BMJ open

Home-based cardiac rehabilitation is an attractive alternative to centre-based cardiac rehabilitation for elderly patients with coronary heart disease. Results from a randomised clinical trial.

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-001820
Article Type:	Research
Date Submitted by the Author:	13-Aug-2012
Complete List of Authors:	Oerkild, Bodil; Bispebjerg University Hospital, Department of Cardiology Frederiksen, Marianne; Bispebjerg University Hospital, Department of Cardiology Hansen, Jørgen; Bispebjerg University Hospital, Department of Cardiology prescott, eva; Bispebjerg University Hospital, Cardiology
Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	CARDIOLOGY, Coronary heart disease < CARDIOLOGY, Ischaemic heart disease < CARDIOLOGY, Heart failure < CARDIOLOGY

Title page:

Home-based cardiac rehabilitation is an attractive alternative to centre-based cardiac rehabilitation for elderly patients with coronary heart disease. Results from a randomised clinical trial.

Bodil Oerkild, MD, ph.d; Marianne Frederiksen, MD, DMSc; Jorgen Fischer Hansen, MD, DMSc and Eva Prescott MD, DMSc.

Department of Cardiology, Bispebjerg University Hospital, Copenhagen, Denmark

Corresponding author:

Bodil Oerkild, MD, ph.d.

Department of Cardiology,

Bispebjerg University Hospital,

Bispebjerg Bakke 23, 11b

DK-2400 Copenhagen NV, Denmark

Phone: +45 20 15 51 54

Fax: +45 35 31 39 82

Email: Oerkild@dadlnet.dk

Keywords: Cardiac rehabilitation; elderly; physical activity; mortality.

Word count: 2512

Abstract:

Objective: To compared home-based cardiac rehabilitation (CR) with usual care in elderly patients not willing to participate in centre-based CR.

Design: Randomised clinical trial with 12 months follow-up and mortality data at 5½ year.

Setting: Rehabilitation Unit, Department of Cardiology, Copenhagen, Denmark.

Participants: Elderly patients ≥ 65 years with coronary heart disease.

Intervention: A physiotherapist made home visits in order to develop an individualised exercise programme that could be performed at home and surrounding outdoor area. Risk factor intervention, medical adjustment, physical and psychological assessments were offered at baseline and after 3, 6 and 12 months.

Main Outcome Measurements: The primary outcome was six minutes walk test (6MWT). Secondary outcomes were blood pressure, body composition, cholesterol profile, cessation of smoking and health related quality of life.

Results: 40 patients participated. The study population was characterised by high age (median age 77 years, range 65-92 years) and high level of comorbidity. Patients receiving home-based CR had a significant increase in the primary outcome 6MWT of 33.5m (95%CI: 6.2, 60.8, P=0.02) at 3 months whereas the usual care group did not significantly improve. However, at 12 months follow-up there was a significant decline in 6MWT in both groups; 55.2m (95%CI: 18.7, 91.7, P<0.01) in the home-based CR group and 52.1m (95%CI: -3.0, 107.1, P=0.06) in the usual care group. There were no significant differences in blood pressure, body composition, cholesterol profile, cessation of smoking and health related quality of life after 3, 6 and 12 months follow-up.

Conclusions: Participation in home-based CR improved exercise capacity among elderly patients with coronary heart disease. However, when intervention ceased effect was rapidly lost.

Article focus

- To compare home-based cardiac rehabilitation with usual care in elderly patients with coronary heart disease.

Key messages

- Home-based cardiac rehabilitation improved exercise capacity among elderly patients with coronary heart disease.
- Elderly patient with coronary heart disease has a high level of co-morbidity and disability.
- When the home-based intervention ceased effect was rapidly lost.

Strengths and limitations of the study

- The randomised design provides a higher level of evidence.
- This population represents the 'real-world' scenario of elderly cardiac patients.
- The duration of the intervention may be too short to maintain changes in exercise capacity at 12 months follow-up.
- The size of the study did not allow sub-group analysis.

Introduction

Participation in cardiac rehabilitation (CR) is often the first step toward optimal secondary treatment and prevention and is recommended to patients with coronary heart disease. The centre-based programmes are the cornerstone in the evidence of CR, with meta-analysis showing an approximately 20% reduction in all-cause and cardiac mortality and 17% reduction in re-infarction rate among patients who participated in the programmes [1;2]. CR is also found to be effective among the elderly age $\geq$ 65 years [3] and this group may benefit the most [4-6]. However, the elderly and patients with co-morbidity are underrepresented in the centre-based programmes. It has been estimated that only 20% of eligible elderly participate [6;7].

In order to improve participation rate, there has been an increasing focus on home-based CR where the entire programme or parts hereof is moved from the centre to the patients home. This could be an attractive alternative to centre-based CR. A recently published Cochrane review [8] established that home-based CR was not inferior to centre-based CR and a review from 2006 [9] found that the home-based programmes at some points were superior to usual care. However, the included populations in the reviews were highly selected with few elderly and excluding patients with co-morbidity and disability. Since elderly patients with coronary heart disease is the fastest growing

sub-group of cardiac patients there is an increasing need for adjusting the CR programmes according to their requirements.

The aim of this study is, in a randomised design, to compare the effect of home-based CR with usual care in a population of patients ≥ 65 years with coronary heart disease who did not want to participate in a centre-based CR programme.

Methods

Trial design

The study is a randomised clinical trial comparing home-based CR with usual care. The study represents patients not willing to participate in centre-based CR, which is offered routinely to all patients with coronary heart disease after discharge from our coronary department. Figure 1 shows the flowchart.

Inclusion criteria were patients ≥ 65 years with a new coronary event i.e. acute myocardial infarction (MI), percutaneous transluminal coronary intervention (PCI) or coronary artery bypass graft (CABG). Exclusion criteria were mental disorders (dementia), social disorders (severe alcoholism and drug abuse), living in a nursing home, language barriers or use of wheelchair. The recruitment period was from January 2007 to July 2008.

Patients were recruited through a database covering all invasive procedures in the catchments area of Bispebjerg University Hospital, Copenhagen. All patients were consecutively invited by letter and non-responders were additionally contacted by telephone. Patients had to give informed consent before any trial related procedures. Patients were randomised in alternated block sizes of 4 to 6 using computer generated randomly permuted blocks. An impartial person not related to the study randomised patients. The result of the randomisation could not be blinded because of the nature of the intervention. Data were collected at Bispebjerg University Hospital before randomisation and

after 3, 6 and 12 months. In addition, overall mortality data were obtained in July 2012, 5½ years after the study was initiated.

The study was approved by the local ethic committee (jr.nr.KF01327990), the Danish Data Protection Agency (j.nr. 2006-41-7212) and is registered at www.clinicaltrial.gov (NCT00489801).

Intervention

The home programme

The home programme was designed to focus on the exercise component of CR, which was moved to the patients home. A physiotherapist made home visits twice with 6 weeks interval in order to develop a training programme that could be performed at home and surrounding outdoor area. A telephone call was made in between the two visits to clarify any questions.

The exercise programmes were individualised but followed the international recommendations with 30 min. exercise per day including 5-10 min. warm up (e.g. slow walking) and 10 min. cool down at a frequency of 6 days per week [10;11] at an intensity of 11-13 on the Borg scale [11]. For very disabled patients the exercise programmes were of shorter duration but then repeated several times a day. Regarding risk factor intervention and medical adjustment a cardiologist counselled the patients at baseline and after 3, 6 and 12 months. At 4 and 5 months a telephone call was made to encourage continuous exercising and to answer any questions. All patients were offered dietary counselling and (if needed) smoking cessation.

Usual care

As for the home group, the patients were offered risk factor intervention and medical adjustment by a cardiologist at baseline and after 3, 6 and 12 months and telephone calls were made at 4 and 5 months. There was no exercise education or dietary counselling, but if needed smoking cessation was offered.

Outcome measures

The primary outcome was change in exercise capacity determined by 6MWT. The secondary outcomes were: sit to stand test (STS), self reported level of physical activity, systolic and diastolic blood pressure, total-, HDL- and LDL-cholesterol, body mass index (BMI), waist-hip ratio, proportion of smokers, and health related quality of life measured by SF-12 and Hospital Anxiety and Depression Scale (HADS). Outcomes were evaluated after 3, 6 and 12 months.

In the STS-test the patients must as fast as possible within 30 sec. change position from sitting on a chair to upright standing, without holding the handgrip, hereby measuring the strength in the lower limb. Self-reported level of physical activity was estimated by a questionnaire originally developed by Saltin and Grimby [12]. It has four categories ranging from a sedentary lifestyle, to performing light activities 2-4 hours/week, activity more than 4 hours/week or highly vigorous physical activity more than 4 hours/week. Patients in the last three categories were classified as having an active lifestyle. Medication included the use of diuretics, beta-blockers, calcium antagonists, lipid lowering drugs, anti-thrombotics, anti-diabetic and anti-depressive treatment. Sociodemographic data included level of education, main employment status, contact to children, living alone and the need of weekly assistance at home. Patients in NYHA II-IV and CCS II-IV were categorised as having dyspnoea and angina, respectively. Co-morbidity was assed by The Charlson Co-Morbidity Index (CMI) [13], which measures the burden of 19 co-morbid conditions through a weighted index. The CMI was categorised in 3 sub-groups: 0 (no co-morbid condition), 1-2 and $\geq$ 3 (high level of co-morbid burden).

Adverse events were recorded in the study period and included admissions for MI, progressive angina, decompensated congestive heart failure, severe bleeding, new malignant disease, and performance of PCI. Moreover, the number and duration of hospital admissions were recorded 1 year after randomisation. Mortality data were obtained from the Civil Registration System, which records the vital status of all citizens in Denmark.

Statistical analysis

Baseline data were compared using two-sided t-test for continuous variables and chi2 test for categorical variables. To test the effect of the interventions at 3 and 12 months a mixed model of regression analysis was used with a time*treatment interaction term. All the models were adjusted for age and gender. We did not adjust the significance levels for multiple testing, since such an adjustment is a too conservative test to perform when data are positively correlated, as in this study. Data were analysed by intention to treat. All statistical analysis was performed using STATA for windows release 10.0.

Table 1 Baseline characteristics according to intervention
Values are mean (SD) unless stated otherwise

Characteristic	Usual care n=21	Home n=19
Age	76.5 (7.7)	77.3 (6.0)
Men n (%)	11 (52.3%)	12 (63.2%)
Risk factors		
Hypertension, n (%)	13 (61.9%)	16 (88.9%)
Hyperlipidemia, n (%)	17 (81.0%)	18 (94.7%)
Diabetes, n (%)	2 (9.5%)	7 (36.8%)*
BMI, kg/m^2	26.2 (3.6)	27.6 (4.5)
Current smokers, n (%)	9 (42.9%)	8 (42.1%)
Medical history		
Previous MI, n (%)	8 (38.1%)	6 (31.7%)
Previous PCI, n (%)	5 (23.8%)	4 (21.1%)
Previous CABG, n (%)	2 (9.5%)	0 (0%)
Heart failure LVEF $\leq$ 45%, n (%)	9 (42.9%)	9 (50.0%)
Event prior to entry into the study		
Post-MI without invasive procedure, n (%)	4 (19.1%)	0 (0%)
Post-PCI, n (%)	14 (66.7%)	16 (84.2%)
Post-CABG, n (%)	3 (14.3%)	3 (15.8%)
Clinical status		
6MWT, m	325.9 (123.1)	290.9 (116.5)
STS	10.9 (3.7)	8.9 (4.8)
Systolic blood pressure, mmHg	138.3 (22.2)	153.6 (27.5)
Diastolic blood pressure, mmHg	72.2 (13.9)	76.1 (13.0)
Waist-hip ratio	0.9 (0.1)	1.0 (0.1)
Dyspnoea, NYHA II-IV, n (%)	13 (61.9%)	11 (57.9%)
Angina, CCS II-IV, n (%)	4 (19.1%)	4 (21.1%)
Self-reported active lifestyle, n (%)	10 (47.6%)	(31.6%)
Co-morbid conditions		
CMI score 0, n (%)	0 (0%)	1 (5.3%)
1-2, n (%)	9 (42.9%)	7 (36.8%)
$\geq$3, n (%)	12 (57.1%)	11 (57.9%)
COPD, n (%)	7 (33.3%)	4 (21.1%)
Peripheral arterial disease, n (%)	3 (14.3%)	5 (26.3%)
Laboratory values		
Total cholesterol, mmol/l	4.5 (1.1)	4.3 (0.9)
HDL cholesterol, mmol/l	1.4 (0.3)	1.3 (0.6)
LDL cholesterol, mmol/l	2.5 (2.2)	2.4 (1.7)
Health related quality of life		
HADS anxiety score	4.7 (3.0)	5.1 (4.9)
HADS depression score	5.3 (3.8)	4.8 (2.7)
SF-12 PCS	39.0 (10.8)	38.0 (9.9)
SF-12 MCS	46.9 (10.1)	48.9 (9.3)

* P< 0.05.
Abbreviations: MI, myocardial infarction; PCI, percutaneous transluminal coronary intervention; CABG, coronary artery bypass graft; LVEF, left ventricular ejection fraction; 6MWT, 6 minutes walk test; STS, sit to stand test; CMI, Charlson co-morbidity index; COPD, chronic obstructive lung disease; HADS, Hospital Anxiety and Depression Scale; PMS, physical composite scale of SF-12; MCS, mental composite scale of SF-12.

Results

A total of 40 patients participated. Baseline characteristics are listed in table 1. Except for a higher incidence of diabetes in the home group there were no significant differences between the two groups. In addition, there were no significant differences in medication and sociodemographic data (data not shown). All patients received anti-thrombotics and lipid lowering drugs and 77.4% received beta-blockers.

Exercise capacity

Figure 2 illustrates the unadjusted means of the primary outcome measurement of 6MWT from baseline to 12 months follow-up. The figure shows a significant increase in walking distance of 33.5m (95%CI: 6.2, 60.8, P=0.02) in the home group after the intervention followed by a significant decline of 55.2m (95%CI: 18.7, 91.7, P<0.01) at 12 months follow-up to a level lower than the baseline value. Patients in the usual care group had a non-significant increase in walking distance of 10.1m (95 %CI: -19.3, 39.5, P=0.5) after 3 months followed by a decline of 52.1m (95%CI: -3.0, 107.1, P=0.06) at the end of the follow-up period. When adjusting for age and gender in a mixed model with a time*treatment interaction term, there were no significant differences between the groups at 3 months (table 2). At 12 months follow-up, a significant decline in 6MWT and STS was found in both groups with no differences between the groups (table 3).

Other outcomes

A higher proportion of patients reported a change from an inactive to an active lifestyle in the home group (27%, P<0.05) compared to the usual care group (-5%, P=0.6) after the intervention with a difference between the two groups of 33% (P<0.05). At 12 months follow-up the proportion of patients with a self-reported active lifestyle declined again in the home group with no changes in the usual care group.

