

# Technology Assessment



## Non-Pharmacological Interventions for Post-Discharge Care in Heart Failure



**Technology  
Assessment Program**

**FINAL REPORT**

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# **Non-Pharmacological Interventions for Post-Discharge Care in Heart Failure**

**FINAL DRAFT**

Technology Assessment Report

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**Tufts-NEMC Evidence-based Practice Center**

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A: Search strategy, sample data extraction form, and bibliography of included studies

B: Study and patient characteristics of included studies

C: Results of costs incurred and combined endpoints

## **Abstract**

**Objective:** To conduct a technology assessment on the effectiveness of non-pharmacological interventions for post-discharge care in heart failure patients.

**Data Sources:** Published English language randomized controlled trials identified in a Medline search through July 2007 and relevant bibliographies.

**Methods:** Certain interventions, specifically, education on self-care management have become usual care, rather than a specific intervention of interest. Thus, increased access to providers and interventions such as telephone support, clinic visits, home visits, home telemonitor, and multidisciplinary discharge care were deemed interventions of interest. The main outcome of interest was the rate of readmission. To assess the relative effects of these interventions compared with usual care on readmission, we grouped studies that utilized similar interventions for post-discharge care and performed meta-analyses using a random effects model.

We performed a qualitative assessment on other outcomes of interest and noted the differences across studies between the intervention and control groups. These outcomes included mortality, length of hospital stay, quality of life and combined endpoints.

**Results:** A total of 49 randomized controlled trials that enrolled 10,572 patients evaluated interventions utilizing delivery models during or after hospitalization, and in the outpatient clinics. There was considerable heterogeneity across studies with regard to individual components of intervention, duration of intervention, length of followup, and description of usual care. Most of the studies were graded good or fair methodological quality. All studies included interventions to educate patients about heart failure symptoms and disease management, and self-care behavioral management. The majority of the studies also evaluated interventions

that included education about diet and sodium restriction, medication review, and daily weight monitoring.

We identified studies that compared increased clinic visits, home visits, home telemonitor, and multidisciplinary care with usual care reduced the risks of readmission. Often the interventions in these studies utilized a combination of secondary components, with telephone followup being the most common. However, when telephone followup was utilized alone, there was no significant difference in all cause readmissions between comparison groups. Studies with intermediate- to long-term followup (>6 month and >12 month), interventions that were initiated in the inpatient setting, and patient ages older than 75 years were associated with a statistically significant reduction in all cause readmissions.

Compared with usual care, one-fourth of the 20 studies reported a significant reduction in all-cause mortality when interventions were initiated during an index hospitalization. Similar significant reduction of length of stay during readmissions was reported when interventions were initiated during an index hospitalization. When interventions were initiated after discharge from an index hospitalization, only one out of 18 studies reported intervention decreased rates of mortality and readmissions, and reduced length of hospital stay during readmissions.

Six randomized controlled trials with a total of 2,654 patients assessed interventions that began in the outpatient clinics. The majority of the studies utilized a pharmacist-led intervention that mostly included medication review. Mortality data was reported in five studies, number of readmissions in four studies, cost incurred in one study, QOL changes in four studies, and composite end point of mortality or readmissions in two studies. Overall, the results do not support the superiority of any particular intervention strategy.

**Conclusions:** Interventions that utilized increased clinic visits, home visits, and multidisciplinary care reduced the risk of readmissions. Studies with intermediate- to long-term followup, interventions initiated in the inpatient setting, and patient ages greater than 75 years were associated with significant reduction of all cause readmissions in the intervention group. These interventions often utilized a combination of components. There was no distinct combination of intervention components that was associated with improved clinical outcomes. The evidence was sparse for interventions beginning in the outpatient clinics.



## Introduction

The Coverage and Analysis Group at the Centers for Medicare and Medicaid Services (CMS) requested from the Technology Assessment Program (TAP) at the Agency for Healthcare Research and Quality (AHRQ) a technology assessment report to evaluate the effectiveness of non-pharmacological interventions for post-discharge care in patients with heart failure (HF) and their relevance to the Medicare population. AHRQ assigned this report to the following Evidence-based Practice Center: Tufts-New England Medical Center Evidence-based Practice Center (Tufts-NEMC EPC) (Contract Number 290-02-0022).

In the United States, HF is the most common hospital discharge diagnosis among elderly. In many developed countries, the prevalence of HF approaches 1 to 4 percent of the population and medical expenditures have been estimated at 1 to 5 percent of health care spending in some settings.<sup>1</sup> HF is an increasingly common condition because recent improvements in medical and surgical therapies along with advancements in diagnostic techniques have increased survival in patients with ischemic cardiovascular disease.<sup>2</sup> Nonetheless, HF carries a substantial risk of death. After an initial diagnosis of HF, increasing age and co-morbidity increases the 30-day and 1-year mortality. The current 1-year mortality estimates range from 18 to 60 percent for elderly with comorbidity.<sup>3-5</sup> About 40 percent of patients are readmitted within 1-year following their first admission for HF and hospitalization accounts for approximately 70 percent of the costs of HF management.<sup>2, 6</sup>

The post-discharge-related adverse events and increased readmissions are often due to potentially modifiable factors, that may include patient-, clinician-, and hospital-related characteristics.<sup>7-9</sup> As a result, management of a HF patient has evolved from the traditional model of crisis intervention toward a more proactive model of managing the disease. Drug

therapy remains the core of therapy for HF. Although invasive procedures are indicated for some patients, the majority of patients are managed with both medications and lifestyle counseling.

Various strategies to manage HF are based on comprehensive care and intensive followup, and are often organized within a formal disease management program. In general, these programs coordinate care across disciplines, provide education to patient and caregiver, enhance patient self-management skills, implement effective followup, and base medication decisions on current clinical practice guidelines for HF.<sup>10</sup> The intervention component in these disease management programs may include education on symptoms and disease management, encouragement of proper self-management behaviors, monitoring of symptoms and weight, dietary advice, sodium restriction, medication review, exercise recommendations, proactive telephone support, social and psychological support, education reinforcement, and home visits. Combinations of components are often employed, and there are considerable variations in the content, intensity, and duration of the components, the setting, and the personnel who coordinate the care. Studies of various interventions reported mixed results concerning their effectiveness.<sup>11,</sup>

<sup>12</sup>

Over the past several years, telephone-based symptom monitoring,<sup>13, 14</sup> automated symptom monitoring,<sup>15</sup> and Internet automated physiologic monitoring by patients (with review by a cardiologist) have been introduced.<sup>16</sup> These are designed to improve outcome and quality of life in elderly HF patients, and they focus on the transition from hospital-to-home and supportive care for self-management.<sup>17</sup> Another intervention strategy introduced in the recent years is pharmacist-led medication support.<sup>18</sup> Given the shortage of specialist nurses in countries such as the UK, the use of pharmacists is seen as extending the scope of post-discharge support. However, published studies indicate that the use of such support failed to benefit the elderly.<sup>18, 19</sup>

The Robert Wood Johnson Foundation (RWJF) and the Institute for Healthcare Improvement (IHI) have started an initiative called Transforming Care at the Bedside (TCAB) to facilitate transition to home. They have created a framework to build safe and reliable care and emphasize vitality and teamwork, patient-centered care, and value-added care processes. Currently, this framework is being tested and has shown some early benefits.

Many non-pharmacological interventions to support post-discharge care have been examined extensively in published systematic reviews or meta-analysis.<sup>12, 20-25</sup> Many previously published studies have varied their eligibility criteria and inclusion of primary studies; thus evaluating different studies. This report aims to comprehensively evaluate data on the effectiveness of non-pharmacological interventions for post-discharge care in patients with HF and their relevance to the Medicare population.

## **Scope and Key Question**

CMS, AHRQ, and EPC staff jointly determined the key question and the definition of terminologies.

1) In HF patients 50 years and older, what is the effectiveness of interventions to support post-discharge care compared with the usual care to prevent readmission?

1a. What is the relationship of the following parameters to the outcome readmission?

- Internal and external validity of the studies (includes inclusion and exclusion criteria of the studies).
- Length of followup
- Concurrent discharge planning in disease management programs
- Place of delivery of discharge planning (home, inpatient, outpatient)

- Components of discharge planning and whether components were individually tailored or generalized
- Intensity of discharge planning, number and frequency of interventions
- Patient characteristics
- Other study characteristics that may affect outcomes

In addition to the rate of readmission, which is the main outcome of interest, CMS requested evaluation of other outcomes that were deemed clinically important. These included all cause mortality, length of hospital stay, costs, quality of life, and combined endpoint consisting of mortality and hospitalization.

## Methods

This report is based on a systematic review of the literature on non-pharmacological interventions for post-discharge care that are currently in use. The approach and criteria used in this technology assessment were agreed upon by consensus of the EPC, CMS, and AHRQ. Several published systematic reviews on this topic indicate that a large number of randomized controlled trials (RCTs) are available. Therefore, we focus only on RCTs in this report.

### Search Strategy

We searched Medline, Medline In-Process & Other Non-Indexed Citations, the Cochrane Library, CINHALL, and Ovid HealthStar from 1990 through July 2007 to identify articles relevant to the key question. We limited the start date of the search to 1990; the time point associated with rapid advances in the medical management of HF, and changing healthcare needs of patients and changes in practice patterns. We reviewed reference lists of published systematic reviews on the same topic, selected narrative reviews, and retrieved primary articles for potentially relevant articles. We also searched ClinicalTrials.gov for registered but not yet published studies and contacted authors of these trials. We combined search terms for discharge plan, case management, and heart failure, and limited the search to English-language RCTs in adult humans. (See **Appendix A** for complete search strategy.)

### Study Selection

We included all comparisons of interventions for post-discharge care that reported at least readmission and/or mortality outcomes among patients with HF. We assessed titles and/or abstracts of citations identified in literature searches. A low threshold was used to retrieve articles for evaluation. Full-text articles of potentially relevant abstracts were retrieved and

reviewed according to the criteria. Results published only in abstract form were not included in our reviews because these reports have generally not been peer-reviewed and therefore lack adequate information to assess the validity of the data.

## **Population**

The population of interest for this report is adults with diagnosed HF. Although the Medicare-eligible populations are age 65 years and above, in consultation with CMS, we used a lower threshold for limiting studies with respect to the age cut-off. Studies were accepted if the mean age of the population was at least 50 years. We also included studies that had subjects who were recruited during the index hospitalization, at the time of discharge from the index hospitalization, or at the outpatient HF clinic. In general, the studies excluded patients discharged to settings other than home (i.e., nursing home or long-term facility) because of the difficulty in followup. We excluded studies with less than 10 patients per arm and studies of secondary analysis of an RCT. When there were multiple publications of the same study, we used the publication that reported the largest number of subjects. We excluded two studies that were included in previous systematic reviews (one had an incorrect citation,<sup>26</sup> and the other could not be retrieved.<sup>27</sup>)

## **Settings**

The site of initiation of an intervention was the key feature of interest among the settings. In the first setting, the intervention(s) was initiated while patients were still in the hospital prior to discharge. In the second setting, the intervention started for recently discharged patients in the outpatient clinic. In the third setting, the intervention was initiated with patients who had been attending a HF management clinic, and at least a proportion of those have had a recent

hospitalization within 3 months of study recruitment. However, in this report, the patients recruited from the third setting were analyzed separately.

## **Interventions**

We accepted descriptions of the components of interventions as they were reported in published articles. Interventions were implemented in hospitals, outpatient settings or in patients' homes. Studies of interventions with any duration were included.

### **Education on symptoms and disease management**

Patients received a simple explanation of the pathophysiology of HF, symptoms, and treatment of HF and were offered advice about when to seek expert help.

### **Instruction on self management behaviors**

Instruction to increase the self-care behavior in patients and includes assessment of self-care ability. Instruction occurs about behaviors to be taken in relation to early signs of worsening HF. The goal is for the patient to understand the role of fluid retention in worsening symptoms and to seek care early. HF diaries or notebooks are sometimes provided to aid self-management.

### **Diet advice, sodium restriction**

Patients were advised to restrict their sodium intake to 1.5 to 2 grams per day, and instructed on how this level could be achieved. The intervention may involve a dietician's visit and an individualized sodium restricted diet or a list of dietary recommendations.

### **Medication review**

The name of each drug and its purpose, dosage, frequency, and significant adverse effects, of specific HF drugs is reviewed by a care provider, and HF drugs (e.g. beta blockers) up titrated slowly as tolerated. It may involve a written medication schedule for complicated medication regimens and increase a patients' adherence to prescribed medications.

### **Education reinforcement**

Review of education goals with patients on subsequent clinic visits or telephone calls was designed to increase the self-care behavior in patients and included an assessment of self-care ability.

### **Exercise recommendations**

This includes recommendations about moderate aerobic exercise training, which can result in improved exercise duration, less fatigue, faster pace of activities, and improved general well-being.

### **Weight monitoring**

Instructions are given to the patients on weight monitoring that may include daily or regular monitoring, and provide HF failure diaries or notebooks to document weight for self-management.

### **Telephone support**

A care provider telephoned the patients in weekly or biweekly intervals for the proactive telephone followup of patients at home after discharge from the hospital. This may involve a review of symptoms and weight and/or questions, which follow a computerized care plan. Support may be provided by a non-physician, usually a nurse, but could also involve a dietician or pharmacist.

### **Increased clinic visits**

Increased clinic visits were additional clinic visits to assess or in response to a change in clinical stability.



## **Home visits**

A member of the multidisciplinary HF team (usually a HF specialist nurse, a pharmacist or dietician) visited the patient in his/her home to assess clinical stability and implement care to correct any variation from care plan.

## **Social and psychological support**

The level of family or career support that is available to the patient was assessed and recommendations were provided to increase support where necessary. Both forms of support are expected to help patients deal better with their social function (e.g., in their role in the family) and, as a result, influence the psychological state (e.g., anxiety or depression) of the patient as he/she copes with the disease.

## **Multidisciplinary care**

All members of the multidisciplinary care team are involved in the care of HF patients. The followup visits include consultation with a cardiologist, HF specialist nurse, physiotherapist, dietician, and psychologist.

## **Comparators**

The acceptable comparators of interest included those defined as usual care, routine care, or standard care. Usual care is generally not structured and consists of instruction on discharge medications by the unit nurse or possibly specialist HF nurse, and includes information on the next appointment with the cardiologist or primary care physician. There were many variations in the description of the usual care among the studies and in general, usual care was not well defined. We also included studies that compared one intervention versus another type of intervention.

## Outcomes

We restricted our evaluation to outcomes deemed clinically important and of greatest interest to CMS. Outcomes of interest included:

- Readmission, all causes
- Mortality, all causes
- Length of hospital stay
- Quality of life, using any validated quality of life measures or any measures of symptom relief
- Other outcomes such as costs or combined endpoint of mortality and hospitalization

## Data Extraction

Items extracted included study year, country where the trial was conducted, setting, funding source, study design, eligibility criteria, patient characteristics, components of intervention, and outcomes (see **Appendix B** for a sample data extraction form). We recorded the method of randomization, allocation concealment, blinding, and whether results were reported on an intention-to-treat basis. Details regarding the duration of HF, history of myocardial disease or other cardiovascular disease, angiotensin converting enzyme (ACE) inhibitor and beta-blocker use, and the intervention were also extracted. For each outcome of interest, baseline, followup, and change from baseline data were extracted, including information on statistical significance. For most outcomes, only data from the last reported time point was included.

