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The effects and costs of home-based rehabilitation for heart failure with reduced ejection fraction: the REACH-HF multicenter randomized controlled trial

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Abstract

Background: Cardiac rehabilitation (CR) improves health-related quality of life (HRQOL) and reduces hospitalizations in patients with heart failure (HF), but international uptake of CR for HF remains low.

Design and methods: The aim of this multicenter randomized trial was to compare the REACH-HF (Rehabilitation EnAblement in CHronicHeart Failure) intervention, a facilitated self-care and home-based CR programme to usual care for adults with HF with reduced ejection fraction (HFrEF). The study primary hypothesis was that the addition of the REACH-HF intervention to usual care would improve disease-specific HRQOL (Minnesota Living with Heart Failure questionnaire [MLHFQ]) at 12 months compared with usual care alone.

Results: The study recruited 216 participants, predominantly men (78%) with an average age of 70 years and mean left ventricular ejection fraction of 34%. Overall, 185 (86%) participants provided data for the primary outcome. At 12 months, there was a significant and clinically meaningful between-group difference in the MLHFQ score of –5.7 points (95% CI –10.6 to –0.7) in favor of the REACH-HF intervention group ($p = 0.025$). With exception of patient self-care ($P < 0.001$) there was no significant difference in other secondary outcomes including clinical events ($P > 0.05$) at follow up compared to usual care. The mean cost of the REACH-HF intervention was £418 per participant.

Conclusions: The novel REACH-HF home-based facilitated intervention for HFrEF was clinically superior in disease-specific HRQoL at 12 months and offers an affordable alternative to traditional centre-based programs to address current low CR uptake rates for HF.

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Key words: cardiac rehabilitation, health-related quality of life, heart failure, home-based, randomized controlled trial, self-management

Introduction

With important gains in mortality achieved through pharmacological and device therapy in patients with heart failure (HF) with reduced ejection fraction (HFrEF) over the past decade,[1] the focus is increasingly shifting towards optimizing health-related quality of life (HRQoL).[2] Patients are prepared to trade off longevity for an improvement in HRQoL,[3] and a Cochrane meta-analysis of exercise-based CR in patients with HF reported important improvements in HRQoL and a reduction in rehospitalizations.[4] International guidelines consistently recommend group- or center-based CR for patients with HFrEF.[5-7] However, less than 10% of people with HF in the United States of America and less than 20% in Europe participate in CR,[8,9] prompting a call to explore newer strategies to improve participation and explore the effectiveness of more accessible alternatives to group or center-based CR.[8]

Home-based CR programs can widen access and have been shown to be as effective as group or hospital-based CR after myocardial infarction and coronary revascularization and with similar costs.[10] The high cost of treating people with HF is well documented,[1] but little evidence (five randomized trials, 511 patients) is available on the clinical and cost-effectiveness of home-based CR in HF.[4] Furthermore, none of the home-based interventions have involved caregivers or have been co-developed with patients, caregivers or clinicians. We therefore developed a novel home-based CR intervention derived from health behavior change theory – the Rehabilitation EnAblement in CHronic Heart Failure (REACH-HF) intervention – for people with HF and their caregivers, which is facilitated by a healthcare professional.[11] We hypothesized that addition of the REACH-HF intervention to usual care would improve disease-specific HRQoL for patients with HFrEF at 12 months' follow-up compared with usual care alone.

Methods

The REACH-HF trial was conducted and reported in accordance with the Consolidated Standards of Reporting Trials guidelines.[12] Our full trial protocol has been published elsewhere.[13]

Study population and design

The REACH-HF trial was a multicenter, two parallel group, randomized, superiority trial in men and women aged ≥ 18 years with a confirmed diagnosis of HFrEF on echocardiography or angiography (i.e., left ventricular ejection fraction < 45%) within the preceding five years. Participants who had undertaken CR within 12 months prior to enrolment were excluded, as were those with a contraindication to exercise testing or exercise training. The published protocol provides a full list of patient inclusion and exclusion criteria.[13] Participants were randomized to the REACH-HF intervention plus usual care (REACH-HF group) or usual care alone (control group).

Participants were recruited from primary and secondary care settings in four centers in the United Kingdom (Birmingham, Cornwall, Gwent, and York). Participants were randomly allocated in a 1:1 ratio, stratified by investigator site and baseline plasma N-terminal proB-type natriuretic peptide levels (≤ 2000 vs > 2000 pg/ml), using minimization to facilitate balance between the groups. Randomization numbers were computer generated and assigned in strict sequence at the point of randomization. To maintain concealment, the Peninsula Clinical Trials Unit used a password-protected, web-based randomization system to allocate participants after consent was obtained and baseline assessment data entered. Treatment allocation was open label given the nature of the intervention, but outcome assessors were masked to participants' allocations. We kept a record of instances when outcome assessors were inadvertently unmasked by participants during assessment visits. The trial statistician and all investigators were blinded to the outcome data and group allocation until after prespecified statistical analyses were completed and interpretation of results was agreed. Between January 2015 and February 2016, 216 participants were randomized.

