Canadian Agency for Drugs and Technologies in Health

RAPID RESPONSE REPORT: SUMMARY WITH CRITICAL APPRAISAL

TITLE: Congestive Heart Failure Follow-up Models: A Review of the Clinical Effectiveness

DATE: 26 March 2012

CONTEXT AND POLICY ISSUES

Heart failure (HF), often termed "congestive heart failure" or CHF, is a complex and progressive condition that has been associated with heavy individual and health system burden.[1] There are approximately 500,000 Canadians living with heart failure and 50,000 new patients are diagnosed with this condition each year.[2] The annual mortality rate of CHF varies from 5% to 50%, depending on the severity of symptoms, heart dysfunction, age and other factors.[2] In developed countries, it is a common cause of hospitalization and hospital re-admission in the aged population.[3] About a quarter of the HF patients who are hospitalized are re-admitted within 30 days and one third of them are re-admitted within one year.[4,5]

Aside from optimization of evidence-based drug and device therapies, addressing causes of HF, and treating comorbidities, strategies to reduce hospitalizations in patients with HF include improved care management programs, that are widely adopted with an intention to prevent or reduce HF-related re-admissions and to improve patient's quality of life and survival.[4,5]

In routine patient care after HF, a single practitioner, usually the treating physician, follows the patient in line with the current standards and guidelines for treatment of patients with HF,[6,7] through regular clinic visits, or telephone follow-up on an "as needed" basis.[8] This type of care is generally not structured.

Various follow-up models in a wide range of settings for HF patients, such as CHF clinics and non-clinic settings (e.g. community health centers or patient's home), are now available after hospital discharge.[1] In a multidisciplinary HF clinic, health care professionals (physicians, nurses, pharmacists, nutritionists, social workers, exercise physiologists and others) with specialized training and skills in HF management provide services of patient education and counseling, detection of early signs and symptoms of deterioration, telephone follow-up, and titration of medications.[6,9,10] In recent years, telehealth (also known as "telemedicine" or "telemonitoring") uses communications technologies to deliver care services to patients from a distant location.[11,12] This is different from the direct phone calls with clinicians.[4]

The purpose of this report is to review the evidence regarding the clinical effectiveness of different CHF follow-up models.

RESEARCH QUESTION

What is the clinical effectiveness of various models of follow-up for congestive heart failure?

KEY MESSAGE

Evidence from nine health technology assessments, systematic reviews, or meta-analyses suggests that some HF follow-up models are associated with lower mortality rates and lower hospital admission when compared with usual care. However, conflicting results are reported for improvement in patients' quality of life.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2012, Issue 2), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and abbreviated list of major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, and meta-analyses. The search was also limited to English language documents published between January 01, 2007 and February 23, 2012.

Selection Criteria and Methods

One reviewer screened the titles and abstracts of the retrieved publications, and evaluated the full-text publications for the final article selection, according to the selection criteria present in Table 1.

Table 1: Selection Criteria

Population	Adult patients with congestive heart failure at all stages
Intervention	Heart failure follow-up models
Comparator	None specified
Outcomes	Clinical effectiveness Primary outcome: hospital readmission rates Secondary outcomes: mortality, quality of life
Study Designs	Health technology assessments, systematic reviews and meta-analyses, and randomized controlled trials

Exclusion Criteria

Studies were excluded if they did not meet the selection criteria, were duplicate publications, were abstracts or conference proceedings, were included in a selected systematic review, were superseded by a more recent systematic review, or were published prior to 2007.

Critical Appraisal of Individual Studies

The quality of the included health technology assessments (HTA), systematic reviews (SR) and meta-analyses (MA) were assessed using the Assessment of Multiple Systematic Reviews (AMSTAR) tool.[13] No additional randomized controlled trials, not already included in a selected review, were identified for critical appraisal.

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search yielded 436 citations. Upon screening titles and abstracts, 397 citations were excluded, and 39 potentially relevant articles were retrieved for full-text review. Of the 39 potentially relevant reports, 30 did not meet the inclusion criteria, and thus nine publications were included in this review.[12,14-21] The study selection process is outlined in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart (Appendix 1). One HTA[14] and eight SRs or MAs[12,15-21] met the inclusion criteria. Two SRs[22,23] were excluded as all included studies were examined in more recent systematic reviews

Summary of Study Characteristics

Three of the SRs[12,18,20] were conducted in Canada, two SRs and one HTA[14,15,21] in the United States of America, one SR[16] in the United Kingdom, one SR[17] in Australia and one SR[19] in Italy. The study designs reviewed in these evidence-based studies included RCTs and non-RCTs.

The characteristics of the selected HTAs, SRs, and MAs are outlined in Appendix 2.