## Quality Assessment

We assessed the methodological quality of studies based on predefined criteria. We used a 3-category (A, B, and C) grading system to denote the methodological quality of each study (defined below). This generic scheme defines a grading system that is applicable within a study design. For randomized trials, we mainly considered the methods used for randomization, allocation concealment, and blinding, as well as the use of intention-to-treat analysis and the report of dropout rate. We also considered the extent to which valid primary outcomes were described, as well as whether information was clearly reported. Studies were not rejected due to poor quality.

### **A (good)**

Category A studies have the least bias, and their results are considered valid. A study that adheres mostly to the commonly held concepts of high quality includes the following: adequate random allocation method; blinded evaluation; clear descriptions of the population, setting, interventions, and comparison groups; appropriate measurement of outcomes; appropriate statistical and analytic methods and reporting; no reporting errors; less than 20 percent dropout; clear reporting of dropouts; and no other obvious bias.

### **B (fair/moderate)**

Category B studies are susceptible to some bias, but not a sufficient amount to invalidate the results. They do not meet all the criteria in category A because they have some deficiencies, but they have not deficiencies that are likely to cause major bias. The study

may be missing information, making it difficult to assess limitations and potential problems.

### **C (poor)**

Category C studies have significant bias that may invalidate the results. These studies have serious errors in design, analysis, or reporting; large amounts of missing information; or major discrepancies in reporting.

## **Applicability Assessment**

Applicability addresses the relevance of a given study to the target population of interest. Every study applies certain eligibility criteria when selecting study subjects. Most of these criteria are explicitly stated (e.g., disease status, age, comorbidities). However, some criteria may be implicit or the recruited study population was affected by unintentional biases, such as those related to location (e.g., multi-center vs. single-center, intensive care vs. all inpatients). The populations and the interventions that are of interest specified by the key questions, as opposed to those of interest to the study investigators, dictate the applicability of a study.

We categorized study populations into 1 of 3 levels of applicability that are defined as follows:

**Wide**      Sample is representative of the Medicare population in relevant settings. Patients' age (older adult), gender, spectrum of disease severity and type, etc. are representative of the population of interest.

**Moderate** Sample is an important subgroup of the population of interest. It is possibly limited to a narrow or young age range, lower New York Heart Association (NYHA) score, type of disease, gender etc.

**Narrow** Sample represents only a narrow, atypical subgroup of the population of interest.

## **Data Synthesis and Meta-analyses**

For studies with binary outcomes, we calculated the relative risk and 95% confidence interval. For studies with continuous outcomes, we calculated the mean difference and standard error of the mean difference.

There was significant heterogeneity among studies, with regard to intervention components, intervention duration, or other factors. In the presence of significant clinical heterogeneity among studies of any interventions compared with usual care, we did not perform meta-analyses to obtain a single effect size estimate for the clinical outcomes of interest.

However, certain individual interventions, specifically, education on symptoms and disease management, instruction on self management, dietary advice (including sodium restriction), medication review, exercise recommendations and weight monitoring have become usual care. Thus, interventions consisting of increased access to providers – telephone support, clinic visits, home visits, home telemonitor, and multidisciplinary discharge care – were deemed interventions of interest. To assess the effectiveness of intervention compared with usual care on readmission, we performed meta-analyses by grouping studies that utilized similar interventions for post-discharge care.

We used DerSimonian and Laird's random effects model for all meta-analyses, which generally provides a wider confidence interval (more conservative) in the presence of

heterogeneity across studies.<sup>28</sup> We tested for heterogeneity using Cochran's Q (statistically significant at  $P < 0.05$ ) and assessed its extent with  $I^2$ , which evaluates the proportion of between study variability that is attributed to heterogeneity rather than chance.<sup>29</sup>

Subgroup analyses were performed to examine the impact of study quality, followup duration, site of initiation of interventions (inpatient versus outpatient), the effects of duration of intervention (<3 months, 3 to 6 months, >6 months), country where the study was conducted (US versus non US), and severity of HF on the rate of readmission.

## Results

Our search yielded 273 abstracts of randomized controlled trials, of which 190 were rejected after initial screening using very broad eligibility criteria (i.e., all comparisons of intervention for post-discharge care that reported at the least readmission and/or mortality outcomes among patients with HF). The review of reference lists of related systematic reviews, selected narrative reviews, and primary articles yielded an additional 13 citations. A total of 96 articles were retrieved for full text examination. Of these, 14 articles were duplicate reports, 28 articles were conducted among mixed population, three studies were not randomized trials, and two studies that could not be retrieved were excluded. Forty-nine unique randomized controlled trials qualified for analysis in this report.<sup>8, 13-18, 30-71</sup> **Figure 1** summarizes the search and selection of articles. **Appendix B** summarizes the data of the included studies.

The characteristics of included studies are reported according to the settings where interventions were initiated among patients either during or after an index hospitalization. Index hospitalization is the time period indicating the beginning of study interventions or the recruitment of patients for the study. The study characteristics description is followed by a review of the key question, and the additional outcomes of interest.

All studies restricted patients' recruitment to those who were discharged to their homes or returned to their community. Studies excluded populations for whom coexisting illnesses were likely to reduce life expectancy and/or living in a nursing home setting. Studies also excluded patients with dementia or any psychiatric illnesses, poorly compensated HF, chronic pulmonary diseases, unstable angina, and acute myocardial infarction. The most commonly reported etiology of HF among patients in the included studies was due to ischemic heart disease. Hypertension was the most frequent coexisting medical disease in these patients. The studies

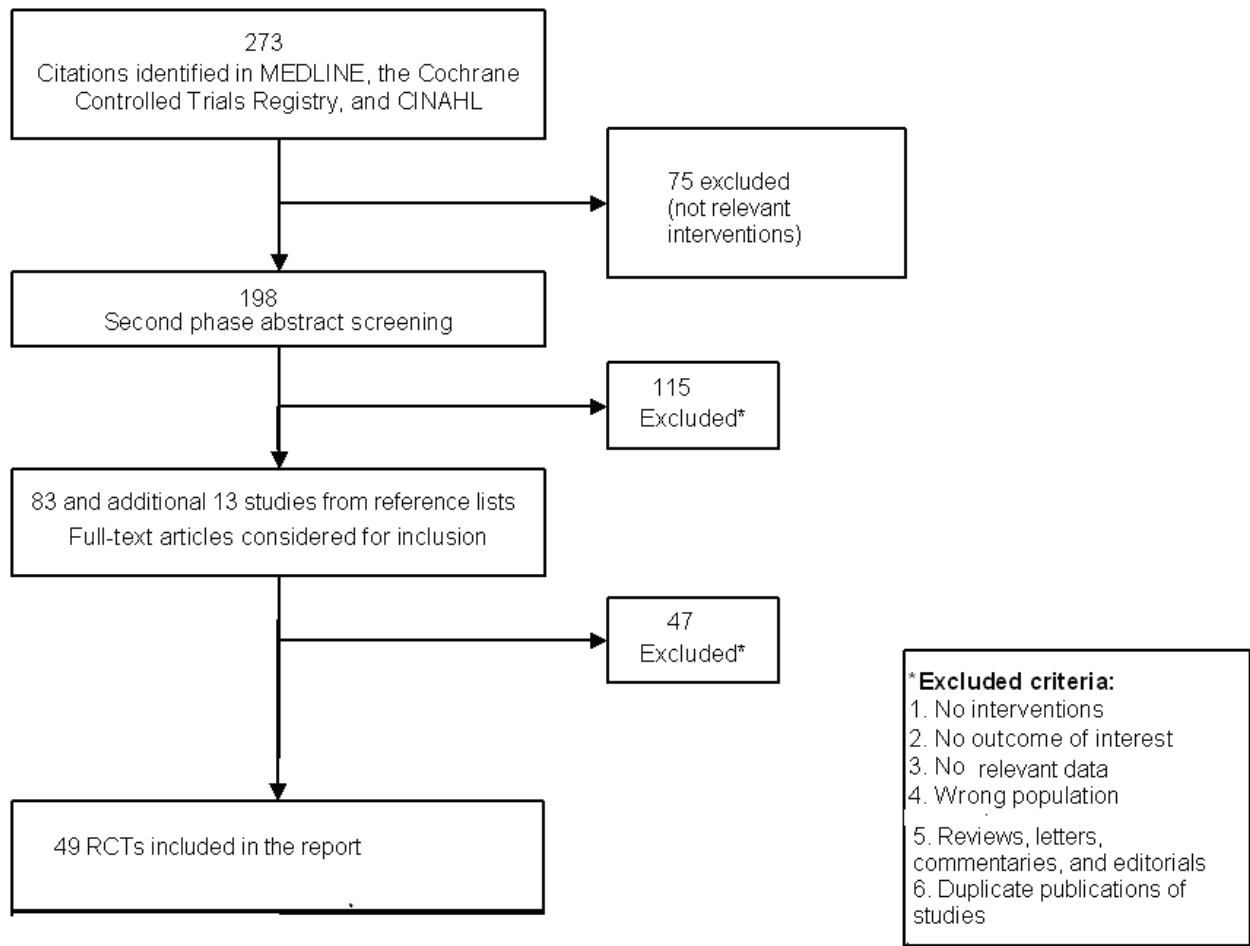
most frequently reported LV systolic dysfunction measured as left ventricular ejection fraction (LVEF).

The severity of HF and the distribution of NYHA class among included patients varied across studies. The studies reported that the therapeutic management of HF patients was optimized as guided by the clinical practice guidelines available at the time of the trials. Among studies, overall at baseline there were no significant differences in demographics, medication use, and co-existing medical illnesses between the intervention and usual care group.

In general, patients in the intervention group had their followup in a HF clinic managed by a study or a specialist nurse under the supervision of a cardiologist. The primary care physicians, or sometimes cardiologists followed HF patients in the usual care group. Generally in the usual care group, studies failed to report care coordination of patients during their transition from an inpatient setting to the post-discharge period or outpatient clinic.



**Figure 1. Flow diagram summarizes the search and selection of articles**



## **Key question 1: In HF patients, what is the effectiveness of interventions to support post-discharge care compared with the usual care to prevent readmission?**

### **Description of studies with all cause readmission data**

Overall 37 studies reported data on all cause readmissions after an index hospitalization. Of which, 20 studies reported interventions beginning in the inpatient setting, and 17 studies that recruited patients beginning in the immediate post-discharge period (Table 2a-3a).<sup>8, 14-16, 18, 30-32, 34, 35, 37-39, 41-46, 48-62, 64-66</sup> In 34 of 37 studies there were a total of 2,054 readmissions in 3,147 patients in the intervention group and 2,589 readmissions in 3,134 patients in the usual care group. Followup duration of these studies ranged from 3 months to 16 months. The remaining three studies reported data on the number of readmissions per patient,<sup>15</sup> on the mean difference of readmissions<sup>57</sup> or on readmissions per patient.<sup>60</sup>

Thirty studies provided quantitative data on the number of readmitted patients in the intervention and control group.<sup>8, 14, 16, 17, 30-33, 36, 37, 39-42, 44-50, 52, 54-57, 59, 60, 62, 65</sup> These studies were categorized according to the type of primary interventions reported in each individual study and combined in meta-analyses. The interventions in these studies included: only telephone followup (13 studies),<sup>14, 31, 39, 40, 42, 45, 46, 48, 50, 54, 57, 59, 62</sup> increased visits to a cardiology clinic (5 studies),<sup>30, 33, 37, 55, 56</sup> home visits (4 studies),<sup>17, 36, 49, 52</sup> home visits and increased clinic visits (1 study),<sup>65</sup> home telemonitoring (1 study),<sup>16</sup> multidisciplinary care (4 studies),<sup>8, 32, 44, 47</sup> self-care instruction only by a care provider or through software (2 studies).<sup>41, 60</sup>

## **Effectiveness of interventions to support post-discharge care compared with the usual care to prevent readmission:**

### **Only Telephone support**

Thirteen studies that included a total of 2,167 HF patients utilized only telephone support intervention, compared to usual care, and reported readmissions.<sup>14, 31, 39, 40, 42, 45, 46, 48, 50, 54, 57, 59, 62</sup> One study that reported no readmission events in both arms was excluded from this meta-analysis.<sup>31</sup> Twelve studies were combined in a meta-analysis (Figure 2).<sup>14, 39, 40, 42, 45, 46, 48, 50, 54, 57, 59, 62</sup> Nine studies were conducted in the US,<sup>14, 31, 39, 46, 48, 50, 54, 59, 62</sup> and the remaining four studies were conducted in Europe.<sup>40, 42, 45, 57</sup> Only two studies were graded poor quality;<sup>14, 46</sup> the remaining studies were good to fair quality. Only one study recruited patients whose mean age were 80 years.<sup>57</sup> The severity of HF varied among the studies. Two studies utilized software assisted telephone followup by the study nurse or a specialist nurse.<sup>14, 62</sup> Only one study reported data on ACE-I titration over the telephone followup.<sup>50</sup>

Our meta-analysis indicated a slight reduction in readmission rates in the telephone followup group compared to the control group, but this failed to reach statistical significance (Figure 2).

### **Clinic visits**

Five studies that included a total of 1,155 HF patients reported quantitative data on all cause readmissions among those who had increased clinic visits to a HF or a specialty clinic.<sup>30, 33, 37, 55, 56</sup> In addition to increased clinic visits, all studies except one utilized telephone followup as an intervention component. One study was conducted in the US,<sup>37</sup> and the remaining studies were conducted in Canada and Europe.<sup>30, 33, 55, 56</sup> One study was graded good quality,<sup>30</sup> two studies were graded fair quality,<sup>37, 56</sup> and two studies were graded poor quality.<sup>33, 55</sup> Only one study reported data on the care coordination during the transition from inpatient setting to post-

discharge followup.<sup>55</sup> This study reported no difference in readmissions between the increased clinic visits group and the control group. The remaining four studies reported reduced readmissions in the intervention group compared with control group, although statistical significance was reached in only two studies. Our meta-analysis identified that the increased clinic visits group had a statistically significant decreased risk for readmission compared with the usual care group (overall RR 0.78; 95%CI 0.64 – 0.95), with considerable between-study heterogeneity.

One poor quality multi-center study conducted in the UK combined increased clinic visits with at least one home visit by the study nurse and compared with the usual care group.<sup>65</sup> This study reported an almost 50 percent reduction in the readmissions compared with the usual care group.

### **Home visits**

Four studies that included a total of 633 HF patients compared readmissions in the home visits intervention group with the usual care group.<sup>17, 36, 49, 52</sup> Individually, each of the four studies reported non-significant, lower rates of readmission in the intervention groups. All four were single-center studies conducted outside of the US. Three studies were graded fair quality,<sup>17, 49, 52</sup> and one study was graded poor quality.<sup>36</sup> The meta-analysis of these studies showed a statistically significant reduction in the readmissions in the intervention group compared with the usual care group (pooled RR 0.82; 95%CI 0.69 – 0.97). There was no significant between-study heterogeneity.

## **Home Telemonitor**

Only one study of 426 HF patients evaluated readmissions in the home telemonitor group compared with the usual care group, and it reported no significant reduction in the readmissions between the groups.<sup>16</sup>

## **Multidisciplinary care (MDC)**

Four studies that included a total of 1,279 HF patients evaluated readmissions in the multidisciplinary care group compared with the usual care group.<sup>8, 32, 44, 47</sup> Three studies were conducted in the US,<sup>8, 44, 47</sup> and one study was conducted in Italy.<sup>32</sup> All four studies were graded fair quality. All four studies noted decreased readmissions with multidisciplinary care intervention, but statistically significant results were noted in only two studies.<sup>8, 32</sup> Two studies followed patients for 3 months,<sup>32, 44</sup> and the remaining two studies followed patient for 1-year.<sup>8, 47</sup> The combined estimate in our meta-analysis indicated statistically significantly reduced readmissions in the multidisciplinary care group compared with the usual care group (pooled RR 0.63; 95%CI 0.44 – 0.90). There was significant heterogeneity between studies.

