patients were coached by a physical therapist trained in motivational interviewing. To support the coaching, pedometers (Yamax Digiwalker SW-200; Yamax, Inc., Tokyo, Japan) were used to provide the patients with continuous objective feedback about daily physical activity level.

After the initial three-month cardiac rehabilitation program, a nine-month after-care program was offered. This program consisted of three 2-hour group sessions with four to eight patients at one, three, and nine months after completion of cardiac rehabilitation. Each session comprised 1 hour of exercise and 1 hour of healthy lifestyle counseling. The counseling sessions focused on permanent adoption

of a healthy lifestyle (i.e. healthy diet and optimal physical activity), but also on psychosocial problems. During these sessions, patients were coached alternately by a physical therapist, dietician, and social worker.

3. *Cardiac rehabilitation plus telephonic counseling*: This intervention was based on the existing Coaching Patients on Achieving Cardiovascular Health (COACH) program.<sup>21</sup> During the initial phase, patients participated only in standard cardiac rehabilitation. After the initial phase, patients participated in a nine-month individual after-care program comprised of five to six telephone coaching sessions at five- to six-week intervals. During the coaching sessions, patients were encouraged to self-monitor their coronary risk factors (e.g. weight, blood pressure, or cholesterol) and make an action plan. In addition, patients developed a personal plan for permanent adoption of a heart-healthy lifestyle (i.e. healthy diet and sufficient physical activity). Progress was discussed during each session.

Patients in all three groups attended usual follow-up appointments with their cardiologist.

In all patients, functional capacity, fatigue, participation in society, physical activity, and sedentary behavior were measured at four occasions: at randomization; at completion of standard cardiac rehabilitation (3 months after randomization); at completion of after-care (12 months after randomization); and 6 months after completion of after-care (18 months after randomization). Measurements were performed by trained research assistants. Both patient and testers were not blinded to group allocation:

- Functional capacity was measured with a 6-minute walk test, performed according to the American Thoracic Society guidelines.<sup>22</sup> Patients were asked to walk back and forth along a 30-m corridor, covering as many meters as they could during 6 minutes without running. Standardized encouragement was given every minute, and the distance walked was recorded in meters. The 6-minute walk test has

found to be a valid and reliable outcome measure and is responsive to relevant clinical changes during cardiac rehabilitation.<sup>23</sup>

- Fatigue was measured using the nine-item Fatigue Severity Scale. The Fatigue Severity Scale is widely used and validated in healthy subjects and patients with sleeping disorders, multiple sclerosis, and stroke.<sup>24–26</sup> The outcome is a continuous score between 0 and 7, with higher scores indicating more severe fatigue.
- Fatigue prevalence was calculated in addition to the Fatigue Severity Scale score.<sup>11,26,27</sup> Being fatigued was defined as a score of one standard deviation above the mean score for healthy persons (score higher than 4) and being severe fatigued as a score of two standard deviations above the mean score for healthy persons (score higher than 5.2).<sup>26</sup>
- Participation in society was assessed using the Utrecht Scale for Evaluation of Rehabilitation-Participation (USER-P), a 32-item questionnaire concerning participation in domestic activities (e.g. housekeeping), occupational activities (e.g. paid and voluntary work), and recreational activities (e.g. going out and leisure activities). The questionnaire addresses three subdomains of participation: frequency, perceived restrictions, and satisfaction. For each subdomain, a separate score from 0 to 100 was calculated, with higher scores indicating better participation. The questionnaire has been validated for cardiac patients.<sup>28</sup>
- Physical activity and sedentary behavior were measured using a tri-axial accelerometer (ActiGraph GT3x, ActiGraph, Pensacola, FL, USA). Patients were asked to wear the accelerometer for eight consecutive days, except while sleeping and during bathing. A valid day was defined as a wear time of at least 11 hours, and measurements were included in the analysis only when the accelerometer was worn for at least four valid days. The ActiGraph converts accelerations on three axes into activity counts. Using ActiLife software, counts were summed over a sampling interval (epoch) of 15 seconds. Using MATLAB version R2011 (MathWorks, Natick, MA, USA), a vector magnitude of