Table 2 Effect of intervention at 3 months follow-up

	Usual care		**Home**			
	Δ 0-3 months	95%CI	Δ 0-3 months	95%CI	Δ 3 months between home-usual care	95%CI
Exercise capacity						
6MWT, m	10.1	-23.6, 43.9	36.3	-0.9, 73.6	26.2	-24.1, 76.5
STS	0.9	-0.8, 2.6	1.0	-0.8, 2.8	0.1	-2.3, 2.6
Clinial status						
Systolic blood pressure, mmHg	2.0	-8.4, 12.4	-12.9	-24.2, -1.6*	-14.9	-30.2, 0.5
Diastolic blood pressure, mmHg	4.1	-2.2, 10.5	-1.5	-8.4, 5.4	-5.7	-15.0, 3.7
BMI, kg/m^2	0.1	-1.3, 1.5	-0.5	-2.1, 1.1	-0.6	-2.7, 1.5
Waist-hip ratio	-0.01	-0.03, 0.01	-0.01	-0.03, 0.01	0	-0.03, 0.03
Laboratory values						
Total cholesterol, mmol/l	-0.2	-0.6, 0.2	-0.1	-0.5, 0.4	0.1	-0.5, 0.7
HDL cholesterol, mmol/l	0.1	-0.01, 0.2	0.1	-0.1, 0.2	-0.04	-0.2, 0.1
LDL cholesterol, mmol/l	-0.2	-0.5, 0.1	-0.1	-0.5, 0.3	0.1	-0.4, 0.6
Cholesterol/HDL ratio	-0.4	-0.7, 0	-0.3	-0.7, 0.1	0.1	-0.5, 0.7
Health related quality of life						
HADS anxiety score	-0.9	-2.3, 0.5	-1.2	-2.7, 0.6	0.3	-2.4, 1.9
HADS depression score	-1.1	-2.6, 0.4	-1.0	-2.7, 0.6	0.1	-2.2, 2.3
SF-12 PCS	2.7	-1.4, 6.8	-0.4	5.1, 4.3	-3.1	-9.4, 3.1
SF-12 MCS	3.5	-0.9, 7.9	2.4	-2.6, 7.5	-1.0	-7.7, 5.6

All data are adjusted for age and gender. Positive data indicates an increase in outcome or is in favour of home-based rehabilitation. * P<0.05.
Abbreviations: CI, confidence interval; 6MWT, 6 minutes walk test; STS, sit to stand test; HADS, hospital anxiety and depression score; PCS, physical component summary scale of SF-12; MCS, mental component summary scale of SF-12.

Table 3 Follow-up data at 12 months

	Usual care		Home			
	Δ 3-12 months	95%CI	Δ 3-12 months	95%CI	Δ 12 months between home-usual care	95%CI
Exercise capacity						
6MWT, m	-50.9	-86.6, -15.3**	-55.0	-94.0, -16.1**	-4.0	-56.8, 48.8
STS	-3.0	-4.7, -1.3**	-2.1	-3.9, -0.3*	0.9	-1.6, 3.4
Clinical status						
Systolic blood pressure, mmHg	0.7	-9.3, 10.6	-2.5	-13.1, 8.2	-3.1	-17.7, 11.4
Diastolic blood pressure, mmHg	-0.6	-6.4, 5.1	1.6	-4.6, 7.8	2.2	-6.2, 10.7
BMI, kg/m^2	0.4	-0.04, 0.8	0.6	0.1, 1.0*	0.2	-0.4, 0.8
Waist-hip ratio	0.01	-0.01, 0.03	0.0	-0.02, 0.02	0.01	-0.04, 0.02
Laboratory values						
Total cholesterol, mmol/l	0.1	-0.3, 0.5	-0.1	-0.5, 0.3	-0.2	-0.8, 0.4
HDL cholesterol, mmol/l	-0.1	-0.2, 0.01	-0.04	-0.1, 0.1	0.1	-0.1, 0.2
LDL cholesterol, mmol/l	0.1	-0.3, 0.2	-0.04	-0.4, 0.3	-0.1	-0.6, 0.4
Cholesterol/HDL ratio	0.3	-0.1, 0.6	0.1	-0.3, 0.5	-0.2	-0.7, 0.3
Health related quality of life						
HADS anxiety score	0.3	-1.3, 1.9	0.4	-1.3, 2.1	0.1	-2.3, 2.4
HADS depression score	0.3	-1.2, 1.8	1.2	-0.3, 2.8	0.9	-1.3, 3.1
SF-12 PCS	-1.4	-5.2, 2.3	-1.1	-5.3, 3.1	0.3	-5.4, 6.0
SF-12 MCS	-0.3	-4.6, 4.0	-1.4	-6.1, 3.3	-1.1	-7.5,5.3

All data are adjusted for age and gender. Positive data indicates an increase in outcome or is in favour of home-based rehabilitation. * P<0.05, **P<0.01.
Abbreviations: CI, confidence interval; 6MWT, 6 minutes walk test; STS, sit to stand test; HADS, hospital anxiety and depression score; PCS, physical component summary scale of SF-12; MCS, mental component summary scale of SF-12.

Except for lower systolic blood pressure in the home group after the intervention, there were no significant differences in diastolic blood pressure, waist-hip ratio, cholesterol profile, cessation of smoking and health related quality of life at 3 and 12 months follow-up either within or between the home and usual care group.

The number and length of acute and non-acute admissions were equally distributed at 12 months follow-up (data not shown). Mortality data showed that nine patients died within 5½ years (usual care group n=5 and home group n=4). There was no loss to follow-up.

Discussion

To our best knowledge, this is the first study to investigate the effect of home-based CR compared to usual care among elderly patients ≥ 65 years with coronary heart disease who did not want to participate in a centre-based programme. The study confirms that elderly patients who decline participation in centre-based CR are a very fragile group with low level of exercise capacity and high level of co-morbidity. For this population home-based CR was found to improve exercise capacity and although this study is small and generalisation thus limited, it identifies an intervention targeting this vulnerable group of patients. However, after ending the home programme the gained improvement in exercise capacity was not sustained.

Exercise capacity

The effect of our home CR programme on exercise capacity is consistent with the findings in the only other study investigating the effect of home-based CR and usual care among elderly with coronary heart disease [14]. In this study, patients in the age groups 45-65 years, 66-75 years and > 75 years significantly improved their exercise capacity after participating in a home programme although the improvement was less among the very old patients (>75 years).

Jolly et all's meta-analyses [9], which included studies of all age groups, investigated the effect of home-based CR and usual care. The meta-analysis showed an improvement in exercise capacity but

could not identify any significant differences between the home and usual care group. The authors explained this by the probability, that patients in usual care groups may receive input that match the home-interventions and thus diminish a possible difference.

At 12 months a significant decline in exercise capacity was found in this study in both the home and usual care group reaching a level lower than at entrance to the study. We identified two other studies with long-term follow-up [14;15], which in contrast to our study found a sustained improvement in exercise capacity after 12 months if the exercise programme was initiated at home. The discrepancy between studies may be caused by the differences in the enrolled population, our population was older, (mean age 77.3 ±6.0 years versus 69.0 ±9.0 years [14] and 64.3 ±0.5 years [15]), and had a high degree of co-morbidity and low level of exercise capacity, which may have contributed significantly to the lack of sustained effect at 12 months. In the only other study targeting the elderly [14] the population was highly selected with exclusions rate of 72% among the very old patients (>75 years) due to co-morbidity, disability and congestive heart failure. In addition, the duration of our home intervention may have been too short to maintain changes in lifestyle at 12 months follow-up.

Coronary heart disease is one of the leading causes of disability and with increasing age other chronic non-cardiac conditions further limit function [16]. Our population of elderly had a very high frequency of co-morbid conditions (57% had CMI $\geq$ 3) and low level of exercise capacity (mean 6MWT=308.4 m ± 120), which probably reflects a true picture of the elderly cardiac population. The 1-year mortality has been reported to be as high as 50 % for patients with CMI $\geq$ 3 [13] and similar mortality rates have been found for patients with a 6MWT below 300 m [17]. However, even when the mortality rate is high, improving exercise capacity is important for quality of life since there is a big difference between living independently of others versus having the need for assistance.

Other outcomes

Except for self-reported active lifestyle and systolic blood pressure, which changed favorable in the home group after the intervention, there were no significant differences in diastolic blood pressure, body composition, cessation of smoking, cholesterol profile and health related quality of life between the home and usual care group. Our population had a good risk factor control at entrance to the study why a further improvement could not be expected.

In central Europe, centre-based CR is the traditional choice of CR services. However, establishing of home-based CR programmes as an alternative for elderly patients could improve CR attendance rate. In English speaking countries and in countries where health services are not free home-base CR is more commonly used, primarily through the use of The Heart Manual. Results from these programmes are promising [18;19], although only limited data is available so far.

The main limitation of this study is the number of patients included, which did not allow any sub-group analysis. With the additionally large variation in the effect of intervention as reflected in the wide confidence intervals there is a risk of type II error. However, wide confidence intervals are often seen in exercise trials and our results are in concordance with other much larger exercise trials [18;20]. The strength of this study is the high co-morbidity, which makes our population more representative of the elderly population in daily clinical practice. The high co-morbidity is explained by our screening procedure which eliminated the referral bias often seen to the CR Units, which is not in favour of the elderly fragile patients with high co-morbidity and disability [4;21-23].

Conclusion

In this study of patient ≥ 65 years with coronary heart disease home-based CR improved exercise capacity. The study confirms that elderly cardiac patients are a very fragile population with high comorbidity and disability and that results from exercise trials excluding this group cannot just be applied to the elderly population. After cessation of the home intervention the gained improvement in exercise capacity was rapidly lost. This emphasises, that close follow-up with continuous

guidance is important beyond the initial rehabilitation period. Larger trials of unselected older patients are needed in order to confirm our findings.

Acknowledgments: Physiotherapists, nurses and dieticians involved in the study.

Patient consent: All patients had to signed standard consent forms approved by the Local ethics committee in Copenhagen, Denmark.

Ethics approval: The study was approved by the Local ethics committee in Copenhagen, Denmark, (jr.nr.KF01327990) and the Danish Data Protection Agency (j.nr. 2006-41-7212).

Funding: This work was supported by VELUX FOUNDATION.

Competing interests: NONE.

Authors Contributors: BO designed and initiated the study, collected the data, wrote the statistical analysis plan, analysed the data, and drafted and revised the paper. She is guarantor. EP wrote the statistical analysis plan, analysed the data, and revised the draft paper. MF designed the study and collected some of the data. JFH designed the study and revised the draft paper.

Data sharing statement: No additional data available.

Reference List

1 Clark AM, Hartling L, Vandermeer B, et al. Meta-analysis: secondary prevention programs for patients with coronary artery disease. Ann Intern Med 2005;**143**:659-672.

2 Taylor RS, Brown A, Ebrahim S, et al. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. Am J Med 2004;**116**:682-692.

3 Pasquali SK, Alexander KP, Peterson ED. Cardiac rehabilitation in the elderly. Am Heart J 2001;**142**:748-755.

4 Nielsen KM, Faergeman O, Foldspang A, et al. Cardiac rehabilitation: health characteristics and socio-economic status among those who do not attend. Eur J Public Health 2008;**18**:479-483.

5 Balady GJ, Jette D, Scheer J, et al. Changes in exercise capacity following cardiac rehabilitation in patients stratified according to age and gender. Results of the Massachusetts Association of Cardiovascular and Pulmonary Rehabilitation Multicenter Database. J Cardiopulm Rehabil 1996;**16**:38-46.

6 Lavie CJ, Milani RV. Cardiac rehabilitation and preventive cardiology in the elderly. Cardiol Clin 1999;**17**:233-242.

7 Ades PA, Waldmann ML, McCann WJ, et al. Predictors of cardiac rehabilitation participation in older coronary patients. Arch Intern Med 1992;**152**:1033-1035.

8 Taylor RS, Dalal H, Jolly K, et al. Home-based versus centre-based cardiac rehabilitation. Cochrane Database Syst Rev 2010:CD007130.

9 Jolly K, Taylor RS, Lip GY, et al. Home-based cardiac rehabilitation compared with centre-based rehabilitation and usual care: a systematic review and meta-analysis. Int J Cardiol 2006;**111**:343-351.

10 Smith SC, Jr., Allen J, Blair SN, et al. AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update: endorsed by the National Heart, Lung, and Blood Institute. Circulation 2006;**113**:2363-2372.

11 Fletcher GF, Balady GJ, Amsterdam EA, et al. Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. Circulation 2001;**104**:1694-1740.

12 Saltin B, Grimby G. Physiological analysis of middle-aged and old former athletes. Comparison with still active athletes of the same ages. Circulation 1968;**38**:1104-1115.

13 Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;**40**:373-383.

14 Marchionni N, Fattirolli F, Fumagalli S, et al. Improved exercise tolerance and quality of life with cardiac rehabilitation of older patients after myocardial infarction: results of a randomized, controlled trial. Circulation 2003;**107**:2201-2206.

15 Smith KM, Arthur HM, McKelvie RS, et al. Differences in sustainability of exercise and health-related quality of life outcomes following home or hospital-based cardiac rehabilitation. Eur J Cardiovasc Prev Rehabil 2004;**11**:313-319.

16 Pinsky JL, Jette AM, Branch LG, et al. The Framingham Disability Study: relationship of various coronary heart disease manifestations to disability in older persons living in the community. Am J Public Health 1990;**80**:1363-1367.

17 Shah MR, Hasselblad V, Gheorghiade M, et al. Prognostic usefulness of the six-minute walk in patients with advanced congestive heart failure secondary to ischemic or nonischemic cardiomyopathy. Am J Cardiol 2001;**88**:987-993.

18 Jolly K, Lip GY, Taylor RS, et al. The Birmingham Rehabilitation Uptake Maximisation study (BRUM): a randomised controlled trial comparing home-based with centre-based cardiac rehabilitation. Heart 2009;**95**:36-42.

19 Dalal HM, Evans PH, Campbell JL, et al. Home-based versus hospital-based rehabilitation after myocardial infarction: A randomized trial with preference arms--Cornwall Heart Attack Rehabilitation Management Study (CHARMS). Int J Cardiol 2007;**119**:202-211.

20 O'Connor CM, Whellan DJ, Lee KL, et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. JAMA 2009;**301**:1439-1450.

21 Cortes O, Arthur HM. Determinants of referral to cardiac rehabilitation programs in patients with coronary artery disease: a systematic review. Am Heart J 2006;**151**:249-256.

22 Cooper AF, Jackson G, Weinman J, et al. Factors associated with cardiac rehabilitation attendance: a systematic review of the literature. Clin Rehabil 2002;**16**:541-552.

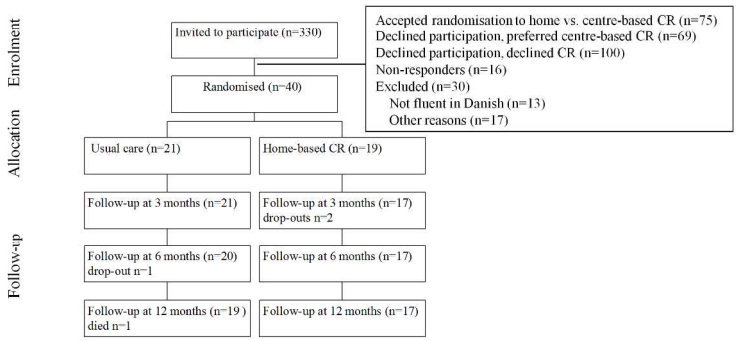
23 Cottin Y, Cambou JP, Casillas JM, et al. Specific profile and referral bias of rehabilitated patients after an acute coronary syndrome. J Cardiopulm Rehabil 2004;**24**:38-44.

