Cost-effectiveness of home-based cardiac rehabilitation: a systematic review

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¹Manchester Centre for Health Economics, The University of Manchester, Manchester, UK ²Faculty of Biology, Medicine and Health. The University of Manchester, Manchester, UK ³Cranmer Consultancy Ltd, Sheffield, UK ⁴Research and Innovation, Greater Manchester Mental Health NHS Foundation Trust, Manchester, UK ⁵School of Psychological Sciences, The University of Manchester, Manchester, UK ⁶Department of Health Sciences, University of York, York, UK

Correspondence to

Gemma E Shields, Manchester Centre for Health Economics, The University of Manchester, Manchester M13 9PL, UK; gemma.shields@manchester. ac.uk

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ABSTRACT

Objective Centre-based cardiac rehabilitation (CR) is recognised as cost-effective for individuals following a cardiac event. However, home-based alternatives are becoming increasingly popular, especially since COVID-19, which necessitated alternative modes of care delivery. This review aimed to assess whether home-based CR interventions are cost-effective (vs centrebased CR).

Methods Using the MEDLINE, Embase and PsycINFO databases, literature searches were conducted in October 2021 to identify full economic evaluations (synthesising costs and effects). Studies were included if they focused on home-based elements of a CR programme or full home-based programmes. Data extraction and critical appraisal were completed using the NHS EED handbook, Consolidated Health Economic Evaluation Reporting Standards and Drummond checklists and were summarised narratively. The protocol was registered on the PROSPERO database (CRD42021286252).

Results Nine studies were included in the review. Interventions were heterogeneous in terms of delivery. components of care and duration. Most studies were economic evaluations within clinical trials (8/9). All studies reported quality-adjusted life years, with the EQ-5D as the most common measure of health status (6/9 studies). Most studies (7/9 studies) concluded that home-based CR (added to or replacing centre-based CR) was cost-effective compared with centre-based options. **Conclusions** Evidence suggests that home-based CR options are cost-effective. The limited size of the evidence base and heterogeneity in methods limits external validity. There were further limitations to the evidence base (eg, limited sample sizes) that increase uncertainty. Future research is needed to cover a greater range of home-based designs, including home-based options for psychological care, with greater sample sizes and the potential to acknowledge patient heterogeneity.



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INTRODUCTION

Globally, cardiovascular diseases (CVDs) represent a significant and increasing burden, with the estimated prevalence having increased by 92% between 1990 and 2019 (from 271 million to 525 million).¹ CVDs are a leading cause of morbidity and mortality, contributing to an estimated 17.8 million deaths and 35.6 million years lived with disability in 2017.² They impose a significant economic burden to healthcare systems and society, with the annual costs to the European Union economy estimated at €210 billion for 2017, including €111 billion in healthcare costs, €54 billion in productivity losses

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Centre-based cardiac rehabilitation (CR) is recognised as a cost-effective intervention, however, home-based alternatives are becoming increasingly popular.

WHAT THIS STUDY ADDS

- ⇒ This review aimed to assess whether homebased CR interventions are cost-effective (versus centre-based CR).
- ⇒ Included studies (n=9) generally found that home-based CR options are cost-effective, compared to, or in addition to, centre-based options. There are some limitations to the evidence base, including the limited number of studies identified, sample sizes and generalisability.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ The COVID-19 pandemic saw a shift towards greater use of home-based CR and this review supports their use as a potentially cost-effective intervention.
- ⇒ Future robust research is needed to cover a greater range of home-based designs, including home-based options for psychological care.

(eg, time absent from work) and €45 billion in informal care costs.³

Cardiac rehabilitation (CR) is a supervised secondary prevention programme, intended to prevent recurrent disease and improve long-term outcomes among people with CVD. CR programmes are complex interventions which typically consist of exercise, health education and psychological intervention and are often delivered by multidisciplinary teams. The benefits of CR are well documented and include reductions in the recurrence of cardiac events, mortality and rehospitalisation (both all-cause and cardiovascular-specific).

CR has traditionally been centre-based, delivered in a medically supervised setting (eg, hospitals).⁵ However, barriers were found to reduce participation (eg, transportation problems and travel costs).⁶ To help combat these issues, home-based CR was introduced with sessions delivered remotely.⁷ Delivery formats (centre-based and home-based) have been found to provide similar clinical and health-related quality of life benefits to people with CVD.⁵ The COVID-19 pandemic saw reductions in healthcare service provision, as providers





focused on prioritising resources to help cope with an increasing number of infections. Cardiac services were no exception, with one global study across 70 countries stating a 76.2% cessation in usual CR services. To aid continuity of care, many services favoured alternative delivery models, with a marked increase in home-based CR observed. To rinstance, in the UK a significant shift from centre-based CR (72%–16%) to home-based (16%–76%) was observed from 2019 to 2020.

Given the patient and economic burden of CVD, in a time where health systems are under increasing pressure, cost-effective intervention is essential. Previous reviews of economic evaluations for CR have found positive evidence (ie, evidence to suggest CR is cost-effective compared with usual care) to support the implementation of CR. ¹³ ¹⁴ However, it has been noted that more evidence is needed to identify the most cost-effective design and delivery of CR. ¹⁵ Given the move towards home-based formats of CR, there is a need for a review focusing on the cost-effectiveness of home-based CR compared with centre-based CR.

This review aims to assess whether home-based interventions in the CR pathway have been demonstrated to be cost-effective compared with conventional delivery (centre-based delivery). The review critically appraises the quality of the existing evidence and identifies evidence gaps, with the intention of guiding future research.

METHODS

A systematic review was conducted to identify economic evaluations of home-based CR packages and/or interventions in comparison with centre-based options. The protocol is available on the PROSPERO international prospective register of systematic reviews (CRD42021286252).

An electronic literature search was conducted in October 2021 using MEDLINE, Embase and PsycINFO databases via Ovid. Search terms for economic evaluations were taken from the Centre for Reviews and Dissemination. ¹⁶ Terms related to CR were taken from previously published search strategies. ⁵ ¹⁷ Terms varied according to database designs and strategies are included in the online supplemental material.

Citations retrieved following database searches were reviewed in two stages; first, titles and abstracts were screened, subsequently full texts of the remaining citations were retrieved and read. Explicit inclusion criteria were applied at each screening stage. The inclusion criteria were as follows: (1) studies focusing on the population offered CR in line with guidelines from the National Institute for Health and Care Excellence (NICE), 18-20 (2) studies reporting on home-based interventions that were either participation in a CR programme or an intervention that may be classed as an individual aspect/component of a comprehensive CR programme, (3) studies reporting a relevant comparator delivered in usual care (ie, centre-based CR) and (4) studies reporting a full economic evaluation (synthesising costs and health benefits). Furthermore, publications needed to be original full-text articles, published in English, and reporting original results. Two reviewers carried out each screening stage independently; differences in opinion were discussed and decided with a third reviewer.