The investigation conforms with the principles outlined in the Declaration of Helsinki and the trial was approved by the North West Lancaster Research Ethics Committee (14/NW/1351). All participants provided written informed consent.

Study intervention

A detailed description of the REACH-HF intervention, its development, and its theoretical underpinnings is published elsewhere.[11] In the trial, participants in both the intervention and control groups continued with medical management and care of HF according to local and national guidelines.[7,14] In the UK, patients with HFrEF are usually seen by a community HF specialist nurse (soon after hospital discharge or at diagnosis, mainly to optimize drug dosages) and their family doctor, and some are followed up by a cardiologist. Most patients with HF do not undertake CR. The REACH-HF intervention is an evidence-informed, patient-centered, theory-based, self-care support program uniquely co-developed with key stakeholders – patients, caregivers and clinicians. This comprehensive intervention includes four core elements (see Figure S1)[11,13]

- REACH-HF Manual for patients with a choice of two structured exercise programs: a chair-based exercise and a progressive walking training program. Patients were advised to exercise ≥3 times per week, starting from their own personal level and gradually building up over 2-3 months in time/distance/walking pace.
- Patient 'Progress Tracker' – an interactive booklet designed to facilitate learning from experience to record symptoms, physical activity, and other actions related to self-care. Patients recorded: (1) how long/far they plan to walk, (2) whether they have done it, (3) how it felt to identify whether they should be moving up or down in efforts next time and (4) their weekly steps per minute (pace).
- 'Family and Friends Resource' – a manual for use by caregivers aimed to increase their understanding of HF and caregiver physical and mental well-being.

- Facilitation by cardiac nurses or physiotherapists, who attended a 3-day training course on the use of person-centered counselling and how to tailor the intervention for the patient and their caregiver.

The intervention was delivered at the patient's home via a mixture of face-to-face and telephone contacts over 12 weeks. The first contact was made by the facilitator and future contacts were agreed by the patient and the facilitator at a mutually convenient time. Patient adherence to the intervention was defined as attendance at the first face-to-face contact with the facilitator and at least two facilitator contacts thereafter – at least one of which must have been face to face.

Usual care

Given that the majority of HF patients do not receive CR,[8,9] usual care in this trial was a no CR approach that included medical management according to national and local guidelines, including specialist HF nurse care.[7] Both REACH-HF and controls groups received this usual care.

Outcome measures

The primary outcome was disease-specific HRQoL at 12 months measured using the Minnesota Living with Heart Failure Questionnaire (MLHFQ).[15] Secondary outcomes were death, hospitalization, generic quality of life (five-dimension EuroQol [EQ-5D-5L] scale),[16] psychological wellbeing (Hospital Anxiety and Depression Scale [HADS]),[17] exercise capacity (incremental shuttle walk test),[18] and physical activity assessed using GeneActiv accelerometer.[19] Additional secondary measures included the HeartQoL questionnaire,[20] and Self-Care of Heart Failure Index.[21]

Outcome data were collected from participants during three clinic visits at baseline and 4 and 12 months and by postal questionnaire at 6 months. At the baseline clinic visit, after obtaining written consent, we collected sociodemographic data and information on past medical history from the participants' hospital and primary care records, including key comorbidities, New York Heart Association classification,[22] concomitant cardiac drugs, and presence of implantable cardiac devices.

Adherence to intervention protocols by the facilitators was ascertained through audio recordings of interviews and a fidelity checklist created as part of the intervention development.[11,13] The findings of the intervention fidelity assessment is summarised in Table S1. .

Serious adverse events were recorded and assessed for their relatedness to the trial processes or the REACH-HF intervention. Adverse events and reactions were regarded as serious if they resulted in death, were life threatening, or required hospitalization. All serious adverse events were reported to the ethics and data monitoring committees.

The use of care services, including those provided by healthcare professionals in the community and secondary care, was documented at each follow-up visit by participants completing healthcare resource-use questionnaires and by collection of data on concomitant drug usage. A detailed cost-effectiveness analysis will be presented elsewhere.

Statistical analysis

The sample size was based on an effect size that represented the minimal clinically important difference in our primary outcome measure – that is, five points on the MLHFQ.[15] With a type I error of 0.05 and power of 90%, 85 participants per group were required to detect a five-point difference in the MLHFQ score, assuming a standard deviation (SD) of 10.[4,13] Assuming an attrition rate of 20% (in accordance with the level of attrition seen in previous trials),[10] 108 participants were required per group.

