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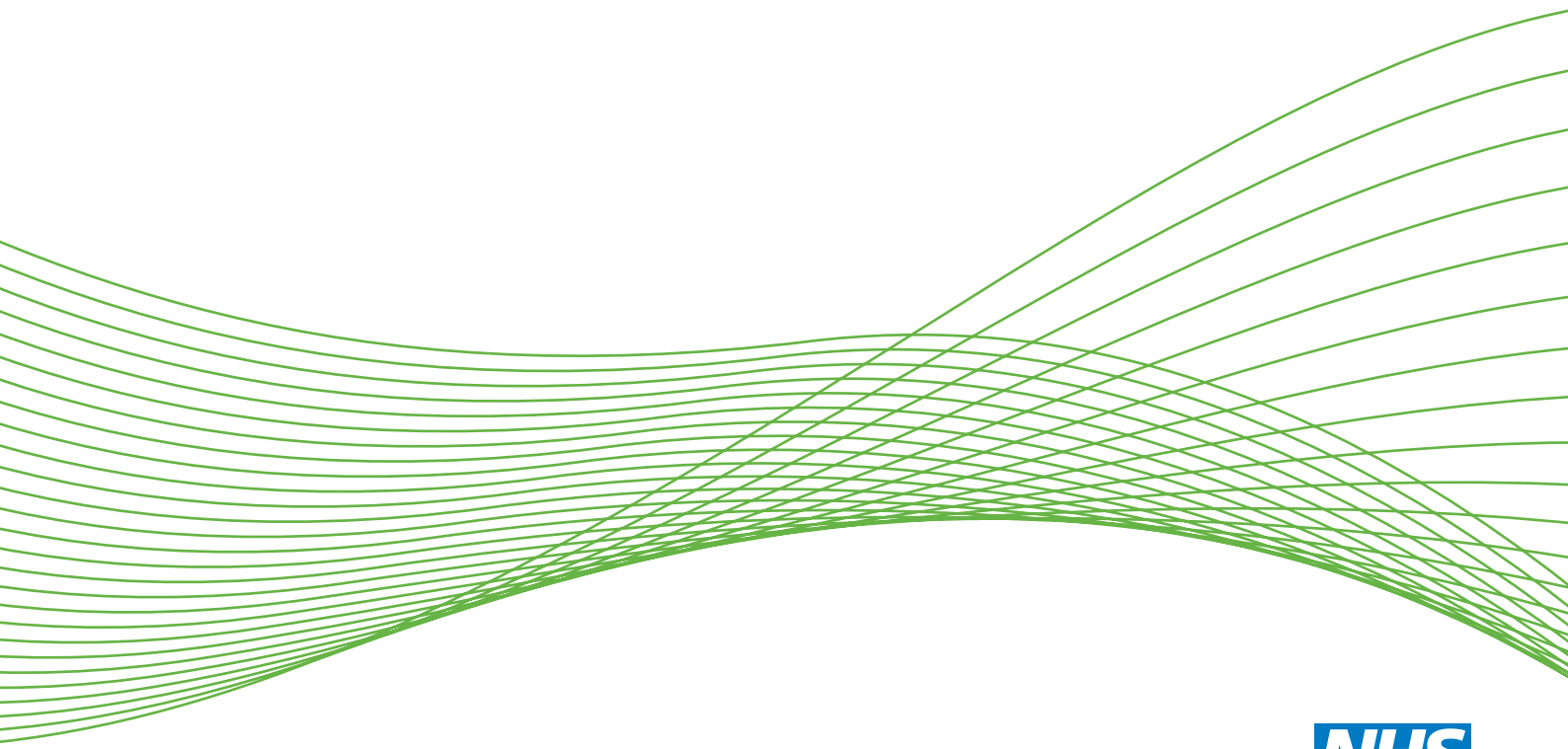

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Abstract

Home telemonitoring or structured telephone support programmes after recent discharge in patients with heart failure: systematic review and economic evaluation

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Background: Remote monitoring (RM) strategies have the potential to deliver specialised care and management to patients with heart failure (HF).

Objective: To determine the clinical effectiveness and cost-effectiveness of home telemonitoring (TM) or structured telephone support (STS) strategies compared with usual care for adult patients who have been recently discharged (within 28 days) from acute care after a recent exacerbation of HF.

Data sources: Fourteen electronic databases (including MEDLINE, EMBASE, PsycINFO and The Cochrane Library) and research registers were searched to January 2012, supplemented by hand-searching relevant articles and contact with experts. The review included randomised controlled trials (RCTs) or observational cohort studies with a contemporaneous control group that included the following RM interventions: (1) TM (including cardiovascular implanted monitoring devices) with medical support provided during office hours or 24/7; (2) STS programmes delivered by human-to-human contact (HH) or human-to-machine interface (HM).

Review methods: A systematic review and network meta-analysis (where appropriate) of the clinical evidence was carried out using standard methods. A Markov model was developed to evaluate the cost-effectiveness of different RM packages compared with usual care for recently discharged HF patients. TM 24/7 or using cardiovascular monitoring devices was not considered in the economic model because of the lack of data and/or unsuitability for the UK setting. Given the heterogeneity in the components of usual care and RM interventions, the cost-effectiveness analysis was performed using a set of costing scenarios designed to reflect the different configurations of usual care and RM in the UK.

Results: The literature searches identified 3060 citations. Six RCTs met the inclusion criteria and were added to the 15 trials identified from the previous systematic reviews giving a total of 21 RCTs included in the systematic review. No trials of cardiovascular implanted monitoring devices or observational studies met the inclusion criteria. The methodological quality of the studies varied widely and reporting was generally poor. Compared with usual care, RM was beneficial in reducing all-cause mortality for STS HH [hazard ratio (HR) 0.77, 95% credible interval (CrI) 0.55 to 1.08], TM during office hours (HR 0.76, 95% CrI 0.49 to 1.18) and TM 24/7 (HR 0.49, 95% CrI 0.20 to 1.18); however, these results were statistically inconclusive. The results for TM 24/7 should be treated with caution because of the poor methodological quality of the only included study in this network. No favourable effect on mortality was observed with STS HM. Similar reductions were observed in all-cause hospitalisations for TM interventions, whereas STS interventions had no major effect. A sensitivity analysis, in which a study was excluded because it provided

better-than-usual support to the control group, showed larger beneficial effects for most outcomes, particularly for TM during office hours. In the cost-effectiveness analyses, TM during office hours was the most cost-effective strategy with an estimated incremental cost-effectiveness ratio (ICER) of £11,873 per quality-adjusted life-year (QALY) compared with usual care, whereas STS HH had an ICER of £228,035 per QALY compared with TM during office hours. STS HM was dominated by usual care. Similar results were observed in scenario analyses performed using higher costs of usual care, higher costs of STS HH and lower costs of TM during office hours.

Limitations: The RM interventions included in the review were heterogeneous in terms of monitored parameters and HF selection criteria and lacked detail in the components of the RM care packages and usual care (e.g. communication protocols, routine staff visits and resources used). As a result, the economic model developed scenarios for different RM classifications and their costs were estimated using bottom-up costing methods. Although the users can decide which of these scenarios is most representative of their setting, uncertainties still remain about the assumptions made in the estimation of these costs. In addition, the model assumed that the effectiveness of the interventions was constant over time, irrespective of the duration of deployment, and that the intervention was equally effective in different age/severity groups.

Conclusion: Despite wide variation in usual care and RM strategies, cost-effectiveness analyses suggest that TM during office hours was an optimal strategy (in most costing scenarios). However, clarity was lacking among descriptions of the components of RM packages and usual care and there was a lack of robust estimation of costs. Further research is needed in these areas.

Study registration: PROSPERO registration no. CRD42011001368.

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Contents

Glossary

Technical terms and abbreviations are used throughout this report. The meaning is usually clear from the context, but a glossary is provided for the non-specialist reader. In some cases, usage differs in the literature, but the term has a constant meaning throughout this review.

Base-case analysis In modelling, the base case is the primary analysis based on the best estimates of each model input (cf. sensitivity analysis).

Baseline risk The probability of an event (e.g. death) occurring in the comparator arm. This is a term used in modelling in which the baseline risk from one data source might be combined with a risk ratio from another source to estimate the probability of an event occurring for patients receiving a different intervention.

Conservative assumption When there is uncertainty, modellers may have a choice of which value to give to a model input. A conservative assumption is when the modeller chooses the parameter in such a way that it cannot bias in favour of the new treatment (and is likely to be biasing in favour of the standard treatment).

Cost-effectiveness acceptability curve A way of illustrating cost-effectiveness results by plotting the probability that the intervention is cost-effective (*y*-axis) against the maximum that society is willing to pay for an improvement in health (*x*-axis).

Cost-effectiveness plane A way of illustrating cost-effectiveness results by plotting the mean incremental cost and effectiveness on a four-quadrant graph. Interventions that are more costly and more effective fall in the north-east quadrant.

Incremental cost-effectiveness ratio The difference in costs between one intervention and an alternative divided by the difference in outcomes.

Length of stay The total number of days that a participant stays in hospital.

Meta-analysis A statistical technique for combining (pooling) the results of a number of studies that address the same question and report on the same outcomes to produce a summary result. The aim is to derive more precise and clear information from a large data pool. It is generally more reliably likely to confirm or refute a hypothesis than the individual trials.

Quality-adjusted life-year A measure of benefit of health care combining the impact of both expected length of life and quality of life.

List of abbreviations

ACE	angiotensin-converting enzyme
ARB	angiotensin receptor blocker
BHF	British Heart Foundation
CAD	coronary artery disease
CEAC	cost-effectiveness acceptability curve
CHARM	Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity
CHF	chronic heart failure
CI	confidence interval
COPD	chronic obstructive pulmonary disease
CrI	credible interval
DRG	diagnosis-related group
EQ-5D	European Quality of Life-5 Dimensions
ESC	European Society of Cardiology
EVPI	expected value of perfect information
GPRD	General Practice Research Database
HDS	Health Distress Score
HF	heart failure
HH	human-to-human contact
HM	human-to-machine interface
Home-HF	Home Heart Failure Study
HR	hazard ratio
HRQoL	health-related quality of life
ICER	incremental cost-effectiveness ratio
LVEF	left ventricular ejection fraction
LVSD	left ventricular systolic dysfunction
LYG	life-years gained
MCMC	Markov chain Monte Carlo
MLHFQ	Minnesota Living with Heart Failure Questionnaire
NICE	National Institute for Health and Care Excellence
NMA	network meta-analysis
NMB	net monetary benefit
NY&Y	NHS North Yorkshire and York
NYHA	New York Heart Association
PSA	probabilistic sensitivity analysis
PSSRU	Personal Social Services Research Unit
QALY	quality-adjusted life-year
QoL	quality of life
RCT	randomised controlled trial
RM	remote monitoring
RR	risk ratio
ScHARR	School of Health and Related Research
SF-12	Short Form questionnaire-12 items

SF-36	Short Form questionnaire-36 items
STS	structured telephone support
TEN-HMS	Trans-European Network – Home-Care Management System
TIM-HF	Telemedical Interventional Monitoring in Heart Failure
TM	telemonitoring
WTP	willingness to pay
WSD	Whole System Demonstrator

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

Scientific summary

Background

Heart failure (HF) is a complex clinical syndrome. It is associated with significant morbidity, mortality and reduced quality of life (QoL) and as such exerts a substantial burden on health-care systems, mainly because of repeated and lengthy admissions to hospital. The highest risk period for rehospitalisation is in the first few weeks after discharge from hospital, with 20–30% of patients being readmitted within a month, rising to 50% at 6 months. Early remote monitoring (RM) of patients (as a component of a care package) using structured telephone support (STS) or telemonitoring (TM) may be one way to meet the growing needs of HF patients.

Objectives

The aim was to determine the clinical effectiveness and cost-effectiveness of home TM or STS strategies compared with usual care for adult patients who have been recently discharged (within 28 days) from an acute care setting after a recent exacerbation of HF. Specifically, the objectives were to (1) update two existing systematic reviews (published between 2009 and 2010) of TM or STS programmes for patients with HF within the scope of the current review; (2) evaluate the effectiveness and cost-effectiveness of home TM and/or STS packages compared with usual post-discharge care; and (3) identify key areas for primary research.

Methods

Fourteen electronic databases (including MEDLINE, EMBASE, PsycINFO and The Cochrane Library) and research registers were searched to January 2012. Searches were supplemented by hand searching of relevant articles (including citation searching) and contacting experts in the field. The systematic review included randomised controlled trials (RCTs) or observational cohort studies with a contemporaneous control group that met the following criteria: remote home TM (using patient-initiated external electronic devices or cardiovascular implanted monitoring devices, with transfer of physiological data from patient to health-care provider using telecommunications technology) or STS programmes (including regular telephone contact between patients and health-care providers and reporting of symptoms and/or physiological data) in adults (≥18 years of age) with a HF diagnosis and discharged from acute care (within 28 days) to home. The methodological quality of each included study was assessed according to established criteria. Where sufficient data existed, a random-effects network meta-analysis (NMA) was conducted using Markov chain Monte Carlo (MCMC) simulation.

A Markov model was developed to evaluate the cost-effectiveness of RM packages compared with usual care for recently discharged HF patients. RM interventions included (1) STS delivered via human-to-machine interface (HM), (2) STS delivered via human-to-human contact (HH) and (3) TM during office hours compared with (4) usual care. TM with medical support provided 24 hours a day, 7 days a week (24/7) or using cardiovascular monitoring devices was not considered in the economic model because of the lack of data and/or unsuitability for the UK setting. Given the heterogeneity among usual care and RM intervention components, cost-effectiveness analyses were performed using several costing scenarios. RM intervention costs included costs of the RM devices, monitoring costs in the RM centre and medical care costs to deal with alerts. Bottom-up costing methods were used to estimate the costs of these scenarios, designed to reflect usual care and different configurations of RM systems available in the UK. Base-case

costs and higher- and lower-cost scenarios were developed for each RM strategy whereas base-case and higher-cost scenarios were developed for usual care.

The costs and quality-adjusted life-years (QALYs) accrued by each strategy were estimated using monthly probabilities of death and of hospitalisations (HF-related complications or other causes), dependent on the type of RM intervention. Cost-effectiveness was assessed using both an incremental cost-effectiveness analysis and a net benefit approach at the £20,000 per QALY threshold. Probabilistic sensitivity analysis (PSA) and expected value of perfect information (EVPI) analysis were performed to capture uncertainty in the model parameters. A 30-year time horizon was taken and the economic perspective of the model was the NHS in England and Wales.

Results

The literature searches identified 3060 citations. Six RCTs met the inclusion criteria and were added to the 15 trials identified from the previous systematic reviews. No trials of cardiovascular implanted monitoring devices or observational studies met the inclusion criteria. The methodological quality of the 21 included studies varied widely and reporting was generally poor on random sequence generation, allocation concealment, blinding of outcome assessment, definition and confirmation of HF diagnosis, and intention-to-treat analysis. Twenty studies contributed to the network comparing different pairs or triplets of treatment for TM or STS programmes with usual care, although not all studies provided information on each outcome. One study was excluded from the NMA because there were no events in either intervention group. For adults who have recently been discharged from an acute care setting after a recent HF exacerbation, the NMA found that, compared with usual care, RM was beneficial in reducing all-cause mortality by 23%, 24% and 51% for STS HH [hazard ratio (HR) 0.77, 95% credible interval (CrI) 0.55 to 1.08], TM with medical support during office hours (HR 0.76, 95% CrI 0.49 to 1.18) and TM 24/7 (HR 0.49, 95% CrI 0.20 to 1.18) respectively; however, the results for TM 24/7 should be treated with caution because of the poor methodological quality of the only study in this network. No beneficial effect on mortality was observed with STS HM. TM with medical support during office hours or 24/7 was associated with 25% (HR 0.75, 95% CrI 0.49 to 1.10) or 19% (HR 0.81, 95% CrI 0.33 to 2.00) reduction in all-cause hospitalisations, respectively, whereas there was no major effect of STS HM (HR 1.06, 95% CrI 0.44 to 2.53) or STS HH (HR 0.97, 95% CrI 0.70 to 1.31). Although there were no major effects on HF-related hospitalisation for STS HM (HR 1.03, 95% CrI 0.66 to 1.54) and TM with medical support during office hours (HR 0.95, 95% CrI 0.70 to1.34), STS HH (HR 0.77, 95% CrI 0.62 to 0.96) was associated with a 23% reduction. The posterior predictive distributions for the HRs estimated from the NMA as predictive intervals (PrIs) also provided similar results as CrIs, albeit with more uncertainty. Whilst data were limited, care packages that included STS and TM generally improved QoL and were acceptable to HF patients.

A sensitivity analysis that excluded data from the Home Heart Failure Study (Home-HF) (as it provided better-than-usual support and optimal medical treatment to patients in the control group and appeared to be inconsistent with the data from the remaining studies, i.e. an outlier) found that TM with medical support during office hours was more effective than STS HH for all-cause mortality (HR 0.62, 95% CrI 0.42 to 0.89 and HR 0.75, 95% CrI 0.59 to 0.96 respectively) and all-cause hospitalisation (HR 0.67, 95% CrI 0.42 to 0.97 and HR 0.96, 95% CrI 0.72 to 1.27 respectively) but not HF-related hospitalisation (HR 0.86, 95% CrI 0.61 to 1.21 and HR 0.76, 95% CrI 0.61 to 0.94 respectively). By excluding this study from the NMA, larger reductions in effects were observed for all-cause mortality, all-cause hospitalisation and HF-related hospitalisation for TM during office hours.

In the cost-effectiveness analyses, base-case monthly costs per patient were estimated using bottom-up costing methods: £27 for usual care, £119 for STS HM, £179 for STS HH and £175 for TM during office hours. Five cost scenarios were also developed to calculate lower and higher estimates of costs of STS HH (£175 and £192 per month respectively) and TM during office hours (£133.50 and £215 per month respectively) along with a higher estimate of usual care costs (£92 per month).

The full incremental cost-effectiveness analysis using the base-case costs found that TM during office hours was likely to be the most cost-effective strategy at a £20,000 per QALY threshold. TM during office hours had an estimated incremental cost-effectiveness ratio (ICER) of £11,873 per QALY compared with usual care, whereas STS HH had an ICER of £228,035 per QALY compared with TM during office hours. STS HM was dominated by usual care. PSA showed substantial uncertainty in the most probable cost-effective strategy. TM during office hours was the most cost-effective strategy in 40% of the PSA runs whereas STS HH was most cost-effective in 35% of the PSA runs. STS HM and usual care were the most cost-effective in 19% and 6% of the runs respectively. Cost-effectiveness analysis performed using the HRs from the NMA that excluded the data from the Home-HF trial showed an improvement in the cost-effectiveness of TM during office hours. STS HM and STS HH were dominated and extendedly dominated, respectively, with the ICER of TM during office hours against usual care estimated as £6942 per QALY. The results from the uncertainty analyses suggest that TM during office hours was cost-effective in 73% of the runs, whereas STS HH and STS HM were cost-effective in 19% and 7% of the runs respectively.

Scenario analysis using higher costs of TM during office hours (£215 per month) increased uncertainty. TM during office hours and STS HH were both cost-effective in 37% of PSA runs, but TM during office hours was dominated by STS HH. The same scenario analysis (i.e. higher cost of TM during office hours of £215 per month) performed using the HRs from the NMA that excluded the data from the Home-HF trial suggested that TM during office hours would still be the most cost-effective strategy with an ICER of £8223 per QALY compared with usual care (STS HH is extendedly dominated by a combination of usual care and TM during office hours). Threshold analysis performed excluding the data from the Home-HF trial suggested that the monthly cost of TM during office hours has to be > £390 to have an ICER > £20,000 per QALY compared with STS HH. The ICER of TM during office hours compared with usual care, at a monthly cost of £390, is £13,357 per QALY. Scenario analyses performed using higher costs of usual care, higher costs of STS HH and lower costs of TM during office hours do not substantially change the conclusions. TM during office hours was estimated to be the most cost-effective strategy in all of these scenarios.

Discussion

Although an extensive literature search was conducted, it is possible that some relevant studies may have been missed. However, such omissions are likely to have been minimal as the search included all identifiable publications in the grey literature (including contact with clinical experts in the field).

Data were analysed exactly by assuming a binomial likelihood function for the sample data. The statistical model acknowledged the fact that events accumulate over time by adjusting for the varying durations of each study using a complementary log-log link function. Parameter estimates, including between-study standard deviation, were estimated using MCMC simulation, which allows for uncertainty in estimates of between-study standard deviation; it also allowed estimation of the predictive distribution of the effect of each intervention in a new study.

The clinical effectiveness findings had several limitations. RM interventions were heterogeneous in terms of monitored parameters and HF selection criteria. Some trials were underpowered to detect the primary clinical outcome and did not report outcome assessor blinding. Furthermore, few trials reported results in such a way as to enable an assessment of intervention effect modifiers (i.e. meta-regression). Consequently, uncertainties remain around determinants of patient responsiveness, suitability of different systems and 'active ingredients' of RM interventions. A limitation of the statistical model (because of having only one observation from each study) was that hazards and relative intervention effects were assumed to be constant over time; nevertheless, this is better than assuming that duration of study has no impact on the data. Similarly, in the cost-effectiveness model, these constant effectiveness parameters were applied to the time-dependent baseline mortality hazard (which is greatest in the early period after discharge and subsequently declines over time) and constant risk of hospitalisation. If the studies reported observations at different time points, time-dependent effectiveness parameters can be estimated and used

in the cost-effectiveness model. Furthermore, optimal duration for each of the RM interventions can also be identified.

None of the reviewed studies provided estimates for patient utility and whether or not there was a difference between the RM and usual care groups; thus, in the economic model, similar utility values were used for HF patients undergoing both RM strategies and usual care. However, the validity of this assumption is unclear. Furthermore, the lack of detail provided in research studies concerning the components of RM packages and usual care (e.g. communication protocols, routine staff visits and resources used) made it difficult to estimate costs. Costing scenarios for different RM classifications were developed and costs were estimated using microcosting methods. Although users can decide which of these analyses is most representative of their setting, uncertainties remain about the assumptions made in the costing estimation. This uncertainty in costing was a limitation, especially given the small difference in QALYs between STS HH and TM during office hours. Hence, a small change in the difference between costs of TM during office hours and STS HH can lead to a marked change in the ICER. A further limitation was that the effectiveness remained the same for the different cost scenarios whereas in reality there might be some correlation between the costs and effectiveness of different RM strategies.

Hazard ratios of mortality and hospitalisation were the key drivers in the cost-effectiveness model, as mortality reductions lead to a gain in QALYs whereas reductions in hospitalisations lead to fewer costs and more QALYs. The intervention costs were only a small part of the overall costs (hospitalisation costs being the main contributor); thus, RM is likely to be cost-effective if it can save lives and reduce hospitalisations to a sufficient extent. However, some uncertainty persisted in the effectiveness parameters as suggested in the EVPI analysis.

Conclusions

In general, although the effectiveness of the interventions varied widely according to the type of RM system used, STS HH and TM with medical support provided during office hours showed beneficial effects, particularly in reducing all-cause mortality for recently discharged patients with HF; however, these results were statistically inconclusive.

Given the variation in usual care and RM strategies, the cost-effectiveness analysis was performed using a set of costing scenarios. These scenarios were designed to reflect the different configurations of usual care and RM interventions present in the UK. The cost-effectiveness analyses suggest that TM during office hours was an optimal strategy in most scenarios.

Research recommendations include:

1. new research should seek to examine the ‘active ingredients’ of RM
2. qualitative research on patient experiences of RM may be useful to understand the processes by which RM works
3. RM studies should publish data in such a way as to identify which patient subgroups benefited most from the intervention
4. RM studies should include clear descriptions of the interventions and usual care to enable robust costing estimations
5. RM studies should report health outcomes at specific time intervals to identify temporal trends in effectiveness
6. future studies should provide greater detail on reconfiguration costs and link more clearly with the financial impact (e.g. cost variation with scale and over time) on provider organisations.

Study registration

This study is registered as PROSPERO registration no. CRD42011001368.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.

Chapter 1 Background

Description of the health problem

Heart failure (HF) is a complex condition in which cardiac abnormality or dysfunction impairs the capacity of the heart to maintain output without a rise in filling pressures. Clinical presentation typically includes dyspnoea, fatigue, effort intolerance and signs of fluid retention (such as swelling in the extremities).[1] HF is often defined as impaired left ventricular ejection fraction (LVEF) of ≤40%. However, uncertainties remain concerning the appropriate threshold for diagnosis.[2,3] For formal diagnosis, clinical examination is usually supplemented with objective assessments of the underlying structural or functional abnormality of the heart and severity of the syndrome, using techniques including electrocardiography, chest radiography and laboratory tests.[1,4]

Aetiology, pathology and prognosis

In Western countries, hypertension and coronary artery disease (CAD) are the most common causes of HF, whereas nutritional cardiac disease and valvular heart disease are more common in the developing world.[5] In one Scottish survey, hypertension and CAD (alone or in combination) were identified as the cause of HF in >90% of cases.[6] HF has also been associated with neurohormonal changes[7] – in particular, to brain natriuretic peptide and noradrenaline. Elevated levels of each of these hormones is an independent predictor of morbidity and mortality among HF patients.[8] Behavioural factors, such as smoking and chronic alcoholism, were strongly associated with HF in a large cohort study of men residing in the USA ($n = 20,900$), with men not adhering to any of the six measured health behaviours (normal weight, not smoking, regular exercise, moderate alcohol intake, consumption of breakfast cereals, consumption of fruit and vegetables) being at the highest risk [21.2%, 95% confidence interval (CI) 16.8 to 25.6%].[9] Finally, socioeconomic status appears to play a role in the development of HF: a national HF audit commissioned by the NHS[10] found that people with a home address in the highest quintile of deprivation are admitted to hospital with HF on average 5 years earlier than those in the lowest quintile (most affluent). A brief list of causal factors is included in *Table 1*.

Severity of HF is usually assessed using the New York Heart Association (NYHA) system. This system classifies HF as mild (stage I–II), moderate (stage III) or severe (stage IV) based on symptomatic markers

TABLE 1 Causes of HF

CAD	Myocardial infarction, ischaemia
Hypertension	
Cardiomyopathy	Dilated (congestive), hypertrophic/obstructive, restrictive (e.g. amyloidosis, sarcoidosis, haemochromatosis)
Valvular and congenital heart disease	Mitral valve disease, aortic valve disease, atrial septal defect, ventricular septal defect
Arrhythmias	Atrial fibrillation
Alcohol and drugs	Alcohol, cardiac depressant drugs (beta-blockers, calcium antagonists)
'High output' failure	Anaemia, thyrotoxicosis, arteriovenous fistulae, Paget's disease
Pericardial disease	Constrictive pericarditis, pericardial effusion
Primary right HF	Pulmonary hypertension, tricuspid incompetence

Source: adapted from Lip *et al.*[5]

(*Table 2*).[11] Although the NYHA class system does not necessarily reflect the severity of underlying heart dysfunction, it is a useful clinical tool which provides a standardised description of symptom severity that can be used to guide clinical management. Furthermore, NYHA class has been shown to be a strong independent predictor of quality of life (QoL) for patients with HF.[12]

Patients with a new HF diagnosis have a 40% risk of mortality within the first year.[13,14] However, post-discharge mortality incidence varies substantially according to the care setting to which patients are admitted. A recent UK HF audit (between April 2010 and March 2011)[14] found annual post-discharge mortality rates of 26.2%, 38.2% and 42.0% for cardiovascular, general medical and other wards respectively ($p<0.001$). On average, patients who are discharged have an approximately 28% risk of mortality within the first year after HF discharge.[14] The highest risk period for further complications is immediately after an acute decompensation.[15] Between 20% and 30% of patients are readmitted within 30 days, rising to 50% at 6 months.[16] Prognosis is poor even among people receiving optimal pharmaceutical therapy and so preventative strategies should ideally be pursued with at-risk patients.[17]

Epidemiology

Given the ongoing debate around appropriate HF diagnostic criteria,[2,3] it is difficult to provide confident estimates of incidence and prevalence of HF. Early epidemiological studies used unreliable diagnostic criteria,[18] and although some later surveys incorporated objective assessments of LVEF using echocardiogram[6,19] they were limited by excluding adults >85 years of age and by restricting HF to those with left ventricular systolic dysfunction (LVSD).[20] More recently, a UK population survey in 2009, drawing on an audit of GP registries, estimated total all-age prevalence of HF to be 0.9% for men and 0.7% for women.[10] The largest recent community-based survey, the Echocardiographic Heart of England Screening (ECHOES) study,[21] utilised objective European Society of Cardiology (ESC) criteria to determine the presence of HF. A LVEF <40% was found in 1.8% of the population >45 years of age (95% CI 1.4 to 2.3%), and definite HF in 2.3% (95% CI 1.9 to 2.8%). In those >75 years of age, prevalence of LVEF of <40% and definite HF rose to 3.7% and 6.9% respectively. A recent British Heart Foundation (BHF) survey of the General Practice Research Database (GPRD) found an all-age prevalence rate of 0.9% for the UK, which was lowest in England (0.9%) and highest in Northern Ireland (1.1%). In those >75 years of age, prevalence rose to 13.7% and 15.3% respectively.[10]

Cowie *et al.*[22] found a crude incidence rate of 1.3 cases per 1000 population in a large West London cohort, rising to 11.6 cases per 1000 population in those >85 years of age. The age-adjusted incidence was higher among men than among women (incidence ratio 1.75, 95% CI 1.34 to 2.29).[22,23] However, there are important regional variations in incidence. Using data from the GPRD, the BHF found that the incidence of HF in the UK was highest in Northern Ireland and lowest in England (58.1 per 100,000 and 37.5 per 100,000 respectively), with the overall incidence rate being approximately 75% higher among men than among women.[10] The Rotterdam cohort study found similar patterns, with an overall incidence rate of 14.4 per 1000 person-years (95% CI 13.4 to 15.5) rising to 47.4 per 1000 person-years among

TABLE 2 New York Heart Association classification system for HF severity[11]

NYHA class	Severity	Symptoms
I	Mild	No limitations. No fatigue, breathlessness or palpitations in response to ordinary levels of physical activity
II	Mild	Comfortable at rest with slight limitation of physical activity. Ordinary physical activity leads to breathlessness, fatigue or angina pectoris
III	Moderate	Marked limitation of physical activity. Comfortable at rest but less than ordinary physical activity leads to symptoms
IV	Severe	Inability to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency present at rest

those aged >90 years, and a higher incidence rate for men than women (17.6 per 1000 man-years, 95% CI 15.8 to 19.5 and 12.5 per 1000 woman-years, 95% CI 11.3 to 13.8 respectively).[23] The Rochester epidemiology project in the USA also found a higher incidence among men than among women (3.78 per 1000, 95% CI 3.61 to 3.95 and 2.89 per 1000, 95% CI 2.77 to 3.00).[24] HF incidence and prevalence in the UK are set to increase in conjunction with life expectancy as medical therapies for cardiac conditions such as hypertension and myocardial infarction improve.[25]

Impact of the health problem

Heart failure is associated with high levels of morbidity and mortality, particularly among those aged >60 years.[10] One-year mortality for HF patients >75 years may be twice as high as for those <75 years.[26] The illness trajectory of HF is unpredictable: NYHA functional classification can improve as well as deteriorate, and sometimes changes unevenly over time.[10] HF also has a substantial impact on patient QoL. In one German cohort study, the Short Form questionnaire-36 items (SF-36) measure was administered to 205 HF inpatients.[12] Using multiple regressions to control for confounders, this research found that NYHA functional class was the only consistent independent predictor of QoL. Evidence suggests a 25–50% prevalence of anxiety and a 18–47% prevalence of depression among HF patients, depending on age, time since diagnosis and other prognostic indicators.[27,28]

Heart failure imposes a significant burden on NHS resources. The cost of inpatient bed-days for HF alone has been estimated at £563M per year,[29] whereas total HF-related costs have been estimated at £625M per year.[30] HF is a leading cause of hospitalisation in the UK, with 58,164 admissions recorded for HF (as first diagnoses) between April 2009 and March 2010 in England and Wales.[30] Around 90% of HF admissions are to emergency departments,[31] with hospitalisations lasting a median of 9 days.[30] As the proportion of people >60 years of age in the UK continues to increase, and improvements are made in treatment for and survival from cardiac disorders, the burden of HF on the NHS looks set to increase.[32,33]

Current service provision

Optimal HF treatment can vary depending on aetiology and severity. Evidence-based treatment guidelines from the National Institute for Health and Care Excellence (NICE)[34] advocate pharmaceutical treatment of HF with angiotensin-converting enzyme (ACE) inhibitors and beta-blockers as first line (*Table 3*). These should be administered initially at a low dose and up-titrated at short intervals until the optimal dosage, or tolerance limit, is reached. If the patient remains symptomatic despite optimal treatment with these agents, a second line of treatment comprising one of three options, an aldosterone antagonist, an angiotensin receptor blocker (ARB) or hydralazine in combination with nitrate, should be considered.[39] For stable patients without clinical contraindications to exercise, supervised, exercise-based group rehabilitation programmes for HF should be offered. Finally, patients should be regularly monitored, although the frequency depends on the clinical status of the patient. Stable patients should be monitored at least every 6 months whereas those with recent changes to medication and/or clinical status should be monitored every few days to every 2 weeks[39] (see *Table 3*).

Ideally, inpatient treatment should be provided by a specialist centre. Patients admitted to specialist cardiology wards have better survival rates while hospitalised and in the first year post discharge – a relationship that remains when age, HF aetiology, echocardiology, heart rhythm, sex and symptoms are adjusted for.[29] Overall, patients admitted to specialist centres are around half as likely to die in hospital as those admitted to general wards.[10] Post-discharge, multidisciplinary disease management programmes comprising patient education, optimal medical treatment and psychosocial care have been associated with decreased hospitalisation and improved clinical outcomes.[40–43] However, access to these services is limited because of funding-related barriers or geographical location.[44,45] Furthermore, there are inequalities in access to services in terms of sex and age. Only 38% of people referred to the UK's HF liaison service between 2008 and 2009 were women and, although approximately 70% of patients <45 years of age were referred to the liaison service, this figure fell across the age groups to <21% in those ≥95 years.[30]

TABLE 3 National and international guidelines for the treatment of HF

Issuing body	Country	Drug therapy[a]	Outpatient monitoring	Device based/ surgical
NICE[34]	England and Wales	First line: ACE inhibitors; beta-blockers. Second line: aldosterone antagonist; angiotensin II receptor antagonist;[b] hydralazine in combination with nitrate[b]	Clinical assessment of functional capacity, fluid status, cardiac rhythm and BNP; regular medication review; serum urea, electrolytes, creatinine and eGFR; review at least every 6 months for stable outpatients or every few days to 2 weeks if recent medication change/clinical deterioration; education, support and group-based exercise rehabilitation	Coronary revascularisation, heart transplantation, CRT
SIGN[35]	Scotland	First line: ACE inhibitors; beta-blockers. Second line: ARBs;[b] aldosterone antagonists;[c] diuretics/loop diuretics/ metolazone (to relieve symptoms of congestion/fluid retention); digoxin;[d] hydralazine and isorbide dinitrate[b,c]	Patient education and communication including a nurse-led, home-based element; behaviour change (smoking cessation, limiting alcohol, supervised exercise training, dietary change); pharmacist input to assess knowledge of drugs and compliance; tailored self-management advice; patient support groups	CRT; assisted ventilation; left ventricular assist devices; cardiac transplantation; intra-aortic balloon counterpulsation
CREST[36]	Northern Ireland	First line: ACE inhibitors; beta-blockers. Second line: aldosterone antagonists;[c] diuretics/loop diuretics (for congestion/fluid overload); digoxin;[c] nitrates and hydralazine[b]	Multidisciplinary, nurse-led management; action plan for all patients; education (exercise training, sexual activity, smoking cessation, alcohol intake, fluid intake, salt intake, daily weighing, obesity, cachexia, immunisations, travel, medication advice); psychological management	Heart transplantation; CRT; coronary revascularisation
ESC[37]	Europe	First line: ACE inhibitors; beta-blockers. Second line: aldosterone antagonists;[c,d] ARBs;[b,d] hydralazine and isorbide dinitrate;[b,d] digoxin (for arrhythmias); diuretics (to relieve congestions); statins (for systolic dysfunction caused by CAD)	Multidisciplinary approach led by HF nurses; early follow-up post-discharge; patient education with emphasis on self-care; physical activity training; self-monitoring of weight, symptoms, diet, fluid intake and alcohol; involve patient in symptom monitoring and flexible diuretic use; remote monitoring; psychosocial support	Revascularisation; valvular surgery; CRT; heart transplantation; left ventricular assist devices and artificial hearts; ultrafiltration (to relieve congestion)
AHA[38]	USA	First line: ACE inhibitors; beta-blockers. Second line: ARBs;[b] aldosterone antagonist;[c] hydralazine and nitrates;[b,c] digitalis; diuretics/loop diuretics and salt restriction (for congestion/fluid overload); vasodilators (to relieve congestion if adequate blood pressure); intravenous inotropes (only in patients with low blood pressure and cardiac output who can be closely monitored)	Close observation and follow-up; exercise training; written educational materials (activity level, diet, discharge medications, follow-up appointment, weight monitoring and response to symptoms); discharge planning with emphasis on medication compliance; psychosocial support; access to palliative services	CRT; coronary revascularisation; cardiac transplantation; left ventricular assist device; pulmonary artery catheter placement; ultrafiltration (if pharmacological diuretic strategies unsuccessful)

AHA, American Heart Association; BNP, B-type natriuretic peptide; CREST, Clinical Resource Efficiency Support Team; CRT, cardiac resynchronisation therapy (including implanted cardiac defibrillators and biventricular pacing); eGFR, estimated glomerular filtration rate; SIGN, Scottish Intercollegiate Guidelines Network.

a Drug therapy is specific to LVSD unless otherwise stated.

b Consider as alternative if first-line treatments contraindicated/not tolerated.

c Indicated for patients with moderate to severe HF.

d Consider if patient remains symptomatic despite optimum treatment.

Description of technology under assessment

Telemedicine is an emerging approach utilising remote monitoring (RM) of prognostic indicators (e.g. weight, arrhythmias, blood pressure, intrathoracic impedance, heart rates during rest and exertion) to facilitate early detection of clinically significant changes, prevent emergency admissions and avoid complications.[46] Guidelines from the ESC currently recommend RM for patients with HF (see *Table 3*). Because the highest risk period for rehospitalisation is the first few weeks after discharge, RM interventions should be performed at least once in the first 28 days following discharge. RM encompasses a range of approaches depending on what physiological data are transferred to clinicians, how the data are transferred (e.g. automatically or manually, by telephone contact or through a secure web server) and how these data are utilised. Broadly speaking, two main approaches have emerged: telemonitoring (TM), in which physiological data are electronically transmitted to a health-care team, and structured telephone support (STS), that is, the use of telephone calls, usually by specialist nurses, to deliver self-care support and/or management.[47,48] For STS, support can be provided by human-to-human contact (HH) or through a human-to-machine interface (HM), that is, STS with an interactive response system. For TM, support can be provided during office hours (9 AM to 5 PM, Monday to Friday) only or 24 hours a day, 7 days a week (24/7), although few studies have used the latter approach. Further details are provided in *Table 4*. Cardiovascular implanted monitoring devices such as modern pacemakers, implantable cardioverter defibrillators or cardiac resynchronisation devices are also capable of delivering remote physiological

TABLE 4 Summary of various RM strategies

	TM		STS	
	Office hours only	24/7	HH	HM
Description	Patients take measurements (manual or automated) of vital parameters (most commonly weight, BP and HR) at home, which are transmitted to a health-care team or HF specialist centre by telephone, mobile telephone, cable network or broadband technology. Transmitted data are reviewed by medical staff (in some cases readings outside of prespecified limits may generate automated warnings) during office hours (including provision of medical support)	Same as TM during office hours but constant presence of medical personnel required to operate the support system, i.e. 24 hours a day, 7 days a week	Patients followed up with regular telephone calls by a care provider. Calls typically from HF specialist nurses and include advice on self-care and medication. STS may also incorporate basic monitoring of physiological parameters (e.g. weight)	Patients monitored by automated telephone-based interactive response system. May include questions about HF symptoms to which patients can respond on telephone keypad
Example	Cleland *et al.*[49] provided patients with a scale and sphygmomanometer. Patients took twice daily measurements of vital parameters (weight, BP, HR and single lead ECG using wristband electrodes). Results were encrypted and sent via a secure web server to a computer at each investigator site. Medical support was provided during office hours	Koehler *et al.*[50] provided a wireless Bluetooth system with a personal digital assistant and three integrated devices: an ECG lead, a BP cuff and weighing scales. Encrypted measurements were sent via a secure server to participating sites. These sites provided physician-led medical support 24 hours a day, 7 days a week	Angermann *et al.*[51] provided telephone-based structured monitoring delivered by trained nurses (supervised by a cardiologist and a psychologist), which included educational material/self-monitoring schemes and multidisciplinary advice	Chaudhry *et al.*[52] used an interactive system that required patients to provide daily readings of vital parameters, which were sent to a secure internet site and reviewed by clinicians on weekdays

BP, blood pressure; ECG, electrocardiogram; HR, heart rate.

monitoring, often without the need for a patient to trigger the transmission of data.[53] The equipment and personnel requirements vary according to the type of RM and a number of systems have been described.[54]

Use of information communication technology may help provide wider access to HF programmes for a larger number of patients, including those constrained by geography, transport or infirmity.[15] When a care plan has been agreed with a patient, TM and STS interventions can promote a rapid response when vital clinical signs fall outside agreed parameters, for example by up-titrating medication or arranging for a clinical visit. RM could also minimise the incidence of difficult-to-treat complications, and use early warning signs to avoid hospitalisation. Conversely, RM may generate false alerts leading to inappropriate hospitalisation[55] and it may not be feasible for health-care providers to contact all patients regularly or provide specialist equipment to all patients who may potentially benefit.

Telemedical interventions for a variety of chronic conditions are currently being investigated and rolled out by a number of UK NHS trusts. For example, NHS North Yorkshire and York (NY&Y) has seen approximately 500 patients with long-term conditions including HF receive a TM intervention. HF patients were supplied with RM equipment, which generated medication prompts, along with weighing scales and a blood pressure and pulse meter (Julie Ryan, Telehealth Project Manager, NHS NY&Y, 2 April 2012, personal communication). NY&Y are in the process of rolling out the initiative to cover 2000 people.[56] In addition, the UK Department of Health released headline findings from the Whole System Demonstrator (WSD) programme for telehealth in December 2011.[57] This randomised evaluation of the impact of telehealth for people with chronic conditions [diabetes, HF and chronic obstructive pulmonary disease (COPD)] included over 6000 patients from sites in Newham, Kent and Cornwall, and reported strongly positive results, including a 45% reduction in mortality. However, these results should be interpreted with caution. The Department of Health's release of these findings before peer review makes their robustness difficult to evaluate, and data on potential confounding factors, such as face-to-face clinical contact, are not yet publicly available. Nevertheless, the early release of these findings underscores the enthusiasm for telehealth among some quarters of the UK health-care authorities.

Two recent meta-analyses demonstrated significant benefits of RM interventions in terms of mortality and hospitalisation[48,58] [it is noteworthy that shortly following approval of this review protocol the original Cochrane systematic review published by Clark *et al.*[59] (search date from January 2002 to May 2006) was superseded by that by Inglis *et al.*[48] (search date from January 2006 to November 2008)]. However, since the publication of the latest of these reviews, randomised controlled trials (RCTs) demonstrating minimal or no clinical benefits have been published.[50,52,60] Furthermore, neither the review by Klersy *et al.*[58] nor that of Clark *et al.*[59] (including the recent update by Inglis *et al.*[48]) included an economic evaluation of telemedicine.

Chapter 2 Definition of the decision problem

Purpose of the decision to be made

The aim of this assessment was to investigate the clinical effectiveness and cost-effectiveness of home TM or STS programmes for adults who have been recently discharged (within 28 days) from an acute care setting after a recent exacerbation of HF (including subgroups such as those with transiently or persistently severe HF).

Clear definition of the intervention

Telemonitoring, defined as the use of information and communication technologies to monitor and transmit items related to patient health status between geographically separated individuals,[54] permits home monitoring of patients (living at home or in nursing or residential care homes) using external electronic devices in conjunction with a telecommunications system (landline or mobile telephone, cable network or broadband technology). TM allows frequent or continuous assessment of HF signs and symptoms measured by patients, family or caregivers at home, while allowing patients to remain under close supervision.[37,59] Symptoms reported by patients can be remotely reviewed by a health-care professional and appropriate action can be initiated. Telephone support is another form of remote management that can be provided through structured telephone contact between patients and health-care providers (with or without home visits) and reporting of symptoms and/or physiological data.[58,59] Cardiovascular implanted monitoring devices such as modern pacemakers, implantable cardioverter defibrillators or cardiac resynchronisation devices are also capable of delivering remote physiological monitoring, often without the need for a patient to trigger the transmission of data.[53]

The highest risk period for rehospitalisation is in the first few weeks after discharge from hospital.[15] STS and/or home TM interventions should be performed at least once within the first 28 days following discharge from hospital and must be targeted towards patients and intended to address patient concerns and problems and not those of caregivers.[59] The optimum time period for TM is unclear; however, it is likely that services will provide TM or STS for at least 4–6 months following discharge from hospital with its usefulness evaluated at 30-day intervals thereafter. The review focuses on the use of home TM or STS programmes for patients who have been discharged from an acute care setting after a recent exacerbation of HF.

Population and relevant subgroups

The population included any adults (defined as ≥18 years of age) of either sex or any ethnic group with a diagnosis of HF and discharged from an acute care setting (including emergency departments and 1-day stay procedures) to home (including a relative's home, nursing home or residential care home). The identification of subgroups of patients for whom home TM or STS programmes are appropriate or inappropriate was governed by the available evidence; however, on a priori grounds, information was sought for people with transiently or persistently severe HF.

Relevant comparators

The relevant comparator was considered to be usual care. This involves standard post-discharge multidisciplinary care without regular follow-up and may include (1) in-person follow-up visits to a primary care physician, (2) attendance at a clinic-based chronic heart failure (CHF) disease management programme and (3) any visits at home by a specialised CHF health-care professional (referred to as enhanced conventional care).[58,59]

Outcomes

The outcomes of the review were mortality (all-cause), all-cause admission to hospital, HF-related admission to hospital, length of stay (days in hospital), health-related quality of life (HRQoL) and acceptability of interventions to patients.

Overall aims and objectives of the assessment

The review had the following objectives:

1. update two existing systematic reviews[48,58] of TM or STS programmes for patients with HF within the scope of the current review
2. evaluate the effectiveness and cost-effectiveness of home TM and/or STS packages compared with usual post-discharge care
3. identify key areas for primary research.

Chapter 3 Assessment of clinical effectiveness

A systematic review of the literature and (network) meta-analysis (where appropriate) was undertaken to evaluate the clinical effectiveness of home TM or STS strategies compared with usual care for adults who have been recently discharged (within 28 days) from an acute care setting after a recent exacerbation of HF.

A review of the evidence was undertaken in accordance with the general principles recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (www.prisma-statement.org/).

Methods for reviewing effectiveness

Identification of studies

Electronic databases

Studies were identified by searching the following electronic databases and research registers:

- MEDLINE(R) In-Process & Other Non-Indexed Citations and MEDLINE(R) (Ovid) 1948–January 2012
- EMBASE (Ovid) 1980–January 2012
- Science Citation Index Expanded (Web of Science) 1899–January 2012
- Conference Proceedings Citation Index – Science (Web of Science) 1990–January 2012
- Cochrane Database of Systematic Reviews (Wiley Online Library) 1996–January 2012
- Cochrane Central Register of Controlled Trials (Wiley Online Library) 1898–January 2012
- Health Technology Assessment database (Wiley Online Library) 1995–January 2012
- Database of Abstracts of Reviews of Effects (Wiley Online Library) 1995–January 2012
- PsycINFO (Ovid) 1806–January 2012
- Cumulative Index to Nursing and Allied Health Literature (EBSCO*host*) 1982–January 2012
- Allied and Complementary Medicine Database (Ovid) 1985–January 2012
- UK Clinical Research Network (CRN) Portfolio Database [National Institute for Health Research (NIHR)] 2001–January 2012
- ClinicalTrials.gov (US NIH) 2000–January 2012
- Institute of Electrical and Electronics Engineers/Institution of Engineering and Technology (IEEE/IET) Electronic Library (IEEE *Xplore*) 1988–January 2012.

Sensitive keyword strategies using free text and, where available, thesaurus terms using Boolean operators and database-specific syntax were developed to search the electronic databases. Synonyms relating to the condition (e.g. HF) were combined with terms for TM. No language restrictions were used on any database; however, the clinical effectiveness searches were restricted by date. The current review updated two existing systematic reviews[48,58] of TM or STS programmes for patients with HF (within the scope of the current review). In the review by Inglis *et al.*[48] the searches examined the period from January 2006 to November 2008 and in Klersy *et al.*[58] the searches examined the period from January 2000 to October 2008. As the search strategies from the existing systematic reviews were of good quality (and clearly reported) it was assumed that all studies prior to 2008 should have been identified. Thus, the clinical effectiveness searches were limited by date from 2008 to January 2012. An example of the MEDLINE search strategy is provided in *Appendix 1*.

Other resources

To identify additional published, unpublished and ongoing studies, the reference lists of all relevant studies (including existing systematic reviews) were checked. Citation searches of relevant articles using the Web

of Science Science Citation Index was also undertaken to identify articles that cite the relevant articles. In addition, key experts in the field were contacted.

All identified citations from the electronic searches and other resources were imported into and managed using Reference Manager bibliographic software (version 12; Thomson Reuters, Philadelphia, PA).

Inclusion and exclusion criteria

The inclusion of potentially relevant articles was undertaken using a two-step process. First, all titles were examined for inclusion by one reviewer. Any citations that clearly did not meet the inclusion criteria, that is, non-human, unrelated to TM and/or HF, were excluded. Second, all abstracts and full-text articles were examined independently by two reviewers. Any disagreements in the selection process were resolved through discussion. The relevance of each article for the systematic review was assessed according to the following criteria.

Study design

All RCTs or observational cohort studies with a contemporaneous control group published from 2008 to January 2012 (as well as those identified by the existing systematic reviews) that evaluated home TM or STS programmes compared with usual post-discharge multidisciplinary care for adults who have been recently discharged (within 28 days) from an acute care setting to home (including a relative's home, nursing home or residential care home) after a recent exacerbation of HF were included. Before-and-after studies without a concurrent control group were excluded because the absence of a control group to record concurrent changes over time means that changes due to the intervention or due to temporal trends, concurrent changes or a Hawthorne effect would be conflated. Such studies therefore represent very weak evidence of effectiveness.

Reviews of primary studies were not included in the analysis but were retained for discussion and identification of additional studies. Moreover, the following publication types were excluded from the review: animal models; preclinical and biological studies; narrative reviews, editorials, opinions; non-English-language papers and reports published as meeting abstracts only when insufficient methodological details are reported to allow critical appraisal of study quality.

Population

The population comprised adults (defined as ≥ 18 years of age) with a diagnosis of HF and discharged from an acute care setting to home (including a relative's home, nursing home or residential care home).

Interventions

The following interventions were included: (1) remote home TM using patient-initiated external electronic devices or cardiovascular implanted monitoring devices, with transfer of physiological data from the patient to the health-care provider by landline or mobile telephone, cable network or broadband technology, (2) STS including regularly scheduled telephone contact between patients and health-care providers and reporting of symptoms and/or physiological data. In addition, STS and/or home TM interventions were required to be performed at least once within the first 28 days following discharge from hospital, and to be targeted towards patients and intended to address patient concerns and problems and not those of caregivers.

Relevant comparators

The relevant comparator was considered as usual care. This involved standard post-discharge multidisciplinary care without regular follow-up and may include (1) in-person follow-up visits to a primary care physician, (2) attendance at a clinic-based CHF disease management programme and (3) any visits at home by a specialised CHF health-care professional (referred to as enhanced conventional care).[58,59]

Outcomes

The outcomes of the review included mortality (all-cause), all-cause admission to hospital, HF-related admission to hospital, length of stay (days in hospital), HRQoL and acceptability of interventions to patients.

Data abstraction strategy

Data abstraction was performed by one reviewer into a standardised data extraction form and independently checked for accuracy by a second. Discrepancies were resolved by discussion between the two reviewers; if agreement could not be reached a third reviewer was consulted. When multiple publications of the same study were identified, data were extracted and reported as a single study. Moreover, as this was an update of two existing reviews,[48,58] all relevant data were extracted from the reviews in the first instance and cross-checked for accuracy with the original papers. When necessary, additional data were extracted from the original papers or, in cases in which information was missing from the articles, authors of the respective studies were contacted to provide further details.

The following information was extracted for all studies when reported: study characteristics (e.g. author, year of publication, country, study design, setting, duration of follow-up, funding), participant details (e.g. inclusion and exclusion criteria, age, sex, autonomy, comorbidities), intervention and comparator details (e.g. description, system activity, frequency of measurement, parameters measured) and outcomes (including definitions).

Quality assessment strategy

The methodological quality of each included study was assessed by one reviewer and independently checked by another. Disagreements were resolved by discussion between the two reviewers and, if agreement could not be reached, a third reviewer was consulted. The study quality characteristics were assessed according to (adapted) criteria based on those proposed by Verhagen *et al.*[61] for RCTs and by Wells *et al.*[62] for observational studies. Further details are provided in *Appendix 2*.

Methods of data synthesis

Primary analyses (recently discharged patients with heart failure)

The extracted data and quality assessment variables were presented for each study both in structured tables and as a narrative description. Mortality (all-cause), all-cause admission to hospital and HF-related admission to hospital were subjected to formal (network) meta-analyses. A network meta-analysis (NMA) allows a comprehensive comparison of all interventions that are linked with respect to at least one common intervention without breaking the randomisation within studies. The summary statistics that were analysed were the number of patients who had an event. In each case the data were analysed using a random-effects model (to allow for heterogeneity in treatment effects across studies) implemented using the WinBUGS software package, version 1.4.3 (MRC Biostatistics Unit, Cambridge, UK).[63,64] The statistical model accounted for the variation in follow-up between studies using a complementary log-log link function (see *Appendix 3*). This model assumed that the parameter being analysed was the event rate (i.e. hazard) from an exponential survivor function and that an intervention effect relative to the baseline treatment was the (log-) hazard ratio (HR). Convergence of the model to its posterior distribution was assessed using the Gelman–Rubin convergence statistic.[65] In each case, convergence occurred within 20,000 iterations so the final analysis used a burn-in of 20,000. There was some suggestion of high autocorrelation between successive iterations of the Markov chains; to compensate for this the Markov chains were thinned every 10 iterations. Parameter estimates were estimated based on 10,000 iterations of the Markov chains. The total residual deviance was used to formally assess whether or not the statistical model provided a reasonable representation of the sample data. The total residual deviance is the mean of the deviance under the current model minus the deviance for the saturated model, so that each data point should contribute about 1 to the deviance. Results of the NMA were reported in terms of the HR and 95% credible interval (CrI) relative to the baseline intervention (i.e. usual care). The posterior median of the between-study standard deviation together with the 95% CrI was also presented. To account for potential

heterogeneity in intervention effects between studies, the posterior predictive distribution for the HR of a new study was also presented.

