The cost effectiveness of REACH-HF and home-based cardiac rehabilitation in the treatment of heart failure with reduced ejection fraction

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The cost effectiveness of REACH-HF and home-based cardiac rehabilitation in the treatment of heart failure with reduced ejection fraction: a decision model-based analysis

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Abstract:	Background The REACH-HF (Rehabilitation EnAblement in CHronic Heart Failure) trial found that the REACH-HF home-based intervention resulted in a clinically meaningful improvement in disease-specific health-related quality of life in patients with reduced ejection fraction heart failure (HFrEF). The aim of this study was to assess the long-term cost-effectiveness of the addition of REACH-HF intervention or home-based CR to usual care compared to usual care alone in patients with HFrEF. Design and methods A Markov model was developed using a patient lifetime horizon and integrating evidence from the REACH-HF trial, a systematic review/meta-analysis of randomised trials, estimates of mortality and hospital admission and UK costs at 2015/6 prices. Taking a UK National Health and Personal Social Services perspective we report the incremental cost per quality-adjusted life-year (QALY) gained, assessing uncertainty using probabilistic and deterministic sensitivity analyses. Results In base case analysis, the REACH-HF intervention was associated with per patient mean QALY gain of 0.30 and an increased mean cost of £126 compared with usual care, resulting in a cost per QALY of £415. Probabilistic sensitivity analysis indicated a 77% probability that REACH-HF is cost effective versus usual care at a threshold of £20,000 per QALY. Results were similar for home-based CR versus usual care. Sensitivity analyses indicate the findings to be robust to changes in model assumptions and parameters Conclusions Our analyses indicate that the addition of the REACH-HF intervention and home-based CR programmes are likely to be cost-effective treatment options versus usual care alone in patients with HFrEF.

2nd Feb 2019

Dear Handling Editor

Ref: Ms. No. EJPC-D-18-01031. The cost effectiveness of REACH-HF and home-based cardiac rehabilitation in the treatment of heart failure with reduced ejection fraction: a decision model-based analysis

Thank you for the further comments on our paper. We have replied to reviewer #4 additional comments and I have emailed our health economist to email an electronic copy of our economic model.

We hope our responses will result in final acceptance of our paper.

Yours sincerely

Prof Rod Taylor on behalf of the co-authors

-----Original Message-----
From: Taylor, Rod
Sent: 02 February 2019 17:34
To: 'susannah sadler' <susisadler@gmail.com>
Cc: 'kvellop@gmail.com' <kvellop@gmail.com>
Subject: FW: Editor Decision - Please Revise
Importance: High

Dear Susie

As requested in 2nd round of peer review of our paper (see below) can I please ask you to email asap an electronic copy of our economic model to reviewer #4 and copy me in. I have copied the reviewer #4 into this email.

Many thanks
Rod

Professor Rod Taylor MSc, PhD
Chair of Population Health Research, Institute of Health and Well Being, University of Glasgow Chair of Health Services Research, Co-Director of Exeter Clinical Trials Unit & NIHR Senior Investigator Institute of Health Research, College of Medicine and Health, University of Exeter

Ms. No. EJPC-D-18-01031 The cost effectiveness of REACH-HF and home-based cardiac rehabilitation in the treatment of heart failure with reduced ejection fraction: a decision model-based analysis – following 2nd round of review

	Author reply	**Revision to manuscript**
Reviewer #3		
In my opinion, authors have adequately responded to the points raised by reviewers.	Thank you.	
Reviewer #4		
You addressed the majority of the comments in a satisfactory way. There are some points that need to be clarified, especially concerning the PSA in order for the paper to be of good quality and correspond to the standards of the journal. In total, I reckon that your paper would be of value to the community. I would like to see the model you used. If you do not mind, you can share it with me in my email address (kvellop@gmail.com). Of course, I would abide by the requested confidentiality.	As indicated in our cover letter to editor in the first round of review, we would be pleased to share the model with you. I have copied you into an email to my health economics colleague (Dr Susi Sadler) to request that she forwards an electronic version of our model to you.	None
The key role of cost efficiency in cardiac rehabilitation has been investigated in more recent evidences: You may wish to comment in your revision (eg. 'Clinical and cost-effectiveness of home-based cardiac rehabilitation compared to conventional, centre-based cardiac rehabilitation: Results of the FIT@Home study' by Kraal JJ; 'Cost-utility analysis of cardiac rehabilitation after conventional heart valve surgery versus usual care' by Hansen TB)	Our presentation of previous published cost effectiveness for cardiac rehabilitation evidence comes from two recent comprehensive systematic reviews (now cited in the manuscript). We agree that as a home-based strategy, the FIT@home publication is important and we added this.	Text added to discussion section