All statistical analyses were conducted to a predefined analysis plan agreed in advance with the trial management group, trial steering committee, and data management committee. Baseline sociodemographic and health-related variables are reported descriptively by treatment arm. The primary analyses for all participant outcomes were based on a between-group, intention-to-treat basis in participants with complete outcome data at 12 months. Outcomes were analyzed using linear regression methods, adjusting for stratification variables and baseline score of the outcome variable, where applicable. Secondary analyses were undertaken on participant outcomes as

repeated-measures analysis using all follow-up assessment points (4, 6, and 12 months). In addition, we did a per-protocol analysis and estimated complier average causal effects analysis of the primary outcome using 12-month follow-up data. We used our definition of adherence to the REACH-HF intervention (see above under 'Study intervention') to specify the per-protocol population. Multiple imputation methods were used as a sensitivity analysis to address the issue of missing outcome data at follow-up. The following predefined subgroups were assessed using interaction terms: the two minimization variables used in randomization (center and N-terminal proB-type natriuretic peptide) plus time since diagnosis of HF and presence of participating caregiver. Serious adverse events are presented descriptively by treatment arm. All between-group outcome comparisons are presented as mean difference with 95% confidence interval (CI). No correction of p values for multiplicity of testing was undertaken. However, the primary outcome analysis was done before all other analyses, and the p values of all subsequent analyses were interpreted in the context of multiple testing. No interim analyses were performed.

Unit costs were applied to resource use reported at the participant level to estimate the delivery costs associated with the REACH-HF intervention.[24] Costs are reported in pounds sterling (£) for 2016. All analyses were performed using Stata version 14.1.

Results

Trial population and interventions

The 216 participants were randomly allocated to the REACH-HF group (n = 107) and control group (n = 109) (Figure 1). Overall, 92 (86%) participants in the REACH-HF group and 93 (85%) in the control group provided data for the primary outcome. Drop out was the result of death (n = 8) or withdrawal (n=20) – 15 participants did not wish to continue, 3 were uncontactable, and 2 were too unwell. Participants were predominantly male (78%) and NHYA class II (59%), with an average age of 70 years and mean left ventricular ejection fraction of 34%. Patient-level characteristics at baseline were well balanced between the groups, apart from more frequent cardiac comorbidity (history of myocardial infarction and atrial fibrillation) and, consequently, higher Charlson comorbidity score in the control group (Table 1).[25] Mean baseline MLHFQ scores for the REACH-HF group were higher (poorer) than for the control group, but secondary baseline outcomes were similar for the two groups (Tables 2 and 3).

Of the 107 patients randomized to the REACH-HF group, 96 (90%) met our definition of intervention adherence**.**

Primary outcome: disease-specific HRQoL

At 12 months, MLHFQ total scores improved in the REACH-HF group but did not change in the control group, with a significant between-group difference of –5.7 points (95% CI –10.6 to –0.7) in favor of the REACH-HF group (p = 0.025; Table 2). This difference was also consistent across per-protocol, complier average causal effects, multiple-imputation, and repeated-measure analyses. The MLHFQ physical score also differed significantly in favor of the REACH-HF group (mean difference at 12 months –3.2 [95% CI –5.7 to –0.6, p = 0.016]) but the MLHFQ emotional score did not (–0.8 [–2.2 to 0.6], p = 0.273). A post-hoc analysis showed that 48 (52%) participants in the REACH-HF group and 31 (33%) in the control group achieved a reduction $\geq$5 MLHFQ points.

Secondary outcomes

The maintenance score on the Self-Care of Heart Failure Index, a measure of self-care, was in favor of the REACH-HF intervention group at 12 months ($p < 0.001$). Within-group improvements from baseline were seen in the REACH-HF group for HADS anxiety and depression, incremental shuttle walk test and Self-Care of Heart Failure Index (management and confidence) but did not reach statistical significance compared with control at 12 months. No differences were seen in the other secondary outcomes i.e. EQ-5D, HeartQoL, and physical activity (Table 2). Similar patterns of primary and secondary results were seen at 4 and 6 months. We found no evidence of a significant subgroup treatment interaction on the primary outcome at 12 months by N-terminal proB-type natriuretic peptide level, presence of caregiver, recruitment site, or duration of HF (see Table S2).