<u>Clinical Effectiveness of Non-Pharmacological Interventions</u>

Two studies examined the effects of non-pharmacological interventions in HF patients.

In the HTA conducted by Raman et al.,[14] non-pharmacological interventions such as telephone support, increased clinic visits, home visits, home telemonitoring and multidisciplinary discharge care were compared with usual care in HF patients. Relevant English-language RCTs were searched for in multiple databases from 1990 through July 2007. The primary outcome of interest was all-cause re-admission rates. Quality of the reviewed studies was assessed using a 3-category (A, B, and C) grading system. A total of 49 RCTs (10,572 patients) evaluating interventions utilizing delivery models during or after hospitalization and in outpatient clinics were identified from the literature search. The duration of follow-up ranged from three months to two years.

Kozak and coworkers performed a meta-analysis on the effectiveness of non-pharmacologic interventions in HF patients.[15] The interventions involved patient education, direct phone calls, home visit, discharge planning, and exercise training via face-to-face or non-face-to-face mode. Relevant English-language RCTs were searched for in multiple databases until June 2006 (the start date was not specified). Quality of the reviewed studies was assessed using Jadad scale. Twenty-six RCTs met the inclusion criteria. The sample sized in these studies ranged from 34 to 462 patients. Duration of follow-up ranged from less than one month to 14 months.

Clinical Effectiveness of Telemedicine

Five studies evaluated the clinical effectiveness of telemedicine versus usual care in adult patients with CHF.

A meta-analysis conducted by Clarke et al. examined the effectiveness of telemonitoring (TM) in patients with CHF.[16] TM was described as home care of patients using specialist telecare devices (telephone or broadband) and is often done for patients with severe symptoms of HF, such as New York Heart Association (NYHA) class III-IV. Relevant RCTs were searched for in multiple databases from January 1969 to October 2009. The authors did not indicate if there was a restriction on language during study selection. Mortality and hospital admission were the most common primary outcomes in the included RCTs. Funnel plots were used to examine publication bias. Quality assessment for the included RCTs was not performed, expect for a summary of the limitations that have been acknowledged in these studies, such as the generalizability of results and the diverse definitions for "usual care" adopted. There were 13 RCTs included in this meta-analysis. The duration of follow-up ranged from three to 15 months.

Inglis and coworkers evaluated the benefits of structured telephone support (STS) and TM in the target population in a meta-analysis.[17] STS referred to monitoring and/or self-care management delivered using simple telephone technology, while TM was digital /broadband /satellite /wireless, or blue-tooth transmission of physiological data such as electrocardiogram, blood pressure, weight, pulse oximetry, respiratory rate, and other data. The authors of this review also published a Cochrane review with the same contents.[24] In this review, RCTs that were published between January 2006 and November 2008 were included. There was no limit on language as inclusion criteria. This review was an update of a previously published review of remote monitoring strategies for CHF, that searched RCTs on TM from January 2002 to May 2006.[8] The primary outcomes were all-cause mortality, and CHF-related and all-cause hospitalizations. The secondary outcomes included quality of life (QoL) and cost. Publication bias was assessed using funnel plots, and the quality of the included studies was examined through adequacy of allocation concealment, adequacy of blinding of outcome assessors, and completeness of outcome assessment and reporting. In total, 30 RCTs were included in this review, which included 9,560 patients. STS was examined in 16 RCTs, TM was examined in 12 RCTs, and in two RCTs, both STS and TM were compared with standard care. The duration of follow-up in these studies ranged from three to 18 months.

Polisena et al. conducted a systematic review and meta-analysis to compare the effectiveness of home TM relative to usual care for CHF.[12] "Home TM" was described as care services delivered to patients in their homes from a distant location, while "usual care" was considered to involve follow-up by a primary care physician or specialist after patient discharge from hospital. This review is based on a published HTA on home telehealth for chronic disease management.[25] RCTs and observational studies for adult and pediatric CHF patients were searched in multiple databases from 1998 to 2008. No language restriction was applied. The outcomes of interest were mortality, QoL and health care resources. Quality of the included studies was assessed with a tool developed by Hailey et al. based on study design and study performance. Twenty-one studies (3,082 patients from 12 RCTs and nine observational studies) were included in this review. The duration of follow-up ranged from 30 days to one year. Of these studies, 11 were rated with fair to high quality and 10 were rated with fair to poor quality.