The cost effectiveness of REACH-HF and home-based cardiac rehabilitation compared to the usual medical care ~~in the treatment of~~ for ~~-~~ heart failure with reduced ejection fraction: a decision model-based analysis

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Previous presentations: none

Disclaimers: none

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Word count: 4979 (including references, tables and figures)

Abstract

Background: The REACH-HF (Rehabilitation EnAblement in CHronic Heart Failure) trial found that the REACH-HF home-based cardiac rehabilitation (CR) intervention resulted in a clinically meaningful improvement in disease-specific health-related quality of life in patients with reduced ejection fraction heart failure (HFrEF). The aims of this study werewas to assess the long-term cost-effectiveness of the addition of REACH-HF intervention or home-based CR to usual care compared to usual care alone in patients with HFrEF.

Design and methods: A Markov model was developed using a patient lifetime horizon and integrating evidence from the REACH-HF trial, a systematic review/meta-analysis of randomised trials, estimates of mortality and hospital admission and UK costs at 2015/6 prices. Taking a UK National Health and Personal Social Services perspective we report the incremental cost per quality-adjusted life-year (QALY) gained, assessing uncertainty using probabilistic and deterministic sensitivity analyses.

Results: In base case analysis, the REACH-HF intervention was associated with per patient mean QALY gain of 0.230 and an increased mean cost of £400126 compared with usual care, resulting in a cost per QALY gained of £1,720415. Probabilistic sensitivity analysis indicated a 787% probability that REACH-HF is cost effective versus usual care at a threshold of £20,000 per QALY gained. Results were similar for home-based CR versus usual care. Sensitivity analyses indicate the findings to be robust to changes in model assumptions and parameters

Conclusions: Our cost-utility analyses indicate that the addition of the REACH-HF intervention and home-based CR programmes are likely to be cost-effective treatment options versus usual care alone in patients with HFrEF.

Key words: cardiac rehabilitation, health-related quality of life, heart failure, home-based, cost-effectiveness, decision model

Introduction

Heart failure with reduced ejection fraction (HFrEF) represents a major health issue and is associated with considerable morbidity and mortality. HF as primary diagnosis accounts for 1-2% of the annual healthcare budget in Europe and USA [1]. The global ~~cost~~ economic burden of HF is estimated at $US108 billion per annum with hospital admission being a key economic driver [2].

Systematic reviews and meta-analyses of cardiac rehabilitation (CR) for HF have shown improvements in health-related quality of life (HRQoL), reductions in re-hospitalisations and demonstrated potential cost-effectiveness [3,4]. This existing evidence is based solely ~~entirely for~~ on hospital (or centre)-based CR programmes and the economic evaluation data is limited in both quantity and quality [3,4].

In spite of national and international guidelines recommending CR for HF [5-7], less than 20% of HF patients in the UK are referred to CR and less than 15% currently participate in CR [8-10], prompting calls for alternative more accessible models of CR provision [8].

REACH-HF (Rehabilitation EnAblement in CHronic Heart Failure) is a home-based CR programme delivered over a 12-weeks by a trained healthcare professional for patients and their caregivers. Uniquely the REACH-HF intervention has been co-developed with patients, caregivers, and clinicians to include core components of comprehensive CR, i.e., education and psychological support, in addition to exercise training [11]. The REACH-HF randomised controlled trial compared the addition of REACH-HF intervention to usual care with usual care alone in patients with HFrEF across four UK sites [12]. At 12-months, the trial found - that the REACH-HF intervention led to a statistically significant and clinically meaningful improvement in HRQoL with a reduction in total Minnesota Living with Heart Failure Questionnaire score of -5.7 points (95% confidence interval: -10.6 to -0.7) and a non-significant reduction in the number of patients experiencing one or more hospital admissions (odds ratio: 0.56, 95% CI: 0.13 to 2.33). [13]. Having estimated the average cost of REACH-HF delivery at £418 per patient [13], we sought to assess if the REACH-HF intervention is likely to be cost-effective for healthcare payers over the long-term.