counts on the three axes ( $\sqrt{x^2 + y^2 + z^2}$ ) was calculated and time in moderate-to-vigorous-intensity physical activity ( $\geq 672.5$  counts per 15 seconds)<sup>29</sup> and sedentary time ( $\leq 37.5$  counts per 15 seconds)<sup>30</sup> were determined. Steps per day were also captured by the accelerometer. To correct for differences in accelerometer wear time between patients, moderate-to-vigorous-intensity physical activity time and sedentary time were expressed as percentages of wear time and the number of steps as mean steps per minute of wear time.

Patients were only included in the data analysis if at least one measurement after baseline was available. We compared baseline differences between patients included and excluded from analysis and baseline differences between patients randomized to standard cardiac rehabilitation or one of the novel interventions using Student's *t*-tests and chi-square tests, to explore unintentional bias. Scores on the subdomain experienced restrictions in participation in society showed severe negative skewness. Therefore, dichotomized scores (no restrictions experienced or restrictions experienced) were used in the analysis. Data for other measures were normally distributed.

Generalized estimating equations with exchangeable correlation structures were performed to determine intervention effects of the two novel interventions compared to standard cardiac rehabilitation on functional capacity, fatigue, and participation in society. First, separate overall models were created for each outcome (functional capacity, fatigue, and participation in society); group allocation was included as a categorical predictor; and baseline values for outcome measures were used as covariates to correct for baseline differences between subjects. Second, time-dependent models were created by adding the variable time (measurement occasions) and an interaction variable of group allocation  $\times$  time. By changing the order of the time variable, between-group differences (intervention effects) could be calculated for improvement between baseline and 3 months, improvement between baseline and 12 months, and improvement between baseline and 18 months.

In all models, standard cardiac rehabilitation served as a reference group, and age and sex were added as confounders. The regression coefficient *B* represented between-group differences (intervention effects) over all measurements for the overall model. In the time-dependent models, *B* represented the between-group difference at different time-points. For dichotomous variables, between-group differences are presented as odds ratios (OR).

In case of missing baseline data, values were imputed five times (multiple imputations), using baseline characteristics and all available follow-up outcomes of the particular outcome as predictors. Missing baseline data were balanced between groups. Because generalized estimating equation models correct for missing data, other time-points (end-points) did not require data imputation.<sup>31</sup>

The generalized estimating equations were performed using the original dataset and all five datasets containing imputed baseline values. Pooled results are reported. We considered a *P*-value smaller than .05 to be statistically significant. Only in case both novel interventions would result in significant intervention effects as compared to standard cardiac rehabilitation, a post hoc comparison between the two novel interventions would be performed with adjustment for multiple testing. SPSS version 21.0 (IBM Corp., Armonk, NY, USA) was used for all analyses.

In case significant intervention effects were found for any of the novel interventions compared to standard cardiac rehabilitation, additional analyses were performed to explore the mediating effects of moderate-to-vigorous-intensity physical activity time, sedentary time, and daily step count. Mediation was expressed as the percentage change in the intervention effect (regression coefficient, *B*) after adding the potential mediator to the overall model. We considered mediating effects to be clinically relevant when the percentage change was 10% or higher.