Figure Legends

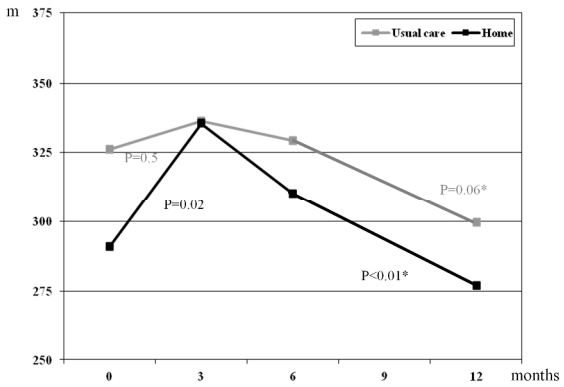
Figure 1 Flowchart

Figure 2 Changes in mean values of 6MWT

* P value between 3 and 12 months



Flowchart
254x190mm (300 x 300 DPI)



Changes in mean values of 6MWT
* P value between 3 and 12 months

254x190mm (300 x 300 DPI)

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	Title page
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	Title page
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3
	2b	Specific objectives or hypotheses	4
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	4
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	-
Participants	4a	Eligibility criteria for participants	4
	4b	Settings and locations where the data were collected	4
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	5
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	6
	6b	Any changes to trial outcomes after the trial commenced, with reasons	No changes made
Sample size	7a	How sample size was determined	-
	7b	When applicable, explanation of any interim analyses and stopping guidelines	Not relevant
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	4
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	4
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	-
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	4

Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	Not possible
	11b	If relevant, description of the similarity of interventions	Not relevant
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	7
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	7
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	9
	13b	For each group, losses and exclusions after randomisation, together with reasons	12
Recruitment	14a	Dates defining the periods of recruitment and follow-up	4
	14b	Why the trial ended or was stopped	4
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Yes
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Figure 1
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Table 2+3
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	Table 2+3
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Table 2+3 + figure 2
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	12
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	14
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	13+14
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	12+13
Other information			
Registration	23	Registration number and name of trial registry	5
Protocol	24	Where the full trial protocol can be accessed, if available	5
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	15

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

Home-based cardiac rehabilitation is an attractive alternative to no cardiac rehabilitation for elderly patients with coronary heart disease. Results from a randomised clinical trial.

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-001820.R1
Article Type:	Research
Date Submitted by the Author:	12-Nov-2012
Complete List of Authors:	Oerkild, Bodil; Bispebjerg University Hospital, Department of Cardiology Frederiksen, Marianne; Bispebjerg University Hospital, Department of Cardiology Hansen, Jørgen; Bispebjerg University Hospital, Department of Cardiology prescott, eva; Bispebjerg University Hospital, Cardiology
Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Rehabilitation medicine
Keywords:	CARDIOLOGY, Coronary heart disease < CARDIOLOGY, Ischaemic heart disease < CARDIOLOGY, Heart failure < CARDIOLOGY

Title page:

Home-based cardiac rehabilitation is an attractive alternative to no cardiac rehabilitation for elderly patients with coronary heart disease. Results from a randomised clinical trial.

Bodil Oerkild, MD, ph.d; Marianne Frederiksen, MD, DMSc; Jorgen Fischer Hansen, MD, DMSc and Eva Prescott MD, DMSc.

Department of Cardiology, Bispebjerg University Hospital, Copenhagen, Denmark

Corresponding author:

Bodil Oerkild, MD, ph.d.

Department of Cardiology,

Bispebjerg University Hospital,

Bispebjerg Bakke 23, 11b

DK-2400 Copenhagen NV, Denmark

Phone: +45 20 15 51 54

Fax: +45 35 31 39 82

Email: Oerkild@dadlnet.dk

Keywords: Cardiac rehabilitation; coronary heart disease; physical activity; mortality.

Word count: 3491

Abstract:

Objective: To compared home-based cardiac rehabilitation (CR) with usual care (control group with no rehabilitation) in elderly patients who declined participation in centre-based CR.

Design: Randomised clinical trial with 12 months follow-up and mortality data after 5½ years (mean follow-up 4½ years).

Setting: Rehabilitation Unit, Department of Cardiology, Copenhagen, Denmark.

Participants: Elderly patients ≥ 65 years with coronary heart disease.

Intervention: A physiotherapist made home visits in order to develop an individualised exercise programme that could be performed at home and surrounding outdoor area. Risk factor intervention, medical adjustment, physical and psychological assessments were offered at baseline and after 3, 6 and 12 months.

Main Outcome Measurements: The primary outcome was six minutes walk test (6MWT). Secondary outcomes were blood pressure, body composition, cholesterol profile, cessation of smoking, health related quality of life (HRQoL), anxiety and depression.

Results: 40 patients participated. The study population was characterised by high age (median age 77 years, range 65-92 years) and high level of co-morbidity. Patients receiving home-based CR had a significant increase in the primary outcome 6MWT of 33.5m (95%CI: 6.2, 60.8, P=0.02) at 3 months whereas the usual care group did not significantly improve, but with no significant differences between the groups. At 12 months follow-up there was a decline in 6MWT in both groups; -55.2m (95%CI: 18.7, 91.7, P<0.01) in the home group and -52.1m (95%CI: -3.0, 107.1, P=0.06) in the usual care group. There were no significant differences in blood pressure, body composition, cholesterol profile, cessation of smoking or HRQoL after 3, 6 and 12 months follow-up.

Conclusions: Participation in home-based CR improved exercise capacity among elderly patients with coronary heart disease, but there was no significant difference between the home intervention

and the control group. In addition, no significant difference was found in the secondary outcomes. When intervention ceased the initial increase in exercise capacity was rapidly lost.

Article focus

- To compare home-based cardiac rehabilitation with usual care in elderly patients with coronary heart disease who decline participation in a centre-based rehabilitation programme.

Key messages

- Home-based cardiac rehabilitation improved exercise capacity among elderly patients with coronary heart disease.
- This population of elderly patient had a high level of co-morbidity and disability.
- When the home-based intervention ceased effect was rapidly lost.

Strengths and limitations of the study

- The randomised design provides a higher level of evidence.
- This population represents the 'real-world' scenario of elderly cardiac patients.
- The duration of the intervention may be too short to maintain changes in exercise capacity at 12 months follow-up.
- The size of the study did not allow sub-group analysis.

Introduction

Participation in cardiac rehabilitation (CR) is often the first step toward optimal secondary treatment and prevention and is recommended to patients with coronary heart disease. The centre-based programmes are the cornerstone in the evidence of CR, with meta-analysis showing an approximately 20% reduction in all-cause and cardiac mortality and 17% reduction in re-infarction rate among patients who participated in the programmes [1;2]. CR is also found to be effective among the elderly age $\geq$ 65 years [3;4]. However, one of the main problems in centre-based CR is the low participation rate among patients in general and among elderly patients in particular. Participation rates are reported to be as low as 30% of eligible patients [5] but among elderly patients participation rate is even lower [4]. In addition, adherence rate to the centre-based programmes are low and drop-out rates are high [6].

In order to improve access and participation rate, there has been an increasing focus on home-based CR where the entire programme or parts hereof is moved from the centre to the patients home. This

could be an attractive alternative to centre-based CR. Several guidelines have advocated for home-based CR [7-9] and these programmes are now the main alternative to the centre-based programmes. We have recently published a randomised clinical trial (RCT) comparing home-based CR with centre-based CR in elderly patients with coronary heart disease [10]. The study showed that home-based CR was not inferior to centre-based CR which is in accordance with a Cochrane review from 2010 [11]. A review from 2006 [12] comparing home-based programmes with usual care (no rehabilitation) found a significantly better outcome in systolic blood pressure and in the likelihood of being a smoker. The home-based programmes had also better outcomes with regard to exercise capacity, total cholesterol, anxiety and depression score although these data did not reach statistical significance. A limitation in the reviews and meta-analyses [11-13] are that the included populations are highly selected with few elderly patients and excluding patients with co-morbidity and disability. Since elderly patients with coronary heart disease is the fastest growing sub-group of cardiac patients there is an increasing need for adjusting the CR programmes according to their requirements.

The aim of this study is, in a randomised design, to compare the effect of home-based CR with usual care (no rehabilitation) in a population of patients ≥ 65 years with coronary heart disease who declined participation in a centre-based CR programme.

Methods

Trial design

The study is a randomised clinical trial comparing home-based CR with usual care. Inclusion criteria were patients ≥ 65 years with a recent coronary event defined as acute myocardial infarction (MI), percutaneous transluminal coronary intervention (PCI) or coronary artery bypass graft (CABG) and who declined participation in centre-based CR. Exclusion criteria were mental

disorders (dementia), social disorders (severe alcoholism and drug abuse), living in a nursing home, language barriers or use of wheelchair. Figure 1 shows the flowchart.

Patients were recruited from our Rehabilitation Unit which offers centre-based CR to all patients with coronary heart disease assigned to the hospital. In order to ensure that all patients receive the CR treatment offer, the referral procedure is centralized and computerized with identification of patients from a database covering diagnosis and all invasive procedures performed in the catchments area of Bispebjerg University Hospital, Copenhagen. Patients are consecutively invited by letter and non-responders are additionally contacted by telephone. At the first visit in the Rehabilitation Unit patients were invited to participate in the previous mentioned RCT comparing home-based CR with centre-based CR [10] or as an alternative encouraged to participate in the centre-based CR programme (outside the study). Patients who declined participation in these offers were invited to participate in this study.

The recruitment period was from January 2007 to July 2008.

Inclusion of patients was not based on a sample size calculation.

Patients had to give informed consent before any trial related procedures. Patients were randomised in alternated block sizes of 4 to 6 using computer generated randomly permuted blocks. An impartial person not related to the study randomised patients. Due to the nature of the intervention concealment of randomisation was not feasible with regard to both patients and researcher. Data were collected at Bispebjerg University Hospital before randomisation and after 3, 6 and 12 months. In addition, overall mortality data were obtained in July 2012, 5½ years after the study was initiated.

The study was approved by the local ethic committee (jr.nr.KF01327990), the Danish Data Protection Agency (j.nr. 2006-41-7212) and is registered at www.clinicaltrial.gov (NCT00489801).

Intervention

The home programme

Patients received two home visits by a physiotherapist in a 6 weeks interval with the purpose of creating a training programme that could be performed at home and outside in local surroundings. Patients were carefully instructed in the training programme and guided to optimal training effort. In between the visits a telephone call was made by the physiotherapist to resolve any questions. The exercise programmes were individualised but followed the international recommendations with 30 min. exercise per day including 5-10 min. warm up (e.g. slow walking) and 10 min. cool down at a frequency of 6 days per week [14;15] at an intensity of 11-13 on the Borg scale [15]. For very disabled patients the exercise programmes were of shorter duration but then repeated several times a day. Regarding risk factor intervention and medical adjustment the patients consulted a cardiologist at baseline and after 3, 6 and 12 months. At 4 and 5 months a telephone call was made by the cardiologist to encourage continuous exercising and to answer any medical questions. All patients were offered dietary counselling and (if required) smoking cessation.

Usual care

This group is equivalent to a non-rehabilitation control group. Patients were not offered exercise education or dietary counselling but as for the home group, offered risk factor intervention and medical adjustment by a cardiologist at baseline and after 3, 6 and 12 months. Telephone calls were made at 4 and 5 months. Thus, this group received solely consultation at a cardiologist which is offered to all patients in daily clinical practise who decline participation in our comprehensive centre-based CR programme.

Outcome measures

Because many patients due to age and co-morbidity is not able to perform a symptom-limited exercise capacity test the primary outcome was change in exercise capacity determined by 6MWT.

The secondary outcomes were: sit to stand test (STS), self reported level of physical activity, systolic and diastolic blood pressure, total-, HDL- and LDL-cholesterol, body mass index (BMI), waist-hip ratio, proportion of smokers, HRQoL measured by SF-12 and anxiety and depression estimated by Hospital Anxiety and Depression Scale (HADS). Outcomes were evaluated after 3, 6 and 12 months.

In the STS-test the patients must as fast as possible within 30 sec. change position from sitting on a chair to upright standing, without holding the handgrip, hereby measuring the strength in the lower limb. Self-reported level of physical activity was estimated by a questionnaire originally developed by Saltin and Grimby [16]. It has four categories ranging from a sedentary lifestyle, to performing light activities 2-4 hours/week, activity more than 4 hours/week or highly vigorous physical activity more than 4 hours/week. Patients in the last three categories were classified as having an active lifestyle. Medication included the use of diuretics, beta-blockers, calcium antagonists, lipid lowering drugs, anti-thrombotics, anti-diabetic and anti-depressive treatment. Sociodemographic data included level of education, main employment status, contact to children, living alone and the need of weekly assistance at home. Patients in NYHA II-IV and CCS II-IV were categorised as having dyspnoea and angina, respectively. Co-morbidity was assed by The Charlson Co-Morbidity Index (CMI) [17], which measures the burden of 19 co-morbid conditions through a weighted index. The CMI was categorised in 3 sub-groups: 0 (no co-morbid condition), 1-2 and $\geq$ 3 (high level of co-morbid burden).

Adverse events were recorded in the study period and included admissions for MI, progressive angina, decompensated congestive heart failure, severe bleeding, new malignant disease, and performance of PCI. Moreover, the number and duration of hospital admissions were recorded 1 year after randomisation. Mortality data were obtained from the Civil Registration System, which records the vital status of all citizens in Denmark.

Statistical analysis

To test the effect of the interventions at 3 and 12 months a mixed model of regression analysis was used with a time*treatment interaction term. We used a mixed model in order to analyse the effect of the interventions, since this statistical model allow us to include all data into one analysis. All the models were adjusted for age and gender. We did not adjust the significance levels for multiple testing, since such an adjustment is a too conservative test to perform when data are positively correlated, as in this study.

Data were analysed by intention to treat. All statistical analysis was performed using STATA for windows release 10.0.

Table 1 Baseline characteristics according to intervention
Values are mean (SD) unless stated otherwise

Characteristic	Usual care n=21	Home n=19
Age	76.5 (7.7)	77.3 (6.0)
Men n (%)	11 (52.3%)	12 (63.2%)
Risk factors		
Hypertension, n (%)	13 (61.9%)	16 (88.9%)
Hyperlipidemia, n (%)	17 (81.0%)	18 (94.7%)
Diabetes, n (%)	2 (9.5%)	7 (36.8%)
BMI, kg/m^2	26.2 (3.6)	27.6 (4.5)
Current smokers, n (%)	9 (42.9%)	8 (42.1%)
Medical history		
Previous MI, n (%)	8 (38.1%)	6 (31.7%)
Previous PCI, n (%)	5 (23.8%)	4 (21.1%)
Previous CABG, n (%)	2 (9.5%)	0 (0%)
Heart failure LVEF $\leq$ 45%, n (%)	9 (42.9%)	9 (50.0%)
Event prior to entry into the study		
Post-MI without invasive procedure, n (%)	4 (19.1%)	0 (0%)
Post-PCI, n (%)	14 (66.7%)	16 (84.2%)
Post-CABG, n (%)	3 (14.3%)	3 (15.8%)
Clinical status		
6MWT, m	325.9 (123.1)	290.9 (116.5)
STS	10.9 (3.7)	8.9 (4.8)
Systolic blood pressure, mmHg	138.3 (22.2)	153.6 (27.5)
Diastolic blood pressure, mmHg	72.2 (13.9)	76.1 (13.0)
Waist-hip ratio	0.9 (0.1)	1.0 (0.1)
Dyspnoea, NYHA II-IV, n (%)	13 (61.9%)	11 (57.9%)
Angina, CCS II-IV, n (%)	4 (19.1%)	4 (21.1%)
Self-reported active lifestyle, n (%)	10 (47.6%)	6 (31.6%)
Co-morbid conditions		
CMI score 0, n (%)	0 (0%)	1 (5.3%)
1-2, n (%)	9 (42.9%)	7 (36.8%)
$\geq$3, n (%)	12 (57.1%)	11 (57.9%)
COPD, n (%)	7 (33.3%)	4 (21.1%)
Peripheral arterial disease, n (%)	3 (14.3%)	5 (26.3%)
Laboratory values		
Total cholesterol, mmol/l	4.5 (1.1)	4.3 (0.9)
HDL cholesterol, mmol/l	1.4 (0.3)	1.3 (0.6)
LDL cholesterol, mmol/l	2.5 (2.2)	2.4 (1.7)
HRQoL, anxiety and depression		
HADS anxiety score	4.7 (3.0)	5.1 (4.9)
HADS depression score	5.3 (3.8)	4.8 (2.7)
SF-12 PCS	39.0 (10.8)	38.0 (9.9)
SF-12 MCS	46.9 (10.1)	48.9 (9.3)

Abbreviations: MI, myocardial infarction; PCI, percutaneous transluminal coronary intervention; CABG, coronary artery bypass graft; LVEF, left ventricular ejection fraction; 6MWT, 6 minutes walk test; STS, sit to stand test; CMI, Charlson co-morbidity index; COPD, chronic obstructive lung disease; HRQoL, health related quality of life; HADS, Hospital Anxiety and Depression Scale; PMS, physical composite scale of SF-12; MCS, mental composite scale of SF-12.