Following the finalisation of the included studies, data extraction was conducted using pre-specified forms. Data extraction fields included study objectives, design, methods and results (including uncertainty analysis). Two reviewers performed data extraction, with 25% of data extraction cross-checked (no issues identified). Cost data were converted to

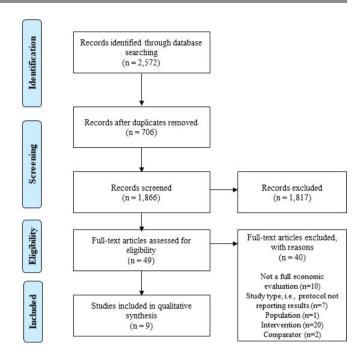


Figure 1 Search results.

2022 pound sterling to allow for comparison between studies.²¹ Studies were critically appraised using the Drummond checklist and the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist.²² ²³

A narrative synthesis was used to summarise findings. A formal quantitative synthesis of findings would have been limited by heterogeneity across the studies, as is typical in reviews of economic evaluations.²⁴

Patient and public involvement

Patients and/or the public were not involved in the research.

RESULTS

Nine studies met the inclusion/exclusion criteria and were included in the review (figure 1).²⁵ An overview of the design of included studies is reported in table 1.

Critical appraisal

Studies were appraised using two checklists, which are provided in full in the online supplemental materials. ²² ²³ The quality of reporting (assessed using CHEERS) differed across studies, with no publication reporting full details for all items. Methods and results had the most variability in reporting. Health economic analysis plans, methods used to characterise heterogeneity, distributional effects and stakeholder engagement were underreported. Some of these are partially explained as new items were added to the checklist recently. From the Drummond and Jefferson (1996) checklist, the overall methodological quality of the identified publications appears to be good, as most publications comply with most of the items from the checklist. More details on specific aspects of the studies are provided below.

Population and sample

The populations that can access CR services vary according to local recommendations and multiple patient groups can access CR services. Participants across the studies included those with coronary artery disease, heart disease or failure and myocardial

Study	Population	Setting and country	Intervention	Comparator	Study type	Analysis type and outcome	Perspective	Time horizon
	tre-based CR programn		intervention	Comparator	Study type	outcome	reispective	110112011
Hwang <i>et al²⁶</i>	Chronic heart failure	Home-based and outpatient care in Australia	Telerehabilitation	Centre-based rehabilitation	Trial-based, two- arm, multi-centre randomised controlled trial (n=53)*	CUA (QALY using the EQ-5D)	Healthcare provider	6 months
Kidholm <i>et al²⁷</i>	Artery sclerosis, coronary artery bypass surgery, valve surgery and heart failure	Home-based and outpatient care in Denmark	Cardiac telerehabilitation programme	Traditional CR programme at the hospital or healthcare centre	Trial-based, two- arm multi-centre randomised controlled trial (n=141)*	CUA (QALY using the SF-6D)	Health sector	1 year
Taylor <i>et al²⁸</i>	Uncomplicated acute myocardial infarction	Home-based and hospital-based care in the UK	Home-based CR	Hospital-based CR	Trial-based, two- arm, randomised controlled trial (n=104)*	CUA (QALY using the EQ-5D)	National health service	9 months
	re, home-based CR vs ce	entre-based CR compone	ent					
Kraal <i>et al³³</i>	Low-to-moderate cardiac risk patients entering CR	Home-based and outpatient care in the Netherlands	Home-based training with telemonitoring guidance	Centre-based CR	Trial-based, two-arm, single- blind randomised controlled trial (n=90)	CUA (QALY using the SF-36)	Societal	1 year
Initiated in cent	re, home-based CR prog	ramme thereafter vs cer	ntre-based CR program	mes				
Niewada <i>et al³⁴</i>	Heart failure	Home-based and standard of care (outpatient or inpatient care) in Poland	Hybrid telerehabilitation programme	TAU appropriate for the patient's clinical status (ie, outpatient or inpatient CR)	Model-based, which utilised data exclusively from a two-arm, multi-centre, randomised controlled trial (n=795)*	CUA (QALY using the SF-36 and the EQ-5D)	Public payer	Lifetime (average survival of 3.9 years)
Home-based CR	in addition to centre-ba	ased CR vs centre-based	CR programmes					
Frederix <i>et al²⁹</i>	Coronary artery disease and/or chronic heart failure	Home-based and outpatient care in Belgium	Telerehabilitation plus conventional centre-based CR	Conventional centre- based CR	Trial-based, two- arm, single-blind, multi-centre randomised controlled trial (n=140)	CUA (QALY using the EQ-5D)	Society and patient	1 year
Frederix <i>et al³⁰</i>	Coronary artery disease and/or chronic heart failure	Home-based and outpatient care in Belgium	Telerehabilitation plus conventional centre-based CR	Conventional centre- based CR	Trial-based, two- arm, single-blind, multi-centre randomised controlled trial (n=126)	CUA (QALY using the EQ-5D)	Patient and healthcare	2 years
Maddison <i>et</i> al ³¹	Ischaemic heart disease	Home-based and community care in New Zealand	Mobile phone delivered HEART intervention (mHealth) plus TAU	TAU (including community-based CR and potential supervised exercise)	Trial-based, two-arm, single- blind randomised controlled trial (n=171)	CUA (QALY using the EQ-5D)	Health service	6 months
Maddison <i>et</i> al ³²	Coronary heart disease	Home-based, inpatient, outpatient, and community-based care in New Zealand	Real-time remotely monitored exercise- based cardiac telerehabilitation (REMOTE-CR) plus TAU	Centre-based CR (TAU)	Trial-based, two-arm, single- blind randomised controlled trial (n=162)	CUA (QALY using the EQ-5D)	Healthcare system	6 months

infarction, among others. Heterogeneity across sampled populations in studies and pooling of participants with different cardiac conditions within studies means that we cannot separate/distinguish results for specific groups.