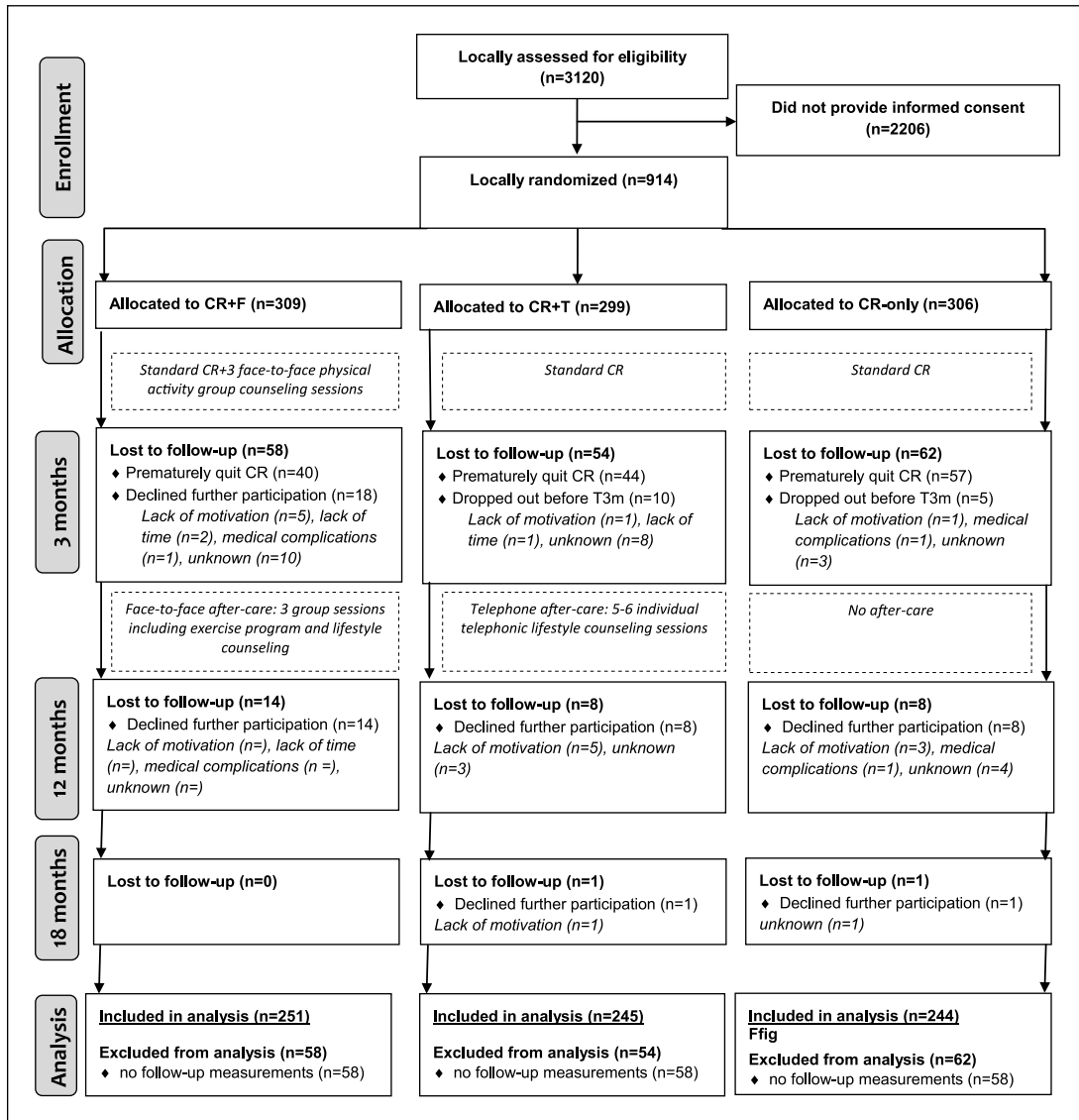
## Results

In total, 914 patients with acute coronary syndrome were enrolled, of whom 141 patients quit cardiac rehabilitation prematurely due to reasons unrelated to the study. An additional 33 patients dropped out

of the study before the second measurement due to logistic reasons or lack of motivation (Figure 1). The excluded patients were, on average, two years younger ( $P = .017$ ), more likely to have a history of smoking ( $P < .001$ ), and less likely to use statins ( $P < .001$ ). The remaining 740 patients (mean age (SD) = 57.2 (9.1) years, 600 (81.1%) male) were included in the analysis (Table 1). The three groups were balanced with respect to baseline characteristics (see Table 1). Physical activity and sedentary behavior (potential mediating factors) were measured in a subsample consisting of 589 of the 740 patients (80%) included in the analysis.