The original intention was to use meta-regression in an attempt to explain any heterogeneity in the effects of the interventions amongst the studies. Potential treatment effect modifiers were quality of usual care, different telehealth intervention settings, adherence, age, sex and autonomy (i.e. single vs couple). However, because of the lack of availability of data on these study-level covariates, meta-regressions were not performed.

Additional analyses (patients with stable heart failure)

Following advice from clinical experts, additional analyses were undertaken to assess whether or not the results from the primary analysis differed markedly from results in those with stable HF who were managed in the community. In this supplementary analysis the following studies were included: RCTs comparing HF management delivered via STS, TM or cardiovascular implanted monitoring devices with HF management delivered via usual post-discharge care in stable HF patients (defined as having no acute event or deterioration in the past 28 days) who were managed in the community setting (ambulatory or outpatient care). Studies that included intensified management with additional home or clinic visits were excluded. Although no formal critical appraisal of these studies was undertaken, the results were meta-analysed (as per the methods of the primary analysis) and presented for information only. All studies published before 2008 were identified from Inglis *et al.*[48] and Klersy *et al.*,[58] whereas more recent studies (meeting these criteria) were identified using the current review.

Results of the clinical effectiveness review

This section first provides a brief overview of the evidence from the two existing systematic reviews[48,58] of RM for HF [including a methodological quality assessment using a measurement tool developed by Shea *et al*.[66] for the 'assessment of multiple systematic reviews' (AMSTAR)]. Second, this section presents the results of the current systematic review, including additional analyses.

Overview of existing systematic reviews

The first of the two existing systematic reviews and meta-analyses was published by Clark *et al.* in 2007[59] and later updated by Inglis *et al*. in 2010.[48] The review included RCTs comparing HF management strategies delivered via STS or TM with usual post-discharge care in HF patients recently discharged from an acute care setting to home or while managed in the community setting. Any interventions that included home visits by specialised HF health-care professionals or study personnel for the purpose of education or clinical assessment, other than an initial visit to set up equipment, were excluded. The primary outcomes of interest were all-cause mortality, HF-related admission to hospital and all-cause readmissions to hospital. Secondary outcomes included length of stay, QoL, health-care cost savings in patients with HF and acceptability of the intervention to patients with HF. Overall, 30 RCTs of STS and TM were identified (25 peer-reviewed publications and five abstracts). Of the 25 peer-reviewed studies, 11 evaluated TM and 16 evaluated STS, with two testing both STS and TM in separate intervention arms compared with usual care.

The second review was conducted by Klersy *et al.*[58] and was published in December 2009. The review included RCTs and observational studies comparing HF management strategies delivered via STS (with or without home visits), TM or cardiovascular implanted monitoring devices with usual post-discharge care in HF patients. Overall, 32 studies were identified (20 RCTs and 12 cohort studies). Of the 20 RCTs, 11 evaluated STS, 7 evaluated TM (including cardiovascular implanted monitoring devices) and 2 tested both STS and TM. Of the 12 cohort studies, 6 were between-arm studies. The outcomes of interest included all-cause mortality, all-cause hospitalisation, HF-related hospitalisation and a composite end point comprising all-cause hospitalisation or death from any cause. Despite ostensibly being reviews of the same literature, as their objectives would suggest (except for studies of cardiovascular implanted monitoring devices), there was limited overlap between the two reviews in terms of the primary studies that were

included. The lack of overlap of included studies may be largely explained by the differences in their search strategies (including search dates) and inclusion/exclusion criteria. For example, Inglis *et al.*[48] searched 15 electronic databases (including research registers) from 1966 to November 2008 and included RCTs that had interventions without home visits or intensified clinic follow-up. In contrast, Klersy *et al.*[58] searched five electronic databases from January 2000 to October 2008 and included RCTs and observational studies that had interventions with or without home visits. A summary of all of the included studies in both reviews (including discordance) is presented in *Appendix 4*.

The methodological quality of both systematic reviews was judged to be high, indicating low risk of bias: Inglis *et al.*[48] met 9 of the 11 criteria whereas Klersy *et al.*[58] met 7 of the 11 criteria (see *Appendix 5*). Both reviews provided an 'a priori' design, had at least two authors conduct data extraction independently, provided lists and comprehensive details of included studies, assessed the likelihood of publication bias and assessed the scientific quality of the meta-analysed trials. In addition, Klersy *et al.*[58] utilised appropriate methods for data synthesis and Inglis *et al.*[48] conducted a comprehensive literature search and reported potential conflicts of interest from both the review authors and the authors of the included trials. However, Klersy *et al.*[58] did not report supplementing their literature search by consulting current contents, reviews, textbooks, specialised registers and reference lists of identified literature nor did they explicitly state that they searched for reports regardless of their publication type. In addition, they did not refer to the quality of the synthesised literature when formulating recommendations and did not refer to the sources of support received by authors of the included trials. Inglis *et al.*[48] also did not refer to the quality of the included trials when making recommendations and did not use appropriate statistical methods for synthesising heterogeneous results (all analyses were performed using a fixed-effects model). It is also worth noting that Klersy *et al.*[58] did not specify their HF patient population of interest. Inglis *et al.*[48] included both recent discharge HF patients and stable HF patients managed in the community, although they did not specify their interpretation of recent discharge.

Quantity and quality of research available in the current (and existing[48,58]) systematic reviews

Number of studies identified/included

The literature searches identified 3060 citations. Of these, six RCTs[52,60,67–70] met the inclusion criteria and were added to the 15 trials[49,51,71–83] from the previous systematic reviews.[48,58] No trials of cardiovascular implanted monitoring devices or observational studies met the inclusion criteria of the current review. A flow chart describing the process of identifying relevant literature can be found in *Figure 1*.

Number and type of studies excluded

A total of 153 full-text articles were excluded as they did not meet all of the prespecified inclusion criteria. The majority of the articles were excluded primarily on the basis of inappropriate study design (not RCTs or cohort studies without concurrent controls), incorrect intervention (not home TM or STS for patients with HF) or unsuitable publication type (reviews, commentaries or editorials). A full list of excluded studies with reasons for exclusion is presented in *Appendix 6*.

Assessment of effectiveness

Description of included studies (design and patient characteristics)

The design and patient characteristics of the 21 included studies that evaluated home TM or STS programmes for adults who have been recently discharged (within 28 days) from an acute care setting after a recent exacerbation of HF are summarised in *Tables 5* and *6* respectively. Of these, 11 studies evaluated STS [10 used standard telephone equipment using HH[51,69,72,74,77–82] and one provided support via an automated telephone interactive response system (HM) with an alert system[52]], nine studies assessed TM,[60,67,68,70,71,73,75,76,83] and one study assessed both STS and TM compared with usual care.[49] Almost all of the studies used different measures and devices as part of the STS and TM interventions.

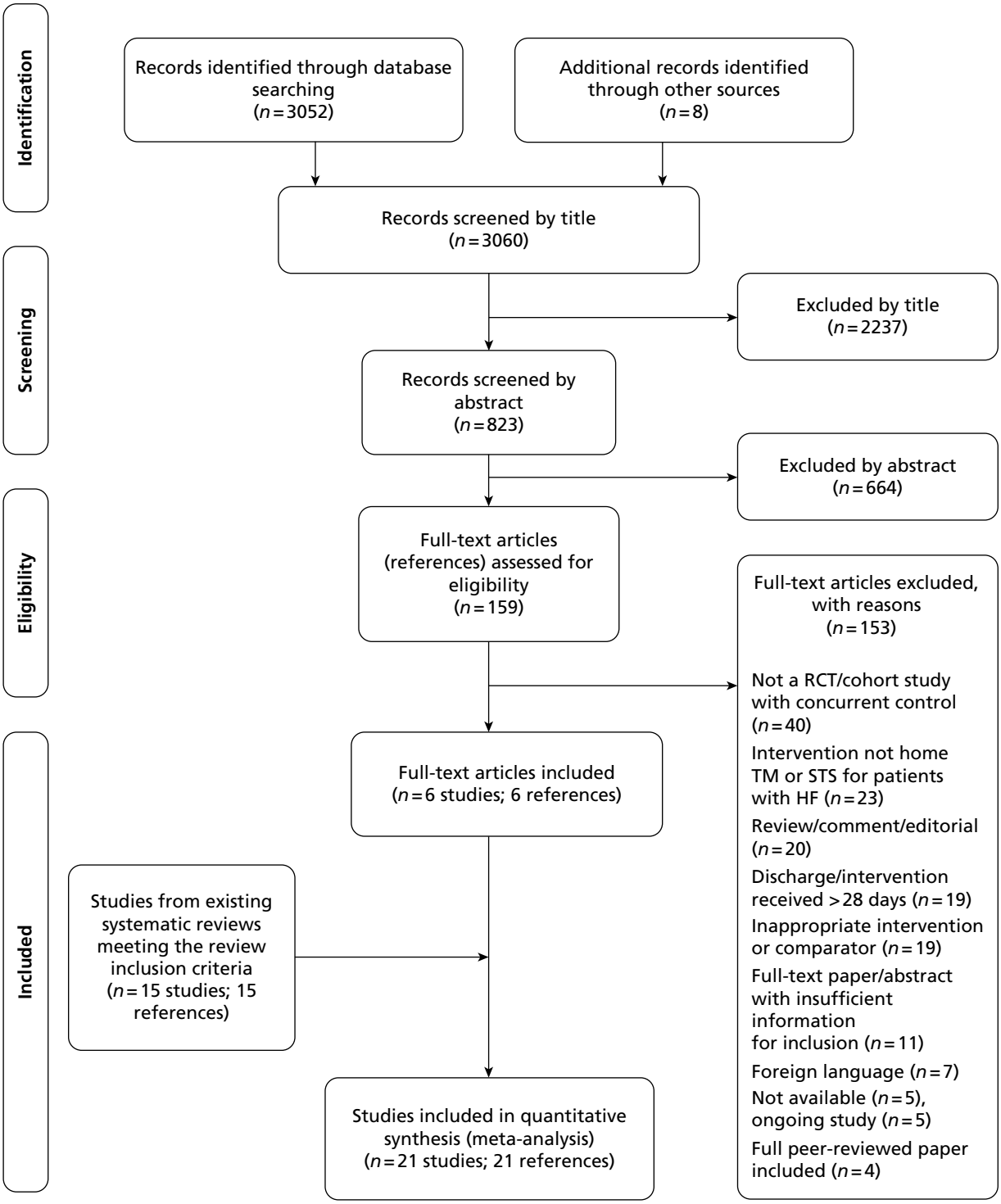

FIGURE 1 Flow chart (adapted): clinical effectiveness.[84]

TABLE 5 Summary of design characteristics

Author, year	Country (sites)	Total patients	Intervention	Comparator	Follow-up duration	Primary outcome	Funding
STS HH vs TM vs usual care							
[b]Cleland *et al.* 2005 (TEN-HMS)[49]	Germany, Netherlands, UK (16 sites)	258	Structured (monthly) telephone-based monitoring (of symptoms and current medication) and education ($n = 173$). Managed by a HF specialist nurse	Standard care. Followed up by GP with pharmacological treatment according to individualised patient management plan ($n = 85$)	240 days and 450 days	Composite of any hospital admission or mortality	Joint European Union (Trans-European Network) and Philips Medical Systems
		253	Home TM. Twice-daily measurement, automatic transmission of weight, BP, HR and single-lead ECG ($n = 168$). Specialist nurse-led support (following automated alert, nurses provided advice directly or through GP for long-term changes in therapy) together with monthly telephone calls to assess the patient's symptoms and current medication. Management of patients according to preset guidelines	Standard care. Followed up by GP with pharmacological treatment according to individualised patient management plan ($n = 85$)	240 days and 450 days	Composite of any hospital admission or mortality	Joint European Union (Trans-European Network) and Philips Medical Systems
STS HM (e.g. telephone-based interactive response system) vs usual care							
Chaudhry *et al.* 2010 (Tele-HF)[52]	USA (33 cardiology practices)	1653	Structured (daily) telephone-based monitoring (of symptoms and weight) using an interactive voice response system ($n = 826$). Reviewed by a clinician every weekday except on holidays. Guideline-based therapy	Standard optimal care. Followed by local physician. Guideline-based therapy ($n = 827$)	6 months	Composite of readmission for any reason or death	National Heart, Lung, and Blood Institute, USA
STS HH vs usual care							
[a]Angermann *et al.* 2011 (INH)[51]	Germany (nine hospitals)	708	Structured (weekly during the first month, then individualised: fortnightly in NYHA class III and IV, monthly in NYHA class I and II) telephone-based monitoring (of symptoms and current medication) and modular education ($n = 352$). Managed by trained nurses who were supervised by a cardiologist and a psychologist	Standard care. Followed up by GP plus 6-monthly visits to a HF clinic ($n = 363$)	6 months	Composite of time to all-cause death or rehospitalisation	German Ministry of Education and Research, German Competence Network Heart Failure, University of Wurzburg, Germany

continued

TABLE 5 Summary of design characteristics (*continued*)

Author, year	Country (sites)	Total patients	Intervention	Comparator	Follow-up duration	Primary outcome	Funding
[a,b]Barth 2001[72]	USA (one hospital)	34	Structured (at 72 hours, 144 hours and then fortnightly) telephone-based monitoring (of signs, symptoms and weight) and education ($n = 17$). Nurse-managed	Standard care (no details provided) ($n = 17$)	3 months	NR	NR
[a,b]DeBusk *et al.* 2004[74]	USA (five hospitals)	462	Structured (weekly for 6 weeks, biweekly for 8 weeks and then monthly and bimonthly) telephone-based HF lifestyle education and medication management ($n = 228$). Physician-directed nurse-managed case management	NR; however, standard care appeared to involve a high frequency of all kinds of follow-up clinic visit (13 in 12 months following hospitalisation) ($n = 234$)	12 months	Composite of rehospitalisation for HF or all-cause rehospitalisation	National Heart, Lung, and Blood Institute, USA
Domingues *et al.* 2011[69]	Brazil (one tertiary hospital)	120	Structured (weekly for first month, every 15 days for following 2 months) telephone-based education and monitoring of signs and symptoms of decompensation ($n = 57$). Nurse managed	Standard care (no details provided) ($n = 63$)	3 months	Level of HF awareness and self-care knowledge	Fundação Instituto de Pesquisas Econômicas (FIPE) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Brazil
[a,b]Laramee *et al.* 2003[77]	USA (one hospital)	287	Structured (weekly for first 4 weeks, then biweekly) telephone-based monitoring (of signs and symptoms) and education ($n = 141$). Nurse managed	Standard care. Followed up by local physician (44% received some home care services) ($n = 146$)	3 months	All-cause readmission	University of Vermont General Clinical Research Centre and Novartis Pharmaceuticals

Author, year	Country (sites)	Total patients	Intervention	Comparator	Follow-up duration	Primary outcome	Funding
[a]Rainville 1999[78]	USA (one site)	38	Structured (at days 3, 7, 30 and 90 and 12 months) telephone-based education, medication review and management and weight monitoring ($n = 19$). Pharmacist led	Standard care. Followed up by pharmacist at 30 days, 90 days and 12 months to determine readmissions ($n = 19$)	12 months	Composite of hospital readmission for HF or mortality	NR
[a,b]Riegel *et al.* 2002[79]	USA (two hospitals)	358	Structured (at day 5 and thereafter at a frequency guided by the software and case manager) telephone-based education and monitoring of signs and symptoms (e.g. weight, fluid retention, dyspnoea) ($n = 130$). Nurse managed with guidance and liaison with primary care physician	Non-standardised care (no details provided) ($n = 228$)	6 months	HF rehospitalisations	Pfizer Inc., USA
[a,b]Riegel *et al.* 2006[80]	USA (two hospitals)	135	Structured (at day 5 and thereafter at a frequency guided by the software and case manager) telephone-based education and monitoring of signs and symptoms indicating worsening illness ($n = 70$). Nurse managed with guidance and liaison with primary care physician	Non-standardised care (no details provided) ($n = 65$)	6 months	HF rehospitalisations	American Heart Association, USA
[a]Tsuyuki *et al.* 2004 (REACT)[81]	Canada (10 hospitals)	276	Structured (at 2 and 4 weeks and then monthly for 6 months) telephone-based education and monitoring of signs and symptoms (including salt and fluid restriction and weight) ($n = 140$). Managed by local research co-ordinator with recommended follow-up by local physician for pharmacological therapy	Standardised care (no details provided) ($n = 136$)	6 months	Medication adherence	Pfizer, Canada and University of Alberta Hospital Foundation, Canada
[a]Wakefield *et al.* 2008[82]	USA (one hospital)	148	Structured (three times in first week, then weekly for 11 weeks) telephone- or videophone-based education and monitoring of signs and symptoms (including weight, BP and ankle circumference) ($n = 99$). Managed by trained nurses	NR; however, subjects contacted their primary care nurse case manager by telephone if needed ($n = 49$)	12 months	Readmission rates	Veterans Health Administration, Health Services Research & Development Service, USA

continued

TABLE 5 Summary of design characteristics (*continued*)

Author, year	Country (sites)	Total patients	Intervention	Comparator	Follow-up duration	Primary outcome	Funding
TM vs usual care							
[a]Antonicelli *et al.* 2008[71]	Italy (one hospital)	57	Home TM. Weekly measurement, manual transmission of weight, BP, HR, 12-lead ECG, 24-hour urine output ($n = 28$). Reviewed by HF team at least once per week and patient management (including therapeutic regimens) modified accordingly	Standard care. Followed by a HF specialist team (including routinely scheduled clinic visits) ($n = 29$)	12 months	Composite of mortality and hospitalisation	Italian Ministry of Health, Italy
[a]Capomolla *et al.* 2004[73]	Italy (one hospital)	133	Home TM. Daily measurement, manual transmission (using touchpad of home or mobile telephone to an interactive voice response system) of weight, systolic BP, HR and symptoms ($n = 67$). Automated alert (via computer software) prompting a telephone call by nurse or physician to the patient at home. Individualised care plan designed by the physician	Standard care. Followed up by GP with support of a cardiologist. During follow-up the process of care was governed by different providers with a heterogeneous range of strategies: emergency room management, hospital admission and outpatient access ($n = 66$)	12 months	Composite of rehospitalisation, emergency room access and total mortality	Ministero della Salute, Italy
Dar *et al.* 2009 (Home-HF)[67]	UK (three acute hospitals)	182	Home TM. Daily measurement, manual transmission of weight, BP, HR, oxygen saturation and symptoms ($n = 91$). Data were reviewed daily (Monday to Friday) by HF nurses. Variation of parameters outside predefined limits triggered an alert and resulted in a telephone call for further assessment	Standard care. Each site had a specialist HF service including at least one cardiologist or physician with an interest in HF and at least one HF specialist nurse. Regular clinical follow-ups were scheduled at the discretion of the HF team and telephone support was available during office hours ($n = 91$)	6 months	Days alive and outside of hospital	Honeywell HomMed, UK

Author, year	Country (sites)	Total patients	Intervention	Comparator	Follow-up duration	Primary outcome	Funding
Dendale *et al.* 2011 (TEMA-HF 1)[68]	Belgium (seven hospitals)	160	Home TM. Daily measurement, automatic transmission of weight, BP, HR ($n = 80$). Automated email alert to GP and HF clinic. Followed up by GP visit or contact. Guideline-based therapy	Standard care. Followed up by GP (with referral to specialist cardiologist if needed). Guideline-based therapy. No intervention by study nurse or HF clinical team ($n = 80$)	6 months	All-cause mortality	Belgian Government Health Insurance Institute and Leo Pharma, Belgium
[a,b]Goldberg *et al.* 2003 (WHARF)[75]	USA (16 sites)	280	Home TM. Daily measurement, manual transmission of weight and symptoms ($n = 138$). Data reviewed daily by nurses (7 days a week, 365 days a year; however, system was not active 24 hours a day) and concerns reported to a treating physician. Guideline-driven HF care (with additional nursing resources)	Standard care. Followed up by treating physician (at discretion) in a dedicated outpatient HF programme with additional nursing resources. In addition, patients undertook daily weight measurements and were instructed to contact their physician for weight increases of more than a prespecified amount or if their symptoms of HF worsened ($n = 142$)	6 months (mean)	Hospital readmission	Alere Medical, Inc., USA
[a,b]Kielblock *et al.* 2007[76]	Germany (sites NR)	502	Home TM. Daily measurement, automatic transmission of weight ($n = 251$). Automated alert to the HF specialist team, which prompted a telephone call by a designated personal adviser. Followed up by GP (24-hour on-demand telephone service including medical support)	Standard care (no details provided) ($n = 251$)	12 months	Hospital stay	NR

continued

TABLE 5 Summary of design characteristics (*continued*)

Author, year	Country (sites)	Total patients	Intervention	Comparator	Follow-up duration	Primary outcome	Funding
[a]Kulshreshtha *et al.* 2010[60]	USA (one hospital)	110	Home TM. Daily measurement, manual transmission of weight, BP, pulse and pulse oximetry ($n = 68$). Nurse-led support (including physician or cardiologist notification, referral to emergency room) together with weekly telephone calls to provide additional information (including evaluation of home TM readings and telephone assessment) and monitor adherence	Standard care (no details provided) ($n = 42$)	6 months	All-cause rehospitalisation rate	Partners Healthcare, USA
Scherr *et al.* 2009 (MOBITEL)[70]	Austria (eight centres)	120	Home TM. Daily measurement, manual transmission of weight, BP, HR and dosage of HF medication ($n = 66$). Automated e-mail alert prompting a telephone call from a physician via mobile telephone. Guideline-based therapy	Standard care. Pharmacological treatment according to guideline-based therapy ($n = 54$)	6 months	Composite of cardiovascular mortality/hospital readmission for worsening HF	Novartis Pharma, Roche Pharma and Mobikom, Austria
[a,b]Woodend *et al.* 2008[83]	Canada (one site)	121	Home TM. Daily measurement, manual transmission of weight, BP and 12-lead ECG (periodic) ($n = 62$). Reviewed weekly by telehome-care nurse via video conference (frequent in first few weeks and tapered over 3 months). Triage protocol-based management	Standard care. Followed up by community physician or cardiologist (no further details provided) ($n = 59$)	3 and 12 months	NR	Richard Ivey Foundation, Change Foundation and Merck-Frosst Canada

BP, blood pressure; ECG, electrocardiogram; Home-HF, Home Heart Failure Study; HR, heart rate; INH, Interdisciplinary Network for Heart Failure; MOBITEL, MOBIle TELemonitoring in Heart Failure Patients Study; NR, not reported; REACT, Review of Education on ACE Inhibitors in Congestive Heart Failure Treatment; TEMA-HF, TElemonitoring in the MAnagement of Heart Failure; TEN-HMS, Trans-European Network – Home-Care Management System; WHARF, Weight Monitoring in Heart Failure.

a Identified in review by Inglis *et al.*[48]

b Identified in review by Klersy *et al.*[58]

TABLE 6 Summary of patient characteristics at baseline

Author, year	Population	Mean age (years)	Male (%)	NYHA class	Autonomy (living alone) (%)	LVEF for inclusion	Period between remote intervention and hospital discharge
STS HH vs TM vs usual care							
[a,b]Cleland *et al.* 2005 (TEN-HMS)[49]	Patients (aged ≥18 years) with a recent admission for HF and LVEF <40%	67	77	I–IV	NR	<40%	<6 weeks (assumed majority received intervention <4 weeks from discharge)
STS HM (e.g. telephone-based interactive response system) vs usual care							
Chaudhry *et al.* 2010 (Tele-HF)[52]	Patients recently hospitalised for HF	NR	58	I–IV (6% I; 37% II; 51% III; 7% IV)	NR	NR	<30 days (assumed majority received intervention <4 weeks from discharge)
STS HH vs usual care							
[a]Angermann *et al.* 2011 (INH)[51]	Patients (aged ≥18 years) hospitalised with signs and symptoms of decompensated (systolic) HF with evidence of pulmonary congestions on chest radiography and LVEF ≤40% (echocardiography)	69	71	I–IV (2% I; 58% II; 36% III; 4% IV)	33	≤40%	<28 days
[a,b]Barth 2001[72]	Patients discharged from acute care to home with primary diagnosis of HF	75	47	NR	32	NR	<72 hours
[a,b]DeBusk *et al.* 2004[74]	Patients hospitalised with a provisional diagnosis of HF (based on clinical signs and symptoms or evidence of pulmonary congestions on chest radiography)	72	51	I–IV (49% I–II; 51% III–IV)	NR	NR	<2 weeks
Domingues *et al.* 2011[69]	Hospitalised patients (aged ≥18 years) with HF (diagnosed using Boston diagnostic criteria) and LVEF ≤45%	63	64	NR	NR	≤45%	<1 week
[a,b]Laramee *et al.* 2003[77]	Patients admitted to hospital with primary or secondary diagnosis of HF (based on clinical signs and symptoms, left ventricular dysfunction <40% or radiological evidence of pulmonary oedema and symptomatic improvement following diuresis)	71	54	I–IV (16% I; 43% II; 33% III; 2% IV; missing, 6%)	NR	<40%	1–3 days

continued

TABLE 6 Summary of patient characteristics at baseline (*continued*)

Author, year	Population	Mean age (years)	Male (%)	NYHA class	Autonomy (living alone) (%)	LVEF for inclusion	Period between remote intervention and hospital discharge
[a]Rainville 1999[78]	Patients (aged ≥50 years) discharged from hospital with HF	70	50	II–IV	NR	NR	<3 days
[a,b]Riegel *et al.* 2002[79]	Patients discharged from hospital with HF	74	49	II–IV (3% II; 38% III; 59% IV)	NR	NR	<5 days
[a,b]Riegel *et al.* 2006[80]	Hospitalised Hispanic patients with a primary or secondary diagnosis of HF, living in the community	72	46	II–IV (19% II; 46% III; 35% IV)	NR	NR	<5 days
[a]Tsuyuki *et al.* 2004 (REACT)[81]	Patients (aged >18 years) discharged from hospital with HF	72	58	I–IV (13% I; 50% II; 33% III; 4% IV)	NR	NR	<2 weeks
[a]Wakefield *et al.* 2008[82]	Patients hospitalised for HF exacerbation (e.g. volume overload, pulmonary oedema)	69	99	II–IV (28% II; 65% III; 7% IV)	NR	NR	<1 week
TM vs usual care							
[a]Antonicelli *et al.* 2008[71]	Patients (aged ≥70 years) hospitalised for worsening symptoms and signs of HF (NYHA classes II–IV) with evidence of pulmonary congestion on chest radiography and ejection fraction on echocardiography	78	61	II–IV (58% II; 37% III; 5% IV)	NR	NR	<1 week
[a]Capomolla *et al.* 2004[73]	Patients discharged from specialist HF unit to home	57	88	II–IV (67% II; NR III; NR IV)	NR	NR	<1 day
Dar *et al.* 2009 (Home-HF)[67]	Patients discharged after hospitalisation with HF (defined by ESC criteria: either a new diagnosis or an acute decompensation of CHF) and NYHA class II–IV symptoms	71	66	II–IV	NR	NR	Mean 4 days (after randomisation)

Author, year	Population	Mean age (years)	Male (%)	NYHA class	Autonomy (living alone) (%)	LVEF for inclusion	Period between remote intervention and hospital discharge
Dendale *et al.* 2011 (TEMA-HF 1)[68]	Patients hospitalised for fluid overload due to HF requiring an increase or initiation of diuretic therapy (treated with ACE inhibitor or angiotensin II receptor antagonist with beta-blocker, if tolerated)	76	65	≥ III	NR	NR	<1 day
[a,b]Goldberg *et al.* 2003 (WHARF)[75]	Patients admitted to hospital with decompensated advanced HF (NYHA classes III–IV) secondary to systolic dysfunction (LVEF <35%, measured within 6 months of enrolment)	59	68	III–IV (74% III; 26% IV)	20	≤35%	<1 day
[a,b]Kielblock *et al.* 2007[76]	Patients discharged after hospitalisation with HF or with a confirmed diagnosis from ICD codes from hospital insurance data	74	51	I–IV (NR I; NR II, 17% III; 28% IV)	NR	NR	<2 weeks
[a]Kulshreshtha *et al.* 2010[60]	Hospitalised (current admission or recently discharged within previous 2 weeks) or high risk for readmission (cardiac-related reasons or ejection fraction ≤20%), non-homebound patients (age >18 years) with HF	68	64	NR	NR	≤20%	<14 days
Scherr *et al.* 2009 (MOBITEL)[70]	Patients (aged 18–80 years) with acute worsening of HF (acute cardiac decompensation) with hospitalisation >24 hours in the last 4 weeks	NR	71	NR	NR	NR	<4 weeks
[a,b]Woodend *et al.* 2008[83]	Patients with symptomatic HF (NYHA class II or greater)	68	72	II–IV	NR	NR	<2 days

Home-HF, Home Heart Failure Study; ICD, *International Classification of Diseases*; INH, Interdisciplinary Network for Heart Failure; MOBITEL, MOBIle TELemonitoring in Heart Failure Patients Study; NR, not reported; REACT, Review of Education on ACE Inhibitors in Congestive Heart Failure Treatment; TEMA-HF, TElemonitoring in the MAnagement of Heart Failure; TEN-HMS, Trans-European Network – Home-Care Management System; WHARF, Weight Monitoring in Heart Failure.

a Identified in review by Inglis *et al.*[48]

b Identified in review by Klersy *et al.*[58]

STS programmes generally included regular scheduled telephone contact between patients and health-care providers (usually on a weekly/monthly basis) and incorporated telephone-based education and monitoring of signs and symptoms of worsening HF. The TM programmes generally used patient-initiated external electronic devices with daily transfer of physiological data (mainly weight, blood pressure and heart rate) from the patient to the health-care provider using a landline, a mobile telephone or broadband technology. With the exception of one study (which provided 24/7 medical support),[76] all transmitted data (including alerts) in TM programmes were reviewed by medical staff (nurses and/or physicians) and support provided during office hours (in one study[75] nurses reviewed transmitted data on a daily basis 7 days a week, 365 days a year; however, the system was not active 24/7).

All studies were published between 1999 and 2011. The studies were carried out in a variety of countries and regions including Europe [Austria, $n = 1$; Belgium, $n = 1$; Germany, $n = 2$; Italy, $n = 2$; UK, $n = 1$; and a combination of countries (Germany, Netherlands and the UK), $n = 1$], North America (USA, $n = 10$; Canada, $n = 2$) and South America (Brazil, $n = 1$). The duration of follow-up ranged from 3 months[69,72,77,83] to 15 months.[49] Although all of the included studies were required to perform STS and/or home TM interventions at least once within the first 28 days following discharge from hospital, two studies performed the intervention outside this period (within 30 days[52] or within 6 weeks).[49] For both of these studies it was assumed that the majority of patients would have received the intervention within 28 days of discharge. Of the 21 studies, 10 received funding from one or more commercial sponsors.[49,60,67,68,70,75,77,79,81,83] The sample sizes of the included studies ranged from 34[72] to 1653[52] patients, with the mean age of participants ranging from 57 years[73] to 78 years.[71] Only three studies recruited more women than men,[72,79,80] with the number of male participants ranging from 46%[80] to 99%.[82] One trial was restricted to patients with a LVEF of <35%,[75] three trials were restricted to patients with a LVEF of ≤40%,[49,51,77] one trial was restricted to patients with a LVEF of <45%[69] and the LVEF inclusion criterion was not reported in 16 studies.[52,60,67,68,70–74,76,78–83]

Quality characteristics

The overall methodological quality of the 21 included studies is summarised in *Figure 2* and *Table 7*. Generally, nine studies performed well,[49,51,52,67,68,74,75,80,81] receiving a positive assessment of at least six out of nine methodological quality items. Potential sources of high bias most frequently identified in studies concerned baseline comparability of important prognostic factors (24%), adequate power to detect differences in the primary outcome (19%) and reporting of numbers and reasons for loss to follow-up

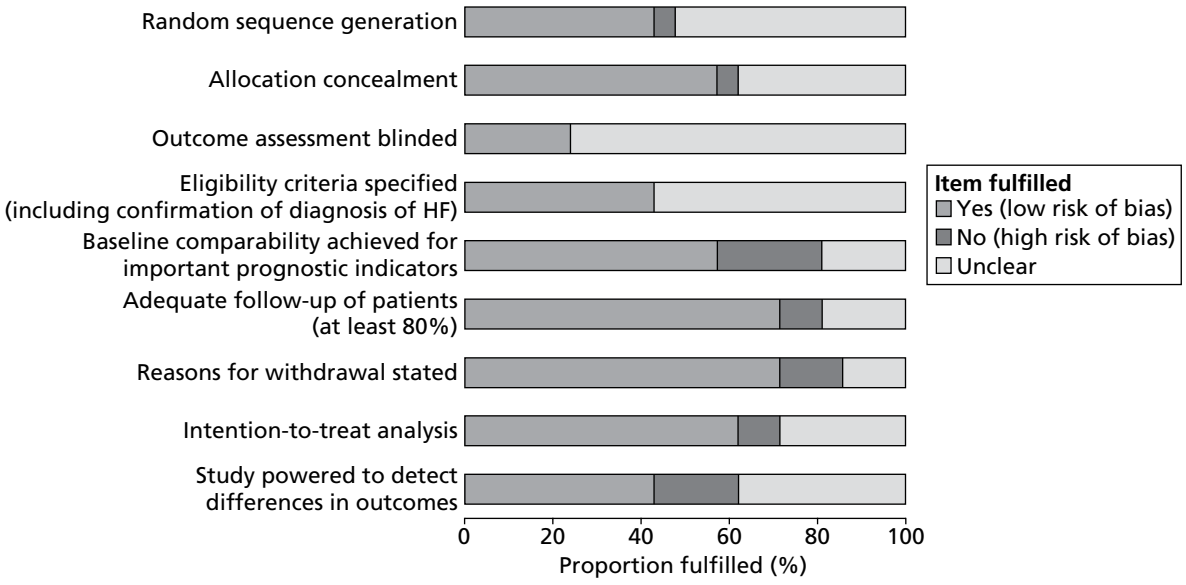

FIGURE 2 Methodological quality graph: review authors' judgements about each methodological quality item as percentages across all included studies.

TABLE 7 Methodological quality summary: review authors' judgements about each methodological quality item for each included study

	Methodological assessment criteria[a]								
Author, year	1	2	3	4	5	6	7	8	9
[b]Angermann *et al.* 2011 (INH)[51]	Y	Y	Y	Y	Y	Y	Y	Y	Y
Antonicelli *et al.* 2008[71]	U	U	U	Y	Y	U	N	U	Y
Barth 2001[72]	U	U	U	U	Y	U	N	U	U
Capomolla *et al.* 2004[73]	U	U	U	U	Y	Y	U	U	U
[b]Chaudhry *et al.* 2010 (Tele-HF)[52]	Y	Y	Y	U	Y	Y	Y	Y	Y
[b]Cleland *et al.* 2005 (TEN-HMS)[49]	Y	Y	U	U	U	Y	Y	Y	Y
[b]Dar *et al.* 2009 (Home-HF)[67]	Y	Y	U	Y	Y	Y	Y	Y	N
[b]DeBusk *et al.* 2004[74]	Y	Y	Y	Y	Y	Y	Y	Y	Y
[b]Dendale *et al.* 2011 (TEMA-HF 1)[68]	Y	U	U	U	Y	Y	Y	Y	Y
Domingues *et al.* 2011[69]	U	U	U	Y	Y	Y	Y	N	U
[b]Goldberg *et al.* 2003 (WHARF)[75]	U	Y	Y	Y	Y	Y	Y	Y	U
Kielblock *et al.* 2007[76]	N	U	U	Y	N	U	U	U	U
Kulshreshtha *et al.* 2010[60]	U	N	U	U	Y	Y	Y	Y	U
Laramee *et al.* 2003[77]	U	U	U	Y	N	N	Y	U	U
Rainville 1999[78]	U	Y	U	U	N	Y	Y	N	U
Riegel *et al.* 2002[79]	U	Y	U	U	N	U	U	U	N
[b]Riegel *et al.* 2006[80]	U	Y	Y	U	U	Y	Y	Y	Y
Scherr *et al.* 2009 (MOBITEL)[70]	Y	Y	U	U	U	Y	Y	Y	N
[b]Tsuyuki *et al.* 2004 (REACT)[81]	Y	Y	U	U	N	Y	Y	Y	Y
Wakefield *et al.* 2008[82]	Y	Y	U	U	Y	N	Y	Y	N
Woodend *et al.* 2008[83]	U	U	U	Y	U	Y	N	Y	Y

Home-HF, Home Heart Failure Study; INH, Interdisciplinary Network for Heart Failure; MOBITEL, MOBIle TELemonitoring in Heart Failure Patients Study; N, no (high risk of bias); REACT, Review of Education on ACE Inhibitors in Congestive Heart Failure Treatment; TEMA-HF, TElemonitoring in the MAnagement of Heart Failure; TEN-HMS, Trans-European Network – Home-Care Management System; U, unclear (insufficient detail to make judgement); WHARF, Weight Monitoring in Heart Failure; Y, yes (low risk of bias).

a 1 = Was the method used to assign participants to the treatment groups really random?; 2 = Was allocation concealment to each group performed adequately (e.g. centrally) and group assignment revealed after provision of consent?; 3 = Were the outcome assessors/data analysts blinded to the treatment allocations?; 4 = Were the eligibility criteria for study entry specified (including confirmation of diagnosis of HF); 5 = Was baseline comparability achieved for the most important prognostic indicators?; 6 = Was follow-up of patients adequate (at least 80%)?; 7 = Were the reasons for withdrawal stated?; 8 = Was an intention-to-treat analysis included?; 9 = Was the study powered to detect differences in outcomes?

b Study received a positive assessment on at least six of the nine quality assessment items.

(14%). The majority of publications poorly described the following aspects: random sequence generation (52%), allocation concealment (38%), blinding of outcome assessment (76%) and intention-to-treat analysis (29%). Although all studies specified eligibility criteria for study entry, the majority (57%) poorly described the definition and confirmation of diagnosis of HF.

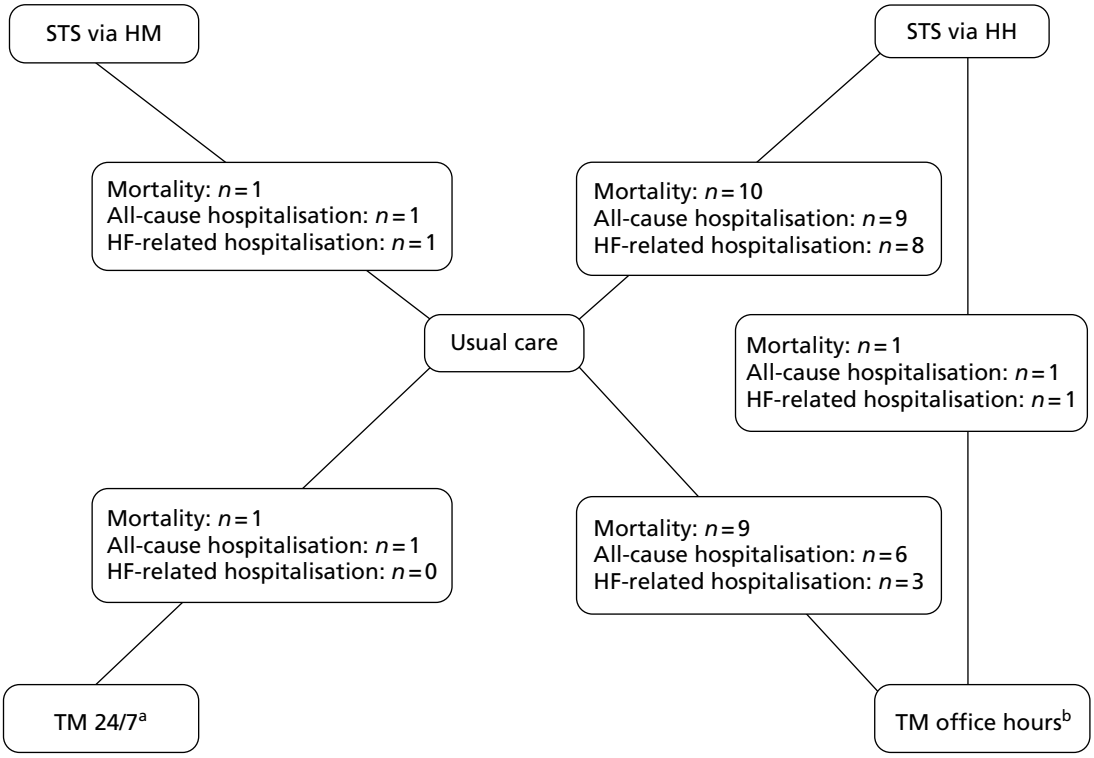

FIGURE 3 Network diagram of different RM programmes compared with usual care in recently discharged patients with HF. The nodes are the interventions. The numbers against each outcome represent the numbers of times that each pair of interventions has been compared. There was one multiarm study comparing STS via HH, TM during office hours and usual care. a, Transmitted data reviewed by medical staff (or medical support provided) 24 hours per day, 7 days per week. b, Transmitted data reviewed by medical staff (or medical support provided) during office hours.

Effects of interventions

A NMA was undertaken to compare the comparative efficacy of RM (STS or TM) and usual care. *Figure 3* presents the network of evidence. A total of 21 studies comparing different pairs or triplets of interventions provided information on at least one of the outcomes being analysed, although not all studies provided information on each outcome. One study[72] was excluded from the network analysis because there were no events in each intervention arm and, as a consequence, it provided no information about the intervention effects.[86] A sensitivity analysis was performed excluding data from Dar *et al*.[67] (Home Heart Failure Study; Home-HF) because it provided better-than-usual support and optimal medical treatment to patients in the control groups and also appeared to be inconsistent with the data from the remaining studies (i.e. an outlier). A summary of all of the trials (data) included in the base-case NMA is presented in *Appendix 7*.

Primary analyses (recently discharged patients with heart failure)

All-cause mortality All-cause mortality data were available from 20 studies,[49,51,52,60,67–71,73–83] including one three-arm study (STS HM, $n = 1$; STS HH, $n = 10$; TM with medical support provided during office hours, $n = 9$; TM 24/7, $n = 1$). *Table 8* summarises the all-cause mortality data for the NMA of RM compared with usual care.

The NMA model fitted the data reasonably well, with a residual deviance close to the total number of data points included in the analysis. The total residual deviance was 42.87, which compared favourably with the 40 non-zero data points being analysed. However, the model did not represent the data from the Dar *et al.* (Home-HF)[67] and Dendale *et al.* (TEMA-HF 1; TElemonitoring in the MAnagement of Heart Failure)[68] studies particularly well. The between-study standard deviation was estimated to be 0.34 (95% CrI 0.03

TABLE 8 All-cause mortality in recently discharged patients with HF: posterior distribution for the HRs relative to usual care (random effects)

	HR and CrI			Predictive interval	
Treatment	Median	2.5%	97.5%	2.5%	97.5%
STS					
HM	0.98	0.41	2.33	0.30	3.23
HH	0.77	0.55	1.08	0.31	1.86
TM					
Office hours[a]	0.76	0.49	1.18	0.30	1.91
24/7[b]	0.49	0.20	1.18	0.14	1.73
Usual care					
Reference	Reference	Reference	Reference	Reference	Reference
Between-study standard deviation (log-HR scale)	0.34	0.03	0.75	–	–

a Transmitted data reviewed by medical staff (or medical support provided) during office hours.
b Transmitted data reviewed by medical staff (or medical support provided) 24 hours per day, 7 days per week.

to 0.75). This indicated that there was small to moderate heterogeneity between studies in the treatment effect. All interventions showed a beneficial trend in reducing all-cause mortality compared with usual care. The intervention that exhibited the greatest effect was TM 24/7 (HR 0.49; 95% CrI 0.20 to 1.18); however, this result should be treated with caution because of the poor methodological quality of the only included study in this network.[76] STS HH (HR 0.77; 95% CrI 0.55 to 1.08) and TM during office hours (HR 0.76; 95% CrI 0.49 to 1.18) both had similar effects on all-cause mortality. In addition, the heterogeneity in the effect of RM between studies means that the intervention effects in a randomly chosen study vary substantially depending on the characteristics of the study.

A sensitivity analysis was performed excluding the Home-HF study[67] (*Table 9*). The heterogeneity in intervention effects between studies was considerably reduced. The interventions that exhibited the greatest effects were TM 24/7 (HR 0.49; 95% CrI 0.26 to 0.88) (although this result should be treated with caution because of the poor methodological quality of the only included study in this network[76]), TM during office hours (HR 0.62; 95% CrI 0.42 to 0.89) and STS HH (HR 0.75; 95% CrI 0.59 to 0.96).

All-cause hospitalisation All-cause hospitalisation data were available from 16 studies,[49,51,52,67,69,70,71,74–77,79–83] including one three-arm study (STS HM, $n = 1$; STS HH, $n = 9$; TM with medical support provided during office hours, $n = 6$; TM 24/7, $n = 1$). *Table 10* summarises the all-cause hospitalisation data for the NMA of RM compared with usual care.

The NMA model fitted the data reasonably well, with a residual deviance (36.85) close to 33, the total number of data points included in the analysis. However, the model did not represent the data from Antonicelli *et al.*[71] particularly well. The between-study standard deviation was estimated to be 0.38 (95% CrI 0.13 to 0.74). This indicated that there was small to moderate heterogeneity between studies in the treatment effect. The intervention that exhibited the greatest effect was TM with medical support provided during office hours (HR 0.75; 95% CrI 0.49 to 1.10). In addition, the heterogeneity in the effect of RM between studies means that the intervention effects in a randomly chosen study vary substantially depending on the characteristics of the study.

A sensitivity analysis was performed excluding the Home-HF study[67] (*Table 11*). There was little impact on the heterogeneity in intervention effects between studies. As before, the intervention that exhibited

TABLE 9 All-cause mortality in recently discharged patients with HF (excluding Dar et al.[67]): posterior distribution for the HRs relative to usual care (random effects)

	HR and CrI			Predictive interval	
Treatment	Median	2.5%	97.5%	2.5%	97.5%
STS					
HM	0.98	0.58	1.62	0.49	1.95
HH	0.75	0.59	0.96	0.45	1.27
TM					
Office hours[a]	0.62	0.42	0.89	0.35	1.09
24/7[b]	0.49	0.26	0.88	0.23	1.04
Usual care					
Reference	Reference	Reference	Reference	Reference	Reference
Between-study standard deviation (log-HR scale)	0.14	0.01	0.47	–	–

a Transmitted data reviewed by medical staff (or medical support provided) during office hours.
b Transmitted data reviewed by medical staff (or medical support provided) 24 hours per day, 7 days per week.

TABLE 10 All-cause hospitalisation in recently discharged patients with HF: posterior distribution for the HRs relative to usual care (random effects)

	HR and CrI			Predictive interval	
Treatment	Median	2.5%	97.5%	2.5%	97.5%
STS					
HM	1.06	0.44	2.53	0.31	3.61
HH	0.97	0.70	1.31	0.38	2.43
TM					
Office hours[a]	0.75	0.49	1.10	0.28	1.91
24/7[b]	0.81	0.33	2.00	0.23	2.85
Usual care					
Reference	Reference	Reference	Reference	Reference	Reference
Between-study standard deviation (log-HR scale)	0.38	0.13	0.74	–	–

a Transmitted data reviewed by medical staff (or medical support provided) during office hours.
b Transmitted data reviewed by medical staff (or medical support provided) 24 hours per day, 7 days per week.

the greatest effect was TM with medical support provided during office hours (HR 0.67; 95% CrI 0.42 to 0.97), although the heterogeneity in the effect of RM between studies means that the intervention effects in a randomly chosen study vary substantially depending on the characteristics of the study.

Heart failure-related hospitalisation Heart failure-related hospitalisation data were available from 11 studies,[49,51,52,67,74,75,77–81] including one three-arm study (STS HM, $n = 1$; STS HH, $n = 8$; TM with medical support provided during office hours, $n = 3$). *Table 12* summarises the HF-related hospitalisation data for the NMA of RM compared with usual care.

TABLE 11 All-cause hospitalisation in recently discharged patients with HF (excluding Dar et al.[67]): posterior distribution for the HRs relative to usual care (random effects)

	HR and CrI			Predictive interval	
Treatment	Median	2.5%	97.5%	2.5%	97.5%
STS					
HM	1.06	0.48	2.32	0.35	3.22
HH	0.96	0.72	1.27	0.42	2.18
TM					
Office hours[a]	0.67	0.42	0.97	0.26	1.53
24/7[b]	0.81	0.36	1.81	0.27	2.50
Usual care					
Reference	Reference	Reference	Reference	Reference	Reference
Between-study standard deviation (log-HR scale)	0.33	0.08	0.69	–	–

a Transmitted data reviewed by medical staff (or medical support provided) during office hours.
b Transmitted data reviewed by medical staff (or medical support provided) 24 hours per day, 7 days per week.

TABLE 12 HF-related hospitalisation in recently discharged patients with HF: posterior distribution for the HRs relative to usual care (random effects)

	HR and CrI			Predictive interval	
Treatment	Median	2.5%	97.5%	2.5%	97.5%
STS					
HM	1.03	0.66	1.54	0.58	1.77
HH	0.77	0.62	0.96	0.50	1.19
TM					
Office hours[a]	0.95	0.70	1.34	0.59	1.62
24/7[b]	NA	NA	NA	NA	NA
Usual care					
Reference	Reference	Reference	Reference	Reference	Reference
Between-study standard deviation (log-HR scale)	0.11	0.00	0.42	–	–

NA, not applicable.
a Transmitted data reviewed by medical staff (or medical support provided) during office hours.
b Transmitted data reviewed by medical staff (or medical support provided) 24 hours per day, 7 days per week.

The NMA model fitted the data reasonably well, with a residual deviance (22.18) close to 23, the total number of data points included in the analysis. However, the model did not represent the data from the Dar *et al.* (Home-HF)[67] and Rainville[78] studies particularly well. The between-study standard deviation was estimated to be 0.11 (95% CrI 0.00 to 0.42). This indicated that there was small heterogeneity between studies in the treatment effect. The intervention that exhibited the greatest effect was STS HH (HR 0.77; 95% CrI 0.62 to 0.96).

A sensitivity analysis was performed excluding the Home-HF study[67] (*Table 13*). There was little impact on the heterogeneity in intervention effects between studies. As before, the intervention that exhibited the greatest effect was STS HH (HR 0.76; 95% CrI 0.61 to 0.94).

Length of stay Of the 11 studies reporting on STS intervention programmes compared with usual care,[51,52,69,73,74,77–82] six studies reported length of stay data.[52,77,79–82] Of these, only the study by Tsuyuki *et al.*[81] reported a statistically significant reduction in the length of stay in hospital between the STS programme and the usual care group (total: 627 vs 1082 days respectively, $p<0.001$; average: 6.6 vs 11.0 days respectively, $p<0.001$). Of the nine studies reporting on TM intervention programmes compared with usual care, two studies reported length of stay data.[67,83] These studies found no significant differences between the groups in the number of days spent in hospital at 180 days (17 vs 13 days respectively, $p=0.99$)[67] or in the first year post discharge (7.13 vs 6.71 days respectively, $p=$ not significant).[83] The study that assessed both STS and TM intervention programmes reported no significant differences in the length of stay for hospital admissions between groups during 240 days of follow up ($p=$ not significant for all comparisons).[49]

Quality of life Quality of life was a secondary outcome measure in eight of the 21 included studies.[51,67,71,72,75,80,82,83] These were either a direct comparison between intervention and control groups at study conclusion[51,67,80,83] or a comparison between baseline and study conclusion within the study arm.[71,72,75,82] A range of psychometric measures were used including both generic and HF-specific measures: SF-36,[51,71,83] the Short Form questionnaire-12 items (SF-12),[76] the Health Distress Score (HDS),[75] the Minnesota Living with Heart Failure Questionnaire (MLHFQ),[67,72,75,80,82,83] and the European Quality of Life-5 Dimensions (EQ-5D).[67,80]

Three of the four STS studies reported improvements in QoL, with significant improvements in physical ($p=0.03$)[51] and overall (MLHFQ, $p<0.001$)[72,82] measures. One study found no significant differences between groups in either the MLHFQ or the EQ-5D measure.[80] Four TM studies measured QoL.[67,71,75,83] Of these, two reported improvements in QoL (SF-36 health perception, $p=0.046$;[71] MLHFQ, $p=0.025$ and SF-36, $p<0.05$[83]). Although Goldberg *et al.*[75] observed improvements in QoL, none of the measures was significant (MLHFQ, $p=0.22$; SF-12, $p>0.05$; HDS, $p=0.57$). Similarly, Dar *et al.*[67] found no significant

TABLE 13 HF-related hospitalisation in recently discharged patients with HF (excluding Dar et al.[67]): posterior distribution for the HRs relative to usual care (random effects)

	HR and CrI			Predictive interval	
Treatment	**Median**	**2.5%**	**97.5%**	**2.5%**	**97.5%**
STS					
HM	1.02	0.70	1.49	0.61	1.69
HH	0.76	0.61	0.94	0.51	1.13
TM					
Office hours[a]	0.86	0.61	1.21	0.54	1.38
24/7[b]	NA	NA	NA	NA	NA
Usual care					
Reference	Reference	Reference	Reference	Reference	Reference
Between-study standard deviation (log-HR scale)	0.10	0.00	0.39	–	–

NA, not applicable.

a Transmitted data reviewed by medical staff (or medical support provided) during office hours.

b Transmitted data reviewed by medical staff (or medical support provided) 24 hours per day, 7 days per week.

differences between groups in either the MLHFQ ($p = 0.6$) or the EQ-5D ($p = 0.5$) measure over a 6-month follow-up period.

System acceptability and patient satisfaction Only 5 of the 21 included studies reported adherence (compliance) rates to the intervention.[51,52,67,73,75] Adherance was measured at 55.1%[52]–84.0%[51] for STS and 81.0%[73]–98.5%[75] for TM. Some further data were available on system acceptability and patient satisfaction. Cleland *et al.*[49] reported an overall acceptance rate of 91.2% with 96% of participants expressing satisfaction with the system and 97% reporting that the device was easy to use. Riegel *et al.*[79] reported significantly higher satisfaction among patients receiving TM than among those receiving usual care ($p = 0.01$), and Laramee *et al.*[77] reported higher satisfaction among STS patients than among usual care patients ($p < 0.01$). Kielblock *et al.*[76] reported very high satisfaction among TM patients, with 57% rating the programme 'very good' and the remaining 43% rating it as 'quite good'. Woodend *et al.*[83] reported satisfaction scores of between 92 and 97 out of 100 on a 10-item checklist. Scherr *et al.*[70] reported early termination of their study because of an increasing number of patients who were unable to operate the TM equipment, with 12 participants (10%) failing to transmit any readings and a further four requesting early termination. Finally, Kulshreshtha *et al.*[60] reported that, of 82 patients offered TM, 40 refused participation: 24 patient refusals and 16 physician refusals.