Over the 12 months of the trial, eight (4%) participants died: four deaths in each group and four deaths related to HF (one REACH-HF, three controls). In the REACH-HF group, 19 participants had at least one hospital admission during follow-up to 12 months compared with 24 patients in the control group (odds ratio [OR] 0.72 [95% CI 0.35 to 1.51], $p = 0.386$). Three REACH-HF versus 6 patients experienced one or more hospital admissions related to HF (0.56, 0.13 to 2.33, $p = 0.422$) Overall, there were 33 admissions (four related to HF) in the REACH-HF group and 35 (10 related to HF) in the control group. The independent data monitoring committee considered none of the 37 serious adverse events in the REACH-HF to be related to the intervention.

Costs

To calculate costs, facilitator contact sheets were completed at 12 months and were available for 94 (98%) participants in the REACH-HF intervention group. The mean number of facilitator contacts was 6.5 per participant, and total contact time and non-contact time inputs were 5.3 and 2.9 hours per participant, respectively, with overall time input at 8.25 hours per participant. Taking into account these contact times, facilitator training, and travel and consumables, the mean total cost for delivery of the REACH-HF intervention was estimated at £418.39 per participant (Table S3).

Discussion

In this randomized, multicenter trial, participants with HFrEF who received the novel REACH-HF home-based CR intervention for 12 weeks in addition to usual care had superiority in disease-specific HRQoL and self-management at 12 months compared with usual care alone. The magnitude of improvement in total MLHFQ (mean between group difference –5.7 (95% CI –10.6 to –0.7) points) was not only statistically significant but also clinically meaningful (i.e. a reduction ≥ 5 points).[16] The MLHFQ score is a key outcome indicator for patient well-being that has been shown to be independently related to survival.[26] The cost of the REACH-HF intervention (£418.39 per participant) falls within the National Health Service tariff for CR in England of £477 per patient.[27]

The REACH-HF intervention was also associated with better patient ratings of self-care maintenance assessed using the Self-Care of Heart Failure Index, indicating enhanced engagement in activities such as monitoring their weight and increased exercise, looking for signs of fluid retention, and using a system to help remember daily drugs.[21]

The results of our trial are consistent with existing evidence on the impact of CR for HF. The 2014 Cochrane meta-analysis of exercise-based CR included 33 trials and reported a mean benefit in MLHFQ score of –5.8 (95% CI –9.2 to –2.4) points (p = 0.0007) compared with control.[4] However, it is important to note that most of this evidence came from trials of hospital- and center-based models of CR, as only six of the included trials (413 participants) assessed CR undertaken exclusively in a home-based setting.[4] Furthermore, our findings are in keeping with recent studies that support the use of home-based interventions as an alternative to centre-based CR.[28,29] Mobile and internet modes of delivery offer the opportunity to improve CR uptake in the elderly.[30]

We believe that this study is the first randomized trial of a home-based CR intervention for HF derived from health behavior change theory and that was co-developed with patients, caregivers and clinicians. We recently published the findings of a single centre pilot trial which supported the feasibility and acceptability of the REACH-HF intervention in HF patients with preserved ejection

fraction and indicates that it would be possible to recruit and retain participants in a full randomized trial of our intervention in patients with HFpEF.[31]

This multicenter trial in patients with HFrEF recruited to target, had excellent intervention adherence (90%), and had a relatively low level of attrition (< 15% loss) over the 12 months of participant follow-up. There are number of possible explanations for the lack of a significant between-group difference in other outcomes. First, participants may have insufficiently engaged with the REACH-HF intervention to stimulate an improvement in outcomes. For example, failure to adequately engage in the exercise training program, would explain the lack of between difference in exercise capacity and physical activity. Second, the trial was not formally powered to detect differences in secondary outcomes, in particular clinical events. Third, REACH-HF is a comprehensive, multifactorial intervention, with individual patients likely to have experienced different pathways to improved HRQoL, which may include reduced stress or anxiety; improved pacing of physical activity, exercise capacity, or sleep quality; and better medication management. In addition, the baseline characteristics of our study population indicated high levels of comorbidity. The lack of impact on exercise capacity and physical activity may therefore be attributed to the 'heavy burden of comorbid disease' that can affect outcomes in older patients with HF.[32] For example, substantive numbers of patients had atrial fibrillation/flutter (50%) and osteoarthritis or rheumatoid arthritis(37%) which could have limited the participants' intensity and frequency of exercise and physical activity . Finally, there is a growing evidence base demonstrating the limited sensitivity of the EQ-5D in mild-to-moderate HF.[33-35] Consistent with our study, the HF-ACTION study found no difference in the EQ-5D utility score after exercise-based CR compared with control at 12 months.[35] In contrast, the EQ-5D has been shown to be a valid and sensitive measure in patients with advanced HF.[2]