## **Self-care**

Two studies that included a total of 438 HF patients evaluated readmissions with interventions that included increased emphasis on HF care compared with usual care.<sup>41, 60</sup> Increased emphases on HF care were provided to patients either during their regularly scheduled visits or through educational software. Both studies were conducted in Sweden; one study was graded fair and the other poor quality. The combined estimate for reduction in readmissions was not significantly different between the groups (pooled RR 0.97; 95%CI 0.83 – 1.14).

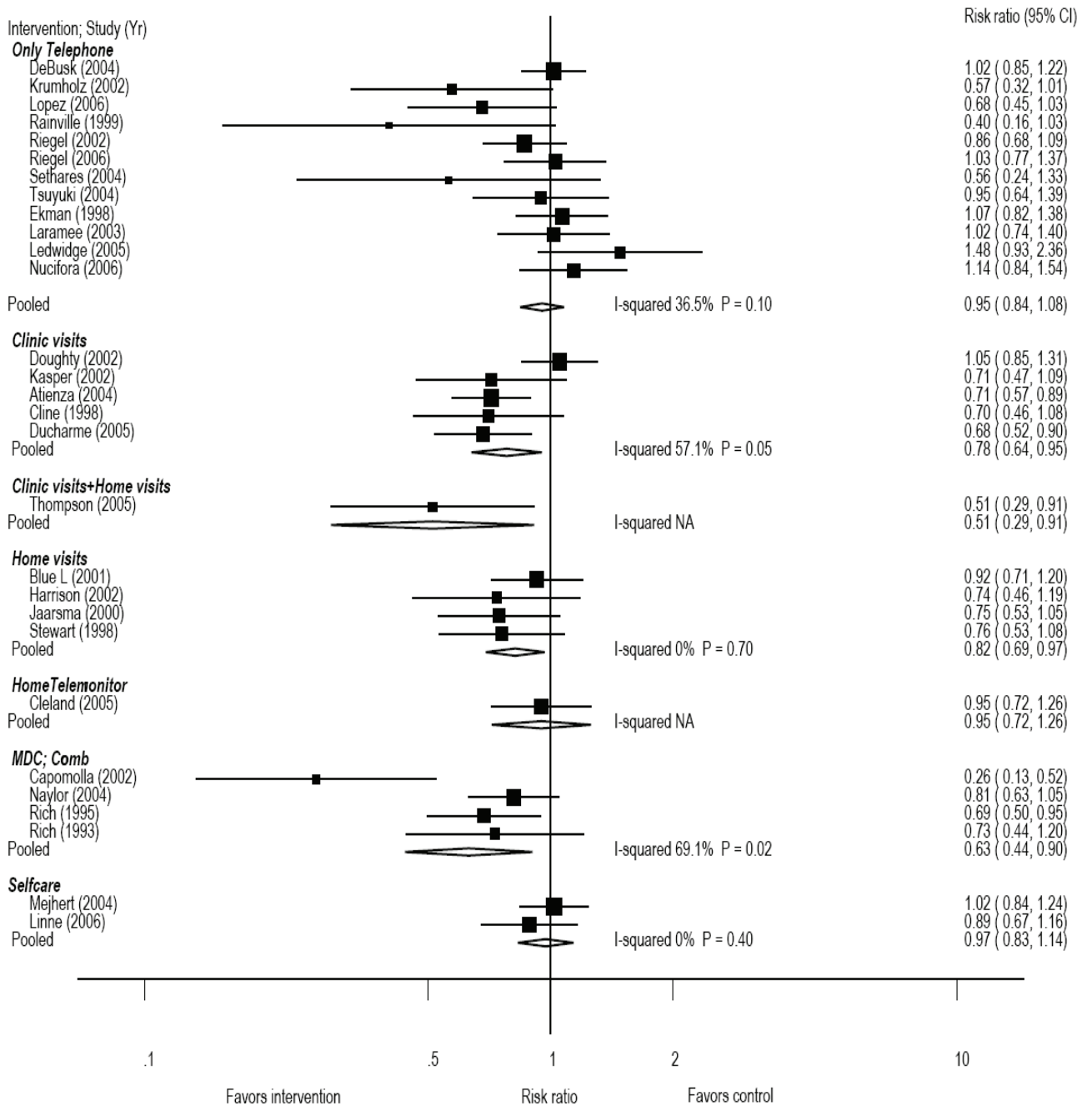
## **Key question 1a: What is the relationship of the study and clinical parameters to the outcome readmission?**

When data were available, we analyzed the impact of characteristics such as internal and external validity of the studies on readmission rates. Factors considered for analyses included length of followup, concurrent discharge planning in disease management programs, place of delivery of discharge planning (inpatient, outpatient), components of discharge planning and whether components were individually tailored or generalized, intensity of discharge planning, number and frequency of interventions, and patient characteristics on the outcome of all cause readmissions (**Table 1**). Among these factors only intermediate- to long-term followup (>6 month or >12 month versus <6 month), interventions initiated in the inpatient setting, and the age of the patient (>75 years) had a statistically significant impact on all cause readmission.

### **Summary of evidence**

- In the meta-analyses, interventions of home visits, increased clinic visits, and multidisciplinary care along with a combination of components of education reinforcement and telephone followup reduced the risk of all cause readmission significantly compared with the usual care group.
- The intermediate- to long-term (>6 month and >12 month) followup interventions initiated in the inpatient setting, and the age of the patient (>75 years) had a statistically significant impact on all cause readmission.

**Figure 2. Meta-analyses of the effect of post-discharge care interventions compared with the usual care on readmissions**



**Table1. Meta-analyses by subgroups comparing interventions for post-discharge care with the usual care in HF patients**

	Subgroups	N studies	Categories	Relative risk (95% CI)	I <sup>2</sup>	P value
Readmission risk intervention vs. usual care	Country: USA	11	Yes	0.84 (0.74, 0.96)	31.6%	0.15
		18	No	0.85 (0.75, 0.96)	60.2%	0.001
	Followup	6	<6 mo	0.86 (0.66, 1.11)	49.9%	0.08
		12	>6 – <12 mo	<b>0.87 (0.78, 0.97)</b>	29.5%	0.16
		11	≥12 mo	<b>0.80 (0.67, 0.94)</b>	69.1%	0.0
	Center	19	Single-center	0.84 (0.74, 0.96)	60.0%	0.0
		10	Multi-center	0.84 (0.76, 0.94)	25.2%	0.21
	Recruitment Setting	19	Inpatient	<b>0.80 (0.71, 0.90)</b>	45.8%	0.02
		10	Outpatient	0.92 (0.82, 1.03)	46.9%	0.05
	Age	2	<65 y	0.45 (0.17, 1.22)	83.7%	0.01
		15	65 y - <75 y	0.90 (0.81, 1.0)	49.6%	0.02
		12	≥75 y	<b>0.82 (0.73, 0.93)</b>	25.7%	0.19
	Quality	2	Good (A)	0.85 (0.59, 1.21)	74.0%	0.05
		20	Fair (B)	<b>0.86 (0.77, 0.96)</b>	54.3%	0.002
		7	Poor (C)	<b>0.81 (0.68, 0.97)</b>	44.9%	0.09
	Severe HF	20	Yes	0.89 (0.81, 0.98)	43.9%	0.02
		8	No	0.76 (0.62, 0.94)	59.0%	0.02
		1	ND	0.68 (0.52, 0.90)	NA	NA
	Readmission outcome	11	Primary outcome	0.78 (0.67, 0.92)	60.6%	0.005
		18	Combined endpoint	0.88 (0.79, 0.98)	44.5%	0.022

Within each subgroup, categories that are statistically significantly different appear in bold



## Interventions beginning as inpatient

### Study characteristics

We identified 25 RCTs with a total of 4,795 patients; these trials assessed the effectiveness of non-pharmacological interventions for post-discharge care in HF patients that began in the inpatient setting during an index hospitalization (Table 2.).<sup>8, 15-17, 30-50</sup> The majority of the trials compared interventions with usual care.<sup>8, 15, 16, 30, 32-34, 36, 39-45, 47-50</sup> One trial compared 3 months intervention with an extended 6 months intervention.<sup>40</sup> One study was a 3-arm trial that compared nurse telephone followup, home telemonitor, and the usual care.<sup>16</sup> Sixteen trials included interventions led by nurses only.<sup>8, 15-17, 31, 33, 35-40, 43, 44, 47, 48</sup> All or most of the studies included interventions to educate patients about HF symptoms and disease management. However, the studies were unclear if the usual care group received educational information on HF symptoms and disease management similar to the intervention group. Only 10 of 25 studies emphasized exercise education and educational reinforcement programs as part of the education information on HF.<sup>17, 31, 32, 37, 39, 40, 43, 45, 46, 50</sup> All or most of the studies utilized telephone followup as one of the components in the intervention group. The main care provider either followed patients actively at frequent intervals or the provider was readily available to be contacted during business hours. Additional interventions to follow HF patients included home telemonitor (two studies), home visits (six studies), increased clinic visits (four studies), and multidisciplinary care (four studies). The description of usual care varied among the studies (Appendix B). The duration of interventions ranged from 1 week to 12 months.

The studies followed patients from 3 months to 16 months. Sixteen studies were single-center, and nine studies were multi-center. The studies mostly included patients with a mean age

of 65 years and above. Eleven trials were conducted in the US,<sup>8, 15, 31, 35, 37-39, 44, 46-48</sup> 11 trials in European countries,<sup>16, 30, 32-34, 36, 40-43, 45</sup> two trials in Canada,<sup>17, 50</sup> and one in Australia.<sup>49</sup> There were three good (A),<sup>30, 34, 38</sup> 16 fair (B),<sup>8, 15-17, 32, 37, 39, 40, 42-45, 47-50</sup> and six poor (C) studies.<sup>31, 33, 35, 36, 41, 46</sup> The six studies were graded poor (C) quality due to various methodological reasons including lack of clear reporting of randomization methods, lack of reporting on the number of patients who met the eligibility criteria were enrolled and randomized, lack of reporting of baseline data, and errors in reporting. Data on available clinical outcomes included readmissions in 25 studies (Figure 3), mortality in 20 studies,<sup>15, 16, 30, 32-47, 49</sup> length of hospital stay in nine studies, cost incurred in 12 studies, and QOL changes in 14 studies. Of the 25 included studies, 11 studies evaluated composite end point of mortality or readmissions as the primary outcome.

## **Mortality**

Twenty studies that began an intervention in the inpatient setting during index hospitalization reported that mortality rates in the intervention group ranged from 2 percent to 31 percent over the study duration of 3 to 16 months (Table 2a).<sup>15, 16, 30, 32-47, 49</sup> The mortality rates in the control or the usual care group ranged from 1 percent to 49 percent over the study duration of 3 to 16 months. Only four studies reported statistically significant decreased relative risk of mortality (0.16 to 0.62) in the intervention group when compared with control group (Table 2a).<sup>15, 30, 32, 42</sup> These studies were conducted in European countries and the US, recruited more than 100 patients, and had a considerable heterogeneity in the duration of followup, interventions utilized (active telephone followup, increased clinic visits, and multidisciplinary care) and care providers (nurses, pharmacists, and cardiologist) (Figure 4). The intervention duration ranged from 6 months to 1-year and the followup duration ranged from 6 months to 1.4 year.

An additional 10 studies reported statistically non-significant decreased mortality rates in the intervention group compared with control group (Figure 4).<sup>16, 34, 37-39, 43, 44, 46, 47, 49</sup> Data with regard to intervention components were assessed across all studies that reported a decrease in mortality. There was no distinct combination of intervention components that were associated with decreased rates of mortality except for one intervention component – active telephone followup – which was utilized along with increased clinic visits, home visits, home telemonitoring or multidisciplinary care. Of note, across studies there was considerable heterogeneity with regard to individual components of intervention, duration of intervention, length of followup, and description of usual care.

Six studies reported a statistically non-significant increased relative risk of mortality (1.07 to 3.5) in the intervention group when compared with control group.<sup>33, 35, 36, 40, 41, 45</sup> Five of these six studies were conducted in single-centers; these five studies utilized nurses as the main provider who could be contacted by telephone when needed.<sup>33, 35, 36, 40, 45</sup> Utilizing educational software only as the intervention tool increased the risk of mortality to almost four fold in the intervention group compared with the control group.<sup>41</sup>

## **Length of stay during readmissions**

Nine studies reported data on the length of stay as number of days of stay in the hospital per patient in the intervention group compared with the usual care group (Table 2a.).<sup>8, 17, 33, 35, 39, 42, 45, 47, 50</sup> Only three of nine studies reported statistically significant decreases in the intervention group compared with the control group.<sup>33, 47, 50</sup> In these studies, the study quality ranged from fair (B) to poor (C) quality, the recruitment was less than 100 to more than 200 patients, and the length of stay ranged from 3.9 to 6.4 days in the intervention group compared with 6.2 to 11.6 days in the control group. The studies utilizing specialist nurses led one or more of the following

interventions: active telephone followup, home visits, increased clinic visits, and multidisciplinary care.

## **Quality of life**

Fourteen studies provided data on patient-perceived health status using one or more validated QOL instruments (e.g., MLHF, SF-36) (Table 2a.).<sup>8, 15, 17, 30, 31, 34-38, 42, 43, 45, 48</sup> Although the majority of studies reported improved scores in the intervention group during followup compared with baseline scores, only three of 14 studies reported statistically significantly improved QOL scores in the intervention group compared with the control group at followup.<sup>8, 17, 37</sup> Two studies were single-center, and one was multi-center. All recruited less than 100 patients per group and received a fair (B) quality grade. These three studies utilized one or more of nurse- or multidisciplinary team-led interventions that included active telephone followup, home visits, increased clinic visits, or multidisciplinary care and 3 to 6 months of followup. There was no discernible combination of intervention components when studies reporting significant results were compared with those reporting non-significant results.

## **Costs**

Twelve studies reported quantitative data on the total costs incurred in the intervention group compared with the control group (Appendix C).<sup>8, 30-34, 37-39, 43, 44, 49</sup> Two of 12 studies reported statistically significant lower total costs in the intervention group compared with the usual care.<sup>38, 44</sup> Studies were graded good (A) or fair (B), followed more than 200 patients from 6 to 12 months, and were conducted in US. The studies utilized one or more nurse-led interventions that included home visits and multidisciplinary care, and education. The remaining studies generally reported statistically non-significant but lower total costs in the intervention group compared

with the usual care.<sup>8, 30-34, 37, 39, 43, 49</sup> There was no distinct combination of intervention components that was associated with decreased total costs.

## **Composite outcome of mortality or readmission**

Ten studies reported data on the combined endpoint of mortality or readmission. Eight of these reported this endpoint as their primary outcome (Appendix C).<sup>30, 33-35, 37, 38, 40, 41, 45, 49</sup> Six studies of good (A)<sup>30, 34, 38</sup> to fair (B)<sup>37, 40, 49</sup> quality reported statistically significant decreased rates for composite outcome of mortality or readmission in the intervention group compared with the control group. All six studies evaluated composite endpoint as their primary outcome of interest. However these six studies varied in the intervention evaluated, were conducted in different countries (US, Europe, and Australia), and randomized almost 50 to 200 patients per group. There was no distinct combination of intervention components that was associated with improved outcome.