In the studies conducted within a trial, sample sizes ranged from 53 to 171 participants. In the single modelling study, a

larger trial was used (n=795). The mean age (when reported) ranged from 59 to 67 years, and samples were predominantly male (proportion of females ranging from 9% to 25% across studies). Exclusion criteria reported for trial papers included clinical characteristics (eg, outside of target groups), physical or cognitive disabilities, location (eg, living too far from treatment

Study	Intervention	Comparator
Home CR vs centr	e-based CR programmes	
Hwang <i>et al²⁶</i>	Home-based telerehabilitation (12 weeks) Exercise (remotely supervised by a physiotherapist using a sphygmomanometer and finger pulse oximeter) and education (delivered virtually with discussions facilitated by a physiotherapist and nurse) for small groups	Centre-based rehabilitation (12 weeks) Exercise (aerobic and strength training) and education sessions delivered to groups in hospital and supervised by a physiotherapist and nurse
Kidholm <i>et al²⁷</i>	Telerehabilitation programme (12 weeks) Individualised programme involving a digital toolbox (containing rehabilitation topics, activities and videos), measurement (using a sphygmomanometer, digital weight scale, accelerometer and ECG) and communication (between healthcare professionals, patients and their families) accessed via tablet	Traditional centre-based rehabilitation based on CR guidelines (duration not reported) Traditional rehabilitation delivered at the hospital or healthcare centre based on CR guidelines (details/duration not reported)
Taylor <i>et al²⁸</i>	Home-based CR (6 weeks) Nurse facilitated support using a self-help manual (the Heart Manual)	Hospital-based CR (8–10 week) Group-based rehabilitation provided by a multidisciplinary team (specialist nurse, physiotherapist or exercise therapist and assistant clinical psychologist)
	home-based CR vs centre-based CR component	
Kraal et al ³³	Home-based training with telemonitoring guidance with remaining aspects of CR delivered as usual (12 weeks) Individually tailored home training (remotely supervised by physical therapists using a heart rate monitor, accelerometer and web application) with feedback provided weekly via telephone	Centre-based CR (12 weeks) Individually tailored group-based training (involving a cycle ergometer or treadmill) in the outpatient clinic, supervised by physical therapists/ exercise specialists
Initiated in centre,	home-based CR programme thereafter vs centre-based CR programmes	
Niewada <i>et al</i> ³⁴	Hybrid telerehabilitation programme initiated in inpatient stay and delivered remotely after discharge (8 weeks) Remotely supervised exercise training at home combined with multi-parameter telemonitoring	Treatment as usual (8 weeks) Treatment as usual appropriate for the patient's clinical status, with som able to participate in outpatient or inpatient CR
Home-based CR ir	addition to centre-based CR vs centre-based CR programmes	
Frederix <i>et al</i> ²⁹	Telerehabilitation programme (24 weeks) in addition to TAU (12 weeks) An internet-based programme involving patient-specific exercises, tailored dietary and smoking cessation recommendations (delivered via text/email), continuous monitoring (using an accelerometer) and feedback (provided by a semi-automatic tele coaching system)	Treatment as usual comprising conventional centre-based CR (12 weeks) Pluridisciplinary* rehabilitation sessions with weekly exercise sessions, including walking/running, cycling and/or arm cranking.
Frederix <i>et al</i> ³⁰	Telerehabilitation programme (24 weeks) in addition to TAU (12 weeks) As detailed above	Treatment as usual comprising conventional centre-based CR (12 weeks) As detailed above
Maddison <i>et al</i> ³¹	Mobile phone delivered HEART intervention in addition to TAU (24 weeks) Personalised, automated text messages (encouraging exercise and behaviour change) delivered to the patients mobile, with details to a website (containing resources on healthy behaviours) also provided	Treatment as usual (including community-based CR and supervised exercise) (24 weeks) Treatment as usual, with encouragement to be physically active and attend a cardiac club providing supervised exercise
Maddison <i>et al</i> ³²	Real time remotely monitored exercise-based cardiac telerehabilitation (REMOTE-CR) (12 weeks) Individualised exercise intervention with remote monitoring (using a smartphone and chest-worn sensor) and feedback (provided by exercise/CR specialists)	Traditional centre-based programmes (CBexCR) (12 weeks) Supervised exercise delivered by clinical exercise physiologists in CR clinics

centres), language, pregnancy, participation in similar studies, and no access to the internet and/or a computer at home. None of the identified studies included subgroup analyses.

Interventions

An overview of interventions and comparators is provided in table 2. Variability in intervention design and delivery is observed. As shown, three studies compare home-based CR with centre-based CR. ^{26–28} Six studies considered hybrid CR, with components or stages (eg, initiation) of CR being delivered in a centre, with the remainder being delivered in home settings. Four studies look at home-based intervention in addition to centre-based CR compared with centre-based CR. ^{29–32} A single study looked at an exercise component of CR that (following initiation in a centre) could be delivered at home, or in a centre, while the remainder of CR remained centre-based. ³³ Another study initiated CR within an inpatient setting and transitioned to home-based care on discharge. ³⁴ One study (the oldest) investigated the use of a self-help manual (the Heart Manual), with

regular follow-up with cardiac nurses through either telephone or home-visits.²⁸ The remaining studies included a telerehabilitation component.²⁶ ²⁷ ²⁹⁻³⁴ All interventions were either exercise-focused or included an exercise element/component. The majority of studies (7/9) used devices to monitor physical activity. 26 27 29 30 32-34 One study provided limited detail on the content and design of the programme.³⁴ No studies explicitly reported a psychological component within their intervention, and only two cited an educational component. 26 32 Most studies reported equal access to specialists across home-based and centre-based CR interventions. ²⁶ ²⁷ ^{29–33} However, in one study, home-based CR was delivered exclusively by a cardiac nurse, while centre-based CR patients accessed a multidisciplinary care team.²⁸ Note that some of the exercise training was delivered asynchronously (independent of interactions with CR staff), whereas other training was delivered synchronously (during interaction with CR staff), though this was not frequently reported or clear.