Paré et al. performed a systematic review to evaluate the effects of home TM in patients diagnosed with diabetes, asthma, heart failure and hypertension.[18] "Home TM" was defined as

"an application of telemedicine in which physiological and biological data were transferred from the patients' home to the TM center to monitor patients, interpret the data, and make clinical decisions". Randomized or non-randomized studies published from January 1966 through December 2008 were searched in multiple databases. Only English-language studies were included. The strength of evidence of the included studies was assessed using the classification system devised by Jovell and Navarro-Rubio, in that study design was specified as one of nine levels in descending order of strength. Patient outcomes (such as mortality and QoL) and efficiency in care delivery (such as hospital re-admission rates) were commonly reported in studies involved HF patients. In total, 17 studies (five large RCTs, eight small RCTs and four non-RCTs) were identified.

In the meta-analysis conducted by Klersy and coworkers, effectiveness of remote patient monitoring (RPM) on HF patients was evaluated.[19] This intervention referred to 1) a telephone monitoring approach including regularly scheduled structured telephone contact between patients and 2) health care providers, and electronic transfer of physiological data using remote access technology via external, wearable, or implantable electronic devices. RMP was compared with a multidisciplinary HF care approach implemented by in-person follow-up visits, which was deemed usual care. RCTs and non-RCTs published between January 2000 and October 2008 were searched. Articles written in English, Spanish, German, French or Italian were included. Quality of these studies was assessed based on adherence to the CONSORT and STROBE statements and graded on a 0 to 10 visual analog scale. Twenty RCTs (6,258 patients, median follow-up duration was six months) and 12 cohort studies (2,354 patients, median follow-up duration was 12 months) were included.

Clinical Effectiveness of Pharmacist Care

Koshman and coworkers conducted a systematic review on the role of pharmacist care in improving clinical outcomes for HF patients.[20] The pharmacist-specific interventions in this review involved education on both HF and HF medications, including self-monitoring, medication management, and facilitation of compliance. Pharmacists were either a key driver of the intervention or acted as one member in a multidisciplinary team. Relevant RCTs were searched in multiple databases from their inception until August 2007. Quality of the reviewed studies was assessed using the Jadad scale along with a tool to evaluate the adequacy of allocation concealment. In total, 12 RCTs enrolled 2,060 patients were included. The duration of follow-up ranged from six to 12 months.

Clinical Effectiveness of Self-Management Education

One systematic review evaluated the clinical effectiveness of self-management education in adult patients with CHF.[21] RCTs that examined the CHF self-management education programs were searched in multiple databases from 1966 through 2007. The education topics from all studies were categorized into one of four groups: knowledge and management, social interaction and support, fluids management, and diet and activity. Patient outcomes of interest included satisfaction, learning, behavior, medications, clinical status, social functioning, mortality, medical resource utilization and cost. Quality of the included studies was assessed using Jadad scale. In total, 35 RCTs that involved 7,413 patients were included. The duration of the intervention and follow-up ranged from three to 18 months. The education programs were carried out through verbal presentations and communications by the educators and various forms of printed educational materials.

Summary of Critical Appraisal

The details on the critical appraisal of individual included studies are presented in Appendix 3.

Overall, the included HTA, SRs and MAs were well-conducted, with clearly described research questions and selection criteria. Multiple databases were searched in all reviews. In most SRs (n=9), the quality of the primary studies was appraised using predefined quality assessment instruments. Conflicts of interest and funding sources were recorded in all but two reviews. The results were not reported in sufficient detail in some reviews. For instance, a description of the comparator (usual care) was not provided, or there was insufficient detail reported for outcome measures such as QoL. There were overlaps in the data reported between the SRs. For example, both the Inglis review[17] and Clarke review[16] included similar studies and reported comparable clinical outcome improvements.

Publication bias was assessed in two SRs using funnel plots. Strong publication bias was suggested in the Inglis review,[17] while no publication bias was observed in the Clarke review.[16]

Summary of Findings

The results of clinical effectiveness of various HF follow-up models versus standard care are presented in Appendix 4.

Mortality

Non-Pharmacologic Interventions

Results from the meta-analysis by Kozak et al.[15] showed significant reduction in all-cause death rates in the non-pharmacologic interventions group compared to usual care (pooled risk ratio [RR] 0.69, 95% confidence interval [CI] 0.56 to 0.85).

Telemedicine (TM)

In the meta-analysis by Clarke et al.,[16] TM reduced the risk of all-cause mortality by 23% when compared with usual care (pooled RR 0.77, P = 0.02).

In the meta-analysis by Inglis et al.,[17] TM reduced the risk of all-cause mortality by 34% when compared with standard care (pooled RR 0.66, P < 0.0001).

The pooled all-cause mortality from five RCTs and one observational study in Polisena's review[12] indicated that patients in the home TM group had lower risk of death compared with usual care (pooled RR 0.64, 95% CI 0.48 to 0.85).

In the Paré review,[18] mortality was found to be significantly lower in the TM group compared to standard care in two large RCTs; similar mortality rates were reported in the TM and usual care groups in another two large RCTs; similar cardiac mortality rates in the TM and usual care groups were reported in one large RCT. The authors did not provide details for this outcome.