Results

A total of 40 patients participated. Baseline characteristics are listed in table 1. All patients received anti-thrombotics and lipid lowering drugs and 77.4% received beta-blockers.

Of eligible patients to receive CR (n=284) a total of 49% (n=140) declined to participate in the centre-based programme, figure 1. Of these 29% accepted to participate in this study and 71% (n=100) did not receive any rehabilitation.

Exclusion rate was 10% mainly because of language barriers (n=13), social disorders (n=5), dementia (n=5) and other reasons (n=7).

Exercise capacity

Figure 2 illustrates the unadjusted means of the primary outcome measurement of 6MWT from baseline to 12 months follow-up. The figure shows a significant increase in walking distance of 33.5m (95%CI: 6.2, 60.8, P=0.02) in the home group after the intervention followed by a significant decline of -55.2m (95%CI: 18.7, 91.7, P<0.01) at 12 months follow-up to a level lower than the baseline value. Patients in the usual care group had a non-significant increase in walking distance of 10.1m (95 %CI: -19.3, 39.5, P=0.5) after 3 months followed by a decline of -52.1m (95%CI: -3.0, 107.1, P=0.06) at the end of the follow-up period. When adjusting for age and gender in a mixed model with a time*treatment interaction term, there were no significant differences between the groups at 3 months (table 2). At 12 months follow-up, a significant decline in 6MWT and STS was found in both groups with no differences between the groups (table 3).

Other outcomes

A higher proportion of patients reported a change from an inactive to an active lifestyle in the home group (27%, P<0.05) compared to the usual care group (-5%, P=0.6) after the intervention with a difference between the two groups of 33% (P<0.05). At 12 months follow-up the proportion of patients with a self-reported active lifestyle declined again in the home group with no changes in the usual care group.

Table 2 Effect of intervention at 3 months follow-up
All data are adjusted for age and gender. * P<0.05.
Abbreviations: CI, confidence interval; 6MWT, 6 minutes walk test; STS, sit to stand test; HRQoL, health related quality of life; HADS, hospital anxiety and depression score; PCS, physical component summary scale of SF-12; MCS, mental component summary scale of SF-12.

	Usual care		**Home**			
	Δ 0-3 months	95%CI	Δ 0-3 months	95%CI	Between groups comparison	95%CI
Exercise capacity						
6MWT, m	10.1	-23.6, 43.9	36.3	-0.9, 73.6	26.2	-24.1, 76.5
STS	0.9	-0.8, 2.6	1.0	-0.8, 2.8	0.1	-2.3, 2.6
Clinial status						
Systolic blood pressure, mmHg	2.0	-8.4, 12.4	-12.9	-24.2, -1.6*	-14.9	-30.2, 0.5
Diastolic blood pressure, mmHg	4.1	-2.2, 10.5	-1.5	-8.4, 5.4	-5.7	-15.0, 3.7
BMI, kg/m^2	0.1	-1.3, 1.5	-0.5	-2.1, 1.1	-0.6	-2.7, 1.5
Waist-hip ratio	-0.01	-0.03, 0.01	-0.01	-0.03, 0.01	0	-0.03, 0.03
Laboratory values						
Total cholesterol, mmol/l	-0.2	-0.6, 0.2	-0.1	-0.5, 0.4	0.1	-0.5, 0.7
HDL cholesterol, mmol/l	0.1	-0.01, 0.2	0.1	-0.1, 0.2	-0.04	-0.2, 0.1
LDL cholesterol, mmol/l	-0.2	-0.5, 0.1	-0.1	-0.5, 0.3	0.1	-0.4, 0.6
Cholesterol/HDL ratio	-0.4	-0.7, 0	-0.3	-0.7, 0.1	0.1	-0.5, 0.7
HRQoL, anxiety and depression						
HADS anxiety score	-0.9	-2.3, 0.5	-1.2	-2.7, 0.6	-0.3	-2.4, 1.9
HADS depression score	-1.1	-2.6, 0.4	-1.0	-2.7, 0.6	0.1	-2.2, 2.3
SF-12 PCS	2.7	-1.4, 6.8	-0.4	5.1, 4.3	-3.1	-9.4, 3.1
SF-12 MCS	3.5	-0.9, 7.9	2.4	-2.6, 7.5	-1.0	-7.7, 5.6

Table 3 Follow-up data at 12 months

All data are adjusted for age and gender. * P<0.05, **P<0.01.
Abbreviations: CI, confidence interval; 6MWT, 6 minutes walk test; STS, sit to stand test; HRQoL, health related quality of life; HADS, hospital anxiety and depression score; PCS, physical component summary scale of SF-12; MCS, mental component summary scale of SF-12.

	Usual care		**Home**			
	Δ 3-12 months	95%CI	Δ 3-12 months	95%CI	Between groups comparison	95%CI
Exercise capacity						
6MWT, m	-50.9	-86.6, -15.3**	-55.0	-94.0, -16.1**	-4.0	-56.8, 48.8
STS	-3.0	-4.7, -1.3**	-2.1	-3.9, -0.3*	0.9	-1.6, 3.4
Clinical status						
Systolic blood pressure, mmHg	0.7	-9.3, 10.6	-2.5	-13.1, 8.2	-3.1	-17.7, 11.4
Diastolic blood pressure, mmHg	-0.6	-6.4, 5.1	1.6	-4.6, 7.8	2.2	-6.2, 10.7
BMI, kg/m^2	0.4	-0.04, 0.8	0.6	0.1, 1.0*	0.2	-0.4, 0.8
Waist-hip ratio	0.01	-0.01, 0.03	0.0	-0.02, 0.02	0.01	-0.04, 0.02
Laboratory values						
Total cholesterol, mmol/l	0.1	-0.3, 0.5	-0.1	-0.5, 0.3	-0.2	-0.8, 0.4
HDL cholesterol, mmol/l	-0.1	-0.2, 0.01	-0.04	-0.1, 0.1	0.1	-0.1, 0.2
LDL cholesterol, mmol/l	0.1	-0.3, 0.2	-0.04	-0.4, 0.3	-0.1	-0.6, 0.4
Cholesterol/HDL ratio	0.3	-0.1, 0.6	0.1	-0.3, 0.5	-0.2	-0.7, 0.3
HRQoL, anxiety and depression						
HADS anxiety score	0.3	-1.3, 1.9	0.4	-1.3, 2.1	0.1	-2.3, 2.4
HADS depression score	0.3	-1.2, 1.8	1.2	-0.3, 2.8	0.9	-1.3, 3.1
SF-12 PCS	-1.4	-5.2, 2.3	-1.1	-5.3, 3.1	0.3	-5.4, 6.0
SF-12 MCS	-0.3	-4.6, 4.0	-1.4	-6.1, 3.3	-1.1	-7.5,5.3

There were no significant differences in clinical status, exercise capacity, laboratory values, HRQoL or anxiety and depression score at 3 and 12 months follow-up either within or between the groups.

The number and length of acute and non-acute admissions were equally distributed at 12 months follow-up (data not shown).

A total of nine patients died during a mean follow-up of 4½ years (usual care group n=5 and home group n=4). There was no loss to follow-up.

Discussion

To the best of our knowledge, this is the first study to investigate the effect of home-based CR compared to usual care (no rehabilitation) among elderly patients ≥ 65 years with coronary heart disease who declined participation in a centre-based programme. In many countries, including Denmark, centre-based programmes are often the only cardiac rehabilitation programme available, and the limited access to CR may be an important barrier for optimal secondary treatment and prevention in elderly patients with coronary heart disease.

The study found that elderly patients who decline participation in centre-based CR had a low level of exercise capacity and a high level of co-morbidity. For this population who is often found not to be eligible to centre-based CR, home-based CR was feasible. There was a trend towards clinical relevant improvement in 6MWT but these changes were not statistically significant compared to the control group. Although the study is small and conclusions must be drawn with caution, it could identify an intervention targeting this group of patients. After having ended the home programme the gained improvement in exercise capacity was not sustained.

Exercise capacity

The effect of our home CR programme on exercise capacity is consistent with the findings in the only other study investigating the effect of home-based CR and usual care among elderly with coronary heart disease [3]. In this study, patients in the age groups 45-65 years, 66-75 years and > 75 years significantly improved their exercise capacity after participating in a home programme although the improvement was less among the very old patients (>75 years).

The meta-analysis by Jolly et al [12], which included studies of all age groups, investigated the effect of home-based CR and usual care. The meta-analysis showed an improvement in exercise capacity

but could not identify any significant differences between the home and usual care group. The authors explained this by the possability that patients in usual care groups may receive input that match the home-interventions and thus diminish a possible difference. This could also have been the case in our study.

At 12 months a significant decline in exercise capacity was found in both the home and usual care group reaching a level lower than at entrance to the study. We identified two other studies with long-term follow-up [3;18]. In contrast to our study they both found a sustained improvement in exercise capacity after 12 months if the exercise programme was initiated at home. The discrepancy could be caused by the duration of our home intervention that may have been too short to maintain changes in lifestyle at 12 months follow-up, but our home intervention is in line with other home-based programmes [12;13]. The majority of programmes have a duration of 6-12 weeks [7;9;11-13]. It has been suggested that more intensive programmes with prolonged duration beyond 12 weeks have a more successful long term outcome [19;20]. However, in a previous study of heart failure patients [21] even a prolonged centre-based maintenance programme with supervised sessions every two weeks in addition to home exercise training could not maintain the improvements achieved during initial CR [21]. Furthermore, in the very large HF-ACTION trial [22] patients participated in an initial centre-based exercise programme of 36 sessions in 3 months followed by a home-based exercise programme with intensive follow-up and were equipment for home training was provided. In this study there were no changes in exercise capacity at 12 months follow-up. This was explained partly by insufficient adherence to training that was below the target set at all time points. The HF-ACTION trial mainly included middle aged men with no major co-morbidities or limitations that could interfere with training. Thus, in spite of intensive exercise programmes with close follow-up in patients with no significant concomitant co-morbidities it is difficult to motivate patients to adhere to training. Feasible solutions to overcome this have not yet been identified.

The discrepancy between studies may also be due to the differences in the enrolled populations. Our population was significantly older (mean age 77.3 ±6.0 years versus 69.0 ±9.0 years [3] and 64.3 ±0.5 years [18]) and had a high degree of co-morbidity and low level of exercise capacity. Age, co-morbidity and disability are all found to be negative correlated with physical activity [15;23] and adherence to training [6;24;25] and thus may have contributed significantly to the lack of sustained effect at 12 months. In addition, the only other study targeting the elderly [3] the population was highly selected with exclusions rate of 72% among the very old patients (>75 years) due to co-morbidity, disability and congestive heart failure, leading to a much "healthier" population compared to our population were only 10% were excluded.

Coronary heart disease is one of the leading causes of disability and with increasing age other chronic non-cardiac conditions further limit function [26]. Our population of elderly had a very high frequency of co-morbid conditions (57% had CMI $\geq$ 3). For comparison, a recent very large nationwide study including 234 000 patients (median age 68 years in men and 75 years in women) with first time acute myocardial infarction found that only 6% of that population had CMI$\geq$3 [27]. In addition to the high frequency of co-morbidity we found a low level of exercise capacity at baseline, with mean 6MWT=308.4 m ± 120. In healthy elderly subjects mean 6MWT is found to be approximately 659 m ± 74 m [28] and in a recent RCT study from our group comparing home-based CR with centre-based CR[10] we found a baseline mean 6MWT of 340 m ± 122 m in the centre group [10]. These characteristics indicate that the group of elderly patients who decline participation in centre-based rehabilitation is very vulnerable and not necessarily comparable with the population who accept centre-based CR. Our finding is in concordance with previous studies who found that older age, high burden of co-morbidity and low level of exercise capacity was negatively correlated with participation rate in centre-based CR programmes [6;24].

The high burden of co-morbidity in this population is most likely explained by the computerized identification of patients which eliminated the selection and referral bias often seen to rehabilitation units, which is not in favour of the elderly and patients with co-morbidity [24;29-31].

Other outcomes

Self-reported active lifestyle and systolic blood pressure changed favorably in the home group after the intervention but there were no significant differences in diastolic blood pressure, body composition, cessation of smoking, cholesterol profile and HRQoL between the groups. Our population had a good risk factor control and low anxiety and depression score (HADS score < 8 is within normal rage) [32;33] at entrance to the study why a further improvement could not be expected. We did not find any significant changes in HRQoL measured by SF-12. This is partly due to lack of statistical power and the limited duration of our home intervention but is in concordance with the meta-analysis by Jolly et al [12] and with a recent published review concerning CR and HRQoL [34].

We did not have any specific psychological intervention but the type of intervention (comprehensive programmes, exercise only or mainly psychological interventions) do not seem to affect these results [12;34].

In central Europe, centre-based CR is the traditional choice of CR services. However, establishing of home-based CR programmes as an alternative for elderly patients could improve CR attendance rate. In English speaking countries and in countries where health services are not free home-base CR programmes are more commonly used, primarily through the adoption of The Heart Manual [35;36]. This is currently not an option in non-English speaking countries, in many of which there is a stronger tradition of centre-based CR.

In the everyday scenario at the rehabilitation units there is only one CR programme available and this is often a centre-based programme. Patients who decline enrolment in these programmes do not have alternatives. A total of 29% of patients who initially declined centre-based CR did accept to participate in this study and the proportion could have been even higher if the home-based CR

programme was not part of a RCT study. Thus, with alternative concomitant CR programmes, accessibility increases and participation rate will be expected to rise.

The main limitation of this study is the number of patients included. With the additionally large variation in the effect of intervention as reflected in the wide confidence intervals there is a risk of type II error. However, wide variations in effect of intervention are often seen in exercise trials and our results are in concordance with other much larger exercise trials [22;35]. The strength of our study is the randomised design and the unselected population of elderly patients with high co-morbidity, which probably makes our population more representative of the elderly population in daily clinical practice.

Conclusion

In this study of patient ≥ 65 years with coronary heart disease home-based CR improved exercise capacity, but there was no significant difference between the home intervention and the control group. In addition, no significant difference was found in the secondary outcomes. The study found that elderly cardiac patients who declined participation in centre-based CR had high level of co-morbidity and low exercise capacity. These characteristics indicate that results from exercise trials excluding this group of patients should be cautiously applied to the elderly population. After cessation of the home intervention the gained improvement in exercise capacity was rapidly lost. This emphasises, that close follow-up with continuous guidance beyond the initial rehabilitation period is important. This study could contributes to the scientific gap on how to manage the large population of elderly cardiac patients who are not interested in (or cable of) participating in a centre-based CR programme. Larger trials of unselected older patients are needed in order to confirm our findings and ways to overcome the barriers for adherence to exercise training has to be established.

Acknowledgments: Physiotherapists, nurses and dieticians involved in the study.

Patient consent: All patients had to signed standard consent forms approved by the Local ethics committee in Copenhagen, Denmark.

Ethics approval: The study was approved by the Local ethics committee in Copenhagen, Denmark, (jr.nr.KF01327990) and the Danish Data Protection Agency (j.nr. 2006-41-7212).

Funding: This work was supported by VELUX FOUNDATION.

Competing interests: NONE.