We report the results of a model-based cost-effectiveness analyses that extrapolates the findings of REACH-HF trial to estimate the long-term cost-effectiveness of REACH-HF intervention. We also report the long-term cost-effectiveness of home-based CR based on a meta-analysis of randomised trials.

Methods

This analysis was reported in accord with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement [14] and the reference case of the UK National Institute for Health and Care Excellence (NICE) [15]. The analyses were conducted from the perspective of the UK NHS and Personal Social Services. We estimated the cost-effectiveness of REACH-HF plus usual care versus usual care alone and home-based CR plus usual care versus usual care alone, based on the estimated incremental cost per quality-adjusted life-years (QALY). - a cost-utility analysis.

Study Population

Data were used from the REACH HF trial [13] where participants with HFrEF were recruited from primary and secondary care in 4 UK centres during 2015–2016 and were randomly assigned to the REACH-HF intervention plus usual care or usual care alone (current standard therapy in the UK for most patients with HF) [12]. In the UK, only a minority of patients with HF receive CR and 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 [13]. Details of REACH-HF intervention are presented elsewhere [12,13].

Model Structure

Consistent with the economic evaluation literature in HF [16], a Markov cohort model (eFigure 1) was developed that captured the impact on hospital admissions, and a related increase in the mortality rate, for people with HF. In this case a cohort Markov model was considered appropriate since this estimates the average effect of the intervention on morbidity, mortality, cost and HRQoL. The model uses a lifetime horizon (follows patients from a starting age of 78 to age 100) and costs and QALYs were discounted at 3.5% [15]. The model consisted of three primary health states: (1) HF with no HF-related hospital admission, (2) HF with HF-related hospital admission, and (3) death. The model uses a one-month cycle length, in order to capture the effects of hospital admission events which are short term events but may recur several times in a year. Tunnel states are used in the model to reflect an increased mortality risk in the period (1 to 38 months) after hospital admission/discharge. Patients begin in a stable HF health state (HF with no HF-related hospitalisation). From this state, patients can either remain in the same state, or experience an HF-related hospitalisation or death. If the patients experience an HF-related hospitalisation, they automatically progress to the first of 38 post-hospitalisation tunnel states, where they will progress one state each month until month 38 post-hospitalisation, when they will return to the HF with no HF-related hospitalisation state. During the tunnel states, patients can also experience an additional hospitalisation or death at any time. , and

~~the model uses the patient lifetime duration to estimate and compare the costs and QALYs for patients receiving REACH-HF or home-based CR.~~ The model was developed in Microsoft Excel and programmed in Visual Basic for Applications.

Model inputs

The model parameters and assumptions about transitions between health states are outlined in Table 1.

CR Effectiveness

We used data from REACH-HF trial for the difference in risk of hospital admission (odds ratio: 0.56, 95% CI: 0.13 to 2.33) [13]. We also undertook a meta-analysis that combined REACH-HF trial data with two other randomised trials of home-based CR versus no CR usual care [17,18] to estimate the pooled risk of hospital admission following home-based CR compared to usual care (odds ratio: 0.70, 95% CI: 0.27 to 1.60) (see eFigure 1 for meta-analysis forest plot and methodology). This reduction in risk was assumed to last for four years from the start of the model, after which hospital admission rates are assumed to return to baseline. We assessed the impact on estimates of cost-effectiveness of variations in this assumption using sensitivity analyses.

Hospital Admissions

We applied hospital admission data for HF specific admissions from a UK cohort study reflective of a UK primary care setting, with patients experiencing both first and subsequent hospital admissions [19] (see Table 1). In sensitivity analyses, we tested the robustness of model outcomes to changes in hospital admission rates, using data from the UK Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure (EMPHASIS) trial [20], which provided a lower estimate of admission rates (10% HF-related admissions; 20% all cause admissions per annum), and a meta-analysis of randomised trials [21] reporting relatively high admission rates (34% HF-related admissions; 85% all cause admission per annum). We used the same admission rate for all patients in the model irrespective of age and previous admissions.

Mortality

Survival parameters in the model are based on a recently published analysis of UK mortality rates in The Health Improvement Network (THIN) dataset, 1998-2012 [22], a retrospective cohort of 54,313 HF patients aged over 45. In a sensitivity analysis, we applied the overall survival reported by Mohuiddin et al [23] for patients in another large UK cohort, who had already experienced a hospital admission for HF and therefore are expected to have a worse prognosis. This study showed increased risk for time since admission in people 0-1 months,

1-3 months, 3-6 months, 6-12 months, 12-24 months and 24-38 months after admission. The reported hazard ratios were applied in the model.