Additional analyses (patients with stable heart failure)

Additional analyses were undertaken to assess whether or not the results from the primary analysis differed markedly from the results in those with stable HF who were managed in the community. In this supplementary analysis the following studies were included: RCTs comparing HF management delivered via STS, TM or cardiovascular implanted monitoring devices with HF management delivered via usual post-discharge care in stable HF patients (defined as having no acute event or deterioration in the past 28 days) who were managed in the community setting (ambulatory or outpatient care). Studies that included intensified management with additional home or clinic visits were excluded. Although no formal critical appraisal of these studies was undertaken, the results were meta-analysed (as per the methods of the primary analysis) and are presented in this section for information only. All studies published before 2008 were identified from Inglis *et al.*[48] and Klersy *et al.*[58] whereas more recent studies (meeting these criteria) were identified from the current review. The design and patient characteristics of the 21 included studies that evaluated home TM (including cardiovascular implanted monitoring devices) or STS programmes for adults with stable HF are briefly summarised in *Appendix 8*. A network of 18 studies comparing different pairs or triplets of treatments is shown in *Figure 4* (data included in the base-case NMA are presented in *Appendix 9*).

All-cause mortality

Structured telephone support or telemonitoring compared with usual care All-cause mortality data were available from 17 studies,[50,87–102] including one three-arm study (STS HM, $n = 2$; STS HH, $n = 6$; TM with medical support provided during office hours, $n = 7$; TM 24/7, $n = 3$). *Table 14* summarises the all-cause mortality data for the NMA of RM compared with usual care.

The residual deviance, 28.76, was <35, the total number of data points included in the analysis, suggesting that the meta-analysis model may not be a good representation of the data. The between-study standard deviation was estimated to be 0.12 (95% CrI 0.01 to 0.38). This indicated that there was little heterogeneity between studies in the treatment effect. All interventions except for STS HM showed a beneficial trend in reducing all-cause mortality compared with usual care, although these effects were not conclusive.

Cardiovascular implanted monitoring devices compared with non-monitoring cardiovascular implanted monitoring devices (usual care) Of the three studies[103–105] that compared cardiovascular implanted monitoring devices with non-monitoring cardiovascular implanted monitoring devices (usual care), there was an indication of small to extreme heterogeneity between the studies in the treatment effect.

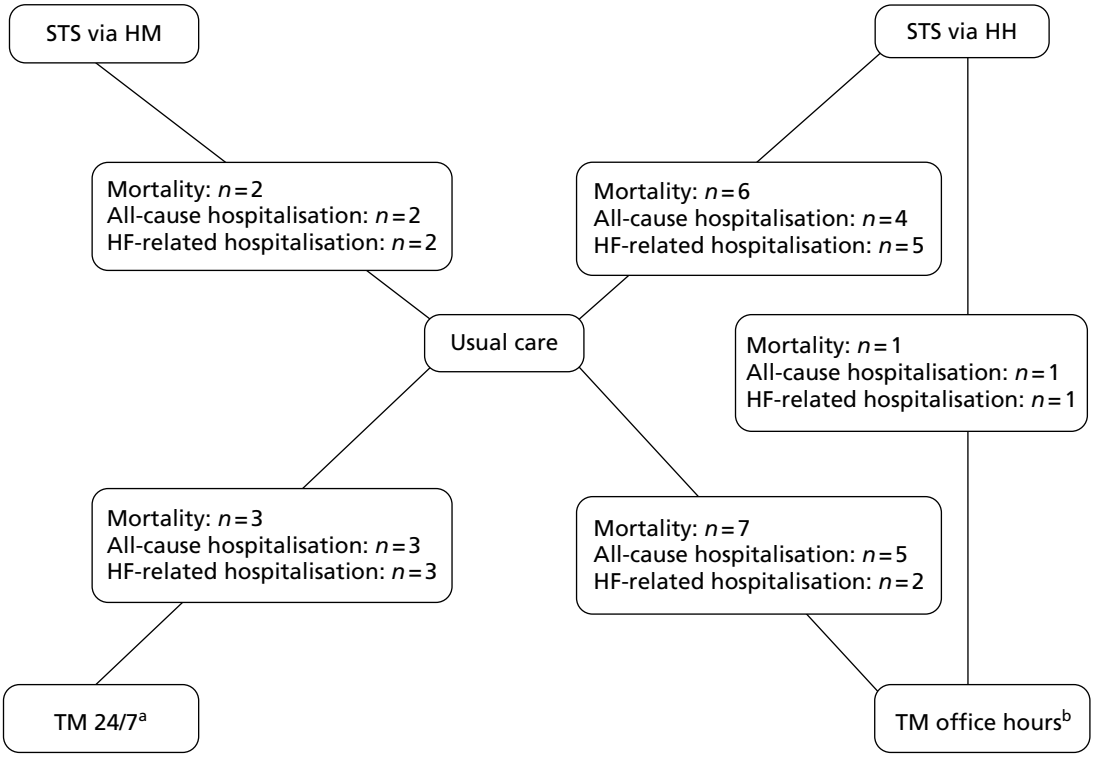

FIGURE 4 Network diagram of different RM programmes compared with usual care in patients with stable HF. The nodes are the interventions. The numbers against each outcome represent the number of times that each pair of interventions has been compared. There was one multiarm study comparing STS via HH, TM during office hours and usual care. a, Transmitted data reviewed by medical staff (or medical support provided) 24 hours per day, 7 days per week. b, Transmitted data reviewed by medical staff (or medical support provided) during office hours.

TABLE 14 All-cause mortality in patients with stable HF: posterior distribution for the HRs relative to usual care (random effects)

	HR and CrI			Predictive interval	
Treatment	**Median**	**2.5%**	**97.5%**	**2.5%**	**97.5%**
STS					
HM	1.35	0.78	2.36	0.71	2.67
HH	0.87	0.69	1.14	0.57	1.42
TM					
Office hours[a]	0.85	0.59	1.20	0.52	1.37
24/7[b]	0.85	0.58	1.27	0.47	1.39
Usual care					
Reference	Reference	Reference	Reference	Reference	Reference
Between-study standard deviation (log-HR scale)	0.12	0.01	0.38	–	–

a Transmitted data reviewed by medical staff (or medical support provided) during office hours.

b Transmitted data reviewed by medical staff (or medical support provided) 24 hours per day, 7 days per week.

The between-study standard deviation was estimated to be 0.26 (95% CrI 0.01 to 1.63). Although cardiovascular implanted monitoring devices appeared to be associated with a reduction in mortality compared with usual care, this result was inconclusive (*Table 15*). In addition, the heterogeneity in the effect of cardiovascular implanted monitoring devices between studies means that the intervention effect in a randomly chosen study varies substantially depending on the characteristics of the study.

All-cause hospitalisation All-cause hospitalisation data were available from 13 studies,[50,88,90–93,95,97–102] including one three-arm study (STS HM, $n = 2$; STS HH, $n = 4$; TM with medical support provided during office hours, $n = 5$; TM 24/7, $n = 3$). *Table 16* summarises the all-cause hospitalisation data for the NMA of RM compared with usual care.

The NMA model fitted the data well, with a residual deviance (27.11) close to 27, the total number of data points included in the analysis. The between-study standard deviation was estimated to be 0.23 (95% CrI 0.07 to 0.49). This indicated that there was little heterogeneity between studies in the treatment effect. All interventions except for TM with medical support provided during office hours showed a beneficial trend in reducing all-cause hospitalisation compared with usual care, although these effects were not conclusive.

TABLE 15 All-cause mortality in patients with stable HF: posterior distribution for the HRs relative to non-monitoring cardiovascular implanted monitoring devices (random effects)

	HR and CrI			Predictive interval	
Treatment	Median	2.5%	97.5%	2.5%	97.5%
Cardiovascular implanted monitoring devices	0.90	0.31	2.49	0.12	5.21
Usual care[a]					
Reference	Reference	Reference	Reference	Reference	Reference
Between-study standard deviation (log-HR scale)	0.26	0.01	1.63	–	–

a Usual care defined as non-monitoring cardiovascular implanted monitoring devices.

TABLE 16 All-cause hospitalisation in patients with stable HF: posterior distribution for the HRs relative to usual care (random effects)

	HR and CrI			Predictive interval	
Treatment	Median	2.5%	97.5%	2.5%	97.5%
STS					
HM	0.87	0.54	1.29	0.44	1.74
HH	0.86	0.62	1.17	0.45	1.62
TM					
Office hours[a]	1.17	0.89	1.59	0.62	2.18
24/7[b]	0.84	0.54	1.15	0.40	1.47
Usual care					
Reference	Reference	Reference	Reference	Reference	Reference
Between-study standard deviation (log-HR scale)	0.23	0.07	0.49	–	–

a Transmitted data reviewed by medical staff (or medical support provided) during office hours.
b Transmitted data reviewed by medical staff (or medical support provided) 24 hours per day, 7 days per week.

Heart failure-related hospitalisation

Structured telephone support or telemonitoring compared with usual care Heart failure-related hospitalisation data were available from 11 studies,[50,88,90–93,97,99,100,102,106] including one three-arm study (STS HM, $n = 2$; STS HH, $n = 5$; TM with medical support provided during office hours, $n = 2$; TM 24/7, $n = 3$). *Table 17* summarises the HF-related hospitalisation data for the NMA of RM compared with usual care.

The NMA model fitted the data reasonably well, with a residual deviance (26.50) close to 23, the total number of data points included in the analysis. The between-study standard deviation was estimated to be 0.31 (95% CrI 0.03 to 1.05). This indicated that there was small to extreme heterogeneity between studies in the treatment effect. All interventions showed a beneficial trend in reducing all-cause hospitalisation compared with usual care, although these effects were not conclusive. In addition, the heterogeneity in the effect of interventions between studies means that the effect in a randomly chosen study varies substantially depending on the characteristics of the study.

Cardiovascular implanted monitoring devices compared with non-monitoring cardiovascular implanted monitoring devices (usual care) Of the three studies[103–105] that compared cardiovascular implanted monitoring devices with non-monitoring cardiovascular implanted monitoring devices (usual care), there was an indication of small to moderate heterogeneity between studies in the treatment effect. The between-study standard deviation was estimated to be 0.24 (95% CrI 0.01 to 0.64). Although cardiovascular implanted monitoring devices appeared to be associated with a reduction in HF-related hospitalisation, this result was inconclusive (*Table 18*).

Discussion

The NMA showed that, compared with usual care, STS HH, TM with medical support provided during office hours and TM 24/7 were associated with a 23%, 24% and 51% reduction in all-cause mortality, respectively, among adults who have been recently discharged (<28 days) from an acute care setting after a recent exacerbation of HF. However, the results for TM 24/7 should be treated with caution because of the poor methodological quality of the only included study in this network.[76] No beneficial effect on mortality was observed with STS HM. TM with medical support during office hours and TM 24/7 were associated with a 25% and 19% reduction in all-cause hospitalisations, respectively, whereas there was

TABLE 17 Heart failure-related hospitalisation in patients with stable HF: posterior distribution for the HRs relative to usual care (random effects)

	HR and CrI			Predictive interval	
Treatment	Median	2.5%	97.5%	2.5%	97.5%
STS					
HM	0.69	0.34	1.43	0.23	2.11
HH	0.67	0.37	1.05	0.22	1.75
TM					
Office hours[a]	0.70	0.34	1.50	0.19	2.30
24/7[b]	0.64	0.34	1.14	0.23	1.89
Usual care					
Reference	Reference	Reference	Reference	Reference	Reference
Between-study standard deviation (log-HR scale)	0.31	0.03	1.05	–	–

a Transmitted data reviewed by medical staff (or medical support provided) during office hours.
b Transmitted data reviewed by medical staff (or medical support provided) 24 hours per day, 7 days per week.

TABLE 18 HF-related hospitalisation in patients with stable HF: posterior distribution for the HRs relative to cardiovascular implanted non-monitoring devices (random effects)

	HR and CrI			Predictive interval	
Treatment	Median	2.5%	97.5%	2.5%	97.5%
Cardiovascular implanted monitoring devices	0.72	0.32	1.37	0.14	3.01
Usual care[a]					
Reference	Reference	Reference	Reference	Reference	Reference
Between-study standard deviation (log-HR scale)	0.24	0.01	0.64	–	–

a Usual care defined as cardiovascular implanted non-monitoring devices.

no major effect of STS HM or STS HH. STS HH was associated with a reduction of 23% in HF-related hospitalisations. There was no major effect of STS HM and TM with medical support during office hours on HF-related hospitalisations. In addition, despite the limited data, STS and TM generally improved QoL and were acceptable to patients.

Although the present findings broadly support the conclusions of the latest review and meta-analysis by Inglis *et al.*,[48] there were some points on which the results differed. Despite differences between the two reviews in the classification of the RM strategies and in the statistical approaches to conducting the meta-analyses, STS HH was found to have a larger effect on mortality reduction than the pooled results of STS trials in the Inglis *et al.*[48] review [HR 0.77, 95% CrI 0.55 to 1.08 vs risk ratio (RR) 0.88, 95% CI 0.76 to 1.01]. Effects on all-cause hospitalisation (HR 0.97; 95% CrI 0.70 to 1.31 vs RR 0.92, 95% CI 0.85 to 0.99) and HF-related hospitalisation (HR 0.77, 95% CrI 0.62 to 0.96 vs RR 0.77, 95% CI 0.68 to 0.87) were similar between the two reviews. However, the findings from the analysis of STS HM were less favourable than those of Inglis *et al.*[48] for all-cause mortality (HR 0.98, 95% CrI 0.41 to 2.33 vs RR 0.88, 95% CI 0.76 to 1.01), all-cause hospitalisation (HR 1.06, 95% CrI 0.44 to 2.53 vs RR 0.92, 95% CI 0.85 to 0.99) and HF-related hospitalisation (HR 1.03, 95% CrI 0.66 to 1.54 vs RR 0.77, 95% CI 0.68 to 0.87). In addition, the present results were less favourable for TM during office hours (i.e. transmitted data reviewed by medical staff or medical support provided during office hours) for all-cause mortality (HR 0.76, 95% CrI 0.49 to 1.18 vs RR 0.66, 95% CI 0.54 to 0.81, respectively), but more favourable for all-cause hospitalisation (HR 0.75, 95% CrI 0.49 to 1.10 vs RR 0.91, 95% CI 0.84 to 0.99), and worse for HF-related hospitalisation (HR 0.95, 95% CrI 0.70 to 1.34 vs RR 0.79, 95% CI 0.67 to 0.94). Notably, when a sensitivity analysis excluding the results from the Home-HF study[67] was conducted, the findings for TM effectiveness were similar to those observed in the Inglis *et al.*[48] review.

When interpreting these diverging results, a number of differences in the methodology and data sets used in the respective reviews should be borne in mind. Most importantly, the present NMA distinguished between two types of STS (HH and HM) and two types of TM (transmitted data reviewed by medical staff or support provided during office hours, or transmitted data reviewed by medical staff or support provided 24/7). As the analysis showed, effectiveness varied substantially according to the type of system used, with, in particular, greater favourability towards STS HH than STS HM. Furthermore, the present analysis included the Home-HF study,[67] which was excluded from the Inglis *et al.* review[48] because of the use of an initial nurse visit (for equipment installation and use) as part of the care package. Inclusion of this trial in the analysis substantially reduced TM clinical effectiveness. However, given the low mortality rate in the control group of the Home-HF trial,[67] the results of this study may not be generalisable to the wider HF population. This review also had a more stringent definition of the population of interest than the Inglis review[48] (i.e. patients who commenced RM ≤28 days post discharge). Given what is known about the risk of mortality following decompensation,[15] it may be that the present review focused on a patient population for whom RM is particularly efficacious. If this assumption holds, it might appear surprising that the NMA did not find substantially greater benefits of RM than those observed in the Inglis

et al. review.[48] However, it should be noted that the standard and quality of usual care for HF continues to evolve (generally this was poorly reported in all included studies); thus, the impact of the age of the study on the treatment effects may have been an important confounding factor in the observed results.

In addition to the studies from the Inglis *et al.* review,[48] six new studies[52,60,67–70] of RM were included in the present review. These trials were of variable methodological quality with only three studies[52,67,68] performing well and receiving a positive assessment of at least six out of nine methodological quality items. Perhaps most notable was the inclusion of the largest trial of STS to date ($n = 1653$),[52] which has already generated considerable debate.[107–109] The Tele-HF trial[52] delivered STS using HM and found no benefit over usual care. Although this trial was well designed and reported (see *Table 7*), a low patient adherence rate was observed (55%) and the control group received good quality of care. In response to such criticisms of Tele-HF, Chaudhry *et al.*[52] have pointed out that patients were given individual counselling to support engagement with RM and thus the 55% adherence rate probably represents the 'best case scenario' for real-world clinical practice.[109] These investigators further argued that the >50% event rate (rehospitalisation or death) in the usual care group did not suggest an excellent standard of care. There may, however, be further questions raised by the Tele-HF trial. For example, it is possible that interpersonal interaction with a care provider is an important active component of STS. It seems plausible that regular telephone contact with a care provider provides psychosocial benefits that feed into self-care practices and QoL, particularly among socially isolated older people. Similarly, Anker *et al.*[46] suggested that remote contact between patients and care providers could help detect depression, which is associated with poor outcomes in HF. Furthermore, the mortality rate of 11.4% in the usual care group of the Tele-HF study was low compared with usual clinical practice.[14]

The Home-HF study[67] was a RCT that compared TM with usual care. The trial included 182 patients from the UK with a recent hospital admission for HF and in NYHA classes II–IV. There was a higher incidence of mortality among the TM group than among the usual care group (17 vs 5 using the intention-to-treat approach or 14 vs 4 after TM equipment installation). These results may appear surprising at first glance and could even be read as showing a detrimental effect of TM compared with usual care. However, the 6-month mortality rate in the usual care group (5.5%) was substantially lower than would be expected in a HF cohort receiving care outside the context of a clinical trial (i.e. between 13% and 21%).[14] The authors stated that the standard of usual care was of high quality in the Home-HF trial, consisting of an initial home visit from a specialist nurse and access to telephone support during working hours. In addition, most patients were receiving optimal medical treatment including ACE inhibitors (70%), beta-blockers (56%) and loop diuretics (93%). Whatever the reason for the lack of effectiveness in the Home-HF[67] and Tele-HF[52] trials, the results at least serve as caution that all RM interventions (i.e. packages of care) are not necessarily effective in all contexts.

One TM study from Germany,[76] which was conducted in collaboration with a health insurance company, reported provision of round-the-clock support to address participants' questions about medication and the TM system. The 24-hour call centre approach has been reccomended elsewhere on the grounds that HF is a dynamic illness and so patients may need quick medical response 24 hours a day.[110] In comparison with office hours-only services, the 24-hour provision appeared to confer additional benefits for mortality but not for all-cause hospitalisation or HF-related hospitalisation. However, the results from the trial of 24/7 monitoring should be treated with caution as the study had serious methodological shortcomings (see *Table 7*). In particular, the method used to assign groups (i.e. by date of birth) was not ideally random and the intervention group ($n = 251$) was significantly younger than the control group ($n = 251$) (73 years vs 78 years, $p < 0.001$). Even if the results from this study are interpreted as a reduction in short- and medium-term mortality arising from maximisation of medical therapy, it is unlikely that out-of-hours events were sufficiently frequent to result in alterations of therapy that would not have occurred in an office hours-only system. Moreover, in the UK, an existing round-the-clock response system is available through the 999 emergency response route; thus, RM interventions provided by the NHS have been during office hours only.

Additional analyses were performed to assess whether or not the findings from the present review (primary analysis) differed markedly in patients with stable HF (i.e. defined as having no acute event or detrioration in the past 28 days and managed in an ambulatory or outpatient care setting). These analyses suggested that inclusion of stable patients reduced the effectiveness of STS (both HH and HM) for mortality but provided additional reductions in both all-cause hospitalisation and HF-specific hospitalisation. With respect to TM during office hours, inclusion of stable patients yielded a marginally greater hazard reduction for mortality, a substantially greater reduction for HF-related hospitalisation and a substantially worse outcome for all-cause hospitalisation. Inclusion of stable patients in the 24/7 TM interventions yielded a substantially lower hazard reduction for all-cause mortality, a marginally lower hazard reduction for all-cause hospitalisation and a greater hazard reduction for HF-related hospitalisation. It is not clear how these apparently contradictory results should be interpreted, particularly given that no formal assessment of study quality was conducted on the studies involving stable patients. Finally, inclusion of stable patients allowed an analysis of RM effectiveness in three studies of implanted cardiac devices.[103–105] The findings showed a trend towards a reduction in all-cause mortality (HR 0.90, 95% CrI 0.31 to 2.49) and HF-related hospitalisation (HR 0.72, 95% CrI 0.32 to 1.37).

There are a number of limitations to the findings of this meta-analysis. Perhaps most importantly, the interventions were heterogeneous in terms of the physiological parameters remotely transmitted and the type of RM system utilised (see *Table 4*), so it may be argued that this review is a meta-analysis of a family of similar interventions rather than a single standardised intervention. For the 10 included TM studies, the most commonly monitored parameters were weight ($n = 10$) followed by blood pressure ($n = 8$) and heart rate ($n = 7$). Of the two UK trials, the TEN-HMS (Trans-European Network – Home-Care Management System) study[49] monitored weight, blood pressure, electrocardiogram and heart rate, whereas the Home-HF study[67] monitored weight, blood pressure, heart rate, oxygen saturation and symptoms (breathlessness, orthopnoea, dizziness and ankle swelling). However, this meta-analysis was unable to establish whether or not monitoring different parameters provided different levels of clinical benefit. STS interventions were somewhat more homogeneous in terms of monitored parameters, with the majority including an educational component and questions about worsening symptoms. However, the frequency of monitoring varied widely in these studies, from three times in the first week[82] to monthly.[49] In addition, it is important to note that usual care for HF has improved over recent decades. Diagnosis may occur earlier because of initiatives to improve HF awareness among primary care physicians and because of the increased availability of diagnostic tests. Furthermore, HF self-management programmes led by specialist nurses, which have been shown to reduce mortality and morbidity, are now widely used in HF care.[45] The estimated 6-month survival rate for HF in the UK rose from 74.5% in 1996–7 (95% CI 70.6% to 77.9%) to approximately 85.7% in 2004–5 (95% CI 81.8% to 88.8%).[111] With these improvements, it is possible that present usual care delivery may confound the effects of RM. A final issue for trial comparability was the diagnostic criteria used to confirm HF. More than half of the included trials did not report how the presence of HF was assessed,[49,52,60,68,70,72,73,78–82] and among the remaining trials a variety of criteria were used.

The difficulty in interpreting the findings from these trials is further compounded by the fact that few studies presented outcomes in such a way as to allow stratification by age and sex in meta-regression – a problem also noted in the previous Inglis *et al.* review.[48] Hence, the analysis was unable to establish patient subgroups in which RM is particularly effective. Another limitation concerns the quality of reporting in the included studies, which varied widely (see *Table 7*). In particular, a substantial number of studies were underpowered to detect differences in the primary outcome measures,[60,67,69,70,72,73,75–79,82] although this is not a concern in terms of the meta-analysis. However, there was evidence of several further potential sources of bias among the included studies. In particular, either outcome assessors were unblinded or blinding status was unclear in 16 trials.[49,60,67–73,76–79,81–83] Another issue for external validity was the commercial funding reported by 10 studies[49,60,67,68,70,75,77,79,81,83] as receipt of such funding has also been shown to systematically bias trials in favour of the products made by the companies that fund the research.[112]

Further, foreign language studies were excluded and no cohort studies met the inclusion criteria for this review. Although RCTs are generally viewed as representing the most robust form of evidence for treatment efficacy, they have been criticised for a narrow focus on highly selected populations and outcomes.[113] Cohort studies, on the other hand, are more open to potential sources of bias but may offer a more realistic representation of how outcomes play out in the complex real world of clinical practice.[114] A previous meta-analysis by Klersy *et al.*[58] included 12 cohort studies of RM. The pooled results showed that RM was associated with a significantly lower number of deaths ($n = 6$ studies, RR 0.53, 95% CI 0.29 to 0.96, $p < 0.001$) and hospitalisations ($n = 3$ studies, RR 0.52, 95% CI 0.28 to 0.96, $p < 0.001$). However, the included studies had a number of internal/external validity issues. In particular, half of the studies used a pre/post-test design without a concurrent control (which could result in a Hawthorne effect being mistaken for a genuine clinical effect) and several included a programme of home visits in the RM intervention (further details are provided in *Overview of existing systematic reviews* and *Appendix 4*). The literature search for this meta-analysis identified one cohort study of implanted RM devices, which included stable HF patients[115] and was therefore not eligible for inclusion in the meta-analysis. All of the cohort studies from the Klersy *et al.*[58] review were also excluded because of the application of more stringent inclusion criteria. Clearly, well-designed cohort studies with concurrent control groups are lacking among the RM evidence base. Another limitation of the present meta-analysis was that, given the heterogeneity in the RM systems, the analysis was unable to establish the precise 'active ingredients' of RM. Given that RM is a complex intervention (i.e. made up of a variety of interconnected, socially situated factors), it is important to understand not only whether RM works, but also how, why and under what circumstances.[116] One way to explore these issues would be to include qualitative research on patient experiences of RM in subsequent updates.

Finally, it should be noted that this review did not include data from the Department of Health's WSD programme.[117] The WSD programme is the largest randomised trial of RM to date, including 6191 patients from 238 GP practices across three areas: Newham, Kent and Cornwall. The trial included people with one of three chronic conditions (HF, diabetes and COPD) and the headline results[57] suggest an even more dramatic reduction in mortality (45%) than the pooled results reported here. An effect size as large as this has the potential to substantially alter the point estimates of the NMA. However, until data from the WSD programme become publicly available in peer-reviewed publications, it is difficult to evaluate the true magnitude and direction of effect in recently discharged patients with HF (or people with stable HF). As one perceptive commentator has noted, the Department of Health report states that telehealth can deliver the stated 45% mortality reduction 'if used correctly'[118] – and at present it is unclear what correct usage entails.

Chapter 4 Assessment of cost-effectiveness

This chapter details the methods and results of the health economic model, which has been developed to compare different strategies for adult patients who have been discharged from an acute care setting after a recent exacerbation of HF. It includes a brief review of existing economic evaluations and a detailed explanation of the methods and results of a de novo economic model. The first section presents the results of the systematic review of economic literature. The modelling approach adopted to estimate the cost-effectiveness of RM interventions is then presented followed by the results of the analysis. The chapter concludes with a discussion of the results.

Review of cost-effectiveness evidence

The objective of this review was to identify and evaluate studies exploring the cost-effectiveness of TM or STS programmes for patients with HF.

Identification of studies

Electronic databases

Studies were identified by searching the following electronic databases:

- MEDLINE(R) In-Process & Other Non-Indexed Citations and MEDLINE(R) (Ovid) 1948–January 2012
- EMBASE (Ovid) 1980–January 2012
- Science Citation Index Expanded (Web of Science) 1899–January 2012
- Conference Proceedings Citation Index – Science (Web of Science) 1990–January 2012
- NHS Health Economic Evaluation Database (Wiley Online Library) 1995–January 2012
- Health Technology Assessment database (Wiley Online Library) 1995–January 2012
- Database of Abstracts of Reviews of Effects (Wiley Online Library) 1995–January 2012
- PsycINFO (Ovid) 1806–January 2012
- Cumulative Index to Nursing and Allied Health Literature (EBSCO*host*) 1982–January 2012
- Allied and Complementary Medicine Database (Ovid) 1985–January 2012
- Health Economic Evaluations Database (OHE-IFPHA) 1967–January 2012.

Sensitive keyword strategies using free text and, where available, thesaurus terms using Boolean operators and database-specific syntax were developed to search the electronic databases. Synonyms relating to the condition (e.g. heart failure) were combined with sensitive economic evaluations (where applicable) or QoL search filters aimed at restricting results to economic and cost-related studies (used in the searches of MEDLINE, Cumulative Index to Nursing and Allied Health Literature and EMBASE). Essentially, the cost-effectiveness search strategy is the same as the clinical effectiveness search strategy albeit with the addition of an economic filter. The MEDLINE search strategy is provided in *Appendix 10*.

Other resources

To identify additional published, unpublished and ongoing studies, the reference lists of all relevant studies (including existing systematic reviews) were hand searched. A citation search of relevant articles (using the Web of Science Science Citation Index Expanded) was also undertaken. All identified citations from the electronic searches and other resources were imported into and managed using Reference Manager 12.

Inclusion and exclusion criteria

Studies were selected for inclusion according to predetermined inclusion and exclusion criteria. Studies were included if they reported an economic evaluation of disease management strategies or RM strategies

for HF patients and estimated the benefits in terms of life-years gained (LYG) or quality-adjusted life-years (QALYs).

Studies that performed economic evaluations alongside trials were excluded if they did not extrapolate the outcomes beyond the trial duration, as these economic analyses are valid only for the trials under consideration. Studies that were considered to be methodologically unsound, that were not reported in sufficient detail to extract costs and outcome estimates (including abstracts) or that did not report an estimate of cost-effectiveness (e.g. costing studies) were also excluded. Papers not published in the English language were also excluded.

The inclusion of potentially relevant articles was undertaken using a two-step process. First, all titles were examined for inclusion by one reviewer. Any citations that clearly did not meet the inclusion criteria, that is, non-human, unrelated to TM and/or HF, were excluded. Second, all abstracts and full-text articles were examined independently by two reviewers. Any disagreements in the selection process were resolved through discussion.

Quality assessment strategy

The methodological quality of each included study was assessed using a combination of key components of the Drummond and Jefferson checklist for economic evaluations[119,120] and the Eddy checklist for mathematical models used in technology assessments.[121] The use of the checklist ensured a consistent approach to assessing the quality of each economic evaluation.

Results of the cost-effectiveness review

The electronic literature searches identified 1696 potentially relevant publications. Of these, two studies[122,123] met the inclusion criteria. A flow chart describing the process of identifying relevant literature can be found in *Figure 5*. A full list of excluded studies is presented in *Appendix 11*. Further details of the included studies including an assessment of methodological quality are provided below.

Miller *et al.*[122] developed a Markov model to assess the long-term effect of a STS programme compared with usual care for patients diagnosed with systolic HF. The model considered three levels of severity corresponding to (1) NYHA class I, (2) NYHA class II and (3) a combination of NYHA classes III and IV. The input data for the model were abstracted from an 18-month trial in 1069 HF patients in south Texas.[87] This study was not included in the NMA as the STS programme included HF disease management from registered nurses. The authors used SF-36 data collected from the trial to calculate the utilities for each severity class using the methods suggested by Brazier *et al.*[124] The study was carried out from the health-care system perspective and the analysis estimated the incremental cost-effectiveness ratio (ICER) of the disease management group against usual care. STS compared with usual care had an estimated ICER equal to $43,650 per QALY gained, and the univariate sensitivity analysis suggested that the incremental cost per QALY gained varied from $28,691 (with the use of different death rates for the control and intervention groups) to $129,738 (with an increased disease management programme cost of $246 per patient per month).

The study by Miller *et al*.[122] performed satisfactorily on the majority of items in the critical appraisal checklists[119–121] used to assess the overall methodological quality of the model. Costs were extracted from the trial data by estimating the resource usage of different patient groups classified by morbidity and health state. Most of the costs were presented in a detailed and systematic way; however, the authors provided only an average cost of the STS programme and did not provide the breakdown of the individual cost components. One-way sensitivity analysis was performed; however, the authors did not perform a probabilistic sensitivity analysis (PSA). Both costs and QALYs were discounted at a rate of 3% per year.

Klersy *et al.*[123] assessed the cost-effectiveness of remote home TM for HF compared with usual care from a third payer perspective. A decision tree approach was used to compare the two strategies and the only outcome measured was admission for HF. To evaluate the clinical effectiveness of RM, a meta-analysis of

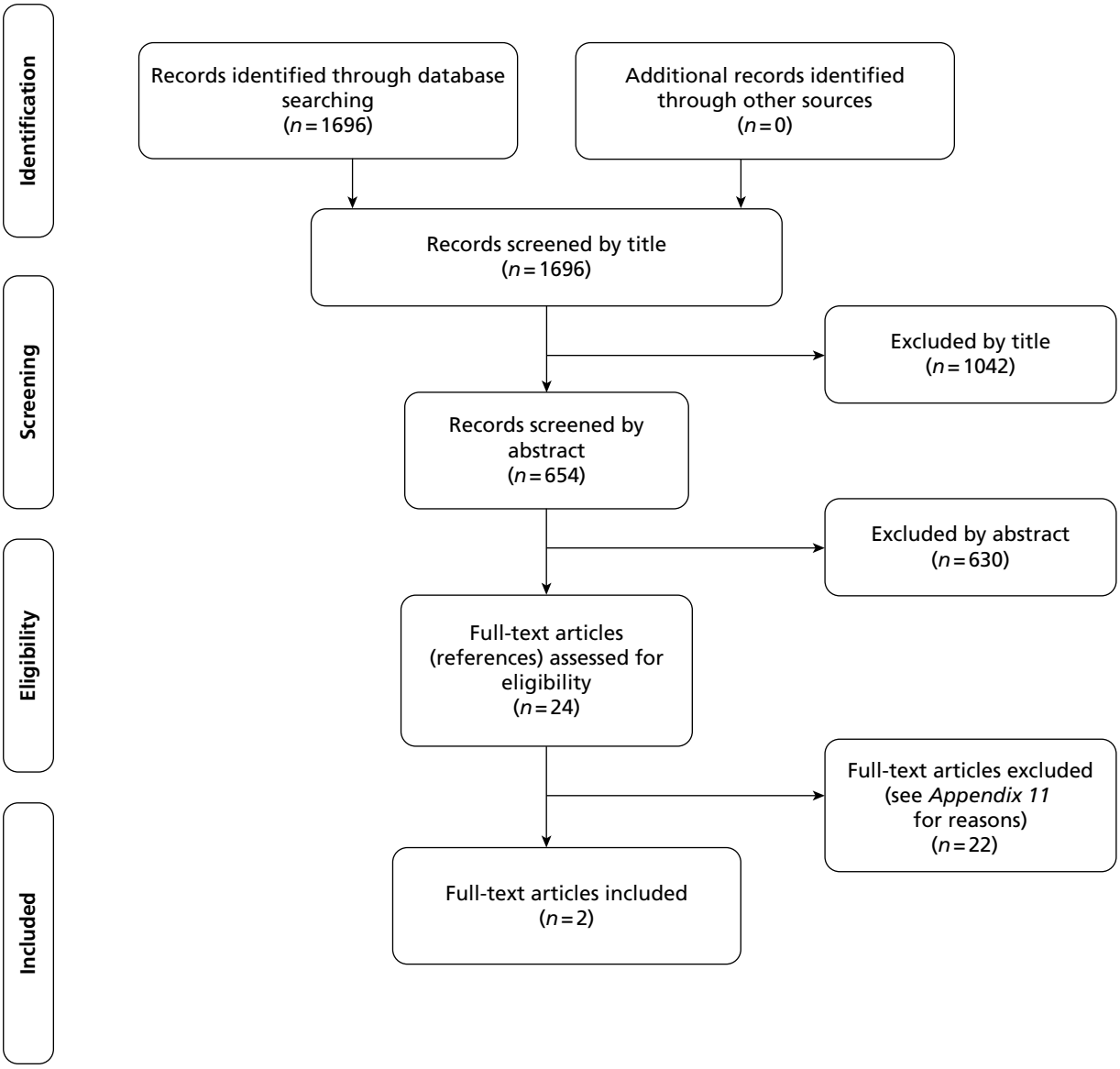

FIGURE 5 Study flow chart (adapted): cost-effectiveness.[84]

21 clinical trials assessing RM was carried out for this study. A budget impact analysis was presented and the different diagnosis-related group (DRG) reimbursement tariffs were considered with cost savings per patient ranging between €306.80 and €992.94.

Klersy *et al.*[123] focused mainly on the effectiveness rather than the costs and used a time horizon of 1 year. The study was limited to the budget impact and the cost-effectiveness was evaluated in this study by comparing the differences in costs and QALYs between RM and usual care. The effectiveness of RM was based on a meta-analysis of diverse studies evaluating interventions ranging from TM with home visits to STS. The authors used utilities of 0.612 and 0.662 for the usual care and RM groups respectively, based on a RCT reported by Hebert *et al.*[125] However, the study by Hebert *et al.*[125] was undertaken in an ethnically diverse urban community in Harlem, New York, and so the results might not be applicable to the UK HF population. Regarding costs, only hospitalisation costs were included and other costs such as RM costs, outpatient visits and drug costs were not considered. The authors stated that the monitoring costs were not considered because of the heterogeneity in the costs of RM. The authors used the DRG reimbursement tariff for HF hospitalisations as a proxy for real-life costs of hospitalisations. The authors performed

scenario analyses using different DRG costs as part of the budget analysis to address the uncertainty in the hospitalisation costs, but neither deterministic sensitivity analysis nor PSA was performed.

Cost-effectiveness review summary

Although two cost-effectiveness analysis studies of RM were identified through the literature searches, there are a number of limitations associated with generalising the findings of these studies. The analysis reported by Miller *et al.*[122] was based on a single trial of STS, whereas Klersy *et al.*[123] included data from a meta-analysis of a wide range of studies of RM and the analysis did not differentiate between the different RM approaches. It is important to consider different RM approaches separately as they have different clinical effectiveness and costs associated with them.

There was heterogeneity in terms of the components of both usual care and RM interventions reported in the cost-effectiveness studies; this was also evident within the clinical effectiveness review (see *Chapter 3*, *Results of the clinical effectiveness review*). This made the identification of the parameters (e.g. costs) associated with the interventions difficult. Standard/specific RM approaches need to be described before estimating the cost-effectiveness of the interventions. Potential uncertainty in the description of interventions can be overcome by performing scenario analyses and sensitivity analyses.

The review also identified different approaches to the modelling of disease progression in HF patients. The analysis reported by Miller *et al.*[122] used the NYHA classification system to model disease progression whereas Klersy *et al.*[123] applied a Markov model with constant probabilities for mortality and hospitalisation. A systematic review by Goehler *et al*.[126] identified another approach that uses the number of rehospitalisations to model the disease progression pathway in HF. Hospital readmission- and NYHA classification-based models have significant data requirements (such as transition probabilities between NYHA classes) and this information was not reported in all of the RM studies included in the meta-analysis in *Chapter 3* (see *Results of the clinical effectiveness review*). For hospital readmission- or NYHA classification-based models, a few selected studies that report the transition probabilities will have to be chosen to provide data for the models. This is in conflict with the aim of performing a robust analysis that takes all relevant evidence into account. Because all of the studies included in the meta-analysis provided mortality and/or hospitalisation rates for each type of remote disease management for HF, a two-state Markov model consisting of an 'alive' state and a 'death' state with a constant probability of rehospitalisation and changing mortality rate over time was chosen as the preferred approach for the de novo economic model detailed in the following section.

Independent economic assessment methods

This section details the methods and assumptions of the de novo economic model constructed to evaluate the cost-effectiveness of several strategies for RM compared with usual care for patients recently discharged with HF.

Overview of modelling methodology and objectives

A Markov model using a UK NHS perspective was developed to explore the costs and health outcomes associated with RM interventions for patients recently discharged with HF. Scenarios for costs of usual care and the RM interventions were developed through discussions with an expert advisory group (including clinicians and RM experts) and a review of the published literature and other sources that report details of resource use and unit costs of equipment, infrastructure and staff time. Data from the Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity (CHARM) study[127] were used to estimate baseline mortality rates for patients in usual care, and the baseline risks associated with hospitalisation were estimated from Klersy *et al.*[123] The results from the NMA in *Chapter 3* (see *Results of the clinical effectiveness review*) were used to model the HRs of event rates for patients with RM, separating HRs for mortality, HF-related hospitalisations and all-cause hospitalisations. Utilities were identified from evidence reported in the literature. Input parameters were assigned probability distributions to reflect

their imprecision and Monte Carlo simulations were performed to produce expected incremental costs and QALYs for each strategy. Results were presented in terms of expected discounted QALYs and costs for each strategy, discounted incremental costs per QALY over a lifetime and net benefits using a threshold of £20,000 to value QALYs.

The objectives of the cost-effectiveness analysis were to:

1. estimate the cost-effectiveness of strategies for monitoring recently discharged HF patients, in terms of the incremental cost-effectiveness of each strategy, and to estimate the subsequent rates of death and hospitalisation among the modelled study population
2. identify the strategy that is most likely to be cost-effective for monitoring recently discharged HF patients in the NHS, defined as the most cost-effective strategy at a willingness-to-pay (WTP) threshold of £20,000–30,000 per QALY gained
3. identify the expected cost of uncertainty in the monitoring of HF patients and whether or not future research would be valuable by estimating the expected value of perfect information (EVPI) using a target population of 54,779 (number of first admissions for HF estimated from the National Heart Failure Audit for April 2010–March 2011[14]).

A brief description of the key aspects of the economic analysis is provided in the following sections.

Model structure

A Markov model was developed to estimate the costs and health outcomes associated with different strategies for a hypothetical cohort of patients discharged in the last 28 days with HF-related hospitalisations. The model took a lifetime horizon and the economic perspective of the model was the NHS in England and Wales. In the model, as shown in *Figure 6*, two different states were considered:

(a) alive at home
(b) dead.

The Markov model used a monthly cycle length with half-cycle correction and assigned each patient a monthly probability of death based on the time since discharge and the type of treatment. In each period the patients who were alive were under the risk of an average number of monthly rehospitalisations, that is, readmissions to a hospital for HF-related complications or other causes. Each patient then accrued lifetime QALYs and health-care costs according to their hospitalisation and treatment status.

Population

To address the research question laid out in the scope, the economic model utilised a hypothetical cohort of HF patients, discharged from hospital within 28 days. Patient age was not explicitly modelled because it was assumed that HF mortality was the dominant factor and other-cause mortality was implicitly included in the all-cause mortality. However, the mean age of HF patients as reported by the authors of the National

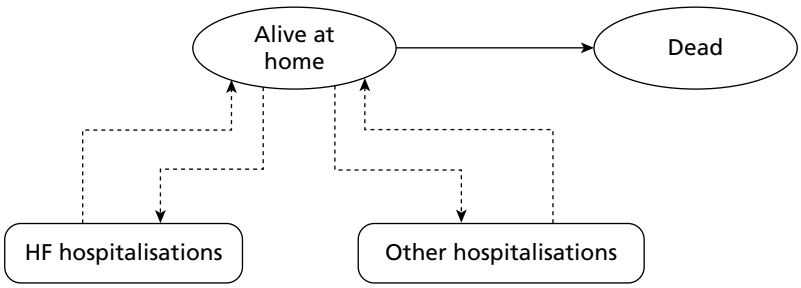

FIGURE 6 Markov model of recently discharged HF patients.

Heart Failure Audit for 2010[30] was 75.85 years, which is similar to the mean age of 77.3 years at first HF admission reported in the National Heart Failure Audit for April 2010–March 2011.[14]

Intervention

The systematic review presented in *Chapter 3* identified considerable heterogeneity across studies with respect to how the RM activities were performed. As multiple alternative specifications of the RM approaches were reported in the studies included within the systematic review, the interventions were classified and specified as reported in *Chapter 3*. In the economic model, the following strategies were evaluated compared with current usual care in the NHS:

(a) STS HH
(b) STS HM
(c) TM during office hours (i.e. TM with transmitted data reviewed by medical staff or medical support provided during office hours).

A base-case cost scenario, low-cost scenario and high-cost scenario were developed for each of these strategies based on discussions with an expert advisory group, as described in *Costs*.

Comparator

The comparator was usual care for patients recently discharged after HF hospitalisation in the NHS. Detailed reporting of the resources involved in usual care was severely lacking in most of the clinical trials. The base case for usual care in the economic model was estimated from the TEN-HMS study[49] as it included patients from the UK. Following discussions with the expert advisory group a high-cost scenario for usual care was also developed.

Time horizon

A lifetime time horizon of 30 years was used. Patients progress through the model until they either die or reach the end of the 30-year time horizon. The proportion of patients alive in the usual care arm after 15 years predicted from the model is 5.67%; <0.5% of the patients were alive after 30 years, suggesting that a 30-year time horizon was adequate.

Treatment duration

It was assumed that the interventions and usual care were provided for the first 6 months following discharge from hospital. At the end of 6 months all patients were assumed to receive usual care as per the NICE clinical guideline for the management of adults with HF,[34] irrespective of whether or not they received the intervention or post-discharge usual care during the treatment period.

It was assumed that the treatment costs and effectiveness last only for the treatment duration of 6 months, after which the cost of usual care (as recommended by the NICE guideline on HF[34]) was applied along with the baseline risks of hospitalisation and mortality.

Perspective

A UK NHS perspective was used throughout; hence, productivity lost through illness or costs incurred directly by patients were not included.

Discount rate

Both the costs and QALYs were discounted at a monthly discount rate of 0.28709%, which was estimated from the annual discount rate of 3.5%, recommended by NICE, using the formula $1 + (\text{monthly discount rate}/100) = [1 + (\text{annual rate}/100)]^{1/12}$.[128]

The key modelling methods together with the evidence sources and assumptions used to populate the model are discussed in detail in the following sections.

Selecting the classification of remote monitoring strategies

The systematic review in *Chapter 3* identified heterogeneity in the components of interventions within the broad class of RM. Aspects of heterogeneity included the equipment available in the patient's home, the physiological measures monitored (e.g. weight, blood pressure and heart rate), the method of communicating the patient information to the RM team, the extent and timing of routine communication from the RM team to the patient, the use of automated computerised assessment of information to screen for prespecified alert levels, the method of assessment by the team and the staffing levels and types of staff.

As shown in *Figure 7*, the generalised structure of any remote disease management model includes monitoring, triage and a protocol for response/follow-up of the patient.

The strategies can differ in terms of monitoring type, frequency and mode. Monitoring type relates to the data transmitted; this can include vital signs, physiological symptom monitoring and questionnaires. Frequency relates to how often the data are transmitted and is usually instantaneous, daily or weekly. The mode of input varies according to the intervention; it can be via the telephone verbally or via a telephone keypad, television or electronic device. The transmission can be via cables/wires or wireless (telephone lines, modem, 3G, broadband).

Triage involves investigation of the patient's alert/problem once it is discovered by the RM system. A problem could be discovered by software using prespecified algorithms or by manual examination of patient data by health professionals. Nurses or physicians will then determine whether it is a false alarm or whether the patient needs to be followed up based on the perceived severity of the problem.

If the problem is not labelled as a false alarm, a formal follow-up process is initiated by the health professional as shown in *Figure 8*. Depending on the diagnosis of the alarm, the follow-up process could vary from no further action to an emergency admission to the hospital. Based on the severity of diagnosis, other forms of follow-up include adjustment of medicine, adjustment of disease management protocol or an outpatient clinic visit.

Variation in the RM interventions in terms of differences in the arrangements for monitoring, triage and a protocol for response/follow-up of the patient was used to develop a subclassification. RM was classified into three distinct categories: (1) STS HH, (2) STS HM and (3) TM during office hours (*Table 19* and *Figure 9*). Cost-effectiveness analysis was performed for each of these intervention strategies compared with usual care and with each other.

Although a fourth subclassification of 24/7 TM (i.e. transmitted data are reviewed by medical staff or medical support is provided 24 hours a day, 7 days a week) was examined separately as part of the NMA in *Chapter 3*, this strategy was not included in the economic analysis. There were two reasons for this. First, there were no UK-based 24/7 TM trials identified in the systematic review and the data for 24/7 TM would

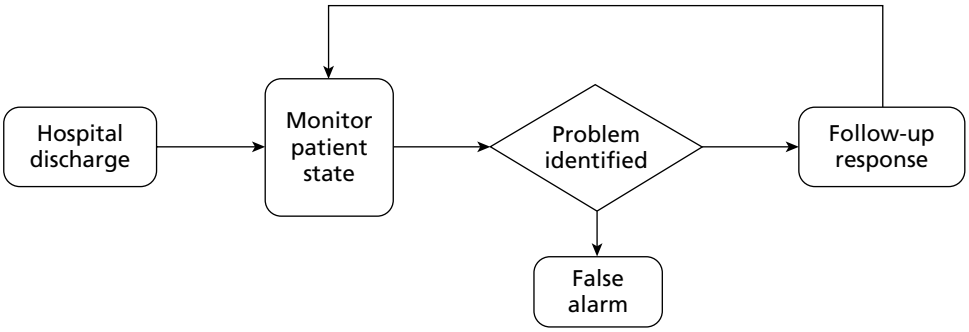

FIGURE 7 Generalised patient pathway for RM.

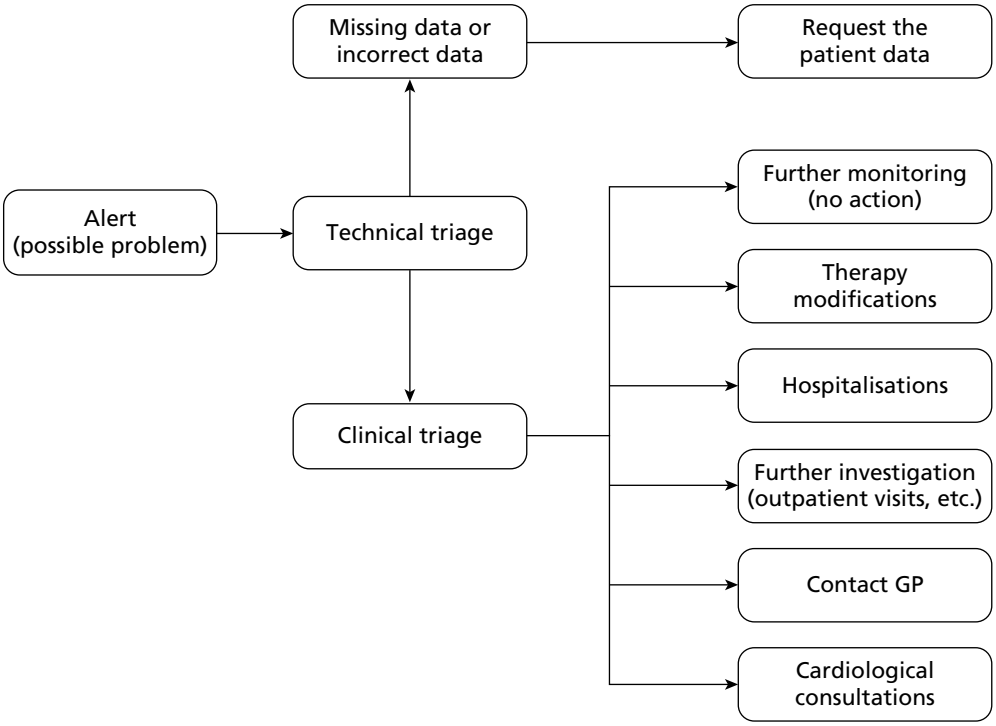

FIGURE 8 Follow-up process of RM for HF patients.

TABLE 19 Different RM interventions

TM activity	STS HH	STS HM	TM during office hours
Monitoring	Undertaken via timetabled structured telephone calls from the service to the patient	Undertaken by the patient according to a predefined schedule related to their wake-up time	Undertaken via transmission of electronic data from the equipment in the patient's home to the monitoring centre
Triage	Most of the time the triage is carried out in real time while gathering information from the patient	Undertaken daily (5–7 days a week) by the nurse at a predefined time	Undertaken daily (5–7 days a week) by the nurse at a predefined time
Protocol for response/ follow-up	According to the severity of the case, either the case is handled by the nurse or the physician is consulted		

have been based on a single study.[76] This study[76] was subject to methodological weaknesses as described in *Chapter 3* (see *Results of the clinical effectiveness review*). Second, the expert advisory group suggested that the 24/7 home monitoring is currently not a realistic option for the UK setting as an existing round-the-clock response system is already available via the 999 emergency response route.

Baseline mortality and hospitalisation risks related to time since discharge

Patients with HF are at increased risk of both fatal and non-fatal major adverse cardiovascular events. The main outcomes of interest were all-cause mortality and hospitalisations. The model estimated the subsequent prognosis of each patient by using a monthly probability of death and monthly risks for hospitalisation (both HF-related and other causes) depending on the patient characteristics and the type of treatment. This section details the baseline risks of hospitalisation and death (i.e. for usual care without RM) estimated using data from the literature.

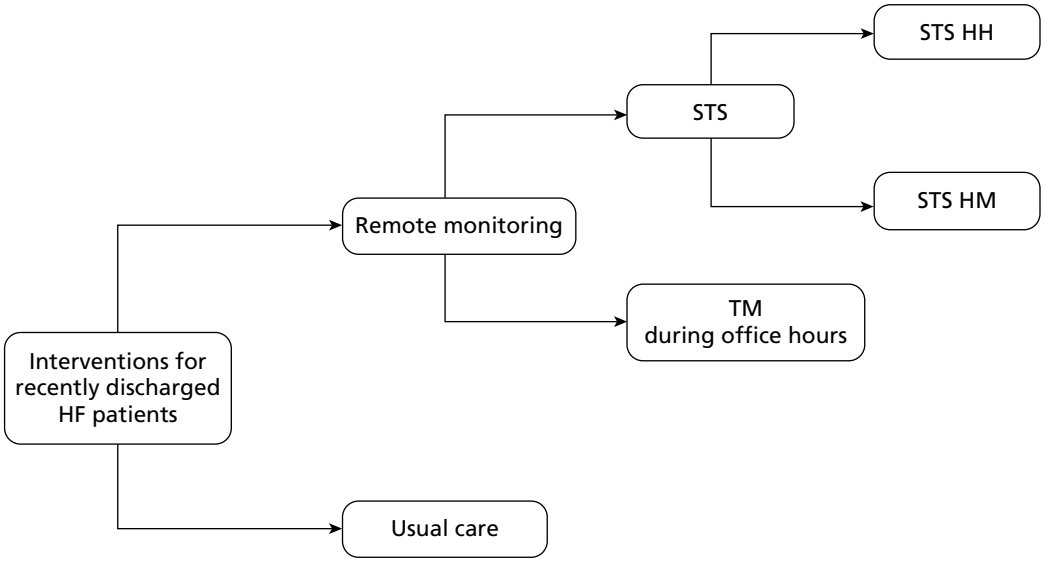

FIGURE 9 Interventions for remote disease management for patients with HF.

Mortality risk

The influence of time from non-fatal hospitalisation on subsequent mortality rates for HF patients was estimated based on the data from the CHARM study,[127] which included 7572 patients followed up for 38 months. The monthly probability of death was also estimated from the CHARM study,[127] which showed that the mortality risk was highest immediately after hospital discharge and then decreased over time. This section describes the process of estimation of the mortality risk for HF patients from the data reported in the CHARM study.[127]

The HRs of all-cause mortality of hospitalised HF patients compared with non-hospitalised HF patients in the CHARM[127] study are reported and are replicated in *Table 20*. The mortality risk of non-hospitalised patients was estimated from the CHARM study,[127] which reported 1233 deaths in 4884 non-hospitalised patients over 38 months. The instantaneous mortality hazard rate (r) for non-hospitalised patients was calculated as 0.00765 using the formula $r = -[\ln(1 - P_d)]/t$ assuming a constant instantaneous rate, where P_d (= 0.252, i.e. 1233/4884) was the probability of death for non-hospitalised patients over a period of time ($t = 38$ months).

The instantaneous mortality hazard rates for hospitalised HF patients in different time periods since discharge from HF-related hospitalisation, as shown in *Table 21*, were estimated by multiplying the HRs in *Table 20* by the constant mortality hazard rate of non-hospitalised HF patients.