Similar to the intervention, there was variability across the comparator arms. This would be expected as the design of traditional CR differs across settings. However, it limits generalisability.³⁵

Health benefit

All the studies were cost-utility analyses and used qualityadjusted life years (QALYs) as the summary measure of health benefit. These are appropriate in the context of CR as interventions aim to reduce morbidity and mortality, and subsequently a multi-dimensional health outcome is useful. ⁴ The most common measures of health status were the EQ-5D (n=7) and the Short-Form 36-Items (SF-36) (n=3), both generic measures of health status. Both measures have been demonstrated to be reliable in the cardiovascular population.^{36 37} One study additionally reported a cost-effectiveness analysis with cost per metabolic equivalent hour of walking as the outcome.³¹ While a relevant outcome, this only captures a narrow consequence from CR. All the studies that were conducted alongside a trial collected health status measures from participants over the trial follow-up. The single modelling study identified EQ-5D derived utility outcomes by synthesising data across three studies identified from a literature review (associated with New York Heart Association class) in the base case and in an alternative scenario used SF-36 data from trial data.³⁴

Resource use and costs

Types of cost included by studies are reported in the online supplemental materials. A minority of studies took a societal perspective (table 1).^{29 33} A single study included productivity losses. However, these are less relevant in this population (people receiving CR are often above/around retirement age).^{33 38} Only one study reported costs relevant to informal care, which are of relevance in older populations.³³ Commonly included costs included intervention costs, hospitalisation and outpatient care. Two studies only included intervention costs, which ignores any potential impact on wider healthcare costs.^{31 34} Two linked studies only included costs related to cardiovascular reasons, which overlooks the relationship between cardiovascular health and other healthcare conditions/aspects of health and the subsequent impact on costs.^{29 30}

One study was unclear on how resource use and costs had been quantified. ³¹ Across the remaining studies, six used routine data (eg, healthcare system records) ²⁶ ²⁷ ²⁹ ³⁰ ³² ³⁴ and two used a combination of self-reported and routine data (eg, patient self-reported data validated using hospital records). ²⁸ ³³ While administrative data is useful, it can be limited in terms of the data provided and while self-reported data can be comprehensive, it has its own limitation (eg, recall bias). ³⁹ Variations in service provision and costing estimates limit generalisability.

Risk of bias

All studies were conducted using data from randomised controlled trials (RCTs), minimising bias. However, the reliance on RCT evidence does have limitations. Most notably, the majority of studies had time horizons of less than 1 year and in the context of CR, which can reduce premature mortality and recurrent cardiovascular events, this may underestimate costs and outcomes. One paper used data from a trial within an economic model (structure unspecified) and subsequently was able to report a longer timeframe. With the exception of one trial, all sample sizes were below 200 (reported in table 1). These limited sample sizes and inclusion criteria may not fully

represent the heterogeneous populations accessing CR. No studies were powered for economic outcomes, which is typical as trials are most commonly powered on clinical outcomes, meaning economic outcomes are underpowered.⁴¹ Two studies were stated to be non-inferiority in design (ie, rather than aiming to show intervention is clinically superior, they aim to demonstrate that the difference between intervention and comparator is non-inferior).²⁷ ³² ⁴² However, while interventions may be equivalent in terms of their clinical aspects, they may not be in terms of economic outcomes.⁴³

Study results

Key study results are presented in table 3. Over half of studies reported a reduction in costs in the intervention arm (ie, suggesting intervention may result in reduction in service use, such as hospitalisations, leading to a decrease in costs) (5/9). Only some of these cost savings were reported to be significant (3/5). While most studies (6/9) reported an increase in health, these were rarely reported as statistically significant. One study reported equivalent effectiveness between the intervention and comparator arms. The two remaining studies reported negative health gains (ie, the intervention is less effective) though the between-group differences were non-significant in both studies, suggesting no difference. One of these studies was a noninferiority trial (in which the intervention was associated with statistically significantly increased costs), with the remaining non-inferiority trial-based economic evaluation finding a small QALY gain and cost reduction. 27 32 Subsequently, overall study findings were predominantly positive (ie, dominant or costeffective), although rarely statistically significant. A single study found intervention was not cost-effective. However, authors did note that it may have the potential to increase uptake of CR, and economies of scale might be beneficial.²⁷

Note, direct comparison studies (ie, studies in which intervention participants had no access to centre-based CR) may appear to have less favourable results. However, there is limited literature (n=3) and two of these conclude that home-based care is equally effective and either cost saving or cost neutral.²⁶ ²⁸ All studies in which participants receiving home-based care retained access to centre-based CR found intervention to be cost-effective.

When the probability of cost-effectiveness at different willingness to pay thresholds was reported, it was reasonably high (>66%). Two-thirds of the studies included some one-way sensitivity analyses, in which the most common parameters varied were healthcare and intervention costs. ^{26–28} ^{32–34} The modelling study, which was able to investigate a longer time horizon, also examined the impact of adjusting discounting and the effect of persistence of CR (which would increase health gains and reduce the incremental cost-effectiveness ratio (ICER)). ³⁴ One study completed a scenario analysis evaluating the intervention as an ongoing nationwide programme rather than a trial (reducing intervention costs). ³² The results of one-way sensitivity analyses demonstrated that while studies were sensitive to the changes (particularly in costing approaches), they typically did not change study conclusions.

DISCUSSION

Nine studies evaluating the cost-effectiveness of home-based intervention versus conventional centre-based delivery of CR were identified. Results were mainly favourable, suggesting that home-based intervention (as an add-on or alternative to centre-based CR) is a potentially cost-effective option that should be considered by decision makers. However, it should be noted that

Table 3 St	tudy results						
Study	Intervention	Comparator	Net QALYs	Net cost†	Incremental Cost- Effectiveness Ratio (ICER)†‡	Probability of cost-effectiveness¶	Author summary of cost-effectiveness
Home CR vs cer	ntre-based CR programn	nes					
Hwang <i>et al²⁶</i>	Home-based telerehabilitation	Centre-based rehabilitation	0.00	-£884**	-£2 311/QALY	The majority of iterations§ were cost saving, with roughly similar iterations health gaining vs reducing (demonstrated on cost-effectiveness plane)	Less costly and equally effective
Kidholm <i>et al</i> ²⁷	Telerehabilitation programme	Traditional centre- based rehabilitation based on CR guidelines	0.004	£1323*	£412 083/QALY	Iterations are distributed across the cost- effective planes, particularly in the Northeast and Northwest quadrants (cost increasing and health gaining/reducing)	Not cost-effective
Taylor <i>et al</i> ²⁸	Home-based CR	Hospital based CR	-0.06	£113	-£937/QALY	Iterations are distributed across all quadrants of the cost-effectiveness plane	No difference
Initiated in cent	re, home-based CR vs c	entre-based CR compone	ent				
Kraal <i>et al</i> ³³	Home-based training with telemonitoring guidance	Centre-based CR	0.01	-£5963 (societal perspective)	Dominant (societal perspective)	75% (WTP €100 000) to 97% (WTP €0) from a societal perspective	Cost-effective
Initiated in cent	re, home-based CR prog	gramme thereafter vs cer	ntre-based CR pro	grammes			
Niewada <i>et</i> al ³⁴	Hybrid telerehabilitation programme	Treatment as usual	► 0.0269 (SF- 36)0.044 (EQ-5D)	£1149	► £26 117/ QALY (EQ-5D)£42 719/QALY (SF-36)	68% (WTP 155 514 PLN/QALY)	Cost-effective
Home-based CR	R in addition to centre-b	ased CR vs centre-based	CR programmes				
Frederix <i>et al</i> ²⁹	Telerehabilitation programme in addition to conventional centre- based CR	Conventional centre- based CR	0.026	-£543**	Dominant	The vast majority of iterations were dominant (demonstrated on cost-effectiveness plane)	Cost-effective
Frederix <i>et al</i> ³⁰	Telerehabilitation programme in addition to conventional centre- based CR	Conventional centre- based CR	0.22**	-£846	Dominant	The majority of iterations were dominant (demonstrated on cost-effectiveness plane)	Cost-effective
Maddison <i>et</i> al ³¹	Mobile phone delivered HEART intervention in addition to treatment as usual	Treatment as usual (including community- based CR and supervised exercise)	0.03	NR	£16 436/QALY	72% (WTP NZ\$20 000) to 90% (WTP NZ\$50 000)	Likely cost-effective
Maddison <i>et</i> <i>al</i> ³²	Real-time remotely monitored exercise- based cardiac telerehabilitation (REMOTE-CR)	Traditional centre- based programmes (CBexCR)	-0.03	-£2496	NR (as no significant difference in QALYs)	NR	Cost -effective