## **Summary of evidence**

- Almost three-quarters of the studies with interventions beginning as inpatient were of good (A) to fair (B) methodological quality and wide to moderate applicability to the population of interest.
- The studies compared different combinations of intervention components with usual care group.
- The majority of the studies utilized an education intervention component and active telephone followup.

- Less than one-quarter of the studies utilized intervention components that increase access to care providers. Most of the studies utilized active telephone followup as one of their components of intervention.
- Three-quarters of the studies reported data on mortality. Studies were inadequately powered to ascertain meaningful differences between the interventions and usual care groups for mortality outcomes.
- Less than one-half of the studies reported data on length of stay and quality of life. No studies reported on adverse effects.
- There was considerable heterogeneity across studies with regard to individual components of intervention, duration of intervention, length of followup, and description of usual care.
- Five of 20 studies that initiated interventions in the inpatient setting noted statistically significantly decreased risk of mortality in HF patients who had a broad array of interventions (home visits, increased clinic visits, and multidisciplinary care) compared with the usual care group. All of these interventions utilized telephone followup as one of their components of intervention.
- Interventions of home visits, increased clinic visits, and multidisciplinary care also decreased length of stay, and improved quality of life compared with usual care in several studies.

Study characteristics			Education intervention components										Increased access to providers interventions			
Author	Year	N	Followup duration (mo)	Intervention duration	Education about HF	Self management	Weight monitoring	Sodium restriction / Diet advice	Exercise motivation	Medication review	Education reinforcement	Active telephone	Telephone on demand	Home telemonitor	Home visits	Increased clinic visits
Atienza 2004 <sup>30</sup>		338	16	nd	x	x				x			x			x
Koelling 2005 <sup>38</sup>		223	6	<1 wk	x	x	x	x								
DeSindaco 2007 <sup>34</sup>		173	6	6 mo	x					x						x
Cleland 2005 <sup>16</sup>		426	8	7 mo			x						x	x		
Laramiee 2003 <sup>39</sup>		287	3	3 mo	x	x	x	x		x	x					
Rich 1995 <sup>8</sup>		282	3	3 mo	x	x	x	x		x					x	
Goldberg 2003 <sup>15</sup>		280	6	6 mo	x	x	x	x						x		
Tsuyuki 2004 <sup>50</sup>		276	6	6 mo	x	x	x	x	x	x	x					
Naylor 2004 <sup>44</sup>		239	12	3 mo	x	x									x	
Capomolla 2002 <sup>32</sup>		234	12	nd	x	x	x	x	x							
Kasper 2002 <sup>37</sup>		200	6	6 mo	x			x	x	x						
Nucifora 2006 <sup>45</sup>		200	6	1 wk	x	x	x	x	x							x
Harrison 2002 <sup>17</sup>		192	3	2 wk	x	x	x	x	x						x	
Lopez 2006 <sup>42</sup>		134	12	1 y	x			x		x					x	
Ledwidge 2005 <sup>40</sup>		130	3	3 mo	x	x	x	x	x	x	x					
Rich 1993 <sup>47</sup>		98	3	3 mo	x	x	x	x	x						x	
McDonald 2002 <sup>43</sup>		98	3	3 mo	x	x	x	x	x	x	x					
Stewart 1998 <sup>49</sup>		97	6	1 wk						x					x	
Sethares 2004 <sup>48</sup>		70	3	1 mo		x										
Linne 2006 <sup>41</sup>		230	6	2 wk	x			x		x						
Cline 1998 <sup>33</sup>		190	12	1 y	x	x	x	x	x	x					x	
Jaarsma 2000 <sup>36</sup>		179	9	nd	x			x							x	
Dunagan 2005 <sup>35</sup>		151	12	2 wk		x		x		x						
Rainville 1999 <sup>46</sup>		34	12	>1 wk	x	x	x	x	x	x	x					
Barth 2001 <sup>31</sup>		34	3	3 mo	x	x	x	x	x	x	x					

Mo, months of followup; N, Total number; Nurse (S), heart failure specialist nurse; wk, week; y, year

1. When specified nurse; these studies were unclear to whether the nurse had any training in HF care.

Author Year	Country	Intervention		Mortality		Readmission rate	LOS (d)	QOL Mean	
		Study y	Duration (mo)	%Event in Control	RR (95% CI)				%Event in Control
Atienza 2004 <sup>30</sup>	Spain	1999-2000	16	338	29	<b>0.62</b> (0.42, 0.93)	58	0.71 (0.57, 0.89)	A
Koelling 2005 <sup>38</sup>	USA	2001-2002	6	223	9	0.76 (0.30, 1.92)	nd	MLHF↓ +3.0 ns	A
Del Sindaco 2007 <sup>34</sup>	Italy	2001-2002	6	173	37	0.85 (0.56, 1.30)	nd	MLHF↓ ns	A
Cleland 2005 <sup>a16</sup>	Europe	2000-2002	8	426	24	0.73 (0.44, 1.22)	47	0.95 (0.72, 1.26)	B
Laramée 2003 <sup>39</sup>	USA	1999-2000	3	287	10	0.90 (0.44, 1.82)	37	1.02 (0.74, 1.40)	B
Rich 1995 <sup>8</sup>	USA	1990-94	3	282	nd		42	<b>0.69</b> (0.50, -36.6% HFQ)† <b>0.95</b>	B
Goldberg 2003 <sup>15</sup>	USA	1998-2000	6	280	18	<b>0.44</b> (0.22, 0.85)	nd	MLHF↓ -4.5	B
Tsuyuki 2004 <sup>60</sup>	Canada	1999-2000	6	276	nd		28	0.95 (0.64, 1.39)	B
Naylor 2004 <sup>44</sup>	USA	1997-2001	12	239	11	0.87 (0.41, 1.86)	55	0.81 (0.63, 1.05)	B
Capomolla 2002 <sup>32</sup>	Italy	1999-2000	12	234	17	<b>0.16</b> (0.05, 0.51)	30	<b>0.27</b> (0.13, 0.52)	B
Kasper 2002 <sup>37</sup>	USA	1996-1998	6	200	13	0.52 (0.22, 1.24)	36	0.71 (0.47, 1.09)	B
Nucifora 2006 <sup>45</sup>	Italy	1999-2001	6	200	8	1.79 (0.78, 4.07)	43	1.14 (0.84, 1.54)	B
Harrison 2002 <sup>17</sup>	Canada	1996-98	3	192	nd		31	0.74 (0.46, 1.19)	B
Lopez 2006 <sup>42</sup>	Spain	2000-2002	12	134	30	<b>0.43</b> (0.21, 0.89)	48	0.68 (0.45, 1.03)	B
Ledwidge 2005 <sup>40</sup>	Ireland	nd	3	130	21	1.25 (0.67, 2.35)	29	1.48 (0.93, 2.36)	B
Rich 1993 <sup>47</sup>	USA	1988-1989	3	98	49	<b>0.43</b> (0.24, 0.77)	46	0.73 (0.44, 1.21)	B

CI, confidence interval; HFQ, Chronic Heart Failure Questionnaire; Ctrl, control; d, days; diff, difference; EQOL, Euroqol; Int, intervention; LOS, length of stay; mo, month; MLHF, Minnesota Living with Heart Failure; m, mental score; mo, months of followup; N, number; nd, not documented; ns, not significant; p, physical score; QOL, quality of life; RR, rate ratio; SE, standard error; wk, week; y, year; † Lower score indicates improved function; ‡ Higher score

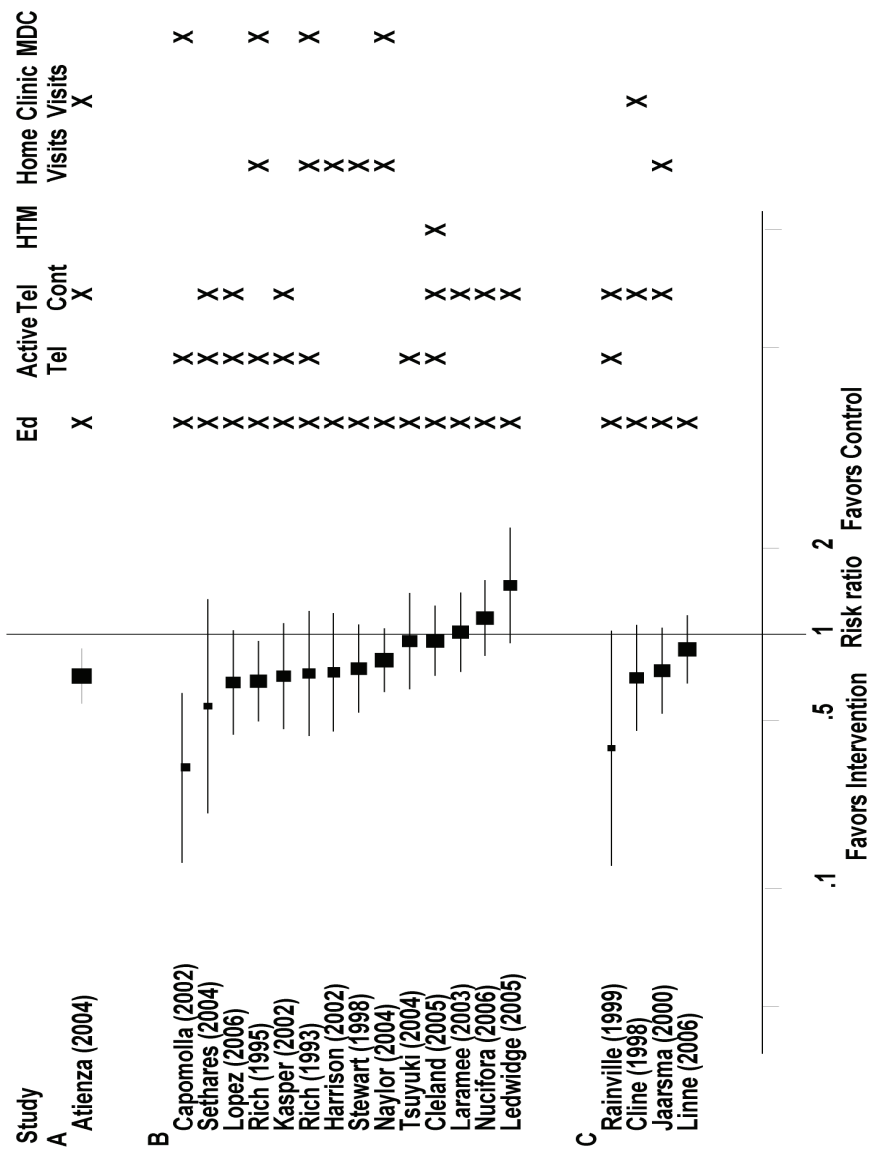




Author Year	Country	Intervention	Duration (mo)	Mortality		RR (95% CI)	Readmission rate	LOS (d)	QOL
				%Event in Control	%Event in Control				
McDonald 2002 <sup>43</sup>	UK	1998-2000	3	98	6	0.92 (0.20, 4.34)	nd	nd	-10.2 ns
Stewart 1998 <sup>49</sup>	Australia	nd	6	97	10	0.20 (0.02, 1.62)	65	0.76 (0.53, 1.08)	B
Sethares 2004 <sup>48</sup>	USA	1999-2000	3	70	nd	0.56 (0.24, 1.33)	32	MLHF $\ddagger$	-4.70 ns
Linne 2006 <sup>41</sup>	Sweden	1998-2002	6	230	1	3.54 (0.4, 31.20)	50	0.89 (0.67, 1.17)	C
Cline 1998 <sup>33</sup>	Sweden	1991-1993	12	190	28	1.07 (0.68, 1.67)	39	0.70 (0.46, 1.08)	-3.9 (nd)
Jaarsma 2000 <sup>36</sup>	Netherlands	1994-1997	9	179	17	1.56 (0.88, 2.76)	nd	nd	ns
Dunagan 2005 <sup>35</sup>	USA	1999	12	151	15	1.17 (0.56, 2.44)	nd	-1.2 MLHFm $\ddagger$ (nd)	ns
Rainville 1999 <sup>46</sup>	USA	1996-1997	12	34	24	0.25 (0.03, 2.01)	59	0.40 (0.16, 1.03)	-0.7 ns
Barth 2001 <sup>31</sup>	USA	nd	3	34	0	0	0	nd	ns

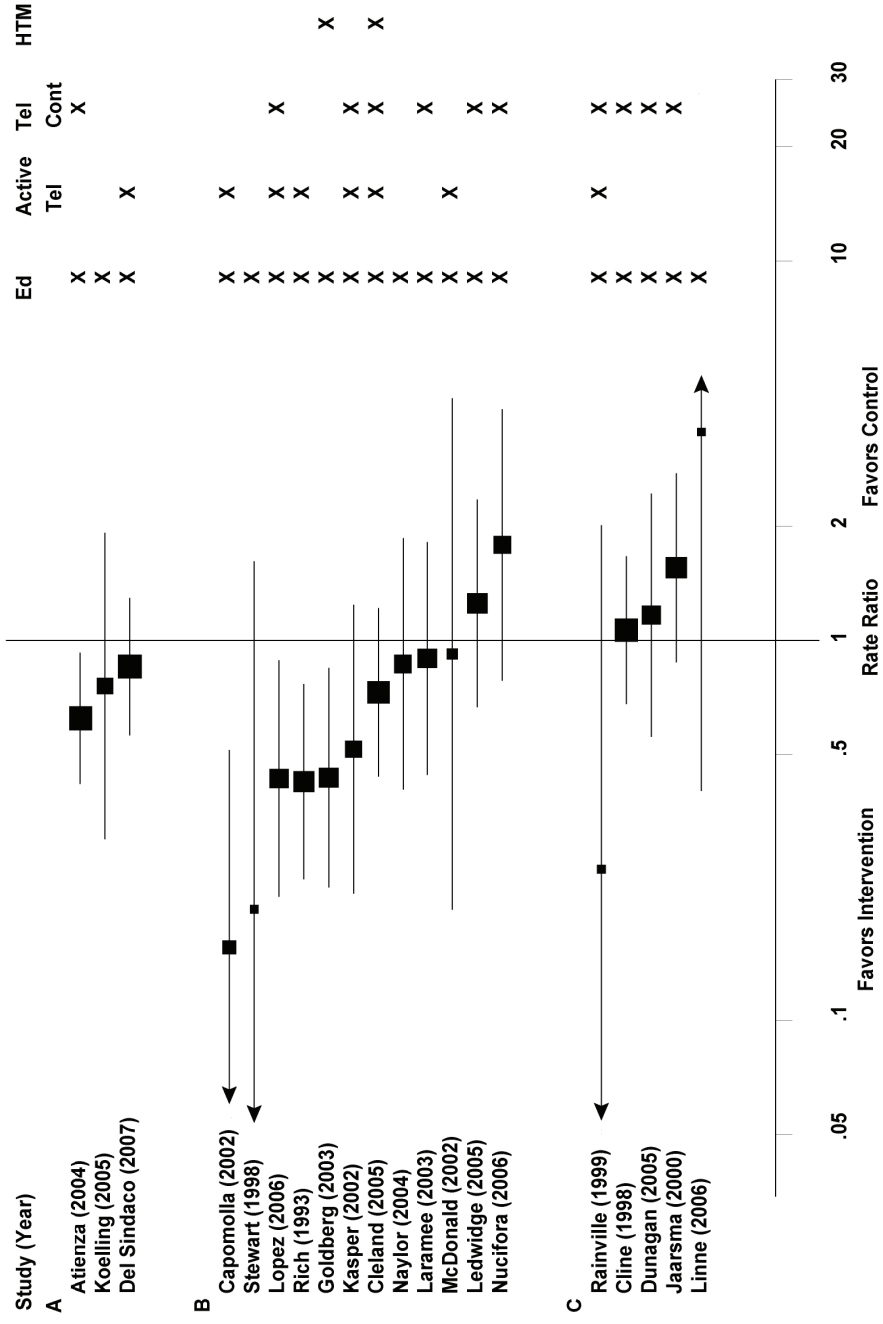
CI, confidence interval; HFQ, Chronic Heart Failure Questionnaire; Ctrl, control; d, days; diff, difference; EQOL, Euroqol; Int, intervention; LOS, length of stay; mo, month; MLHF, Minnesota Living with Heart Failure; m, mental score; N, number; nd, not documented; ns, not significant; p, physical score; QOL, quality of life; RR, rate ratio; SE, standard error; wk, week; y, year;  $\ddagger$  Lower score indicates improved function;  $\ddagger$  Higher score indicates better function

beginning in the inpatient compared with the usual care group.