Mortality rates have been shown to vary with hospital admission and after discharge both in trials [24] and in the wider UK HF population ~~more generally~~ [25] with those in hospital and closer to discharge having higher death rates. Following the approach of Thokala et al [26], we reflected this in the model using the hazard ratio for all-cause mortality reported by Solomon et al [24] for patients within 1 to over 24 months from discharge for their HF hospital admission. For hospital mortality, we derived a~~n additional~~ hazard ratio for survival for patients in hospital compared to within 30 days of discharge~~,~~ from the UK HF Audit [25], which reports outcomes from data on more than 73% of all English and Welsh HF admissions. We calibrated the baseline mortality rate so that the overall survival curves generated by the model matched the survival curves based on parameters taken from the THIN analysis [21]. We conservatively assumed that the hazard ratio of death for subsequent hospital admissions was the same as for the first hospital admission. We assumed that survival followed an exponential curve which has previously been shown to provide a good fit in this population [23,27].

Costs

Costs were included in pounds sterling using the 2015/16 price year. The following costs were considered: (i) home-based CR, (ii) costs associated with HF hospital admission, (iii) costs associated with other cause hospital admission, and (iv) primary and secondary usual health care costs (excluding hospital admission) associated with HF (see Table 1). For intervention cost we use the UK NHS tariff for CR of £477/patient) [28] and the estimated cost for delivery of the REACH-HF intervention of £418/patient [13]. This cost was applied to all patients at the start of the model. Ongoing costs for usual care for HF, primary care, secondary care, Accident & Emergency department attendances and drug costs, are included for time spent in the HF non-hospital admission state (£815/patient per year), informed by UK national data for HF and the THIN dataset, a large UK HF cohort study [22]. The cost for hospital admission is based on data from the English NHS National Schedule of Reference Costs 2015/16 [28], for HF hospital admission we use a weighted average cost of a single hospital stay for the health resource groups (HRGs) EB03A to D. The cost of non-HF hospital admissions is a background cost in each cycle of the model, where patients are alive with HF. We discounted costs and QALYs at an annual rate of 3.5% in accord the NICE reference case [15].

Health state values

We calculated QALYs by multiplying the health value for the state by the time spent in that state. We use data from Systolic Heart failure treatment with the inhibitor ivabradine Trial (SHIFT) to inform health state values, applying a health state value of 0.736 for the HF health state, and a reduction (decrement) of 0.084 where people experience a HF related hospital admission [30]. For non-HF hospital admissions, we apply a decrement of 0.032 for events. The impact of hospital events on health state values is applied for the one-month cycle of hospital admission after which individuals were assumed to return to baseline values. Data from the SHIFT trial, was considered to be the most appropriate for our model given the reporting of EQ-5D data for the HF state and separately for a HF specific hospital admission.

Analysis

We present deterministic estimates of the cost per QALY gained and use probabilistic sensitivity analysis (PSA) and the incremental net monetary benefit (iNMB) approach [31,32] to address uncertainty around the results. The iNMB approach uses parameters representing the maximum amount that the Payer (i.e. NHS) is 'willing to pay' to gain one QALY. We conservatively used the lower NICE threshold value of £20,000 per QALY gained in calculating iNMB [15]. An iNMB value > 0 would indicate that the intervention (home based CR) is cost-effective. The cost-effectiveness acceptability curve (CEAC) ~~to~~ demonstrates how the willingness-to-pay threshold affects the probability that the intervention is considered cost-effective [32]. Monte Carlo simulation was used to draw a randomly selected estimate of each model parameter from the distributions described in Table 1 and to calculate the iNMB. Beta distributions represent the uncertainty in the probability parameters (mortality, hospital admission) and parameters for health state values because these values are typically bounded at zero and one. Log-normal distributions were used to estimate uncertainty in hazard rates and ratios. We used 5,000 iterations to empirically estimate the uncertainty surrounding the mean iNMB.