In the Klersy review,[19] results from RCTs and non-RCTs showed significantly fewer patients in the RMP group died compared with those in the usual care group (pooled RR in RCTs 0.83, P = 0.006; pooled RR in non-RCTs 0.53, P < 0.001).

Structured Telephone Support (STS)

In the meta-analysis by Inglis et al.,[17] STS reduced the risk of all-cause mortality by 12% when compared with standard care (pooled RR 0.88, P = 0.08). The different was not statistically significant.

Pharmacist Care

In the Koshman review,[20] there was no significant difference with respect to all-cause mortality between comparison groups (odds ratio [OR] 0.84, 95% CI 0.61 to 1.15).

Self-Management Education Programs

In the 13 studies that measured all-cause mortality in the Boren review,[21] three reported reduced mortality rates in the intervention group.

Hospitalization

Non-Pharmacological Interventions

In the HTA by Raman et al.,[14] significant reductions in all-cause re-admission rates were observed for increased clinic visits (RR 0.78, 95% CI 0.64 to 0.95), home visits (RR 0.82, 95% CI 0.69 to 0.97), home TM (RR 0.95, 95% CI 0.72 to 1.26), and multidisciplinary care (RR 0.63, 95% CI 0.44 to 0.90). Interventions of telephone support only or self-care failed to show statistically significant difference over usual care in terms of hospital re-admission rates.

Results from the meta-analysis by Kozak et al.[15] showed significant reduction in HF-related hospitalization in the non-pharmacologic interventions group compared to usual care (pooled RR 0.41, 95% CI 0.30 to 0.56).

Telemedicine (TM)

In the meta-analysis by Clarke et al.,[16] TM had similar effect on all-cause hospitalization rate as usual care (pooled RR 0.99, P = 0.84). However, TM significantly reduced the CHF-related hospitalization rate by 27% (pooled RR 0.73, P = 0.0004).

In the meta-analysis by Inglis et al.,[17] TM reduced the proportion of patients hospitalized due to chronic HF by 21% when compared with standard care (pooled RR 0.79, P = 0.008). TM reduced the all-cause hospitalization rate by 9% (pooled RR 0.91, P = 0.02).

The pooled all-cause hospitalization rate from three RCTs and one observational study in Polisena's review[12] indicated that patients in the home TM group were less likely to be admitted to hospital compared with those in the usual care group (RR 0.77, 95% CI 0.65 to 0.90).

In the Paré review,[18] hospital re-admission rates were significantly lower in the TM group compared with the standard care group in two large RCTs; similar rates were found between the TM and usual care groups in one large RCT; conflict results were reported in small RCTs and non-RCTs for this outcome. The authors did not provide details for this outcome.

In the Klersy review,[19] results from RCTs and non-RCTs showed significantly lower hospitalization rates in the RPM group compared with the usual care group (pooled RR in RCTs 0.93, P = 0.03; pooled RR in non-RCTs 0.52, P < 0.001). Pooled analysis of results from RCTs showed significantly lower HF-related hospitalization rates in the RPM group (pooled RR 0.71, P < 0.001).

Structured Telephone Support (STS)

In the meta-analysis by Inglis et al.,[17] STS reduced the proportion of patients hospitalized due to chronic HF by 23% when compared with standard care (pooled RR 0.77, P < 0.0001). STS reduced the all-cause hospitalization rates by 8% (pooled RR 0.92, P = 0.02).

Pharmacist Care

In the Koshman review,[20] significant reductions in all-cause hospitalization rates (OR 0.71, 95% CI 0.54 to 0.94) and HF-related hospitalization rates were found in the pharmacist care group compared to usual care (OR 0.69, 95% CI 0.51 to 0.94).

Health-related quality of life (QoL)

Telemedicine (TM)

In the Clarke review,[16] conflicting results were reported for the outcomes of QoL. Some included studies reported improvement in QoL in terms of knowledge about CHF, vitality, and health perception. However, the intervention arm did not show significant improvement in patient health in some studies.

In the Inglis review,[17] three included RCTs examined the effectiveness of TM and reported significant improvements in QoL, without reporting the results in detail.

In Polisena's review,[12] seven studies reported no significant differences in QoL outcomes between the TM and usual care groups, while five studies reported better QoL and higher patient satisfaction in TM group compared with usual care.

In the Paré review,[18] one large RCT reported no significant difference in QoL improvement between TM and standard care groups; another large RCT found significant QoL improvement in the TM group compared with the standard care group. The authors did not provide details for this outcome.