The monthly mortality probabilities were then estimated from the instantaneous hazard rates using the formula $p = 1 - \exp(-\text{rate})$. The risk of death is greatest in the early period after discharge after a hospitalisation for HF and subsequently declines over time as seen in *Table 22*. The probability of death in the first month after discharge is an estimated threefold higher than the probability of mortality beyond 2 years from discharge.

The survival curve showing the proportion of patients alive (under usual care) over time is shown in *Figure 10*. It can be seen that most of the deaths occur in the initial period after discharge, which is in line with the assumptions that the mortality risk is higher in the time immediately after discharge and the effect of the intervention lasts only for the first 6 months. The survival rate changes at 1 month, 3 months, 6 months, 12 months and 24 months as expected from *Table 22*. Finally, the patients are assumed to have a constant mortality rate beyond the 24-month period, as seen in the smooth exponential curve.

TABLE 20 Hazard ratios of mortality for HF patients discharged from hospital compared with non-hospitalised HF patients according to time since discharge (replicated from the CHARM[127] study)

Time since discharge (months)	HR	95% CI
0–1	6.18	4.81 to 7.93
>1–3	4.39	3.50 to 5.50
>3–6	3.54	2.86 to 4.39
>6–12	3.11	2.59 to 3.75
>12–24	2.46	2.06 to 2.94
>24	1.93	1.48 to 2.52

TABLE 21 Instantaneous mortality hazard rates for HF patients discharged from hospital according to time since discharge

Time since discharge (months)	Mortality hazard	95% CI
0–1	0.04732	0.03683 to 0.06072
>1–3	0.03361	0.02680 to 0.04211
>3–6	0.02711	0.02190 to 0.03361
>6–12	0.02381	0.01983 to 0.02871
>12–24	0.01884	0.01577 to 0.02251
>24	0.01478	0.01133 to 0.01930

TABLE 22 Monthly mortality probability according to time since discharge for HF patients in usual care

Time since discharge (months)	Mortality probability per month	95% CI
0–1	0.04622	0.03616 to 0.05891
>1–3	0.03306	0.02644 to 0.04124
>3–6	0.02674	0.02166 to 0.03306
>6–12	0.02353	0.01964 to 0.02831
>12–24	0.01866	0.01565 to 0.02226
>24	0.01467	0.01127 to 0.01911

According to the survival curve, 4.7%, 10.8% and 17.7% of HF patients would have died by 1 month, 3 months and 6 months respectively. Furthermore, 28% of the patients would have died by the end of 1 year and 43% would have died at 2 years post discharge. This is in line with the findings from the HF audit as reported in *Chapter 1* (see *Aetiology, pathology and prognosis*).

Risk of hospitalisation

The other main outcomes included in the model are HF-related and other-cause hospitalisations. The other-cause hospitalisations are modelled as all-cause hospitalisations minus the HF-related hospitalisations. The mean number of annual hospitalisations were estimated from the meta-analysis reported by Klersy *et al.*[123] and are presented in *Table 23*. For HF hospitalisations, Klersy *et al.*[123] reviewed 17 trials from different countries (2089 patients) and reported an annual incidence rate of 42.1 per 100 patients. For all-cause hospitalisations the authors reviewed 18 trials (2332 patients) and reported an annual incidence rate of 105.1 per 100 patients. These rates of hospitalisation were divided by 12 to estimate the monthly risk of

hospitalisations in the economic model. *Table 23* shows the parameters used in the model per patient in usual care.

Effect of the interventions

Hazard ratios for all-cause mortality, all-cause hospitalisations and HF-related hospitalisations were used as effectiveness parameters in the model during the treatment period (i.e. the first 6 months following discharge from the hospital). It should be noted that the clinical systematic review identified considerable heterogeneity in the manner in which RM and usual care were performed. Clear descriptions of the interventions were not provided in many of the studies identified in the systematic review, which made it difficult to understand exactly what was provided as part of the intervention and what was provided as part of usual care. This lack of detail meant that the HR estimates from the meta-analyses were a conglomeration of estimates from heterogeneous comparisons. For example, study 1, which compared RM variant 1 with usual care variant 1, was pooled with study 2, which compared RM variant 2 with usual care variant 2, and so on. There was insufficient information regarding how usual care variant 1 differed from usual care variant 2 to make adjustments to effectiveness difference estimates. Furthermore, as some of the studies were undertaken across multiple centres, usual care variant 1 itself could be a pooled estimate of usual care variant 1a, usual care variant 1b and usual care variant 1c. Thus, this lack of detail in research studies concerning the design of the RM and especially the usual care arm has implications for the robustness of any analysis of effectiveness. The statistical analysis of the extent of heterogeneity was discussed fully in *Chapter 3*.

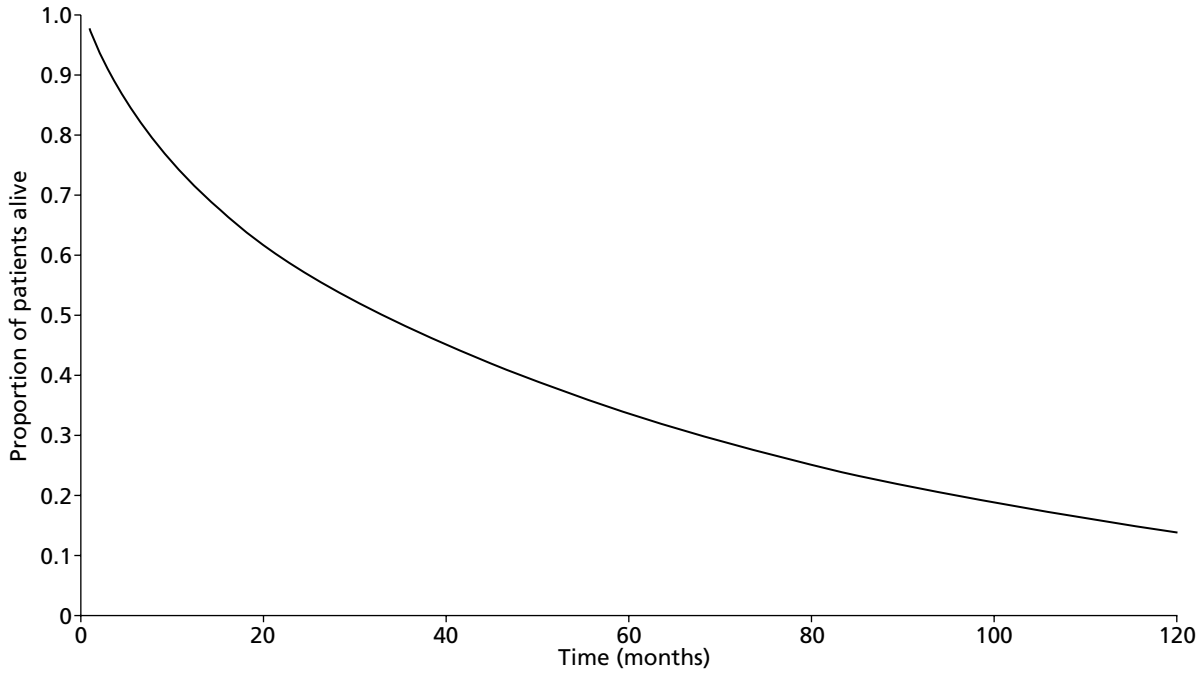

FIGURE 10 Baseline survival curve of recently discharged HF patients.

TABLE 23 Monthly risk of hospitalisations per patient in usual care

Hospitalisation	Source	Estimate	95% CI
HF-related hospitalisations	Klersy *et al.*[123]	0.0350	0.0325 to 0.0375
All-cause hospitalisations	Klersy *et al.*[123]	0.0875	0.0841 to 0.0908

The HRs estimated from the NMA, as reported in *Chapter 3* (see *Results of the clinical effectiveness review*), for the different categories (i.e. STS HM, STS HM and TM during office hours) are presented in *Tables 24a* and *b*. All analyses were performed using an intention-to-treat analysis, that is, all patients were analysed in the groups to which they were allocated, regardless of whether or not they received the treatment.

A sensitivity analysis was performed excluding the Home-HF study[67] as described in *Chapter 3* (see *Results of the clinical effectiveness review*) and the HRs are presented in *Tables 25a* and *b*. For decision-makers deciding which of these scenarios is most representative of their setting, the key questions relate to the inclusion of the Home-HF study[67] in the effectiveness meta-analyses. If one believes that usual care is best represented by the usual care arm in the Home-HF study,[67] which is the only study showing a statistically significant difference in effectiveness of usual care over RM, then perhaps the results including the Home-HF study[67] might be considered more relevant than those without. If, on the other hand, one believes that the performance of usual care is better represented by the other studies and that usual care in the Home-HF study[67] is not representative of current usual care, then the results excluding the Home-HF study[67] might be considered more relevant.

The monthly mortality probabilities for the interventions were estimated by applying the HRs to the baseline mortality probability using the formula $P_{intervention} = 1-(1-P_{baseline})^{HR}$, where $P_{intervention}$ is the monthly mortality probability of the intervention and $P_{baseline}$ is the baseline monthly mortality probability. This is equivalent to multiplying the HR of the intervention with the baseline hazard rate to estimate the hazard rate of the intervention, and then converting the hazard rate into a monthly probability.

Health-related quality of life

This section provides a discussion of the evidence available for four aspects of QoL: baseline HRQoL for HF patients under usual care, the impact caused by hospital readmission for HF, the impact caused by hospital readmission for other causes and whether or not there is any evidence that patients who are not readmitted experience better HRQoL with RM than with usual care.

TABLE 24a Hazard ratios for interventions compared with usual care for mortality (all-cause) and hospitalisations (all-cause and HF-related) using CrIs

	All-cause mortality		HF-related hospitalisations		All-cause hospitalisations	
Intervention	Median HR	95% CrI	Median HR	95% CrI	Median HR	95% CrI
STS HH	0.77	0.55 to 1.08	0.77	0.62 to 0.96	0.97	0.70 to 1.31
STS HM	0.98	0.41 to 2.33	1.03	0.66 to 1.54	1.06	0.44 to 2.53
TM during office hours	0.76	0.49 to 1.18	0.95	0.70 to 1.34	0.75	0.49 to 1.10

TABLE 24b Hazard ratios for interventions compared with usual care for mortality (all-cause) and hospitalisations (all-cause and HF-related) using predictive distributions

	All-cause mortality		HF-related hospitalisations		All-cause hospitalisations	
Intervention	Median HR	95% PrI	Median HR	95% PrI	Median HR	95% PrI
STS HH	0.77	0.31 to 1.86	0.77	0.50 to 1.19	0.97	0.38 to 2.43
STS HM	0.98	0.30 to 3.23	1.03	0.58 to 1.77	1.06	0.31 to 3.61
TM during office hours	0.76	0.30 to 1.91	0.95	0.59 to 1.62	0.75	0.28 to 1.91

PrI, predictive interval.

TABLE 25a Hazard ratios for interventions compared with usual care for mortality (all-cause) and hospitalisations (all-cause and HF-related) excluding the Home-HF[67] study

	All-cause mortality		HF-related hospitalisations		All-cause hospitalisations	
Intervention	Median HR	95% CrI	Median HR	95% CrI	Median HR	95% CrI
STS HH	0.75	0.59 to 0.96	0.76	0.61 to 0.94	0.96	0.72 to 1.27
STS HM	0.98	0.58 to 1.62	1.02	0.70 to 1.49	1.06	0.48 to 2.32
TM during office hours	0.62	0.42 to 0.89	0.86	0.61 to 1.21	0.67	0.42 to 0.97

TABLE 25b Hazard ratios for interventions compared with usual care for mortality (all-cause) and hospitalisations (all-cause and HF-related) using predictive distribution and excluding the Home-HF[67] study

	All-cause mortality		HF-related hospitalisations		All-cause hospitalisations	
Intervention	Median HR	95% PrI	Median HR	95% PrI	Median HR	95% PrI
STS HH	0.75	0.45 to 1.27	0.76	0.51 to 1.13	0.96	0.42 to 2.18
STS HM	0.98	0.49 to 1.95	1.02	0.61 to 1.69	1.06	0.35 to 3.22
TM during office hours	0.62	0.35 to 1.09	0.86	0.54 to 1.38	0.67	0.26 to 1.53

PrI, predictive interval.

To estimate the HRQoL for recently discharged HF patients under usual care, a rapid review was conducted and four studies were found. Capomolla *et al.*[73] reported HRQoL for recently discharged CHF patients as 0.63 and Calvert *et al*.[129] reported the utility to be 0.6 for advanced HF patients (NYHA class III or IV). Iqbal *et al.*[130] reported the utility of HF patients as 0.57 but the population had multiple comorbidities. Miller and Cox[131] estimated the utilities from SF-36 data collected during the trial using the methods suggested by Brazier *et al.*[124] and reported them as 0.58 for advanced HF (NYHA class III or IV) and 0.67 for the weighted average for patients in NYHA class I or II.

Reviewing the evidence showed that there was uncertainty about the difference in patients' QoL in different arms, that is, whether or not HRQoL is different for patients in the usual care and RM groups. In a previous economic model of RM, Klersy *et al*.[123] used utilities of 0.612 and 0.662 for the usual care and RM groups respectively. However, the utilities used by Klersy *et al*.[123] were based on a RCT by Herbert *et al*.,[125] which was undertaken in an ethnically diverse urban community in Harlem, New York; hence, the results might not be applicable to the UK HF patient population. Furthermore, none of the studies identified in the systematic review in *Chapter 3* reported any difference in the utility of patients in the usual care and RM groups. As there was no quantified evidence on the extent to which RM improves HRQoL of patients, the same utility values were used for HF patients receiving both usual care and (each of the three) RM strategies in the economic model.

Evidence on the disutility caused by rehospitalisation for HF was not clear. A disutility of 0.1 was incorporated for every HF-related hospitalisation based on a study by Yao *et al.*,[132] who estimated the disutility to be equivalent to the utility of one health state lower in terms of NYHA class. The disutility was assumed to last for 1 year.

Evidence on the disutility caused by rehospitalisation for other causes (not directly HF related) was also limited. In the absence of evidence it was assumed that there was no disutility caused by rehospitalisation for other causes.

In the economic model, different values of utility were used for unstable patients (i.e. recently discharged patients) and stable patients (i.e. 1 year since hospitalisation). A utility score of 0.58 was used for patients in the first year since discharge and a utility of 0.67 was used after the first year. Any HF-related hospitalisation was assumed to result in a disutility of 0.1 for a whole year, that is, the utility of the patient for that year was $0.67 - 0.1 = 0.57$. Within the PSA, the uncertainty in the utility values was represented using a normal distribution using the deterministic value as mean with a standard deviation of 0.015, estimated based on the difference between utilities reported by Capomolla *et al.*[73] and Iqbal *et al.*,[130] and the disutility was represented using a triangular distribution with (–0.08,0.11) as the range with –0.1 as the mode.

Costs

The costs in the model are described in detail in the following sections.

Clear descriptions of the interventions and usual care were not provided in many of the studies identified in the systematic review. This lack of detail concerning the design of the RM interventions and especially the usual care arms (e.g. communication protocols, routine staff visits, resources used) has implications for estimating the costs of interventions and usual care. As the resources used in each intervention variant were not always clear, three different cost scenarios for RM interventions (base case, lower and upper) and two different cost scenarios for usual care (base case and upper) were developed as described in *Costs of remote monitoring care interventions* and *Usual care costs*.

Costs of remote monitoring care interventions

The RM costs were highly variable because of the heterogeneity in devices, monitoring and follow-up processes. The costs of RM comprised three main components:

- costs of the RM devices and equipment within the patient's home, including the device hub, peripherals and communication costs
- maintenance/monitoring costs in the RM centre
- medical care costs to deal with events/alerts, for example GP and nurse visit costs or further hospital-based outpatient visits (excludes rehospitalisation costs).

The costs of the RM devices were elicited from the expert advisory group. The maintenance/monitoring costs were estimated using activity-based costing for the resources spent by staff on triage and follow-up based on evidence from the literature. The costs of medical care were estimated from the TEN-HMS study,[49] which reported the medical care received in the usual care, STS and TM arms.

The RM device, responsible for the collection and transmission of data (which can include vital signs, symptoms and questionnaires), can take different levels of complexity and the cost of the device is based on this complexity. Each monitoring device consists of a hub and can have a number of peripherals (medical devices with specific functionality that measure the vital signs and transmit them to the hub). These peripherals can be wired or wireless with the costs of wireless peripherals being higher than the costs of wired peripherals. The communication costs include the cost of data transfer along with server costs for the management of patient data.

In terms of monitoring, the characteristics of the system/infrastructure and the composition of the monitoring team also have an impact on the cost of the monitoring through triage costs. Triage costs also vary depending on whether the triage is performed by individuals (such as technicians, nurses or physicians) or a dedicated clerical triage team that monitors the patients. Triage costs also depend on the type of software used.

The medical care costs associated with the follow-up of patients consist of A&E visits, GP/cardiologist visits and nurse visits (both home and office visits). These were examined in two stages: the mean number of visits for each patient and the unit costs per visit.

Medical care costs to deal with events/alerts: evidence and assumptions used

The evidence used to estimate the mean numbers of medical care visits is taken from the TEN-HMS study,[49] conducted across 16 hospitals in Germany, the Netherlands and the UK between August 2000 and March 2002. A total of 426 patients were assigned randomly to home TM, nurse telephone support and usual care in a 2 : 2 : 1 ratio. This study reported the frequency of different health visits for each of the three arms over a 240-day period as shown in *Table 26*.

The unit costs of staff time were estimated based on data from the Personal Social Services Research Unit (PSSRU)[133] and *NHS Reference Costs 2009–10*.[134] The unit costs of staff time used in estimating the intervention costs are shown in *Table 27*.

TABLE 26 Frequency of medical care visits based on the TEN-HMS study[49]

Medical care visits	Usual care	STS	TM
Number of patients	85	170	163
Total days at risk	16,089	33,803	33,641
Emergency room visits			
Visits	8	54	60
Total/1000 days at risk (95% CI)	0.5 (0.2 to 0.8)	1.6 (1.2 to 2.0)	1.8 (1.3 to 2.2)
Office visits			
Family practitioner	119	602	454
Specialist	34	117	100
Nurse and other	36	104	100
Total	189	823	654
Total/1000 days at risk (95% CI)	11.7 (10.1 to 13.4)	24.3 (22.7 to 26.0)	19.4 (18.0 to 20.9)
Home visits			
Family practitioner	42	185	162
Specialist	0	3	1
Nurse and other	27	206	128
Total	69	394	291
Total/1000 days at risk (95% CI)	4.3 (3.3 to 5.9)	11.7 (10.5 to 12.8)	8.7 (7.7 to 9.6)
All face-to-face patient contacts			
Total	300	1388	1115
Total/1000 days at risk (95% CI)	18.6 (16.6 to 20.7)	41.1 (38.9 to 43.2)	33.1 (31.2 to 35.1)
Telephone calls			
Total	90	914	1180
Total/1000 days at risk (95% CI)	5.6 (4.4 to 6.8)	27.0 (25.3 to 28.8)	35.1 (33.1 to 37.0)
All patient contacts			
Total contacts	390	2302	2295
Total/1000 days at risk (95% CI)	24.2 (21.9 to 26.6)	68.1 (65.4 to 70.8)	68.2 (65.5 to 70.9)

TABLE 27 Unit costs of staff time

Medical staff	Unit of time	Cost (£)	Source
GP	One office visit	46	PSSRU 2011,[133] section 10.8b, p. 149[a]
Specialist	One office visit	46	PSSRU 2011[133b]
GP	One home visit	104	PSSRU 2011,[133] section 10.8b, p. 150[c]
Community nurse	One home visit	38	Department of Health,[134] District Nursing Services: Adult: Face To Face, Currency Code: CN301AF
Community nurse	One office visit	25	PSSRU 2011,[133] section 10.7, p. 147[d]
Hospital nurse	1 hour	40	PSSRU 2011,[133] section 14.3, p. 193[e]
Clinical support worker (hospital)	1 hour	20	PSSRU 2011,[133] section 14.5, p. 195

a Per clinic consultation lasting 17.2 minutes (complex consultation).
b Assumed to be equivalent to GP.
c Per home visit lasting 23.4 minutes (includes travel time), excluding staff costs.
d Surgery consultation by clinical nurse specialist.
e Per hour, nurse (day ward), including qualification.

Scale of typical remote monitoring service

Three alternative scenarios for each RM classification (i.e. STS HM, STS HH and TM during office hours) were developed and their costs were estimated after discussions with the expert advisory group. The three alternative scenarios for each RM classification correspond to a base-case scenario, a low-cost scenario and a high-cost scenario. These scenarios were designed to reflect the different configurations of the RM systems present in the UK.

The costs of RM interventions were estimated for a RM centre that monitored 250 patients for a period of 6 months. This was based on the median size of NHS foundation trusts in the UK and the proportion of those people eligible for RM. According to the National Heart Failure Audit for 2010-11,[14] the median number of HF patients discharged annually with HF as their primary diagnosis from the different hospital foundation trusts in England and Wales was 380. Hull Foundation Trust, which had 380 HF patients admitted in 2011, has 250 CHF patients under RM. Thus, taking into consideration that the number of HF patients admitted to the Hull and East Yorkshire Hospitals NHS Trust was equal to the median number of HF patients admitted to different foundation trusts in England and Wales, it was assumed that a typical RM centre would have an average capacity to monitor 250 patients. This number was also deemed sensible by the expert advisory group.

Cost of the structured telephone support human-to-machine interface intervention

The breakdown of the costs of the device, maintenance/monitoring costs and medical care costs for the base-case STS HM intervention is shown in *Table 28*.

The costs of the telephone and peripherals for STS HM were elicited from the expert advisory group and a baseline yearly cost of £78 was used. For the low-cost STS HM scenario a yearly cost of £32 was used for a basic telephone device, and for the high-cost STS HM scenario a yearly cost of £235 was used for a telephone device with more peripherals (see *Table 31*).

The costs of monitoring for STS HM were estimated from Boyne *et al.*,[135] who conducted a RCT at three hospitals in the South-Limburg area of the Netherlands. The study included 382 patients with 197 in the RM group and 185 in the usual care group. Boyne *et al.*[135] reported that an average time of 2 minutes and 20 seconds was dedicated by the triage nurse each day for monitoring an individual patient. This

time spent daily was multiplied by 182.5 to estimate the staff time spent for each patient over 6 months; this gave a total of 7 hours. The costs associated with monitoring over 6 months were estimated by multiplying this nurse time by their hourly rate. It was assumed in the model that the triage is performed by a hospital nurse and a £40 per hour rate was used according to the PSSRU.[133] Also, the cost of the patient management software (£5000) for the RM centre was converted into a cost per patient based on a 3-year depreciation period (i.e. assuming that new software will be required in 3 years) and sharing the overall cost of the software out amongst the number of patients who would benefit from the service over 3 years (estimated as 1500 patients, i.e. 250 every 6 months, assuming a 6-month treatment duration and no delays for removal and installation of the monitoring device).

The costs of medical care (excluding hospital readmissions) were estimated based on the data from the TEN-HMS trial.[49] The numbers of visits reported in the trial for patients in the nurse telephone support arm ($n = 170$) over a 240-day period (see *Table 26*) were used to estimate the average numbers of visits per patient over 6 months (see *Table 28*). These average numbers of visits were multiplied by the corresponding unit cost per contact, based on the staff involved, to estimate medical costs of £392 per patient over 6 months.

Thus, the total cost per patient for the STS HM intervention over 6 months was estimated to be £715, that is, a monthly cost of £119 per patient.

Cost of the structured telephone support human-to-human contact intervention

For STS HH intervention costs, it was assumed that only the monitoring costs were different between the STS HM and STS HH interventions. The costs of monitoring for STS HH were estimated from Riegel *et al*.,[79] who reported the workload of the staff responsible for implementing a STS intervention to be equal to 16 hours per patient for 6 months. Using the same device and medical costs as for STS HM, the total base-case cost per patient receiving the STS HH intervention for 6 months was estimated to be £1075, that is, a monthly cost of £179 per patient (*Table 29*).

Cost of telemonitoring during office hours

The total costs of TM during office hours were broken down into the costs of the device, maintenance/monitoring costs and medical care costs for the TM during office hours as shown in *Table 30*.

The cost of the TM device was elicited from the expert advisory group – a baseline yearly cost of £708 was used. For the high-cost TM scenario a yearly cost of £1176 was used for a TM device with more peripherals, as detailed in *Table 31*.

The costs of monitoring were assumed to be the same as the STS HM monitoring costs estimated from Boyne *et al*.[135] as the triage and follow-up process was similar for both interventions. The cost of the software was also assumed to be the same and was estimated using a 3-year depreciation period for 1500 patients (i.e. for six cohorts of 250 patients each). For the low-cost TM scenario it was assumed that the time spent by the hospital nurse on triage and follow-up was 1 hour for each patient for 6 months.

The data from the TEN-HMS trial[49] were used to estimate the medical costs. The numbers of visits reported in the trial for patients in the home TM arm ($n = 163$) over a 240-day period, reproduced in *Table 26*, were used to estimate the average numbers of visits per patient for 6 months as reported in *Table 30*. These average numbers of visits were multiplied by the corresponding unit cost per contact, based on the staff involved, to estimate medical costs of £336 per patient over 6 months.

The total cost per patient for the office hours TM intervention for 6 months was estimated to be £1051, that is, a monthly cost of £173 per patient (see *Table 30*).

TABLE 28 Breakdown of the base-case STS HM intervention costs per patient for 6 months

	Resource usage	Source	Unit cost (£)	Source	Cost per 6 months (£)
Breakdown of device costs					
Cost of telephone + peripherals (scale and blood pressure cuff)	0.5 (for 6 months)	Based on advice from clinical experts	78 (per year)	Expert advisory input	39
Total cost of the device per patient for 6 months					39
Breakdown of monitoring costs					
Triage, decision-making by nurse	7 hours	Boyne *et al.*[135]	40 (per hour)	PSSRU 2011[133]	280
Data management software	1/1500[a]		5000 (per site licence)		3
Total STS HM monitoring cost per patient for 6 months					283
	Frequency per patient	**Source**	**Unit cost per contact (£)**	**Source**	**Cost per 6 months (£)**
Breakdown of medical care costs					
Emergency room visits	0.30	Cleland *et al.* (TEN-HMS)[49]	130	Department of Health[134]	39
Office visits: family practitioner	3.37	Cleland *et al.* (TEN-HMS)[49]	46	PSSRU 2011[133]	155
Office visits: specialist	0.66	Cleland *et al.* (TEN-HMS)[49]	46	PSSRU 2011[133]	30
Office visits: nurse and other	0.58	Cleland *et al.* (TEN-HMS)[49]	25	PSSRU 2011[133]	15
Home visits: family practitioner	1.04	Cleland *et al.* (TEN-HMS)[49]	104	PSSRU 2011[133]	108
Home visits: specialist	0.02	Cleland *et al.* (TEN-HMS)[49]	104	PSSRU 2011[133]	2
Home visits: nurse and other	1.15	Cleland *et al.* (TEN-HMS)[49]	38	Department of Health[134]	43
Total medical care costs per patient for 6 months					392
Total cost of STS HM intervention per patient for 6 months					715

a 1500 patients (assuming 250 patients monitored for 6 months over 3 years).

Cost scenarios for the remote monitoring interventions

It was not possible to validate the robustness of the costs of the base-case scenarios as clear descriptions of the interventions were not provided in the trials of RM. Furthermore, large variation was observed in the costs of the devices from the pricing data accessed and there was uncertainty in the monitoring resources used within studies reporting different estimates. This heterogeneity made it difficult to provide a single description (and cost) of the interventions in each RM classification.

To this end, two further costing scenarios were developed for each RM classification, that is, STS HM, STS HH and TM during office hours, and their costs were estimated. These costing scenarios evaluate a high and low estimate of the costs for each RM classification to understand the impact of cost on the cost-effectiveness of the interventions. The differences in assumptions between the new scenarios and the base-case scenarios along with the new estimated costs (per patient for 6 months) are shown in *Table 31*.

TABLE 29 Breakdown of the base-case STS HH intervention costs per patient for 6 months

	Resource usage	Source	Unit cost (£)	Source	Cost per 6 months (£)
Breakdown of device costs					
Cost of telephone + peripherals (scale and blood pressure cuff)	0.5 (for 6 months)	Based on advice from clinical experts	78 (per year)	Expert advisory input	39
Total cost of the device per patient for 6 months					39
Breakdown of monitoring costs					
Triage, decision-making by nurse	16 hours	Riegel *et al.*[79]	40 (per hour)	PSSRU 2011[133]	640
Data management software	1/1500[a]		5000 (per site licence)	Expert advisory input	3
Total STS HH monitoring cost per patient for 6 months					643
	Frequency per patient	**Source**	**Unit cost per contact (£)**	**Source**	**Cost per 6 months (£)**
Breakdown of medical care costs					
Emergency room visits	0.30	Cleland *et al.* (TEN-HMS)[49]	130	Department of Health[134]	39
Office visits: family practitioner	3.37	Cleland *et al.* (TEN-HMS)[49]	46	PSSRU 2011[133]	155
Office visits: specialist	0.66	Cleland *et al.* (TEN-HMS)[49]	46	PSSRU 2011[133]	30
Office visits: nurse and other	0.58	Cleland *et al.* (TEN-HMS)[49]	25	PSSRU 2011[133]	15
Home visits: family practitioner	1.04	Cleland *et al.* (TEN-HMS)[49]	104	PSSRU 2011[133]	108
Home visits: specialist	0.02	Cleland *et al.* (TEN-HMS)[49]	104	PSSRU 2011[133]	2
Home visits: nurse and other	1.15	Cleland *et al.* (TEN-HMS)[49]	38	Department of Health[134]	43
Total medical care costs per patient for 6 months					392
Total cost of STS HH intervention per patient for 6 months					1075

a 1500 patients (assuming 250 patients monitored for 6 months over 3 years).

Usual care costs

There is variation between different local settings in the usual care applied in current clinical practice, as described in Chapter 1 (see *Current service provision*). The current NICE guidelines[34] provide recommendations for the management of adults with HF; however, a clear description of the current service is not available. The recommendations in the NICE guidelines state that: 'The frequency of monitoring should depend on the clinical status and stability of the patient. The monitoring interval should be short (days to 2 weeks) if the clinical condition or medication has changed, but is required at least 6-monthly for stable patients with proven heart failure'.

Furthermore, the studies identified in the systematic review presented in *Chapter 3* did not report clearly or in detail what was involved in the usual post-discharge care, thus making it difficult to estimate the costs of usual care. The key resource costs for usual care for HF patients are the visits to the GP and the nurse visits immediately after discharge. As the usual post-discharge care was not reported clearly in the studies within the systematic review, it was assumed that the cost of the base-case usual post-discharge care was

TABLE 30 Breakdown of the base-case TM during office hours costs per patient for 6 months

	Resource usage	Source	Unit cost (£)	Source	Cost per 6 months (£)
Breakdown of device costs					
Cost of hub + peripherals	0.5 (for 6 months)	Based on advice from clinical experts	703 (per year)	Based on advice from clinical experts	352
Communication (patient to centre)	0.5 (for 6 months)	Based on advice from clinical experts	160 (per year)	Based on advice from clinical experts	80
Total cost of the device per patient for 6 months					433
Breakdown of monitoring costs					
Triage, decision-making	7 hours	Boyne *et al.*[135]	40 (per hour)	PSSRU 2011[133]	280
Data management software	1/1500[a]		5000		3
Total monitoring cost per patient for 6 months					283
	Frequency per patient	**Source**	**Unit cost per contact (£)**	**Source**	**Cost per 6 months (£)**
Breakdown of medical care costs					
Emergency room visits	0.35	Cleland *et al.* (TEN-HMS)[49]	130	Department of Health[134]	45
Office visits: family practitioner	2.65	Cleland *et al.* (TEN-HMS)[49]	46	PSSRU 2011[133]	122
Office visits: specialist	0.58	Cleland *et al.* (TEN-HMS)[49]	46	PSSRU 2011[133]	27
Office visits: nurse and other	0.58	Cleland *et al.* (TEN-HMS)[49]	25	PSSRU 2011[133]	15
Home visits: family practitioner	0.95	Cleland *et al.* (TEN-HMS)[49]	104	PSSRU 2011[133]	98
Home visits: specialist	0.01	Cleland *et al.* (TEN-HMS)[49]	104	PSSRU 2011[133]	1
Home visits: nurse and other	0.75	Cleland *et al.* (TEN-HMS)[49]	38	Department of Health[134]	28
Total medical care costs per patient for 6 months					336
Total costs					1051

a 1500 patients (assuming 250 patients monitored for 6 months over 3 years).

the same as that described in the TEN-HMS study.[49] A high-cost usual post-discharge care scenario was also developed based on discussions with the expert advisory group.

Base-case usual post-discharge care cost scenario

Data from the TEN-HMS study[49] were used to estimate the costs of usual post-discharge care in the base-case scenario, which consisted of nurse visits, GP/cardiologist visits and A&E visits. The numbers of visits reported in the trial for patients in the usual care arm ($n = 85$) over a 240-day period, reproduced in *Table 26*, were used to estimate the average numbers of visits per patient for 6 months (*Table 32*). These average numbers of visits were multiplied by the corresponding unit cost per contact, based on the staff involved, to estimate usual care costs of £161 per patient for 6 months.

TABLE 31 Costs of RM scenarios per patient for 6 months

Scenario	Assumption	Source	Total cost (£)
STS HM scenarios			
Base-case scenario	–	–	715
Low-cost scenario	Telephone cost of £31.60 per year	Clinical input	623
High-cost scenario	Telephone cost of £235 per year (with more peripherals)	Clinical input	794
STS HH scenarios			
Base-case scenario	–	–	1075
Low-cost scenario	Telephone cost of £31.60 per year	Clinical input	1051
High-cost scenario	Telephone cost of £235 per year (with more peripherals)	Clinical input	1152
TM during office hours scenarios			
Base-case scenario	–	–	1051
Low-cost scenario	1 hour of triage and follow-up per patient	Clinical input/Dar *et al.*[67]	801.20
High-cost scenario	Device cost of £1176 per year (with more peripherals)	Clinical input	1287.50

High-cost usual post-discharge care cost scenario

As the usual care was not reported clearly in the studies in the systematic review, a high-cost usual post-discharge care scenario was developed after discussions with the expert advisory group. It was assumed that on discharge one HF hospital nurse visits the patient at home on a weekly basis for 3–4 weeks, and subsequently the district nurse visits a further three to four times in the period between week 4 and week 8 after discharge. It was assumed that patients also have monthly GP consultations. It was also assumed that monitoring costs include the medical costs of patients such as the costs of diagnostic and pathology laboratory tests once every 6 months. These numbers of visits were multiplied by the corresponding unit cost per contact, based on the data from PSSRU 2011[133] reported in *Table 27*, to estimate a cost for each patient of £592 for 6 months (*Table 33*).

Usual care beyond the treatment duration of 6 months

It was assumed that at the end of the 6-month treatment period all patients receive usual care as recommended in the NICE clinical guidelines for the management of adults with HF,[34] irrespective of whether they received the intervention or post-discharge usual care during the treatment period. Usual care for patients beyond the 6-month treatment period, based on the description in the NICE guidelines, is shown in *Table 34*.

Hospitalisation costs

The hospitalisation costs are one of the major cost drivers for HF; the estimated mean costs of the hospitalisations are presented in *Table 35*. The mean inpatient admission cost for HF-related hospitalisations was calculated from the weighted average of the costs for the Healthcare Resource Group (HRG) 'Heart Failure or Shock' (EB03H, EB03I) based on the data obtained from the *NHS Reference Costs 2009–10*.[134] For hospital admissions for any cause other than HF it was assumed that the cost was the same as the mean cost of hospital admission for the general population. This was estimated as a weighted average of elective inpatient admissions and non-elective inpatient admissions (including both short and long stay) based on data from the *NHS Reference Costs 2009–10*.[134]

TABLE 32 Usual post-discharge care costs based on data from the TEN-HMS trial[49]

Medical care	Frequency per patient	Source	Unit cost per contact (£)	Source	Cost per 6 months (£)
Emergency room visits	0.09	Cleland *et al.* (TEN-HMS)[49]	130	Department of Health[134]	12
Office visits: family practitioner	1.33	Cleland *et al.* (TEN-HMS)[49]	46	PSSRU 2011[133]	61
Office visits: specialist	0.38	Cleland *et al.* (TEN-HMS)[49]	46	PSSRU 2011[133]	18
Office visits: nurse and other	0.40	Cleland *et al.* (TEN-HMS)[49]	25	PSSRU 2011[133]	10
Home visits: family practitioner	0.47	Cleland *et al.* (TEN-HMS)[49]	104	PSSRU 2011[133]	49
Home visits: specialist	–	Cleland *et al.* (TEN-HMS)[49]	104	PSSRU 2011[133]	–
Home visits: nurse and other	0.30	Cleland *et al.* (TEN-HMS)[49]	38	Department of Health[134]	11
Total medical care costs per patient for 6 months					161

TABLE 33 Usual care cost scenarios for 6 months

Scenario	Assumption	Source	Total cost (£)
Base-case usual care cost	–	Cleland *et al.* (TEN-HMS)[49]	161
High-cost usual care cost	Expert advisory group	PSSRU 2011[133]	592

TABLE 34 Usual care for patients post treatment

Medical care	Frequency per patient	Source	Unit cost per contact (£)	Source	Cost per 6 months (£)
Clinical assessment	1	[a]NICE clinical guidelines[34]	46	[b]PSSRU 2011[133], section 10.8b, p. 149	46
Laboratory tests[c]	1	[d]NICE clinical guidelines[34]	3	[e]Department of Health[134]	3
Total medical care costs per patient for 6 months					49

a Recommendation 1.4.1.3.
b Complex consultation lasting 17.2 minutes.
c Serum urea, electrolytes, creatinine and estimated glomerular filtration rate.
d Recommendation 1.4.1.1.
e Equivalent to haematology (code: DAP823).

Drug costs

Drug costs were not clearly reported for many of the trials and there was little description of the difference in drug use or drug costs between usual care and RM amongst studies identified in the systematic review; thus, it was assumed in the model that the drug costs were the same in the usual care and RM groups.

TABLE 35 Heart failure-related and other-cause hospitalisation costs

Hospitalisation	Average cost (lower and upper quartile) (£)
HF-related hospitalisations[a]	2514.49 (1857.10 to 2809.95)
Other-cause hospitalisations[b]	1529.79 (1129.84 to 1709.55)

a 'Heart Failure or Shock' (EB03H, EB03I): non-elective inpatient (long stay) including excess bed-days.[134]
b Non-elective inpatient (long and short stay) including excess bed-days.[134]

Summary of modelling input parameters

The Markov model assigned each patient a monthly probability of death, and in each monthly period the patients who are alive were under monthly risks of HF-related hospitalisations or other-cause hospitalisations. The risks of death and hospitalisation for RM interventions were estimated by applying the HRs from the meta-analysis to the baseline risks of mortality and hospitalisation. The effect of the intervention was assumed to last for a period of 6 months and after this it was assumed that patients reverted back to usual care. Each patient alive accumulated costs and QALYs every period based on their hospitalisation and treatment status. The model used a 30-year time horizon and the economic perspective of the model was the NHS in England and Wales. A summary of the model parameters is provided in *Table 36*.

Methods to estimate cost-effectiveness

The cost-effectiveness of the different interventions was estimated using both the ICER and the net benefit approaches. Uncertainty was incorporated in the modelling by performing PSA. Descriptions of these terms and approaches are provided in the following sections.

Definitions of cost-effectiveness terms

The ICER measures the relative value of two strategies and is calculated as the mean incremental cost divided by the mean incremental benefits. A strategy is dominated when another strategy accrues more QALYs for less cost. Extended dominance occurs when a combination of two alternative strategies can produce the same QALYs as a chosen strategy but at a lower cost. Strategies that are neither dominated nor extendedly dominated constitute the cost-effectiveness frontier, and the ICER is reported for these strategies compared with the next least effective strategy.

The WTP threshold is the amount of money that the decision-maker is willing to pay to gain 1 additional QALY. The usual threshold for decision-making at NICE is considered to be around £20,000–30,000 per QALY.

The net monetary benefit (NMB) is defined as the QALYs multiplied by a value for the QALYs (e.g. £20,000) minus the costs of obtaining them, that is, NMB = QALYs × lambda − cost, where lambda is the WTP threshold. The NMB approach is simpler to calculate and gives equivalent findings (but requires an explicit assumption regarding the value of lambda).

Uncertainty analysis

The results presented in the following section include the effects of accounting for uncertainty in the model parameters (the costs, utilities, risks and HRs for mortality, HF-related hospitalisations and all-cause hospitalisations), characterised as probability distributions. PSA is undertaken whereby the model is rerun (10,000 times), each time with a different value for the risks, HRs, costs and utilities, which is sampled from the probability distributions.

The cost-effectiveness plane shows the incremental costs (*y*-axis) and incremental QALYs (*x*-axis) compared with usual care. In this chart, if a model run for a strategy had exactly the same costs and QALYs as usual care then the 'sample' for that model run would appear at the origin. Samples plotted to the right of the

TABLE 36 Summary of model parameters

Parameter	Central estimate	Distribution	Source
Monthly mortality probability			
Months 0–1	0.04622[a]	0.005716[b]	Solomon *et al.* (CHARM)[127]
Months >1–3	0.03306[a]	0.003719[b]	Solomon *et al.* (CHARM)[127]
Months >3–6	0.02674[a]	0.002864[b]	Solomon *et al.* (CHARM)[127]
Months >6–12	0.02353[a]	0.002178[b]	Solomon *et al.* (CHARM)[127]
Months >12–24	0.01866[a]	0.001661[b]	Solomon *et al.* (CHARM)[127]
Months >24	0.01467[a]	0.001970[b]	Solomon *et al.* (CHARM)[127]
Number of monthly hospitalisations			
HF-related	0.0350[a]	0.001256[b]	Klersy *et al.*[123]
All-cause	0.0875[a]	0.001700[b]	Klersy *et al.*[123]
HR for mortality			
STS HM	0.98[c]	Samples	NMA
STS HH	0.77[c]	Samples	NMA
TM	0.76[c]	Samples	NMA
HR for HF-related hospitalisations			
STS HM	1.03[c]	Samples	NMA
STS HH	0.77[c]	Samples	NMA
TM	0.95[c]	Samples	NMA
HR for all-cause hospitalisations			
STS HM	1.06[c]	Samples	NMA
STS HH	0.97[c]	Samples	NMA
TM	0.75[c]	Samples	NMA
HRQoL			
Year 1	0.58[a]	0.015[b]	Miller *et al.*[131]
>Year 1	0.67[a]	0.015[b]	Miller *et al.*[131]
Disutility for HF-related hospitalisation	–0.1[a]	Triangular (–0.08, –0.1, 0.11)	Yao *et al.*[132]
Cost (£) per 6 months			
Usual care	161[d]	592[e]	Cleland *et al.* (TEN-HMS),[49] clinical input
STS HM	715[d]	623–794[f]	Clinical input
STS HH	1075[d]	1051–1152[f]	Clinical input
TM	1051[d]	801–1288[f]	Clinical input
Cost (per month) (£) after 6 months			
Usual care after 6 months	8.23	–	NICE clinical guidelines[34]

a Mean estimate.
b Standard deviation.
c Median value.
d Base-case cost.
e High-cost scenario.
f Low- and high-cost scenarios.

y-axis have more QALYs than usual care and samples plotted above the *x*-axis have more costs. Samples plotted to the right of a straight line with slope lambda passing through the origin are cost-effective whereas those plotted to the left are not. The cost-effectiveness acceptability curve (CEAC) shows the proportion of model runs for which each strategy is cost-effective over a range of potential WTP thresholds (i.e. lambda).

Another measure of uncertainty is the overall EVPI. This calculation is carried out based on the theory that the decision-maker will choose the most cost-effective option but could acquire additional evidence to reduce the uncertainties in the decision, for example know exactly what the HRs for mortality and hospitalisations are for each treatment. In the EVPI calculation it can be estimated how often making the decision based on current evidence could be wrong, and also how many QALYs (and costs) would be lost by choosing the strategy that is expected to be most cost-effective given current evidence when in fact one of the other strategies is truly the most cost-effective. One can estimate a monetary value lost by making a 'wrong' decision to choose a strategy based on current evidence by valuing the QALYs using the WTP threshold for this possible loss, that is, the net benefit lost on each of the occasions when another strategy would be optimal. This can be multiplied by the number of patients per year and the expected lifetime of the decision to estimate the population EVPI. The interpretation of this number is that if one could fund research to eliminate the uncertainty in effectiveness for all of the HRs for each strategy (e.g. by a large or infinitely large four-arm clinical trial) then the value of eliminating the uncertainty through such research would be expected to be the population EVPI.

Results of the independent economic assessment

This section details the results of the cost-effectiveness analyses estimated for a single HF patient as mean values of 10,000 PSA runs, each PSA run with a different estimate for the risks, HRs, costs and utilities sampled from the probability distributions reported in *Table 36*.

Results are presented using different effectiveness parameters (i.e. HRs) estimated from the NMA summarised in *Tables 24* and *25*. The cost-effectiveness analysis was performed using the base-case costs shown in *Table 31* for these four estimates of effectiveness, that is, HRs based on CrIs and predictive distributions from the NMA, both including and excluding data from the Home-HF study.[67] Results are also presented for five cost scenarios: (1) higher usual care cost scenario, (2) lower cost scenario of TM during office hours, (3) higher cost scenario of TM during office hours, (4) lower STS cost scenario and (5) higher STS cost scenario. The cost-effectiveness for each of these scenarios was performed using the four estimates of effectiveness, that is, HRs based on CrIs and predictive distributions from the NMA, both including and excluding data from the Home-HF study.[67]

This approach was taken to address the uncertainty in the cost and effectiveness evidence. For decision-makers deciding which of these sets of results is most representative of their setting, the key questions relate to the inclusion of the Home-HF study in the effectiveness meta-analyses. If one believes that usual care is best represented by the usual care arm in the Home-HF study,[67] which is the only study showing a statistically significant difference in effectiveness between usual care over RM, then perhaps the results including the Home-HF study[67] might be considered more relevant than those without. If, on the other hand, one believes that the performance of usual care is better represented by the other studies and that usual care in the Home-HF trial[67] is not representative of current usual care, then the results excluding this trial might be considered more relevant. Similarly, the users of the results should decide which cost scenario best reflects their local practice.

In each case, the expected estimates of cost-effectiveness and the uncertainty around them are presented, along with the probability that each of the four strategies, STS HM, STS HH, TM during office hours and usual care, is the most cost-effective. The EVPI, a measure of how valuable it would be to eliminate all of the existing uncertainty, is also provided for each scenario.

Results of the primary analyses

Results for base-case costs

The results of the NMA with HRs based on CrIs and including the Home-HF study[67] suggest that both TM during office hours and STS HH are similar in terms of mean HRs for mortality (0.779 for TM during office hours vs 0.780 for STS HH). STS HH is the most effective in terms of HF-related hospitalisation reduction with TM during office hours being the second most effective (mean HR 0.778 for STS HH vs 0.966 for TM during office hours). However, STS HH is the second most effective in terms of all-cause hospitalisation reduction after TM during office hours (mean HR 0.977 for STS HH vs 0.761 for TM during office hours) (*Table 37*). All mean HRs for STS HM are >1, suggesting that STS HM is not effective in reducing mortality or hospitalisations. It should be noted that the mean HRs are calculated as an average of the 10,000 PSA HR samples provided by the NMA for input into the model.

Structured telephone support with human-to-human contact is the most costly strategy over a 6-month period (average monthly cost over treatment duration of first 6 months = £179 for STS HH compared with £175 for TM during office hours). Thus, it is necessary to estimate the incremental cost-effectiveness compared with the other interventions to answer the question, 'Is the additional effect estimated for STS HH using the NMA worth the additional costs of the strategy?'

The survival results suggest that the lower HR for mortality would result in an estimated survival gain for TM during office hours over usual care of 0.202 years (mean undiscounted life expectancy = 4.912 years for TM vs 4.710 for usual care). This 0.202 life-years (just over 10 weeks, i.e. 73 days) mean additional survival for TM during office hours is slightly higher than the additional 0.199 LYG with STS HH, which has a mean life expectancy of 4.909 years. Similar survival benefits for STS HH and TM during office hours can be attributed to their similar mean HRs for mortality as seen in *Table 37*.

However, the QALY results show a reverse pattern to those for survival, with STS HH showing a higher QALY gain over usual care of 0.1059 compared with an additional 0.1038 QALYs gained with TM during office hours (equivalent to an additional 37.7 and 38.6 quality-adjusted days average gain for STS HH and TM respectively). This is because of fewer QALYs lost to HF hospitalisation by STS HH (–0.1638) than TM (–0.1673), in line with the higher effectiveness of STS HH in terms of HF-related hospitalisation reduction (HR of 0.778 for STS HH vs 0.966 for TM).

The expected costs over a lifetime (30-year time horizon) differ for each strategy, with STS HH having the highest costs at £9604 followed by TM during office hours (£9470), STS HM (£9001) and usual care (£8478). The main contribution to the overall costs comes from the hospitalisation costs, with the intervention and usual care costs being significantly lower.

Compared with usual care, STS HH has an additional discounted cost of approximately £1126; the majority of this cost difference was due to the difference in the costs of treatment in the treatment period, that is, the first 6 months (it was assumed that all of the patients revert to standard usual care after 6 months). There were also slightly higher hospitalisation costs, which were dependent on the number of people alive and the risks of hospitalisation for each intervention, that is, the HRs for mortality and hospitalisation respectively. For example, STS HH has an additional HF-related hospitalisation cost of around £70 per person over and above that of usual care and an additional £207 for other-cause hospitalisations. This is because STS HH patients live longer than usual care patients and, despite the lower risk of HF-related hospitalisation per month (HR 0.778) and the slightly lower risk of all-cause hospitalisation (HR 0.977), this leads to higher hospitalisation costs.

The additional discounted cost of £1126 for STS HH is higher than that of TM during office hours, which has an additional expected lifetime cost over and above that of usual care of £992 per person. This is because the higher HF-related hospitalisation costs of TM during office hours are offset by lower costs of other hospitalisations.

TABLE 37 Results of the economic analysis using base-case costs

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.074	0.780	0.779
HF-related hospitalisation HR	1.000	1.045	0.778	0.966
All-cause hospitalisation HR	1.000	1.173	0.977	0.761
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	71.45	75.34	75.38
5 years (%)	33.75	33.43	35.25	35.27
Life expectancy over 30 years (years)	4.710	4.666	4.909	4.912
Difference in life expectancy vs usual care (years)	–	–0.04	0.199	0.202
Cost results (£)				
Discounted cost of usual care	491	343	362	362
Discounted cost of treatment	0	632	978	957
Discounted cost of HF-related hospitalisations	4187	4169	4257	4348
Discounted cost of other hospitalisations	3800	3858	4007	3803
Total costs	8478	9001	9604	9470
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–148	–129	–129
Discounted cost of treatment	0	632	978	957
Discounted cost of HF-related hospitalisations	0	–19	70	161
Discounted cost of other hospitalisations	0	57	207	3
Total difference in costs	0	523	1126	992
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5509	2.6834	2.6848
HF-related hospitalisation decrement	–0.1611	–0.1604	–0.1638	–0.1673
Total discounted QALYs	2.4137	2.3905	2.5196	2.5175
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0239	0.1086	0.1100
HF-related hospitalisation decrement	0.0000	0.0007	–0.0027	–0.0062
Total difference in discounted QALYs	0.0000	–0.0232	0.1059	0.1038
Total discounted QALYs rank (1 = highest)	3	4	1	2
Probabilistic ICER vs usual care (£/QALY)		Dominated	10,629	9552
Probabilistic sequential ICER (£/QALY)		Dominated	63,240[a]	9552

continued

TABLE 37 Results of the economic analysis using base-case costs (*continued*)

	Usual care	STS HM	STS HH	TM during office hours
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	2	18	36	44
Expected total costs from PSA (£)	8478	9001	9604	9470
Expected total QALYs from PSA	2.4137	2.3905	2.5196	2.5175
Expected net benefit from PSA (£)	39,795	38,809	40,788	40,880
Difference from usual care costs (£)	0	523	1126	992
Difference from usual care QALYs	0.0000	–0.0232	0.1059	0.1038
Difference from usual care net benefit (£)	0	–986.75	993	1084
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at WTP of 20,000 per QALY (£)	826			
Population EVPI (£)	45,247,202			

a Last strategy in the cost-effectiveness frontier.

To assess whether or not the additional costs are worthwhile, the incremental cost per QALY gained is estimated. Comparing STS HH with usual care, the incremental cost per QALY gained is £1126/0.1059 = £10,629, which is below the typical NICE threshold of £20,000–30,000 per QALY gained. The ICER for TM during office hours compared with usual care is £992/0.1038 = £9552, which is also below the threshold of £20,000–30,000 per QALY gained.

However, when there are multiple possible strategies, one needs to calculate ICERs between different pairs, comparing each strategy with the next most effective strategy. Strategies that are dominated (or extendedly dominated) are removed from the cost-effectiveness frontier and the ICER is reported for these strategies compared with the next least effective strategy. Here, STS HM is dominated as usual care resulted in better health outcomes (2.4137 QALYs) and lower costs (£8478) than STS HM (2.3905 QALYs and £9001). As TM during office hours is the next most effective strategy compared with usual care, the ICER of TM during office hours against usual care is estimated at £9522 per QALY. The ICER of STS HH compared with TM during office hours is estimated as (£9604 – £9470)/(2.5196 – 2.5175) = £136/0.0021 = £63,240 per QALY, which suggests that STS HH cannot be considered more cost-effective than TM during office hours at the typical NICE threshold of £20,000–30,000 per QALY gained. In this situation, TM during office hours is estimated to be the most cost-effective option with an ICER of £9522 per QALY.

Another way to present these results is to calculate the NMB of each strategy. The NMB of TM during office hours is (2.5175 × £20,000) – £9470 = £40,880. This approach takes away the need to calculate the ICER and simplifies the interpretation for decision-makers as the strategy with the highest expected incremental NMB is the most cost-effective. Using a threshold value of £20,000 per QALY, the estimated incremental NMB of TM during office hours compared with usual care is estimated to be £40,880 – £39,795 = £1084. Mathematically, as this difference is positive (i.e. >0), the ICER must be <£20,000 (the ICER of TM during office hours compared with usual care is £9522 per QALY).

In terms of NMB then, if one accepts a cost-effectiveness threshold of £20,000 per QALY, the results show that TM during office hours is estimated to be the most cost-effective, with STS HH second and STS HM the least cost-effective.

In the cost-effectiveness plane shown in *Figure 11*, the samples to the right of the dotted line through the origin would have an incremental cost per QALY compared with usual care of < £20,000 and so would be considered cost-effective compared with usual care. *Figure 11* shows that the majority of the TM during office hours and STS HH samples fall to the right of the dotted line, suggesting that they have a high chance of being cost-effective compared with usual care. The figure shows that the uncertainty in QALYs is larger for STS HM than it is for the other two strategies, because of the greater uncertainty in the HRs reported. There is less uncertainty in costs than QALYs in this base-case scenario. This is because in this scenario we have assumed that the monthly costs of the interventions are fixed at £119, £179 and £175 during the treatment period of 6 months for STS HM, STS HH and TM during office hours respectively. Thus, the uncertainty in costs shown in *Figure 11* is actually a function of the uncertainty in the HRs for hospitalisations (more or fewer hospitalisations occurring, which are then multiplied by fixed unit costs) and mortality (more or less time alive, during which there is a risk of hospitalisation per month).