Study limitations

This study had potential limitations. First is the lack of blinding – given the nature of the intervention and control, we could not mask participants to treatments, so our results may reflect patient

expectation bias. However, we used self-reported outcome measures and outcome assessor blinding procedures to reduce researcher assessment bias. Second, around 15% of data were missing for the primary outcome measure at follow-up. However, our sensitivity analyses show that the between-group inferences in our trial were robust to data imputation. To take account of the observed baseline between-group imbalance, we adjusted all analyses for baseline outcome scores and the presence of cardiac morbidity (myocardial infarction, atrial fibrillation, and atrial flutter). Third, the assessment of adherence is notoriously challenging in home-based interventions (given the self-direct nature of the intervention, we were not a able to capture consistent patient-level data on their level of intervention adherence, such as their exercise training programme.[36]

Conclusions

The REACH-HF home-based CR intervention for the management of HFrEF results in superior and clinically important improvements in disease-specific HRQoL and self-management. These findings support the benefits of an affordable, novel home-based CR intervention that offers patients, clinicians and healthcare commissioners an additional option to center-based CR to address current low rates of uptake.

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Data sharing: All of the individual participant data collected during the trial (including the data dictionary) will be available, after deidentification, immediately after completion of trial funding (end of June 2018) with no end date. The trial protocol has been published. All proposals requesting data access will need to specify how it is planned to use the data, and all proposals will need approval of the trial's co-chief investigators (HMD and RST) before data release.

Supplementary information

Additional supplementary information can be found in the online version of this article.

Table S1. Fidelity of intervention delivery summary scores

Table S2. Interactions on primary outcome at 12 months.

Table S3. REACH-HF intervention contacts and costs

Figure S1. Components of the Rehabilitation EnAblement in CHronic Heart Failure (REACH-HF) intervention.

Author contribution: HMD and RST contributed equally. HMD, RST, KJ, RCD, PD, JM, RvL, CGreen, JW, NB, CGreaves, CA, and SSingh designed the trial, were responsible for its conduct, and obtained the trial funding. CGreaves led the design of the intervention, with strong contributions from JW, PD, the Heart Manual Department (Edinburgh), and the REACH-HF service user advisory group. VE and CH were responsible for trial and data collection management. FW, SSadler, and CGreen and MH analyzed the data. KP provided patient and public involvement. All authors including CCL, KS, and SSadler contributed to writing and editing of the manuscript, with the lead taken by HMD and RST. All authors commented on the manuscript and agreed the final version. HMD and RST are the guarantors. The corresponding author had full access to all of the data in the trial and had final responsibility for the decision to submit.

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Legends

Figure 1. Trial profile. *Per protocol: REACH-HF participant must attend first face-to-face contact with facilitator and at least two facilitator contacts thereafter, at least one of which must be face-to-face. †One REACH-HF and two control participants had completed questionnaires insufficiently to allow scoring of primary outcome. REACH-HF, Rehabilitation EnAblement in CHronic Heart Failure

Figure 1 Trial profile. *Per protocol: REACH-HF participant must attend first face-to-face contact with facilitator and at least two facilitator contacts thereafter, at least one of which must be face-to-face. †One REACH-HF and two control participants had completed questionnaires insufficiently to allow scoring of primary outcome. REACH-HF, Rehabilitation EnAblement in CHronic Heart Failure