Structured Telephone Support (STS)

In the Inglis review,[17] six included RCTs examined the effectiveness of STS and reported significant improvements in QoL, without reporting the results in detail.

Pharmacist Care

In the Koshman review,[20] conflicting results were reported for QoL: two studies showed a significant difference between groups in favor of pharmacist care, 1 study showed significant difference in favor of usual care, and 6 studies did not show significant difference between groups.

Self-Management Education program

In the Boren review,[21] 11 out of 20 studies assessing patients' social functioning reported significant improvement in the intervention group. Studies assessing depression or patient's global self-assessment failed to detect a significant improvement.

Cost

Telemedicine (TM) and Structured Telephone Support (STS)

In the Inglis review, eight out of 11 included studies indicated that TM/STS intervention was associated with reduction in cost (either cost per admission or overall reduction in healthcare costs), and the cost reduction ranged between 14% and 86%. However, the authors did not specify the countries/settings of these primary studies; in addition, it was unclear if the cost reduction was a result of using TM or STS.

Limitations

The HTA, SRs, and MAs in this report examined data from numerous systematic reviews of RCTs and non-randomized studies. There were some overlapping of primary studies due to the similar selection criteria (population: adult patients with HF; intervention: HF follow-up models such as telemonitoring; comparators: usual care; outcome measures: mortality rates and hospital admissions) adopted by these SRs. There is a risk when summarizing such data, due to the possibility of overestimating the benefits of HF follow-up models if these data were repeatedly used.

There was considerable heterogeneity across studies with regard to individual components of intervention, duration of intervention, length of follow-up and description of usual care. In many studies, "usual care" was not well defined. Given the substantial diversity in the currently available HF follow-up models, it would be challenging to determine the relative effectiveness between these models.

The experience of the service providers may also have an impact on the effectiveness of the investigated interventions.

Most of the primary studies included in the HTA/SRs were conducted in the US and European countries, while some enrolled Canadian patients. The results are likely to be generalizable to a Canadian HF population, due to the similarity of the components in the HF follow-up models such as telemonitoring, patient education program, multidisciplinary care team and usual care. However, more research involving Canadian patients will allow a better understanding of the effectiveness of various HF follow-up programs in Canada.

The risk of publication bias exists, particularly for small studies such that negative results are often not published. Publication bias was examined in only two reviews, with strong bias being reported in one report.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

The clinical effectiveness of disease management programs has been evaluated in a number of systematic reviews and meta-analyses. Evidence from nine HTA, SRs and MAs are presented in our report.

In summary, non-pharmacologic interventions (involving increased clinic visits, home visits, home telemonitoring and multidisciplinary care) significantly reduce mortality and hospital admission in HF patients; telemedicine is associated with significantly lower mortality and hospital admission rates; the pharmacist care modal shows benefit in lowering hospital admission rate, yet it is not associated with lower death rates. The effect of self-management education programs on patient outcomes has yet to be confirmed based on the available evidence. In terms of QoL in HF patients, conflicting results were commonly report across the included reviews. Cost data was briefly reported; therefore, we are not allowed to thoroughly examine the cost reduction related to the adoption of HF models. The improvements for some of the health outcomes are statistically significant. For example, compared with usual care, RR was 0.93 for all-cause hospitalization for remote patient monitoring in the Klersy review[19], RRs were 0.91 and 0.92 for all-cause hospitalization for telemonitoring and structured telephone support respectively in the Inglis review;[17] however, whether such a small difference is clinically important in practice remains unclear.

Long-term studies with better study design and clear definitions of HF care models, particularly enrolling Canadian patients, are warranted to provide more compelling evidence on the effectiveness of such models in the target populations.