The model is rerun 10,000 times, each time with a different value for the HRs, costs and utilities sampled from the probability distribution, and in some of the sampled model runs TM during office hours could be more effective than STS HH because of the overlap in the probability distributions of their HRs. There is a chance that the HR for TM during office hours could be lower, that is, better, than that for STS HH. The CEAC in *Figure 12* shows the proportion of model runs for which each strategy is cost-effective over a range of potential WTP thresholds. The percentage of model runs in which TM during office hours was the most cost-effective strategy (at a £20,000 per QALY threshold) was 44%, with the percentage of model runs in which STS HH, STS HM and usual care were the most cost-effective being 36%, 18% and 2% respectively.

A CEAC in which the best strategy is cost-effective less than half of the time (44%) indicates that there is substantial uncertainty as to which strategy is the optimal in terms of net benefit. This uncertainty can also be measured as the overall EVPI, which is the average of the net benefits lost by making the decision now to choose TM during office hours. The EVPI in this case is £826 per patient for whom the decision is made, and the population EVPI per annum was estimated at £45,247,202 by multiplying the EVPI per patient with the annual incidence of first HF-related hospital admissions in England and Wales (i.e. £826×54,779).

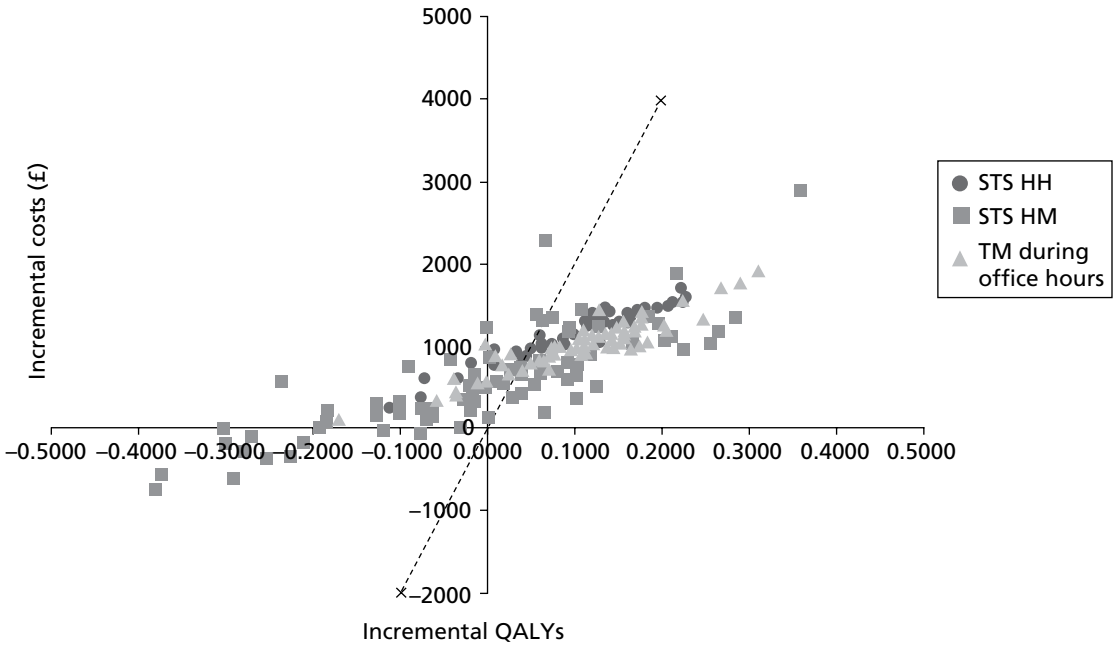

FIGURE 11 Cost-effectiveness plane for the economic analysis using base-case costs with effectiveness data from the NMA including the Home-HF study.[67]

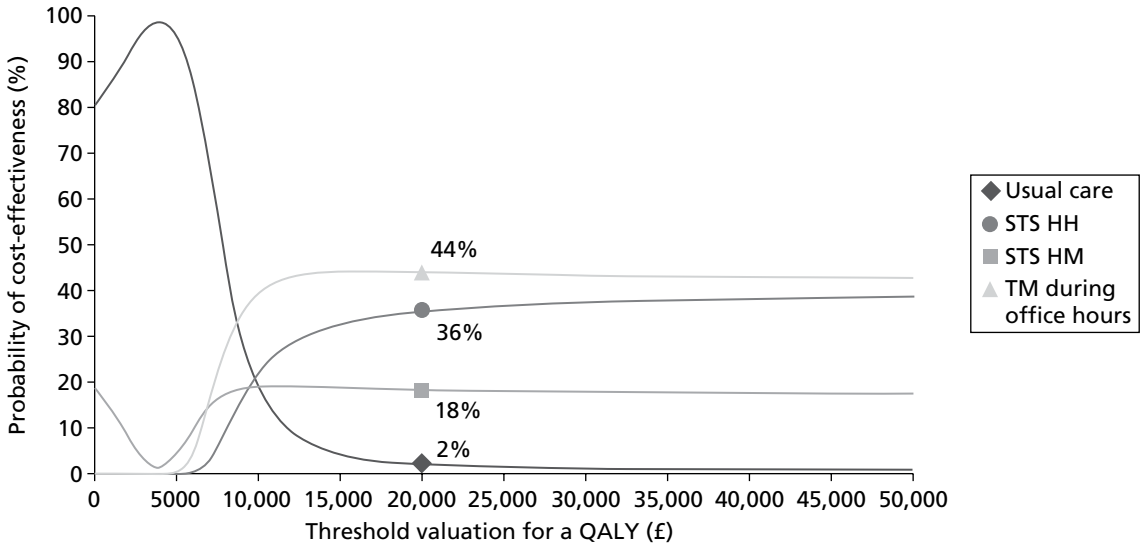

FIGURE 12 Cost-effectiveness acceptability curve for the economic analysis using base-case costs.

Results for base-case costs using effectiveness data from predictive distributions

The same analyses were performed using HRs from predictive distributions of the NMA including the Home-HF study[67] and the results are presented in *Table 38*. As explained in *Chapter 3* (see *Results of the clinical effectiveness review*), the predictive distributions place more emphasis on heterogeneity between studies and provide wider estimates than CrIs. In this analysis, the most effective strategy in terms of the mortality HR is again TM during office hours (mean HR 0.843), with STS HH being the second best strategy (mean HR 0.849).

In terms of NMB, TM during office hours has the highest followed by STS HH, with mean incremental NMBs of £656 and £534, respectively, compared with usual care, suggesting that the ICERs for TM during office hours and STS HH compared with usual care are < £20,000 per QALY. In terms of incremental analysis, again TM during office hours is the most cost-effective option assuming a NICE cost-effectiveness threshold of £20,000 per QALY gained, with an ICER for TM during office hours compared with usual care of £11,873 per QALY gained, whereas STS HH has an ICER of £228,035 per QALY gained compared with TM during office hours.

The cost-effectiveness results estimated here were similar to the results with effectiveness data from the CrIs of the NMA including the Home-HF study.[67] However, the ICER for TM during office hours compared with usual care using HRs from the predictive distributions is £11,873, which is slightly higher than the ICER of £9522 estimated using HRs from the CrIs. This is due to the higher estimates of HRs in the predictive distributions (mean mortality HR 0.843) than the HRs based on CrIs (mean mortality RR 0.779).

Furthermore, the results using HRs from the predictive distributions are also more uncertain, as seen in the wider distribution of the samples in the cost-effectiveness plane shown in *Figure 13* than in the cost-effectiveness plane shown in *Figure 11*, estimated using HRs based on CrIs. This is because the HRs estimated from the predictive distributions of the NMA have more uncertainty than those estimated from HRs based on CrIs.

The proportion of model runs in which TM during office hours was the most cost-effective strategy (at a £20,000 per QALY threshold) was 40%, with the proportion of model runs in which STS HH, STS HM and usual care were the most cost-effective being 35%, 19% and 6% respectively (*Figure 14*). As described earlier, the results are slightly more uncertain when HRs from predictive distributions are used [the proportion of model runs in which TM during office hours was the most cost-effective strategy (at a £20,000 per QALY threshold) when HR estimates from CrIs were used was 44%]. This uncertainty is also

TABLE 38 Results of the economic analysis using the base-case costs with effectiveness data from predictive distributions of the NMA including the Home-HF study[67]

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.180	0.849	0.843
HF-related hospitalisation HR	1.000	1.063	0.790	0.982
All-cause hospitalisation HR	1.000	1.302	1.074	0.835
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	70.61	74.58	74.66
5 years (%)	33.75	33.04	34.89	34.93
Life expectancy over 30 years (years)	4.710	4.614	4.862	4.867
Difference in life expectancy vs usual care (years)	–	–0.10	0.151	0.157
Cost results (£)				
Discounted cost of usual care	491	339	358	359
Discounted cost of treatment	0	627	972	951
Discounted cost of HF-related hospitalisations	4187	4130	4221	4316
Discounted cost of other hospitalisations	3800	3869	4023	3811
Total costs	8478	8965	9574	9437
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–152	–132	–132
Discounted cost of treatment	0	627	972	951
Discounted cost of HF-related hospitalisations	0	–57	33	129
Discounted cost of other hospitalisations	0	69	223	11
Total difference in costs	0	487	1096	959
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5223	2.6575	2.6605
HF-related hospitalisation decrement	–0.1611	–0.1589	–0.1624	–0.1661
Total discounted QALYs	2.4137	2.3633	2.4950	2.4944
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0525	0.0827	0.0857
HF-related hospitalisation decrement	0.0000	0.0022	–0.0013	–0.0050
Total difference in discounted QALYs	0.0000	–0.0504	0.0814	0.0808
Total discounted QALYs rank (1 = highest)	3	4	1	2
Probabilistic ICER vs usual care (£/QALY)		Dominated	13,473	11,873
Probabilistic sequential ICER (£/QALY)		Dominated	228,035[a]	11,873

continued

TABLE 38 Results of the economic analysis using the base-case costs with effectiveness data from predictive distributions of the NMA including the Home-HF study[67] (*continued*)

	Usual care	STS HM	STS HH	TM during office hours
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	6	19	35	40
Expected total costs from PSA (£)	8478	8965	9574	9437
Expected total QALYs from PSA	2.4137	2.3633	2.4950	2.4944
Expected net benefit from PSA (£)	39,795	38,301	40,327	40,452
Difference from usual care costs (£)	0	487	1096	959
Difference from usual care QALYs	0.0000	–0.0504	0.0814	0.0808
Difference from usual care net benefit (£)	0	–1494.07	531	656
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	1831			
Population EVPI (£)	100,299,791			

a Last strategy in the cost-effectiveness frontier.

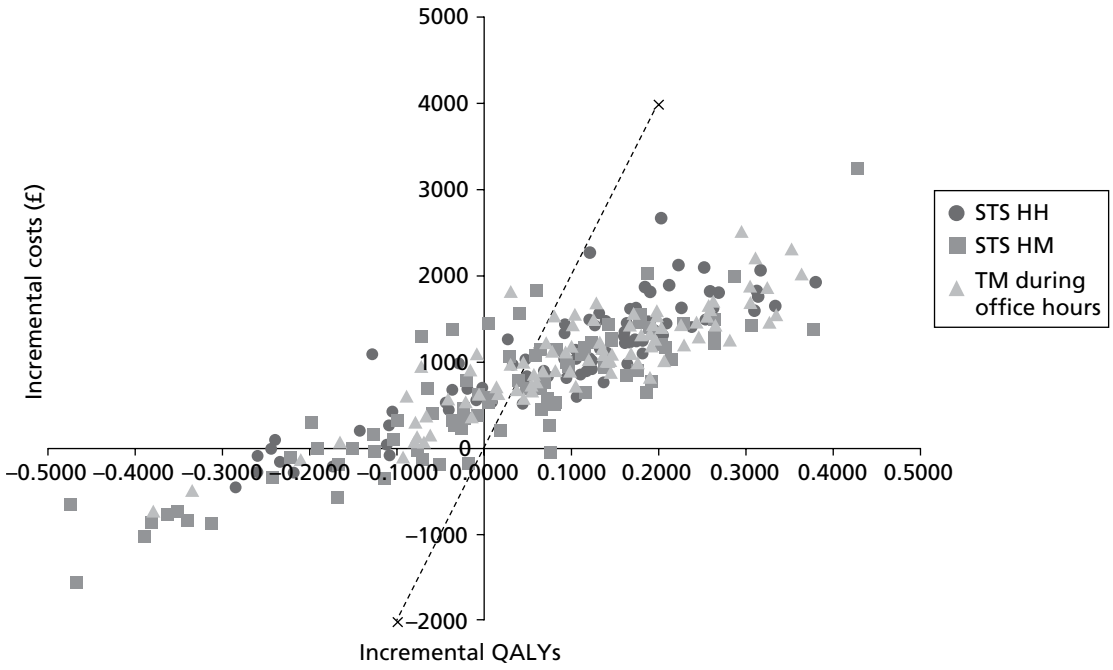

FIGURE 13 Cost-effectiveness plane for the economic analysis using base-case costs with effectiveness data from predictive distributions.

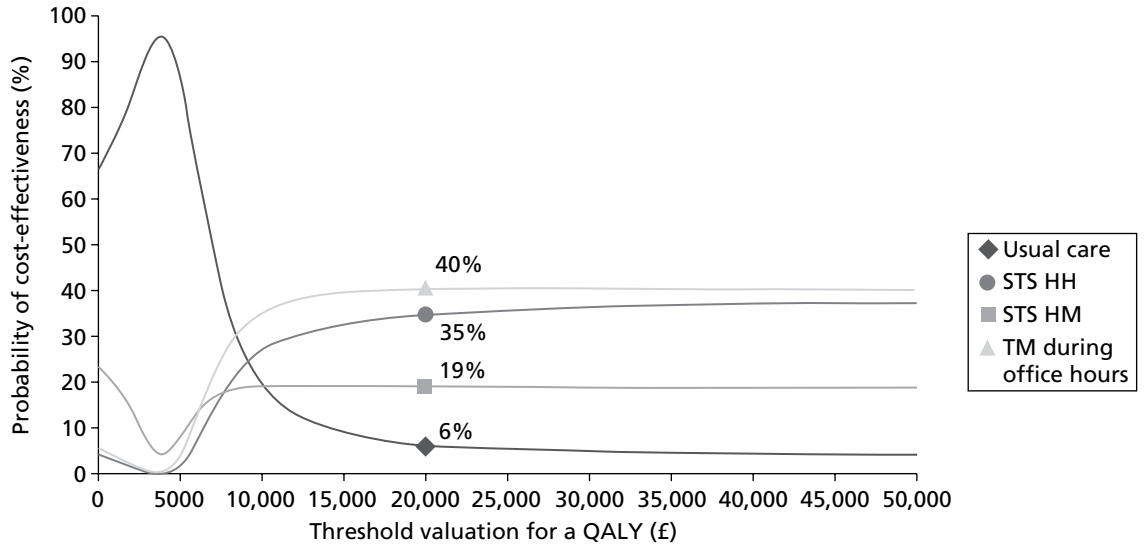

FIGURE 14 Cost-effectiveness acceptability curve for the economic analysis using base-case costs with effectiveness data from predictive distributions.

reflected in the higher EVPI of £1831 per patient when HR estimates from predictive distributions were used compared with £826 when HR estimates from CrIs were used (as reported in *Results for base-case costs*). The population EVPI per annum was £100M compared with £45M when HR estimates from CrIs were used.

Results for base-case costs using effectiveness data excluding the Home-HF study[67]

The results of the NMA excluding the Home-HF study[67] suggest that TM during office hours is substantially more effective in terms of mortality risk reduction (HR 0.627) than the second most effective strategy STS HH (HR 0.757), with STS HM slightly worse than usual care (HR 1.007). Cost-effectiveness analysis was performed with these HR estimates and the results are presented in *Table 39*.

Telemonitoring during office hours was estimated to be the most cost-effective option with an ICER of £6616 per QALY gained, with STS HM and STS HH being dominated and extendedly dominated respectively. In terms of the incremental NMB compared with usual care, again TM during office hours was the best strategy with an incremental NMB of £2371; STS HH was the second best strategy with an incremental NMB of £1181. These estimates for TM during office hours show improved cost-effectiveness (i.e. lower ICER and higher incremental NMB) than the estimates when the Home-HF study[67] was included in the NMA (ICER of £9522 per QALY and NMB of £1084). This is because the heterogeneity in intervention effects between studies was considerably reduced when the Home-HF study[67] was excluded, resulting in better effectiveness in terms of mortality risk reduction than when the Home-HF study[67] was included (HR 0.627 vs HR 0.779).

This can also be observed in the cost-effectiveness plane, with the samples based on estimates of effectiveness when the Home-HF study[67] was excluded from the NMA shifting to the right in the cost-effectiveness plane, as shown in *Figure 15*, compared with the samples in the cost-effectiveness plane shown in *Figure 11*, which is based on the estimates of effectiveness when the Home-HF study[67] was included in the NMA.

The proportion of model runs in which TM during office hours was the most cost-effective strategy (at a £20,000 per QALY threshold) was 83%, with STS HH at 12%, STS HM at 5% and usual care at 0% (*Figure 16*). This proportion of model runs (83%) in which TM was the most cost-effective strategy at £20,000 per QALY is much higher than the proportion of model runs in which TM was the most cost-effective strategy (44%) when the Home-HF study[67] was included in the NMA. This reduction in

TABLE 39 Results of the economic analysis using base-case costs with effectiveness data from the NMA excluding the Home-HF study[67]

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.007	0.757	0.627
HF-related hospitalisation HR	1.000	1.042	0.766	0.872
All-cause hospitalisation HR	1.000	1.134	0.969	0.678
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	72.14	75.67	77.63
5 years (%)	33.75	33.75	35.40	36.32
Life expectancy over 30 years (years)	4.710	4.7103	4.930	5.052
Difference in life expectancy vs usual care (years)	–	0.0003	0.220	0.342
Cost results (£)				
Discounted cost of usual care	491	346	363	373
Discounted cost of treatment	0	635	981	972
Discounted cost of HF-related hospitalisations	4187	4206	4269	4426
Discounted cost of other hospitalisations	3800	3873	4021	3879
Total costs	8478	9060	9635	9650
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–144	–127	–118
Discounted cost of treatment	0	635	981	972
Discounted cost of HF-related hospitalisations	0	18	82	239
Discounted cost of other hospitalisations	0	73	221	79
Total difference in costs	0	582	1157	1172
Overall cost rank (1 = lowest cost)	1	2	3	4
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5747	2.6949	2.7612
HF-related hospitalisation decrement	–0.1611	–0.1619	–0.1643	–0.1703
Total discounted QALYs	2.4137	2.4128	2.5306	2.5908
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0002	0.1200	0.1864
HF-related hospitalisation decrement	0.0000	–0.0007	–0.0032	–0.0092
Total difference in discounted QALYs	0.0000	–0.0009	0.1169	0.1772
Total discounted QALYs rank (1 = highest)	3	4	2	1
Probabilistic ICER vs usual care (£/QALY)		Dominated	9897	6616
Probabilistic sequential ICER (£/QALY)		Dominated	Extendedly dominated	6616[a]

TABLE 39 Results of the economic analysis using base-case costs with effectiveness data from the NMA excluding the Home-HF study[67] (*continued*)

	Usual care	STS HM	STS HH	TM during office hours
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	0	5	12	83
Expected total costs from PSA (£)	8478	9060	9635	9650
Expected total QALYs from PSA	2.4137	2.4128	2.5306	2.5908
Expected net benefit from PSA	39,795	39,196	40,976	42,167
Difference from usual care costs (£)	0	582	1157	1172
Difference from usual care QALYs	0.0000	–0.0009	0.1169	0.1772
Difference from usual care net benefit (£)	0	–599.54	1181	2371
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	133			
Population EVPI (£)	7,285,566			

a Last strategy in the cost-effectiveness frontier.

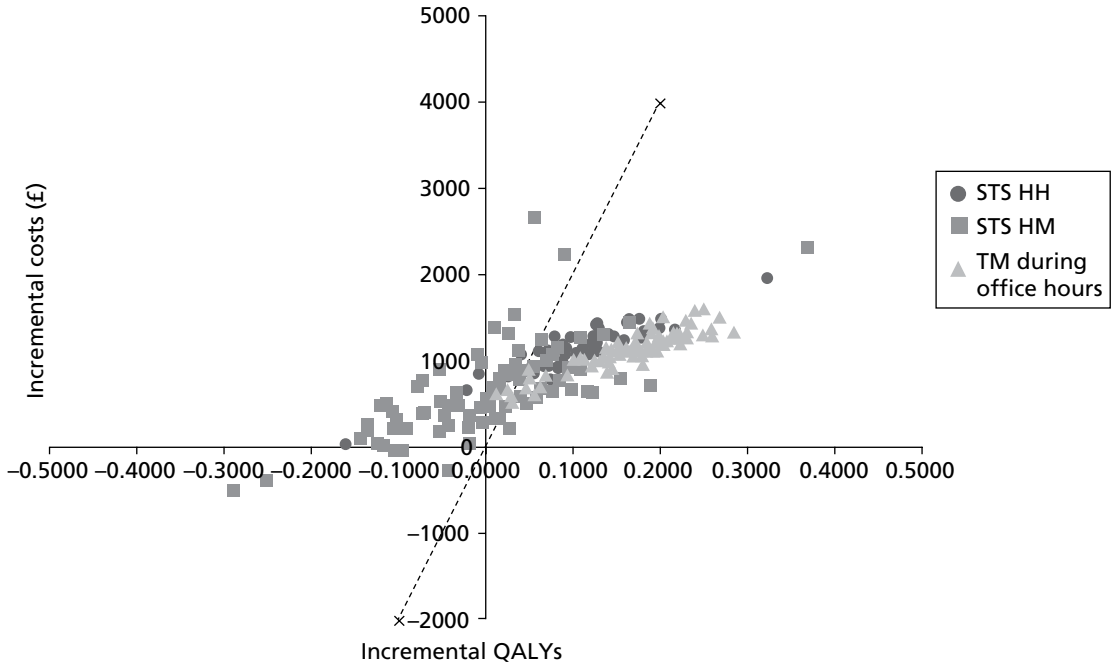

FIGURE 15 Cost-effectiveness plane for the economic analysis using base-case costs with effectiveness data excluding the Home-HF study.[67]

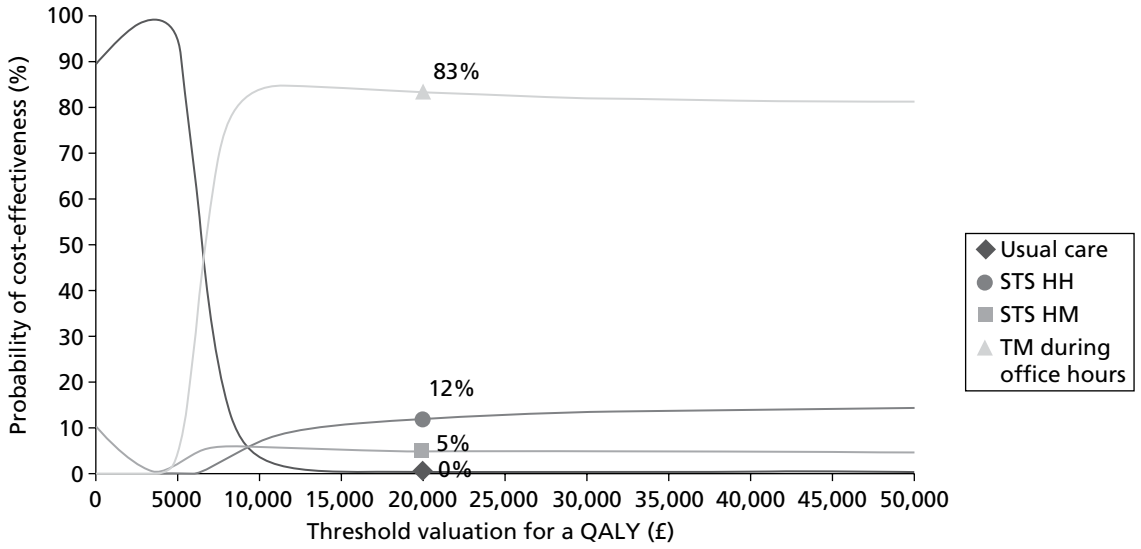

FIGURE 16 Cost-effectiveness acceptability curve for the economic analysis using base-case costs with effectiveness data excluding the Home-HF study.[67]

uncertainty is also reflected in the lower EVPI of £133 per patient when the Home-HF study[67] was excluded from the NMA compared with £826 when the Home-HF study[67] was included (as reported in *Results for base-case costs*).

Therefore, excluding the Home-HF study[67] from the NMA suggests that TM during office hours is the most cost-effective strategy and that there is less uncertainty involved in suggesting that this is the most cost-effective strategy than when the Home-HF study[67] is included in the NMA. Users can decide which of these analyses is most representative of the UK setting, that is, whether or not the usual care in the Home-HF study[67] is representative of usual care in the UK and whether or not this study should be included in the meta-analysis.

Results for base-case costs with effectiveness data from predictive distributions excluding the Home-HF study[67]

The results of the cost-effectiveness analysis using HRs from predictive distributions of the NMA excluding the data from the Home-HF study[67] suggest that the most effective strategy in terms of mortality reduction is TM during office hours (mean mortality HR 0.642), with STS HH the second most effective strategy (mean mortality HR 0.776) and STS HM worse than usual care (mean mortality HR 1.032). The cost-effectiveness analysis was performed with these HRs and the results are presented in *Table 40*.

In terms of incremental analysis, STS HM and STS HH are dominated and extendedly dominated respectively, with TM during office hours being the most cost-effective option with an ICER of £6942 per QALY. In terms of NMB, TM during office hours is again the most cost-effective strategy with a NMB of £2233; STS HH is the second most cost-effective strategy with a NMB of £1006.

The cost-effectiveness results estimated here were similar to the results using effectiveness data based on CrIs of the NMA excluding the Home-HF study.[67] However, the central estimates are slightly higher with an ICER of £6942 for TM during office hours compared with usual care using HRs from predictive distributions compared with an ICER of £6616 using HRs based on CrIs. This is due to the higher estimates of the HRs in the predictive distributions (mean mortality HR 0.642) than the HRs based on CrIs (mean mortality RR 0.627).

Furthermore, the results using predictive distributions are also more uncertain, as seen in the wider distribution of the samples in the cost-effectiveness plane shown in *Figure 17* compared with the

TABLE 40 Results of the economic analysis using base-case costs with effectiveness data from predictive distributions of the NMA excluding the Home-HF study[67]

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.032	0.776	0.642
HF-related hospitalisation HR	1.000	1.058	0.778	0.883
All-cause hospitalisation HR	1.000	1.235	1.048	0.731
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	71.89	75.44	77.44
5 years (%)	33.75	33.63	35.30	36.23
Life expectancy over 30 years (years)	4.71	4.69	4.92	5.04
Difference in life expectancy vs usual care (years)	0.00	–0.02	0.21	0.33
Cost results (£)				
Discounted cost of usual care	491	345	362	372
Discounted cost of treatment	0	634	979	971
Discounted cost of HF-related hospitalisations	4187	4200	4262	4422
Discounted cost of other hospitalisations	3800	3909	4055	3901
Total costs	8478	9087	9658	9665
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–145	–128	–119
Discounted cost of treatment	0	634	979	971
Discounted cost of HF-related hospitalisations	0	12	75	234
Discounted cost of other hospitalisations	0	108	255	101
Total difference in costs	0	609	1180	1187
Overall cost rank (1 = lowest cost)	1	2	3	4
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5659	2.6870	2.7548
HF-related hospitalisation decrement	–0.1611	–0.1616	–0.1640	–0.1701
Total discounted QALYs	2.4137	2.4043	2.5230	2.5847
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0089	0.1122	0.1800
HF-related hospitalisation decrement	0.0000	–0.0004	–0.0029	–0.0090
Total difference in discounted QALYs	0.0000	–0.0093	0.1093	0.1710
Total discounted QALYs rank (1 = highest)	3	4	2	1
Probabilistic ICER vs usual care (£/QALY)		Dominated	10,798	6942
Probabilistic sequential ICER (£/QALY)		Dominated	Extendedly dominated	6942[a]

continued

TABLE 40 Results of the economic analysis using base-case costs with effectiveness data from predictive distributions of the NMA excluding the Home-HF study[67] (*continued*)

	Usual care	STS HM	STS HH	TM during office hours
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	1	7	19	73
Expected total costs from PSA (£)	8478	9087	9658	9665
Expected total QALYs from PSA	2.4137	2.4043	2.5230	2.5847
Expected net benefit from PSA (£)	39,795	39,000	40,801	42,029
Difference from usual care costs (£)	0	609	1180	1187
Difference from usual care QALYs	0.0000	–0.0093	0.1093	0.1710
Difference from usual care net benefit (£)	0	–795.73	1006	2233
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	410			
Population EVPI (£)	22,459,265			

a Last strategy in the cost-effectiveness frontier.

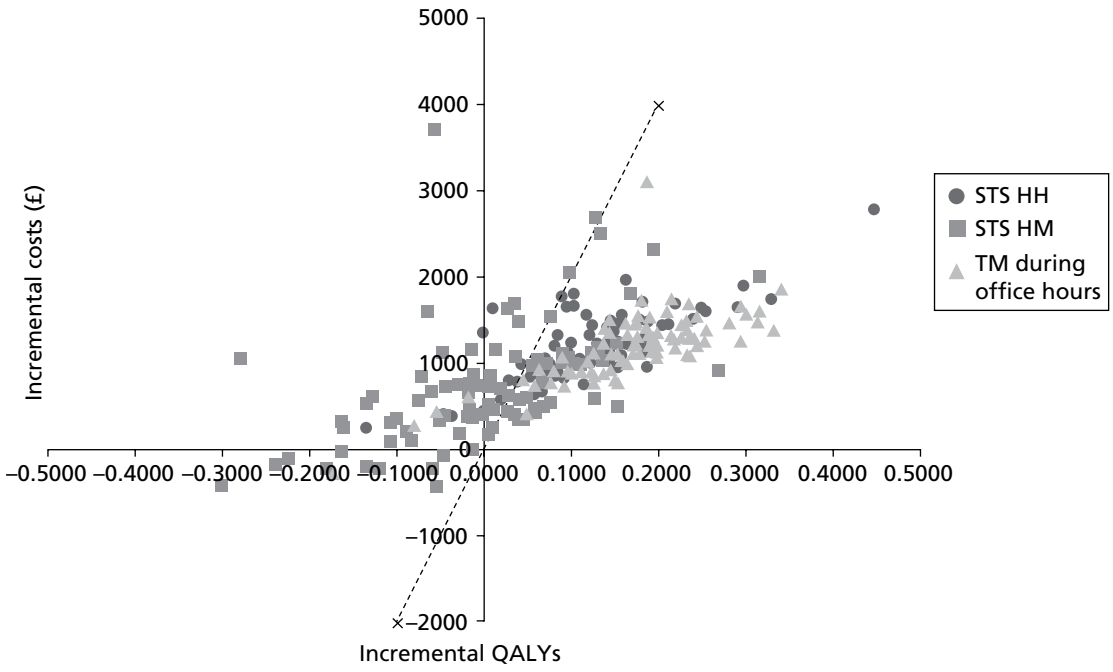

FIGURE 17 Cost-effectiveness plane using base-case costs with effectiveness data from predictive distributions excluding the Home-HF study.[67]

cost-effectiveness plane shown in *Figure 15*, estimated using HRs from CrIs. This is because the HRs for the predictive distribution of a new study are more uncertain than the HRs for the population mean of the studies.

The percentage of model runs in which TM during office hours was the most cost-effective strategy (at a £20,000 per QALY threshold) was 73%, with the percentage of model runs in which STS HH, STS HM and usual care were the most cost-effective being 19%, 7% and 1% respectively (*Figure 18*). The lower percentage of model runs in which TM during office hours was the most cost-effective strategy when estimates from the predictive NMA were used compared with when estimates from CrIs were used (83%) reflects the higher uncertainty in the HRs estimated from the predictive NMA than in those estimated based on CrIs.

Summary of the results for base-case costs

Table 41 provides the summary of the cost-effectiveness results using the base-case costs. TM during office hours appears to be the most cost-effective strategy at a threshold of £20,000 per QALY in all four analyses, that is, HRs based on CrIs and predictive distributions of the NMA, including and excluding the Home-HF study.[67] TM during office hours is also the most effective strategy (i.e. highest QALYs gained) in the analyses that excluded the Home-HF study.[67] TM during office hours is not the most effective strategy in the analyses that included the Home-HF study,[67] with STS HH providing the highest number of expected QALYs. However, the additional QALYs gained by STS HH are not worth the additional costs of the strategy as seen in the ICERs (compared with TM during office hours), which are greater than the threshold of £20,000 per QALY.

In the analyses that included the Home-HF study,[67] the cost-effectiveness of TM during office hours has high uncertainty as there is a 44% and 40% chance of TM during office hours being cost-effective for analyses using HR estimates from CrIs and predictive distributions respectively. However, this uncertainty is lower in the analyses using HRs from the NMA that excluded the Home-HF study,[67] with TM during office hours having an 83% and 73% chance of being cost-effective for analyses using estimates from CrIs and predictive distributions respectively.

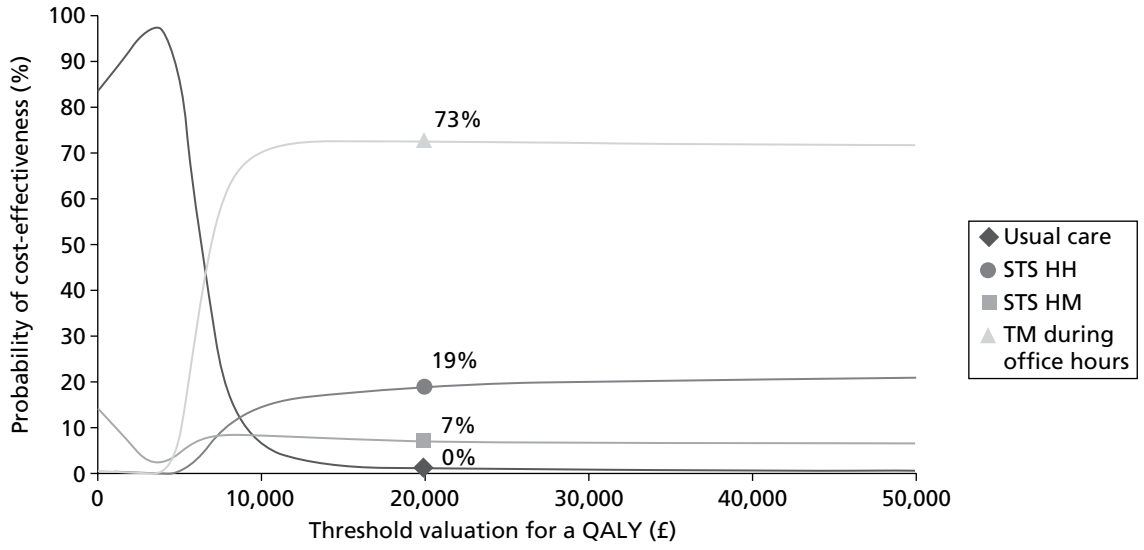

FIGURE 18 Cost-effectiveness acceptability curve for the economic analysis using base-case costs with effectiveness data from predictive distributions excluding the Home-HF study.[67]

TABLE 41 Summary of the economic analysis results using base-case costs

	Usual care	STS HM	STS HH	TM during office hours
Total costs (£)				
CrI	8478	9001	9604	9470
PrI	8478	8965	9574	9437
CrI excluding Home-HF[67]	8478	9060	9635	9650
PrI excluding Home-HF[67]	8478	9087	9658	9665
Difference in costs (£)				
CrI	–	523	1126	992
PrI	–	487	1096	959
CrI excluding Home-HF[67]	–	582	1157	1172
PrI excluding Home-HF[67]	–	609	1180	1187
Total QALYs				
CrI	2.4137	2.3905	2.5196	2.5175
PrI	2.4137	2.3633	2.4950	2.4944
CrI excluding Home-HF[67]	2.4137	2.4128	2.5306	2.5908
PrI excluding Home-HF[67]	2.4137	2.4043	2.5230	2.5847
Difference in QALYs				
CrI	–	–0.0232	0.1059	0.1038
PrI	–	–0.0504	0.0814	0.0808
CrI excluding Home-HF[67]	–	–0.0009	0.1169	0.1772
PrI excluding Home-HF[67]	–	–0.0093	0.1093	0.1710
ICER (£/QALY)				
CrI	–	Dominated	63,240[a]	9552
PrI	–	Dominated	228,035[a]	11,873
CrI excluding Home-HF[67]	–	Dominated	Extendedly dominated	6616[a]
PrI excluding Home-HF[67]	–	Dominated	Extendedly dominated	6942[a]
Expected incremental NMB (£)				
CrI	–	–986.75	993	1084
PrI	–	–1494.07	531	656
CrI excluding Home-HF[67]	–	–599.54	1181	2371
PrI excluding Home-HF[67]	–	–795.73	1006	2233
Probability of cost-effectiveness (%)				
CrI	2	18	36	44
PrI	6	19	35	40
CrI excluding Home-HF[67]	0	5	12	83
PrI excluding Home-HF[67]	1	7	19	73

PrI, predictive interval.

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Scenario analyses

Results for the high usual care cost scenario

A high cost usual care scenario in which the cost of usual care was £98.70 per patient per month during the treatment period (compared with the base-case usual care cost of £27), as described in *Usual care costs*, was incorporated to address the heterogeneity and uncertainty in the usual care cost data. All of the other parameters in this analysis were the same and the results summarised in *Table 42* are also presented in detail in *Appendix 12*.

In general, the higher usual care cost makes only a small difference to the results. For the high usual care cost scenario analysis, all of the intervention strategies showed an increase in cost-effectiveness. The ICER for TM during office hours compared with usual care decreased from £9522 per QALY in the base-case

TABLE 42 Summary of the economic analysis results using the high usual care cost

	Usual care	STS HM	STS HH	TM during office hours
Total costs (£)				
CrI	8861	9001	9604	9470
PrI	8861	8965	9574	9437
CrI excluding Home-HF[67]	8861	9060	9635	9650
PrI excluding Home-HF[67]	8861	9087	9658	9665
Difference in costs (£)				
CrI	–	140	743	609
PrI	–	104	713	576
CrI excluding Home-HF[67]	–	199	774	789
PrI excluding Home-HF[67]	–	226	797	804
Total QALYs				
CrI	2.4137	2.3905	2.5196	2.5175
PrI	2.4137	2.3633	2.4950	2.4944
CrI excluding Home-HF[67]	2.4137	2.4128	2.5306	2.5908
PrI excluding Home-HF[67]	2.4137	2.4043	2.5230	2.5847
Difference in QALYs				
CrI	–	–0.0232	0.1059	0.1038
PrI	–	–0.0504	0.0814	0.0808
CrI excluding Home-HF[67]	–	–0.0009	0.1169	0.1772
PrI excluding Home-HF[67]	–	–0.0093	0.1093	0.1710
ICER (£/QALY)				
CrI	–	Dominated	63,240[a]	5864
PrI	–	Dominated	228,035[a]	7133
CrI excluding Home-HF[67]	–	Dominated	Extendedly dominated	4455[a]
PrI excluding Home-HF[67]	–	Dominated	Extendedly dominated	4703[a]

continued

TABLE 42 Summary of the economic analysis results using the high usual care cost (*continued*)

	Usual care	STS HM	STS HH	TM during office hours
Expected incremental NMB (£)				
CrI	–	–603.90	1375	1467
PrI	–	–1111.22	914	1039
CrI excluding Home-HF[67]	–	–216.70	1564	2754
PrI excluding Home-HF[67]	–	–412.88	1389	2616
Probability of cost-effectiveness (%)				
CrI	1	18	36	44
PrI	4	19	35	41
CrI excluding Home-HF[67]	0	5	12	83
PrI excluding Home-HF[67]	1	7	19	73

PrI, predictive interval.
a Last strategy in the cost-effectiveness frontier.

cost scenario to £5864 per QALY in the high usual care cost scenario estimated using HRs from CrIs of the NMA. Similarly, the probability of TM being cost-effective increased from 44% in the base-case cost scenario to 45% in the high usual care cost scenario, and the probability of usual care being cost-effective decreased from 2% to 1%. Similar patterns were observed in the other analyses (using HRs based on CrIs excluding the Home-HF study[67] as well as predictive distributions of the NMA including and excluding the Home-HF study[67]). This is because the difference in costs between the interventions and usual care decreases as the cost of usual care increases, resulting in better cost-effectiveness for the interventions.

Results of the lower cost of telemonitoring during office hours scenario

Similar scenario analysis using a lower cost for TM during office hours of £133.50 per patient per month was repeated using effectiveness evidence from all four NMAs (HRs based on CrIs as well as predictive distributions of NMA, including and excluding the Home-HF study[67]). The results of this analysis are presented in *Appendix 13* and summarised in *Table 43*.

For the lower cost of TM during office hours scenario analysis, TM during office hours showed an increase in cost-effectiveness. The ICER of TM during office hours compared with usual care estimated using HRs from CrIs of the NMA decreased from £9522 per QALY in the base-case cost scenario to £7367 per QALY in the low-cost TM scenario. Similarly, the probability of TM during office hours being cost-effective increased from 44% in the base-case cost scenario to 50% in the low-cost TM scenario. Similar patterns were observed in the other analyses (using HRs based on CrIs excluding the Home-HF study[67] as well as predictive distributions of the NMA including and excluding the Home-HF study[67]). Again, this is because delivering the same health outcomes at a lower cost increases the cost-effectiveness.

Results of the higher cost of telemonitoring during office hours scenario

Similar scenario analysis using a higher cost of TM during office hours of £215 per patient per month was repeated using effectiveness evidence from all four NMAs (HRs based on CrIs as well as predictive distributions of the NMA, including and excluding the Home-HF study[67]). Results of these analyses are presented in *Appendix 14* and are summarised in *Table 44*.

The probability of TM during office hours being cost-effective decreased from 44% in the base-case cost scenario to 38% in the high-cost TM during office hours scenario estimated using HRs from CrIs of the NMA. Furthermore, TM during office hours is dominated by STS HH when the expected values of the

TABLE 43 Summary of the economic analysis results using a lower cost for TM during office hours

	Usual care	STS HM	STS HH	TM during office hours
Total costs (£)				
CrI	8478	9001	9604	9243
PrI	8478	8965	9574	9211
CrI excluding Home-HF[67]	8478	9060	9635	9420
PrI excluding Home-HF[67]	8478	9087	9658	9435
Difference in costs (£)				
CrI	–	523	1126	765
PrI	–	487	1096	733
CrI excluding Home-HF[67]	–	582	1157	942
PrI excluding Home-HF[67]	–	609	1180	957
Total QALYs				
CrI	2.4137	2.3905	2.5196	2.5175
PrI	2.4137	2.3633	2.4950	2.4944
CrI excluding Home-HF[67]	2.4137	2.4128	2.5306	2.5908
PrI excluding Home-HF[67]	2.4137	2.4043	2.5230	2.5847
Difference in QALYs				
CrI	–	–0.0232	0.1059	0.1038
PrI	–	–0.0504	0.0814	0.0808
CrI excluding Home-HF[67]	–	–0.0009	0.1169	0.1772
PrI excluding Home-HF[67]	–	–0.0093	0.1093	0.1710
ICER (£/QALY)				
CrI	–	Dominated	170,629[a]	7367
PrI	–	Dominated	605,112[a]	9080
CrI excluding Home-HF[67]	–	Dominated	Extendedly dominated	5315[a]
PrI excluding Home-HF[67]	–	Dominated	Extendedly dominated	5595[a]
Expected incremental NMB (£)				
CrI	–	–986.75	993	1311
PrI	–	–1494.07	531	882
CrI excluding Home-HF[67]	–	–599.54	1181	2602
PrI excluding Home-HF[67]	–	–795.73	1006	2463
Probability of cost-effectiveness (%)				
CrI	2	17	31	50
PrI	6	18	33	44
CrI excluding Home-HF[67]	0	4	9	87
PrI excluding Home-HF[67]	1	6	16	77

PrI, predictive interval.

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TABLE 44 Summary of the economic analysis results using a higher cost of TM during office hours

	Usual care	STS HM	STS HH	TM during office hours
Total costs (£)				
CrI	8478	9001	9604	9686
PrI	8478	8965	9574	9652
CrI excluding Home-HF[67]	8478	9060	9635	9870
PrI excluding Home-HF[67]	8478	9087	9658	9884
Difference in costs (£)				
CrI	–	523	1126	1207
PrI	–	487	1096	1174
CrI excluding Home-HF[67]	–	582	1157	1392
PrI excluding Home-HF[67]	–	609	1180	1406
Total QALYs				
CrI	2.4137	2.3905	2.5196	2.5175
PrI	2.4137	2.3633	2.4950	2.4944
CrI excluding Home-HF[67]	2.4137	2.4128	2.5306	2.5908
PrI excluding Home-HF[67]	2.4137	2.4043	2.5230	2.5847
Difference in QALYs				
CrI	–	–0.0232	0.1059	0.1038
PrI	–	–0.0504	0.0814	0.0808
CrI excluding Home-HF[67]	–	–0.0009	0.1169	0.1772
PrI excluding Home-HF[67]	–	–0.0093	0.1093	0.1710
ICER (£/QALY)				
CrI	–	Dominated	£10,629[a]	Dominated
PrI	–	Dominated	£13,473[a]	Dominated
CrI excluding Home-HF[67]	–	Dominated	Extendedly dominated	7854[a]
PrI excluding Home-HF[67]	–	Dominated	Extendedly dominated	8223[a]
Expected incremental NMB (£)				
CrI	–	–986.75	993	869
PrI	–	–1494.07	531	442
CrI excluding Home-HF[67]	–	–599.54	1181	2152
PrI excluding Home-HF[67]	–	–795.73	1006	2014
Probability of cost-effectiveness (%)				
CrI	3	19	40	38
PrI	7	20	37	37
CrI excluding Home-HF[67]	0	6	16	78
PrI excluding Home-HF[67]	1	8	23	68

PrI, predictive interval.

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ICERs are estimated. The reason for this difference is the similarity in the estimates of the effectiveness parameters, which means that the ICERs are estimated based on very small differences in benefits (STS HH results in 0.0021 QALYs more than TM during office hours). Thus, a small change in the incremental costs of TM during office hours compared with STS HH (from –£134 to +£82) led to a marked change in the ICER of TM during office hours compared with STS HH.

In the analyses performed using HRs from the predictive distributions of the NMA that excluded the Home-HF study,[67] TM during office hours is still the most cost-effective strategy with an ICER of £8223 per QALY compared with usual care (STS HH is extendedly dominated by a combination of usual care and TM during office hours). Threshold analysis suggested that the monthly cost of TM during office hours needs to be >£390 for it not to be cost-effective, that is, to have an ICER >£20,000 per QALY compared with STS HH. At this monthly cost of £390, TM during office hours has an ICER of £13,357 per QALY compared with usual care.

Results of the high-cost structured telephone support human-to-human contact scenario

Scenario analysis was also performed using a higher STS HH cost of £192 per patient per month during the treatment period. This scenario analysis was performed with effectiveness evidence from all four NMAs (HRs based on CrIs as well as predictive distributions of the NMA, including and excluding the Home-HF study[67]). The results of this analysis are presented in *Appendix 15* and summarised in *Table 45*.

TABLE 45 Summary of the economic analysis results using a higher STS HH cost

	Usual care	STS HM	STS HH	TM during office hours
Total costs (£)				
CrI	8478	9001	9675	9470
PrI	8478	8965	9645	9437
CrI excluding Home-HF[67]	8478	9060	9706	9650
PrI excluding Home-HF[67]	8478	9087	9729	9665
Difference in costs (£)				
CrI	–	523	1197	992
PrI	–	487	1167	959
CrI excluding Home-HF[67]	–	582	1228	1172
PrI excluding Home-HF[67]	–	609	1251	1187
Total QALYs				
CrI	2.4137	2.3905	2.5196	2.5175
PrI	2.4137	2.3633	2.4950	2.4944
CrI excluding Home-HF[67]	2.4137	2.4128	2.5306	2.5908
PrI excluding Home-HF[67]	2.4137	2.4043	2.5230	2.5847
Difference in QALYs				
CrI	–	–0.0232	0.1059	0.1038
PrI	–	–0.0504	0.0814	0.0808
CrI excluding Home-HF[67]	–	–0.0009	0.1169	0.1772
PrI excluding Home-HF[67]	–	–0.0093	0.1093	0.1710

continued

TABLE 45 Summary of the economic analysis results using a higher STS HH cost (*continued*)

	Usual care	STS HM	STS HH	TM during office hours
ICER (£/QALY)				
CrI	–	Dominated	97,300[a]	9552
PrI	–	Dominated	346,341[a]	11,873
CrI excluding Home-HF[67]	–	Dominated	Extendedly dominated	6616[a]
PrI excluding Home-HF[67]	–	Dominated	Extendedly dominated	6942[a]
Expected incremental NMB (£)				
CrI	–	–986.75	922	1084
PrI	–	–1494.07	460	656
CrI excluding Home-HF[67]	–	–599.54	1110	2371
PrI excluding Home-HF[67]	–	–795.73	935	2233
Probability of cost-effectiveness (%)				
CrI	2	19	34	46
PrI	6	19	34	41
CrI excluding Home-HF[67]	0	5	11	84
PrI excluding Home-HF[67]	1	7	18	74

PrI, predictive interval.
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For the high-cost STS scenario analyses, the probability of STS HH being cost-effective decreased whereas the probability of TM during office hours being cost-effective increased compared with the analysis with base-case costs. Similar patterns were also observed in the other analyses (using HRs based on CrIs excluding the Home-HF study[67] as well as predictive distributions of the NMA including and excluding the Home-HF study[67]).

Results of the low-cost structured telephone support human-to-human contact scenario

Scenario analysis was also performed using a lower cost of STS HH of £175 per patient per month during the treatment period. This scenario analysis was performed using the effectiveness evidence from all four NMAs (HRs based on CrIs as well as predictive distributions of NMA, including and excluding the Home-HF study[67]). The results of this analysis are presented in *Appendix 16* and summarised in *Table 46*.

Structured telephone support with human-to-human contact is still not cost-effective at a threshold of £20,000 per QALY, although the ICER of STS HH compared with TM during office hours estimated using the HRs from CrIs of the NMA decreased from £63,240 per QALY in the base-case scenario to £52,951 per QALY in the low-cost STS HH scenario. Assuming that the effectiveness parameters are constant, STS HH has to cost < £163 per month to be cost-effective at a threshold of £20,000 per QALY compared with TM during office hours. In the analyses excluding the Home-HF study,[67] STS HH has to cost < £105 per month to not be extendedly dominated by a combination of usual care and TM during office hours.

Scenario analysis using 12 months' treatment duration

Scenario analysis using 12 months' treatment duration was performed using effectiveness evidence from all four NMAs (HRs based on CrIs as well as predictive distributions of the NMA, including and excluding

TABLE 46 Summary of the economic analysis results using a lower STS HH cost

	Usual care	STS HM	STS HH	TM during office hours
Total costs (£)				
CrI	8478	9001	9582	9470
PrI	8478	8965	9553	9437
CrI excluding Home-HF[67]	8478	9060	9613	9650
PrI excluding Home-HF[67]	8478	9087	9636	9665
Difference in costs (£)				
CrI	–	523	1104	992
PrI	–	487	1075	959
CrI excluding Home-HF[67]	–	582	1135	1172
PrI excluding Home-HF[67]	–	609	1158	1187
Total QALYs				
CrI	2.4137	2.3905	2.5196	2.5175
PrI	2.4137	2.3633	2.4950	2.4944
CrI excluding Home-HF[67]	2.4137	2.4128	2.5306	2.5908
PrI excluding Home-HF[67]	2.4137	2.4043	2.5230	2.5847
Difference in QALYs				
CrI	–	–0.0232	0.1059	0.1038
PrI	–	–0.0504	0.0814	0.0808
CrI excluding Home-HF[67]	–	–0.0009	0.1169	0.1772
PrI excluding Home-HF[67]	–	–0.0093	0.1093	0.1710
ICER (£/QALY)				
CrI	–	Dominated	52,951[a]	9552
PrI	–	Dominated	193,206[a]	11,873
CrI excluding Home-HF[67]	–	Dominated	Extendedly dominated	6616[a]
PrI excluding Home-HF[67]	–	Dominated	Extendedly dominated	6942[a]
Expected incremental NMB (£)				
CrI	–	–986.75	1014	1084
PrI	–	–1494.07	553	656
CrI excluding Home-HF[67]	–	–599.54	1203	2371
PrI excluding Home-HF[67]	–	–795.73	1028	2233
Probability of cost-effectiveness (%)				
CrI	2	18	36	43
PrI	6	19	35	40
CrI excluding Home-HF[67]	0	5	12	83
PrI excluding Home-HF[67]	1	7	19	72

PrI, predictive interval.

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the Home-HF study[67]). The results of this analysis are presented in *Appendix 17* and summarised in *Table 47*.

In general, the 12-month treatment duration scenario produced similar results. The probability of the different interventions being cost-effective remained the same as in the 6-month treatment duration scenario. The ICER of TM during office hours compared with usual care estimated using the HRs from CrIs of the NMA increased from £9522 per QALY in the base-case 6-month treatment duration scenario to £10,353 per QALY in the 12-month treatment duration scenario. Similar patterns were observed in the other analyses (using HRs based on CrIs excluding the Home-HF study[67] as well as predictive distributions of the NMA including and excluding the Home-HF study[67]).