Ed, one or more of the educational component; HTM, home telemonitor; MDC, multidisciplinary care; Active Tel, active telephone followup; Tel cont, Telephone contact

beginning in the inpatient compared with the usual care group.



Ed, one or more of the educational component; HTM, home telemonitor; MDC, multidisciplinary care; Active Tel, active telephone followup;

Tel cont, Telephone contact



## Interventions beginning post-discharge

### Study characteristics

We identified 18 RCTs with a total of 3,123 patients that assessed the effectiveness of non-pharmacological interventions for post-discharge care immediately after an index hospitalization in HF patients (Table 3).<sup>14, 18, 51-66</sup> Patients were recruited or consented to the trial during their index hospitalization, but interventions began 1 to 3 weeks after their discharge from the hospital. Sixteen trials compared interventions versus usual care.<sup>14, 18, 52-57, 59-66</sup> One trial compared home visits intervention with a nurse telesupport group.<sup>51</sup> One 3-arm trial compared nurse telephone followup, home telecare, and usual care.<sup>58</sup> Twelve trials included interventions led by nurses only.<sup>51-54, 57-61, 63-65</sup> Interventions included active telephone followup (eight studies); availability of provider telephone contact (two studies); home telemonitoring (two studies), multiple home visits (six studies), increased clinic visits (two studies), and multidisciplinary care (one study). The description of usual care varied among the studies. The duration of interventions ranged from 2 weeks to 12 months.

The studies followed patients for 6 months to 12 months. In general, a clinic visit for the patients in the intervention group was scheduled at 2 to 3 weeks after discharge. In some studies, the study nurse or pharmacist visited the patients' home following their discharge to provide the first educational intervention. Twelve studies were single-center, and six studies were multi-center. The studies mostly included patients with a mean age of 70 years and above. Six trials were conducted in the US; nine trials were from European countries; one trial was from Canada; and one each from Australia and New Zealand. There were four good (A),<sup>18, 62-64</sup> seven fair (B),<sup>51, 52, 54, 56, 57, 59, 60</sup> and seven poor (C)<sup>14, 53, 55, 58, 61, 65, 66</sup> studies. The seven studies that were graded poor (C) quality had various methodological deficiencies, including reporting errors and a

failure to clearly report randomization methods, eligibility criteria, number enrolled and randomized, or baseline data.

Data on available clinical outcomes included mortality in 13 studies,<sup>18, 52-54, 56-60, 63-66</sup> readmissions in 17 studies (Figure 5),<sup>14, 18, 51-62, 64-66</sup> length of hospital stay in 10 studies,<sup>14, 51, 52, 57-60, 62, 64, 66</sup> QOL changes in nine studies,<sup>18, 51, 56, 60-63, 65, 66</sup> and cost incurred in seven studies. Of the 18 included studies, five studies evaluated composite end point of mortality or readmissions as the primary outcome.<sup>55, 59, 63-65</sup>

## **Mortality**

Thirteen studies that began an intervention in the 1 to 3 week period after discharge from an index hospitalization reported mortality rates in the intervention group ranged from 1 percent to 40 percent (Table 3a.).<sup>18, 52-54, 56-60, 63-66</sup> The mortality rates in the control or the usual care group ranged from 0 percent to 37 percent over the study duration of 3 to 16 months. Only one study reported statistically significant decreased relative risk of mortality (0.36), and the remainder of the studies reported non-significant decreased risk in the intervention group when compared with usual care group.<sup>52, 64</sup> This study was conducted in Europe, recruited less than 100 patients per group, had 1-year of followup, utilized increased clinic visits during their followup, and was graded good (A) quality. The study also utilized nurse-led interventions and reported the primary endpoint as the composite clinical outcome of mortality or readmission.

Two studies reported statistically non-significantly increased relative risk of mortality (1.20, 1.21) in the intervention group when compared with usual care group.<sup>18, 60</sup> Of note, these two studies utilized only educational interventions and medication review, and did not utilize interventions of increased access to providers (Figure 6).

## Length of stay during readmission

Nine studies reported data on the length of stay during readmission as the number of days of stay in the hospital per patient in the intervention group compared with the usual care group (Table 3a).<sup>14, 52, 57-60, 62, 64, 66</sup> The tenth study compared nurse telemanagement with home visits and provided data on the total number of hospitalization days.<sup>51</sup>

Only three studies reported statistically significant decreases in the length of stay in the intervention group compared with the control group.<sup>51, 64, 66</sup> A good (A) quality study from Sweden with 106 patients reported a significant decrease in the length of stay per patient in the intervention group compared with the usual care group (1.4 versus 3.9 days) during a 1-year followup.<sup>64</sup> The patients in the intervention group had the nurse-led education along with increased clinic visits during followup. A fair (B) quality study by Benatar that compared nurse telemanagement with home visits reported a significant decrease in the total number of hospitalization days in the nurse telemanagement group during 1-year followup.<sup>51</sup> The third study, graded as poor (C) quality, utilized home visits by study nurses along with multidisciplinary care intervention and reported a significant decrease in the length of stay per patient (9.3 versus 12.5 days) compared with the usual care group.<sup>66</sup> The three studies utilized different interventions to increase access to care providers, and there was no distinct combination of intervention components that was associated with improved outcomes.

## Quality of life

Nine studies provided data on the patient-perceived health status using one or more validated QOL instruments — MLHF, SF-36, and Nottingham health profile (Table 3a).<sup>18, 51, 56, 60-63, 65, 66</sup> Two single-center studies reported significantly improved QOL scores in the intervention group at followup.<sup>56, 61</sup> One study was graded fair (B) and the other poor (C) quality. Both studies



utilized nurse or multidisciplinary team-led education with medication review for compliance, and followed patients for 6 months. In the intervention group, Ducharme reported significantly improved self assessed scores of MLHF from baseline,<sup>56</sup> while Morcillo reported significantly higher on the physical and mental health SF-36 scale from baseline.<sup>61</sup> For comparisons between the intervention and usual care group there were no differences between those two groups.

## **Costs**

Seven studies reported data on the total costs incurred in the intervention group compared with the control group (Appendix C).<sup>14, 51, 58, 59, 61-63</sup> Two studies that utilized active telephone followup or education only in the intervention reported statistically significant lower total costs compared with the usual care.<sup>59, 61</sup> One study was graded fair (B) and the other poor (C) quality; they followed less than 100 patients for 6 to 12 month, and was conducted in US and Spain. Two other studies that evaluated home visits reported higher total costs in the intervention group, but were not statistically significant compared with usual care or nurse telemanagement.<sup>51, 58</sup> The remainder of the studies reported lower costs but were not statistically significant in the intervention group compared with the control group.<sup>14, 62, 63</sup>

## **Composite outcome of mortality or readmission**

Five studies reported the combined endpoint of mortality or readmission as their primary endpoint (Appendix C).<sup>55, 59, 63-65</sup> Three studies of good (A) or fair (B) quality reported statistically significant decreased risk for composite outcome of mortality or readmission. All three studies varied in the intervention evaluated, were conducted in different countries (US, Europe, and Australia) and randomized less than 100 to 200 patients in each. Across studies,

there was no distinct combination of intervention components that was associated with improved outcomes.

## **Summary of evidence**

- Almost two-thirds of the studies with interventions beginning post-discharge were of good (A) or fair (B) methodological quality and wide to moderate applicability to the population of interest.
- The studies compared different combinations of intervention components with usual care.
- The majority of the studies utilized educational intervention components and active telephone followup.
- Less than one-quarter of the studies utilized intervention components that increased access to care providers. Telephone followup was either used alone or in combination with other interventions in most of the studies.
- Across studies there was considerable heterogeneity with regard to individual components of intervention, duration of intervention, length of followup, and description of usual care.
- In only one study, increased clinic visits along with telephone support that was initiated after an index hospitalization statistically significantly reduced mortality in the intervention group compared with usual care group.



Study characteristics			Education components										Increased access to providers					Main Care Provider <sup>1</sup> Quality
Author	Year	N	Followup duration (mo)	Intervention duration	Education about HF	Self management	Weight monitoring	Sodium restriction / diet advice	Exercise motivation	Medication review	Education reinforcement	Active telephone	Telephone on demand	Home telemonitor	Home visits	Increased clinic visits	Multidisciplinary care	
Holland	2007 <sup>18</sup>	293	6	8 wk	x	x	x	x	x	x	x						Pharmacist	A
Stewart	1999 <sup>63</sup>	200	6	2 wk	x	x	x	x	x	x				x			Nurse	A
Riegel	2006 <sup>62</sup>	134	6	6 mo	x	x	x	x	x			x					Software + Nurse	A
Stromberg	2003 <sup>64</sup>	106	12	1 y	x	x	x	x							x		Nurse	A
DeBusk	2004 <sup>54</sup>	262	12	1 y	x	x	x	x	x	x	x	x					Nurse	B
Ducharme	2005 <sup>56</sup>	230	6	6 mo	x		x	x		x		x				x	Nurse+Cardiologist	B
Benatar	2003 <sup>51</sup>	216	12	6 mo	x				x					x			Nurse	B
Meijert	2004 <sup>60</sup>	208	18	ind	x	x	x	x		x							Nurse	B
Blue	2001 <sup>52</sup>	165	12	1 y	x	x	x	x	x					x			Nurse (S)	B
Ekman	1998 <sup>57</sup>	160	6	6 mo	x	x	x	x		x			x				Nurse (S)	B
Krumholz	2002 <sup>59</sup>	88	12	1 y	x	x					x						Nurse (S)	B
Riegel	2002 <sup>14</sup>	358	ND	6 mo	x	x	x	x	x			x					Software + Nurse	C
Doughty	2002 <sup>55</sup>	197	12	1 y	x	x	x	x	x						x		GP+Nurse	C
Wierchowicki	2006 <sup>66</sup>	160	12	1 y	x	x	x	x	x			x		x		x	MDC staff	C
Capomolla	2004 <sup>53</sup>	133	12	1 y	x	x	x	x				x	x	x			Nurse	C
Thompson	2005 <sup>65</sup>	106	6	6 mo	x	x	x	x							x	x	Nurse (S)	C
Morcillo	2005 <sup>61</sup>	70	6	6 mo	x	x	x	x		x							Nurse	C
Jerant	2001 <sup>58</sup>	37	6	6 mo	x	x	x	x	x			x		x	x		Nurse	C

Mo, Months ; N, Total number; Nurse (S), heart failure specialist nurse; wk, week; y, year

1. When specified nurse; these studies were unclear to whether the nurse had any training in HF care.

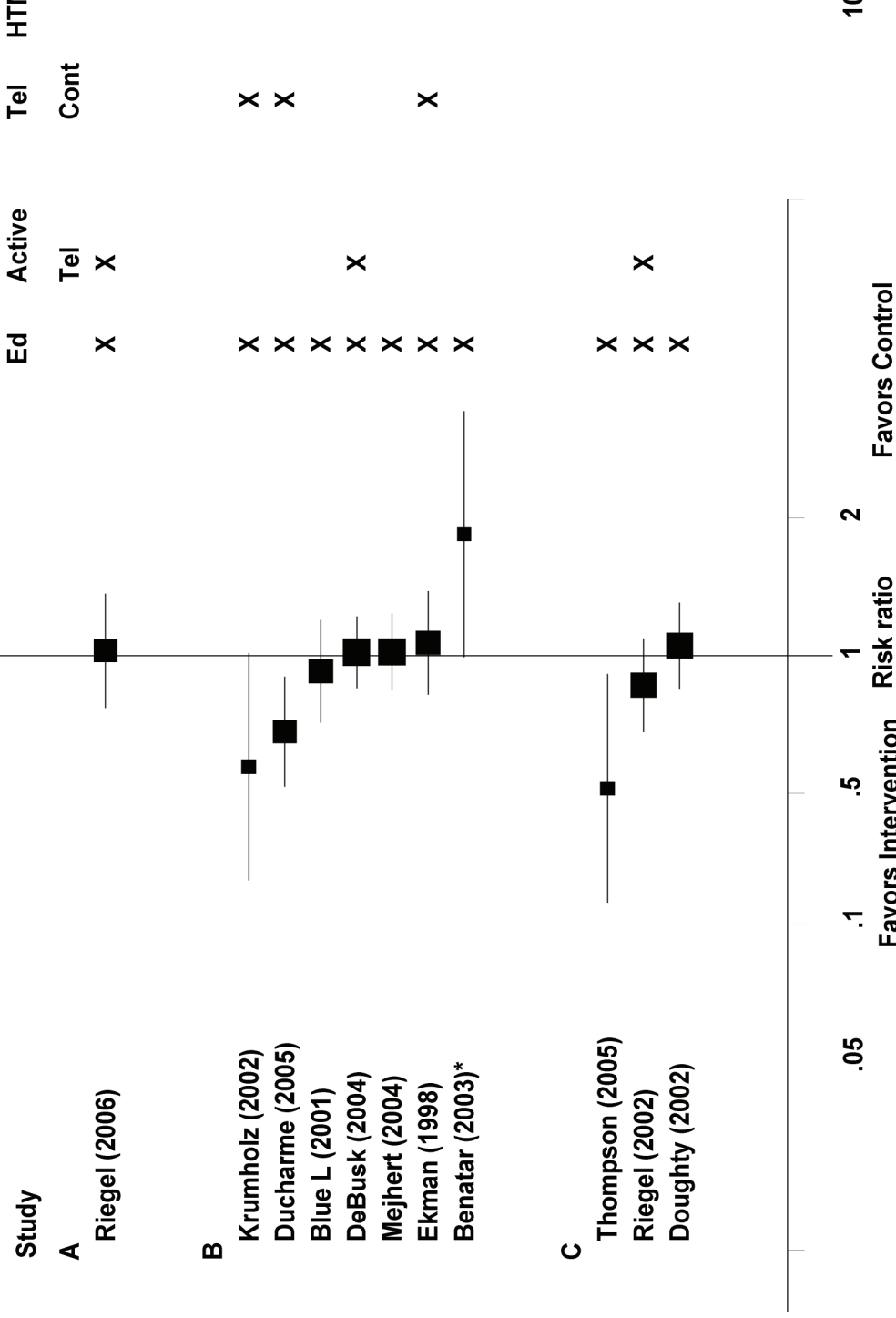
Author Year	Intervention			Mortality			Readmitted patients			LOS			QOL			
	Country	Study y	Duration (mo)	N	Control	RR (95% CI)	%Event Control	RR (95% CI)	RR (95% CI)	Mea n diff (SE)	Score	P-value	Quality	Mea n diff	P-value	Quality
Holland 2007 <sup>18</sup>	UK	2003-2005	6	293	17	1.21 (0.74, 1.96)	nd	nd	nd	MLHF↓	+3.40	ns	A			
Stewart 1999 <sup>63</sup>	Australia	1997-1998	6	200	28	0.64 (0.38, 1.09)	nd	nd	nd				A			
Riegel 2006 <sup>62</sup>	USA	2002-2004	6	134	nd	57	1.03 (0.77, 1.37)	57	1.03 (0.77, 1.37)	+1.1 (1.6)			A			
Stromberg 2003 <sup>64</sup>	Sweden	1997-1999	12	106	37	<b>0.36 (0.17, 0.79)</b>	nd	nd	nd	-2.5 (nd)			A			
DeBusk 2004 <sup>54</sup>	USA	1998-2000	12	262	12	0.74 (0.44, 1.26)	50	50	1.02 (0.85, 1.22)				B			
Ducharme 2005 <sup>56</sup>	Canada	1998-2000	6	230	17	0.63 (0.32, 1.24)	57	57	<b>0.68 (0.52, 0.90)</b>	MLHF↓	nd	ns	B			
Benatar 2003 <sup>a51</sup>	USA	1997-2000	12	216	nd	12	1.85 (0.99, 3.43)	12	1.85 (0.99, 3.43)	MLHF↓	+6.83	ns	B			
Mejhert 2004 <sup>60</sup>	Sweden	1996-1999	18	208	32	1.2 (0.83, 1.73)	66	66	1.02 (0.84, 1.24)	-0.4 (nd)	NHP↓	-8.0	B			
Blue 2001 <sup>52</sup>	UK	1997-1998	12	165	7	0.16 (0.02, 1.31)	60	60	0.93 (0.71, 1.20)	-6.4 (3.4)			B			
Ekman 1998 <sup>57</sup>	Sweden	1994-1996	6	160	28	0.96 (0.57, 1.59)	57	57	1.07 (0.82, 1.39)	-8 (4.1)			B			
Krumholz 2002 <sup>59</sup>	USA	1997-1998	12	88	30	0.69 (0.33, 1.45)	48	48	0.57 (0.32, 1.01)	-5 (3.7)			B			
Riegel 2002 <sup>14</sup>	USA	nd	6	358	nd	50	0.86 (0.68, 1.09)	50	0.86 (0.68, 1.09)	-1.3 (0.8)			C			
Doughty 2002 <sup>55</sup>	NZ	1997-1998	12	197	nd	61	1.05 (0.85, 1.31)	61	1.05 (0.85, 1.31)				C			
Wierchowicki 2006 <sup>66</sup>	Poland	nd	12	160	5	0.75 (0.17, 3.24)	nd	nd	nd	-3.2	MLHF↓	-15	C			
Capomolla 2004 <sup>53</sup>	Italy	2000-2001	12	133	11	0.7 (0.24, 2.11)	nd	nd	nd				C			