Regarding functional capacity, significant intervention effects were found between baseline and 12 months for cardiac rehabilitation plus face-to-face counseling (Tables 2, 3 and Supplemental Figure S1). On average, participants in the cardiac rehabilitation plus face-to-face counseling group improved 12.49 m more on the 6-minute walk test between baseline and 12 months than patients in the standard cardiac rehabilitation group ( $P = .041$ ; outcomes corrected for age and sex). This difference was no longer present at 18 months. No intervention effects were found for cardiac rehabilitation plus telephonic counseling (Table 3). Exploratory analysis revealed that the intervention effects for cardiac rehabilitation plus face-to-face counseling were mediated by moderate-to-vigorous-intensity physical activity time (15.8%), sedentary time (5.3%), and daily step count (36.9%).

Regarding fatigue, patients randomized to cardiac rehabilitation plus face-to-face counseling had a greater improvement in Fatigue Severity Scale scores between baseline and 18 months compared to patients randomized to standard cardiac rehabilitation ( $P = .053$ , outcomes corrected for age and sex) (See Table 2 and Table 3). Furthermore, prevalence of fatigue and severe fatigue decreased more between baseline and 18 months in the cardiac rehabilitation plus face-to-face counseling group compared to the standard cardiac rehabilitation group ( $P = .010$ ;  $P = .038$ , outcomes corrected for age and sex) (Table 3). No intervention effects were found for cardiac rehabilitation plus telephonic counseling (Table 3; Supplemental Figure S1). Exploratory mediation analysis revealed



**Figure 1.** Consort flow diagram.

CR+F, cardiac rehabilitation plus face-to-face group counseling; CR+T, cardiac rehabilitation plus individual telephonic counseling; CR-only, standard cardiac rehabilitation.

that physical activity and sedentary behavior did not explain the intervention effects observed for fatigue. No intervention effects were found on any subdomain of participation in society for either novel intervention (Table 3).

## Discussion

Extending cardiac rehabilitation with a face-to-face behavioral group intervention focused on permanent healthy lifestyle adoption resulted in small additional improvements in functional capacity up to 12 months and more substantial improvements