TABLE 47 Summary of the economic analysis results using 12 months' treatment duration

	Usual care	STS HM	STS HH	TM during office hours
Total costs (£)				
CrI	8562	9571	10,603	10,353
PrI	8562	9564	10,582	10,326
CrI excluding Home-HF[67]	8562	9645	10,655	10,663
PrI excluding Home-HF[67]	8562	9708	10,707	10,698
Difference in costs (£)				
CrI	–	1009	2040	1791
PrI	–	1002	2019	1764
CrI excluding Home-HF[67]	–	1082	2093	2101
PrI excluding Home-HF[67]	–	1146	2145	2136
Total QALYs				
CrI	2.4137	2.3857	2.5935	2.5898
PrI	2.4137	2.3536	2.5589	2.5576
CrI excluding Home-HF[67]	2.4137	2.4155	2.6117	2.7159
PrI excluding Home-HF[67]	2.4137	2.4044	2.6005	2.7065
Difference in QALYs				
CrI	–	–0.0280	0.1798	0.1761
PrI	–	–0.0601	0.1452	0.1439
CrI excluding Home-HF[67]	–	0.0019	0.1980	0.3022
PrI excluding Home-HF[67]	–	–0.0093	0.1868	0.2928
ICER (£/QALY)				
CrI	–	Dominated	68,189[a]	10,167
PrI	–	Dominated	205,812[a]	12,257
CrI excluding Home-HF[67]	–	Dominated	Extendedly dominated	6953[a]
PrI excluding Home-HF[67]	–	Dominated	Extendedly dominated	7296[a]

continued

TABLE 47 Summary of the economic analysis results using 12 months' treatment duration (*continued*)

	Usual care	STS HM	STS HH	TM during office hours
Expected incremental NMB (£)				
CrI	–	–1568.71	1555	1732
PrI	–	–2202.89	884	1114
CrI excluding Home-HF[67]	–	–1045.41	1868	3942
PrI excluding Home-HF[67]	–	–1331.28	1590	3720
Probability of cost-effectiveness (%)				
CrI	2	18	35	44
PrI	7	19	34	40
CrI excluding Home-HF[67]	0	5	12	83
PrI excluding Home-HF[67]	1	7	19	73

PrI, predictive interval.
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Telemonitoring during office hours for 12 months was also compared with TM during office hours for 6 months to identify whether or not it was cost-effective to keep the patients on TM during office hours beyond 6 months. In the analysis using HRs from CrIs of the NMA, TM during office hours for 12 months was still cost-effective compared with TM during office hours for 6 months with an ICER of £12,213 per QALY. Similar patterns were observed in the other analyses as shown in *Table 48* (£8097 per QALY using HRs based on CrIs excluding the Home-HF study,[67] £14,066 per QALY using predictive distributions of the NMA including the Home-HF study[67] and £8481 per QALY using predictive distributions of the NMA excluding the Home-HF study[67]).

More importantly, given the potential capacity constraints for the TM devices, health organisations might choose to treat double the number of patients with TM during office hours for 6 months rather than using TM during office hours for 12 months. For example, assuming a capacity of 100 TM devices at a local health organisation, 200 patients could be treated in 1 year using TM during office hours for 6 months compared with 100 patients treated using TM during office hours for 12 months with the rest of the 100 patients under usual care (because of the lack of TM devices). This scenario was evaluated to find the most cost-effective strategy. In the analysis using HRs from CrIs of the NMA, treating 2*n* patients with TM during office hours for 6 months was cost-effective with an ICER of £793 per QALY compared with a combination of treating *n* patients with TM during office hours for 12 months and treating *n* patients under usual care. Again, similar patterns were observed in the other analyses as shown in *Table 49*. These results suggest that, in situations with a limited number of TM devices, it is cost-effective to treat patients with TM during office hours for 6 months rather than with TM during office hours for 12 months with the rest of the patients under usual care.

Discussion of the cost-effectiveness results

The effectiveness parameters (HRs of mortality and hospitalisation) are the key drivers in the model. Mortality reduction leads to a gain in QALYs whereas reduction in hospitalisations leads to fewer costs and less disutility. As the intervention costs are only a small part of the overall costs (hospitalisation costs are the main contributor), RM is likely to be cost-effective if it can save lives and reduce hospitalisations.

TABLE 48 Cost-effectiveness of TM during office hours for 12 months compared with TM during office hours for 6 months

	TM during office hours for 6 months		TM during office hours for 12 months		ICER (TM for 12 months vs TM for 6 months) (£/QALY)
	Cost (£)	QALYs	Cost (£)	QALYs	
CrI	9470	2.5175	10,353	2.5898	12,213
PrI	9437	2.4944	10,326	2.5576	14,066
CrI excluding Home-HF[67]	9650	2.5908	10,663	2.7159	8097
PrI excluding Home-HF[67]	9665	2.5847	10,698	2.7065	8481

PrI, predictive interval.

TABLE 49 Cost-effectiveness of TM during office hours for 12 months compared with TM during office hours for 6 months in situations with a limited number of TM devices

	2*n* patients on TM during office hours for 12 months[a]		2*n* patients on TM during office hours for 6 months[b]		ICER (TM for 6 months vs TM for 12 months) (£/QALY)
	Cost (£)	QALYs	Cost (£)	QALYs	
CrI	18,915	5.0035	18,940	5.0350	793
PrI	18,888	4.9713	18,874	4.9888	Dominant
CrI excluding Home-HF[67]	19,225	5.1296	19,300	5.1816	1442
PrI excluding Home-HF[67]	19,260	5.1202	19,330	5.1694	1423

PrI, predictive interval.

a The costs and QALYs of *n* patients under TM during office hours for 12 months plus the costs and QALYs of *n* patients under usual care.

b The costs and QALYs of 2*n* patients under TM during office hours for 6 months.

The results of the base-case cost-effectiveness analyses suggest that TM during office hours is expected to be the most cost-effective strategy at a threshold of £20,000 per QALY. However, there is uncertainty involved in suggesting that TM during office hours is the most probable cost-effective strategy and, in particular, there is higher uncertainty when the Home-HF study[67] is included in the NMA than when it is excluded. This uncertainty also increased marginally when the HRs from the predictive distributions of the NMA were used instead of the HRs based on the CrIs of the NMA.

Scenario analyses performed using a higher usual care cost, lower TM during office hours cost and higher STS cost did not substantially change the conclusions regarding the relative cost-effectiveness of TM during office hours.

In the scenario analysis performed using a higher cost for TM during office hours (£215 per month) with HRs based on the predictive distributions of the NMA that included the Home-HF study,[67] TM during office hours is dominated by STS HH. This is because a small change in the difference between the cost of TM during office hours and the cost of STS HH led to a marked change in the ICER, given the small difference in expected QALYs (0.0006) between STS HH and TM during office hours. However, the same scenario analysis (i.e. a higher cost of TM during office hours of £215 per month) performed using the HRs from the NMA that excluded the data from the Home-HF study[67] suggested that TM during office hours is still the most cost-effective strategy. This is because of the much larger difference in the expected QALYs

between STS HH and TM during office hours (0.0617), meaning that the small change in the difference between the cost of TM during office hours and the cost of STS HH did not lead to a marked change in the ICER.

Scenario analysis using a 12-month treatment duration produced similar results as in the 6-month treatment duration scenarios. The ICER of TM during office hours compared with usual care increased from £11,873 per QALY in the base-case 6-month treatment duration scenario to £12,257 per QALY in the 12-month treatment duration scenario. TM during office hours for 12 months was also cost-effective compared with TM during office hours for 6 months with an ICER of £14,066 per QALY, which suggests that it is cost-effective to keep patients on TM during office hours beyond 6 months. However, in situations with a limited number of TM devices, it is cost-effective to treat patients with TM during office hours for 6 months rather than 12 months with the rest of the patients under usual care.

Users can decide which of these base-case analyses is most representative of the UK setting, that is, whether or not the usual care in the Home-HF study[67] is representative of usual care in the UK. If the usual care in the Home-HF study[67] is not representative of usual care in the UK, then the modelling suggests that TM during office hours becomes the most cost-effective strategy with much reduced uncertainty.

Chapter 5 Assessment of factors relevant to the NHS and other parties

Chronic conditions are set to be the major challenge for the NHS over coming years, and already account for approximately 70% of health-care expenditure in the UK.[137] RM may be an opportunity to optimise care quality while controlling costs by bringing care to patients in a way that would be difficult to achieve in conventional hospital-based clinical pathways. For example, in the clinic, collection of vital signs tends to be organised around hospital routine rather than patient needs, and the information is sometimes left in handwritten notes until the patient has another consultation with a senior clinician. Also contrary to usual clinical care, in which follow-up appointments tend to be organised for a prespecified time, RM can be more responsive to important changes in physiological parameters. Furthermore, RM is gradually being shown to be a viable addition to conventional service delivery for chronic conditions, with more than 100 telehealth pilots currently taking place in the NHS.[137] For instance, in Sheffield, 30 high-risk patients with COPD were offered a TM intervention for a period of 5 months. Throughout that time, patients measured their own vital signs, which were remotely transmitted to the care provider. The use of RM decreased hospital admissions by around 50%, saving the trust between £35,000 and £40,000.[37] As previously discussed, early results from the largest trial of RM (the WSD study) also seem promising.[117] However, a number of issues need to be considered if the NHS is to roll out RM as standard care for HF.

First, NHS purchasers need to consider the business model by which RM is provided. As pointed out by Inglis *et al.*,[48] purchasing RM equipment will involve large start-up costs and relatively low running costs, whereas renting the equipment would involve relatively low start-up costs and high running costs. Another relevant consideration is the speed with which RM equipment is changing and developing, which brings a series of further challenges and opportunities for care provision. Purchasing RM equipment may offer the benefits of stability with the risk of equipment rapidly becoming outdated. Conversely, renting may allow the NHS to maintain up-to-date service provision while running the risk of uncertainty, high costs of new technologies and start-up difficulties for new systems. More generally, the logistical and cost challenges of rolling out RM should not be underestimated.[138] The WSD trial cost over £30M to run, and provision of RM as standard for HF patients would require considerable reorganisation of services in the short term.

Second, selection of appropriate patients for RM is an important consideration. Although the acceptability of RM technologies was generally high in the synthesised literature, they will not be suited to everyone. Nor will RM necessarily be effective among those for whom it is acceptable: in the meta-analysed trials, compliance was inconsistently reported, with one large, high-quality trial reporting a low rate.[52] Best practice patient selection methods are therefore critical to guarantee the success of RM interventions. These might include selection of patients who are keen to incorporate RM into their care, and using physiological parameters, such as those described by Fonarow *et al.*,[139] to identify particularly at-risk patients prior to discharge. Indeed, it has been argued that null results in some trials [Telemedical Interventional Monitoring in Heart Failure (TIM-HF[50]) and Tele-HF[52]] may have been attributable to patients with less severe, well-controlled HF.[140]

The NHS should also consider the duration of RM interventions, as this will have important implications for clinical effectiveness and cost-effectiveness. The highest risk period for mortality and rehospitalisation for patients with a new diagnosis of HF is the period immediately following hospitalisation,[15] so offering early RM is likely to deliver the maximum benefit. What is less clear is the time period for which use of RM could continue to confer benefits. The duration of the RM interventions included in this meta-analysis varied from 2 months[72] to 12 months.[74,78,104] However, because of inconsistent reporting of intervention duration, it was not possible to evaluate the relative efficacy of RM interventions by duration in a meta-regression. Further research is required to inform NHS decisions on how long to offer RM to patients with HF.

Finally, as Kaplan and Litewka[141] note, RM 'is not only a technological improvement, but a reengineering of healthcare processes requiring consideration of socio-technical aspects of their design and development' (p. 402). This raises two important issues. First, health-care providers will require appropriate training to ensure stable and high-quality provision. Experience from the system-wide use of RM technologies in the US Veterans Health Administration suggests national or common training support facilities could be one viable way to achieve this.[137] Second, by further shifting the onus of health care from hospital to home, RM has the potential to fundamentally change what it means to be a patient with a chronic condition, which raises ethical issues that go beyond confidentiality and secure data transfer.[141] It is beyond the scope of this review to comprehensively address these issues here but, at the very least, frameworks and guidelines are required to ensure that RM is conducted to deliver benefits to patients in an equitable and genuinely empowering way.[142]

Chapter 6 Discussion

Statement of principal findings

For adults who have recently (<28 days) been discharged from an acute care setting after a recent exacerbation of HF, the NMA found that, compared with usual care, RM was beneficial in reducing all-cause mortality by 23%, 24% and 51% for STS HH (HR 0.77, 95% CrI 0.55 to 1.08), TM with medical support provided during office hours (HR 0.76, 95% CrI 0.49 to 1.18) and TM 24/7 (HR 0.49, 95% CrI 0.20 to 1.18) respectively. However, the results for TM 24/7 should be treated with caution because of the poor methodological quality of the only included study in this network. No beneficial effect on mortality was observed with STS HM. TM with medical support during office hours and TM 24/7 were associated with a 25% (HR 0.75, 95% CrI 0.49 to 1.10) and a 19% (HR 0.81, 95% CrI 0.33 to 2.00) reduction in all-cause hospitalisations, respectively, whereas there was no major effect of STS HM (HR 1.06, 95% CrI 0.44 to 2.53) or STS HH (HR 0.97, 95% CrI 0.70 to 1.31). Although there was no major effect of STS HM (HR 1.03, 95% CrI 0.66 to 1.54) and TM with medical support during office hours (HR 0.95, 95% CrI 0.70 to 1.34) on HF-related hospitalisation, STS HH (HR 0.77, 95% CrI 0.62 to 0.96) was associated with a reduction of 23%. No trials of cardiovascular implanted monitoring devices or observational studies met the inclusion criteria of the current review. Although data were limited, care packages that included STS and TM generally improved QoL and were acceptable to recently discharged patients with HF.

A sensitivity analysis, which excluded data from the Home-HF trial[67] (as it appeared to be inconsistent with the data from the remaining studies, i.e. an outlier), found that TM with medical support provided during office hours was generally more effective than STS HH for all-cause mortality (TM during office hours: HR 0.62, 95% CrI 0.42 to 0.89; STS HH: HR 0.75, 95% CrI 0.59 to 0.96) and all-cause hospitalisations (TM during office hours: HR 0.67, 95% CrI 0.42 to 0.97; STS HH: HR 0.96, 95% CrI 0.72 to 1.27) but not HF-related hospitalisations (TM during office hours: HR 0.86, 95% CrI 0.61 to 1.21; STS HH: HR 0.76, 95% CrI 0.61 to 0.94). By excluding this study from the NMA, larger reductions in effect were observed for all-cause mortality, all-cause hospitalisations and HF-related hospitalisations for TM during office hours.

Additional analyses were undertaken to assess whether or not the results from the primary analysis differed markedly from the results in those with stable HF who were managed in the community. Of the 21 included studies of TM (including cardiovascular implanted monitoring devices) or STS programmes for adults with stable HF, 18 studies contributed to the network comparing different pairs or triplets of treatment using TM or STS programmes and usual care. For all-cause mortality, the NMA found that the effects of STS HH and TM during office hours were similar to the effects in patients who have recently (<28 days) been discharged from an acute care setting after a recent exacerbation of HF. In terms of all-cause hospitalisations and HF-related hospitalisations, RM appears to be beneficial, although the effects of each intervention are not consistent relative to adults who were recently discharged. An analysis of the effect of cardiovascular implanted monitoring devices compared with cardiovascular implanted non-monitoring devices ($n = 3$ studies) found a trend in favour of a reduction in all-cause mortality (HR 0.90, 95% CrI 0.31 to 2.49) and HF-related hospitalisations (HR 0.72, 95% CrI 0.32 to 1.37). However, these effects were not conclusive.

Base-case monthly costs per patient were estimated using microcosting methods as £27 for usual care, £119 for STS HM, £179 for STS HH and £175 for TM during office hours. Five cost scenarios were also developed to calculate lower and higher estimates of costs of STS HH (£175 and £192 per month respectively) and TM during office hours (£133.50 and £215 per month respectively) along with a higher estimate of usual care costs (£92 per month).

The results of the full incremental cost-effectiveness analysis using the base-case costs suggest that TM during office hours is likely to be the most cost-effective strategy at a threshold of £20,000 per QALY for both analysis using CrIs and PrIs of the NMA as HRs in the model. In the analysis performed using PrIs from NMA as HRs, TM during office hours had an estimated ICER of £11,873 per QALY, compared with usual care whereas STS HH had an ICER of £228,035 per QALY compared with TM during office hours. STS HM was dominated by usual care. Thus, although STS HH is the most effective strategy providing the highest number of expected QALYs (2.4950), with TM the second most effective (2.4944 QALYs), the additional QALYs gained by STS HH are not worth the additional costs of the strategy, as seen in the ICER, which is greater than the threshold of £20,000 per QALY.

The PSA showed substantial uncertainty over the most probable cost-effective strategy. TM during office hours was the most cost-effective strategy in 40% of the PSA runs whereas STS HH was most cost-effective in 35% of the PSA runs. STS HM and usual care were the most cost-effective in 19% and 6% of the runs respectively. The EVPI per patient was estimated at £1831 and the population EVPI per annum was estimated at £100,299,791 assuming an annual incidence of first HF admissions in England and Wales of 54,779.

Cost-effectiveness analysis performed using the HRs from the predictive distributions of the NMA that excluded the data from the Home-HF trial[67] showed an improvement in the cost-effectiveness of TM during office hours. STS HM and STS HH were dominated and extendedly dominated, respectively, with the ICER for TM during office hours compared with usual care estimated as £6492 per QALY. In this analysis, TM during office hours is also the most effective strategy (2.5847 QALYs for TM vs 2.5230 QALYs for STS HH). Furthermore, the results from the uncertainty analysis suggest that TM during office hours is cost-effective in 73% of the runs whereas STS HH and STS HM are cost-effective in 19% and 7% of the runs respectively. This reduction in the uncertainty was also reflected in the lower EVPI per patient, estimated as £410, and the lower population EVPI per annum, estimated as £22,459,265.

Scenario analysis performed using a higher cost of TM during office hours (£215 per month) increased the uncertainty. Both TM during office hours and STS HH were cost-effective in 37% of the PSA runs. But, TM during office hours is dominated by STS HH. This is because the estimated ICER is based on very small differences in benefits (STS HH results in 0.0006 QALYs more than TM during office hours) and so a small increase in the difference between costs of TM during office hours and STS HH leads to a marked change in the ICER. The same scenario analysis (i.e. a higher cost of TM during office hours of £215 per month), performed using the HRs from the NMA that excluded the data from the Home-HF trial,[67] suggested that TM during office hours would still be the most cost-effective strategy with an ICER of £8223 per QALY compared with usual care (STS HH is extendedly dominated by a combination of usual care and TM during office hours). Threshold analysis suggested that the monthly cost of TM during office hours has to be >£390 to produce an ICER >£20,000 per QALY compared with STS HH. At a monthly cost of £390, the ICER of TM during office hours compared with usual care is £13,357 per QALY.

Scenario analyses performed using a higher cost of usual care, a higher cost of STS HH and a lower cost of TM during office hours do not substantially change the conclusions. TM during office hours was estimated to be the most cost-effective strategy in all of these scenarios.

Strengths and limitations of the assessment

Although an extensive literature search was conducted, it is possible that some relevant studies may have been missed. However, such omissions are likely to have been minimal as the search included all identifiable publications in the grey literature (including contact with clinical experts in the field).

The data were analysed by assuming a binomial likelihood function for the sample data. The statistical model acknowledged the fact that events accumulate over time by adjusting for the varying durations of

each study using a complementary log-log links function. Parameter estimates, including the between-study standard deviation, were estimated using Markov chain Monte Carlo (MCMC), which allows for uncertainty in the estimate of the between-study standard deviation; it also allowed the estimation of the predictive distribution of the effect of each intervention in a new study.

The clinical effectiveness findings had a number of limitations. In particular, the RM interventions were heterogeneous in terms of monitored parameters and selection criteria for HF. This was the case even within each of the four specific types of RM (STS HH, STS HM, TM with medical support during office hours, TM with medical support 24/7). Clear descriptions of the RM interventions were not provided in many of the studies included in the systematic review, making it difficult to understand exactly what was provided as part of the intervention. In addition, a number of trials were underpowered to detect the clinical outcome of interest and did not report blinding of outcome assessors. A limitation of the statistical model (as a consequence of having only one observation from each study) was that it assumed that the hazards and relative intervention effects were constant over time; nevertheless, this is better than assuming that study duration has no impact on the data. Moreover, because of the differences in the HF populations (e.g. definition of HF, LVEF inclusion criteria) of the included studies the true estimate of treatment effect may be unclear. However, the NMA analysis used a random-effects distribution together with 95% CrIs to reflect the uncertainty associated with the population mean. In addition, the predictive distribution of a randomly chosen study in the population was presented. This reflects not only uncertainty in the population mean but also the heterogeneity in treatment effects between studies. Unfortunately, it was not possible to model the heterogeneity between studies using a meta-regression technique because of the lack of suitable data on potential treatment effect modifiers.

The cost-effectiveness analysis has been undertaken assuming that the NMA results represent the best knowledge regarding the relative uncertainty between treatments. Therefore, although the treatment effects estimated from the NMA were statistically inconclusive, the joint uncertainty about these effectiveness parameters was used to populate the economic model. The expected values of costs and QALYs produced, which were used to estimate the cost-effectiveness of the RM interventions, thus are also aligned with the best knowledge on relative effectiveness. The uncertainty within the cost-effectiveness results was quantified by estimating the probability of each intervention being the most cost-effective at different WTP thresholds, and the EVPI was calculated to explicitly quantify the cost of reducing the decision uncertainty by undertaking further research.

Any limitations in the evidence base also manifest as limitations of the cost-effectiveness model. Most of the included studies in the NMA provided information on mortality and/or hospitalisation rates, which allowed synthesis using meta-analytical methods, but only a few studies reported any data about other potentially relevant states/events (such as stroke, having a pacemaker fitted), which did not extend to reporting any differences between the usual care and RM arms. Given the lack of evidence, it was deemed prudent to use a two-state Markov model even though it involved simplifications and assumptions that may not exactly reflect clinical practice. An advantage of using this simple model is that it can be easily updated to include other states or events should there be future evidence demonstrating differences between the usual care and RM arms.

A limitation of the cost-effectiveness model was that there was no age-specific analysis. Another limitation was that the constant hazards and relative intervention effects over time were applied to the time-dependent baseline mortality hazard (which is greatest in the early period after discharge after a hospitalisation for HF and subsequently declines over time) and constant risk of hospitalisation. If the studies reported observations at different time points, time-dependent effectiveness parameters can be estimated and used in the cost-effectiveness model. Furthermore, the optimal duration for each of the RM interventions can also be identified.

None of the studies identified in the review provided an estimate for the utility of the patients and whether or not there was a difference between the RM and usual care groups. Thus, in the economic model,

similar utility values were used for HF patients in both the RM and usual care groups; however, the validity of this assumption is unclear. Furthermore, the lack of detail provided in research studies concerning the components of RM packages and usual care (e.g. communication protocols, routine staff visits and resources used) made it difficult to estimate costs. Costing scenarios for different RM classifications were developed and their costs were estimated using microcosting methods. Although the users can decide which of these analyses is most representative of their setting, uncertainties still remain about the assumptions made in the estimation of these costs. This uncertainty in the costs is a limitation, especially as, given the small difference in QALYs between STS HH and TM during office hours, a small change in the difference between the cost of TM during office hours and the cost of STS HH can lead to marked changes in the ICER. A further limitation is that the effectiveness remained the same for the different cost scenarios whereas in reality there might be some correlation between the cost and the effectiveness of different RM strategies.

Uncertainties

In the cost-effectiveness model, the HRs of mortality and hospitalisation were the key drivers as mortality reductions lead to a gain in QALYs whereas reductions in hospitalisations lead to fewer costs and more QALYs. The intervention costs were only a small part of the overall costs (hospitalisation costs are the main contributor); thus, RM is likely to be cost-effective if it can save lives and reduce hospitalisations to a large enough extent. However, there was still some uncertainty in the effectiveness parameters as suggested in the EVPI analysis.

At the time of writing, the long-awaited results of the WSD programme[117] had not been published in a peer-reviewed journal. This study is a large UK-based RCT of telehealth compared with usual care, which included over 6000 patients with HF, diabetes mellitus or COPD. Although early headline results, published by the UK Department of Health,[57] suggest a substantial reduction in mortality by 45%, the magnitude and direction of effect in recently discharged patients with HF is unclear (including people with stable HF). Given the large sample size, it is anticipated that the effectiveness results from the WSD programme will help reduce some of the uncertainty reported in the model results for recently discharged patients with HF.

Chapter 7 Conclusions

Implications for service provision

In general, although the effectiveness of the interventions varied widely according to the type of RM system used, STS HH and TM with medical support provided during office hours showed beneficial effects, particularly in reducing all-cause mortality for recently discharged patients with HF; however, these effects were statistically inconclusive.

Given the variation in usual care and RM strategies, the cost-effectiveness analysis was performed using a set of costing scenarios. These scenarios were designed to reflect the different configurations of usual care and RM interventions present in the UK. The cost-effectiveness analyses suggest that TM during office hours was an optimal strategy in most of the scenarios.

Suggested research priorities

Despite the growing evidence base for RM, a number of key questions are yet to be addressed. First, it would be helpful to have more direct comparisons of STS and TM. To our knowledge, only one study of recently discharged patients (TEN-HMS[49]) has made this comparison. The results of this trial suggested that TM was somewhat more beneficial than STS – in particular, TM had a substantially greater effect on reducing the duration of hospitalisation and the number of home or clinical visits. This broadly coheres with our findings (particularly from the sensitivity analyses excluding the Home-HF study[67]) that TM interventions showed a greater risk reduction than STS for mortality and hospitalisation. In addition, patients with HF are at increased risk of atrial fibrillation, which can lead to deterioration and hospitalisation. Further research on the precipitants of admission for HF (including atrial fibrillation, infection and non-compliance) and how they might be detected and managed early is required.

Given the complex nature of RM interventions, new research should seek to examine the 'active ingredients' of RM. For instance, the NMA was unable to compare the effectiveness of TM interventions that monitored different physiological parameters. Well-known risk factors such as low LVEF, NYHA class and heart rate perform well in predicting mortality but it is not yet clear which factors in which combination can provide optimal clinical benefit for RM. As a complex intervention (i.e. made up of multiple, socially meaningful, interconnected factors), it is important to understand the processes by which RM works, and qualitative research on patient experiences of RM may help throw light on the issue.[116] In relation to STS, one interesting question is whether contact with a care professional is required to deliver benefits, or whether it can work as an automated human-to-machine interface. RCTs of STS that manipulate the presence of a human caregiver as the primary experimental variable could help address this issue. It also remains unclear how RM affects clinical decision-making. Further research should seek to establish in what ways RM might improve such decision-making, and conversely whether it may, in some circumstances, act as an impediment to good care. More importantly, it is worth echoing the recommendation made by Inglis *et al.*[48] that future RM studies should publish data in such a way as to identify which patient subgroups benefited most from the intervention. For example, there might be differential effectiveness in different age groups and future trials should explore these issues. If particular groups tend to benefit more, the potential for RM to exacerbate health inequalities should be carefully considered, and strategies should be pursued to minimise this.

Furthermore, to aid robust cost-effectiveness estimations, the costs associated with usual care and RM interventions need to be reported in detail (including the costs of HF treatment pathways). The costs need to be linked to the activities or items involved in the intervention using activity-based costing or unit

costing approaches respectively. In addition, QoL, patient severity status transitions (e.g. NYHA class) and hospitalisations need to be reported with observations at specific time points to enable the estimation effectiveness of RM over time and also to identify the optimal duration of RM interventions.

Implementation costs (such as set-up costs, staff training costs, costs for dual running of usual care and RM services) were often missing from the studies in the review. Future studies should provide greater detail of the costs of reconfiguration and link more clearly with the financial impact (e.g. cost variation with scale and over time) on provider organisations. Wider adaptation of RM in the NHS can be facilitated by providing financial impact data along with the cost-effectiveness information.

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Contribution of authors

Abdullah Pandor (Senior Research Fellow) co-ordinated the review and was responsible for the acquisition of data, analysis and interpretation of data (for the systematic reviews) and drafting and revision of the final report.

Praveen Thokala (Research Fellow) and **Hassan Baalbaki** (Research Associate) were responsible for the acquisition of data, analysis and interpretation of data and model construction (for the health economic evaluation) and drafting and revision of the final report.

Tim Gomersall (Research Associate) was responsible for the acquisition of data, analysis and interpretation of data (for the systematic reviews) and drafting and revision of the final report.

John Stevens (Senior Lecturer in Statistics) and **Jenny Wang** (Research Assistant Statistician) were responsible for the statistical analyses, interpretation of data and drafting and revision of the final report.

Ruth Wong (Information Specialist) was responsible for developing and undertaking the electronic literature searches.

Alan Brennan (Professor of Health Economics and Decision Modelling) oversaw the modelling and reviewed the final report.

Patrick Fitzgerald was responsible for the conception and design of the study.

About the School of Health and Related Research

The School of Health and Related Research (ScHARR) is one of the nine departments that constitute the Faculty of Medicine, Dentistry and Health at the University of Sheffield. ScHARR specialises in health services and public health research and the application of health economics and decision science to the development of health services and the improvement of public health.

The ScHARR Technology Assessment Group (ScHARR-TAG) synthesises research on the clinical effectiveness and cost-effectiveness of health-care interventions for the NIHR Health Technology Assessment programme on behalf of a range of policy-makers, including NICE. ScHARR-TAG is part of a wider collaboration of a number of units from other regions including Southampton Health Technology Assessment Centre (SHTAC), University of Southampton; Aberdeen Health Technology Assessment Group (Aberdeen HTA Group), University of Aberdeen; Liverpool Reviews & Implementation Group (LRiG), University of Liverpool; Peninsula Technology Assessment Group (PenTAG), University of Exeter; the NHS Centre for Reviews and Dissemination, University of York; Warwick Evidence, University of Warwick; the BMJ Group and Kleijnen Systematic Reviews.

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Appendix 1 Home telemonitoring or structured telephone support programmes for patients with heart failure: literature search strategy, a MEDLINE example

Database searched: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R).
Platform or provider used: Ovid SP.

Date of coverage: 1948–January 2012.

Search undertaken: January 2012.

1. exp Heart Failure/
2. ((heart or cardiac) adj failure).tw.
3. 1 or 2
4. exp Telecommunications/
5. Telemetry/
6. (telemetr$or telemed$or tele-med$or telehealth$or tele-health$or telecare or tele-care or telecardiol$or tele-cardiol$or telehome or tele-home).tw.
7. (telemonitor$or tele-monit$or teleconsult$or tele-consult$or teleconferenc$or tele-conferenc$or telecommunicat$or tele-communicat$).tw.
8. (telephon$or phone$).tw.
9. Remote consultation/
10. (remote$adj3 (consult$or monitor$)).tw.
11. remote patient monitoring.tw.
12. Monitoring, Ambulatory/
13. ((implantable or wearable) and (monitor$or system$or sensor$)).tw.
14. Patient Care Planning/
15. Case Management/
16. disease management/
17. disease management.tw.
18. exp Comprehensive Health Care/
19. Home Care Services/
20. Home Care Services, Hospital-Based/
21. Clinical Protocols/
22. Nurse Clinicians/
23. Nurse Practitioners/
24. (nurse adj led).tw.
25. or/4–24
26. 3 and 25

Appendix 2 Methodological assessment (adapted) criteria for randomised controlled trials[61] and observational studies[62]

Criteria		Criteria met	Criteria defined (if applicable)
RCTs			
1.	Was the method used to assign participants to the treatment groups really random?	Yes	Computer-generated random numbers, random number tables, random permuted blocks, sealed assignment, sequentially numbered sealed opaque envelopes
		No	Use of alternation, case record numbers, date of birth or days of the week
		Unclear	Insufficient detail to make judgement
2.	Was the allocation of treatment concealed?	Yes	Allocation to each group performed adequately (e.g. centrally) and group assignment revealed after provision of consent
		No	Group assignment revealed prior to subject consent, non-opaque sealed envelopes, case record numbers, date of birth or days of the week, open random number lists
		Unclear	Insufficient detail to make judgement
3.	Were the outcome assessors/ data analysts blinded to the treatment allocations (it was not considered plausible that patients could be blinded to these types of interventions)?	Yes	Independent outcome assessors and data analysts were blinded to which group patients belonged to
		No	Outcomes assessed and data analysed by those involved in the intervention, or those who are aware of group membership
		Unclear	Insufficient detail to make judgement
4.	Were the eligibility criteria for study entry specified including confirmation of diagnosis of HF?	Yes	Eligibility criteria for study entry specified *and* diagnosis of HF (systolic or preserved) recorded and confirmed using clinical criteria, echocardiography or BNP
		No	Eligibility criteria for study entry not specified *or* diagnosis of HF not defined
		Unclear	Insufficient detail to make judgement
5.	Was baseline comparability achieved for the most important prognostic indicators?	Yes	The baseline characteristics of each study group (in particular age, NYHA class and/or LVEF) were clearly outlined and any differences identified were accounted for
		No	The baseline characteristics (in particular, age, NYHA class and/or LVEF) of each study group were not outlined or differences were not accounted for
		Unclear	Insufficient detail to make judgement
6.	Adequate follow-up of patients (at least 80%)	Yes	Proportion and characteristics of those participants lost to follow-up (≤20%) clearly reported for each group and outcome. A clear outline is provided as to how losses of participants were handled
		No	Proportion and characteristics of those participants lost to follow-up >20%. No clear outline is provided as to how losses of participants were handled
		Unclear	Insufficient detail to make judgement

Criteria		Criteria met	Criteria defined (if applicable)
7.	Were the reasons for withdrawal stated?	Yes	
		No	
		Unclear	Insufficient detail to make judgement
8.	Was an intention-to-treat analysis included?	Yes	All patients randomly assigned to one of the treatments are analysed together, regardless of whether or not they completed or received that treatment
		No	All patients randomly assigned to one of the treatments are not analysed together, regardless of whether or not they completed or received that treatment, e.g. per protocol
		Unclear	Insufficient detail to make judgement
9.	Was the study powered to detect differences in outcomes?	Yes	A power calculation was performed and reported. The study was adequately powered to detect differences in outcomes
		No	A power calculation was not performed; a power calculation was performed and reported but the study was not adequately powered to detect differences in outcomes; or a power calculation was performed but not reported – the study states that it was adequately powered to detect differences in outcomes
		Unclear	Insufficient detail to make judgement
Observational studies			
1.	Was the sample representative of the average HF patient?	Yes	
		No	
		Unclear	
2.	Were the intervention and control cohort drawn from the same community?	Yes	
		No	
		Unclear	
3.	Were groups comparable in terms of major confounding/ prognostic factors?	Yes	
		No	
		Unclear	
4.	Was the attrition rate acceptable (≤20%)?	Yes	
		No	
		Unclear	
5.	Was the length of follow-up sufficiently long for the outcome to occur?	Yes	
		No	
		Unclear	
6.	Were all potential confounding factors and outcomes measured accurately and objectively?	Yes	
		No	
		Unclear	
7.	Was an attempt made to control for confounders in the analysis (e.g. regression or stratification)?	Yes	
		No	
		Unclear	

BNP, B-type natriuretic peptide.

Appendix 3 Statistical model used to analyse the data

The analysis assumed that the studies are exchangeable in the sense that the investigators would be willing to assign each of the patients in the studies to any of the interventions.

A random-effects NMA was conducted with the baseline treatment being defined as usual care.

The studies presented data in terms of the number of patients who had an event (i.e. all-cause mortality, all-cause hospitalisation and HF-related hospitalisation). To account for the variation in follow-up between studies,[86] it was assumed that the data arose according to a Poisson process for each trial arm, with a constant event rate, λ_{ik}, for arm k in study i, so that T_{ik}, the time until an event occurs in arm k of study i, is distributed exponentially such that:

$$T_{ik} \sim Exp(\lambda_{ik}) \tag{1}$$

Therefore, the probability that there are no events by time f_i in arm k of study i (i.e. the survivor function of an exponential distribution) is:

$$S(f_i) = P\left(T_{ik} > f_i\right) = 1 - F(f_i) = e^{-\lambda_{ik} f_i} \tag{2}$$

Then for each study, i, p_{ik}, the probability of an event in arm k of study i after follow-up time f_i, can be written as:

$$P_{ik} = 1 - P(T_{ik} > f_i) = 1 - e^{-\lambda_{ik} f_i} \tag{3}$$

which is time dependent.

Therefore, the event rate, λ_{ik}, was modelled using the complimentary log-log link function such that:

$$\begin{aligned}
\theta_{ik} &= cloglog(p_{ik}) \\
&= \ln(-\ln(1 - p_{ik})) \\
&= \ln(-\ln(1 - [1 - \exp(-\lambda_{ik} f_i)])) \\
&= \ln(-\ln[\exp(-\lambda_{ik} f_i)]) \\
&= \ln(-(-\lambda_{ik} f_i)) = \ln(\lambda_{ik} f_i) \\
&= \ln(\lambda_{ik}) + \ln(f_i) \\
&= \mu_i + \delta_{i,bk} I_{\{k \neq 1\}} + \ln(fi)
\end{aligned} \tag{4}$$

where $\delta_{i,bk}$ are the treatment effects of interest and are also the log-HRs relative to the baseline treatment.

This model assumes that the hazards for each intervention are constant irrespective of follow-up. Although this is a strong assumption, it is preferable to assuming that the follow-up has no impact on the number of events that are accumulated over time.

Appendix 4 Comparison of included studies from existing reviews

Author, year		
Studies included by Inglis *et al.*[48a]	Studies included by Klersy *et al.*[58b]	Comment
STS vs usual care; TM vs usual care		
Cleland *et al.* 2005 (TEN-HMS)[49]	Cleland *et al.* 2005 (TEN-HMS)[49]	RCT (three arm), patients discharged from hospital (and received intervention) within 28 days of exacerbation of HF (assumed majority received intervention <28 days from discharge)
Mortara *et al.* 2009 (HHH)[88,143]		RCT (three arm), stable HF patients
STS vs usual care		
Angermann *et al.* 2007 (INH) (Abstract)[144]		RCT, patients discharged from hospital (and received intervention) within 28 days of exacerbation of HF, telephone-based human interaction
Barth 2001[72]	Barth 2001[72]	RCT, patients discharged from hospital (and received intervention) within 28 days of exacerbation of HF, telephone-based human interaction
DeBusk *et al.* 2004[74]	DeBusk *et al.* 2004[74]	RCT, patients discharged from hospital (and received intervention) within 28 days of exacerbation of HF, telephone-based human interaction
Laramee *et al.* 2003[77]	Laramee *et al.* 2003[77]	RCT, patients discharged from hospital (and received intervention) within 28 days of exacerbation of HF, telephone-based human interaction
Rainville 1999[78]		RCT, patients discharged from hospital (and received intervention) within 28 days of exacerbation of HF, telephone-based human interaction
Riegel *et al.* 2002[79]	Riegel *et al.* 2002[79]	RCT, patients discharged from hospital (and received intervention) within 28 days of exacerbation of HF, telephone-based human interaction
Riegel *et al.* 2006[80]	Riegel *et al.* 2006[80]	RCT, patients discharged from hospital (and received intervention) within 28 days of exacerbation of HF, telephone-based human interaction
Tsuyuki *et al.* 2004 (REACT)[81]		RCT, patients discharged from hospital (and received intervention) within 28 days of exacerbation of HF, telephone-based human interaction; excluded by Klersy *et al.*[58] because of the following reason: not pertinent
Wakefield *et al.* 2008[82]		RCT, patients discharged from hospital (and received intervention) within 28 days of exacerbation of HF, telephone-based human interaction
DeWalt *et al.* 2006[89]		RCT, stable HF patients, telephone-based human interaction
Galbreath *et al.* 2004[87]	Galbreath *et al.* 2004[87]	RCT, stable HF patients, telephone-based human interaction
Gattis *et al.* 1999 (PHARM)[90]		RCT, stable HF patients, telephone-based human interaction
GESICA investigators 2005 (DIAL)[91]	GESICA investigators 2005 (DIAL)[91]	RCT, stable HF patients, telephone-based human interaction
Ramachandran *et al.* 2007[106]		RCT, stable HF patients, telephone-based human interaction; excluded by Klersy *et al.*[58] because of the following reason: not pertinent
Sisk *et al.* 2006[92,125]	Sisk *et al.* 2006[92,125]	RCT, stable HF patients, telephone-based human interaction
Tonkin *et al.* 2009 (CHAT) (Abstract)[93,145,146]		RCT, stable HF patients, telephone-based interactive response system, telephone-based human interaction; excluded by Klersy *et al.*[58] because of the following reason: not pertinent

Author, year		
Studies included by Inglis *et al.*[48a]	Studies included by Klersy *et al.*[58b]	Comment
TM vs usual care		
Antonicelli *et al.* 2008[71]		RCT, patients discharged from hospital (and received intervention) within 28 days of exacerbation of HF, transmitted data reviewed by medical staff (including medical support) during office hours
Capomolla *et al.* 2004[73]		RCT, patients discharged from hospital (and received intervention) within 28 days of exacerbation of HF, transmitted data reviewed by medical staff (including medical support) during office hours
Goldberg *et al.* 2003 (WHARF)[75]	Goldberg *et al.* 2003 (WHARF)[75]	RCT, patients discharged from hospital (and received intervention) within 28 days of exacerbation of HF, transmitted data reviewed by medical staff (including medical support) 7 days a week but not 24/7
Kielblock *et al.* 2007[76]	Kielblock *et al.* 2007[76]	RCT, patients discharged from hospital (and received intervention) within 28 days of exacerbation of HF, medical support available 24/7 (note: classified as cohort study by Klersy *et al.*[58])
Woodend *et al.* 2008[83]	Woodend *et al.* 2008[83]	RCT, patients discharged from hospital (and received intervention) within 28 days of exacerbation of HF, transmitted data reviewed by medical staff (including medical support) during office hours
Balk *et al.* 2008[94]		RCT, stable HF patients, transmitted data reviewed by medical staff (including medical support) during office hours
Blum *et al.* 2007 (MCCD) (Abstract)[95,147]		RCT, stable HF patients, transmitted data reviewed by medical staff (including medical support) during office hours
de Lusignan *et al.* 2001[96]		RCT, stable HF patients, transmitted data reviewed by medical staff (including medical support) during office hours; excluded by Klersy *et al.*[58] because of the following reason: not pertinent
Giordano *et al.* 2009[97]		RCT, stable HF patients, transmitted data reviewed by medical staff (including medical support) during office hours
Soran *et al.* 2008 (HFHC)[98]		RCT, stable HF patients, transmitted data reviewed by medical staff (including medical support) 7 days a week but not 24/7
Villani *et al.* 2007 (ICAROS) (Abstract)[99]		RCT, stable HF patients, transmitted data reviewed by medical staff (including medical support) during office hours; excluded by Klersy *et al.*[58] because of the following reason: study protocol
Zugck *et al.* 2008 (HiTel) (Abstract)[148]		RCT, stable HF patients, transmitted data reviewed by medical staff (including medical support) during office hours
Cardiovascular implanted devices with monitoring vs cardiovascular implanted devices without monitoring (usual care)		
	Bourge *et al.* 2008[105]	RCT, stable HF patients
Other		
	Blue *et al.* 2001[149]	TM, RCT; excluded by Inglis *et al.*[48] because of the following reason: intervention included home visits
	Dunagan *et al.* 2005[150]	STS, RCT; excluded by Inglis *et al.*[48] because of the following reason: intervention included home visits
	Jerant *et al.* 2001[151]	TM, RCT; excluded by Inglis *et al.*[48] because of the following reason: intervention included home visits
	Kashem *et al.* 2008[152]	TM, RCT; excluded by Inglis *et al.*[48] because of the following reason: web-based intervention
	Kasper *et al.* 2002[153]	TM, RCT; excluded by Inglis *et al.*[48] because of the following reason: intervention included home visits

Author, year		
Studies included by Inglis *et al.*[48a]	Studies included by Klersy *et al.*[58b]	Comment
	Krumholz *et al.* 2002[154]	TM, RCT; excluded by Inglis *et al.*[48] because of the following reason: frequent clinic and home visits
	McDonald *et al.* 2002[155]	TM, RCT; excluded by Inglis *et al.*[48] because of the following reason: frequent clinic visits with unstructured telephone follow-up
	Schwarz *et al.* 2008[156]	TM, RCT; excluded by Inglis *et al.*[48] because of the following reason: intervention involved caregivers as well as the patient with HF
	Adamson *et al.* 2003[157]	Cardiovascular implanted monitoring devices, cohort study without contemporaneous control group
	Gambetta *et al.* 2007[158]	TM, cohort study, stable HF patients
	Hudson *et al.* 2005[159]	TM; excluded by Inglis *et al.*[48] because of the following reason: not a RCT (before-and-after study)
	Myers *et al.* 2006[160]	TM, cohort study, stable HF patients
	Morguet *et al.* 2008[161]	TM; excluded by Inglis *et al.*[48] because of the following reason: not a RCT (cohort study with stable HF patients)
	Oeff *et al.* 2005[162]	TM; excluded by Inglis *et al.*[48] because of the following reason: not a RCT (before-and-after study)
	Roth *et al.* 2004[163]	TM, cohort study without contemporaneous control group
	Scalvini *et al.* 2004[164]	TM; excluded by Inglis *et al.*[48] because of the following reason: not a RCT (cohort study without contemporaneous control group)
	Scalvini *et al.* 2005[165]	TM; excluded by Inglis *et al.*[48] because of the following reason: not a RCT (cohort study with stable HF patients)
	Scalvini *et al.* 2006[166]	TM; excluded by Inglis *et al.*[48] because of the following reason: GP monitoring vs home-based monitoring (cohort study)
	Scholfield *et al.* 2005[167]	TM, before-and-after study

CHAT, Chronic Heart-failure Assistance by Telephone; DIAL, Randomized Trial of Telephone Intervention in Chronic Heart Failure; GESICA, Grupo de Estudio de Sobrevida en la Insuficiencia Cardíaca en la Argentina; HFHC, Heart Failure Home Care; HHH, Home or Hospital in Heart Failure; HiTel, Heart In – sufficiency TELemonitoring Study; ICAROS, Integrated Care vs Conventional Intervention in Cardiac Failure Patients: Randomized Open Label Study; INH, Interdisciplinary Network for Heart Failure; MCCD, Medicare Coordinated Care Demonstration; PHARM, Pharmacist in Heart Failure Assessment Recommendation and Monitoring; REACT, Review of Education on ACE Inhibitors in Congestive Heart Failure Treatment; WHARF, Weight Monitoring in Heart Failure.

a The criteria for inclusion were as follows: *population* – patients (aged ≥18 years) with a definitive diagnosis of HF and recently discharged from an acute care setting to home (excluding nursing homes or convalescent homes) or recruited while managed in the community setting; interventions – STS or TM interventions initiated by a health-care professional and targeted towards the patient and not caregivers; delivered as the only HF disease management intervention, without home visits or intensified clinic follow-up; comparator – consisted of standard post-discharge care without intensified attendance at cardiology clinics or clinic-based HF disease management programme or home visits; outcomes – death (from any cause), hospitalisation (from any cause or HF related), length of stay, cost of the intervention or cost reductions, QoL, acceptability and adherence; study design – RCTs; other criteria – full peer-reviewed journals published between January 2006 and November 2008 (this review updated a previously published review by the same authors that examined the period between 1966 and May 2006).

b The criteria for inclusion were as follows: population – patients with chronic HF; interventions – telephone monitoring approach including regularly scheduled structured telephone contact between patients and health-care providers (with or without home visits) and reporting of symptoms and/or physiological data; a technology-assisted monitoring approach relying on information communication technology, with transfer of physiological data collected via remote (at the patient's home) external monitors or via cardiovascular implantable electronic devices; comparator – usual care approach, which referred to in-person visits at the doctor's office, at a multidisciplinary outpatient clinic or at an emergency department without additional telephone calls to and from the patient; outcomes – death (from any cause), first hospitalisation (from any cause or HF related) and composite of individual outcomes; study design – RCTs and cohort studies; other criteria – full-text articles in peer-reviewed journals published between January 2000 and October 2008 and published in English, Spanish, German, French or Italian.

Appendix 5 Methodological assessment tool for systematic reviews and meta-analysis[66]

	Inglis *et al.*[48]	Klersy *et al.*[58]
1. *Was an 'a priori' design provided?* The research question and inclusion criteria should be established before the conduct of the review	✓ Yes No Can't answer Not applicable	✓ Yes No Can't answer Not applicable
2. *Was there duplicate study selection and data extraction?* There should be at least two independent data extractors and a consensus procedure for disagreements should be in place	✓ Yes No Can't answer Not applicable	✓ Yes No Can't answer Not applicable
3. *Was a comprehensive literature search performed?* At least two electronic sources should be searched. The report must include years and databases used [e.g. Cochrane Central Register of Controlled Trials (CENTRAL), EMBASE and MEDLINE]. Key words and/or medical subject heading (MeSH) terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialised registers or experts in the particular field of study, and by reviewing the references in the studies found	✓ Yes No Can't answer Not applicable	Yes ✓ No Did not report consulting current contents, reviews, specialised registers or experts in field Can't answer Not applicable
4. *Was the status of publication (i.e. grey literature) used as an inclusion criterion?* The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review) based on their publication status, language, etc.	✓ Yes No Can't answer Not applicable	Yes ✓ No Authors searched for full-text peer-reviewed publications only Can't answer Not applicable
5. *Was a list of studies (included and excluded) provided?* A list of included and excluded studies should be provided	✓ Yes No Can't answer Not applicable	✓ Yes No Can't answer Not applicable
6. *Were the characteristics of the included studies provided?* Data from the original studies on the participants, interventions and outcomes should be provided in an aggregated form such as a table. The ranges of characteristics in all of the studies analysed, e.g. age, race, sex, relevant socioeconomic data, disease status, duration, severity or other diseases, should be reported	✓ Yes No Can't answer Not applicable	✓ Yes No Can't answer Not applicable

	Inglis *et al.*[48]	Klersy *et al.*[58]
7. *Was the scientific quality of the included studies assessed and documented?* 'A priori' methods of assessment should be provided [e.g. for effectiveness studies if the author(s) chose to include only randomised, double-blind, placebo-controlled studies, or allocation concealment as inclusion criteria]; for other types of studies alternative items will be relevant	✓ Yes No Can't answer Not applicable	✓ Yes No Can't answer Not applicable
8. *Was the scientific quality of the included studies used appropriately in formulating conclusions?* The results of the methodological rigour and scientific quality should be considered in the analysis and the conclusions of the review and explicitly stated in formulating recommendations	Yes ✓ No Authors did not consider recommendations in light of the quality of included trials Can't answer Not applicable	Yes ✓ No Authors did not refer to study quality when discussing implications for practice Can't answer Not applicable
9. *Were the methods used to combine the findings of studies appropriate?* For the pooled results a test should be carried out to ensure that the studies were combinable, to assess their homogeneity (i.e. chi-squared test for homogeneity, I^2). If heterogeneity exists a random-effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e. is it sensible to combine?)	Yes ✓ No 'Owing to differences in patient populations programme characteristics and length of follow-up, all meta-analyses were performed using a fixed-effects model' (p. 8) Can't answer Not applicable	✓ Yes No Can't answer Not applicable
10.Was the likelihood of publication bias assessed? An assessment of publication bias should include a combination of graphical aids (e.g. funnel plot, other available tests) and/or statistical tests (e.g. Egger regression test)	✓ Yes No Can't answer Not applicable	✓ Yes No Can't answer Not applicable
11.Was the conflict of interest stated? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies	✓ Yes No Can't answer Not applicable	Yes ✓ No Authors listed their own sources of sponsorship but not those of the included trials Can't answer Not applicable

Appendix 6 Clinical effectiveness review: table of excluded studies with rationale

	Author, year	Reason for exclusion
1.	Anon 2009[168]	Foreign language (review article)
2.	Abraham *et al.* 2011[103]	Patients discharged within the previous 12 months for HF but TM intervention performed <28 days after being implanted with a cardiovascular monitoring device (CHAMPION)
3.	Adamson *et al.* 2011[169]	Patients discharged within the previous 12 months for HF but TM intervention performed <28 days after being implanted with a cardiovascular monitoring device (CHAMPION)
4.	Adamson *et al.* 2011[104]	Patients discharged within the previous 12 months for HF but TM intervention performed <28 days after being implanted with a cardiovascular monitoring device (REDUCEhf)
5.	Adlbrecht *et al.* 2009[170]	Not TM or STS
6.	Al-Khatib *et al.* 2010[171]	Not RM for HF – RM of device vs quarterly device interrogation
7.	Anand *et al.* 2010[172]	Not TM or STS
8.	Anand *et al.* 2011[173]	Not TM or STS
9.	Antonicelli *et al.* 2010[174]	Not available
10.	Arya *et al.* 2008[175]	Ongoing study (IN-TIME)
11.	Bardy and McCullough 2008[176]	Editorial/comment
12.	Bardy *et al.* 2008[177]	Not RM or STS
13.	Bento *et al.* 2009[178]	Not RM or STS
14.	Benvenuto *et al.* 2008[179]	Not RCT/cohort with concurrent control
15.	Benvenuto *et al.* 2009[180]	Not RCT/cohort with concurrent control
16.	Berkley *et al.* 2010[181]	Not RCT/cohort with concurrent control
17.	Biddiss *et al.* 2009[182]	Not RCT/cohort with concurrent control
18.	Bocchi *et al.* 2008[183]	Intervention included education and face-to-face (individual/group) support
19.	Boehmer *et al.* 2009[184]	Not RCT/cohort with concurrent control
20.	Boriani *et al.* 2009[185]	Editorial/comment
21.	Boveda *et al.* 2009[186]	Not RM or STS
22.	Bover *et al.* 2009[187]	Control group did not have usual care
23.	Bowles and Horowitz 2008[188]	Intervention included home visits
24.	Bowles *et al.* 2009[189]	Intervention included home visits
25.	Boxer *et al.* 2010[190]	Insufficient information for inclusion (e.g. population, intervention, comparator, outcomes)
26.	Boyne *et al.* 2009[191]	Discharge/intervention received > 28 days (TEHAF)
27.	Boyne *et al.* 2011[135]	Discharge/intervention received >28 days (TEHAF)
28.	Boyne *et al.* 2011[192]	Discharge/intervention received >28 days (TEHAF)

	Author, year	Reason for exclusion
29.	Boyne *et al.* 2011[193]	Discharge/intervention received >28 days (TEHAF)
30.	Boyne *et al.* 2011[100]	Discharge/intervention received >28 days (TEHAF)
31.	Brandon *et al.* 2009[194]	Pre-test and post-test study design
32.	Brandon *et al.* 2009[195]	Pre-test and post-test study design
33.	Braunschweig *et al.* 2008[196]	Not RM for HF – paper states that there was no transfer of physiological data via technology (DOT-HF)
34.	Broesch and Heywood 2009[197]	Not RCT/cohort with concurrent control
35.	Brotons *et al.* 2009[198]	Foreign language
36.	Burri *et al.* 2010[199]	Ongoing study (MORE-CARE)
37.	Cardozo *et al.* 2010[200]	Intervention included home visits
38.	Carson and Bella 2009[201]	Not RCT/cohort with concurrent control
39.	Catanzariti *et al.* 2009[202]	Not TM or STS
40.	Chen *et al.* 2010[203]	Not RCT/cohort with concurrent control
41.	Clark *et al.* 2007[59]	Systematic review and meta-analysis
42.	Clark *et al.* 2010[204]	Systematic review and meta-analysis (abstract)
43.	Cleland *et al.* 2011[205]	Discharge/intervention received >28 days (TEHAF)
44.	Conraads *et al.* 2011[115]	Discharge/intervention received >28 days (cohort study) (SENSE-HF)
45.	Copeland *et al.* 2010[206]	Intervention included education and behaviour change
46.	Cowie 2010[207]	Editorial/comment
47.	Cowie *et al.* 2009[208]	Discharge/intervention received >28 days (cohort study) (SENSE-HF)
48.	Crawford and Volkman 2010[209]	Not RCT/cohort with concurrent control
49.	Crossley *et al.* 2008[210]	Not RM for HF – RM of arrhythmias (CONNECT)
50.	Crossley *et al.* 2009[211]	Population not specific to HF (no useable data)
51.	Crossley *et al.* 2011[212]	Not RM for HF – RM of arrhythmias (CONNECT)
52.	Dansky *et al.* 2008[213]	Intervention included home visits
53.	Dansky *et al.* 2008[214]	Not available
54.	Dansky *et al.* 2009[215]	Intervention initiated after formal home care and not hospital discharge
55.	Dar *et al.* 2008[216]	Abstract (full text included) (Home-HF)
56.	De Vries *et al.* 2010[217]	Ongoing study (IN TOUCH)
57.	Delaney and Apostolidis 2010[218]	Pre-test and post-test study design
58.	Desai *et al.* 2010[219]	Editorial/comment
59.	Domingo *et al.* 2011[220]	Intervention included education (CARME)
60.	Domingo *et al.* 2011[221]	Intervention included education (CARME)
61.	Duffy *et al.* 2010[222]	Intervention included home visits
62.	Ewald *et al.* 2009[223]	Not RCT/cohort with concurrent control
63.	Ewald *et al.* 2009[224]	Not RCT/cohort with concurrent control
64.	Fan *et al.* 2010[225]	Not available
65.	Ferrante *et al.* 2010[226]	Discharge/intervention received >28 days (extension study of the DIAL trial)