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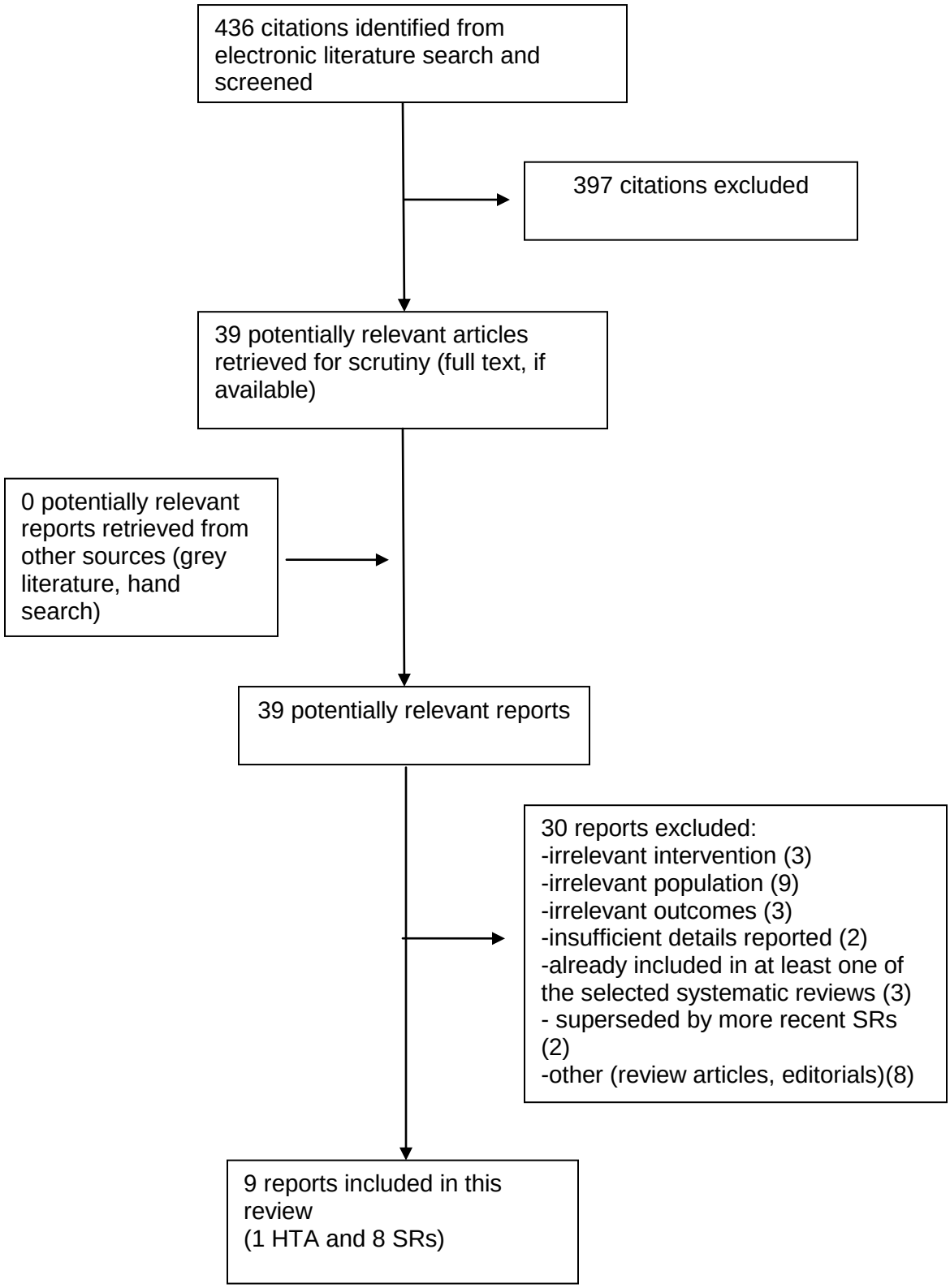
APPENDIX 1: Selection of Included Studies



APPENDIX 2: Characteristics of Included Studies

First Author, Publication Year, Country	Study Design	Patient Characteristics	Intervention	Comparator(s)	Main Outcomes
Clarke, 2011, UK[16]	SR and MA (included RCTs)	Patients with CHF	TM	Usual care	Mortality, hospitalizations, QoL
Inglis, 2011, Australia[17]	SR and MA (included RCTs)	Patients with chronic HF	TM and STS	Standard care	All-cause mortality, hospitalizations, QoL
Polisena, 2010, Canada[12]	SR and MA (included RCTs and observational studies)	Adult and pediatric CHF patients	Home TM	Usual care	Mortality, QoL, health-care resources
Paré, 2010, Canada[18]	SR (included RCTs and observational studies)	Patients with diabetes, asthma, HF and hypertension	Home TM	Usual care	Mortality, hospitalization, re-admission, QoL
Klersy, 2009, Italy[19]	SR and MA (included RCTs and observational studies	Patients with chronic HF	RPM	Usual care (multidisciplinary HF care by in-person follow-up visits)	Mortality; hospitalization
Boren, 2009, USA[21]	SR (included RCTs)	Adult patients with CHF	Self-management education programs	No description of comparator(s)	Satisfaction, learning, mortality, medical resource utilization and cost
Raman, 2008, USA[14]	HTA (included RCTs)	Patients with HF	Non-pharmacological interventions for post-discharge care	Usual care	Re-admission rates, mortality
Koshman, 2008, Canada[20]	SR and MA (included RCTs)	Patients with HF	Pharmacist care	Usual care without pharmacist counseling or education	All-cause or HF-related hospitalization, all-cause mortality
Kozak, 2007, USA[15]	SR and MA (included RCTs)	Patients with HF	Non-pharmacological interventions	Usual care	HF-related hospitalizations, mortality