**Results**

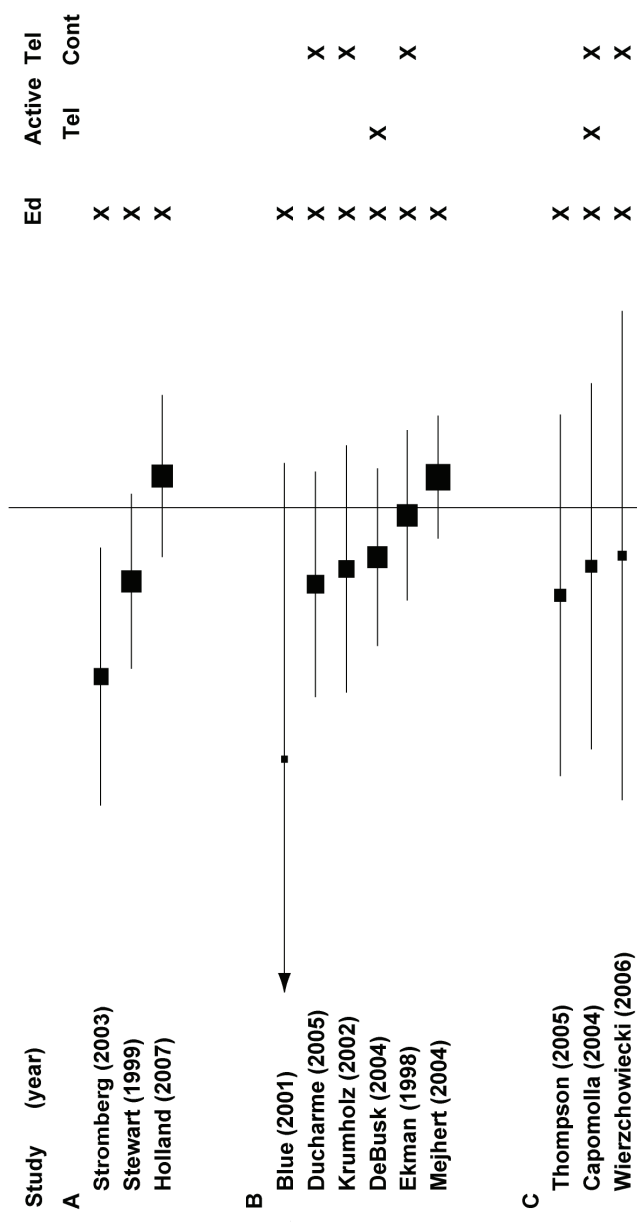
Author Year	Country	Intervention		Mortality		Readmission		LOS (d)	QOL
		Year	Duration (mo)	% Even Control	RR (95% CI)	% Even Control	RR (95% CI)		
Thompson 2005 <sup>65</sup>	UK	nd	6	106	15	0.59 (0.20, 1.74)	44	0.51 (0.29, 0.91)	MLHF $\downarrow$ +1.20 ns
Morcillo 2005 <sup>61</sup>	Spain	2001-2002	6	70	nd	nd	nd	SF36 $\uparrow$ +14.2 ns	C
Jerant 2001 <sup>68</sup>	USA	1999-2000	6	37	0	5% in home telecare	nd	-5.2 (5.3)	C

CI, confidence interval; HFQ, Chronic Heart Failure Questionnaire; Ctrl, control; d, days; diff, difference; Int, intervention; LOS, length of stay; mo, month; MLHF, Minnesota Living with Heart Failure; m, mental score; mo, Months; N, number; nd, not documented; NHP, Nottingham health profile; ns, not significant; p, physical score; QOL, quality of life; RR, rate ratio; SE, standard error; SF, Short form; wk, week; y, year;  $\downarrow$  Lower score indicates improved function;  $\uparrow$  Higher score indicates better function

interventions after discharge compared with the usual care group.



Ed, one or more of the educational component; HTM, home telemonitor; MDC, multidisciplinary care; Active Tel, active telephone followup; Tel cont, Telephone contact; \* Home visits versus nurse telesupport



Ed, one or more of the educational component; HTM, home telemonitor; MDC, multidisciplinary care; Active Tel, active telephone followup; Tel cont, Telephone contact





## Interventions in the outpatient clinics

We identified six RCTs with a total of 2,654 patients that assessed the effectiveness of interventions among HF patients in the outpatient clinics (Table 4).<sup>13, 67-71</sup> Patients were recruited during their visits to the outpatient clinics, including specialist HF clinics, registered in the national multi-center HF registry, general medicine or geriatric clinics, and academic primary care group practice. In addition, a proportion of patients were recruited from their inpatient setting in two trials.<sup>67, 71</sup> Five trials compared interventions versus usual care.<sup>67-71</sup> One trial also utilized some components from the usual care in the intervention group.<sup>13</sup> Four trials included interventions led by a pharmacist,<sup>67-69, 71</sup> and two trials were led by nurses.<sup>13, 70</sup> Five studies included interventions to educate patients about HF symptoms and disease management,<sup>13, 68-71</sup> and one study utilized only medication review as an intervention.<sup>67</sup> The studies also evaluated interventions that included education about diet and sodium restriction, self-care behaviors, exercise, and daily weight monitoring. Three studies emphasized interventions on active telephone followup. The studies did not utilize additional interventions to followup HF patients that included home telemonitor, multiple home visits, increased clinic visits, and multidisciplinary care. The description of usual care varied among the studies. The durations of interventions ranged from 6 to 12 months in four studies and were not documented in two studies.

The studies followed patients from 6 to 16 months. The patients in the intervention group had their followup in a clinic managed by a nurse under the supervision of a cardiologist or a physician or in outpatient pharmacies. The primary care physicians and/or physician assistant or nurse practitioner managed the patients in the usual care group. Two studies were single-center,

and four were multi-center. The studies mostly included patients with a mean age of 60 years and above. Three trials were conducted in the US, two trials in European countries, and one trial in Argentina. There were three good (A),<sup>13, 68, 70</sup> two fair (B),<sup>67, 69</sup> and one poor (C)<sup>71</sup> quality studies. The poor quality study had errors in reporting, and lacked clear reporting of randomization methods and baseline data.

The severity of HF, LVEF and distribution of NYHA class among included patients varied across studies. All studies restricted the recruitment of patients to those who were ambulant. The most commonly reported etiology of HF and/or coexisting medical disease was ischemic heart disease.

Data on available clinical outcomes included mortality in five studies,<sup>13, 67, 68, 70, 71</sup> number of readmissions in four studies,<sup>67, 69-71</sup> cost incurred in one study, QOL changes in four studies,<sup>13, 67, 70, 71</sup> and composite end point of mortality or readmissions in two studies.<sup>13, 67</sup> No study reported length of hospital stay during readmissions.

## **Mortality**

Five studies that began an intervention in the outpatient clinics reported mortality rates in the intervention group ranging from 3 percent to 17 percent (Table 4a).<sup>13, 67, 68, 70, 71</sup> The mortality rates in the control or the usual care group ranged from 5 percent to 21 percent over the study duration. The studies reported a non-significantly decreased relative risk of mortality in the intervention group when compared with usual care group (Figure 7).

## **Readmissions**

Four studies reported data on the number of all cause readmissions that included the number of all cause readmissions and/or patients readmitted (i.e., with at least one readmission) (Table 4a).<sup>67, 69-71</sup> Three studies that followed patients for 6 months to 1-year reported a total of 189

readmissions in 319 patients in the intervention group, compared with 249 readmissions in 322 patients in the usual care group.<sup>67, 70, 71</sup> One other study reported data on mean readmissions per patient.<sup>69</sup> Only one study reported a significantly decreased number of readmissions in the intervention group compared with the usual care group.<sup>71</sup> This single-center study was conducted in Ireland, recruited less than 50 patients per group, had 1-year of followup, and was graded poor (C) quality. A pharmacist led the followup interventions in this study that emphasized disease symptoms and management, self-care behaviors, weight monitoring, and medication review.<sup>71</sup>

Two studies reported non-significantly decreased rates of readmitted patients in the intervention group (31 percent and 34 percent) compared with usual care group (36 percent and 39 percent) (Figure 8).<sup>13, 70</sup>

### **Quality of life**

Four studies provided data on the patient perceived health status using one or more validated QOL instruments — MLHF and SF-36 (Table 4a.).<sup>13, 67, 70, 71</sup> Two of the four studies reported significantly improved QOL scores in the intervention group at followup.<sup>13, 70</sup> Both were multi-center studies, graded good (A) quality, utilized nurse education with active telephone followup, and followed patients for 1 to 1.4 years. Both studies reported statistically significantly improved QOL in the intervention group compared with the usual care group. Sisk reported significantly improved self-assessed scores of MLHF (38.6 versus 47.3,  $P<0.05$ ), and higher SF-12 physical scores (39.9 versus 36.3,  $P<0.05$ ).<sup>70</sup> The DIAL trial reported significantly improved scores of MLHF during followup in the intervention group compared with the usual care group (30.6 versus 35,  $P=0.001$ ).<sup>13</sup>

## **Costs**

One study reported quantitative data on the total costs incurred in the intervention group compared with the control group (Appendix C).<sup>69</sup> This pharmacist-led medication review intervention study reported lower total costs in the intervention group (–\$2960 per patient) compared with the usual care.<sup>69</sup> The multi-center study conducted in the US was graded fair (B) quality and followed more than 300 patients for up to 1-year.

## **Composite outcome of mortality or readmission**

Two studies reported data on the combined endpoint of mortality or readmission (Appendix C).<sup>13, 67</sup> Of these, the DIAL trial reported combined endpoint of mortality or readmission as their primary outcome and noted statistically significantly decreased relative risk in the intervention group compared with the usual care group. The trial was conducted in Argentina and randomized 1,518 outpatients with stable HF to an active telephone followup or usual care. The study reported a significant relative risk reduction of 20% (95% confidence interval 3 to 34).<sup>13</sup>

## **Summary of evidence**

- A limited number of studies evaluated interventions beginning in the outpatient clinics.
- Studies compared different combinations of intervention components with usual care.
- The majority of the studies utilized a pharmacist-led intervention that mostly included medication review.
- Across studies, there was considerable heterogeneity with regard to individual components of intervention, duration of intervention.
- The data does not support any firm conclusions with regard to superiority of any particular intervention strategy.

patients

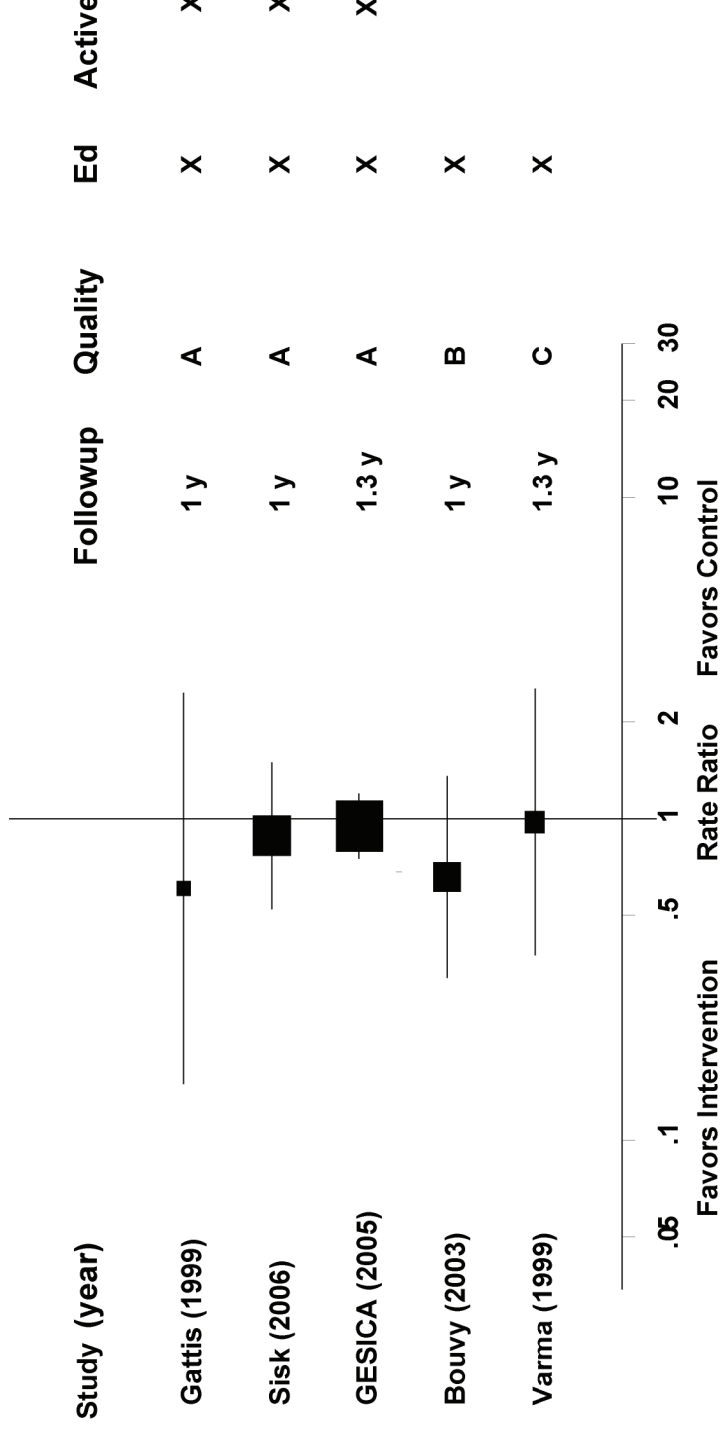
<u>Study characteristics</u>		<u>Education components</u>										<u>Increased access to providers</u>				
<u>Author</u>	<u>Year</u>	<u>N</u>	<u>Intervention duration (mo)</u>	<u>Education about HF</u>	<u>Self management</u>	<u>Weight monitoring</u>	<u>Sodium restriction / diet advice</u>	<u>Exercise motivation</u>	<u>Medication review</u>	<u>Education reinforcement</u>	<u>Active telephone</u>	<u>Telephone on demand</u>	<u>Home telemonitor</u>	<u>Home visits</u>	<u>Increased clinic visits</u>	
GESICA 2005 <sup>63</sup>		1518	nd	x	x	x	x	x	x		x					
Sisk 2006 <sup>70</sup>		406	12	x	x	x	x	x			x					
Gattis 1999 <sup>68</sup>		181	6	x					x						x	
Murray 2007 <sup>69</sup>		314	9	x					x							
Bouvy 2003 <sup>67</sup>		152	6						x							
Varma 1999 <sup>71</sup>		83	nd	x	x	x			x							