	Author, year	Reason for exclusion
66.	Finkelstein and Dennison 2010[227]	Not RCT/cohort with concurrent control
67.	Finkelstein *et al.* 2010[228]	Not RCT/cohort with concurrent control
68.	Fursse *et al.* 2008[229]	Not RCT/cohort with concurrent control
69.	Germany *et al.* 2009[230]	Not RCT/cohort with concurrent control
70.	Goernig *et al.* 2009[231]	Foreign language
71.	Goernig *et al.* 2009[232]	Insufficient information on population, intervention, comparator or outcomes for inclusion
72.	Gonzalez *et al.* 2010[233]	Intervention included education
73.	Haddour 2008[234]	Foreign language (intervention included clinic and home visits)
74.	Hannah *et al.* 2010[235]	Not RCT/cohort with concurrent control
75.	HAYES Inc. 2008[236]	Not available
76.	Holden *et al.* 2011[237]	Insufficient information on population, intervention, comparator or outcomes for inclusion
77.	Houston-Feenstra *et al.* 2008[238]	Not TM or STS
78.	Howlett *et al.* 2011[239]	Insufficient information on population, intervention, comparator or outcomes for inclusion
79.	Inglis *et al.* 2010[48]	Systematic review and meta-analysis
80.	Jacobs 2011[240]	Not TM or STS
81.	Kashem *et al.* 2008[152]	Web-based intervention
82.	Katra *et al.* 2010[241]	Not RCT/cohort with concurrent control
83.	Klersy *et al.* 2009[58]	Systematic review and meta-analysis
84.	Knotter *et al.* 2010[242]	Not RCT/cohort with concurrent control
85.	Koehler *et al.* 2010[243]	Discharge > 28 days (TIM-HF)
86.	Koehler *et al.* 2011[52]	Discharge > 28 days (TIM-HF)
87.	Konstam *et al.* 2011[244]	Intervention included home visits
88.	Kraai *et al.* 2010[245]	Ongoing study (IN TOUCH)
89.	Kriegeskorte 2008[246]	Foreign language (editorial/comment)
90.	Kulshreshtha *et al.* 2008[247]	Abstract (full text included)
91.	Kurtz *et al.* 2011[248]	Not RCT/cohort with concurrent control
92.	LaFramboise *et al.* 2009[249]	Not RCT/cohort with concurrent control
93.	Mainardi *et al.* 2010[250]	Foreign language
94.	Margolis *et al.* 2010[251]	Population not specific to HF (no useable data)
95.	Margolis *et al.* 2010[252]	Population not specific to HF (no useable data)
96.	Maric *et al.* 2010[253]	Web-based intervention
97.	Masella *et al.* 2008[254]	Not RCT/cohort with concurrent control
98.	McEntee *et al.* 2010[255]	Not RCT/cohort with concurrent control
99.	Melillo *et al.* 2009[256]	Review article
100.	Merchant *et al.* 2010[257]	Review article
101.	Meriggi *et al.* 2009[258]	Not RCT/cohort with concurrent control

	Author, year	Reason for exclusion
102.	Metten *et al.* 2011[259]	Discharge/intervention received >28 days (cohort study)
103.	Morguet *et al.* 2008[260]	Population not specific to HF (no useable data)
104.	Mullens *et al.* 2008[261]	Not RCT/cohort with concurrent control
105.	Naccarella *et al.* 2008[262]	Editorial/comment
106.	Nathani *et al.* 2010[263]	Insufficient information on population, intervention, comparator or outcomes for inclusion
107.	Nikus *et al.* 2009[264]	Not RCT/cohort with concurrent control
108.	Oliveira *et al.* 2009[265]	Not RCT/cohort with concurrent control
109.	Paget *et al.* 2010[266]	Not RCT/cohort with concurrent control
110.	Perl *et al.* 2011[267]	Insufficient information on population, intervention, comparator or outcomes for inclusion
111.	Persson *et al.* 2011[268]	Insufficient information on population, intervention, comparator or outcomes for inclusion
112.	Ramaekers *et al.* 2009[269]	Discharge/intervention received >28 days (TEHAF)
113.	Raval *et al.* 2011[270]	Patients discharged within the previous 12 months for HF but TM intervention performed <28 days after being implanted with a cardiovascular monitoring device (CHAMPION)
114.	Ricci *et al.* 2008[271]	Not RCT/cohort with concurrent control
115.	Riley 2011[272]	Review article
116.	Riley and Cowie 2009[15]	Review article
117.	Riley *et al.* 2008[273]	Abstract (full text included) (Home-HF)
118.	Riley *et al.* 2009[274]	Abstract (full text included) (Home-HF)
119.	Rosa 2008[275]	Review article
120.	Rosati 2009[276]	Insufficient information on population, intervention, comparator or outcomes for inclusion
121.	Santamore and Homko 2008[277]	Review article
122.	Scalvini *et al.* 2010[278]	Not RCT/cohort with concurrent control
123.	Schwarz *et al.* 2008[156]	Intervention involved caregivers as well as the patient with HF
124.	Schweinzer 2009[279]	Not available
125.	Seibert *et al.* 2008[280]	Not RCT/cohort with concurrent control
126.	Seto *et al.* 2011[281]	Insufficient information on population, intervention, comparator or outcomes for inclusion
127.	Smith *et al.* 2011[282]	Insufficient information on population, intervention, comparator or outcomes for inclusion
128.	Sonntag *et al.* 2010[283]	Not RCT/cohort with concurrent control
129.	Sprenger and Oeff 2009[284]	Not RCT/cohort with concurrent control
130.	Stevenson 2010[285]	Editorial/comment
131.	Stewart *et al.* 2010[286]	Not TM or STS
132.	Stork *et al.* 2009[287]	Foreign language (review article)
133.	Strobeck *et al.* 2008[288]	Review article
134.	Takahashi *et al.* 2010[289]	Population not specific to HF (no useable data)

	Author, year	Reason for exclusion
135.	Talukder and Pray 2009[290]	Review article
136.	Tang *et al.* 2010[291]	Ongoing study (OptiVol® Care Pathway study)
137.	Tang *et al.* 2010[292]	Not TM or STS
138.	Taylor 2008[293]	Not RCT/cohort with concurrent control
139.	Thompson 2008[294]	Editorial/comment
140.	Tompkins and Orwat 2010[295]	Intervention included education and intensive care management
141.	Trembath *et al.* 2009[296]	Not RCT/cohort with concurrent control
142.	van Veldhuisen *et al.* 2011[297]	Not RM for HF – paper states that there was no transfer of physiological data via technology (DOT-HF trial)
143.	Vanderheyden *et al.* 2010[298]	Not RCT/cohort with concurrent control
144.	Varma *et al.* 2011[299]	Not RM for HF – RM of arrhythmias (TRUST)
145.	Varma *et al.* 2010[300]	Not RM for HF – RM of arrhythmias (TRUST)
146.	Vercauteren *et al.* 2009[301]	Not RCT/cohort with concurrent control
147.	Wade *et al.* 2011[101]	Discharge/intervention received >28 days
148.	Weintraub *et al.* 2010[302]	Intervention included home visits
149.	Wexler 2010[303]	Editorial/comment
150.	Whellan *et al.* 2010[304]	Not RCT/cohort with concurrent control
151.	Wootton *et al.* 2009[305]	Intervention included education and face-to-face support
152.	Zile *et al.* 2008[306]	Patients discharged within the previous 12 months for HF but TM intervention performed <28 days after being implanted with a cardiovascular monitoring device (subgroup analysis of the COMPASS-HF trial)
153.	Zucca *et al.* 2010[307]	Insufficient information on population, intervention, comparator or outcomes for inclusion

CARME, CAtalan Remote Management Evaluation; CHAMPION, CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Patients; COMPASS-HF, Chronicle Offers Management to Patients with Advanced Signs and Symptoms of Heart Failure; CONNECT, Clinical Evaluation of Remote Notification to Reduce Time to Clinical Decision; DIAL, Randomized Trial of Telephone Intervention in Chronic Heart Failure; DOT-HF, Diagnostic Outcome Trial in Heart Failure; IN-TIME, the INfluence of home monitoring on The clinIcal Management of heart failurE patients with impaired left ventricular function; IN TOUCH, INnovative ICT guided disease management and Telemonitoring in OUtpatient clinics for Chronic Heart failure patients; MORE-CARE, MOnitoring Resynchronization dEvices and CARdiac patiEnts; REDUCEhf, Reducing Decompensation Events Utilizing Intracardiac Pressures in Patients With Chronic Heart Failure; SENSE-HF, Sensitivity of the InSync Sentry OptiVol Feature for the Prediction of HF; TEHAF, Tailored Telemonitoring in Patients with Heart Failure; TRUST, Lumos-T Safely Reduces Routine Office Device Follow-up.

Appendix 7 Summary of the trials included in the base-case network meta-analysis of recently discharged patients with heart failure

	All-cause mortality				All-cause hospitalisation				HF-related hospitalisation			
	Intervention		Control		Intervention		Control		Intervention		Control	
Author, year	Events	Total *n*	Events	Total *n*	Events	Total *n*	Events	Total *n*	Events	Total *n*	Events	Total *n*
STS												
HM (e.g. telephone-based interactive response system) vs usual care												
Chaudhry *et al.* 2010 (Tele-HF)[52]	92	826	94	827	407	826	392	827	227	826	223	827
HH vs usual care												
Angermann *et al*. 2011 (INH)[51]	32	352	52	363	119	352	112	363	36	352	46	363
[a]Barth 2001[72]	0	17	0	17					0	17	0	17
[b]Cleland *et al*. 2005 (TEN-HMS)[49]	27	173	20	85	85	173	46	85	34	173	24	85
DeBusk *et al*. 2004[74]	21	228	29	234	116	228	117	234	38	228	43	234
Domingues *et al*. 2011[69]	8	57	13	63	20	57	23	63				
Laramee *et al*. 2003[77]	13	141	15	146	49	141	46	146	18	141	21	146
Rainville 1999[78]	1	19	4	19					4	19	10	19
Riegel *et al*. 2002[79]	16	130	32	228	56	130	114	228	23	130	63	228
Riegel *et al*. 2006[80]	6	70	8	65	39	70	37	65	21	70	22	65
Tsuyuki *et al*. 2004 (REACT)[81]	16	140	12	136	59	140	51	136	37	140	38	136
Wakefield *et al*. 2008[82]	25	99	11	49	41	99	29	49				

Author, year	All-cause mortality				All-cause hospitalisation				HF-related hospitalisation			
	Intervention		Control		Intervention		Control		Intervention		Control	
	Events	Total *n*	Events	Total *n*	Events	Total *n*	Events	Total *n*	Events	Total *n*	Events	Total *n*
TM vs usual care												
Data reviewed/support provided by medical staff during office hours												
Antonicelli *et al*. 2008[71]	3	28	5	29	9	28	26	29				
Capomolla *et al*. 2004[73]	5	67	7	66								
[b]Cleland *et al*. 2005 (TEN-HMS)[49]	28	168	20	85	80	168	46	85	40	168	24	85
Dar *et al*. 2009 (Home-HF)[67]	17	91	5	91	33	91	23	91	17	91	10	91
Dendale *et al*. 2011 (TEMA-HF 1)[68]	4	80	14	80								
Goldberg *et al*. 2003 (WHARF)[75]	11	138	26	142	65	138	67	142	71	251	82	251
Kulshreshtha *et al*. 2010[60]	4	42	4	68								
Scherr *et al*. 2009 (MOBITEL)[70]	0	66	1	54	11	66	17	54				
Woodend *et al*. 2008[83]	5	62	4	59	60	62	54	59				
Data reviewed/support provided by medical staff 24/7												
Kielblock *et al*. 2007[76]	37	251	69	251	157	251	176	251				

INH, Interdisciplinary Network for Heart Failure; MOBITEL, MOBIle TELemonitoring in Heart Failure Patients Study; REACT, Review of Education on ACE Inhibitors in Congestive Heart Failure Treatment; TEMA-HF, TElemonitoring in the MAnagement of Heart Failure; WHARF, Weight Monitoring in Heart Failure.

a Study data excluded from the NMA: comparisons with zero events in both groups provide no information on the magnitude of the treatment effect.[86]

b Three-arm trial.

Appendix 8 Additional analyses: summary of the design and patient characteristics of included studies of stable patients with heart failure

Author, year	Population	Intervention	Comparator	Primary outcome	Duration
Boyne *et al.* 2010 (TEHAF)[135,192,205,269]	Adults with confirmed HF diagnosis, NYHA class II–IV symptoms	STS. Monitoring of HF symptoms, knowledge of HF and self-care behaviour; delivered via telephone-based interactive response system ($n = 197$)	Usual care (follow-up from HF nurse specialist and cardiologist) ($n = 185$)	Time to first HF admission	12 months
Tonkin *et al.* 2009 (Abstract) (CHAT)[93]	Adults with HF diagnosed in last 5 years, confirmed LVEF <40%, confirmed by echocardiography, NYHA class II–IV symptoms	STS. Monitored parameters NR; delivered via interactive voice response system ($n = 188$)	Usual care (follow-up from GP) ($n = 217$)	Packer clinical composite score	12 months
DeWalt *et al.* 2006[89]	Confirmed HF patients (aged 30–80 years) with NYHA class II–IV symptoms and LVEF <40%	STS. Weight and self-monitoring education; delivered via HH ($n = 62$)	Usual care (follow-up from GP) ($n = 65$)	Composite of mortality and hospitalisation and HF-related QoL	12 months
Galbreath *et al.* 2004[87]	Patients (aged ≥18 years) with symptoms of CHF and documented systolic (LVEF 35%) or diastolic dysfunction (echocardiographically confirmed)	STS. Education and monitoring; delivered via HH ($n = 710$)	Usual care (follow-up from GP) ($n = 359$)	All-cause mortality	18 months
Gattis *et al.* 1999 (PHARM)[90]	Adults with HF (based on signs and symptoms) and LVEF <45%	STS. Pharmacist-led medication review and education; delivered via HH ($n = 90$)	Usual care (follow-up from attending physician, physician assistant or HF nurse specialist) ($n = 91$)	All-cause mortality and HF-related clinical events	6 months
GESICA investigators 2005 (DIAL)[91]	Adult outpatients with stable CHF (defined as no admissions in previous 2 months)	STS. Monitored adherence to diet and treatment, symptoms, control of fluid retention and daily physical activity; delivered via HH ($n = 760$)	Usual care (follow-up from attending cardiologist) ($n = 758$)	All-cause mortality and HF-related hospitalisation	16 months
Mortara *et al.* 2009 (HHH)[88a]	HF patients (aged 18–85 years) with NYHA class II–IV symptoms and LVEF ≤40%	STS. Education and clinical status monitoring; delivered via HH ($n = 106$) TM. Measurement of weight, BP and symptoms, reviewed by medical staff, support available during office hours ($n = 195$)	Usual care (not described) ($n = 160$)	Bed-days for HF and composite of cardiac death and HF-related hospitalisation	12 months

Author, year	Population	Intervention	Comparator	Primary outcome	Duration
Ramachandran *et al.* 2007[106]	Adult outpatients (aged 16–65 years) with HF and LVEF <40%	STS. Education, monitoring and medication management; delivered via HH ($n = 25$)	Usual care (follow-up in HF specialist clinic) ($n = 25$)	QoL	6 months
Sisk *et al.* 2006[92]	Hispanic and non-Hispanic patients (aged ≥18 years) with documented systolic dysfunction	STS. Clinical status monitoring and self-monitoring advice; delivered via HH ($n = 203$)	Usual care (patients received guidelines for managing systolic dysfunction) ($n = 203$)	All-cause hospitalisation and QoL	12 months
Balk *et al.* 2008[94]	Stable adult outpatients with HF and NYHA class I–IV symptoms	TM. Measurement/transmission of BP and weight, with education provision; data reviewed by HF specialist nurses available during office hours ($n = 101$)	Usual care (follow-up from cardiologists and HF nurse specialists) ($n = 113$)	Hospital-days and days alive outside hospital	10 months
Blum *et al.* 2007 (Abstract) (MCCD)[95]	Patients with hospitalisation for HF within previous year	TM. Measurement/transmission of weight, BP, heart rate and heart rhythm; data reviewed by HF specialist nurses available during office hours ($n = 102$)	Usual care (patients not contacted until 6-month assessment follow-up) ($n = 102$)	Hospitalisations, QoL, mortality and BNP	12 months
de Lusignan *et al.* 2001[96]	Adult patients with HF confirmed by cardiologist, identified from the database of an academic general practice	TM. Measurement/transmission of pulse, BP and weight and video consultations with HF nurses; data reviewed by HF nurses on weekdays ($n = 10$)	Usual care (follow-up from GP) ($n = 10$)	Mortality, satisfaction, adherence and QoL	12 months
Giordano *et al.* 2009[97]	Adult HF patients (clinically stable with optimised pharmacotherapy) with LVEF <40% and at least one hospitalisation for acute HF in the last year	TM. Measurement/transmission of one-lead ECG; reviewed by clinical staff who were available 24/7 for teleconsultations ($n = 230$)	Usual care (follow-up from GP and cardiologist) ($n = 230$)	Hospital readmission for cardiovascular reasons	12 months
Koehler *et al.* 2011 (TIM-HF)[50]	Stable adult HF outpatients (NYHA II or III symptoms, LVEF ≤35%) and cardiac decompensation with hospitalisation for HF within 24 months or LVEF ≤25%, measured twice within last 6 months	TM. Measurement/transmission of BP, weight and three-lead ECG; reviewed by staff at telemedical centre with physician-led medical support available 24/7 ($n = 354$)	Usual care (follow-up from GP) ($n = 356$)	All-cause mortality	22 months
Soran *et al.* 2008 (HFHC)[98]	Stable patients (aged ≥65 years) with HF diagnosis secondary to systolic dysfunction (LVEF ≤40%)	TM. Measurement/transmission of weight and HF symptoms; reviewed by nurses 7 days a week, daytime only, and concerns reported to physician ($n = 160$)	Usual care (enhanced patient education from clinicians and follow-up) ($n = 155$)	Composite of cardiovascular death or HF-related rehospitalisation (including length of stay)	6 months

Author, year	Population	Intervention	Comparator	Primary outcome	Duration
Villani *et al.* 2007 (Abstract) (ICAROS)[99]	Stable adult HF patients (LVEF ≤40%, NYHA II or III symptoms)	TM. Measurement/transmission of weight, urine output, fluid intake, BP and heart rate; reviewed by medical staff during office hours ($n = 33$)	Usual care (content NR) ($n = 44$)	Mortality, hospitalisations, emergency room visits and hospital-days per patient	12 months
Wade *et al.* 2011[101]	Medicare Advantage patients with HF (inpatient admission or two or more emergency department visits for any cause in past 6 months; medical claims for CHF in past 3 years; resident in NJ, NY or PA, USA)	TM. Measurement/transmission of weight and BP; reviewed by HF case management team during office hours, with automatic warnings if measurements outside preset parameters ($n = 1477$)	Usual care (follow-up from nurse case managers) ($n = 723$)	Composite of all-cause hospitalisation, A&E visit and death	6 months
Zugck *et al.* 2008 (Abstract) (HiTEL)[102]	Adult HF patients with NYHA II–IV symptoms on optimum therapy	TM. Measurement/transmission of weight, BP and 12-lead ECG; medical advice from physicians available 24/7 ($n = 58$)	Usual care (content NR) ($n = 30$)	Mortality, hospitalisations and length of stay	12 months
Abraham *et al.* 2011 (CHAMPION)[103]	HF patients with NYHA class III symptoms (for at least 3 months), irrespective of LVEF or cause and previous HF-related hospitalisation in past 12 months	Home TM via cardiovascular implanted monitoring device; daily continuous measurement, automatic transmission of pulmonary artery pressure to a secure patient database with clinician access ($n = 270$)	Home TM via cardiovascular implanted monitoring device; daily continuous measurement, automatic transmission of pulmonary artery pressure to a secure patient database with no clinician access ($n = 280$)	Rate of HF-related hospitalisations	6 months

Author, year	Population	Intervention	Comparator	Primary outcome	Duration
Adamson *et al.* 2011 (REDUCEhf)[104]	HF patients with NYHA class II or III symptoms, an indication for an implantable cardioverter defibrillator and HF hospitalisation in the past 12 months	Home TM via cardiovascular implanted monitoring device; daily continuous measurement, weekly manual transmission of intercardiac pressures to secure internet-based information system ($n = 202$)	Home TM via cardiovascular implanted monitoring device; daily continuous measurement of intercardiac pressures; however, haemodynamic data not used to guide management ($n = 198$)	Composite of HF-related events (hospitalisations >24 hours or <24 hours requiring intravenous HF therapy, emergency department visits and urgent clinic visits requiring intravenous therapy)	12 months
Bourge *et al* 2008 (COMPASS-HF)[105]	HF patients receiving optimised pharmacological therapy with NYHA class II or III symptoms and HF hospitalisation in the past 6 months	Home TM via cardiovascular implanted monitoring device; daily continuous measurement, weekly manual transmission of intercardiac pressures to secure server with clinician access ($n = 134$)	Home TM via cardiovascular implanted monitoring device; daily continuous measurement, weekly manual transmission of intercardiac pressures to secure server with no clinician access ($n = 140$)	Composite of HF-related events (hospitalisations, emergency department visits and urgent clinic visits requiring intravenous therapy)	6 months

BNP, B-type natriuretic peptide; BP, blood pressure; CHAMPION, CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Patients; CHAT, Chronic Heart-failure Assistance by Telephone; COMPASS-HF, Chronicle Offers Management to Patients with Advanced Signs and Symptoms of Heart Failure; DIAL, Randomized Trial of Telephone Intervention in Chronic Heart Failure; ECG, electrocardiogram; HFHC, Heart Failure Home Care; HHH, Home or Hospital in Heart Failure; ICAROS, Integrated Care vs Conventional Intervention in Cardiac Failure Patients: Randomized Open Label Study; MCCD, Medicare Coordinated Care Demonstration; NR, not reported; PHARM, Pharmacist in Heart Failure Assessment Recommendation and Monitoring; REDUCEhf, Reducing Decompensation Events Utilizing Intracardiac Pressures in Patients With Chronic Heart Failure; TEHAF, Tailored Telemonitoring in Patients with Heart Failure.

a Three-arm trial comparing TM, STS and usual care.

Appendix 9 Summary of the trials included in the base-case network meta-analysis of patients with stable heart failure

Author, year	All-cause mortality				All-cause hospitalisation				HF-related hospitalisation			
	Intervention		Control		Intervention		Control		Intervention		Control	
	Events	Total *n*	Events	Total *n*	Events	Total *n*	Events	Total *n*	Events	Total *n*	Events	Total *n*
STS												
HM (e.g. telephone-based interactive response system) vs usual care												
Boyne *et al.* 2010 (TEHAF)[100]	18	197	12	185	93	197	78	185	18	197	25	185
Tonkin *et al.* 2009 (Abstract) (CHAT)[93]	17	188	16	217	74	188	114	217	23	188	35	217
HH vs usual care												
DeWalt *et al.* 2006[89]	3	62	4	65								
Galbreath *et al.* 2004[87]	54	710	39	359								
Gattis *et al.* 1999 (PHARM)[90]	3	90	5	91	17	90	30	91	1	90	11	91
GESICA investigators 2005 (DIAL)[91]	116	760	122	758	261	760	296	758	128	760	169	758
Mortara *et al.* 2009 (HHH)[88a]	9	106	9	160	37	106	48	160	18	106	28	160
Ramachandran *et al.* 2007[106]									6	25	4	25
Sisk *et al.* 2006[92]	22	203	22	203	62	203	74	203	18	203	29	203
TM vs usual care												
Data reviewed/support provided by medical staff during office hours												
Balk *et al.* 2008[94]	9	101	8	113								
Blum *et al.* 2007 (Abstract) (MCCD)[95]	17	102	21	102	42	102	28	102				
de Lusignan *et al.* 2001[96]	2	10	3	10								
Mortara *et al.* 2009[88a]	15	195	9	160	69	195	48	160	35	195	28	160
Soran *et al.* 2008 (HFHC)[98]	11	160	17	155	75	160	66	155				
Villani *et al.* 2007 (Abstract) (ICAROS)[99]	5	33	9	44	22	33	28	44	6	33	17	44
Wade *et al.* 2011[101]	6	164	6	152	57	164	49	152				

Author, year	All-cause mortality				All-cause hospitalisation				HF-related hospitalisation			
	Intervention		Control		Intervention		Control		Intervention		Control	
	Events	Total *n*	Events	Total *n*	Events	Total *n*	Events	Total *n*	Events	Total *n*	Events	Total *n*
Data reviewed/support provided by medical staff 24/7												
Giordano *et al.* 2009[97]	21	230	32	230	67	230	96	230	43	230	73	230
Koehler *et al.* 2011 (TIM-HF)[50]	54	354	55	356	192	354	179	356	64	354	74	356
Zugck *et al.* 2008 (Abstract) (HiTel)[102]	3	58	1	30	24	58	17	30	18	58	16	30
Cardiovascular implanted monitoring devices vs cardiovascular implanted non-monitoring devices (usual care)												
Abraham *et al.* 2011 (CHAMPION)[103]	15	270	20	280	229	270	263	280	83	270	120	280
Adamson *et al.* 2011 (REDUCEhf)[104]	7	202	9	198					72	202	78	198
Bourge *et al.* 2008 (COMPASS-HF)[105]	13	134	11	140					37	134	57	140

CHAMPION, CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Patients; CHAT, Chronic Heart-failure Assistance by Telephone; COMPASS-HF, Chronicle Offers Management to Patients with Advanced Signs and Symptoms of Heart Failure; DIAL, Randomized Trial of Telephone Intervention in Chronic Heart Failure; HFHC, Heart Failure Home Care; HHH, Home or Hospital in Heart Failure; ICAROS, Integrated Care vs Conventional Intervention in Cardiac Failure Patients: Randomized Open Label Study; MCCD, Medicare Coordinated Care Demonstration; PHARM, Pharmacist in Heart Failure Assessment Recommendation and Monitoring; REDUCEhf, Reducing Decompensation Events Utilizing Intracardiac Pressures in Patients With Chronic Heart Failure; TEHAF, Tailored Telemonitoring in Patients with Heart Failure.

a Three-arm trial comparing TM, STS and usual care.

Appendix 10 MEDLINE search strategy for the cost-effectiveness review

1. exp Heart Failure/
2. ((heart or cardiac) adj failure).tw.
3. 1 or 2
4. exp Telecommunications/
5. Telemetry/
6. (telemetr$ or telemed$ or tele-med$ or telehealth$ or tele-health$ or telecare or tele-care or telecardiol$ or tele-cardiol$ or telehome or tele-home).tw.
7. (telemonitor$ or tele-monit$ or teleconsult$ or tele-consult$ or teleconferenc$ or tele-conferenc$ or telecommunicat$ or tele-communicat$).tw.
8. (telephon$ or phone$).tw.
9. Remote consultation/
10. (remote$ adj3 (consult$ or monitor$)).tw.
11. remote patient monitoring.tw.
12. Monitoring, Ambulatory/
13. ((implantable or wearable) and (monitor$ or system$ or sensor$)).tw.
14. Patient Care Planning/
15. Case Management/
16. disease management/
17. disease management.tw.
18. exp Comprehensive Health Care/
19. Home Care Services/
20. Home Care Services, Hospital-Based/
21. Clinical Protocols/
22. Nurse Clinicians/
23. Nurse Practitioners/
24. (nurse adj led).tw.
25. or/4-24
26. 3 and 25
27. exp "costs and cost analysis"/
28. economics/
29. exp economics, hospital/
30. exp economics, medical/
31. economics, nursing/
32. exp models, economic/
33. economics, pharmaceutical/
34. exp "fees and charges"/
35. exp budgets/
36. budget$.tw
37. ec.fs
38. cost$.ti
39. (cost$ adj2 (effective$ or utilit$ or benefit$ or minimi$)).ab
40. (economic$ or pharmacoeconomic$ or pharmaco-economic$).ti
41. (price$ or pricing$).tw
42. (financial or finance or finances or financed).tw
43. (fee or fees).tw
44. (value adj2 (money or monetary)).tw
45. quality-adjusted life years/

46. (qaly or qalys).af.
47. (quality adjusted life year or quality adjusted life years).af.
48. or/27-48
49. 26 and 48

Quality-of-life filter in MEDLINE

1. "Quality of Life"/
2. (qol or (quality adj2 life)).ab,ti.
3. (value adj2 (money or monetary)).tw.
4. value of life/
5. quality adjusted life year/
6. quality adjusted life.tw.
7. (qaly$ or qald$ or qale$ or qtime$).tw.
8. disability adjusted life.tw.
9. daly$.tw.
10. health status indicators/
11. (sf36 or sf 36 or short form 36 or shortform 36 or sf thirtysix or sf thirty six or shorform thirtysix or shortform thirty six or short form thirtysix or short form thirty six).tw.
12. (sf 6 or sf6 or short form 6 or shortform 6 or sf six or sfsix or shortform six or short form six).tw.
13. (sf12 or sf 12 or short form 12 or shortform 12 or sf twelve or sftwelve or shortform twelve or short form twelve).tw.
14. (sf16 or sf 16 or short form 16 or shortform 16 or sf sixteen or sfsixteen or shortfrom sixteen or short form sixteen).tw.
15. (sf20 or sf 20 or short form 20 or shortform 20 or sf twenty or sftwenty or shortform twenty or short form twenty).tw.
16. (euroqol or euro qol or eq5d or eq 5d).tw.
17. (hql or hqol or h qol or hrqol or hr qol).tw.
18. (hye or hyes).tw.
19. health$ year$ equivalent$.tw.
20. health utilit$.tw.
21. (hui or hui1 or hui2 or hui3).tw.
22. disutilit$.tw.
23. rosser.tw.
24. (quality adj2 wellbeing).tw.
25. qwb.tw.
26. (willingness adj2 pay).tw.
27. standard gamble$.tw.
28. time trade off.tw.
29. time tradeoff.tw.
30. tto.tw.
31. letter.pt.
32. editorial.pt.
33. comment.pt.
34. 31 or 32 or 33
35. or/1-30
36. 35 not 34
37. 36 and 26 above

Appendix 11 Table of excluded cost-effectiveness studies

Author, year	Reason for exclusion
1. Almond *et al*. 2011[308]	Budget impact analysis, not a cost-effectiveness analysis
2. Barth 2001[72]	Not a cost-effectiveness study
3. Benatar *et al*. 2003[309]	Trial-based analysis
4. Berg *et al*. 2004[310]	Trial-based cost analysis
5. Chan *et al*. 2008[311]	Not RM
6. Davalos *et al*. 2009[312]	Not a cost-effectiveness study
7. Eapen *et al*. 2011[313]	Not RM
8. Gregory *et al*. 2006[314]	Not RM
9. Herbert *et al*. 2008[125]	Cost evaluation
10. Perl *et al*. 2011[267]	Cost evaluation
11. Postmus *et al*. 2011[315]	Cost evaluation
12. Riegel *et al*. 2002[85]	Commentary
13. Rojas *et al*. 2008[316]	Systematic review
14. Scalvini *et al*. 2004[317]	Cost evaluation
15. Scalvini *et al*. 2005[165]	Not a cost-effectiveness study
16. Seto 2008[318]	Not a cost-effectiveness study
17. Smith *et al*. 2008[319]	Cost evaluation
18. Soran *et al*. 2010[320]	Not a cost-effectiveness study
19. Stafylas *et al*. 2008[321]	Trial-based analysis
20. Stewart *et al*. 2002[322]	Not a cost-effectiveness study
21. Stone 2009[323]	Trial included home visit, trial-based cost-effectiveness analysis (not model based)
22. Van Montfort *et al.* 2006[324]	Not a cost-effectiveness study

Appendix 12 Results for higher usual care cost scenarios

Economic analysis using base-case estimates

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.074	0.780	0.779
HF-related hospitalisation HR	1.000	1.045	0.778	0.966
All-cause hospitalisation HR	1.000	1.173	0.977	0.761
Treatment costs assumed per month (£)	99	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	71.45	75.34	75.38
5 year (%)	33.75	33.43	35.25	35.27
Life expectancy over 30 years (years)	4.71	4.67	4.91	4.91
Difference in life expectancy vs usual care (years)	0.00	–0.04	0.20	0.20
Cost results (£)				
Discounted cost of usual care	873	343	362	362
Discounted cost of treatment	0	632	978	957
Discounted cost of HF-related hospitalisations	4187	4169	4257	4348
Discounted cost of other hospitalisations	3800	3858	4007	3803
Total costs	8861	9001	9604	9470
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–530	–512	–511
Discounted cost of treatment	0	632	978	957
Discounted cost of HF-related hospitalisations	0	–19	70	161
Discounted cost of other hospitalisations	0	57	207	3
Total difference in costs	0	140	743	609
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5509	2.6834	2.6848
HF-related hospitalisation decrement	–0.1611	–0.1604	–0.1638	–0.1673
Total discounted QALYs	2.4137	2.3905	2.5196	2.5175
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0239	0.1086	0.1100
HF-related hospitalisation decrement	0.0000	0.0007	–0.0027	–0.0062

	Usual care	STS HM	STS HH	TM during office hours
Total difference in discounted QALYs	0.0000	–0.0232	0.1059	0.1038
Total discounted QALYs rank (1 = highest)	3	4	1	2
Probabilistic ICER vs usual care (£/QALY)		Dominated	7015	5864
Probabilistic sequential ICER (£/QALY)		Dominated	63,240[a]	5864
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	1	18	36	44
Expected total costs from PSA (£)	8861	9001	9604	9470
Expected total QALYs from PSA	2.4137	2.3905	2.5196	2.5175
Expected net benefit from PSA (£)	39,413	38,809	40,788	40,880
Difference from usual care costs (£)	0	140	743	609
Difference from usual care QALYs	0.0000	–0.0232	0.1059	0.1038
Difference from usual care net benefit (£)	0	–603.90	1375	1467
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	820			
Population EVPI (£)	44,918,530			

a Last strategy in the cost-effectiveness frontier.

Economic analysis using data from predictive distributions

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.180	0.849	0.843
HF-related hospitalisation HR	1.000	1.063	0.790	0.982
All-cause hospitalisation HR	1.000	1.302	1.074	0.835
Treatment costs assumed per month (£)	99	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	70.61	74.58	74.66
5 years (%)	33.75	33.04	34.89	34.93
Life expectancy over 30 years (years)	4.710	4.614	4.862	4.867
Difference in life expectancy vs usual care (years)	–	–0.100	0.151	0.157
Cost results (£)				
Discounted cost of usual care	873	339	358	359
Discounted cost of treatment	0	627	972	951
Discounted cost of HF-related hospitalisations	4187	4130	4221	4316

	Usual care	STS HM	STS HH	TM during office hours
Discounted cost of other hospitalisations	3800	3869	4023	3811
Total costs	8861	8965	9574	9437
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–534	–515	–515
Discounted cost of treatment	0	627	972	951
Discounted cost of HF-related hospitalisations	0	–57	33	129
Discounted cost of other hospitalisations	0	69	223	11
Total difference in costs	0	104	713	576
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5223	2.6575	2.6605
HF-related hospitalisation decrement	–0.1611	–0.1589	–0.1624	–0.1661
Total discounted QALYs	2.4137	2.3633	2.4950	2.4944
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0525	0.0827	0.0857
HF-related hospitalisation decrement	0.0000	0.0022	–0.0013	–0.0050
Total difference in discounted QALYs	0.0000	–0.0504	0.0814	0.0808
Total discounted QALYs rank (1 = highest)	3	4	1	2
Probabilistic ICER vs usual care (£/QALY)		Dominated	8768	7133
Probabilistic sequential ICER (£/QALY)		Dominated	228,035[a]	7133
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	4	19	35	41
Expected total costs from PSA (£)	8861	8965	9574	9437
Expected total QALYs from PSA	2.4137	2.3633	2.4950	2.4944
Expected net benefit from PSA (£)	39,413	38,301	40,327	40,452
Difference from usual care costs (£)	0	104	713	576
Difference from usual care QALYs	0.0000	–0.0504	0.0814	0.0808
Difference from usual care net benefit (£)	0	–1111.22	914	1039
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	1811			
Population EVPI (£)	99,204,217			

a Last strategy in the cost-effectiveness frontier.

Economic analysis using data excluding the Home-HF study[67]

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.007	0.757	0.627
HF-related hospitalisation HR	1.000	1.042	0.766	0.872
All-cause hospitalisation HR	1.000	1.134	0.969	0.678
Treatment costs assumed per month (£)	99	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	72.14	75.67	77.63
5 years (%)	33.75	33.75	35.40	36.32
Life expectancy over 30 years (years)	4.710	4.710	4.930	5.052
Difference in life expectancy vs usual care (years)	–	–0.0003	0.2200	0.3420
Cost results (£)				
Discounted cost of usual care	873	346	363	373
Discounted cost of treatment	0	635	981	972
Discounted cost of HF-related hospitalisations	4187	4206	4269	4426
Discounted cost of other hospitalisations	3800	3873	4021	3879
Total costs	8861	9060	9635	9650
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–527	–510	–501
Discounted cost of treatment	0	635	981	972
Discounted cost of HF-related hospitalisations	0	18	82	239
Discounted cost of other hospitalisations	0	73	221	79
Total difference in costs	0	199	774	789
Overall cost rank (1 = lowest cost)	1	2	3	4
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5747	2.6949	2.7612
HF-related hospitalisation decrement	–0.1611	–0.1619	–0.1643	–0.1703
Total discounted QALYs	2.4137	2.4128	2.5306	2.5908
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0002	0.1200	0.1864
HF-related hospitalisation decrement	0.0000	–0.0007	–0.0032	–0.0092
Total difference in discounted QALYs	0.0000	–0.0009	0.1169	0.1772
Total discounted QALYs rank (1 = highest)	3	4	2	1
Probabilistic ICER vs usual care (£/QALY)		Dominated	6621	4455
Probabilistic sequential ICER (£/QALY)		Dominated	Extendedly dominated	4455[a]

	Usual care	STS HM	STS HH	TM during office hours
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	0	5	12	83
Expected total costs from PSA (£)	8861	9060	9635	9650
Expected total QALYs from PSA	2.4137	2.4128	2.5306	2.5908
Expected net benefit from PSA (£)	39,413	39,196	40,976	42,167
Difference from usual care costs (£)	0	199	774	789
Difference from usual care QALYs	0.0000	–0.0009	0.1169	0.1772
Difference from usual care net benefit (£)	0	–216.70	1564	2754
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	133			
Population EVPI (£)	7,285,566			

a Last strategy in the cost-effectiveness frontier.

Economic analysis using data from predictive distributions excluding the Home-HF study[67]

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.032	0.776	0.642
HF-related hospitalisation HR	1.000	1.058	0.778	0.883
All-cause hospitalisation HR	1.000	1.235	1.048	0.731
Treatment costs assumed per month (£)	99	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	71.89	75.44	77.44
5 years (%)	33.75	33.63	35.30	36.23
Life expectancy over 30 years (years)	4.71	4.69	4.92	5.04
Difference in life expectancy vs usual care (years)	0.00	–0.02	0.21	0.33
Cost results (£)				
Discounted cost of usual care	873	345	362	372
Discounted cost of treatment	0	634	979	971
Discounted cost of HF-related hospitalisations	4187	4200	4262	4422
Discounted cost of other hospitalisations	3800	3909	4055	3901
Total costs	8861	9087	9658	9665

	Usual care	STS HM	STS HH	TM during office hours
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–528	–511	–502
Discounted cost of treatment	0	634	979	971
Discounted cost of HF-related hospitalisations	0	12	75	234
Discounted cost of other hospitalisations	0	108	255	101
Total difference in costs	0	226	797	804
Overall cost rank (1 = lowest cost)	1	2	3	4
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5659	2.6870	2.7548
HF-related hospitalisation decrement	–0.1611	–0.1616	–0.1640	–0.1701
Total discounted QALYs	2.4137	2.4043	2.5230	2.5847
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0089	0.1122	0.1800
HF-related hospitalisation decrement	0.0000	–0.0004	–0.0029	–0.0090
Total difference in discounted QALYs	0.0000	–0.0093	0.1093	0.1710
Total discounted QALYs rank (1 = highest)	3	4	2	1
Probabilistic ICER vs usual care (£/QALY)		Dominated	7295	4703
Probabilistic sequential ICER (£/QALY)		Dominated	Extendedly dominated	4703[a]
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	1	7	19	73
Expected total costs from PSA (£)	8861	9087	9658	9665
Expected total QALYs from PSA	2.4137	2.4043	2.5230	2.5847
Expected net benefit from PSA (£)	39,413	39,000	40,801	42,029
Difference from usual care costs (£)	0	226	797	804
Difference from usual care QALYs	0.0000	–0.0093	0.1093	0.1710
Difference from usual care net benefit (£)	0	–412.88	1389	2616
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	406			
Population EVPI (£)	22,240,150			

a Last strategy in the cost-effectiveness frontier.

Appendix 13 Results for lower-cost telemonitoring during office hours scenarios

Economic analysis using base-case estimates

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.074	0.780	0.779
HF-related hospitalisation HR	1.000	1.045	0.778	0.966
All-cause hospitalisation HR	1.000	1.173	0.977	0.761
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	71.45	75.34	75.38
5 years (%)	33.75	33.43	35.25	35.27
Life expectancy over 30 years (years)	4.71	4.67	4.91	4.91
Difference in life expectancy vs usual care (years)	0.00	–0.04	0.20	0.20
Cost results (£)				
Discounted cost of usual care	491	343	362	362
Discounted cost of treatment	0	632	978	730
Discounted cost of HF-related hospitalisations	4187	4169	4257	4348
Discounted cost of other hospitalisations	3800	3858	4007	3803
Total costs	8478	9001	9604	9243
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–148	–129	–129
Discounted cost of treatment	0	632	978	730
Discounted cost of HF-related hospitalisations	0	–19	70	161
Discounted cost of other hospitalisations	0	57	207	3
Total difference in costs	0	523	1126	765
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5509	2.6834	2.6848
HF-related hospitalisation decrement	–0.1611	–0.1604	–0.1638	–0.1673
Total discounted QALYs	2.4137	2.3905	2.5196	2.5175
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0239	0.1086	0.1100
HF-related hospitalisation decrement	0.0000	0.0007	–0.0027	–0.0062

	Usual care	STS HM	STS HH	TM during office hours
Total difference in discounted QALYs	0.0000	–0.0232	0.1059	0.1038
Total discounted QALYs rank (1 = highest)	3	4	1	2
Probabilistic ICER vs usual care (£/QALY)		Dominated	10,629	7367
Probabilistic sequential ICER (£/QALY)		Dominated	170,629[a]	7367
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	2	17	31	50
Expected total costs from PSA (£)	8478	9001	9604	9243
Expected total QALYs from PSA	2.4137	2.3905	2.5196	2.5175
Expected net benefit from PSA (£)	39,795	38,809	40,788	41,107
Difference from usual care costs (£)	0	523	1126	765
Difference from usual care QALYs	0.0000	–0.0232	0.1059	0.1038
Difference from usual care net benefit (£)	0	–986.75	993	1311
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	707			
Population EVPI (£)	38,728,537			

a Last strategy in the cost-effectiveness frontier.

Economic analysis using data from predictive distributions

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.180	0.849	0.843
HF-related hospitalisation HR	1.000	1.063	0.790	0.982
All-cause hospitalisation HR	1.000	1.302	1.074	0.835
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	70.61	74.58	74.66
5 years (%)	33.75	33.04	34.89	34.93
Life expectancy over 30 years (years)	4.710	4.614	4.862	4.867
Difference in life expectancy vs usual care (years)	–	–0.100	0.151	0.157
Cost results (£)				
Discounted cost of usual care	491	339	358	359
Discounted cost of treatment	0	627	972	726
Discounted cost of HF-related hospitalisations	4187	4130	4221	4316
Discounted cost of other hospitalisations	3800	3869	4023	3811
Total costs	8478	8965	9574	9211

	Usual care	STS HM	STS HH	TM during office hours
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–152	–132	–132
Discounted cost of treatment	0	627	972	726
Discounted cost of HF-related hospitalisations	0	–57	33	129
Discounted cost of other hospitalisations	0	69	223	11
Total difference in costs	0	487	1096	733
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5223	2.6575	2.6605
HF-related hospitalisation decrement	–0.1611	–0.1589	–0.1624	–0.1661
Total discounted QALYs	2.4137	2.3633	2.4950	2.4944
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0525	0.0827	0.0857
HF-related hospitalisation decrement	0.0000	0.0022	–0.0013	–0.0050
Total difference in discounted QALYs	0.0000	–0.0504	0.0814	0.0808
Total discounted QALYs rank (1 = highest)	3	4	1	2
Probabilistic ICER vs usual care (£/QALY)		Dominated	13,473	9080
Probabilistic sequential ICER (£/QALY)		Dominated	605,112[a]	9080
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	6	18	33	44
Expected total costs from PSA (£)	8478	8965	9574	9211
Expected total QALYs from PSA	2.4137	2.3633	2.4950	2.4944
Expected net benefit from PSA (£)	39,795	38,301	40,327	40,677
Difference from usual care costs (£)	0	487	1096	733
Difference from usual care QALYs	0.0000	–0.0504	0.0814	0.0808
Difference from usual care net benefit (£)	0	–1494.07	531	882
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	1702			
Population EVPI (£)	93,233,339			

a Last strategy in the cost-effectiveness frontier.

Economic analysis using data excluding the Home-HF study[67]

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.007	0.757	0.627
HF-related hospitalisation HR	1.000	1.042	0.766	0.872
All-cause hospitalisation HR	1.000	1.134	0.969	0.678
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	72.14	75.67	77.63
5 years (%)	33.75	33.75	35.40	36.32
Life expectancy over 30 years (years)	4.710	4.710	4.930	5.052
Difference in life expectancy vs usual care (years)	–	–0.0003	0.2200	0.3420
Cost results (£)				
Discounted cost of usual care	491	346	363	373
Discounted cost of treatment	0	635	981	742
Discounted cost of HF-related hospitalisations	4187	4206	4269	4426
Discounted cost of other hospitalisations	3800	3873	4021	3879
Total costs	8478	9060	9635	9420
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–144	–127	–118
Discounted cost of treatment	0	635	981	742
Discounted cost of HF-related hospitalisations	0	18	82	239
Discounted cost of other hospitalisations	0	73	221	79
Total difference in costs	0	582	1157	942
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5747	2.6949	2.7612
HF-related hospitalisation decrement	–0.1611	–0.1619	–0.1643	–0.1703
Total discounted QALYs	2.4137	2.4128	2.5306	2.5908
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0002	0.1200	0.1864
HF-related hospitalisation decrement	0.0000	–0.0007	–0.0032	–0.0092
Total difference in discounted QALYs	0.0000	–0.0009	0.1169	0.1772
Total discounted QALYs rank (1 = highest)	3	4	2	1
Probabilistic ICER vs usual care (£/QALY)		Dominated	9897	5315
Probabilistic sequential ICER (£/QALY)		Dominated	Extendedly dominated	5315[a]

	Usual care	STS HM	STS HH	TM during office hours
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	0	4	9	87
Expected total costs from PSA (£)	8478	9060	9635	9420
Expected total QALYs from PSA	2.4137	2.4128	2.5306	2.5908
Expected net benefit from PSA (£)	39,795	39,196	40,976	42,397
Difference from usual care costs (£)	0	582	1157	942
Difference from usual care QALYs	0.0000	–0.0009	0.1169	0.1772
Difference from usual care net benefit (£)	0	–599.54	1181	2602
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	100			
Population EVPI (£)	5,477,869			

a Last strategy in the cost-effectiveness frontier.

Economic analysis using data from predictive distributions excluding the Home-HF study[67]

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.032	0.776	0.642
HF-related hospitalisation HR	1.000	1.058	0.778	0.883
All-cause hospitalisation HR	1.000	1.235	1.048	0.731
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	71.89	75.44	77.44
5 years (%)	33.75	33.63	35.30	36.23
Life expectancy over 30 years (years)	4.71	4.69	4.92	5.04
Difference in life expectancy vs usual care (years)	0.00	–0.02	0.21	0.33
Cost results (£)				
Discounted cost of usual care	491	345	362	372
Discounted cost of treatment	0	634	979	741
Discounted cost of HF-related hospitalisations	4187	4200	4262	4422
Discounted cost of other hospitalisations	3800	3909	4055	3901
Total costs	8478	9087	9658	9435

	Usual care	STS HM	STS HH	TM during office hours
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–145	–128	–119
Discounted cost of treatment	0	634	979	741
Discounted cost of HF-related hospitalisations	0	12	75	234
Discounted cost of other hospitalisations	0	108	255	101
Total difference in costs	0	609	1180	957
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5659	2.6870	2.7548
HF-related hospitalisation decrement	–0.1611	–0.1616	–0.1640	–0.1701
Total discounted QALYs	2.4137	2.4043	2.5230	2.5847
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0089	0.1122	0.1800
HF-related hospitalisation decrement	0.0000	–0.0004	–0.0029	–0.0090
Total difference in discounted QALYs	0.0000	–0.0093	0.1093	0.1710
Total discounted QALYs rank (1 = highest)	3	4	2	1
Probabilistic ICER vs usual care (£/QALY)		Dominated	10,798	5595
Probabilistic sequential ICER (£/QALY)		Dominated	Extendedly dominated	5595[a]
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	1	6	16	77
Expected total costs from PSA (£)	8478	9087	9658	9435
Expected total QALYs from PSA	2.4137	2.4043	2.5230	2.5847
Expected net benefit from PSA (£)	39,795	39,000	40,801	42,259
Difference from usual care costs (£)	0	609	1180	957
Difference from usual care QALYs	0.0000	–0.0093	0.1093	0.1710
Difference from usual care net benefit (£)	0	–795.73	1006	2463
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	353			
Population EVPI (£)	19,336,879			

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Appendix 14 Results for higher-cost telemonitoring during office hours scenarios

Economic analysis using base-case estimates

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.074	0.780	0.779
HF-related hospitalisation HR	1.000	1.045	0.778	0.966
All-cause hospitalisation HR	1.000	1.173	0.977	0.761
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	71.45	75.34	75.38
5 years (%)	33.75	33.43	35.25	35.27
Life expectancy over 30 years (years)	4.71	4.67	4.91	4.91
Difference in life expectancy vs usual care (years)	0.00	–0.04	0.20	0.20
Cost results (£)				
Discounted cost of usual care	491	343	362	362
Discounted cost of treatment	0	632	978	1173
Discounted cost of HF-related hospitalisations	4187	4169	4257	4348
Discounted cost of other hospitalisations	3800	3858	4007	3803
Total costs	8478	9001	9604	9686
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–148	–129	–129
Discounted cost of treatment	0	632	978	1173
Discounted cost of HF-related hospitalisations	0	–19	70	161
Discounted cost of other hospitalisations	0	57	207	3
Total difference in costs	0	523	1126	1207
Overall cost rank (1 = lowest cost)	1	2	3	4
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5509	2.6834	2.6848
HF-related hospitalisation decrement	–0.1611	–0.1604	–0.1638	–0.1673
Total discounted QALYs	2.4137	2.3905	2.5196	2.5175

	Usual care	STS HM	STS HH	TM during office hours
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0239	0.1086	0.1100
HF-related hospitalisation decrement	0.0000	0.0007	–0.0027	–0.0062
Total difference in discounted QALYs	0.0000	–0.0232	0.1059	0.1038
Total discounted QALYs rank (1 = highest)	3	4	1	2
Probabilistic ICER vs usual care (£/QALY)		Dominated	10,629	11,633
Probabilistic sequential ICER (£/QALY)		Dominated	10,629[a]	Dominated
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	3	19	40	38
Expected total costs from PSA (£)	8478	9001	9604	9686
Expected total QALYs from PSA	2.4137	2.3905	2.5196	2.5175
Expected net benefit from PSA (£)	39,795	38,809	40,788	40,664
Difference from usual care costs (£)	0	523	1126	1207
Difference from usual care QALYs	0.0000	–0.0232	0.1059	0.1038
Difference from usual care net benefit (£)	0	–986.75	993	869
Net benefit rank (1 = highest)	3	4	1	2
Overall EVPI per patient at ICER of £20,000 per QALY (£)	829			
Population EVPI (£)	45,411,538			

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Economic analysis using data from predictive distributions

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.180	0.849	0.843
HF-related hospitalisation HR	1.000	1.063	0.790	0.982
All-cause hospitalisation HR	1.000	1.302	1.074	0.835
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	70.61	74.58	74.66
5 years (%)	33.75	33.04	34.89	34.93
Life expectancy over 30 years (years)	4.710	4.614	4.862	4.867
Difference in life expectancy vs usual care (years)	–	–0.100	0.151	0.157

	Usual care	STS HM	STS HH	TM during office hours
Cost results (£)				
Discounted cost of usual care	491	339	358	359
Discounted cost of treatment	0	627	972	1166
Discounted cost of HF-related hospitalisations	4187	4130	4221	4316
Discounted cost of other hospitalisations	3800	3869	4023	3811
Total costs	8478	8965	9574	9652
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–152	–132	–132
Discounted cost of treatment	0	627	972	1166
Discounted cost of HF-related hospitalisations	0	–57	33	129
Discounted cost of other hospitalisations	0	69	223	11
Total difference in costs	0	487	1096	1174
Overall cost rank (1 = lowest cost)	1	2	3	4
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5223	2.6575	2.6605
HF-related hospitalisation decrement	–0.1611	–0.1589	–0.1624	–0.1661
Total discounted QALYs	2.4137	2.3633	2.4950	2.4944
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0525	0.0827	0.0857
HF-related hospitalisation decrement	0.0000	0.0022	–0.0013	–0.0050
Total difference in discounted QALYs	0.0000	–0.0504	0.0814	0.0808
Total discounted QALYs rank (1 = highest)	3	4	1	2
Probabilistic ICER vs usual care (£/QALY)		Dominated	13,473	14,532
Probabilistic sequential ICER (£/QALY)		Dominated	13,473[a]	Dominated
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	7	20	37	37
Expected total costs from PSA (£)	8478	8965	9574	9652
Expected total QALYs from PSA	2.4137	2.3633	2.4950	2.4944
Expected net benefit from PSA (£)	39,795	38,301	40,327	40,237
Difference from usual care costs (£)	0	487	1096	1174
Difference from usual care QALYs	0.0000	–0.0504	0.0814	0.0808
Difference from usual care net benefit (£)	0	–1494.07	531	442
Net benefit rank (1 = highest)	3	4	1	2
Overall EVPI per patient at ICER of £20,000 per QALY (£)	1871			
Population EVPI (£)	102,490,939			

a Last strategy in the cost-effectiveness frontier.