Authors Contributors: BO designed and initiated the study, collected the data, wrote the statistical analysis plan, analysed the data, and drafted and revised the paper. She is guarantor. EP contributed with design, wrote the statistical analysis plan, analysed the data, and revised the draft paper. MF designed the study and collected some of the data and revised the paper. JFH designed the study and revised the draft paper.

Data sharing statement: No additional data available.

Reference List

(1) Clark AM, Hartling L, Vandermeer B, McAlister FA. Meta-analysis: secondary prevention programs for patients with coronary artery disease. *Ann Intern Med* 2005; 143(9):659-672.

(2) Taylor RS, Brown A, Ebrahim S, Jolliffe J, Noorani H, Rees K et al. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *Am J Med* 2004; 116(10):682-692.

(3) Marchionni N, Fattirolli F, Fumagalli S, Oldridge N, Del Lungo F, Morosi L et al. Improved exercise tolerance and quality of life with cardiac rehabilitation of older patients after myocardial infarction: results of a randomized, controlled trial. *Circulation* 2003; 107(17):2201-2206.

(4) Pasquali SK, Alexander KP, Peterson ED. Cardiac rehabilitation in the elderly. *Am Heart J* 2001; 142(5):748-755.

(5) Jackson L, Leclerc J, Erskine Y, Linden W. Getting the most out of cardiac rehabilitation: a review of referral and adherence predictors. *Heart* 2005; 91(1):10-14.

(6) Worcester MU, Murphy BM, Mee VK, Roberts SB, Goble AJ. Cardiac rehabilitation programmes: predictors of non-attendance and drop-out. *Eur J Cardiovasc Prev Rehabil* 2004; 11(4):328-335.

(7) Giannuzzi P, Saner H, Bjornstad H, Fioretti P, Mendes M, Cohen-Solal A et al. Secondary prevention through cardiac rehabilitation: position paper of the Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology. *Eur Heart J* 2003; 24(13):1273-1278.

(8) Graham I, Atar D, Borch-Johnsen K, Boysen G, Burell G, Cifkova R et al. European guidelines on cardiovascular disease prevention in clinical practice: full text. Fourth Joint Task Force of the European Society of Cardiology and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of nine societies and by invited experts). *Eur J Cardiovasc Prev Rehabil* 2007; 14 Suppl 2:S1-113.

(9) Thomas RJ, King M, Lui K, Oldridge N, Pina IL, Spertus J et al. AACVPR/ACC/AHA 2007 performance measures on cardiac rehabilitation for referral to and delivery of cardiac rehabilitation/secondary prevention services endorsed by the American College of Chest Physicians, American College of Sports Medicine, American Physical Therapy Association, Canadian Association of Cardiac Rehabilitation, European Association for Cardiovascular Prevention and Rehabilitation, Inter-American Heart Foundation, National Association of Clinical Nurse Specialists, Preventive Cardiovascular Nurses Association, and the Society of Thoracic Surgeons. *J Am Coll Cardiol* 2007; 50(14):1400-1433.

(10) Oerkild B, Frederiksen M, Hansen JF, Simonsen L, Skovgaard LT, Prescott E. Home-based cardiac rehabilitation is as effective as centre-based cardiac rehabilitation among elderly

with coronary heart disease: results from a randomised clinical trial. *Age Ageing* 2011; 40(1):78-85.

(11) Taylor RS, Dalal H, Jolly K, Moxham T, Zawada A. Home-based versus centre-based cardiac rehabilitation. *Cochrane Database Syst Rev* 2010;(1):CD007130.

(12) Jolly K, Taylor RS, Lip GY, Stevens A. Home-based cardiac rehabilitation compared with centre-based rehabilitation and usual care: a systematic review and meta-analysis. *Int J Cardiol* 2006; 111(3):343-351.

(13) Dalal HM, Zawada A, Jolly K, Moxham T, Taylor RS. Home based versus centre based cardiac rehabilitation: Cochrane systematic review and meta-analysis. *BMJ* 2010; 340:b5631.

(14) Smith SC, Jr., Allen J, Blair SN, Bonow RO, Brass LM, Fonarow GC et al. AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update: endorsed by the National Heart, Lung, and Blood Institute. *Circulation* 2006; 113(19):2363-2372.

(15) Fletcher GF, Balady GJ, Amsterdam EA, Chaitman B, Eckel R, Fleg J et al. Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. *Circulation* 2001; 104(14):1694-1740.

(16) Saltin B, Grimby G. Physiological analysis of middle-aged and old former athletes. Comparison with still active athletes of the same ages. *Circulation* 1968; 38(6):1104-1115.

(17) Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40(5):373-383.

(18) Smith KM, Arthur HM, McKelvie RS, Kodis J. Differences in sustainability of exercise and health-related quality of life outcomes following home or hospital-based cardiac rehabilitation. *Eur J Cardiovasc Prev Rehabil* 2004; 11(4):313-319.

(19) Perk J, De BG, Gohlke H, Graham I, Reiner Z, Verschuren M et al. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J* 2012; 33(13):1635-1701.

(20) Clark AM, Catto S, Bowman G, Macintyre PD. Design matters in secondary prevention: individualization and supervised exercise improves the effectiveness of cardiac rehabilitation. *Eur J Cardiovasc Prev Rehabil* 2011; 18(5):761-769.

(21) Prescott E, Hjardem-Hansen R, Dela F, Orkild B, Teisner AS, Nielsen H. Effects of a 14-month low-cost maintenance training program in patients with chronic systolic heart failure: a randomized study. *Eur J Cardiovasc Prev Rehabil* 2009; 16(4):430-437.

(22) O'Connor CM, Whellan DJ, Lee KL, Keteyian SJ, Cooper LS, Ellis SJ et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 2009; 301(14):1439-1450.

(23) Kaplan MS, Newsom JT, McFarland BH, Lu L. Demographic and psychosocial correlates of physical activity in late life. *Am J Prev Med* 2001; 21(4):306-312.

(24) Cooper AF, Jackson G, Weinman J, Horne R. Factors associated with cardiac rehabilitation attendance: a systematic review of the literature. *Clin Rehabil* 2002; 16(5):541-552.

(25) Witt BJ, Jacobsen SJ, Weston SA, Killian JM, Meverden RA, Allison TG et al. Cardiac rehabilitation after myocardial infarction in the community. *J Am Coll Cardiol* 2004; 44(5):988-996.

(26) Pinsky JL, Jette AM, Branch LG, Kannel WB, Feinleib M. The Framingham Disability Study: relationship of various coronary heart disease manifestations to disability in older persons living in the community. *Am J Public Health* 1990; 80(11):1363-1367.

(27) Schmidt M, Jacobsen JB, Lash TL, Botker HE, Sorensen HT. 25 year trends in first time hospitalisation for acute myocardial infarction, subsequent short and long term mortality, and the prognostic impact of sex and comorbidity: a Danish nationwide cohort study. *BMJ* 2012; 344:e356.

(28) Jenkins S, Cecins N, Camarri B, Williams C, Thompson P, Eastwood P. Regression equations to predict 6-minute walk distance in middle-aged and elderly adults. *Physiother Theory Pract* 2009; 25(7):516-522.

(29) Nielsen KM, Faergeman O, Foldspang A, Larsen ML. Cardiac rehabilitation: health characteristics and socio-economic status among those who do not attend. *Eur J Public Health* 2008; 18(5):479-483.

(30) Cortes O, Arthur HM. Determinants of referral to cardiac rehabilitation programs in patients with coronary artery disease: a systematic review. *Am Heart J* 2006; 151(2):249-256.

(31) Cottin Y, Cambou JP, Casillas JM, Ferrieres J, Cantet C, Danchin N. Specific profile and referral bias of rehabilitated patients after an acute coronary syndrome. *J Cardiopulm Rehabil* 2004; 24(1):38-44.

(32) Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002; 52(2):69-77.

(33) Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67(6):361-370.

(34) Shepherd CW, While AE. Cardiac rehabilitation and quality of life: a systematic review. *Int J Nurs Stud* 2012; 49(6):755-771.

(35) Jolly K, Lip GY, Taylor RS, Raftery JP, Mant JW, Lane D et al. The Birmingham Rehabilitation Uptake Maximisation study (BRUM): a randomised controlled trial comparing home-based with centre-based cardiac rehabilitation. *Heart* 2008.

(36) Dalal HM, Evans PH, Campbell JL, Taylor RS, Watt A, Read KL et al. Home-based versus hospital-based rehabilitation after myocardial infarction: A randomized trial with preference arms--Cornwall Heart Attack Rehabilitation Management Study (CHARMS). *Int J Cardiol* 2007; 119(2):202-211.

Figure Legends

Figure 1 Flowchart

Figure 2 Changes in mean values of 6MWT

* P value between 3 and 12 months

Title page:

Home-based cardiac rehabilitation is an attractive alternative to no ~~centre-based~~ cardiac rehabilitation for elderly patients with coronary heart disease. Results from a randomised clinical trial.

Bodil Oerkild, MD, ph.d; Marianne Frederiksen, MD, DMSc; Jorgen Fischer Hansen, MD, DMSc and Eva Prescott MD, DMSc.

Department of Cardiology, Bispebjerg University Hospital, Copenhagen, Denmark

Corresponding author:

Bodil Oerkild, MD, ph.d.

Department of Cardiology,

Bispebjerg University Hospital,

Bispebjerg Bakke 23, 11b

DK-2400 Copenhagen NV, Denmark

Phone: +45 20 15 51 54

Fax: +45 35 31 39 82

Email: Oerkild@dadlnet.dk

Keywords: Cardiac rehabilitation; coronary heart disease~~elderly~~; physical activity; mortality.

Word count: ~~2512~~3491

Abstract:

Objective: To compared home-based cardiac rehabilitation (CR) with usual care (control group with no rehabilitation) in elderly patients ~~not willing to~~ who declined participatione in centre-based CR.

Design: Randomised clinical trial with 12 months follow-up and mortality data ~~at~~after 5½ years (mean follow-up 4½ years).

Setting: Rehabilitation Unit, Department of Cardiology, Copenhagen, Denmark.

Participants: Elderly patients ≥ 65 years with coronary heart disease.

Intervention: A physiotherapist made home visits in order to develop an individualised exercise programme that could be performed at home and surrounding outdoor area. Risk factor intervention, medical adjustment, physical and psychological assessments were offered at baseline and after 3, 6 and 12 months.

Main Outcome Measurements: The primary outcome was six minutes walk test (6MWT). Secondary outcomes were blood pressure, body composition, cholesterol profile, cessation of smoking, ~~and~~ health related quality of life (HRQoL), anxiety and depression.

Results: 40 patients participated. The study population was characterised by high age (median age 77 years, range 65-92 years) and high level of co-morbidity. Patients receiving home-based CR had a significant increase in the primary outcome 6MWT of 33.5m (95%CI: 6.2, 60.8, P=0.02) at 3 months whereas the usual care group did not significantly improve, but with no significant differences between the groups. ~~However, at~~ At 12 months follow-up there was a ~~significant~~ decline in 6MWT in both groups; -55.2m (95%CI: 18.7, 91.7, P<0.01) in the home~~-based CR~~ group and -52.1m (95%CI: -3.0, 107.1, P=0.06) in the usual care group. There were no significant differences in blood pressure, body composition, cholesterol profile, cessation of smoking or~~and~~ HRQoL ~~health related quality of life~~ after 3, 6 and 12 months follow-up.

Conclusions: Participation in home-based CR improved exercise capacity among elderly patients with coronary heart disease, but there was no significant difference between the home intervention and the control group. In addition, no significant difference was found in the secondary outcomes. ~~However, w~~When intervention ceased the initial increase in exercise capacity~~effect~~ was rapidly lost.

Article focus

- To compare home-based cardiac rehabilitation with usual care in elderly patients with coronary heart disease who decline participation in a centre-based rehabilitation programme.

Key messages

- Home-based cardiac rehabilitation improved exercise capacity among elderly patients with coronary heart disease.
- This population of ~~E~~elderly patient ~~with coronary heart disease~~ has~~d~~s a high level of co-morbidity and disability.
- When the home-based intervention ceased effect was rapidly lost.

Strengths and limitations of the study

- The randomised design provides a higher level of evidence.
- This population represents the 'real-world' scenario of elderly cardiac patients.
- The duration of the intervention may be too short to maintain changes in exercise capacity at 12 months follow-up.
- The size of the study did not allow sub-group analysis.

Introduction

Participation in cardiac rehabilitation (CR) is often the first step toward optimal secondary treatment and prevention and is recommended to patients with coronary heart disease. The centre-based programmes are the cornerstone in the evidence of CR, with meta-analysis showing an approximately 20% reduction in all-cause and cardiac mortality and 17% reduction in re-infarction rate among patients who participated in the programmes [1;2]. CR is also found to be effective among the elderly age ≥ 65 years [3;4] ~~and this group may benefit the most~~. However, one of the main problems in centre-based CR is the low participation rate among patients in general and among elderly patients in particular. Participation rates are reported to be as low as 30% of eligible patients [5] but among elderly patients participation rate is even lower [4]. In addition, adherence rate to the centre-based programmes are low and drop-out rates are high [6]. ~~the elderly and patients with co-~~

Formatted: Font: Times New Roman, 12 pt

Formatted: Plain Text

Field Code Changed

~~morbidity are underrepresented in the centre based programmes. It has been estimated that only 20% of eligible elderly participate [4;5].~~

In order to improve access and participation rate, there has been an increasing focus on home-based CR where the entire programme or parts hereof is moved from the centre to the patients home. This could be an attractive alternative to centre-based CR. Several guidelines have advocated for home-based CR [7-9] and these programmes are now the main alternative to the centre-based programmes. ~~A~~ We have recently published a randomised clinical trial (RCT) comparing home-based CR with centre-based CR in elderly patients with coronary heart disease [10]. The study showed that home-based CR was not inferior to centre-based CR which is in accordance with a Cochrane review from 2010 [116]. ~~established that home based CR was not inferior to centre based CR and a~~ A review from 2006 [127] ~~found~~ comparing ~~that the~~ home-based programmes with usual care (no rehabilitation) found a significantly better outcome in systolic blood pressure and in the likelihood of being a smoker. The home-based programmes had also better outcomes with regard to exercise capacity, total cholesterol, anxiety and depression score although these data did not reach statistical significance. ~~at some points were superior to usual care. However,~~ A limitation in the reviews and meta-analyses [11-13] are that the included populations ~~in the reviews were~~ are highly selected with few elderly patients and excluding patients with co-morbidity and disability. Since elderly patients with coronary heart disease is the fastest growing sub-group of cardiac patients there is an increasing need for adjusting the CR programmes according to their requirements.

The aim of this study is, in a randomised design, to compare the effect of home-based CR with usual care (no rehabilitation) in a population of patients ≥ 65 years with coronary heart disease who declined participation ~~did not want to participate~~ in a centre-based CR programme.

Formatted: Do not check spelling or grammar, Superscript

Formatted: Do not check spelling or grammar, Superscript

Field Code Changed

Field Code Changed

Formatted: Do not check spelling or grammar, Superscript

Methods

Trial design

The study is a randomised clinical trial comparing home-based CR with usual care. Inclusion criteria were patients > 65 years with a recent coronary event defined as acute myocardial infarction (MI), percutaneous transluminal coronary intervention (PCI) or coronary artery bypass graft (CABG) and who declined participation in centre-based CR. Exclusion criteria were mental disorders (dementia), social disorders (severe alcoholism and drug abuse), living in a nursing home, language barriers or use of wheelchair. ~~The study represents patients not willing to participate in centre-based CR, which is offered routinely to all patients with coronary heart disease after discharge from our coronary department.~~ Figure 1 shows the flowchart.