N, Total number of patients

**Results**

Intervention		Mortality		Readmitted patients		LOS		QOL					
Author	Year	Countr y	Study y	Followup Duration (mo)	N	%Control group	RR (95% CI)	%Control group	RR (95% CI)	RR Mea n diff (SE)	LOS (d)	Mea n diff P- valu e	Quality y
GESICA	2005 <sup>13</sup>	1518	2000-01	16	1518	16	0.95 (0.75, 1.20)	39	0.88 (0.77, 1.0)	nd	MLHF↓0.001	-4.4	A
Sisk	2006 <sup>70</sup>	406	2000-02	12	406	13	0.89 (0.52, 1.50)	37	0.84 (0.64, 1.10)	nd	MLHF↓ <0.05 SF12p +3.2	-8.7	A
Gattis	1999 <sup>68</sup>	181	1996-97	12	181	5	0.61 (0.15, 2.46)	nd	nd	nd	nd	nd	A
Murray	2007 <sup>69</sup>	314	2001-04	6	314	nd	0.66 (0.32, 1.36)	nd	0.98 (0.38, 2.54)	nd	MLHF↓	+6.8	B
Bouvy	2003 <sup>67</sup>	152	1998-00	12	152	21	0.98 (0.38, 2.54)	nd	0.98 (0.38, 2.54)	nd	MLHF↓	-3.0	B
Varma	1999 <sup>71</sup>	83	nd	16	83	17	0.98 (0.38, 2.54)	nd	0.98 (0.38, 2.54)	nd	MLHF↓	ns	C

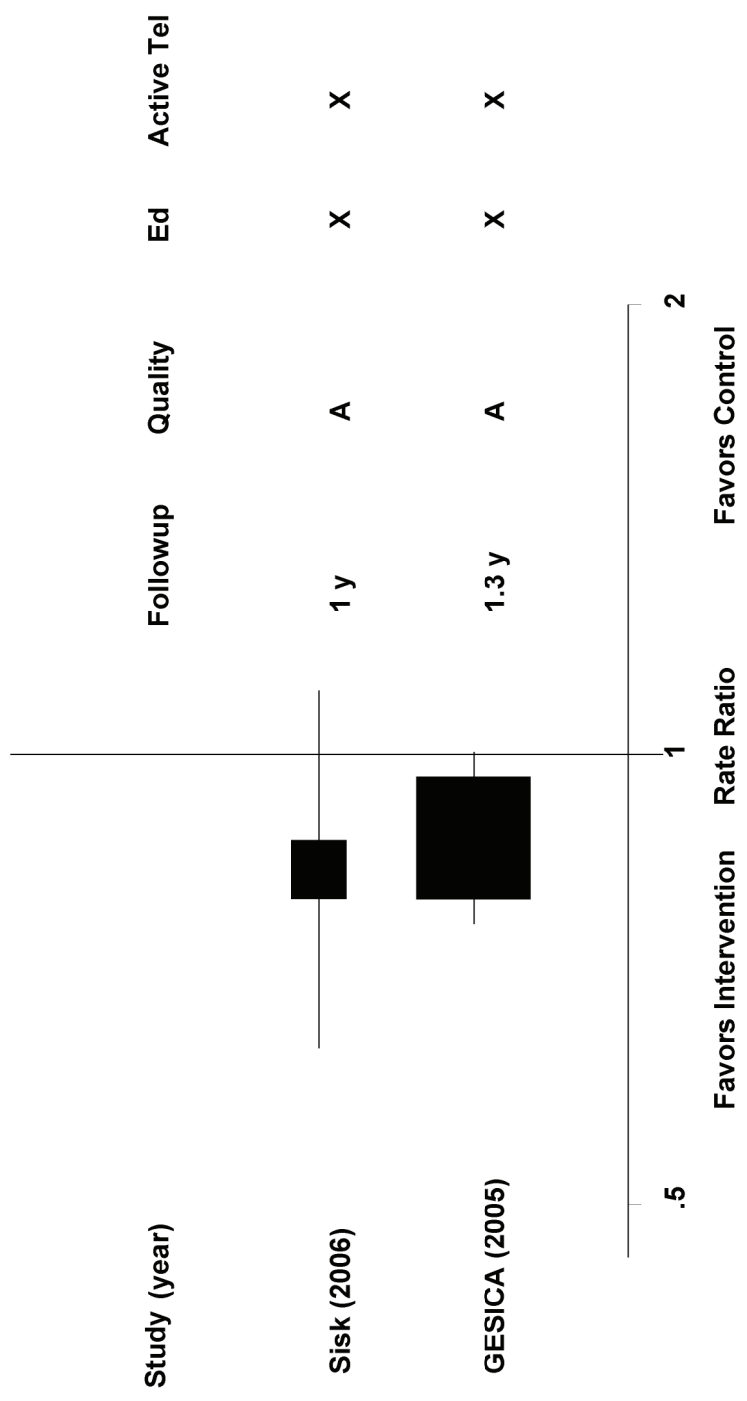
CI, confidence interval; Ctrl, control; d, days; diff, difference; Int, intervention; LOS, length of stay; mo, month; MLHF, Minnesota Living with Heart Failure; m, mental score; N, number; nd, not documented; ns, not significant; p, physical score; QOL, quality of life; RR, rate ratio; SE, standard error; SF, Short form; wk, week; y, year; ↓ Lower score indicates improved function; ↑ Higher score indicates better function



Ed, one or more of the education component; Active Tel, Active telephone followup; y, year



usual care group.<sup>b</sup>



## Review of recent published systematic reviews

At least seven systematic reviews and/or meta-analyses have been published since 2004 that reported comprehensive data relevant to the present review.<sup>12, 20-25</sup> Because of the span of publication years and variations in the eligibility criteria, the number of studies included in each systematic review ranged from 16 studies involving 1,627 patients (Taylor 2005<sup>12</sup>), to 30 studies involving 8,158 patients (Holland 2005<sup>22</sup>). In majority of these systematic reviews, with the exception of Gonseth 2004<sup>21</sup> and Roccaforte 2005,<sup>25</sup> the results were stratified according to either the intervention type or categories of organizational type of post-discharge support.

McAlister 2004 found that the strategies that incorporated followup by a specialized multidisciplinary team (either in a clinic or non-clinic setting) reduced mortality, HF hospitalizations, and all-cause hospitalizations.<sup>23</sup> Interventions that focused on enhancing self-care activities reduced hospitalizations but had no effect on mortality. Telephone followup that advised patients to seek care by their primary care physician in the event of deterioration reduced hospitalization for HF but did not reduce mortality.

Gonseth 2004 reported that strategies within disease management programs, regardless of the type of organizational delivery, whether they were home-based or clinic-based, reduced readmissions for HF and all cause readmissions.<sup>21</sup> This review included both randomized and non-randomized studies and reported that the disease management programs also reduced the frequency of the combined endpoint of re-admission or death among HF patients.

Phillips 2004 studied only strategies with comprehensive discharge planning that included post-discharge support.<sup>24</sup> Each type of support resulted in significantly fewer readmissions except for the strategy of increased clinic visits and frequent telephone contact. However,

overall, Phillips found that such strategies for older patients with HF resulted in 25% relative reduction in the risk of readmission, a trend toward 12% relative reduction in all-cause mortality and for a smaller subset of studies, improvement in QOL scores, and no increase in the cost of medical care. In a later meta-regression analysis, Phillips 2005 found that “complex programs” that included hospital discharge planning and no delay in post-discharge clinical followup showed a trend toward 70% reduction in risk for first readmission, two fewer days utilized per patient per readmission, and a 70% reduction in risk of HF readmission compared to usual care.<sup>11</sup> Less complex programs without hospital discharge planning resulted in less than half the effect in reduction of risk of HF readmission.

A Cochrane systematic review published in 2005 (Taylor 2005) concluded that there was weak evidence that case management interventions are associated with a reduction in admissions for HF, and that it was unclear which components of case management interventions are effective.<sup>12</sup>

In another systematic review published in 2005, Roccaforte reported that mortality and all-cause and HF-related hospitalizations were significantly reduced by interventions to manage HF.<sup>25</sup> This review found that high quality studies and programs lasting 3 to 6 months were those most consistently associated with a significant reduction in all outcomes considered. However, a subsequently published RCT, which compared interventions for 3 month with extended 6 month, found no measured clinical advantage in terms of death and/or HF readmission in extending a structured hospital-based disease management program beyond 3 months of discharge.<sup>40</sup>

In a systematic review on remote telemonitoring programs for HF patients, Clark 2007 found that remote monitoring programs for patients with HF reduced admissions to the hospital and all cause mortality by nearly 20 percent while improving health-related quality of life, but had no

significant effect on all cause admission to the hospital. Clark 2007 determined that telemonitoring may be more effective at shortening hospital stay than in reducing admissions, since it is likely to produce false alarms and preemptive admissions in patients who are deteriorating but not yet in crisis.<sup>20</sup> Moreover, telemonitoring may also lead to early discharge because the patient has a high level of monitoring at home. Clark builds on earlier systematic reviews by McAlister 2004 and Phillips 2004 on multidisciplinary interventions by examining uncertainties relating to the specific effect of telephone-based programs.

The systematic review by Holland 2005 aimed to determine the impact of select intervention components delivered at specific sites on the outcomes.<sup>22</sup> The investigators were interested in the relative merits of the site of care, whether the care was delivered in the home (home visits), by telemonitoring, by telephone, in the clinic, or in the primary care physician's office. Meta-analysis showed a significant reduction in all cause readmission, though significant heterogeneity was present. Subgroup analysis showed that home visits reduced all cause readmission to the hospital, but specialty clinic-based interventions had no effect on readmission. Meta-analysis showed a significant reduction in HF readmission, which was notable and similar for home- and telephone-type interventions. Meta-analysis also showed a significant decrease in all cause mortality, especially in the telemonitoring and telephone followup interventions.

## Conclusions

Living with HF is a challenge to the sufferers of this condition. It also represents a significant burden for the caregivers. The effective management of HF is achieved through optimal medical therapy. In addition, current emphasis has been geared toward a comprehensive and proactive support for self-management utilizing delivery models before, during, and after hospitalizations. These self-management models use multiple intervention components of comprehensive patient education, self care behaviors, medication review, proactive nurse followup, and increased access to providers.

This report identified 49 randomized controlled trials that evaluated interventions utilizing various combinations of individual components initiated in three different settings. We included studies published since 1990 — the time point associated with rapid advances in the medical management of HF, and changing health needs of the patients and changes in the practice patterns. The majority of the included studies reported readmissions as the primary outcome of interest. A few studies also evaluated combined endpoint of readmissions or death as the primary outcome of interest. In general, studies were not adequately powered to evaluate the clinical outcome of mortality. We performed meta-analysis and subgroup analyses to address the key question of the effectiveness of interventions of post-discharge support to prevent readmissions. Our report used lax inclusion criteria, thereby reviewing a large body of literature. We identified those interventions that utilized increased clinic visits, home visits, and multidisciplinary care to reduce the risk of readmissions in the intervention group compared with the usual care group. Often these interventions utilized a combination of secondary components, with telephone followup being the most common across the studies; however, when telephone followup was

utilized alone, it did not demonstrate a significant difference in all cause readmissions compared with usual care.

In our subgroup analyses, the characteristics of intermediate- to long-term followup (>6 month and >12 month), interventions initiated in the inpatient setting, and patient age greater than 75 years had a statistically significant impact on the all cause readmissions in the intervention group. Inpatient setting benefits may be explained due to better transition care from the inpatient to home care in the intervention group. Generally studies did not report adequate information about the transition of care coordination in the usual care group. Improvements with longer followup suggest increased compliance and motivation.

Compared to usual care, one-quarter of the 20 studies reported a significant reduction in all-cause mortality when interventions were initiated during an index hospitalization. Similar significantly decreased length of stay during readmissions was reported when interventions were initiated during an index hospitalization. Individual studies were not adequately powered to ascertain meaningful differences between the interventions and usual care groups for mortality outcomes; however, there was no distinct combination of intervention components and improved outcomes of QOL changes, and miscellaneous clinical outcomes (costs, and composite endpoint of mortality or readmission).

Eighteen randomized controlled trials compared self-management delivery models beginning after discharge from an index hospitalization. Only one of 18 studies suggested decreased event rates in mortality, readmissions, and reduction in length of hospital stay during readmissions with interventions. Also, the evidence was sparse for interventions beginning in the outpatient clinics.

The studies were heterogeneous with regard to intervention components, intervention duration, followup duration, and components of usual care. In addition, some studies utilized components of usual care along with their intervention components. The studies were performed in a range of settings, in patients with a wide range of HF severity, across various countries, over a long time period during which the standards of HF care have changed considerably, and in patients with different underlying risks of clinical events. Studies often utilized several different combinations of intervention components, resulting in considerable heterogeneity that was difficult to dissect and ascertain the effects of individual components.

The consistency of results in the settings of diverse studies adds credibility to the conclusion that patient outcomes can be improved with optimized transition of care coordination between the inpatient settings to home care, and a combination of interventions that increase access to providers. However, there was no easily discernable pattern based on a particular intervention component, time period (year), intervention duration, and specific coexisting medical illnesses. Across studies, similar rates of coexisting medical illnesses, and proportions of patients who received ACE inhibitors, beta-blockers, and/or diuretics were reported at baseline among patients in the intervention and control group. Of note, no studies evaluated or provided data on adverse effects due to the interventions.