**Table 1.** Participant baseline characteristics (*n* = 740).

Characteristics	CR+F ( <i>n</i> = 251)	CR+T ( <i>n</i> = 245)	CR-only ( <i>n</i> = 244)	Between-group differences
Male, <i>n</i> (%)	202 (80.5)	202 (82.4)	196 (80.3)	0.799
Age, mean (SD), years	57.5 (8.8)	56.7 (9.2)	57.5 (9.2)	0.533
Partnered, <i>n</i> (%) <sup>a</sup>	169 (80.5)	168 (84.0)	171 (83.4)	0.599
Employed, <i>n</i> (%) <sup>b</sup>	123 (64.7)	112 (60.5)	107 (56.0)	0.220
Therapeutic intervention index event, <i>n</i> (%)				0.711
No revascularization	17 (6.8)	24 (9.8)	18 (7.4)	
Percutaneous coronary intervention	201 (80.1)	180 (73.5)	193 (79.1)	
Coronary artery bypass graft	33 (13.1)	41 (16.7)	33 (13.5)	
Cardiac history, <i>n</i> (%)				
Myocardial infarction	20 (8)	21 (8.6)	20 (8.2)	0.970
Angina pectoris	12 (4.8)	14 (5.7)	14 (5.7)	0.865
Percutaneous coronary intervention	23 (9.2)	23 (9.4)	25 (10.2)	0.912
Coronary artery bypass graft	3 (1.2)	1 (0.4)	5 (2.0)	0.254
Stroke/transient ischemic attack	10 (4.0)	3 (1.2)	5 (2.0)	0.122
Medication, <i>n</i> (%)				
Acetylsalicylic acid	240 (95.6)	240 (98.0)	237 (97.1)	0.312
Oral anticoagulant	13 (5.2)	17 (6.9)	11 (4.5)	0.478
Thienopyridine	211 (84.1)	196 (80.0)	210 (86.1)	0.185
Cholesterol lowering medication	240 (95.6)	236 (96.3)	237 (97.1)	0.668
Beta-blocker	208 (82.9)	200 (81.6)	200 (82.0)	0.933
ACE inhibitor	181 (72.1)	171 (69.8)	169 (69.3)	0.761
Angiotensin II receptor blocker	32 (12.7)	31 (12.7)	33 (13.5)	0.952
Calcium blocker	34 (13.5)	37 (15.1)	36 (14.8)	0.874
Nitrate	104 (41.4)	76 (31.0)	86 (35.2)	0.052
Diuretic	27 (10.8)	27 (11.0)	24 (9.8)	0.905
Psychotropic	11 (4.4)	15 (6.1)	16 (6.6)	0.541
Risk factors, <i>n</i> (%)				
Diabetes	34 (13.5)	24 (9.8)	35 (14.3)	0.268
Dyslipidemia	70 (27.9)	87 (35.5)	101 (41.4)	0.007
Family history	134 (53.4)	128 (52.2)	136 (55.7)	0.732
Smoking history	109 (43.4)	95 (38.8)	89 (36.5)	0.272
Hypertension	109 (43.4)	96 (39.2)	98 (40.2)	0.602
Overweight	194 (77.3)	186 (75.9)	187 (76.6)	0.906
Cardiac rehabilitation compliance				
Number of training sessions, mean (SD)	23.5 (6.4)	22.9 (5.2)	23.0 (5.6)	0.475
Educational sessions, <i>n</i> (%) <sup>c</sup>	199 (79.2)	185 (75.5)	184 (75.4)	0.844
Counseling sessions, <i>n</i> (%) <sup>c</sup>	88 (35.0)	82 (33.5)	72 (28.7)	0.539
Additional face-to-face sessions, <i>n</i> (%) <sup>c</sup>	243 (96.8)	–	–	
Additional telephonic sessions, <i>n</i> (%) <sup>c</sup>	–	196 (80.0)	–	

CR+F, cardiac rehabilitation plus face-to-face group counseling; CR+T, cardiac rehabilitation plus individual telephonic counseling; CR-only, standard cardiac rehabilitation.

<sup>a</sup>Data missing for *n* = 41 (CR+F), *n* = 45 (CR+T), and *n* = 39 (CR-only).

<sup>b</sup>Data missing for *n* = 61 (CR+F), *n* = 60 (CR+T), and *n* = 53 (CR-only).

<sup>c</sup>Number of patients participating in at least one session.

**Table 2.** Observed data for functional capacity, fatigue, and participation in society for all three groups.

	CR+F				CR+T				CR-only			
	Baseline	3 months	12 months	18 months	Baseline	3 months	12 months	18 months	Baseline	3 months	12 months	18 months
Functional capacity, mean ± SD												
6MWT, m	564 ± 82	608 ± 84	611 ± 87	600 ± 85	567 ± 76	601 ± 89	590 ± 75	597 ± 79	557 ± 80	598 ± 82	594 ± 76	596 ± 82
Fatigue, mean ± SD	3.29 ± 1.48	2.81 ± 1.30	2.62 ± 1.22	2.56 ± 1.18	3.32 ± 1.52	2.91 ± 1.38	2.82 ± 1.45	2.74 ± 1.33	3.33 ± 1.38	3.00 ± 1.37	2.78 ± 1.38	2.87 ± 1.46
FSS score												
Fatigue, prevalence (%)	15.9	10.3	8.9	7.7	17.9	18.2	13.5	13.3	24.9	15.5	13.2	14.1
Fatigue (FSS > 4.0)	13.8	5.6	4.5	4.2	15.1	7.0	7.7	6.0	9.7	7.5	7.5	10.2
Severe fatigue (FSS > 4.0)												
Participation in society, mean ± SD												
Frequency score	38.6 ± 11.1	37.2 ± 10.9	36.8 ± 9.6	36.5 ± 11.1	35.9 ± 10.6	37.3 ± 10.6	35.9 ± 11.9	36.2 ± 10.6	37.9 ± 10.7	36.7 ± 10.6	36.6 ± 10.4	36.2 ± 10.4
Restriction score	90.9 (22:100) <sup>a</sup>	100 (37:100) <sup>a</sup>	100 (7:100) <sup>a</sup>	100 (62:100) <sup>a</sup>	89.4 ± (6:100) <sup>a</sup>	100 ± (29:100) <sup>a</sup>	100 (4:100) <sup>a</sup>	100 (33:100) <sup>a</sup>	90.0 (10:100) <sup>a</sup>	100 (56:100) <sup>a</sup>	100 (0:100) <sup>a</sup>	100 (7:100) <sup>a</sup>
Satisfaction score	68.0 ± 15.6	73.8 ± 15.8	74.3 ± 14.2	74.5 ± 15.6	68.6 ± 14.8	74.5 ± 15.1	73.6 ± 15.8	76.3 ± 13.6	69.7 ± 15.9	73.4 ± 15.8	75.1 ± 16.0	73.8 ± 16.4