Patients were recruited from our Rehabilitation Unit which offers centre-based CR to all patients with coronary heart disease assigned to the hospital. In order to ensure that all patients receive the CR treatment offer, the referral procedure is centralized and computerized with identification of patients from a database covering diagnosis and all invasive procedures performed in the catchments area of Bispebjerg University Hospital, Copenhagen. Patients are consecutively invited by letter and non-responders are additionally contacted by telephone. At the first visit in the Rehabilitation Unit patients were invited to participate in the previous mentioned RCT comparing home-based CR with centre-based CR [10] or as an alternative encouraged to participate in the centre-based CR programme (outside the study). Patients who declined participation in these offers were invited to participate in this study.

~~Inclusion criteria were patients ≥ 65 years with a new coronary event i.e. acute myocardial infarction (MI), percutaneous transluminal coronary intervention (PCI) or coronary artery bypass graft (CABG). Exclusion criteria were mental disorders (dementia), social disorders (severe alcoholism and drug abuse), living in a nursing home, language barriers or use of wheelchair.~~

The recruitment period was from January 2007 to July 2008.

Inclusion of patients was not based on a sample size calculation.

Formatted: Do not check spelling or grammar, Superscript

~~Patients were recruited through a database covering all invasive procedures in the catchments area of Bispebjerg University Hospital, Copenhagen.~~

~~All patients were consecutively invited by letter and non-responders were additionally contacted by telephone.~~

Patients had to give informed consent before any trial related procedures. Patients were randomised in alternated block sizes of 4 to 6 using computer generated randomly permuted blocks. An impartial person not related to the study randomised patients. ~~The result of the randomisation could not be blinded because of the nature of the intervention.~~ Due to the nature of the intervention concealment of randomisation was not feasible with regard to both patients and researcher. Data were collected at Bispebjerg University Hospital before randomisation and after 3, 6 and 12 months. In addition, overall mortality data were obtained in July 2012, 5½ years after the study was initiated.

The study was approved by the local ethic committee (jr.nr.KF01327990), the Danish Data Protection Agency (j.nr. 2006-41-7212) and is registered at www.clinicaltrial.gov (NCT00489801).

Intervention

The home programme

~~The home programme was designed to focus on the exercise component of CR, which was moved to the patients home. A physiotherapist made home visits twice with 6 weeks interval~~ Patients received two home visits by a physiotherapist in a 6 weeks interval with the purpose of creating~~in order to develop~~ a training programme that could be performed at home and outside in local surroundings~~surrounding outdoor area~~. ~~A~~Patients were carefully instructed in the training programme and guided to optimal training effort. In between the visits~~telephone~~ a telephone call was made by the physiotherapist ~~in between the two visits to clarify~~ to resolve any questions.

The exercise programmes were individualised but followed the international recommendations with 30 min. exercise per day including 5-10 min. warm up (e.g. slow walking) and 10 min. cool down at

a frequency of 6 days per week [14;15~~8;9~~] at an intensity of 11-13 on the Borg scale [15~~9~~]. For very disabled patients the exercise programmes were of shorter duration but then repeated several times a day.

Field Code Changed

Field Code Changed

Regarding risk factor intervention and medical adjustment the patients consulted a cardiologist ~~counselled the patients~~ at baseline and after 3, 6 and 12 months. At 4 and 5 months a telephone call was made by the cardiologist to encourage continuous exercising and to answer any medical questions. All patients were offered dietary counselling and (if required~~needed~~) smoking cessation.

Usual care

This group is equivalent to a non-rehabilitation control group. Patients were not offered exercise education or dietary counselling but as~~As~~ for the home group, ~~the patients were~~ offered risk factor intervention and medical adjustment by a cardiologist at baseline and after 3, 6 and 12 months. ~~and t~~Telephone calls were made at 4 and 5 months. ~~There was no exercise education or dietary counselling, but if needed smoking cessation was offered.~~ Thus, this group received solely consultation at a cardiologist which is offered to all patients in daily clinical practise who decline participation in our comprehensive centre-based CR programme.

Outcome measures

Because many patients due to age and co-morbidity is not able to perform a symptom-limited exercise capacity test ~~The~~the primary outcome was change in exercise capacity determined by 6MWT. The secondary outcomes were: sit to stand test (STS), self reported level of physical activity, systolic and diastolic blood pressure, total-, HDL- and LDL-cholesterol, body mass index (BMI), waist-hip ratio, proportion of smokers, ~~and health related quality of life~~ HRQoL measured by SF-12 and anxiety and depression estimated by Hospital Anxiety and Depression Scale (HADS). Outcomes were evaluated after 3, 6 and 12 months.

In the STS-test the patients must as fast as possible within 30 sec. change position from sitting on a chair to upright standing, without holding the handgrip, hereby measuring the strength in the lower limb. Self-reported level of physical activity was estimated by a questionnaire originally developed by Saltin and Grimby [16~~10~~]. It has four categories ranging from a sedentary lifestyle, to performing light activities 2-4 hours/week, activity more than 4 hours/week or highly vigorous physical activity more than 4 hours/week. Patients in the last three categories were classified as having an active lifestyle. Medication included the use of diuretics, beta-blockers, calcium antagonists, lipid lowering drugs, anti-thrombotics, anti-diabetic and anti-depressive treatment. Sociodemographic data included level of education, main employment status, contact to children, living alone and the need of weekly assistance at home. Patients in NYHA II-IV and CCS II-IV were categorised as having dyspnoea and angina, respectively. Co-morbidity was assed by The Charlson Co-Morbidity Index (CMI) [17~~11~~], which measures the burden of 19 co-morbid conditions through a weighted index. The CMI was categorised in 3 sub-groups: 0 (no co-morbid condition), 1-2 and ≥ 3 (high level of co-morbid burden).

Field Code Changed

Field Code Changed

Adverse events were recorded in the study period and included admissions for MI, progressive angina, decompensated congestive heart failure, severe bleeding, new malignant disease, and performance of PCI. Moreover, the number and duration of hospital admissions were recorded 1 year after randomisation. Mortality data were obtained from the Civil Registration System, which records the vital status of all citizens in Denmark.

Statistical analysis

~~Baseline data were compared using two-sided t-test for continuous variables and chi2 test for categorical variables.~~ To test the effect of the interventions at 3 and 12 months a mixed model of regression analysis was used with a time*treatment interaction term. We used a mixed model in order to analyse the effect of the interventions, since this statistical model allow us to include all data into one analysis. All the models were adjusted for age and gender. We did not adjust the

significance levels for multiple testing, since such an adjustment is a too conservative test to perform when data are positively correlated, as in this study.

Data were analysed by intention to treat. All statistical analysis was performed using STATA for windows release 10.0.

Table 1 Baseline characteristics according to intervention
Values are mean (SD) unless stated otherwise

Characteristic	Usual care n=21	Home n=19
Age	76.5 (7.7)	77.3 (6.0)
Men n (%)	11 (52.3%)	12 (63.2%)
Risk factors		
Hypertension, n (%)	13 (61.9%)	16 (88.9%)
Hyperlipidemia, n (%)	17 (81.0%)	18 (94.7%)
Diabetes, n (%)	2 (9.5%)	7 (36.8%)*
BMI, kg/m^2	26.2 (3.6)	27.6 (4.5)
Current smokers, n (%)	9 (42.9%)	8 (42.1%)
Medical history		
Previous MI, n (%)	8 (38.1%)	6 (31.7%)
Previous PCI, n (%)	5 (23.8%)	4 (21.1%)
Previous CABG, n (%)	2 (9.5%)	0 (0%)
Heart failure LVEF ≤ 45%, n (%)	9 (42.9%)	9 (50.0%)
Event prior to entry into the study		
Post-MI without invasive procedure, n (%)	4 (19.1%)	0 (0%)
Post-PCI, n (%)	14 (66.7%)	16 (84.2%)
Post-CABG, n (%)	3 (14.3%)	3 (15.8%)
Clinical status		
6MWT, m	325.9 (123.1)	290.9 (116.5)
STS	10.9 (3.7)	8.9 (4.8)
Systolic blood pressure, mmHg	138.3 (22.2)	153.6 (27.5)
Diastolic blood pressure, mmHg	72.2 (13.9)	76.1 (13.0)
Waist-hip ratio	0.9 (0.1)	1.0 (0.1)
Dyspnoea, NYHA II-IV, n (%)	13 (61.9%)	11 (57.9%)
Angina, CCS II-IV, n (%)	4 (19.1%)	4 (21.1%)
Self-reported active lifestyle, n (%)	10 (47.6%)	6 (31.6%)
Co-morbid conditions		
CMI score 0, n (%)	0 (0%)	1 (5.3%)
1-2, n (%)	9 (42.9%)	7 (36.8%)
≥3, n (%)	12 (57.1%)	11 (57.9%)
COPD, n (%)	7 (33.3%)	4 (21.1%)
Peripheral arterial disease, n (%)	3 (14.3%)	5 (26.3%)
Laboratory values		
Total cholesterol, mmol/l	4.5 (1.1)	4.3 (0.9)
HDL cholesterol, mmol/l	1.4 (0.3)	1.3 (0.6)
LDL cholesterol, mmol/l	2.5 (2.2)	2.4 (1.7)
~~**Health related quality of life**~~		
HRQoL, anxiety and depression		
HADS anxiety score	4.7 (3.0)	5.1 (4.9)
HADS depression score	5.3 (3.8)	4.8 (2.7)
SF-12 PCS	39.0 (10.8)	38.0 (9.9)
SF-12 MCS	46.9 (10.1)	48.9 (9.3)

~~*P<0.05~~

Abbreviations: MI, myocardial infarction; PCI, percutaneous transluminal coronary intervention; CABG, coronary artery bypass graft; LVEF, left ventricular ejection fraction; 6MWT, 6 minutes walk test; STS, sit to stand test; CMI, Charlson co-morbidity index; COPD, chronic obstructive lung disease; HRQoL, health related quality of life; HADS, Hospital Anxiety and Depression Scale; PMS, physical composite scale of SF-12; MCS, mental composite scale of SF-12.

Results

A total of 40 patients participated. Baseline characteristics are listed in table 1. ~~Except for a higher incidence of diabetes in the home group there were no significant differences between the two groups. In addition, there were no significant differences in medication and sociodemographic data (data not shown).~~ All patients received anti-thrombotics and lipid lowering drugs and 77.4% received beta-blockers.

Of eligible patients to receive CR (n=284) a total of 49% (n=140) declined to participate in the centre-based programme, figure 1. Of these 29% accepted to participate in this study and 71% (n=100) did not receive any rehabilitation.

Exclusion rate was 10% mainly because of language barriers (n=13), social disorders (n=5), dementia (n=5) and other reasons (n=7).

Exercise capacity

Figure 2 illustrates the unadjusted means of the primary outcome measurement of 6MWT from baseline to 12 months follow-up. The figure shows a significant increase in walking distance of 33.5m (95%CI: 6.2, 60.8, P=0.02) in the home group after the intervention followed by a significant decline of -55.2m (95%CI: 18.7, 91.7, P<0.01) at 12 months follow-up to a level lower than the baseline value. Patients in the usual care group had a non-significant increase in walking distance of 10.1m (95 %CI: -19.3, 39.5, P=0.5) after 3 months followed by a decline of -52.1m (95%CI: -3.0, 107.1, P=0.06) at the end of the follow-up period. When adjusting for age and gender in a mixed model with a time*treatment interaction term, there were no significant differences between the groups at 3 months (table 2). At 12 months follow-up, a significant decline in 6MWT and STS was found in both groups with no differences between the groups (table 3).

Other outcomes

A higher proportion of patients reported a change from an inactive to an active lifestyle in the home group (27%, P<0.05) compared to the usual care group (-5%, P=0.6) after the intervention with a

difference between the two groups of 33% (P<0.05). At 12 months follow-up the proportion of patients with a self-reported active lifestyle declined again in the home group with no changes in the usual care group.

Table 2 Effect of intervention at 3 months follow-up

	Usual care		**Home**			
	Δ 0-3 months	95%CI	Δ 0-3 months	95%CI	Between groups comparison ~~Δ 3 months between home - usual care~~	95%CI
Exercise capacity						
6MWT, m	10.1	-23.6, 43.9	36.3	-0.9, 73.6	26.2	-24.1, 76.5
STS	0.9	-0.8, 2.6	1.0	-0.8, 2.8	0.1	-2.3, 2.6
Clinial status						
Systolic blood pressure, mmHg	2.0	-8.4, 12.4	-12.9	-24.2, -1.6*	-14.9	-30.2, 0.5
Diastolic blood pressure, mmHg	4.1	-2.2, 10.5	-1.5	-8.4, 5.4	-5.7	-15.0, 3.7
BMI, kg/m^2	0.1	-1.3, 1.5	-0.5	-2.1, 1.1	-0.6	-2.7, 1.5
Waist-hip ratio	-0.01	-0.03, 0.01	-0.01	-0.03, 0.01	0	-0.03, 0.03
Laboratory values						
Total cholesterol, mmol/l	-0.2	-0.6, 0.2	-0.1	-0.5, 0.4	0.1	-0.5, 0.7
HDL cholesterol, mmol/l	0.1	-0.01, 0.2	0.1	-0.1, 0.2	-0.04	-0.2, 0.1
LDL cholesterol, mmol/l	-0.2	-0.5, 0.1	-0.1	-0.5, 0.3	0.1	-0.4, 0.6
Cholesterol/HDL ratio	-0.4	-0.7, 0	-0.3	-0.7, 0.1	0.1	-0.5, 0.7
~~**Health related quality of life**~~ **HRQoL, anxiety and depression**						
HADS anxiety score	-0.9	-2.3, 0.5	-1.2	-2.7, 0.6	-0.3	-2.4, 1.9
HADS depression score	-1.1	-2.6, 0.4	-1.0	-2.7, 0.6	0.1	-2.2, 2.3
SF-12 PCS	2.7	-1.4, 6.8	-0.4	5.1, 4.3	-3.1	-9.4, 3.1
SF-12 MCS	3.5	-0.9, 7.9	2.4	-2.6, 7.5	-1.0	-7.7, 5.6

All data are adjusted for age and gender. ~~Positive data indicates an increase in outcome or is in favour of home based rehabilitation.~~ * P<0.05.

Abbreviations: CI, confidence interval; 6MWT, 6 minutes walk test; STS, sit to stand test; HRQoL, health related quality of life; HADS, hospital anxiety and depression score; PCS, physical component summary scale of SF-12; MCS, mental component summary scale of SF-12.

Formatted Table

Table 3 Follow-up data at 12 months

	Usual care		Home			
	Δ 3-12 months	95%CI	Δ 3-12 months	95%CI	Between groups comparison ~~Δ 12 months between home- usual care~~	95%CI
Exercise capacity						
6MWT, m	-50.9	-86.6, -15.3**	-55.0	-94.0, -16.1**	-4.0	-56.8, 48.8
STS	-3.0	-4.7, -1.3**	-2.1	-3.9, -0.3*	0.9	-1.6, 3.4
Clinical status						
Systolic blood pressure, mmHg	0.7	-9.3, 10.6	-2.5	-13.1, 8.2	-3.1	-17.7, 11.4
Diastolic blood pressure, mmHg	-0.6	-6.4, 5.1	1.6	-4.6, 7.8	2.2	-6.2, 10.7
BMI, kg/m^2	0.4	-0.04, 0.8	0.6	0.1, 1.0*	0.2	-0.4, 0.8
Waist-hip ratio	0.01	-0.01, 0.03	0.0	-0.02, 0.02	0.01	-0.04, 0.02
Laboratory values						
Total cholesterol, mmol/l	0.1	-0.3, 0.5	-0.1	-0.5, 0.3	-0.2	-0.8, 0.4
HDL cholesterol, mmol/l	-0.1	-0.2, 0.01	-0.04	-0.1, 0.1	0.1	-0.1, 0.2
LDL cholesterol, mmol/l	0.1	-0.3, 0.2	-0.04	-0.4, 0.3	-0.1	-0.6, 0.4
Cholesterol/HDL ratio	0.3	-0.1, 0.6	0.1	-0.3, 0.5	-0.2	-0.7, 0.3
~~**Health related quality of life**~~ **HRQoL, anxiety and depression**						
HADS anxiety score	0.3	-1.3, 1.9	0.4	-1.3, 2.1	0.1	-2.3, 2.4
HADS depression score	0.3	-1.2, 1.8	1.2	-0.3, 2.8	0.9	-1.3, 3.1
SF-12 PCS	-1.4	-5.2, 2.3	-1.1	-5.3, 3.1	0.3	-5.4, 6.0
SF-12 MCS	-0.3	-4.6, 4.0	-1.4	-6.1, 3.3	-1.1	-7.5,5.3

All data are adjusted for age and gender. ~~Positive data indicates an increase in outcome or is in favour of home-based rehabilitation.~~ * P<0.05, **P<0.01.
Abbreviations: CI, confidence interval; 6MWT, 6 minutes walk test; STS, sit to stand test; HRQoL, health related quality of life; HADS, hospital anxiety and depression score; PCS, physical component summary scale of SF-12; MCS, mental component summary scale of SF-12.

