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

Project lead:
Abdullah Pandor, Research Fellow
ScHARR Technology Assessment Group (ScHARR-TAG), University of Sheffield, Regent Court, 30 Regent Street, Sheffield S1 4DA
Direct line: 0114 222 0778
Fax: 0114 272 4095
E-mail: a.pandor@sheffield.ac.uk

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.

Dr Abdallah Al-Mohammad, Consultant Cardiologist, Northern General Hospital, Herries Road, Sheffield S5 7AU.
Protocol development (advisor), help interpret data, provide a methodological, policy and clinical perspective on data and review development of background information and clinical effectiveness.

Professor Mark Hawley, Professor of Health Services Research, 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.

Hazel Marsh, Research Nurse, Barnsley Hospital NHS Foundation Trust, Gawber Rd, Barnsley S75 2EP
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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