CR+F, cardiac rehabilitation plus face-to-face group counseling; CR+T, cardiac rehabilitation plus individual telephonic counseling; CR-only, standard cardiac rehabilitation; 6MWT, 6-minute walk test; FSS, Fatigue Severity Scale.

<sup>a</sup>Scores violated normality assumption, therefore median (range) values are displayed.



**Table 3.** Generalized estimating equation<sup>a</sup> results for intervention effects over all time-points, between baseline and 3 months, between baseline and 12 months, and between baseline and 18 months.

		CR+F vs. CR-only			CR+T vs. CR-only		
		B <sup>b</sup>	CI	P-value	B <sup>b</sup>	CI	P-value
<b>Functional capacity (n = 674)</b>							
6MWT, m	Overall	6.83	-3.45, 17.12	.192	3.82	-14.39, 6.74	.477
	ΔT0-3 months	6.84	-5.75, 19.43	.287	-0.14	-13.77, 13.48	.984
	ΔT0-12 months	<b>12.49</b>	<b>0.53, 24.46</b>	<b>.041</b>	-9.20	-20.89, 2.48	.122
	ΔT0-18 months	1.54	-11.86, 14.94	.822	-2.21	-15.66, 11.24	.747
<b>Fatigue (n = 665)</b>							
FSS score	Overall	-0.16	-0.35, 0.03	.095	-0.05	-0.24, 0.14	.619
	ΔT0-3 months	-0.13	-0.35, 0.09	.235	-0.04	-0.26, 0.18	.708
	ΔT0-12 months	-0.13	-0.37, 0.11	.296	-0.02	-0.28, 0.23	.872
	ΔT0-18 months	-0.24	-0.49, 0.03	.053	-0.09	-0.34, 0.15	.453
Prevalence of fatigue (FSS > 4.0)	Overall	<b>0.62<sup>c</sup></b>	<b>0.41, 0.94</b>	<b>.024</b>	0.95 <sup>c</sup>	0.63, 1.45	.832
	ΔT0-3 months	0.75 <sup>c</sup>	0.45, 1.23	.260	1.07 <sup>c</sup>	0.65, 1.77	.778
	ΔT0-12 months	0.63 <sup>c</sup>	0.35, 1.13	.119	1.01 <sup>c</sup>	0.57, 1.79	.969
	ΔT0-18 months	<b>0.47<sup>c</sup></b>	<b>0.26, 0.84</b>	<b>.010</b>	0.76 <sup>c</sup>	0.43, 1.35	.356
Prevalence of severe fatigue (FSS > 5.2)	Overall	0.55 <sup>c</sup>	0.30, 1.01	.056	0.70 <sup>c</sup>	0.38, 1.28	.250
	ΔT0-3 months	0.72 <sup>c</sup>	0.31, 1.63	.428	0.83 <sup>c</sup>	0.37, 1.84	.644
	ΔT0-12 months	0.57 <sup>c</sup>	0.24, 1.35	.199	0.80 <sup>c</sup>	0.34, 1.92	.623
	ΔT0-18 months	<b>0.39<sup>c</sup></b>	<b>0.17, 0.95</b>	<b>.038</b>	0.53 <sup>c</sup>	0.24, 1.17	.117
<b>Participation in society (n = 671)</b>							
Frequency score	Overall	-0.46	-1.92, 1.01	.540	0.73	-0.71, 2.16	.320
	ΔT0-3 months	-0.18	-1.96, 1.60	.842	0.98	-0.79, 2.74	.277
	ΔT0-12 months	-1.06	-2.92, 0.80	.263	-0.03	-2.15, 2.08	.977
	ΔT0-18 months	-0.30	-2.26, 1.65	.760	1.10	-0.77, 2.98	.248
Restrictions score <sup>d</sup>	Overall	1.03 <sup>c</sup>	0.73, 1.46	.858	0.93 <sup>c</sup>	0.66, 1.32	.698
	ΔT0-3 months	1.03 <sup>c</sup>	0.68, 1.55	.903	1.09 <sup>c</sup>	0.70, 1.67	.698
	ΔT0-12 months	0.95 <sup>c</sup>	0.60, 1.51	.824	0.82 <sup>c</sup>	0.51, 1.30	.386
	ΔT0-18 months	1.07 <sup>c</sup>	0.67, 1.70	.777	0.86 <sup>c</sup>	0.54, 1.36	.524
Satisfaction score	Overall	0.32	-1.93, 2.57	.778	1.08	-1.24, 3.39	.361
	ΔT0-3 months	0.67	-1.96, 3.31	.618	1.50	-1.13, 4.12	.264
	ΔT0-12 months	-0.76	-3.59, 2.06	.596	-0.72	-3.68, 2.24	.632
	ΔT0-18 months	1.40	-1.84, 3.65	.518	2.27	-0.49, 5.02	.107