Formatted Table

~~Except for lower systolic blood pressure in the home group after the intervention, there~~ There were no significant differences in clinical status, exercise capacity, laboratory values, HRQoL or anxiety and depression score ~~diastolic blood pressure, waist hip ratio, cholesterol profile, cessation of smoking and health related quality of life~~ at 3 and 12 months follow-up either within or between the ~~home and usual care~~ groups.

The number and length of acute and non-acute admissions were equally distributed at 12 months follow-up (data not shown). ~~Mortality data showed that~~

A total of nine patients died during a mean follow-up of 4½ years ~~nine patients died within 5½ years~~ (usual care group n=5 and home group n=4). There was no loss to follow-up.

Discussion

To the best of our ~~best~~ knowledge, this is the first study to investigate the effect of home-based CR compared to usual care (no rehabilitation) among elderly patients ≥ 65 years with coronary heart disease who ~~did not want to participate~~ declined participation in a centre-based programme. In many countries, including Denmark, centre-based programmes are often the only cardiac rehabilitation programme available, and the limited access to CR may be an important barrier for optimal secondary treatment and prevention in elderly patients with coronary heart disease.

The study found ~~confirms~~ that elderly patients who decline participation in centre-based CR ~~are~~ had a ~~very fragile group with~~ low level of exercise capacity and a high level of co-morbidity. For this population who is often found not to be eligible to centre-based CR, home-based CR was feasible. There was a trend towards clinical relevant improvement in 6MWT but these changes were not statistically significant compared to the control group. ~~found to improve exercise capacity and~~

~~a~~Although th~~e~~is study is small and conclusions must be drawn with caution, ~~generalisation thus limited,~~ it could identify~~ies~~ an intervention targeting this ~~vulnerable~~ group of patients. ~~However,~~

Aafter having endeding the home programme the gained improvement in exercise capacity was not sustained.

Exercise capacity

The effect of our home CR programme on exercise capacity is consistent with the findings in the only other study investigating the effect of home-based CR and usual care among elderly with coronary heart disease[3,12]. In this study, patients in the age groups 45-65 years, 66-75 years and > 75 years significantly improved their exercise capacity after participating in a home programme although the improvement was less among the very old patients (>75 years).

Jolly et all's The meta-analysies by Jolly et al [12,7], which included studies of all age groups, investigated the effect of home-based CR and usual care. The meta-analysis showed an improvement in exercise capacity but could not identify any significant differences between the home and usual care group. The authors explained this by the possibilityprobability, that patients in usual care groups may receive input that match the home-interventions and thus diminish a possible difference. This could also have been the case in our study.

At 12 months a significant decline in exercise capacity was found in this study in both the home and usual care group reaching a level lower than at entrance to the study. We identified two other studies with long-term follow-up [3;18,12;13]., which in In contrast to our study they both found a sustained improvement in exercise capacity after 12 months if the exercise programme was initiated at home. The discrepancy could be caused by the duration of our home intervention that may have been too short to maintain changes in lifestyle at 12 months follow-up, but our home intervention is in line with other home-based programmes [12;13]. The majority of programmes have a duration of 6-12 weeks [7;9;11-13]. It has been suggested that more intensive programmes with prolonged duration beyond 12 weeks have a more successful long term outcome [19;20]. However, in a previous study of heart failure patients [21] even a prolonged centre-based maintenance programme with supervised sessions every two weeks in addition to home exercise training could not maintain the

Field Code Changed

Field Code Changed

Field Code Changed

Formatted: Do not check spelling or grammar, Superscript

Formatted: Do not check spelling or grammar, Superscript

Formatted: Do not check spelling or grammar, Superscript

Formatted: Do not check spelling or grammar, Superscript

improvements achieved during initial CR[21]. Furthermore, in the very large HF-ACTION trial[22] patients participated in an initial centre-based exercise programme of 36 sessions in 3 months followed by a home-based exercise programme with intensive follow-up and were equipment for home training was provided. In this study there were no changes in exercise capacity at 12 months follow-up. This was explained partly by insufficient adherence to training that was below the target set at all time points. The HF-ACTION trial mainly included middle aged men with no major co-morbidities or limitations that could interfere with training. Thus, in spite of intensive exercise programmes with close follow-up in patients with no significant concomitant co-morbidities it is difficult to motivate patients to adhere to training. Feasible solutions to overcome this have not yet been identified.

The discrepancy between studies may also be due to ~~caused by~~ the differences in the enrolled populations. ~~,~~ ~~o~~Our population was significantly older~~,~~ (mean age 77.3 ±6.0 years versus 69.0 ±9.0 years [3~~12~~] and 64.3 ±0.5 years [18~~13~~])~~,~~ and had a high degree of co-morbidity and low level of exercise capacity~~, which~~ Age, co-morbidity and disability are all found to be negative correlated with physical activity [15;23] and adherence to training [6;24;25] and thus may have contributed significantly to the lack of sustained effect at 12 months. In addition, the only other study targeting the elderly [3~~12~~] the population was highly selected with exclusions rate of 72% among the very old patients (>75 years) due to co-morbidity, disability and congestive heart failure~~,~~ leading to a much "healthier" population compared to our population were only 10% were excluded.

~~In addition, the duration of our home intervention may have been too short to maintain changes in lifestyle at 12 months follow-up.~~

Coronary heart disease is one of the leading causes of disability and with increasing age other chronic non-cardiac conditions further limit function [26]. Our population of elderly had a very high frequency of co-morbid conditions (57% had CMI ≥ 3)~~ and~~ For comparison, a recent very large nationwide study including 234 000 patients (median age 68 years in men and 75 years in women)

Formatted: Do not check spelling or grammar, Superscript
Formatted: Do not check spelling or grammar, Superscript
Field Code Changed
Field Code Changed
Formatted: Do not check spelling or grammar, Superscript
Formatted: Do not check spelling or grammar, Superscript
Field Code Changed
Field Code Changed
Formatted: Do not check spelling or grammar, Superscript

with first time acute myocardial infarction found that only 6% of that population had CMI≥3 [27]. In addition to the high frequency of co-morbidity we found a low level of exercise capacity at baseline, ~~(~~with mean 6MWT=308.4 m ± 120~~)~~. In healthy elderly subjects mean 6MWT is found to be approximately 659 m ± 74 m [28] ~~which probably reflects a true picture of the elderly cardiac population.~~ and in a recent RCT study from our group comparing home-based CR with centre-based CR [10] we found a baseline mean 6MWT of 340 m ± 122 m in the centre group [10]. These characteristics indicate that the group of elderly patients who decline participation in centre-based rehabilitation is very vulnerable and not necessarily comparable with the population who accept centre-based CR. Our finding is in concordance with previous studies who found that older age, high burden of co-morbidity and low level of exercise capacity was negatively correlated with participation rate in centre-based CR programmes [6;24]. The high burden of co-morbidity in this population is most likely explained by the computerized identification of patients which eliminated the selection and referral bias often seen to rehabilitation units, which is not in favour of the elderly and patients with co-morbidity [24;29-31].

~~The 1-year mortality has been reported to be as high as 50 % for patients with CMI ≥ 3 [11] and similar mortality rates have been found for patients with a 6MWT below 300 m. However, even when the mortality rate is high, improving exercise capacity is important for quality of life since there is a big difference between living independently of others versus having the need for assistance.~~

Other outcomes

~~Except for s~~Self-reported active lifestyle and systolic blood ~~pressure, which changed~~pressure changed favorably~~favorable~~ in the home group after the intervention~~,~~ but there were no significant differences in diastolic blood pressure, body composition, cessation of smoking, cholesterol profile and HRQoL ~~health related quality of life~~ between the ~~home and usual care~~ groups. Our population

Formatted: Underline

Formatted: Do not check spelling or grammar, Superscript

Formatted: Do not check spelling or grammar, Superscript

Formatted: Do not check spelling or grammar, Superscript

Formatted: Do not check spelling or grammar, Superscript

Formatted: Do not check spelling or grammar, Superscript

Formatted: Do not check spelling or grammar, Superscript

had a good risk factor control and low anxiety and depression score (HADS score < 8 is within normal rage)[32;33] at entrance to the study -why a further improvement could not be expected. We did not find any significant changes in HRQoL measured by SF-12. This is partly due to lack of statistical power and the limited duration of our home intervention but is in concordance with the meta-analysis by Jolly et al[12] and with a recent published review concerning CR and HRQoL[34]. We did not have any specific psychological intervention but the type of intervention (comprehensive programmes, exercise only or mainly psychological interventions) do not seem to affect these results[12;34].

In central Europe, centre-based CR is the traditional choice of CR services. However, establishing of home-based CR programmes as an alternative for elderly patients could improve CR attendance rate. In English speaking countries and in countries where health services are not free home-base CR programmes are~~is~~ more commonly used, primarily through the adoption~~use~~ of The Heart Manual[35;36]. This is currently not an option in non-English speaking countries, in many of which there is a stronger tradition of centre-based CR. ~~Results from these programmes are promising[16;17], although only limited data is available so far.~~

In the everyday scenario at the rehabilitation units there is only one CR programme available and this is often a centre-based programme. Patients who decline enrolment in these programmes do not have alternatives. A total of 29% of patients who initially declined centre-based CR did accept to participate in this study and the proportion could have been even higher if the home-based CR programme was not part of a RCT study. Thus, with alternative concomitant CR programmes, accessibility increases and participation rate will be expected to rise.

The main limitation of this study is the number of patients included.~~, which did not allow any sub-group analysis.~~ With the additionally large variation in the effect of intervention as reflected in the wide confidence intervals there is a risk of type II error. However, wide variations in effect of intervention ~~confidence intervals~~ are often seen in exercise trials and our results are in concordance

Formatted: Do not check spelling or grammar, Superscript

Formatted: English (U.S.)

Field Code Changed

Formatted: Do not check spelling or grammar, Superscript

Formatted: Do not check spelling or grammar, Superscript

Formatted: Do not check spelling or grammar, Superscript

Formatted: Do not check spelling or grammar, Superscript

with other much larger exercise trials [22;35~~16;18~~]. The strength of our~~this~~ study is the randomised design and the unselected population of elderly patients with high co-morbidity, which probably makes our population more representative of the elderly population in daily clinical practice. ~~The high co-morbidity is explained by our screening procedure which eliminated the referral bias often seen to the CR Units, which is not in favour of the elderly fragile patients with high co-morbidity and disability~~ [~~19-22~~].

Field Code Changed

Conclusion

In this study of patient ≥ 65 years with coronary heart disease home-based CR improved exercise capacity, but there was no significant difference between the home intervention and the control group. In addition, no significant difference was found in the secondary outcomes. The study ~~confirms that~~ found that elderly cardiac patients who declined participation in centre-based CR ~~are a very fragile population with~~ had high level of co-morbidity and low exercise capacity. ~~disability~~ These characteristics indicate ~~and~~ that results from exercise trials excluding this group of patients should be cautiously ~~cannot just be~~ applied to the elderly population. After cessation of the home intervention the gained improvement in exercise capacity was rapidly lost. This emphasises, that close follow-up with continuous guidance ~~is important~~ beyond the initial rehabilitation period is important. This study could contributes to the scientific gap on how to manage the large population of elderly cardiac patients who are not interested in (or cable of) participating in a centre-based CR programme. Larger trials of unselected older patients are needed in order to confirm our findings and ways to overcome the barriers for adherence to exercise training has to be established.

Acknowledgments: Physiotherapists, nurses and dieticians involved in the study.

Patient consent: All patients had to signed standard consent forms approved by the Local ethics committee in Copenhagen, Denmark.

Ethics approval: The study was approved by the Local ethics committee in Copenhagen, Denmark, (jr.nr.KF01327990) and the Danish Data Protection Agency (j.nr. 2006-41-7212).

Funding: This work was supported by VELUX FOUNDATION.

Competing interests: NONE.

Authors Contributors: BO designed and initiated the study, collected the data, wrote the statistical analysis plan, analysed the data, and drafted and revised the paper. She is guarantor. EP contributed with design, wrote the statistical analysis plan, analysed the data, and revised the draft paper. MF designed the study and collected some of the data and revised the paper. JFH designed the study and revised the draft paper.

Data sharing statement: No additional data available.

Reference List

(1) Clark AM, Hartling L, Vandermeer B, McAlister FA. Meta-analysis: secondary prevention programs for patients with coronary artery disease. *Ann Intern Med* 2005; 143(9):659-672.

(2) Taylor RS, Brown A, Ebrahim S, Jolliffe J, Noorani H, Rees K et al. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *Am J Med* 2004; 116(10):682-692.

(3) Marchionni N, Fattirolli F, Fumagalli S, Oldridge N, Del Lungo F, Morosi L et al. Improved exercise tolerance and quality of life with cardiac rehabilitation of older patients after myocardial infarction: results of a randomized, controlled trial. *Circulation* 2003; 107(17):2201-2206.

(4) Pasquali SK, Alexander KP, Peterson ED. Cardiac rehabilitation in the elderly. *Am Heart J* 2001; 142(5):748-755.

(5) Jackson L, Leclerc J, Erskine Y, Linden W. Getting the most out of cardiac rehabilitation: a review of referral and adherence predictors. *Heart* 2005; 91(1):10-14.

(6) Worcester MU, Murphy BM, Mee VK, Roberts SB, Goble AJ. Cardiac rehabilitation programmes: predictors of non-attendance and drop-out. *Eur J Cardiovasc Prev Rehabil* 2004; 11(4):328-335.

(7) Giannuzzi P, Saner H, Bjornstad H, Fioretti P, Mendes M, Cohen-Solal A et al. Secondary prevention through cardiac rehabilitation: position paper of the Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology. *Eur Heart J* 2003; 24(13):1273-1278.

(8) Graham I, Atar D, Borch-Johnsen K, Boysen G, Burell G, Cifkova R et al. European guidelines on cardiovascular disease prevention in clinical practice: full text. Fourth Joint Task Force of the European Society of Cardiology and other societies on cardiovascular disease prevention in clinical practice (constituted by representatives of nine societies and by invited experts). *Eur J Cardiovasc Prev Rehabil* 2007; 14 Suppl 2:S1-113.

(9) Thomas RJ, King M, Lui K, Oldridge N, Pina IL, Spertus J et al. AACVPR/ACC/AHA 2007 performance measures on cardiac rehabilitation for referral to and delivery of cardiac rehabilitation/secondary prevention services endorsed by the American College of Chest Physicians, American College of Sports Medicine, American Physical Therapy Association, Canadian Association of Cardiac Rehabilitation, European Association for Cardiovascular Prevention and Rehabilitation, Inter-American Heart Foundation, National Association of Clinical Nurse Specialists, Preventive Cardiovascular Nurses Association, and the Society of Thoracic Surgeons. *J Am Coll Cardiol* 2007; 50(14):1400-1433.