CHF=congestive heart failure; HF=heart failure; HTA=health technology assessment MA=meta-analysis; RCT=randomized controlled trial; RPM=remote patient monitoring; SR=systematic review; STS=structured telephone support; TM=telemonitoring; QoL=quality of life; UK=United Kingdom; USA=United States of America

APPENDIX 3: Critical Appraisal of Included Studies

First Author, Publication Year	Strengths	Limitations
Clarke, 2011[16]	• Research questions and selection criteria were defined and presented • 2 independent investigators performed data collection • Appropriate methods for data synthesis • Conflict of interests declared	• Not clear if there is a limit on language in literature search • Lack of list of included studies • Lack of list of excluded studies • Quality assessment for the included studies was not performed
Inglis, 2011[17]	• Research questions and selection criteria were defined and presented • Comprehensive literature search based on pre-defined criteria, without limit on language • 2 independent investigators performed data collection • List of included studies • Appropriate methods for data synthesis • Conflict of interests declared	• Results were not reported in sufficient detail for some outcomes such as quality of life and cost • "Standard care" was not defined
Polisena, 2010[12]	• Research questions and selection criteria were defined and presented • Comprehensive literature search based on pre-defined criteria without restriction on language • Quality assessment on the included studies • At least 2 independent investigators performed study selection, and quality assessment • Appropriate methods for data synthesis • Conflict of interest declared	• Lack of list of excluded studies • QoL results were not reported in detail.
Paré, 2010[18]	• Research questions and selection criteria were defined and presented • 2 reviewers selected the studies • the strength of evidence was evaluated • Conflict of interest declared	• Grey literature was not searched • Only English-language studies were included • Quality assessment of the included studies was not performed • Results were not reported in sufficient detail
Klersy, 2009[19]	• Research questions and selection criteria were defined and presented • Comprehensive literature search based on pre-defined criteria • Quality assessment on the included studies • 2 reviewers conducted the study selection; data extraction and quality	• Language was limited to English, Spanish, German, French and Italian • Results were not reported in sufficient detail, such as quality assessment

First Author, Publication Year	Strengths	Limitations
	• Appropriate methods for data synthesis • Conflict of interests declared	
Boren, 2009[21]	• Research questions and selection criteria were defined and presented • Literature search in multiple databases based on pre-defined criteria • Quality assessment on the included studies • 2 reviewers conducted the study selection; data extraction and quality	• Only English-language studies were included • Comparator(s) was not clearly defined • Results were not provided in detail • Conflict of interests not declared
Raman, 2008[14]	• Research questions and selection criteria were defined and presented • Literature search in multiple databases based on pre-defined criteria • Quality assessment on the included studies • Conflict of interest declared	• Only English-language studies were included • Not clear if 2 reviewers conducted study selection and data collection
Koshman, 2008[20]	• Research questions and selection criteria were defined and presented • Literature search in multiple databases based on pre-defined criteria without limit on language • 2 reviewers conducted study selection and data collection • Quality assessment on the included studies • Appropriate methods for data synthesis • Conflict of interests declared	• Lack of list of excluded studies
Kozak, 2007[15]	• Research questions and selection criteria were defined and presented • Literature search in multiple databases based on pre-defined criteria • Quality assessment on the included studies • 2 reviewers conducted study selection and data collection	• Lack of list of excluded studies • Effect of non-pharmacologic interventions was reported as a group; no effect for individual components of the non-pharmacologic intervention was reported • Conflict of interests not declared

APPENDIX 4: Main Study Findings and Authors' Conclusions

First Author, Publication Year	Main Study Findings	Authors' Conclusions
Clarke, 2011[16]	All-cause mortality TM vs. usual care: RR 0.77, 95% CI 0.61-0.97 All-cause hospitalization TM vs. usual care: RR 0.99, 95% CI 0.88-1.11 CHF-related hospitalization TM vs. usual care: RR 0.73, 95% CI 0.62-0.87 QoL Conflicting results were reported in QoL. Some included studies reported improvement in QoL in terms of knowledge about CHF, vitality, and health perception. However, the intervention arm did not show significant improvement in patient's health in some studies.	TM was deemed "effective in the clinical management of patients with CHF" (page 7).
Inglis, 2011[17]	All-cause mortality TM vs. standard care: RR 0.66, 95% CI 0.54-0.81 STS vs. standard care: RR 0.88, 95% CI 0.76-1.01 All-cause hospitalization TM vs. standard care: RR 0.91, 95% CI 0.84-0.99 STS vs. standard care: RR 0.92, 95% CI 0.85-0.99 CHF-related hospitalization TM vs. standard care: RR 0.79, 95% CI 0.67-0.94 STS vs. standard care: RR 0.77, 95% CI 0.68-0.87 QoL TM significantly improved QoL in 3 RCTs, no details provided. STS significantly improved QoL in 6 RCTs, no details provided.	TM and STS both "appear effective interventions to improve outcomes in patients with CHF" (page 1028).
Polisena, 2010[12]	All-cause mortality TM vs. usual care: RR 0.64, 95% CI 0.48-0.85 All-cause hospitalization TM vs. usual care: RR 0.77, 95% CI 0.65-0.90 QoL 7 studies reported no significant differences between groups, while 5 studies reported a better QoL and higher patient satisfaction in the TM group compared with usual care.	"Home TM reduced mortality and lowered number of hospitalizations. Patients' QoL and satisfaction with home TM were similar or better than with usual care" (page 68). The authors suggested the need of more compelling evidence to determine the clinical effectiveness of home TM.
Paré, 2010[18]	Mortality Significantly lower mortality in TM group in 2 large RCTs;	The clinical effectiveness of home TM was yet to be