^{*}Statistically significant (0.05).

the limited size of the evidence base and heterogeneity across the methods limit the external validity of results. Additionally, the critical appraisal determined that while studies were generally of good quality and well reported, issues/challenges remain. Most notably, small trial samples may not be representative or sufficient to conclude differences in cost-effectiveness, limited time horizons may not fully capture differences in outcomes and costs, and some under-reporting prevents studies from being replicated.

The evidence base is subject to limitations. The COVID-19 pandemic triggered changes in service delivery, making home-based options the norm in some settings. ¹⁰ There are many ways in which CR can be delivered in a home setting and the included studies do not capture all of the possible differences in

design/delivery. Exercise interventions were common. However, despite an increased prevalence of anxiety and depression among people with CVD, none of the interventions explicitly featured psychological care. A preference for receiving psychological therapy (vs no psychological therapy) as a component of CR has been demonstrated. Future research is needed to determine whether different forms of home-based psychological care are cost-effective among people receiving CR. No studies acknowledged patient heterogeneity, which neglects to consider that cost-effectiveness may vary across participants/subgroups. Research on patient preferences has demonstrated that there is heterogeneity in preferences for CR design (eg, by gender). Future economic evaluations could aim to explore patient heterogeneity if feasible (eg, if sample size allows). No studies

[†]All costs have been updated from their original currency and price year and converted to £ (GBP) for the 2022 price year using the Campbell and Cochrane Economics Methods Group Evidence for Policy and Practice Information and Co-ordinating Centre Cost Converter.

[‡]ICERs will not be reproducible based on the reported net costs and QALYs due to differences in rounding.

[§]Where explicit probabilities of cost-effectiveness were not reported, a description of the key findings from cost-effectiveness planes has been provided.

[¶]Bootstrap iterations or simulations from probabilistic sensitivity analysis.

^{**}Statistically significant (0.01).

CR, cardiac rehabilitation; EQ-5D, EuroQol 5-Dimensions; ICER, incremental cost-effectiveness ratio; NR, not reported; QALY, quality-adjusted life year; SF-6D, Short-Form 36-Items; WTP, willingness to pay (per QALY).

reported budget impact analysis (which considers affordability) or value of information analyses (which considers the expected value of research to reduce uncertainty), both of which may be useful given the context (ie, high numbers of people undergoing CR) and evidence base (ie, few statistically significant results).

This review is subject to limitations. Search results were limited to English language, increasing the potential for bias. Grey literature was not included, increasing the risk of publication bias.⁴⁷ Literature searches were conducted in October 2021 and as additional evidence becomes available the evidence base should be reassessed. Furthermore, cost-effectiveness evidence should be used alongside other forms of evidence (eg, clinical, qualitative research, patient perspectives) to support decision-making. The review explicitly compared home-based care to care delivered in medical settings; this meant that studies looking at uptake of CR or no intervention comparators were excluded, though they might be of interest to decision makers in some settings. Uptake is a known challenge in CR.48 Increasing uptake in particular might be a strength of home-based care, and research has demonstrated that increasing uptake is cost-effective and there is potential to reduce socioeconomic inequalities.⁴⁹

This review has highlighted some key areas to be addressed by future research, including the need for more consideration of intervention design, psychological intervention and subgroup analyses. Future researchers should consider whether they can overcome some of the issues identified in the current evidence base (eg, increased sample sizes with more representative samples to reduce uncertainty) and subgroup analysis. Researchers should also consider the population and aim to ensure a range of participants eligible for CR in the relevant setting are included (eg, varying cardiac conditions) and that the participants adequately reflect all potential participants (eg, by gender). Robust, large, multicentre RCT trials compared home-based and centre-based care (and including economic outcomes) would help to expand the evidence base. These could then be built on in economic modelling studies which allow the extrapolation of costs and outcomes over a longer time horizon. Furthermore, no economic evidence was identified for low and middle-income countries, despite a high burden of CVDs in these countries and a need to efficiently distribute limited resources.

CONCLUSIONS

Overall, our findings suggest that home-based CR is likely cost-effective (as an add-on or alternative to centre-based care) although this comes with a caveat regarding generalisability due to limited size of the evidence base and heterogeneity across the interventions studied and methods deployed to evaluate cost-effectiveness. Given the global large-scale desire to increase home-based options following the COVID-19 pandemic, this review has the potential to be helpful to clinicians and policy makers in supporting a business case so that future home-based CR is resourced appropriately in clinical practice to derive comparable benefits as seen in robust clinical trials. Future research is needed to evaluate a greater range of home-based designs including staffing models and intervention fidelity for exercise, psychological care and risk factor aligned with clinical minimum standards.

Contributors GES, GD, SN and PD formulated the search questions and strategy. GES, AR, SN and GD conducted the literature search and data extraction, with oversight from HC, PD and LC. GES and AR wrote the first draft of the manuscript. GD, SN, HC, LC and PD contributed to the final writing of the paper. GES was responsible for the overall content as guarantor and accepts full responsibility for the finished work, had access to the data and controlled the decision to publish.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Extracted data are available from the authors on request.