The key element of structural uncertainty identified was ~~the use of increasing~~ HF-related mortality rates during admission and after discharge from hospital ~~for an HF related event~~. This mechanism allows any reductions in admission rate brought about by the intervention to reduce overall mortality in the cohort, with related cost savings and QALY gains estimated. To test how sensitive the results are to the inclusion of this element of model structure we included a sensitivity analysis which uses a base mortality rate (from the THIN cohort [22]) for all patients at all times, regardless of hospital admission (SA1).

In addition, we included further deterministic analyses to test how sensitive the results were to the choice of parameter as follows: the lowest hospital admission rate from trials identified as sources of HF-specific admission (0.88% probability of admission per month, based on

the Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure (EMPHASIS) trial [20] (SA2); the higher hospital admission rate from a large meta-analysis of trials (2.83% probability of admission per month [21] (SA3); survival based on previously-admitted patients in the large combined data in Hospital Episode Statistics (HES) and Office of National Statistics (ONS) dataset [23] (SA4); lower mean intervention cost of £204/patient, based on the lower bound of the 95% confidence interval around estimated cost for REACH-HF intervention (SA5); higher mean intervention cost of £730, based on the upper bound of the 95% confidence interval around estimated cost for the REACH-HF intervention [13]; and assumption for home-based CR effect duration, at 2 years (SA7).

Results

Base-case analysis

REACH-HF intervention

Over the HFrEF patient lifetime, compared to usual care alone, the addition of REACH HF intervention was more costly (mean £400~~126~~/patient) and more effective (mean QALY 0.23~~9~~) with an estimated incremental cost effective ratio of £1720~~415~~/QALY (Table 2). There was a 78~~7~~% probability that REACH-HF was cost-effective at willingness to pay threshold of £20,000/QALY gained (eFigure 3a).

Home-based CR

The estimated mean gain in QALYs for home-based CR compared to usual care was 0.16~~20~~, and the estimated mean incremental cost is £383~~206~~/patient over the lifetime, giving an estimated incremental cost ratio of per £2,413~~1,029~~ per QALY (Table 2). There was 73~~5~~% probability that home-based CR was cost-effective compared to usual care, at £20,000/QALY gained (eFigure 3b).

Sensitivity analyses

Sensitivity analyses (eTables 1a and 1b) indicate the base case analyses to be robust and not sensitive to changes in key structural assumptions in the modelling framework or key input parameters (i.e. mortality effect of hospital admission, probability of hospital admission, probability of mortality, home-based CR, duration of treatment effect) for both REACH-HF and home-based CR. Removing the increase in risk of mortality after hospital admission (SA1) resulted, in home-based CR dominating usual care, with a reduction in costs (cost saving) and no difference QALYs. In this scenario, although QALY gains are reduced, the costs associated with home-based CR also reduce due to the absence of an extended period of life expectancy and the absence of the additional costs associated with extending lives in the home-based CR group.

Discussion

Our estimates suggest that the addition of REACH-HF intervention home-based CR to usual care was cost-effective compared to usual care alone in patients with HFrEF at a cost of £1730~~415~~/QALY and a 7~~87~~% likelihood of being cost-effective at the willingness to pay threshold of £20,000 per QALY gained used by policymakers in UK and many developed health-care economies [15,33]. Our cost-effectiveness estimates for other home-based CR programmes were similar. Our results were mainly driven by a reduction in HF-related hospitalisations with CR.

Two recent systematic reviews of cost-effectiveness of CR have been published [4,34]. ~~To the best of our knowledge~~Based on the results of these reviews, this is first published full economic evaluation of ~~a comprehensive~~ a specific home-based programme (REACH-HF) and home-based CR programmes more broadly in patients with HF. However, our findings are consistent with previously economic evaluations in HF comparing centre-based CR to no CR control ~~[4]~~. Using extrapolated outcome survival data from a single centre randomised controlled trial, Georgiou and colleagues reported an incremental cost-effectiveness ratio of US$2500 per life year gained for exercise training programme at a 10-year time horizon based on US healthcare perspective [3~~4~~]. Using a variety of modelling assumptions and data at 2.5 years follow up from the large HF-ACTION trial undertaken across 82 centres across United States, Canada, and France, Reed et al estimated that the cost-effectiveness of exercise training could vary from dominant (cost saving and more QALYs gained) to US$43,141/QALY [3~~5~~]. Based on data from exercise-based CR programme in Colombia, using modelling Rincón et al estimated an incremental cost per QALY of US$1,065/QALY at 5 years [3~~6~~]. Finally, a Markov model-based analysis by Kühr et al reported a cost per QALY of 29,498 international dollars for a hypothetical cohort of HF patients attending outpatient CR programme from the perspective of the Brazilian Public Healthcare System over a 10-year time horizon [3~~7~~]. Notwithstanding the challenge of directly comparing costs across international jurisdictions and whilst these incremental cost effectiveness ratios vary in their magnitude, they have broadly been interpreted by study authors as demonstrating CR to be a cost-effective strategy in patients with HFrEF.