First Author, Publication Year	Main Study Findings	Authors' Conclusions
	similar mortality in TM and usual care groups in 2 large RCTs; similar cardiac mortality in TM and usual care groups in 1 large RCT Hospital re-admission rates Significantly lower rates in TM group in 2 large RCTs; similar rates in TM and usual care groups in 1 large RCT; conflicting results found in small RCTs and non-RCTs for this outcome. QoL 1 large RCT reported no significant difference in improving QoL between the 2 comparison groups; 1 large RCT reported significant improvement in TM group	confirmed according to the inconsistent findings.
Klersy, 2009[19]	All-cause mortality (RCTs) RPM vs. usual care: RR 0.83, 95% CI 0.73-0.95 All-cause mortality (non-RCTs) RPM vs. usual care: RR 0.53, 95% CI 0.29-0.96 All-cause hospitalization (RCTs) RPM vs. usual care: RR 0.93, 95% CI 0.87-0.99 All-cause hospitalization (non-RCTs) RPM vs. usual care: RR 0.52, 95% CI 0.28-0.96 HF-related hospitalization (RCTs) RPM vs. usual care: RR 0.71, 95% CI 0.64-0.80	"RPM had a significant protective clinical effect in patients with chronic HF compared with usual care" (page 1683).
Boren, 2009[21]	All-cause mortality 3 out of 13 RCTs reported reduced all-cause mortality Medical resource utilization 9 out of 13 RCTs reported significant improvement in hospital re-admission QoL Improvement in social functioning was observed in 11 out of 20 RCTs; No improvement was observed in depression and patient global self-assessment Cost 5 out of 11 RCTs reported no significant decrease in any cost measure	There were mixed findings for outcomes such as clinical improvement, functional status, mortality and health care utilization.
Raman, 2008[14]	All-cause re-admission Telephone support only vs. usual care: RR 0.95, 95% CI 0.84-1.08 Increased clinic visits vs. usual care:	"NPIs that utilized increased clinic visits, home visits and multidisciplinary care reduced the risk of re-

First Author, Publication Year	Main Study Findings	Authors' Conclusions
	RR 0.78, 95% CI 0.64 – 0.95 Home visits vs. usual care: RR 0.82, 95% CI 0.69 – 0.97 Home TM vs. usual care: RR 0.95, 95% CI 0.72-1.26 Multidisciplinary care vs. usual care: RR 0.63, 95% CI 0.44 – 0.90 Self-care vs. usual care: RR 0.97, 95% CI 0.83 – 1.14	admissions" (page 8).
Koshman, 2008[20]	All-cause mortality Pharmacist care vs. usual care: OR 0.84, 95% CI 0.61-1.15 All-cause hospitalization Pharmacist care vs. usual care: OR 0.71, 95% CI 0.54-0.94 HF-related hospitalization Pharmacist care vs. usual care: OR 0.69, 95% CI 0.51-0.94 QoL Conflicting results were reported in included studies: 2 showed significant difference between groups in favor of pharmacist care, 1 showed significant difference in favor of usual care, and 6 studies did not show significant difference between groups.	Pharmacist care reduced the risk of all-cause and HF-related hospitalizations, yet there were no benefits on all-cause mortality.
Kozak, 2007[15]	HF-related hospitalization NPI vs. usual care: RR 0.41, 95% CI 0.30-0.56 All-cause mortality NPI vs. usual care: RR 0.69, 95% CI 0.56-0.85	NPIs were effective in reducing HF-related hospitalization and all-cause mortality rates.

CHF=congestive heart failure; CI=confidence interval; NPI=non-pharmacologic intervention; OR=odds ratio; RPM=remote patient monitoring; RR=risk ratio; STS=structured telephone support; TM=telemonitoring