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ORCID iDs

Gemma E Shields http://orcid.org/0000-0003-4869-7524 Aleix Rowlandson http://orcid.org/0000-0002-9513-7821 Holly Cranmer http://orcid.org/0000-0002-9067-3422 Lora Capobianco http://orcid.org/0000-0001-6877-8650 Patrick Doherty http://orcid.org/0000-0002-1887-0237

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A review of the cost-effectiveness of home-based cardiac rehabilitation

Correspondence to: gemma.shields@manchester.ac.uk

Search strategies

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions(R) <1946 to October 29, 2021>

Search Strategy:

- 1 (cardiac adj rehab\$).mp.
- 2 exp cardiovascular diseases/rh
- 3 exp myocardial infarction/
- 4 mi.tw.
- 5 myocardial ischemia/
- 6 exp angina pectoris/
- 7 exp heart failure, congestive/
- 8 exp heart defects, congenital/
- 9 exp heart valve diseases/
- 10 rheumatic heart disease/
- 11 exp heart transplantation/
- 12 angioplasty, transluminal, percutaneous coronary/
- 13 ptca.tw.
- 14 coronary disease/
- 15 cardiovascular diseases/
- 16 heart diseases/
- 17 coronary artery bypass/
- 18 cabg.tw.
- 19 (heart adj disease\$).mp.
- 20 (myocard\$ adj infarct\$).mp.
- 21 coronary artery disease/
- 22 acute coronary syndrome/
- 23 percutaneous coronary intervention/

- 24 PCI.tw.
- 25 stent.tw.
- 26 unstable angina/
- 27 chronic heart failure/
- 28 CHF.tw.
- 29 implantable cardiac defibrillat\$.mp.
- 30 ICD.tw.
- 31 or/3-30
- 32 rehabilitation/
- 33 rehabilitation cent&.mp.
- 34 rehabilitation nursing/
- 35 rehab\$.tw.
- 36 or/32-35
- 37 1 or 2 or (31 and 36)
- 38 Economics/
- 39 exp "costs and cost analysis"/
- 40 Economics, Dental/
- 41 exp economics, hospital/
- 42 Economics, Medical/
- 43 Economics, Nursing/
- 44 Economics, Pharmaceutical/
- 45 (economic\$ or cost or costs or costly or costing or price or pricing or pharmacoeconomic\$).ti,ab.
- 46 (expenditure\$ not energy).ti,ab.
- 47 value for money.ti,ab.
- 48 budget\$.ti,ab.
- 49 or/38-48
- 50 ((energy or oxygen) adj cost).ti,ab.
- 51 (metabolic adj cost).ti,ab.
- 52 ((energy or oxygen) adj expenditure).ti,ab.
- 53 or/50-52

- 54 49 not 53
- 55 letter.pt.
- 56 editorial.pt.
- 57 historical article.pt.
- 58 or/55-57
- 59 54 not 58
- 60 exp animals/ not humans/
- 61 59 not 60
- 62 limit 61 to yr="2006 -Current"
- 63 37 and 62

Database: Embase <1974 to 2021 October 29>

Search Strategy:

- 1 (cardiac adj rehab\$).mp.
- 2 exp cardiovascular diseases/rh
- 3 exp myocardial infarction/
- 4 mi.tw.
- 5 myocardial ischemia/
- 6 exp angina pectoris/
- 7 exp heart failure, congestive/
- 8 exp heart defects, congenital/
- 9 exp heart valve diseases/
- 10 rheumatic heart disease/
- 11 exp heart transplantation/
- 12 angioplasty, transluminal, percutaneous coronary/
- 13 ptca.tw.
- 14 coronary disease/

- 15 cardiovascular diseases/
- 16 heart diseases/
- 17 coronary artery bypass/
- 18 cabg.tw.
- 19 (heart adj disease\$).mp.
- 20 (myocard\$ adj infarct\$).mp.
- 21 coronary artery disease/
- 22 acute coronary syndrome/
- 23 percutaneous coronary intervention/
- 24 PCI.tw.
- 25 stent.tw.
- 26 unstable angina/
- 27 chronic heart failure/
- 28 CHF.tw.
- 29 implantable cardiac defibrillat\$.mp.
- 30 ICD.tw.
- 31 or/3-30
- 32 rehabilitation/
- 33 rehabilitation cent&.mp.
- 34 rehabilitation nursing/
- 35 rehab\$.tw.
- 36 or/32-35
- 37 1 or 2 or (31 and 36)
- 38 Health Economics/
- 39 exp Economic Evaluation/
- 40 exp Health Care Cost/
- 41 pharmacoeconomics/
- 42 38 or 39 or 40 or 41
- 43 (econom\$ or cost or costs or costly or costing or price or pricing or pharmacoeconomic\$).ti,ab.
- 44 (expenditure\$ not energy).ti,ab.

- 45 (value adj2 money).ti,ab.
- 46 budget\$.ti,ab.
- 47 43 or 44 or 45 or 46
- 48 42 or 47
- 49 letter.pt.
- 50 editorial.pt.
- 51 note.pt.
- 52 49 or 50 or 51
- 53 48 not 52
- 54 (metabolic adj cost).ti,ab.
- 55 ((energy or oxygen) adj cost).ti,ab.
- 56 ((energy or oxygen) adj expenditure).ti,ab.
- 57 54 or 55 or 56
- 58 53 not 57
- 59 animal/
- 60 exp animal experiment/
- 61 nonhuman/
- 62 (rat or rats or mouse or mice or hamster or hamsters or animal or animals or dog or dogs or cat or cats or bovine or sheep).ti,ab,sh.
- 63 59 or 60 or 61 or 62
- 64 exp human/
- 65 human experiment/
- 66 64 or 65
- 67 63 not (63 and 66)
- 68 58 not 67
- 69 conference abstract.pt.
- 70 68 not 69
- 71 limit 70 to yr="2006 -Current"
- 72 37 and 71

Database: APA PsycInfo <1806 to October Week 4 2021>

Search Strategy:

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- 1 (cardiac adj2 rehab\$).ti,ab.
- 2 (cardiovascular adj2 diseas\$).ti,ab.
- 3 myocardial infarction.ti,ab.
- 4 mi.mp.
- 5 myocardial ischemia.ti,ab.
- 6 angina pectoris.ti,ab.
- 7 congestive heart failure.ti,ab.
- 8 congenital heart defects\$.ti,ab.
- 9 heart valve diseases.ti,ab.
- 10 rheumatic heart disease.ti,ab.
- 11 heart transplantation.ti,ab.
- 12 angioplasty, transluminal, percutaneous coronary.ti,ab.
- 13 ptca.mp.
- 14 coronary disease.ti,ab.
- 15 cardiovascular diseases.ti,ab.
- 16 heart diseases.ti,ab.
- 17 coronary artery bypass.ti,ab.
- 18 cabg.mp.
- 19 (heart adj2 disease\$).ti,ab.
- 20 (myocard\$ adj2 infarct\$).ti,ab.
- 21 coronary artery disease.ti,ab.
- 22 acute coronary syndrome.ti,ab.
- 23 percutaneous coronary intervention.ti,ab.
- 24 PCI.mp.
- 25 Stent.mp.
- 26 unstable angina.ti,ab.