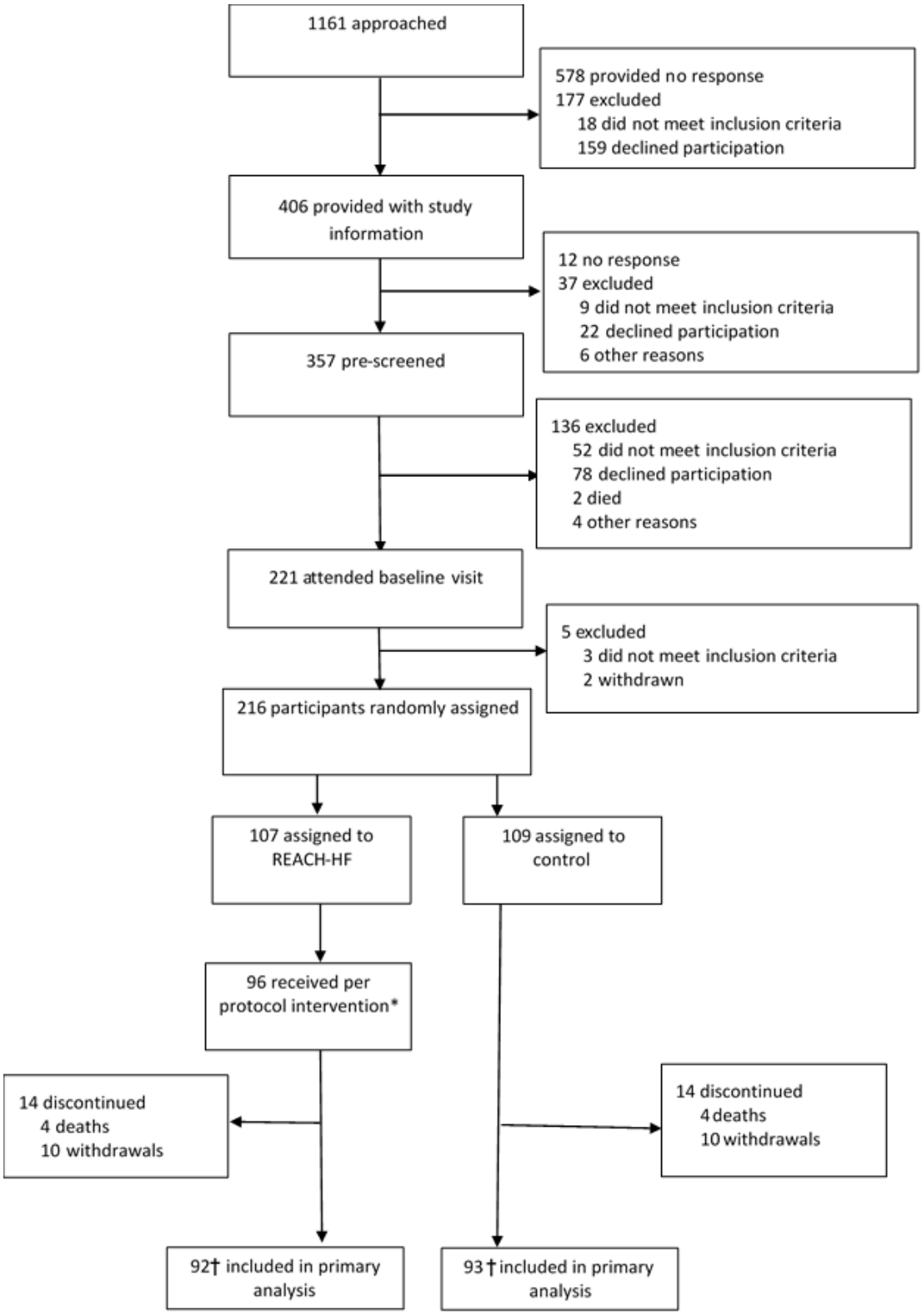

Table 1 Baseline characteristics. Data are n (%) unless otherwise indicated; percentages may not sum to 100 because of rounding

Characteristic	REACH-HF (n = 107)	Control (n = 109)
Mean (SD) age (years)*	69.7 (10.9)	69.9 (11)
Female sex	26 (24)	21 (19)
Median (IQR) BMI (kg/m^2)†	28.1 (25.3–32.4)	28.0 (25–32.2)
Main activity		
Retired	81 (76)	83 (76)
In employment or self-employment	18 (17)	17 (16)
Living alone	28 (26)	22 (20)
Ethnic origin		
White	100 (93)	104 (95)
Other (Black, Asian, other)	7 (7)	5 (5)
NYHA status		
Class I	24 (22)	19 (17)
Class II	63 (59)	63 (58)
Class III	20 (19)	26 (24)
Class IV	–	1 (1)
Ischemic etiology of HF	48 (45)	50 (46)
Time since diagnosis of HF (years)		
<1	35 (33)	35 (32)
1–2	18 (17)	20 (18)
>2	54 (51)	54 (50)

Median (IQR) LVEF (%)‡	34.5 (25–39)	33 (27–36.3)
NT-pro-BNP level (pg/ml)		
≤2000	84 (79)	86 (79)
>2000	23 (22)	23 (21)
Current smoker	6 (6)	6 (6)
Comorbidities (past or present)		
Diabetes mellitus	26 (24)	25 (23)
Myocardial infarction	29 (27)	38 (35)
Hypertension	45 (42)	42 (39)
Chronic renal impairment	14 (13)	19 (17)
Arthritis (osteoarthritis or rheumatoid)	45 (42)	35 (32)
Atrial fibrillation or atrial flutter	48 (45)	60 (55)
COPD	8 (8)	9 (8)
Depression	27 (25)	23 (21)
Charlson comorbidity score >3§	12 (11)	26 (24)
Baseline use of drugs		
Beta-blocker	90 (84)	90 (83)
Angiotensin II receptor antagonist**	31 (29)	24 (22)
ACE inhibitor**	68 (64)	74 (68)
Loop diuretic	70 (65)	68 (62)
Aldosterone antagonist	64 (60)	52 (48)
Digoxin	20 (19)	14 (13)
Baseline use of devices		
ICD	10 (9)	11 (10)