(10) Oerkild B, Frederiksen M, Hansen JF, Simonsen L, Skovgaard LT, Prescott E. Home-based cardiac rehabilitation is as effective as centre-based cardiac rehabilitation among elderly with coronary heart disease: results from a randomised clinical trial. *Age Ageing* 2011; 40(1):78-85.

(11) Taylor RS, Dalal H, Jolly K, Moxham T, Zawada A. Home-based versus centre-based cardiac rehabilitation. *Cochrane Database Syst Rev* 2010;(1):CD007130.

Formatted: English (U.S.), Do not check spelling or grammar

Formatted: Space After: 12 pt

Formatted: Font: Italic, Do not check spelling or grammar

(12) Jolly K, Taylor RS, Lip GY, Stevens A. Home-based cardiac rehabilitation compared with centre-based rehabilitation and usual care: a systematic review and meta-analysis. *Int J Cardiol* 2006; 111(3):343-351.

(13) Dalal HM, Zawada A, Jolly K, Moxham T, Taylor RS. Home based versus centre based cardiac rehabilitation: Cochrane systematic review and meta-analysis. *BMJ* 2010; 340:b5631.

(14) Smith SC, Jr., Allen J, Blair SN, Bonow RO, Brass LM, Fonarow GC et al. AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update: endorsed by the National Heart, Lung, and Blood Institute. *Circulation* 2006; 113(19):2363-2372.

(15) Fletcher GF, Balady GJ, Amsterdam EA, Chaitman B, Eckel R, Fleg J et al. Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. *Circulation* 2001; 104(14):1694-1740.

(16) Saltin B, Grimby G. Physiological analysis of middle-aged and old former athletes. Comparison with still active athletes of the same ages. *Circulation* 1968; 38(6):1104-1115.

(17) Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40(5):373-383.

(18) Smith KM, Arthur HM, McKelvie RS, Kodis J. Differences in sustainability of exercise and health-related quality of life outcomes following home or hospital-based cardiac rehabilitation. *Eur J Cardiovasc Prev Rehabil* 2004; 11(4):313-319.

(19) Perk J, De BG, Gohlke H, Graham I, Reiner Z, Verschuren M et al. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J* 2012; 33(13):1635-1701.

(20) Clark AM, Catto S, Bowman G, Macintyre PD. Design matters in secondary prevention: individualization and supervised exercise improves the effectiveness of cardiac rehabilitation. *Eur J Cardiovasc Prev Rehabil* 2011; 18(5):761-769.

(21) Prescott E, Hjardem-Hansen R, Dela F, Orkild B, Teisner AS, Nielsen H. Effects of a 14-month low-cost maintenance training program in patients with chronic systolic heart failure: a randomized study. *Eur J Cardiovasc Prev Rehabil* 2009; 16(4):430-437.

(22) O'Connor CM, Whellan DJ, Lee KL, Keteyian SJ, Cooper LS, Ellis SJ et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 2009; 301(14):1439-1450.

(23) Kaplan MS, Newsom JT, McFarland BH, Lu L. Demographic and psychosocial correlates of physical activity in late life. *Am J Prev Med* 2001; 21(4):306-312.

Formatted: Font: Italic, Do not check spelling or grammar

(24) Cooper AF, Jackson G, Weinman J, Horne R. Factors associated with cardiac rehabilitation attendance: a systematic review of the literature. *Clin Rehabil* 2002; 16(5):541-552.

(25) Witt BJ, Jacobsen SJ, Weston SA, Killian JM, Meverden RA, Allison TG et al. Cardiac rehabilitation after myocardial infarction in the community. *J Am Coll Cardiol* 2004; 44(5):988-996.

(26) Pinsky JL, Jette AM, Branch LG, Kannel WB, Feinleib M. The Framingham Disability Study: relationship of various coronary heart disease manifestations to disability in older persons living in the community. *Am J Public Health* 1990; 80(11):1363-1367.

(27) Schmidt M, Jacobsen JB, Lash TL, Botker HE, Sorensen HT. 25 year trends in first time hospitalisation for acute myocardial infarction, subsequent short and long term mortality, and the prognostic impact of sex and comorbidity: a Danish nationwide cohort study. *BMJ* 2012; 344:e356.

(28) Jenkins S, Cecins N, Camarri B, Williams C, Thompson P, Eastwood P. Regression equations to predict 6-minute walk distance in middle-aged and elderly adults. *Physiother Theory Pract* 2009; 25(7):516-522.

(29) Nielsen KM, Faergeman O, Foldspang A, Larsen ML. Cardiac rehabilitation: health characteristics and socio-economic status among those who do not attend. *Eur J Public Health* 2008; 18(5):479-483.

(30) Cortes O, Arthur HM. Determinants of referral to cardiac rehabilitation programs in patients with coronary artery disease: a systematic review. *Am Heart J* 2006; 151(2):249-256.

(31) Cottin Y, Cambou JP, Casillas JM, Ferrieres J, Cantet C, Danchin N. Specific profile and referral bias of rehabilitated patients after an acute coronary syndrome. *J Cardiopulm Rehabil* 2004; 24(1):38-44.

(32) Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002; 52(2):69-77.

(33) Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67(6):361-370.

(34) Shepherd CW, While AE. Cardiac rehabilitation and quality of life: a systematic review. *Int J Nurs Stud* 2012; 49(6):755-771.

(35) Jolly K, Lip GY, Taylor RS, Raftery JP, Mant JW, Lane D et al. The Birmingham Rehabilitation Uptake Maximisation study (BRUM): a randomised controlled trial comparing home-based with centre-based cardiac rehabilitation. *Heart* 2008.

(36) Dalal HM, Evans PH, Campbell JL, Taylor RS, Watt A, Read KL et al. Home-based versus hospital-based rehabilitation after myocardial infarction: A randomized trial with preference arms--Cornwall Heart Attack Rehabilitation Management Study (CHARMS). *Int J Cardiol* 2007; 119(2):202-211.

Formatted: Font: Italic, Do not check spelling or grammar

Formatted: Font: Italic, Do not check spelling or grammar

Formatted: Font: Italic, Do not check spelling or grammar

Formatted: Font: Italic, Do not check spelling or grammar

Formatted: Font: Italic, Do not check spelling or grammar

Formatted: Font: Italic, Do not check spelling or grammar

Formatted: Font: Italic, Do not check spelling or grammar

Formatted: Font: Italic, Do not check spelling or grammar

Formatted: Font: Italic, Do not check spelling or grammar

Formatted: Font: Italic, Do not check spelling or grammar

Formatted: Font: Italic, Do not check spelling or grammar

Formatted: Font: Italic, Do not check spelling or grammar

Formatted: Line spacing: single

Reference List

(1) Clark AM, Hartling L, Vandermeer B, McAlister FA. Meta-analysis: secondary prevention programs for patients with coronary artery disease. *Ann Intern Med* 2005; 143(9):659-672.

(2) Taylor RS, Brown A, Ebrahim S, Jolliffe J, Noorani H, Rees K et al. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *Am J Med* 2004; 116(10):682-692.

(3) Pasquali SK, Alexander KP, Peterson ED. Cardiac rehabilitation in the elderly. *Am Heart J* 2001; 142(5):748-755.

(4) Ades PA, Waldmann ML, McCann WJ, Weaver SO. Predictors of cardiac rehabilitation participation in older coronary patients. *Arch Intern Med* 1992; 152(5):1033-1035.

(5) Lavie CJ, Milani RV. Cardiac rehabilitation and preventive cardiology in the elderly. *Cardiol Clin* 1999; 17(1):233-242.

(6) Taylor RS, Dalal H, Jolly K, Moxham T, Zawada A. Home-based versus centre-based cardiac rehabilitation. *Cochrane Database Syst Rev* 2010;(1):CD007130.

(7) Jolly K, Taylor RS, Lip GY, Stevens A. Home-based cardiac rehabilitation compared with centre-based rehabilitation and usual care: a systematic review and meta-analysis. *Int J Cardiol* 2006; 111(3):343-351.

(8) Smith SC, Jr., Allen J, Blair SN, Bonow RO, Brass LM, Fonarow GC et al. AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update: endorsed by the National Heart, Lung, and Blood Institute. *Circulation* 2006; 113(19):2363-2372.

(9) Fletcher GF, Balady GJ, Amsterdam EA, Chaitman B, Eckel R, Fleg J et al. Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. *Circulation* 2001; 104(14):1694-1740.

(10) Saltin B, Grimby G. Physiological analysis of middle-aged and old former athletes. Comparison with still active athletes of the same ages. *Circulation* 1968; 38(6):1104-1115.

(11) Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; 40(5):373-383.

(12) Marchionni N, Fattirolli F, Fumagalli S, Oldridge N, Del Lungo F, Morosi L et al. Improved exercise tolerance and quality of life with cardiac rehabilitation of older patients after myocardial infarction: results of a randomized, controlled trial. *Circulation* 2003; 107(17):2201-2206.

(13) Smith KM, Arthur HM, McKelvie RS, Kodis J. Differences in sustainability of exercise and health-related quality of life outcomes following home or hospital-based cardiac rehabilitation. *Eur J Cardiovasc Prev Rehabil* 2004; 11(4):313-319.

(14) Pinsky JL, Jette AM, Branch LG, Kannel WB, Feinleib M. The Framingham Disability Study: relationship of various coronary heart disease manifestations to disability in older persons living in the community. *Am J Public Health* 1990; 80(11):1363-1367.

(15) Shah MR, Hasselblad V, Gheorghiade M, Adams KF, Jr., Swedberg K, Califf RM et al. Prognostic usefulness of the six-minute walk in patients with advanced congestive heart failure secondary to ischemic or nonischemic cardiomyopathy. *Am J Cardiol* 2001; 88(9):987-993.

(16) Jolly K, Lip GY, Taylor RS, Raftery JP, Mant JW, Lane D et al. The Birmingham Rehabilitation Uptake Maximisation study (BRUM): a randomised controlled trial comparing home-based with centre-based cardiac rehabilitation. *Heart* 2008.

(17) Dalal HM, Evans PH, Campbell JL, Taylor RS, Watt A, Read KL et al. Home-based versus hospital-based rehabilitation after myocardial infarction: A randomized trial with preference arms--Cornwall Heart Attack Rehabilitation Management Study (CHARMS). *Int J Cardiol* 2007; 119(2):202-211.

(18) O'Connor CM, Whellan DJ, Lee KL, Keteyian SJ, Cooper LS, Ellis SJ et al. Efficacy and safety of exercise training in patients with chronic heart failure: HF-ACTION randomized controlled trial. *JAMA* 2009; 301(14):1439-1450.

(19) Nielsen KM, Faergeman O, Foldspang A, Larsen ML. Cardiac rehabilitation: health characteristics and socio-economic status among those who do not attend. *Eur J Public Health* 2008; 18(5):479-483.

(20) Cortes O, Arthur HM. Determinants of referral to cardiac rehabilitation programs in patients with coronary artery disease: a systematic review. *Am Heart J* 2006; 151(2):249-256.

(21) Cooper AF, Jackson G, Weinman J, Horne R. Factors associated with cardiac rehabilitation attendance: a systematic review of the literature. *Clin Rehabil* 2002; 16(5):541-552.

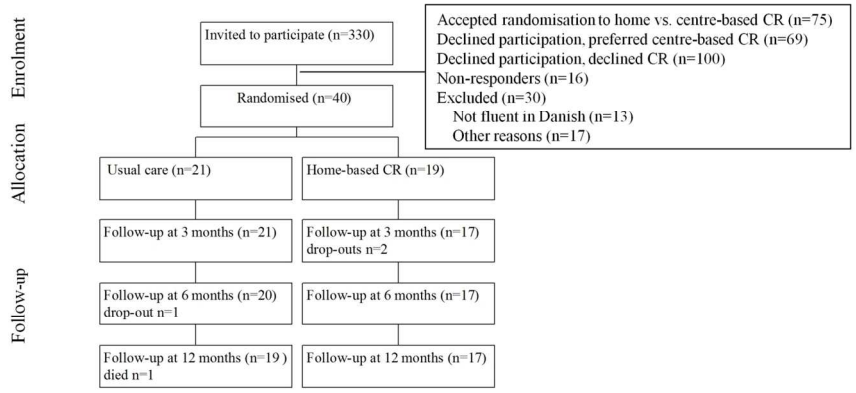
(22) Cottin Y, Cambou JP, Casillas JM, Ferrieres J, Cantet C, Danchin N. Specific profile and referral bias of rehabilitated patients after an acute coronary syndrome. *J Cardiopulm Rehabil* 2004; 24(1):38-44.

Figure Legends

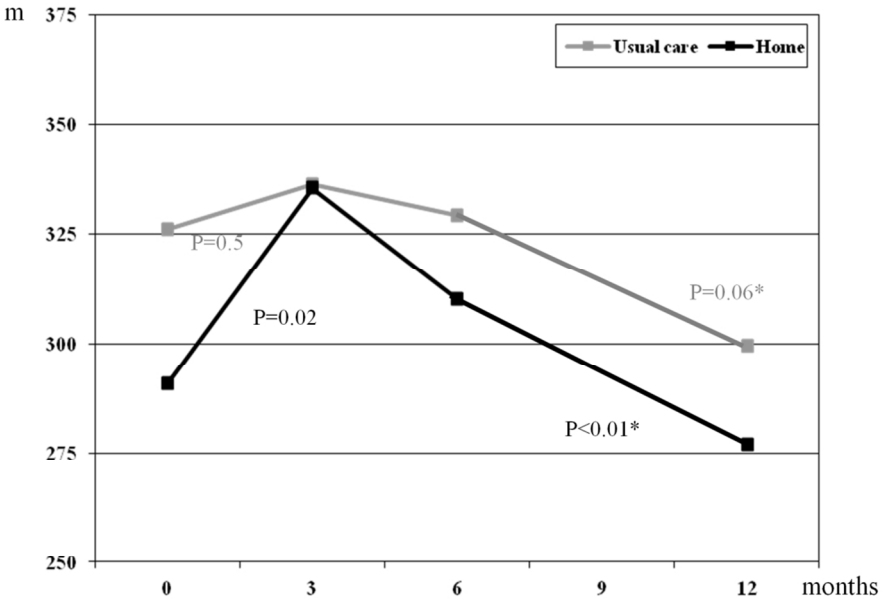
Figure 1 Flowchart

Figure 2 Changes in mean values of 6MWT

* P value between 3 and 12 months



Flowchart
146x90mm (300 x 300 DPI)



Changes in mean values of 6MWT
* P value between 3 and 12 months

104x90mm (300 x 300 DPI)

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	Title page
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	Abstract
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3-4
	2b	Specific objectives or hypotheses	4
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	5-6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	No changes were made
Participants	4a	Eligibility criteria for participants	5
	4b	Settings and locations where the data were collected	6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6-7
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	7-8
	6b	Any changes to trial outcomes after the trial commenced, with reasons	No changes were made
Sample size	7a	How sample size was determined	6
	7b	When applicable, explanation of any interim analyses and stopping guidelines	Not relevant
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	6
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	6
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	6
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to	6

		interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	Not possible
	11b	If relevant, description of the similarity of interventions	Not relevant
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	8-9
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	8-9
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	11
	13b	For each group, losses and exclusions after randomisation, together with reasons	11 + Figure 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up	6-7
	14b	Why the trial ended or was stopped	5
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Yes
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Figure 1
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Table 2+3 12-13
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	Table 2+3
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Table 2+3 Figure 2
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	14
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	18-19
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	14-15
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	14-19
Other information			
Registration	23	Registration number and name of trial registry	6
Protocol	24	Where the full trial protocol can be accessed, if available	6
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	19-20

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.