6MWT, 6-minute walk test; CI, confidence interval; CR+F, cardiac rehabilitation plus face-to-face group counseling; CR+T, cardiac rehabilitation plus individual telephonic counseling; CR-only, standard cardiac rehabilitation; FSS, Fatigue Severity Scale; n = number of patients who had at least one outcome post-baseline on the specified outcome and were included in the analysis.

Significance is P<0.05.

<sup>a</sup>All analyses were adjusted for baseline differences between patients and corrected for confounding effects of gender and age. The CR-only group is the reference group for all analyses.

<sup>b</sup>B, regression coefficient, represents the between-group difference and the intervention effect relative to CR-only over all time-points or at the specified time-point.

<sup>c</sup>Odds ratios are shown for dichotomous variables to indicate the odds (relative risk) relative to CR-only at the specified time-point.

<sup>d</sup>Scores violated normality assumption, dichotomized scores used for analysis.

in prevalence of fatigue up to at least 18 months. The additional improvements in functional capacity seemed to be mediated by improvements in physical activity. Extending cardiac rehabilitation with a telephonic behavioral program did not lead to additional improvements in functional capacity or fatigue. Furthermore, neither the telephonic nor the face-to-face intervention further improved participation in society compared to standard cardiac rehabilitation only.

A previous study indicated that the minimal clinically important difference for the 6-minute walk test for patients after an acute coronary syndrome is 25 m.<sup>32</sup> All three groups in our trial showed improvements far above the 25 m during the initial three-month cardiac rehabilitation period (see Table 2). These improvements remained above 25 m at long-term follow-up. A small additional improvement of 12.5 m was seen at the 12-month follow-up for patients participating in additional face-to-face sessions. Because the additional telephonic sessions did not result in additional improvements in functional capacity, we hypothesize that the stronger focus on physical activity during the face-to-face intervention could be an important element to improve functional capacity. Indeed, an exploratory analysis showed that the found intervention effects were mediated by improvements in both moderate-to-vigorous-intensity physical activity time and daily step count. The additional improvement in functional capacity was not maintained at long-term follow-up. Since relevant and long-lasting improvements were already seen after standard cardiac rehabilitation, we conclude that most patients do not seem to need additional programs regarding functional capacity.