CRT	10 (9)	5 (5)
Combined CRT/ICD	5 (5)	4 (4)
Pacemaker	11 (10)	11 (10)
Location		
Cornwall, England, UK	30 (28)	31 (28)
Gwent, Wales, UK	23 (22)	23 (21)
Birmingham, England, UK	27 (25)	28 (26)
York, England UK	27 (25)	27 (25)
Caregiver present at randomization	53 (50)	44 (40)

REACH-HF = Rehabilitation EnAblement in CHronic Heart Failure; SD = standard deviation; ; IQR = interquartile range; BMI = body mass index; NYHA = New York Heart Association; HF = heart failure; NT-pro-BNP = N-terminal proB-type natriuretic peptide; LVEF = left ventricular ejection fraction; COPD = chronic obstructive pulmonary disease; ICD = implantable cardioverter defibrillator; CRT = cardiac synchronization therapy device; UK = United Kingdom.

*National Audit of Cardiac Rehabilitation (NACR) 2013–14 data for comparison: total mean (SD) age in NACR = 67 (13) years, mean age for patients with HF = 69 (13) years.

**Patients who were intolerant to ACE inhibitor were on Angiotensin II receptor antagonist (e.g. Losartan, Candesartan).

†Numerical values for BMI available for 215 participants (REACH-HF, n = 107; control, n = 108).

‡Numerical values for LVEF available for 156 participants (REACH-HF, n = 76; control, n = 80). Categorical data collected for 60 participants. All participants had an ejection fraction >45% or systolic dysfunction.

§For the REACH-HF trial, we calculated the Charlson comorbidity score but not the Charlson comorbidity index or Charlson comorbidity adjusted life expectancy, as some of our patient population were older than 80 years, which is the limit for these additional scores.

Table 2 Primary and secondary patient reported outcomes at baseline and follow-up. Data are mean (standard deviation [SD], n) unless otherwise indicated

Outcome	Baseline		Follow-up							
			4 months		6 months		12 months			
	REACH-HF	Control	REACH-HF	Control	REACH-HF	Control	REACH-HF	Control	Between group difference	p value
MLHFQ										
Overall	32.8 (23.8, 107)	28.3 (22, 109)	22.7 (18.4, 96)	27.8 (23.2, 100)	28.8 (20.5, 90)	29.5 (21.8, 94)	24.1 (20.9, 92)	27.5 (23.2, 93)	–5.7 (–10.6 to –0.7)	0.025
Physical	16.5 (11.5, 107)	14.7 (11.2, 109)	11.7 (9.0, 96)	14.5 (11.3, 100)	14.7 (10.7, 90)	14.9 (11.2, 94)	12.2 (10.8, 92)	14.5 (11.8, 93)	–3.2 (–5.7 to –0.6)	0.016
Emotional	7.7 (7.3, 107)	6.8 (6.6, 109)	4.8 (5.8, 96)	6.4 (6.9, 100)	6.2 (6.2, 90)	6.8 (6.8, 94)	5.1 (5.8, 92)	5.5 (6.4, 93)	–0.8 (–2.2 to 0.6)	0.273
HADS										
Anxiety	5.1 (4.4, 107)	5.7 (4.3, 109)	4.4 (3.9, 95)	5.2 (4.2, 101)	4.7 (3.7, 89)	5.4 (4.3, 94)	4.2 (3.8, 88)	4.7 (4.5, 92)	0.1 (–0.8 to 1.0)	0.829
Depression	4.4 (3.5, 107)	4.6 (3.3, 109)	3.6 (2.7, 95)	4.5 (3.5, 101)	4.6 (3.2, 89)	4.7 (3.6, 94)	3.6 (3.1, 88)	3.9 (3.4, 92)	–0.2 (–1.1 to 0.6)	0.563