- 27 chronic heart failure.ti,ab.
- 28 CHF.mp.
- 29 implantable cardiac defibrillat\$.ti,ab.
- 30 ICD.mp.
- 31 or/3-30
- 32 rehabilitation.mp.
- 33 rehabilitation cent&.ti,ab.
- 34 rehabilitation nursing.ti,ab.
- 35 rehab\$.mp.
- 36 or/32-35
- 37 1 or 2 or (31 and 36)
- 38 "costs and cost analysis"/
- 39 "Cost Containment"/
- 40 (economic adj2 evaluation\$).ti,ab.
- 41 (economic adj2 analy\$).ti,ab.
- 42 (economic adj2 (study or studies)).ti,ab.
- 43 (cost adj2 evaluation\$).ti,ab.
- 44 (cost adj2 analy\$).ti,ab.
- 45 (cost adj2 (study or studies)).ti,ab.
- 46 (cost adj2 effective\$).ti,ab.
- 47 (cost adj2 benefit\$).ti,ab.
- 48 (cost adj2 utili\$).ti,ab.
- 49 (cost adj2 minimi\$).ti,ab.
- 50 (cost adj2 consequence\$).ti,ab.
- 51 (cost adj2 comparison\$).ti,ab.
- 52 (cost adj2 identificat\$).ti,ab.
- 53 (pharmacoeconomic\$ or pharmaco-economic\$).ti,ab.
- 54 or/38-53
- 55 (task adj2 cost\$).ti,ab,id.
- 56 (switch\$ adj2 cost\$).ti,ab,id.

- 57 (metabolic adj cost).ti,ab,id.
- 58 ((energy or oxygen) adj cost).ti,ab,id.
- 59 ((energy or oxygen) adj expenditure).ti,ab,id.
- 60 or/55-59
- 61 (animal or animals or rat or rats or mouse or mice or hamster or hamsters or dog or dogs or cat or cats or bovine or sheep or ovine or pig or pigs).ab,ti,id,de.
- 62 editorial.dt.
- 63 letter.dt.
- 64 dissertation abstract.pt.
- 65 or/61-64
- 66 54 not (60 or 65)
- 67 limit 66 to yr="2006 -Current"
- 68 37 and 67

CHEERS checklist

Topic	No.	Item	Frederix (2016)	Frederix (2017)	Hwang (2019)	Kidholm (2016)	Kraal (2017)	Niewada (2021)	Taylor (2007)	Maddison (2015)	Maddison (2019)
Title	1	Identify the study as an economic evaluation and specify the interventions being compared.	Fully reported	Not reported	Fully reported	Partially reported	Fully reported	Partially reported	Fully reported	Partially reported	Partially reported
Abstract	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.	Partially reported	Partially reported	Fully reported	Fully reported	Fully reported	Fully reported	Partially reported	Partially reported	Partially reported
Introduction		•		•	•			•	•		
Background and objectives	3	Give the context for the study, the study question, and its practical relevance for decision making in policy or practice.	Fully reported	Fully reported	Fully reported	Partially reported	Fully reported	Partially reported	Fully reported	Fully reported	Fully reported
Methods											
Health economic analysis plan	4	Indicate whether a health economic analysis plan was developed and where available.	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	Fully reported	Not reported	Fully reported	Fully reported					
Setting and location	6	Provide relevant contextual information that may influence findings.	Fully reported	Fully reported	Fully reported	Partially reported	Partially reported	Fully reported	Partially reported	Fully reported	Partially reported
Comparators	7	Describe the interventions or strategies being compared and why chosen.	Fully reported	Partially reported	Fully reported	Partially reported	Fully reported	Fully reported	Fully reported	Fully reported	Partially reported
Perspective	8	State the perspective(s) adopted by the study and why chosen.	Partially reported	Partially reported	Partially reported	Fully reported	Partially reported	Fully reported	Partially reported	Not reported	Partially reported
Time horizon	9	State the time horizon for the study and why appropriate.	Partially reported	Fully reported	Partially reported	Partially reported	Partially reported				
Discount rate	10	Report the discount rate(s) and reason chosen.	NA	Not reported	NA	NA	NA	Fully reported	NA	NA	NA
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).	Fully reported								

Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	Fully reported	Fully reported	Fully reported	Fully reported	Fully reported	Not reported	Fully reported	Fully reported	Fully reported
Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes.	Fully reported	Partially reported	Fully reported	Fully reported	Fully reported	Partially reported	Partially reported	Fully reported	Fully reported
Measurement and valuation of resources and costs	resources 14 Describe how costs were valued.		Fully reported	Fully reported	Fully reported	Fully reported	Fully reported	Partially reported	Fully reported	Partially reported	Fully reported
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.	Partially reported	Partially reported	Fully reported	Fully reported	Fully reported	Partially reported	Fully reported	Fully reported	Fully reported
Rationale and description of model	16	If modelling is used, describe in detail, and why used. Report if the model is publicly available and where it can be accessed.	NA	NA	NA	NA	NA	Not reported	NA	NA	NA
Analytics and assumptions	17	Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	Fully reported	Fully reported	Fully reported	Fully reported	Fully reported	Not reported	Partially reported	Fully reported	Fully reported
Characterising heterogeneity	18	Describe any methods used for estimating how the results of the study vary for subgroups.	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Characterising distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Characterising uncertainty	20	Describe methods to characterise any sources of uncertainty in the analysis.	Not reported	Not reported	Fully reported	Fully reported	Fully reported	Partially reported	Partially reported	Partially reported	Partially reported
Approach to engagement with patients and others	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study.	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported

affected by the study											
Results											
Study parameters	22	Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions.	Partially reported	Partially reported	Fully reported	Fully reported	Partially reported	Partially reported	Fully reported	Partially reported	Partially reported
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure.	Fully reported	Fully reported	Fully reported	Fully reported	Fully reported	Partially reported	Fully reported	Partially reported	Partially reported
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.	Partially reported	Partially reported	Fully reported	Fully reported	Fully reported	Fully reported	Fully reported	Partially reported	Partially reported
Effect of engagement with patients and others affected by the study	25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Discussion											
Study findings, limitations, generalisability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice.	Partially reported	Fully reported	Fully reported	Fully reported	Partially reported	Partially reported	Partially reported	Partially reported	Partially reported
Other relevant in	forma		T	T	T	T	T.	T	•	T	
Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis	Partially reported	Partially reported	Partially reported	Partially reported	Fully reported	Fully reported	Partially reported	Partially reported	Fully reported
Conflicts of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.	Fully reported	Fully reported	Fully reported	Fully reported	Fully reported	Fully reported	Not reported	Fully reported	Fully reported
NA – not applicab	le										