To our knowledge, this is the first study to assess the secondary effects of a lifestyle intervention integrated into cardiac rehabilitation on fatigue. In addition to improving functional capacity, the additional face-to-face sessions improved perceived fatigue (including severe fatigue). Patients reached fatigue levels even lower than those reported for healthy persons (11.9% vs. 18%).<sup>26</sup> In contrast, those randomized to standard cardiac rehabilitation continued to have a high prevalence of fatigue (24.9%). With regard to prevalence of severe

fatigue, the prevalence among those randomized to cardiac rehabilitation with additional face-to-face sessions (4.2%) approached that of healthy persons (3.5%) by study end.<sup>26</sup> As with previous results,<sup>11</sup> the prevalence of severe fatigue in our study remained high following standard cardiac rehabilitation only (10.2%). The improvements to fatigue are clinically important, as fatigue is known to influence quality of life.<sup>9</sup> In contrast to our hypothesis, additional improvements in fatigue were not mediated by changes in physical activity or sedentary behavior. Because the telephonic behavioral intervention did not confer additional benefits to fatigue, an element of the face-to-face group sessions must have been essential for these benefits. Unfortunately, the study design was not appropriate to detect the specific factor for the program's success. Perhaps, the improvements in functional capacity seen after the additional face-to-face sessions lowered the physical strain associated with activities of daily life, which consequently decreased feelings of fatigue.<sup>11</sup> In addition, the face-to-face coaching method (as opposed to individual telephone coaching) may have contributed.

Adding behavioral interventions to standard cardiac rehabilitation (using face-to-face group or individual telephonic coaching) did not affect participation in society. In a previous study, it was found that a lifestyle intervention with a focus on improving physical activity also resulted in improvements in participation in society.<sup>17</sup> However, in this patient group with spinal cord injury, baseline levels for participation in society are lower,<sup>28</sup> leaving more room for improvements. This could probably explain the discrepancy with our results. As participation in society is associated with quality of life,<sup>8</sup> future research should focus on finding effective interventions to improve participation in society. We hypothesize that a more individualized approach, focusing on areas in which participation problems are experienced, may be needed.<sup>8</sup>

Some study limitations deserve discussion. First, patients who were lost to follow-up and excluded from analyses were, on average, younger and more likely to smoke. Cardiac rehabilitation drop-out rates tend to be higher among younger patients and

those with more risk factors.<sup>33,34</sup> Therefore, our results are probably most valid among the more adherent patients. Second, the 6-minute walk test was found to be a valid and reliable test and responsive to clinically meaningful changes in a cardiac rehabilitation population.<sup>23</sup> Nevertheless, a ceiling effect might occur in patients with a higher functional capacity at start of rehabilitation.<sup>23</sup> Third, the power analysis for this randomized controlled trial was performed using the primary outcome SCORE (Systematic COronary Risk Evaluation) risk function.<sup>12</sup> The study was not designed and powered for the outcomes analyzed in this article. Therefore, our results should be considered as exploratory, we cannot rule out that our findings are partly due to coincidence. Nonetheless, post hoc power analysis revealed that we were powered for all three outcomes to detect a between-group difference of at least 10%. Finally, we did not perform official mediation analyses. However, our exploratory analyses do offer insight into possible mediators of findings.

### Clinical messages

- Extending cardiac rehabilitation with face-to-face behavioral sessions resulted in long-term additional improvements in fatigue.
- The face-to-face intervention resulted in small additional improvements in functional capacity up to 12 months.
- Benefits in functional capacity seemed to be mediated by physical activity.
- Extending cardiac rehabilitation with a telephone program provided no benefits.

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### Supplemental material

Supplemental material for this article is available online.

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