Although not recruiting HF patients, the recently published FIT@Home study also showed home-based CR can be a cost-effective strategy [39]. This study randomised 90 low to moderate risk patients following an acute coronary syndrome or revascularisation to three months of either home-based training with telemonitoring guidance or centre-based training. Average healthcare costs were lower in the home-based group (€437 per patient) and had probability of being cost-effective of 97% and 75% at willingness-to-pay of €0 and €100,000 per QALY, respectively.

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Strengths and limitations

This study usesd cost and outcome data from a high quality multicentre randomised controlled trial of REACH-HF in patients with HFrEF with multiple comorbidities reflective of the clinical setting [13]. The use of Markov modelling overcomes the limitations of a within trial economic evaluation, allowing the modelling of costs and outcomes over the longer term of patient lifetime and the assessment of the long-term cost effectiveness beyond the trial period. The use of longer time-horizon is also more compatible with the chronic nature of HF and in accord with NICE methodology guidance [15]. We use high quality data on mortality from a large cohort study consistent with the setting for our economic analysis. Given the variation of hospital admission data, we use a UK dataset in our base case analysis. However, use was made of alternative data sources were used in sensitivity analyses.
A key limitation was that the REACH-HF trial was not powered to detect differences in hospitalisations between arms. However, we sought to overcome this by undertaking a meta-analysis where we included data from two other randomised trials that tested different versions of home-based CR. Furthermore, our probabilistic sensitivity analysis explicitly took account of the uncertainty in the data inputs to the model. Nevertheless, that the overall number of hospitalisations was low (30 events), we acknowledge the need for additional future trials of CR need to consistently collecting and report this the outcome of patient hospitalisation. Furthermore, our probabilistic sensitivity analysis explicitly took account of the uncertainty in the data inputs to the model. We used a simple Markov modelling approach, and whilst this approach is consistent with the wider literature on economic models in HF, we acknowledge it assumes no additional impact from multiple admissions. Whereas in real life patients may suffer from worsening HRQoL after further subsequent hospital stays. This conservative assumption may have led us to have underestimated the cost-effectiveness of REACH-HF and home-based CR. We use HF-related hospital admissions as the main event of interest in the assessment of home-based CR. The absence of any specific modelling of effects on other (non-HF specific) cause of hospital admissions may be a limitation of the modelling, although is also likely to a conservative assumption as CR may positively impact on the risk of admissions due to other cardiovascular related events, such as myocardial infarction or stroke.

Clinical implications

This cost-utility analysis indicates that the REACH-HF intervention and home-based CR programmes are likely to be cost-effective for patients for HFrEF. These economic results have considerable policy relevance given current low levels of uptake of CR for HF across international healthcare systems [4038]. In order to improve CR participation there have been calls for the development of CR programmes that provide an alternative to supervised

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outpatient programmes, such as home-based programmes [8,9,4139]. The results of this analysis are therefore timely and show that home-based CR programmes provide a cost-effective alternative use of healthcare resources. The systematic review of home versus centre-based CR by Wong et al concluded that as costs and outcomes of home-based versus supervised centre-based CR were no different, the choice of the mode of delivery (home- versus centre-based) should be left to healthcare providers and patients [420]. This is further reinforced by the recently updated UK clinical guidelines for the management of HF that patients, which recommend that patients should be offered CR "in a format and setting (at home, in the community or in the hospital) that is easily accessible for the person" [7].

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Conclusion

Over the lifetime of the HFrEF patient, our cost-utility analyses suggest that REACH-HF and home-based CR are cost-effective treatment options in the setting of the United Kingdom health service. These findings should encourage healthcare providers and purchasers to fund home-based CR programmes to improve access and promote participation in CR for people with HF and thereby improve the health-related quality of life and morbidity of this population.