HeartQoL										
Global	1.8 (0.7, 107)	1.8 (0.7, 109)	2.0 (0.7, 95)	1.9 (0.8, 101)	1.8 (0.8, 89)	1.8 (0.8, 91)	1.9 (0.8, 88)	1.9 (0.9, 92)	0.0 (–0.2 to 0.2)	0.823
Physical	1.7 (0.8, 107)	1.7 (0.8, 109)	1.9 (0.8, 95)	1.7 (0.9, 101)	1.6 (0.8, 90)	1.7 (0.9, 92)	1.8 (0.9, 88)	1.7 (0.9, 92)	0.0 (–0.2 to 0.2)	0.869
Emotional	2.1 (0.9, 107)	2.2 (0.8, 109)	2.3 (0.8, 95)	2.2 (0.8, 101)	2.2 (0.8, 89)	2.1 (0.8, 93)	2.3 (0.8, 88)	2.3 (0.8, 92)	0.0 (–0.2 to 0.3)	0.683
EQ-5D-3L	0.739 (0.234, 106)	0.723 (0.236, 108)	0.758 (0.223, 95)	0.753 (0.219, 101)	0.708 (0.265, 88)	0.733 (0.217, 92)	0.752 (0.240, 88)	0.739 (0.263, 92)	–0.024 (–0.091 to 0.044)	0.487
EQ-5D VAS (0 to 100)	69 (20), 97	71 (20), 97	73 (17), 90	74 (17), 93	72 (18), 80	70 (19), 85	74 (18), 85	73 (22), 84	1 (–5 to 6)	0.859
SCHFI										
Maintenance	55.8 (16.5, 107)	54.5 (14.5, 109)	68.3 (13.6, 96)	55.7 (17.0, 101)	65.4 (14.4, 89)	54.7 (16.0, 94)	63.8 (17.0, 87)	55.2 (16.8, 92)	8.0 (3.6 to 12.4)	<0.001
Management	43.1 (25.9, 47)	40.4 (21, 59)	46.8 (24.2, 33)	42.0 (21.0, 48)	52.1 (18.8, 42)	41.9 (21.6, 37)	53.8 (23.4, 39)	43.4 (20.1, 40)	9.4 (–4.0 to 22.8)	0.165
Confidence	61.7 (25.0, 107)	65.3 (23.8, 108)	67.0 (22.3, 94)	64.7 (21.7, 101)	65.4 (22.8, 85)	62.5 (22.7, 93)	70.3 (21.8, 88)	66.4 (21.3, 92)	5.6 (–0.1 to 11.3)	0.056

EQ-5D-3L = three level version of five-dimension EuroQol scale; HADS = Hospital Anxiety and Depression Scale; MLHFQ = Minnesota Living with Heart Failure Questionnaire; REACH-HF = Rehabilitation EnAblement in CHronic Heart Failure; SCHFI = Self-Care of Heart Failure Index; VAS = visual analog scale.

Table 3 Secondary objective outcomes at baseline and follow up. Data are mean (standard deviation (SD), n) unless otherwise indicated

Outcome	Baseline		Follow up					
			4 months		12 months			
	REACH-HF	Control	REACH-HF	Control	REACH-HF	Control	Between-group difference	p value
ISWT (meters)	262.3 (153.4, 99)	239.7 (152.4, 103)	328.5 (181.3, 66)	294.3 (215.5, 75)	328.5 (181.3, 66)	294.3 (215.5, 75)	0.1 (–33.3 to 33.5)	0.995
Number of days/week with at least 10 minutes/day activity >100 milli-g*	5.8 (2.3, 99)	5.9 (1.9, 103)	5.6 (2.4, 78)	5.5 (2.6, 84)	5.6 (2.4, 78)	5.5 (2.6, 84)	0.2 (–0.4 to 0.7)	0.601
Average time/day (minutes)								
≤20 milli-g*	1104 (102, 99)	1106 (114, 103)	1107 (110, 88)	1092 (116, 93)	1092 (124, 78)	1103 (118, 84)	–7 (–29 to 15)	0.534
21–40 milli-g*	141 (35, 99)	136 (35, 103)	140 (35, 88)	138 (30, 93)	142 (39, 78)	138 (34, 84)	–1 (–9 to 8)	0.880
41–60 milli-g*	80 (25, 99)	80 (27, 103)	80 (27, 88)	82 (26, 93)	81 (30, 78)	81 (28, 84)	0 (–6 to 6)	0.901
61–80 milli-g*	45 (21, 99)	46 (21, 103)	45 (22, 88)	48 (22, 93)	48 (23, 78)	46 (22, 84)	2 (–2 to 5)	0.372

81–100 milli-g*	26	27	26	28
	(16, 99)	(16, 103)	(16, 88)	(17, 93)
>100 milli-g*	42	46	43	51
	(34, 99)	(40, 103)	(37, 88)	(46, 93)

*1000 milli-g = 1 g = 9.81 m/s^2, <40 milli-g is approximately equivalent to sedentary activities such as sitting, lying and ≥100 milli-g is approximately equivalent to activities undertaken at a moderate to vigorous intensity.

EQ-5D-3L = three-level version of five-dimension EuroQol scale; HADS = Hospital Anxiety and Depression Scale; ISWT = incremental shuttle walk test; miili-g = milli-gravity unit; MLHFQ = Minnesota Living with Heart Failure Questionnaire; REACH-HF = Rehabilitation EnAblement in CHronic Heart Failure