From: Husereau D, Drummond M, Augustovski F, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Explanation and Elaboration: A Report of the ISPOR CHEERS II Good Practices Task Force. Value Health 2022;25. doi:10.1016/j.jval.2021.10.008

Drummond checklist

	ure 15.5.a: Drummond cklist (Drummond 1996)	Frederix (2016)	Frederix (2017)	Hwang (2019)	Kidholm (2016)	Kraal (2017)	Niewada (2021)	Taylor (2007)	Maddison (2015)	Maddison (2019)
	dy design									
1	The research question is stated.	Not clear	Yes							
2	The economic importance of the research question is stated.	Yes	Yes	Yes	Not clear	Yes	Yes	No	Yes	No
3	The viewpoint(s) of the analysis are clearly stated and justified.	Not clear	Not clear	Yes	Yes	Yes	Yes	Not clear	No	Not clear
4	The rationale for choosing alternative programmes or interventions compared is stated.	Yes	Not clear	Yes	Not clear	Yes	Yes	Yes	Yes	Yes
5	The alternatives being compared are clearly described.	Yes	Yes	Yes	Not clear	Yes	Yes	Yes	Yes	Partly
6	The form of economic evaluation used is stated.	Yes	No	Yes						
7	The choice of form of economic evaluation is justified in relation to the questions addressed.	Not clear	Not clear	Not clear	Not clear	Yes	Yes	Yes	Yes	Yes
Dat	a collection									
8	The source(s) of effectiveness estimates used are stated.	Yes								
9	Details of the design and results of effectiveness study are given (if based on a single study).	Yes	Yes	Yes	Yes	Yes	Partly	No	Yes	Yes
10	Details of the methods of synthesis or meta-analysis of estimates are given (if based on a synthesis of a number of effectiveness studies).	Not appropriate								
11	The primary outcome measure(s) for the economic evaluation are clearly stated.	Not clear	Yes							
12	Methods to value benefits are stated.	Yes								
13	Details of the subjects from whom valuations were obtained were given.	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
14	Productivity changes (if included) are reported separately.	Not appropriate	Not appropriate	Not appropriate	Not appropriate	Yes	Not appropriate	Not appropriate	Not appropriate	Not appropriate

15	The relevance of productivity changes to the study question is discussed.	Yes	Yes	No	No	Yes	Not appropriate	Not appropriate	Not appropriate	Not appropriate
16	Quantities of resource use are reported separately from their unit costs.	Yes	Yes	No	Yes	Not clear	No	Yes	No	No
17	Methods for the estimation of quantities and unit costs are described.	Yes	Yes	Yes	Yes	Not clear	No	Yes	Not clear	Not clear
18	Currency and price data are recorded.	Yes	Not clear	Yes	Yes	Yes	Partly	Yes	Yes	Yes
19	Details of currency of price adjustments for inflation or currency conversion are given.	Not appropriate	No	No	Yes	Not appropriate	No	Yes	Yes	Yes
20	Details of any model used are given.	Not appropriate	Not appropriate	Yes	Not appropriate					
21	The choice of model used and the key parameters on which it is based are justified.	Not appropriate	Not appropriate	Yes	Not appropriate	Not appropriate				
Ana	alysis and interpretation of results									
22	Time horizon of costs and benefits is stated.	Yes								
23	The discount rate(s) is stated.	Not appropriate	No	Not clear	Not appropriate	Not appropriate	Yes	Not appropriate	Not appropriate	Not appropriate
24	The choice of discount rate(s) is justified.	Not appropriate	No	Yes	Not appropriate	Not appropriate	No	Not appropriate	Not appropriate	Not appropriate
25	An explanation is given if costs and benefits are not discounted.	No	No	Not appropriate	No	No	Yes	Yes	No	Yes
26	Details of statistical tests and confidence intervals are given for stochastic data.	Yes	Yes	Yes	Yes	Yes	Not clear	Yes	Not clear	Not clear
27	The approach to sensitivity analysis is given.	No	No	Yes						
28	The choice of variables for sensitivity analysis is justified.	No	No	Yes	Yes	Not clear	Not clear	Yes	Not clear	No
29	The ranges over which the variables are varied are justified.	Not appropriate	Not appropriate	Not clear	Yes	Yes	Yes	Not appropriate	Yes	Not clear
30	Relevant alternatives are compared.	Not clear	No	Yes						
31	Incremental analysis is reported.	Yes	Yes	Yes	Yes	Not clear	Yes	Yes	Yes	Not clear

32	Major outcomes are presented in a disaggregated as well as aggregated form.	Yes	Yes	Yes	Yes	Not clear				
33	The answer to the study question is given.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Not clear
34	Conclusions follow from the data reported.	Yes	Yes	Yes	Yes	Yes	Yes	Not clear	No	Not clear
35	Conclusions are accompanied by the appropriate caveats.	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Included costs

	Frederix et al. (2016)	Frederix et al. (2017)	Hwang et al. (2019)	Kidholm et al. (2016)	Kraal et al (2017)	Niewada et al. (2021)	Taylor et al. (2007)	Maddison et al. (2015)	Maddison et al. (2019)	Proportion of studies
Healthcare costs										
Intervention	√	√	√	√	√	√	√	√	√	100% (9/9)
Hospitalisation	√	✓	✓	✓	✓		✓		✓	78% (7/9)
Outpatient	✓	✓	✓	✓	√				✓	56% (5/9)
Primary/ community care				√	√		√			33% (3/9)
Medication				✓	√		✓		✓	33% (3/9)
Other costs										
Patient out of pocket	✓	✓					✓			22% (2/9)
Productivity losses					✓					11% (1/9)
Informal care					✓					11% (1/9)