Author contribution: HMD, RST, KJ, RCD, PD, JM, JW, NB, CGreaves, CA, and SSingh obtained the funding for the study. SSadler undertook the economic modelling analysis, RST undertook the meta-analysis, and both jointly drafted the manuscript. All authors commented on the manuscript and agreed the final version

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Table

Table 1. Model parameters and assumptions

Parameter		Base case value (mean)	Probabilistic distribution	Standard error	Source
Mortality					
Monthly probability of death*		0.650%	Beta		[22]
RR of death in hospital compared to 30 days of discharge		1.5	Fixed		[25]
HR of mortality rate	≤1	6.18	Lognormal	1.1364	[24]
by months since	>1	4.39	Lognormal	1.1225	
discharge	>3	3.54	Lognormal	1.1150	
	>6	3.11	Lognormal	1.0978	
	>12	2.46	Lognormal	1.0948	
	>24	1.93	Lognormal	1.1450	
Hospital admission					
Monthly probability of HF admission		2.04%	Beta		[19]
Monthly probability of other cause admission		1.97%	Beta		[19]
Average length of stay (days)		8	Fixed		[25]
Intervention effect					
OR for HF admission: REACH-HF		0.56	Lognormal	2.03	[13]
OR for HF admission: home-based CR		0.70	Lognormal	1.60	Meta-analysis (see Appendix 1)
Duration of treatment effect		4 years	Fixed		Assumption
Costs (per patient)					
Admission HF		£3,873~~05~~	~~Fixed~~Gamma		[29]

Admission other causes	£2,240~~0~~8	Gamma~~Fixed~~		[20,29]
Admission all cause	£2,901~~850~~†	~~Fixed~~Gamma		[20,29]
Ongoing monthly healthcare	£96~~8~~‡	Fixed		[24,29,41-43]
REACH-HF	£418	Fixed		[13]
Home-based ~~Rehab~~CR	£477	Fixed		[28]
Utilities				
Utility for HF patients at baseline	0.736	Fixed		[30]
HF hospital admission decrement	-0.084	Beta	0.006	[30]
Other cause hospital admission decrement	-0.032	Beta	0.005	[30]

Assumptions

Usual care was a no CR (either home- or centre-based) **approach that included medical management according to national and local guidelines, including specialist HF nurse care**

~~Usual care was assumed to include no use of centre-based CR~~

Patients can be admitted for HF during any one-month cycle and probability of admission was fixed for all patients at all times regardless of previous admissions.

First and subsequent HF hospitalisations give the same RR of death compared to no hospitalisation.

Other causes hospitalisations don't independently increase risk of death.

Rate of other causes hospitalisations do not change as a result of treatment allocation

The cost and QoL impact of being in any of the post-HF hospitalisation states (from 1 to 38+ months after discharge) were assumed to be the same

*At baseline i.e. never hospitalised or >38 months since last hospitalisation

‡ Based on data for resource use by type, for people with HF: Comprises £~~384~~ 721 pa for drug costs, £3~~36~~ pa for A&E attendances, £~~96~~ 101 pa for outpatient appointments and £30~~20~~ pa for GP appointments monthly

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† We estimate a per month cost for non-HF hospital admission based on a weighted average cost across four common types of non-HF admission (other CVD, renal function, hyperkalaemia and other), using data on proportions of each admission type reported in the EMPHASIS Trial (Zannad et al [20]), combined with unit costs taken from the English National Schedule of Reference Costs 2015/16.

RR: relative risk, OR: odds ratio; HR: hazard ratio

Table

Table 2. Results of cost-effectiveness analyses: REACH-HF intervention and home-based CR vs. usual care

	Discounted Costs £, mean (95% CI)	Discounted QALYs mean (95% CI)	ICER (£ per QALY gained) Vs. usual care	% simulations with iNMB > £0
Usual care alone	£1,5051~~13,031~~ (£1,3844~~12,381~~ to £1,628913,549)	4.24~~4.26~~ (4.05 to 4.43)		
REACH-HF intervention plus usual care	£1,5452~~13,157~~ (£1,4240~~12,563~~ to £1,6780~~14,396~~)	4.47~~4.56~~ (3.83~~3.76~~ to 4.91)	£1,721~~415~~	78~~77~~%
Home-based CR plus usual care	£1,5444~~13,237~~ (£1,4278~~12,598~~ to £1,6781~~14,061~~)	4.40~~4.46~~ (3.89~~3.90~~ to 4.77~~4.79~~)	£2,413~~1,029~~	73~~75~~%

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