Economic analysis using data excluding the Home-HF study[67]

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.007	0.757	0.627
HF-related hospitalisation HR	1.000	1.042	0.766	0.872
All-cause hospitalisation HR	1.000	1.134	0.969	0.678
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	72.14	75.67	77.63
5 years (%)	33.75	33.75	35.40	36.32
Life expectancy over 30 years (years)	4.710	4.710	4.930	5.052
Difference in life expectancy vs usual care (years)	–	–0.0003	0.2200	0.3420
Cost results (£)				
Discounted cost of usual care	491	346	363	373
Discounted cost of treatment	0	635	981	1191
Discounted cost of HF-related hospitalisations	4187	4206	4269	4426
Discounted cost of other hospitalisations	3800	3873	4021	3879
Total costs	8478	9060	9635	9870
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–144	–127	–118
Discounted cost of treatment	0	635	981	1191
Discounted cost of HF-related hospitalisations	0	18	82	239
Discounted cost of other hospitalisations	0	73	221	79
Total difference in costs	0	582	1157	1392
Overall cost rank (1 = lowest cost)	1	2	3	4
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5747	2.6949	2.7612
HF-related hospitalisation decrement	–0.1611	–0.1619	–0.1643	–0.1703
Total discounted QALYs	2.4137	2.4128	2.5306	2.5908
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0002	0.1200	0.1864
HF-related hospitalisation decrement	0.0000	–0.0007	–0.0032	–0.0092
Total difference in discounted QALYs	0.0000	–0.0009	0.1169	0.1772
Total discounted QALYs rank (1 = highest)	3	4	2	1
Probabilistic ICER vs usual care (£/QALY)		Dominated	9897	7854
Probabilistic sequential ICER (£/QALY)		Dominated	Extendedly dominated	7854[a]

	Usual care	STS HM	STS HH	TM during office hours
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	0	6	16	78
Expected total costs from PSA (£)	8478	9060	9635	9870
Expected total QALYs from PSA	2.4137	2.4128	2.5306	2.5908
Expected net benefit from PSA (£)	39,795	39,196	40,976	41,947
Difference from usual care costs (£)	0	582	1157	1392
Difference from usual care QALYs	0.0000	–0.0009	0.1169	0.1772
Difference from usual care net benefit (£)	0	–599.54	1181	2152
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	175			
Population EVPI (£)	9,586,271			

a Last strategy in the cost-effectiveness frontier.

Economic analysis using data from predictive distributions excluding the Home-HF study[67]

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.032	0.776	0.642
HF-related hospitalisation HR	1.000	1.058	0.778	0.883
All-cause hospitalisation HR	1.000	1.235	1.048	0.731
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	71.89	75.44	77.44
5 years (%)	33.75	33.63	35.30	36.23
Life expectancy over 30 years (years)	4.71	4.69	4.92	5.04
Difference in life expectancy vs usual care (years)	0.00	–0.02	0.21	0.33
Cost results (£)				
Discounted cost of usual care	491	345	362	372
Discounted cost of treatment	0	634	979	1190
Discounted cost of HF-related hospitalisations	4187	4200	4262	4422
Discounted cost of other hospitalisations	3800	3909	4055	3901
Total costs	8478	9087	9658	9884
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–145	–128	–119
Discounted cost of treatment	0	634	979	1190

	Usual care	STS HM	STS HH	TM during office hours
Discounted cost of HF-related hospitalisations	0	12	75	234
Discounted cost of other hospitalisations	0	108	255	101
Total difference in costs	0	609	1180	1406
Overall cost rank (1 = lowest cost)	1	2	3	4
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5659	2.6870	2.7548
HF-related hospitalisation decrement	–0.1611	–0.1616	–0.1640	–0.1701
Total discounted QALYs	2.4137	2.4043	2.5230	2.5847
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0089	0.1122	0.1800
HF-related hospitalisation decrement	0.0000	–0.0004	–0.0029	–0.0090
Total difference in discounted QALYs	0.0000	–0.0093	0.1093	0.1710
Total discounted QALYs rank (1 = highest)	3	4	2	1
Probabilistic ICER vs usual care (£/QALY)		Dominated	10,798	8223
Probabilistic sequential ICER (£/QALY)		Dominated	Extendedly dominated	8223[a]
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	1	8	23	68
Expected total costs from PSA (£)	8478	9087	9658	9884
Expected total QALYs from PSA	2.4137	2.4043	2.5230	2.5847
Expected net benefit from PSA (£)	39,795	39,000	40,801	41,809
Difference from usual care costs (£)	0	609	1180	1406
Difference from usual care QALYs	0.0000	–0.0093	0.1093	0.1710
Difference from usual care net benefit (£)	0	–795.73	1006	2014
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	473			
Population EVPI (£)	25,910,322			

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Appendix 15 Results for higher-cost structured telephone support human-to-human contact cost scenarios

Economic analysis using base-case estimates

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.074	0.780	0.779
HF-related hospitalisation HR	1.000	1.045	0.778	0.966
All-cause hospitalisation HR	1.000	1.173	0.977	0.761
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	71.45	75.34	75.38
5 years (%)	33.75	33.43	35.25	35.27
Life expectancy over 30 years (years)	4.71	4.67	4.91	4.91
Difference in life expectancy vs usual care (years)	0.00	–0.04	0.20	0.20
Cost results (£)				
Discounted cost of usual care	491	343	362	362
Discounted cost of treatment	0	632	1049	957
Discounted cost of HF-related hospitalisations	4187	4169	4257	4348
Discounted cost of other hospitalisations	3800	3858	4007	3803
Total costs	8478	9001	9675	9470
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–148	–129	–129
Discounted cost of treatment	0	632	1049	957
Discounted cost of HF-related hospitalisations	0	–19	70	161
Discounted cost of other hospitalisations	0	57	207	3
Total difference in costs	0	523	1197	992
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5509	2.6834	2.6848
HF-related hospitalisation decrement	–0.1611	–0.1604	–0.1638	–0.1673
Total discounted QALYs	2.4137	2.3905	2.5196	2.5175

	Usual care	STS HM	STS HH	TM during office hours
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0239	0.1086	0.1100
HF-related hospitalisation decrement	0.0000	0.0007	–0.0027	–0.0062
Total difference in discounted QALYs	0.0000	–0.0232	0.1059	0.1038
Total discounted QALYs rank (1 = highest)	3	4	1	2
Probabilistic ICER vs usual care (£/QALY)		Dominated	11,300	9552
Probabilistic sequential ICER (£/QALY)		Dominated	97,300[a]	9552
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	2	19	34	46
Expected total costs from PSA (£)	8478	9001	9675	9470
Expected total QALYs from PSA	2.4137	2.3905	2.5196	2.5175
Expected net benefit from PSA (£)	39,795	38,809	40,717	40,880
Difference from usual care costs (£)	0	523	1197	992
Difference from usual care QALYs	0.0000	–0.0232	0.1059	0.1038
Difference from usual care net benefit (£)	0	–986.75	922	1084
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	801			
Population EVPI (£)	43,877,735			

a Last strategy in the cost-effectiveness frontier.

Economic analysis using data from predictive distributions

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.180	0.849	0.843
HF-related hospitalisation HR	1.000	1.063	0.790	0.982
All-cause hospitalisation HR	1.000	1.302	1.074	0.835
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	70.61	74.58	74.66
5 years (%)	33.75	33.04	34.89	34.93
Life expectancy over 30 years (years)	4.710	4.614	4.862	4.867
Difference in life expectancy vs usual care (years)	–	–0.10	0.151	0.157

	Usual care	STS HM	STS HH	TM during office hours
Cost results (£)				
Discounted cost of usual care	491	339	358	359
Discounted cost of treatment	0	627	1043	951
Discounted cost of HF-related hospitalisations	4187	4130	4221	4316
Discounted cost of other hospitalisations	3800	3869	4023	3811
Total costs	8478	8965	9645	9437
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–152	–132	–132
Discounted cost of treatment	0	627	1043	951
Discounted cost of HF-related hospitalisations	0	–57	33	129
Discounted cost of other hospitalisations	0	69	223	11
Total difference in costs	0	487	1167	959
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5223	2.6575	2.6605
HF-related hospitalisation decrement	–0.1611	–0.1589	–0.1624	–0.1661
Total discounted QALYs	2.4137	2.3633	2.4950	2.4944
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0525	0.0827	0.0857
HF-related hospitalisation decrement	0.0000	0.0022	–0.0013	–0.0050
Total difference in discounted QALYs	0.0000	–0.0504	0.0814	0.0808
Total discounted QALYs rank (1 = highest)	3	4	1	2
Probabilistic ICER vs usual care (£/QALY)		Dominated	14,341	11,873
Probabilistic sequential ICER (£/QALY)		Dominated	346,341[a]	11,873
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	6	19	34	41
Expected total costs from PSA (£)	8478	8965	9645	9437
Expected total QALYs from PSA	2.4137	2.3633	2.4950	2.4944
Expected net benefit from PSA (£)	39,795	38,301	40,256	40,452
Difference from usual care costs (£)	0	487	1167	959
Difference from usual care QALYs	0.0000	–0.0504	0.0814	0.0808
Difference from usual care net benefit (£)	0	–1494.07	460	656
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	1806			
Population EVPI (£)	98,930,324			

a Last strategy in the cost-effectiveness frontier.

Economic analysis using data excluding the Home-HF study[67]

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.007	0.757	0.627
HF-related hospitalisation HR	1.000	1.042	0.766	0.872
All-cause hospitalisation HR	1.000	1.134	0.969	0.678
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	72.14	75.67	77.63
5 years (%)	33.75	33.75	35.40	36.32
Life expectancy over 30 years (years)	4.710	4.710	4.930	5.052
Difference in life expectancy vs usual care (years)	–	–0.0003	0.2200	0.3420
Cost results (£)				
Discounted cost of usual care	491	346	363	373
Discounted cost of treatment	0	635	1052	972
Discounted cost of HF-related hospitalisations	4187	4206	4269	4426
Discounted cost of other hospitalisations	3800	3873	4021	3879
Total costs	8478	9060	9706	9650
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–144	–127	–118
Discounted cost of treatment	0	635	1052	972
Discounted cost of HF-related hospitalisations	0	18	82	239
Discounted cost of other hospitalisations	0	73	221	79
Total difference in costs	0	582	1228	1172
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5747	2.6949	2.7612
HF-related hospitalisation decrement	–0.1611	–0.1619	–0.1643	–0.1703
Total discounted QALYs	2.4137	2.4128	2.5306	2.5908
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0002	0.1200	0.1864
HF-related hospitalisation decrement	0.0000	–0.0007	–0.0032	–0.0092
Total difference in discounted QALYs	0.0000	–0.0009	0.1169	0.1772
Total discounted QALYs rank (1 = highest)	3	4	2	1
Probabilistic ICER vs usual care (£/QALY)		Dominated	10,506	6616
Probabilistic sequential ICER (£/QALY)		Dominated	Extendedly dominated	6616[a]

	Usual care	STS HM	STS HH	TM during office hours
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	0	5	11	84
Expected total costs from PSA (£)	8478	9060	9706	9650
Expected total QALYs from PSA	2.4137	2.4128	2.5306	2.5908
Expected net benefit from PSA (£)	39,795	39,196	40,905	42,167
Difference from usual care costs (£)	0	582	1228	1172
Difference from usual care QALYs	0.0000	–0.0009	0.1169	0.1772
Difference from usual care net benefit (£)	0	–599.54	1110	2371
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	125			
Population EVPI (£)	6,847,336			

a Last strategy in the cost-effectiveness frontier.

Economic analysis using data from predictive distributions excluding the Home-HF study[67]

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.032	0.776	0.642
HF-related hospitalisation HR	1.000	1.058	0.778	0.883
All-cause hospitalisation HR	1.000	1.235	1.048	0.731
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	71.89	75.44	77.44
5 years (%)	33.75	33.63	35.30	36.23
Life expectancy over 30 years (years)	4.71	4.69	4.92	5.04
Difference in life expectancy vs usual care (years)	0.00	–0.02	0.21	0.33
Cost results (£)				
Discounted cost of usual care	491	345	362	372
Discounted cost of treatment	0	634	1050	971
Discounted cost of HF-related hospitalisations	4187	4200	4262	4422
Discounted cost of other hospitalisations	3800	3909	4055	3901
Total costs	8478	9087	9729	9665

	Usual care	STS HM	STS HH	TM during office hours
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–145	–128	–119
Discounted cost of treatment	0	634	1050	971
Discounted cost of HF-related hospitalisations	0	12	75	234
Discounted cost of other hospitalisations	0	108	255	101
Total difference in costs	0	609	1251	1187
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5659	2.6870	2.7548
HF-related hospitalisation decrement	–0.1611	–0.1616	–0.1640	–0.1701
Total discounted QALYs	2.4137	2.4043	2.5230	2.5847
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0089	0.1122	0.1800
HF-related hospitalisation decrement	0.0000	–0.0004	–0.0029	–0.0090
Total difference in discounted QALYs	0.0000	–0.0093	0.1093	0.1710
Total discounted QALYs rank (1 = highest)	3	4	2	1
Probabilistic ICER vs usual care (£/QALY)		Dominated	11,449	6942
Probabilistic sequential ICER (£/QALY)		Dominated	Extendedly dominated	6942[a]
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	1	7	18	74
Expected total costs from PSA (£)	8478	9087	9729	9665
Expected total QALYs from PSA	2.4137	2.4043	2.5230	2.5847
Expected net benefit from PSA (£)	39,795	39,000	40,730	42,029
Difference from usual care costs (£)	0	609	1251	1187
Difference from usual care QALYs	0.0000	–0.0093	0.1093	0.1710
Difference from usual care net benefit (£)	0	–795.73	935	2233
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	396			
Population EVPI (£)	21,692,363			

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Appendix 16 Results for lower-cost structured telephone support human-to-human contact cost scenarios

Economic analysis using base-case estimates

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.074	0.780	0.779
HF-related hospitalisation HR	1.000	1.045	0.778	0.966
All-cause hospitalisation HR	1.000	1.173	0.977	0.761
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	71.45	75.34	75.38
5 years (%)	33.75	33.43	35.25	35.27
Life expectancy over 30 years (years)	4.71	4.67	4.91	4.91
Difference in life expectancy vs usual care (years)	0.00	–0.04	0.20	0.20
Cost results (£)				
Discounted cost of usual care	491	343	362	362
Discounted cost of treatment	0	632	956	957
Discounted cost of HF-related hospitalisations	4187	4169	4257	4348
Discounted cost of other hospitalisations	3800	3858	4007	3803
Total costs	8478	9001	9582	9470
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–148	–129	–129
Discounted cost of treatment	0	632	956	957
Discounted cost of HF-related hospitalisations	0	–19	70	161
Discounted cost of other hospitalisations	0	57	207	3
Total difference in costs	0	523	1104	992
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5509	2.6834	2.6848
HF-related hospitalisation decrement	–0.1611	–0.1604	–0.1638	–0.1673
Total discounted QALYs	2.4137	2.3905	2.5196	2.5175

	Usual care	STS HM	STS HH	TM during office hours
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0239	0.1086	0.1100
HF-related hospitalisation decrement	0.0000	0.0007	–0.0027	–0.0062
Total difference in discounted QALYs	0.0000	–0.0232	0.1059	0.1038
Total discounted QALYs rank (1 = highest)	3	4	1	2
Probabilistic ICER vs usual care (£/QALY)		Dominated	10,423	9552
Probabilistic sequential ICER (£/QALY)		Dominated	52,951[a]	9552
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	2	18	36	43
Expected total costs from PSA (£)	8478	9001	9582	9470
Expected total QALYs from PSA	2.4137	2.3905	2.5196	2.5175
Expected net benefit from PSA (£)	39,795	38,809	40,810	40,880
Difference from usual care costs (£)	0	523	1104	992
Difference from usual care QALYs	0.0000	–0.0232	0.1059	0.1038
Difference from usual care net benefit (£)	0	–986.75	1014	1084
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	834			
Population EVPI (£)	45,685,432			

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Economic analysis using data from predictive distributions

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.180	0.849	0.843
HF-related hospitalisation HR	1.000	1.063	0.790	0.982
All-cause hospitalisation HR	1.000	1.302	1.074	0.835
Treatment costs assumed per month (£)	7	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	70.61	74.58	74.66
5 years (%)	33.75	33.04	34.89	34.93
Life expectancy over 30 years (years)	4.710	4.614	4.862	4.867
Difference in life expectancy vs usual care (years)	–	–0.100	0.151	0.157

	Usual care	STS HM	STS HH	TM during office hours
Cost results (£)				
Discounted cost of usual care	491	339	358	359
Discounted cost of treatment	0	627	951	951
Discounted cost of HF-related hospitalisations	4187	4130	4221	4316
Discounted cost of other hospitalisations	3800	3869	4023	3811
Total costs	8478	8965	9553	9437
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–152	–132	–132
Discounted cost of treatment	0	627	951	951
Discounted cost of HF-related hospitalisations	0	–57	33	129
Discounted cost of other hospitalisations	0	69	223	11
Total difference in costs	0	487	1075	959
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5223	2.6575	2.6605
HF-related hospitalisation decrement	–0.1611	–0.1589	–0.1624	–0.1661
Total discounted QALYs	2.4137	2.3633	2.4950	2.4944
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0525	0.0827	0.0857
HF-related hospitalisation decrement	0.0000	0.0022	–0.0013	–0.0050
Total difference in discounted QALYs	0.0000	–0.0504	0.0814	0.0808
Total discounted QALYs rank (1 = highest)	3	4	1	2
Probabilistic ICER vs usual care (£/QALY)		Dominated	13,206	11,873
Probabilistic sequential ICER (£/QALY)		Dominated	193,206[a]	11,873
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	6	19	35	40
Expected total costs from PSA (£)	8478	8965	9553	9437
Expected total QALYs from PSA	2.4137	2.3633	2.4950	2.4944
Expected net benefit from PSA (£)	39,795	38,301	40,348	40,452
Difference from usual care costs (£)	0	487	1075	959
Difference from usual care QALYs	0.0000	–0.0504	0.0814	0.0808
Difference from usual care net benefit (£)	0	–1494.07	553	656
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	1839			
Population EVPI (£)	100,738,020			

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Economic analysis using data excluding the Home-HF study[67]

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.007	0.757	0.627
HF-related hospitalisation HR	1.000	1.042	0.766	0.872
All-cause hospitalisation HR	1.000	1.134	0.969	0.678
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	72.14	75.67	77.63
5 years (%)	33.75	33.75	35.40	36.32
Life expectancy over 30 years (years)	4.710	4.710	4.930	5.052
Difference in life expectancy vs usual care (years)	–	–0.0003	0.2200	0.3420
Cost results (£)				
Discounted cost of usual care	491	346	363	373
Discounted cost of treatment	0	635	959	972
Discounted cost of HF-related hospitalisations	4187	4206	4269	4426
Discounted cost of other hospitalisations	3800	3873	4021	3879
Total costs	8478	9060	9613	9650
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–144	–127	–118
Discounted cost of treatment	0	635	959	972
Discounted cost of HF-related hospitalisations	0	18	82	239
Discounted cost of other hospitalisations	0	73	221	79
Total difference in costs	0	582	1135	1172
Overall cost rank (1 = lowest cost)	1	2	3	4
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5747	2.6949	2.7612
HF-related hospitalisation decrement	–0.1611	–0.1619	–0.1643	–0.1703
Total discounted QALYs	2.4137	2.4128	2.5306	2.5908
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0002	0.1200	0.1864
HF-related hospitalisation decrement	0.0000	–0.0007	–0.0032	–0.0092
Total difference in discounted QALYs	0.0000	–0.0009	0.1169	0.1772
Total discounted QALYs rank (1 = highest)	3	4	2	1
Probabilistic ICER vs usual care (£/QALY)		Dominated	9709	6616
Probabilistic sequential ICER (£/QALY)		Dominated	Extendedly dominated	6616[a]

	Usual care	STS HM	STS HH	TM during office hours
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	0	5	12	83
Expected total costs from PSA (£)	8478	9060	9613	9650
Expected total QALYs from PSA	2.4137	2.4128	2.5306	2.5908
Expected net benefit from PSA (£)	39,795	39,196	40,998	42,167
Difference from usual care costs (£)	0	582	1135	1172
Difference from usual care QALYs	0.0000	–0.0009	0.1169	0.1772
Difference from usual care net benefit (£)	0	–599.54	1203	2371
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	136			
Population EVPI (£)	7,449,902			

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Economic analysis using data from predictive distributions excluding the Home-HF study[67]

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.032	0.776	0.642
HF-related hospitalisation HR	1.000	1.058	0.778	0.883
All-cause hospitalisation HR	1.000	1.235	1.048	0.731
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	71.89	75.44	77.44
5 years (%)	33.75	33.63	35.30	36.23
Life expectancy over 30 years (years)	4.71	4.69	4.92	5.04
Difference in life expectancy vs usual care (years)	0.00	–0.02	0.21	0.33
Cost results (£)				
Discounted cost of usual care	491	345	362	372
Discounted cost of treatment	0	634	957	971
Discounted cost of HF-related hospitalisations	4187	4200	4262	4422
Discounted cost of other hospitalisations	3800	3909	4055	3901
Total costs	8478	9087	9636	9665

	Usual care	STS HM	STS HH	TM during office hours
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–145	–128	–119
Discounted cost of treatment	0	634	957	971
Discounted cost of HF-related hospitalisations	0	12	75	234
Discounted cost of other hospitalisations	0	108	255	101
Total difference in costs	0	609	1158	1187
Overall cost rank (1 = lowest cost)	1	2	3	4
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5659	2.6870	2.7548
HF-related hospitalisation decrement	–0.1611	–0.1616	–0.1640	–0.1701
Total discounted QALYs	2.4137	2.4043	2.5230	2.5847
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0089	0.1122	0.1800
HF-related hospitalisation decrement	0.0000	–0.0004	–0.0029	–0.0090
Total difference in discounted QALYs	0.0000	–0.0093	0.1093	0.1710
Total discounted QALYs rank (1 = highest)	3	4	2	1
Probabilistic ICER vs usual care (£/QALY)		Dominated	10,598	6942
Probabilistic sequential ICER (£/QALY)		Dominated	Extendedly dominated	6942[a]
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	1	7	19	72
Expected total costs from PSA (£)	8478	9087	9636	9665
Expected total QALYs from PSA	2.4137	2.4043	2.5230	2.5847
Expected net benefit from PSA (£)	39,795	39,000	40,823	42,029
Difference from usual care costs (£)	0	609	1158	1187
Difference from usual care QALYs	0.0000	–0.0093	0.1093	0.1710
Difference from usual care net benefit (£)	0	–795.73	1028	2233
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	414			
Population EVPI (£)	22,678,379			

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Appendix 17 Results for 12-month treatment duration scenario

Economic analysis using base-case estimates

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.074	0.780	0.779
HF-related hospitalisation HR	1.000	1.045	0.778	0.966
All-cause hospitalisation HR	1.000	1.173	0.977	0.761
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	71.31	77.58	77.67
5 years (%)	33.75	33.36	36.39	36.44
Life expectancy over 30 years (years)	4.71	4.66	5.05	5.05
Difference in life expectancy vs usual care (years)	0.00	–0.05	0.34	0.34
Cost results (£)				
Discounted cost of usual care	575	306	334	334
Discounted cost of treatment	0	1158	1828	1788
Discounted cost of HF-related hospitalisations	4187	4178	4285	4456
Discounted cost of other hospitalisations	3800	3928	4156	3775
Total costs	8562	9571	10,603	10,353
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–269	–241	–240
Discounted cost of treatment	0	1158	1828	1788
Discounted cost of HF-related hospitalisations	0	–9	97	268
Discounted cost of other hospitalisations	0	128	356	–25
Total difference in costs	0	1009	2040	1791
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5465	2.7583	2.7613
HF-related hospitalisation decrement	–0.1611	–0.1608	–0.1649	–0.1715
Total discounted QALYs	2.4137	2.3857	2.5935	2.5898
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0283	0.1835	0.1865
HF-related hospitalisation decrement	0.0000	0.0003	–0.0037	–0.0103

	Usual care	STS HM	STS HH	TM during office hours
Total difference in discounted QALYs	0.0000	–0.0280	0.1798	0.1761
Total discounted QALYs rank (1 = highest)	3	4	1	2
Probabilistic ICER vs usual care (£/QALY)		Dominated	11,349	10,167
Probabilistic sequential ICER (£/QALY)		Dominated	68,189[a]	10,167
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	2	18	35	44
Expected total costs from PSA (£)	8562	9571	10,603	10,353
Expected total QALYs from PSA	2.4137	2.3857	2.5935	2.5898
Expected net benefit from PSA (£)	39,711	38,143	41,267	41,443
Difference from usual care costs (£)	0	1009	2040	1791
Difference from usual care QALYs	0.0000	–0.0280	0.1798	0.1761
Difference from usual care net benefit (£)	0	–1568.71	1555	1732
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	1401			
Population EVPI (£)	76,745,379			

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Economic analysis using data from predictive distributions

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.180	0.849	0.843
HF-related hospitalisation HR	1.000	1.063	0.790	0.982
All-cause hospitalisation HR	1.000	1.302	1.074	0.835
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	70.31	76.50	76.66
5 years (%)	33.75	32.89	35.88	35.96
Life expectancy over 30 years (years)	4.710	4.596	4.980	4.991
Difference in life expectancy vs usual care (years)	–	–0.110	0.270	0.281
Cost results (£)				
Discounted cost of usual care	575	302	329	330
Discounted cost of treatment	0	1147	1812	1773
Discounted cost of HF-related hospitalisations	4187	4138	4237	4414

	Usual care	STS HM	STS HH	TM during office hours
Discounted cost of other hospitalisations	3800	3977	4204	3809
Total costs	8562	9564	10,582	10,326
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–273	–246	–245
Discounted cost of treatment	0	1147	1812	1773
Discounted cost of HF-related hospitalisations	0	–49	50	227
Discounted cost of other hospitalisations	0	177	404	9
Total difference in costs	0	1002	2019	1764
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5129	2.7219	2.7275
HF-related hospitalisation decrement	–0.1611	–0.1593	–0.1631	–0.1699
Total discounted QALYs	2.4137	2.3536	2.5589	2.5576
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0619	0.1471	0.1527
HF-related hospitalisation decrement	0.0000	0.0019	–0.0019	–0.0087
Total difference in discounted QALYs	0.0000	–0.0601	0.1452	0.1439
Total discounted QALYs rank (1 = highest)	3	4	1	2
Probabilistic ICER vs usual care (£/QALY)		Dominated	13,911	12,257
Probabilistic sequential ICER (£/QALY)		Dominated	205,182[a]	12,257
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	7	19	34	40
Expected total costs from PSA (£)	8562	9564	10,582	10,326
Expected total QALYs from PSA	2.4137	2.3536	2.5589	2.5576
Expected net benefit from PSA (£)	39,711	37,509	40,596	40,826
Difference from usual care costs (£)	0	1002	2019	1764
Difference from usual care QALYs	0.0000	–0.0601	0.1452	0.1439
Difference from usual care net benefit (£)	0	–2202.89	884	1114
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	3034			
Population EVPI (£)	166,199,486			

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Economic analysis using data excluding the Home-HF study[67]

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.007	0.757	0.627
HF-related hospitalisation HR	1.000	1.042	0.766	0.872
All-cause hospitalisation HR	1.000	1.134	0.969	0.678
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	72.25	78.14	81.54
5 years (%)	33.75	33.81	36.67	38.32
Life expectancy over 30 years (years)	4.710	4.716	5.082	5.293
Difference in life expectancy vs usual care (years)	–	0.0062	0.3720	0.5830
Cost results (£)				
Discounted cost of usual care	575	310	336	352
Discounted cost of treatment	0	1168	1835	1837
Discounted cost of HF-related hospitalisations	4187	4227	4303	4580
Discounted cost of other hospitalisations	3800	3939	4180	3895
Total costs	8562	9645	10,655	10,663
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–265	–238	–223
Discounted cost of treatment	0	1168	1835	1837
Discounted cost of HF-related hospitalisations	0	40	116	392
Discounted cost of other hospitalisations	0	139	380	95
Total difference in costs	0	1082	2093	2101
Overall cost rank (1 = lowest cost)	1	2	3	4
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5782	2.7773	2.8921
HF-related hospitalisation decrement	–0.1611	–0.1627	–0.1656	–0.1762
Total discounted QALYs	2.4137	2.4155	2.6117	2.7159
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	0.0034	0.2025	0.3173
HF-related hospitalisation decrement	0.0000	–0.0015	–0.0045	–0.0151
Total difference in discounted QALYs	0.0000	0.0019	0.1980	0.3022
Total discounted QALYs rank (1 = highest)	4	3	2	1
Probabilistic ICER vs usual care (£/QALY)		584,066	10,567	6953
Probabilistic sequential ICER (£/QALY)		Dominated	Extendedly dominated	6953[a]

	Usual care	STS HM	STS HH	TM during office hours
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	0	5	12	83
Expected total costs from PSA (£)	8562	9645	10,655	10,663
Expected total QALYs from PSA	2.4137	2.4155	2.6117	2.7159
Expected net benefit from PSA (£)	39,711	38,666	41,580	43,654
Difference from usual care costs (£)	0	1082	2093	2101
Difference from usual care QALYs	0.0000	0.0019	0.1980	0.3022
Difference from usual care net benefit (£)	0	–1045.41	1868	3942
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	225			
Population EVPI (£)	12,325,275			

a Last strategy in the cost-effectiveness frontier.

Economic analysis using data from predictive distributions excluding the Home-HF study[67]

	Usual care	STS HM	STS HH	TM during office hours
Central estimates of HRs used as input				
Mortality HR	1.000	1.032	0.776	0.642
HF-related hospitalisation HR	1.000	1.058	0.778	0.883
All-cause hospitalisation HR	1.000	1.235	1.048	0.731
Treatment costs assumed per month (£)	27	119	179	175
Survival results (undiscounted)				
1 year (%)	72.14	71.91	77.80	81.26
5 years (%)	33.75	33.65	36.50	38.19
Life expectancy over 30 years (years)	4.71	4.70	5.06	5.28
Difference in life expectancy vs usual care (years)	0.00	–0.01	0.35	0.57
Cost results (£)				
Discounted cost of usual care	575	309	335	350
Discounted cost of treatment	0	1165	1830	1833
Discounted cost of HF-related hospitalisations	4187	4223	4295	4575
Discounted cost of other hospitalisations	3800	4012	4247	3940
Total costs	8562	9708	10,707	10,698

	Usual care	STS HM	STS HH	TM during office hours
Difference in costs from usual care (£)				
Discounted cost of usual care	0	–266	–240	–224
Discounted cost of treatment	0	1165	1830	1833
Discounted cost of HF-related hospitalisations	0	36	108	387
Discounted cost of other hospitalisations	0	212	447	140
Total difference in costs	0	1146	2145	2136
Overall cost rank (1 = lowest cost)	1	2	4	3
Discounted QALY results				
QALYs with no hospitalisation decrement	2.5748	2.5669	2.7657	2.8825
HF-related hospitalisation decrement	–0.1611	–0.1625	–0.1653	–0.1760
Total discounted QALYs	2.4137	2.4044	2.6005	2.7065
Difference in QALYs from usual care				
QALYs with no hospitalisation decrement	0.0000	–0.0079	0.1909	0.3077
HF-related hospitalisation decrement	0.0000	–0.0013	–0.0042	–0.0149
Total difference in discounted QALYs	0.0000	–0.0093	0.1868	0.2928
Total discounted QALYs rank (1 = highest)	3	4	2	1
Probabilistic ICER vs usual care (£/QALY)		Dominated	11,486	7296
Probabilistic sequential ICER (£/QALY)		Dominated	Extendedly dominated	7296[a]
Uncertainty analyses using net benefit at £20,000 per QALY				
Probability that strategy is most cost-effective (%)	1	7	19	73
Expected total costs from PSA (£)	8562	9708	10,707	10,698
Expected total QALYs from PSA	2.4137	2.4044	2.6005	2.7065
Expected net benefit from PSA (£)	39,711	38,380	41,302	43,431
Difference from usual care costs (£)	0	1146	2145	2136
Difference from usual care QALYs	0.0000	–0.0093	0.1868	0.2928
Difference from usual care net benefit (£)	0	–1331.28	1590	3720
Net benefit rank (1 = highest)	3	4	2	1
Overall EVPI per patient at ICER of £20,000 per QALY (£)	693			
Population EVPI (£)	37,961,847			

a Last strategy in the cost-effectiveness frontier.

Appendix 18 Protocol

HTA Reference No. 09/107

1. Title of the project:

Home telemonitoring or structured telephone support programmes for patients with heart failure

2. Name of TAR team and project 'lead'

School of Health and Related Research (ScHARR), Technology Assessment Group, The University of Sheffield

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3. Plain English Summary

Heart failure is a complex clinical syndrome that can result from any structural abnormality or cardiac dysfunction that impairs the ability of the heart to fill with, or eject, a sufficient amount of blood throughout the body.[1] It is characterised by symptoms (such as shortness of breath or fatigue, either at rest or during exertion), and signs of fluid retention (such as pulmonary congestion or ankle swelling) and objective evidence of a structural or functional abnormality of the heart at rest.[2] The severity of heart failure, based on symptoms and physical activity from the New York Heart Association (NYHA) functional classification, is highly variable (there is no definitive progression of NYHA status – a patient's condition can improve as well as deteriorate), and can change unevenly over time.[3] Heart failure is associated with significant morbidity, mortality and reduced quality of life, particularly in those aged over 60 years.[4] It also exerts a significant burden on healthcare systems, with the majority of its economic burden attributable to repeated and lengthy admissions to hospital.[5] Multidisciplinary chronic heart failure (CHF) disease management programmes that include structured follow-up with patient education, optimisation of medical treatment, psychosocial care and access to care have shown promise with decreased hospitalisation rates and improved clinical outcomes.[6,7,8,9,10] However, access to these programmes is limited, as a result of barriers related to funding or inaccessibility by some patients due to geographic location.[11,12]

Remote monitoring using structured telephone support between patients and health care providers or patient initiated electronic monitoring (transfer of physiological data such as weight, blood pressure and electrocardiographic details via a telephone or digital cable from home to healthcare provider) or cardiovascular implanted monitoring devices, may help provide wider access to CHF management programmes to a larger number of patients including those constrained by geography, transport or infirmity.[13,14] Previous systematic reviews and meta-analysis have shown that CHF management programmes that include remote monitoring have a beneficial effect on clinical outcomes in patients with CHF compared with usual care.[15,16,14,9,17] Since the last systematic reviews by Clark *et al*.[14] (search date

from January 2002 to May 2006) and Klersy *et al.*[16] (search date from January 2000 and October 2008) several studies of remote monitoring have become available.[18,19,20,21,22,23,24] Despite the benefits, remote monitoring may generate false alerts leading to inappropriate hospitalisation[25] and it may not be feasible for healthcare providers to telephone all patients on a regular basis and or provide specialised equipment to all patients who may benefit.

The aim of this review is to update earlier systematic reviews[16,14] and evaluate the potential cost-effectiveness of home telemonitoring or structured telephone support strategies compared with usual care for adult patients who have been discharged from an acute care setting after a recent exacerbation of heart failure. A specific focus will be taken in assessing the need for primary research in this area.

4. Decision problem

Purpose of the decision to be made

The assessment will address the question: what is the clinical and cost-effectiveness of home telemonitoring, or structured telephone support programmes for adults who have been discharged from an acute care setting after a recent exacerbation of heart failure (including subgroups such as those with transiently or persistently severe and CHF).

Clear definition of the intervention

Telemonitoring, defined as the use of information and communications technologies to monitor and transmit items related to patient health status between geographically separated individuals,[26] permits home monitoring of patients (living at home, or in nursing or residential care homes) using external electronic devices in conjunction with a telecommunication system (land line or mobile telephone, cable network or broadband technology). Telemonitoring allows frequent or continuous assessment of heart failure signs and symptoms measured by patients, family, or caregivers at home, while allowing patients to remain under close supervision.[2,14] Symptoms reported by patients can be remotely reviewed by a health care professional and appropriate action can be initiated. Telephone support is another form of remote management that can be provided through structured telephone contact between patients and healthcare providers (with or without home visits) and reporting of symptoms and or physiological data.[16,14] Cardiovascular implanted monitoring devices such as modern pacemakers, implantable cardioverter defibrillators or cardiac resynchronisation devices are also capable of delivering remote physiological monitoring often without the need for a patient to trigger the transmission of data.[27]

The highest risk period for rehospitalisation is in the first few weeks after discharge from hospital.[13] Structured telephone support and or home telemonitoring interventions should be performed at least once within the first 28 days following discharge from hospital and must be targeted towards patients and intended to address the patients´ concerns and problems not those of caregivers.[14]

Place of the intervention in the treatment pathway(s)

The review will focus on the use of home telemonitoring or structured telephone support programmes for patients who have been discharged from an acute care setting after a recent exacerbation of heart failure.

International guidelines for heart failure care generally recommend early face to face follow-up of patients following hospitalisation, education to facilitate self care, and ongoing support from a multidisciplinary team that is responsive to the patient´s need.[13,2] Similar guidelines have been adopted in the UK;[3,28,29,30] however, the content and structure of heart failure management programmes vary widely between countries and healthcare settings, and are tailored to meet local needs.[31]

Although specific guidelines for the use of telemonitoring in heart failure have not been developed, the highest risk period for rehospitalisation is in the first few weeks after discharge from hospital.[32] The optimum time period for telemonitoring is unclear; however, it is likely that services will provide

telemonitoring or structured telephone support for at least 4 to 6 months following discharge from hospital with its usefulness evaluated at 30 day intervals thereafter.[13]

Relevant comparators

The relevant comparator is considered as usual care. This involves standard post discharge multidisciplinary care without regular follow-up and may include 1) in person follow-up visits to a primary care physician 2) attendance at a clinic based CHF disease management programme 3) any visits at home by a specialised CHF health care professional (referred to as enhanced conventional care).[16,14]

Population and relevant sub-groups

The population will include any adults (defined as ≥18 years of age) of either sex or ethnic group with a diagnosis of heart failure and discharged from an acute care setting (including emergency departments and one-day stay procedures) to home (including relatives home or to nursing or residential care homes). The identification of subgroups of patients for whom home telemonitoring or structured telephone support programmes are particularly appropriate or inappropriate will be governed by the available evidence. However, on a priori grounds, information will be sought for people with transiently or persistently severe and CHF.

Outcomes

The outcomes of the review are mortality (all cause), all cause admission to hospital, CHF related admission to hospital, length of stay (days in hospital), health-related quality of life (HRQoL) and acceptability of interventions to patients. If the evidence allows, additional outcomes of interest may be include medicine usage, patient satisfaction and functional capacity (e.g. exercise tolerance, and left ventricular ejection fraction).

Key factors to be addressed

The review will aim to evaluate the following objectives:

1. Update two existing systematic reviews[16,14] of telemonitoring or structured telephone support programmes for patients with heart failure within the scope of the current review
2. Evaluate the effectiveness and cost-effectiveness of home telemonitoring and or structured telephone support packages compared with usual post-discharge care
3. Identify key areas for primary research

5. Report methods for synthesis of evidence of clinical effectiveness

A review of the evidence for clinical effectiveness will be undertaken systematically following the general principles recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (http://www.prisma-statement.org/). The review will assess the clinical and cost-effectiveness of home telemonitoring or structured telephone support strategies compared with usual care for adults who have been discharged from an acute care setting after a recent exacerbation of heart failure (including subgroups such as those with transiently or persistently severe and CHF).

Inclusion/Exclusion criteria:

Population

The population will comprise adults (defined as ≥18 years of age) with a diagnosis of heart failure and discharged from an acute care setting to home (including relatives home or to nursing or residential care homes).

Interventions

The following interventions will be included: 1) Remote home-telemonitoring using patient initiated external electronic devices or cardiovascular implanted monitoring devices, with transfer of physiological data from the patient to the health care provider via land line or mobile telephone, cable network or broadband technology, 2) Structured telephone support including regularly scheduled telephone contact between patients and healthcare providers and reporting of symptoms and or physiological data. In addition, structured telephone support and or home telemonitoring interventions were required to be performed at least once within the first 28 days following discharge from hospital and be targeted towards patients and intended to address the patients´ concerns and problems not those of caregivers.

Comparators

Usual care (defined as standard post discharge multidisciplinary care without regular follow-up or enhanced conventional care with home visits by a specialised CHF health care professional)

Outcomes

The outcomes of the review will include mortality (all cause), all cause admission to hospital, CHF related admission to hospital, length of stay (days in hospital), health-related quality of life (HRQoL) and acceptability of interventions to patients. If the evidence allows, additional outcomes of interest may be include medicine usage, patient satisfaction and functional capacity (e.g. exercise tolerance, and left ventricular ejection fraction).

Search strategy

The search strategy will update the two existing systematic reviews[16,14] and comprise the following main elements:

- Searching of electronic databases
- Contact with experts in the field
- Scrutiny of bibliographies of all retrieved papers

The following electronic databases will be searched: MEDLINE; MEDLINE in-Process and Other Non-indexed Citations; EMBASE; all databases in the Cochrane Library including the Cochrane Database of Systematic Reviews, the Cochrane Central Register of Controlled Trials and NHS EED; AMED; CINAHL; PsycINFO; and the ISI Web of Science Citation Index. The search strategy will be adapted across the databases. The clinical effectiveness searches will be limited by date from 2006 (the search strategies from the existing systematic reviews appear to be of good quality [and clearly reported] and as a result all studies prior to 2006 should have been identified) to present and all economic literature searches will be undertaken from inception to present (searches for economic studies was not undertaken in the previous reviews). None of the searches will be restricted by language. An example of the MEDLINE search strategy is shown in *Appendix 1*.

For ongoing, completed and unpublished randomised controlled trials, searches will be carried out in the National Research Register Archive and the ClinicalTrials.gov trials registry. Conference proceedings will be identified through searches in the ISI Conference Proceedings Index, the IEEE/IET Electronic Library and ZETOC.

Additional searches on the outcomes to inform the decision-analytic model where required in the course of the project, will be carried out through consultation between the information specialists and the TAR team.

Inclusion criteria

All randomised controlled trials or observational cohort studies with a contemporaneous control group published from 2006 to present (as well as those identified by the existing systematic reviews) that evaluate home telemonitoring, or structured telephone support programmes with usual post discharge multidisciplinary care for adults who have been discharged from an acute care setting to home (including

relatives home or nursing or residential care homes) after a recent exacerbation of heart failure will be included. Before and after studies without a concurrent control group will be excluded because the absence of a control group to record concurrent changes over time means that changes due to the intervention or due to temporal trends, concurrent changes or a Hawthorne effect would be conflated. Such trials therefore represent very weak evidence of effectiveness. The inclusion of potentially relevant articles will be undertaken using a two-step process. First all titles will be examined for inclusion by one reviewer (any citations that clearly do not meet the inclusion criteria i.e. non-human, unrelated to telemonitoring and or heart failure will be excluded). Second, all abstracts and full text articles will be examined independently by two reviewers. Any disagreements in the selection process will be resolved through discussion.

Exclusion criteria

Reviews of primary studies will not be included in the analysis, but will be retained for discussion and identification of additional studies. Moreover, the following publication types will be excluded from the review: animal models; preclinical and biological studies; narrative reviews, editorials, opinions; non-English language papers and reports published as meeting abstracts only, where insufficient methodological details are reported to allow critical appraisal of study quality. Details of all full text excluded papers (including non-English language citations) will also be provided in the review.

Data extraction strategy

Data will be extracted independently by one reviewer using a standardised data extraction form and independently checked for accuracy by a second. Uncertainties will be resolved by discussion. Where multiple publications of the same study are identified, data will be extracted and reported as a single study. Moreover, as this is an update of two existing reviews,[16,14] all relevant data will be extracted from the reviews in the first instance, but will be cross checked for accuracy with the original papers. If necessary, additional data will be extracted from the original papers.

Quality assessment strategy

The methodological quality of each included study will be assessed according to (adapted) criteria based on those proposed by Verhagen *et al.*[33] for randomised controlled trials and by Wells *et al.*[34] for observational studies.

Consideration of study quality to assess randomised controlled trials will include the following factors: method of randomisation, allocation concealment, blinding of outcome assessors and data-analysts (it is not considered plausible that patients could be blinded to these types of interventions), numbers of participants randomised, baseline comparability between groups, specification of eligibility criteria, whether or not intent to treat analysis is performed, completeness of follow up and whether or not study power calculations are performed and reported.

Consideration of study quality to assess observational studies will include the following factors: representativeness of the exposed cohort, selection of the non exposed cohort, comparability of cohorts on the basis of the design or analysis, assessment of outcome, was follow-up long enough for outcomes to occur and adequacy of follow up of cohorts.

Methods of analysis/synthesis

Data will be tabulated and discussed in a narrative review. Where appropriate (i.e. populations, interventions and outcomes are comparable), meta-analysis will be employed to estimate a summary measure of effect on relevant outcomes based on intention to treat analyses. It is expected that this will incorporate previously identified primary studies from existing reviews and new studies identified by the updated searches.

Meta-analysis will be conducted; however, the choice of methods will depend on the type and magnitude of uncertainty in the data. First, analyses will be conducted using a fixed- or random-effects model, using

the Cochrane Collaboration Review Manager Software (version 5.0).[35] Heterogeneity will be evaluated through consideration of the study populations, methods and interventions, by visualisation of results and, in statistical terms, by the χ^2 test for homogeneity and the I^2 statistic. Second, meta-regression will be employed if the source of heterogeneity is identified and quantifiable (e.g, variability arising due to different health systems, heterogeneous populations, country-specific differences or different care situations). Third, if necessary, Bayesian meta-analysis techniques will be considered.

6. Report methods for synthesising evidence of cost-effectiveness

Methods for estimating quality of life

The time horizon of our analysis will be a patient's lifetime in order to reflect the chronic nature of the disease and potential mortality differences between the intervention strategies. The perspective will be that of the National Health Services and Personal Social Services. Both cost and quality adjusted life years (QALYs) will be discounted at 3.5%.[36]

Identifying and systematically reviewing published cost-effectiveness studies

The review detailed in section 5 will be used to identify studies of cost-effectiveness of home telemonitoring or structured telephone support programmes compared with usual care (standard care or enhanced conventional care) for adult patients who have been discharged from an acute care setting after a recent exacerbation of heart failure. An economic search filter will be incorporated into the search strategy to identify relevant studies (as shown in *Appendix 1*). Identified economic literature will be critically appraised and quality assessed using the critical appraisal checklist for economic evaluations proposed by Drummond and colleagues.[37] Existing cost-effectiveness analyses will also be used to identify sources of evidence to inform structural modelling assumptions and parameter values for the de novo economic model.

Evaluation of costs and cost-effectiveness, which may include development of a de novo *economic model*

A new economic evaluation of the cost-effectiveness of home telemonitoring or structured telephone support programmes for adult patients who have been discharged from an acute care setting after a recent exacerbation of heart failure will be developed and the identification of subgroups of patients will be governed by the available evidence.

The ScHARR modelling team have published papers using different modelling techniques (such as discrete event simulation,[38,39,40] transition state modelling[41] and meta-modelling).[42] The model structure and software used to construct the model will be determined following data collection in order that the most appropriate technique is used for this particular assessment. Clinical experts will be consulted at the conceptual stage to ensure that the structure of the model is appropriate to clinical practice.

Ideally, health related quality-of-life evidence will be available directly from the review literature. In the absence of such evidence, the mathematical model may use indirect evidence on quality of life from alternative sources. Quality-of-life data will be reviewed and used to generate the quality adjustment weights required for the model. In addition to the reviewed literature, national sources (e.g. NHS reference costs,[43] national unit costs,[44] and the British National Formulary (http://bnf.org)) will be used to estimate unit costs for use in the economic model.

It is anticipated that there may be limited evidence for some of the parameters that will be included in the economic model. Therefore, the uncertainty around the parameter estimates will be modelled to take this into account. The uncertainty in the central value for each required parameter will be represented by a distribution, enabling probabilistic sensitivity analysis to be undertaken. This will allow an assessment of the uncertainty to be made.

Value of information techniques will be undertaken within the work. The expected value of perfect information (EVPI)[45] will be explicitly calculated. EVPI is defined as the maximum investment a decision maker would be willing to pay to eliminate all uncertainty from the decision problem. It is initially calculated in terms of a defined unit (typically per patient) and then multiplied by the number of people expected to benefit from eliminating all uncertainty to form an estimate of total EVPI. EVPI per person is relatively high where there is large uncertainty in the adoption decision; conversely where there is only a small probability of error and the impact of an incorrect decision is small the EVPI per person will be relatively low.

Depending upon the resources required more complex methodologies (the expected value of partial perfect information (EVPPI)[45] and the expected value of sample information (EVSI)[46] may be undertaken. EVPPI differs from EVPI as it evaluates the maximum value of removing all uncertainty in one, or a subset of parameters, but it is more computationally expensive as it requires two nested Monte Carlo sampling levels.[47]

EVSI is a more advanced methodology for determining the value of information, which explicitly takes into account that uncertainty will not be removed even with large sample sizes. The EVSI methodology simulates the results from the proposed research and synthesises the simulated data with prior knowledge to form a posterior distribution: the larger the trial size the more the posterior distribution resembles the simulated data which is then used in probabilistic sensitivity analyses. The optimal trial size from the options evaluated can then be estimated based on the costs of conducting the trial and the expected net benefit of the sampled information. The application of EVSI is becoming more widespread and case studies employing this methodology have been published.[39,40]

7. Expertise in this TAR team

TAR Centre

The ScHARR Technology Assessment Group (ScHARR-TAG) undertakes reviews of the effectiveness and cost-effectiveness of healthcare interventions for the NHS R&D Health Technology Assessment Programme on behalf of a range of policy makers in a short timescale, including the National Institute for Health and Clinical Excellence. A list of our publications can be found at: http://www.sheffield.ac.uk/scharr/sections/heds/collaborations/scharr-tag/reports. Much of this work, together with our reviews for the international Cochrane Collaboration, underpins excellence in healthcare worldwide.

Team members' contributions

Abdullah Pandor, Research Fellow: has extensive experience in systematic reviews of health technologies. AP will lead the project and undertake the systematic reviewing. AP will co-ordinate review process, protocol development, abstract assessment for eligibility, quality assessment of studies, data extraction, data entry, data analysis and review development of background information and clinical effectiveness.

Patrick Fitzgerald, Research Fellow: has extensive experience in quantitative data analysis and health economic modelling. PF will be involved in the protocol development, data analysis (including the use of Bayesian meta-analysis techniques) and development of the cost-effectiveness model.

Matt Stevenson, Reader in Health Technology Assessment: has extensive experience in mathematical modelling, undertaking health technology assessments and is a National Institute for Health and Clinical Excellence committee member. MS will act as project advisor for all aspects of the work and is one of the guarantors of the research.

Ruth Wong, Systematic Reviews Information Officer: has extensive experience of undertaking literature searches for the ScHARR Technology Assessment Group systematic reviews and other external projects. RW

will be involved in the protocol development and she will develop the search strategy and undertake the electronic literature searches.

Gill Rooney, Project Administrator:
Retrieval of papers and help in preparing and formatting the report.

Professor John Cleland, Professor of Cardiology, Head of Academic Unit of Cardiology, University of Hull, MRTDS Building, Castle Hill Hospital, Castle Road, Cottingham, Kingston-upon-Hull, HU16 5JQ.
Protocol development (advisor), help interpret data, provide a methodological, policy and clinical perspective on data and review development of background information and clinical effectiveness.

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Protocol development (advisor), help interpret data, provide a methodological, policy and clinical perspective on data and review development of background information and clinical effectiveness.

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Protocol development (advisor), help interpret data, provide a methodological, policy and clinical perspective on data and review development of background information and clinical effectiveness.

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Protocol development (advisor), help interpret data, provide a methodological, policy and clinical perspective on data and review development of background information and clinical effectiveness.

Dr Rachel O'Hara, Lecturer in Public Health, ScHARR, University of Sheffield. Regent Court, 30 Regent Street, Sheffield S1 4DA.
Protocol development (advisor), help interpret data, provide a methodological, policy and clinical perspective on data and review development of background information and clinical effectiveness.

8. Competing interests of authors

None of the authors, except Professor Cleland, have financial interest in the companies who manufacture external electronic devices or cardiovascular implanted monitoring devices for home telemonitoring systems included in this review.

Professor Cleland is Chief Medical Officer on an EU/FP7 grant that includes Philips and Medtronic, providers of telemonitoring equipment. Professor Cleland is also in receipt of research support from Philips and has consulted and received research funding from Bosch and General Electric who have interests in this area.

9. Timetable/milestones

Milestone	
Draft protocol	30 April 2010
Final protocol	5 July 2010
Progress report	28 February 2011
Assessment report	31 March 2011

10. Appendices

Appendix 1: Draft search strategy (Ovid MEDLINE)

Clinical effectiveness search strategy

1. exp Heart Failure/
2. ((heart or cardiac) adj failure).tw.
3. 1 or 2
4. exp Telecommunications/
5. Telemetry/
6. (telemetr$ or telemed$ or tele-med$ or telehealth$ or tele-health$ or telecare or tele-care or telecardiol$ or tele-cardiol$ or telehome or tele-home).tw.
7. (telemonitor$ or tele-monit$ or teleconsult$ or tele-consult$ or teleconferenc$ or tele-conferenc$ or telecommunicat$ or tele-communicat$).tw.
8. (telephon$ or phone$).tw.
9. Remote consultation/
10. (remote$ adj (consult$ or monitor$)).tw.
11. (remote adj patient adj monitoring).tw.
12. Monitoring, Ambulatory/
13. ((implantable or wearable) and monitor$).tw.
14. Patient Care Planning/
15. Case Management/
16. disease management/
17. disease management.tw.
18. exp Comprehensive Health Care/
19. Home Care Services/
20. Home Care Services, Hospital-Based/
21. Clinical Protocols/
22. Nurse Clinicians/
23. Nurse Practitioners/
24. (nurse adj led).tw.
25. or/4-24
26. 3 and 25
27. limit 26 to yr="2007 -Current"

Cost-effectiveness search strategy

For the cost-effectiveness searches, an economic filter will be integrated with the search strategy above.

28. exp "costs and cost analysis"/
29. economics/
30. exp economics, hospital/
31. exp economics, medical/
32. economics, nursing/
33. exp models, economic/
34. economics, pharmaceutical/
35. exp "fees and charges"/
36. exp budgets/
37. budget$.tw
38. ec.fs
39. cost$.ti
40. (cost$ adj2 (effective$ or utilit$ or benefit$ or minimi$)).ab
41. (economic$ or pharmacoeconomic$ or pharmaco-economic$).ti
42. (price$ or pricing$).tw

43. (financial or finance or finances or financed).tw
44. (fee or fees).tw
45. (value adj2 (money or monetary)).tw
46. quality-adjusted life years/
47. (qaly or qalys).af.
48. (quality adjusted life year or quality adjusted life years).af.
49. or/27-48
50. 48 and 26 above

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