Additional limitations of the studies include small sample size and short followup durations, and a substantial number of the studies reported a composite endpoint of mortality or readmission as their primary outcome. It is well-acknowledged that the use of a composite endpoint can erroneously attribute reductions in mortality to interventions that do not actually reduce deaths.<sup>72</sup> The relative effectiveness of the individual components of interventions remains unknown, since none of the studies compared one intervention component with each other. This

lack of clarity on the necessary combination of components of a HF management program may be answered by the future publications. Future research with long-term followup is needed to determine which individual components, if any, in what settings and circumstances, may benefit. A determination should be made as to which patients are most likely to benefit from which combinations of intervention components, and then studies focused on these patients should be conducted. Any future studies should continue to focus primarily on clinical benefits, as short-term intermediate outcomes or composite endpoints are inadequate surrogates for clinically important outcomes.



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# Search strategy

#Search History	Results
1 discharge planning.mp. or exp Patient Discharge/	32632
2 case management.mp. or exp Patient Care Planning/ or exp Case Management/	92238
3 patient readmission.mp.	9266
4 Aftercare/	12568
5 Continuity of Patient Care/	20217
6 Patient Transfer/	8094
7 Post discharg\$.tw.	2180
8 Postdischarg\$.tw.	2738
9 Post hospital\$.tw.	1061
10 Posthospital\$.tw.	1047
11Predischarg\$.tw.	1810
12 Pre discharg\$.tw.	496
13 Patient\$ discharg\$.tw.	7039
14Discharg\$.ti.	24270
15 ((readmission\$ or early or premature or care or medication or destination or decision or decid\$ or support\$ or prepar\$ or process\$ or plan\$ or system\$) adj6 discharg\$.tw.	25564
16 or/1-15	194133
17 exp Heart Failure, Congestive/ or exp Cardiac Output, Low/ or Heart failure.mp.	167913
18 16 and 17	3660
19 limit 18 to english language	3394
20 limit 19 to "all adult (19 plus years)"	2544
21 randomized controlled trial.pt.	688706
22 controlled clinical trial.pt.	221479
23 Randomized controlled trials/	125964
24 random allocation/	112192
25 double-blind method/	252902
26 single-blind method/	27409
27 clinical trial.pt.	157319
28 (random\$ or rct).tw.	900347
29 controlled clinical trials/	39157
30 (clin\$ adj trial\$.tw.	222839
31 ((singl\$ or doubl\$ or trebl\$ or Tripl\$) adj (blind\$ or mask\$)).tw.	275580
32 exp PLACEBOS/	70143
33 placebo\$.tw.	288743
34 cross-over studies/	53318
35 evaluation studies/	214252
36 or/21-35	2048057
37 20 and 36	684
38 animal/ not (animal/ and human/)	3078777
39 37 not 38	684
40 limit 39 to comment and (letter or editorial).pt.	1
41 limit 39 to (addresses or bibliography or biography or case	

reports or congresses or consensus development conference or  
 consensus development conference, nih or dictionary or directory  
 or  
 editorial or festschrift or government publications or interview or  
 lectures or legal cases or legislation or news or newspaper article  
 or patient education handout or periodical index) 9  
 42 39 not (40 or 41) 674  
 43 limit 42 to (guideline or meta analysis or practice guideline or  
 "review") 30  
 44 42 not 43644  
 45 limit 44 to yr=1990-2007 615  
 46 remove duplicates from 45  
 273

Discharge Plan data extraction/summary tables

Study Year			
UI number			
<b>Methods</b>			
Study design description			
Randomization method			
Allocation concealment			
Blinding			
Number of centers			
Recruitment years			
Duration of followup			
<b>Participants</b>			
Country			
Study inclusion criteria			
Study exclusion criteria			
	<b>Overall</b>	<b>Intervention</b>	<b>Controls</b>
N randomized			
Mean age (SD) y			
Males %			
Race / Ethnicity %			
Severity of heart failure (at index admission)		NYHA: LVEF%:	NYHA: LVEF%:
Severity of heart failure (at baseline)		NYHA: LVEF%:	NYHA: LVEF%:
Duration of CHF			
History - Myocardial infarction			
History of other CVD disease			
ACE inhibitor use			
B-blockers			
Diuretics			
Other medications			
<b>Interventions</b>			
Duration of intervention			
Intervention group name			
Description of intervention			
<i>During index hospitalization</i>			
<i>After discharge</i>			
Description of comparator			
Followup times			
<b>Statistical Analyses</b>			
Intention to treat			
Adjusted analyses			
<b>Outcomes description</b>			
Primary endpoint (with definition)			
Secondary endpoint (with definition)			
<b>Notes</b>			
Rationale for sample size			
Reasons for exclusion			
List biases			
Funding source			
Is there any difference between groups at baseline			

Discharge Plan data extraction/summary tables

APPLICABILITY		QUALITY	
	<b>Wide Applicability:</b> sample representative of Medicare population in relevant setting. Patient's age (older adult), gender, spectrum of disease severity and type, etc are representative of population of interest.		<b>A Good quality:</b> Prospective, no obvious biases or reporting errors, <20% dropout, complete reporting of data.
	<b>Moderate Applicability:</b> sample is an important sub-group of population of interest. Possibly limited to a narrow or young age range, type of disease, gender etc.		<b>B Fair quality:</b> Problems with study/paper unlikely to cause major bias..
	<b>Narrow Applicability:</b> sample represents only a narrow, atypical subgroup of population of interest, or old study.		<b>C Poor quality:</b> Cannot exclude possible significant biases. Poor methods, incomplete data, reporting errors.
<b>If applicability is graded <u>narrow</u> or <u>moderate</u>, what are the limiting factors?</b>		<b>If Quality is rated B or C, what are the limiting factors? (i.e., incomplete data, errors in analysis, definitions not clear, poor follow-up, dropouts)</b>	



**SUMMARY TABLE TEMPLATES**

**Randomized Controlled Studies (Intervention vs. Control), For event rates**

Population recruited:

Outcome	Study, Year Country	Followup Duration (Intervention y)	No. Analyzed		Control Used	Severity of CHF	Intervention components	Event Rate		Net change	P within	P Between	Quality
			Interv	Control				Interv	Control				

**Randomized Controlled Studies (Intervention vs. Control), For continuous measures or that provide odds/risk ratio**

Population recruited:

Outcome	Study, Year Country	Followup Duration (Intervention y)	No. Analyzed		Control Used	Severity of CHF	Intervention components	Baseline	Results/Final			Quality	
			Interv	Control					Metric/ Units	Interv	Control		P Between

Text results:

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**Appendix Table B1. Interventions on recruited patients inpatient**

Study, Year, Country	Followup Duration (Intervention y)	Total N Analyzed	Mean Age/% Male	Severity of CHF	Intervention components	Control Description	Quality Applicability
Atienza 2004 Ojeda 2005 Spain	1.4y (1999-2000)	338	69/ 62%	NYHA III/IV 50% LVEF% 36	Cardiologist led education on disease management and reinforcement; individual strategies to self-care, medication compliance telephone followup; heartclinic visit every 3 mo	Received discharge planning with routine hospital protocol and followed by PCP and cardiologists not participating in the study	A Mod
Barth, 2001 USA	3 mo	34	78/ 59%	NYHA: nd LVEF%: nd	At the time of discharge as per the hospital procedure, routine discharge teaching by the hospital nursing staff included instructions on activity, diet, activities of daily living, medication, follow up appointments and when to contact the physician. Nurse led telephone reinforcement of the education on daily weight assessment, CHF symptoms, fluid and salt intake, and medication adherence. Made phone contact for first 72 hrs post discharge and 72 hrs later and then every 2 weeks for 3 mo	Routine care: received only the routine discharge teaching at the time of discharge (as described in the intervention arm)	C Nar
Capomolla 2002 Italy	12 mo (1999-2000)	234	57/ 93%	NYHA III/IV 35% LVEF% 29	Multidisciplinary interventions including cardiovascular risk stratification, tailored therapy, physical training, counseling, checking clinical stability, correction of risk factors for hemodynamic instability, and health care educationA	At discharge patients were referred to their community primary care physician and cardiologists or cardiology dept	B Mod
Cleland, 2005 EU	7-8 mo (2000-2002)	333	67/ 72%	NYHA III/IV 31% LVEF <25% = 48%	Home telemonitoring with electronic weighing scales; an automated sphygmomanometer; single lead ECG and Nurses telephone support	Management plan sent to primary care physician who implemented it Usual care + Nurses telesupport	B Wide
Cleland, 2005 EU	7-8 mo (2000-2002)	248	67/ 72%	NYHA III/IV 31% LVEF <25% = 48%	Home telemonitoring with electronic weighing scales; an automated sphygmomanometer; single lead ECG and Nurses telephone support	Management plan sent to primary care physician who implemented it	B Wide
Cline, 1998 Sweden	12 mo (1991-1993)	190	76/ 53%	NYHA 2.6 LVEF mean 31.6%	Patients received an education programmed from HF nurse consisting of two 30-minute visits. 2 weeks after discharge patients and their families were invited to a one-hour group education	Followed up at the outpatient clinic in the department of cardiology by either cardiologists in private practice or by	C Mod

Study, Year, Country	Followup Duration (Intervention y)	Total N Analyzed	Mean Age/% Male	Severity of CHF	Intervention components	Control Description	Quality Applicability
					session led by the HF nurse. Patients were also offered a 7 day medication dispenser if deemed appropriate. Patients were followed up at a nurse directed o/p clinic and there was a single prescheduled visit by the nurse at 8 mo. after discharge. Patients encouraged contacting the study nurse at their discretion, if unsure, if diuretic adjustments did not ameliorate symptoms in 2-3 d, or if there were "profound changes in self management variables." Patients were offered cardiology outpatient visits 1 and 4 months after discharge.	primary care physicians as considered appropriate by the discharging consultant.	
Del Sindaco, 2007 USA	2 y (2001-2002)	236	77/51%	NYHA: II 32 (37.2%), III 44 (51.2%), IV 10 (11.6%) LVEF%: mean 33.5 ± 11	Managed by a cardiologist, two to four nurses and patient's primary care physician. 1) According to the guidelines components were discharge planning, continuing education, therapy optimization, improved communication with healthcare providers, early notice to signs and symptoms, and flexible diuretic regimen. 1. Nurses home phone calls 2. Visit with a primary care physician 1 to 2 weeks of discharge including reinforcement of education and optimization of therapy.	Usual care: all treatments and services ordered by their primary care physician and/or personal cardiologist Vital status and events were recorded by means of phone calls every 6 mo	A Wide
Dunagan, 2005 USA	6 mo (1999)	151	76/41%	NYHA: 78% LVEF% <40%: 74%	Nurse led education intervention, promotion of self management skills, appropriate diet and adherence to prescribed meds and telephone followup + Usual care	Usual care as provided by primary physician who provided educational packets at the time of hospitalization	C Wide
Goldberg, 2003 US	6 mo (1998-2000)	280	58/70	NYHA III/IV 100% LVEF% <21%	Nurse led education about heart failure, including advice on daily weights, dietary restrictions including sodium and fluid, and signs and symptoms of heart failure decompensation, increased communication with providers encouraged, Technology-based telephone HF monitoring (AlereNe monitoring using the DayLink monitor)	Standard outpatient heart failure therapy in dedicated heart failure program. This included additional nursing resources.	B Wide
Harrison, 2002	12 wk (1996-1998)	192	76/55%	NYHA III/IV: 77%	Comprehensive, evidence based education programmed for heart failure self-	Ideally a multidisciplinary discharge plan within 24	A Wide

Study, Year, Country	Followup Duration (Intervention y)	Total N Analyzed	Mean Age/% Male	Severity of CHF	Intervention components	Control Description	Quality Applicability
Canada				LVEF: nd	management. A nursing transfer letter to the home care nurse detailing clinical status and self-management needs. Phone call from hospital nurse to patient within 24 hours of discharge. Minimum of two-community nurse visits within two weeks of discharge.	hours of admission and weekly discharge planning meetings. Regional home care co-coordinator consults with hospital team as required and may meet patients and their families. Immediately before discharge physician completes referral form for home care and necessary services and supplies are communicated with the home nursing agency.	
Jaarsma, 2000 Netherlands	9 mo (1994-1997)	179	72/60%	NYHA III/IV 100% LVEF% 36	Nurse led intensive education including symptoms of CHF, sodium restriction, fluid balance and compliance, telephone contact, home visits once per week and education, increased communication with providers	Nurse or physician provided education about medication and lifestyle	C Wide
Kasper 2002 USA	~9 mo (1996-1998)	200	64/61%	NYHA III 56% LVEF% 27	Cardiologists designed individualized treatment plan (Usual care) + Nurse telephone followup; monthly clinic visits with nurses; patients received pill sorter, correct medications, list of dietary and exercise recommendations, and education material	CHF cardiologist designed treatment plan for each patient and documented this in patient's chart	B Mod
Koelling 2005 USA	~6 mo (2001-2002)	223	65/58%	LVEF%: 26	Patient education program including 60 min one on one and one time session with a nurse educator, disease and pharmacotherapy management, Salt and water intake management, daily weight monitoring, self-care behaviors + usual care	Standard heart failure specific discharge information Usual care	A Mod
Laramee, 2003	3 mo (1999-2001)	287	71/54%	NYHA III/IV 38% LVEF Mod/severe 90%	Education and early discharge planning and co-ordination of care by nurse case manager; patients received a educational booklet, weight logs, medication lists, a guide for measuring sodium intake, weigh scales and pill boxes; reinforced educational plan and telephone followup	Standard tertiary hospital care, including opportunity for social services evaluation, dietician consult etc. and home care service on discharge. Post-discharge care conducted by primary care physician	B Mod



Study, Year Country	Followup Duration (Intervention y)	Total N Analyzed	Mean Age/% Male	Severity of CHF	Intervention components	Control Description	Quality Applicability
Ledwidge, 2005 Ireland	2 y	130	68/68%	NYHA: IV LVEF%:39±12	Extended heart failure program (EP) 12 weeks of weekly telephone calls from specialist HF nurses (mostly the nurse who had managed the pt during the 1 <sup>st</sup> 3 months following discharge) Specialist nurse-led education and specialist dietician consults on 3 or more occasions during index admission Telephone contact by HF nurse specialist weekly until 12 weeks. Telephone calls determined clinical stability, address questions/concerns and revise key education points deemed necessary by nurse (on daily weight monitoring, disease and medication understanding, compliance with therapy and dietary salt restriction.)	Standard care (SP) group.	B Mod
McDonald 2002; Ledwidge, 2003 Ireland	3 mo (1998-2000)	98	71/63%	NYHA nd LVEF% 36	Specialist nurse-led education including daily weight monitoring, disease and medication understanding and salt restriction. Telephone followup and education reinforcement + usual care	Usual care description not documented	B Mod
Linne 2006 Sweden	6 mo (1998-2002)	224	70/66%	LVEF <40%	Standard information + Additional interactive CD-educational program at and 2 wk after discharge. CD educational program includes disease symptoms and treatment, reasons for deterioration of disease, fluid intake, medication understanding	Standard information on the inpatient ward	C Mod
Lopez, 2006 Spain	(2000-2002)	134	75/41%	NYHA III 56% LVEF% 27	<i>Active Intervention program</i> <i>Information:</i> the day of hospital discharge, a personal interview with patient and his caregiver a. information on the disease b.diet education c. information on drug therapy contact telephone Telephone strengthening monthly during the first 6 mos of followup and subsequently ever 2 months, a telephone call was made to the home of the patient.	“standard care” not further defined. However, during regular followup visits (at 2,6, and 12 months after discharge) the cardiologist carried out a conventional clinical assessment according to the standard practice. Pharmacists evaluated the following parameters: treatment compliance (was patient reliable, partially	B Mod

Study, Year, Country	Followup Duration (Intervention y)	Total N Analyzed	Mean Age/% Male	Severity of CHF	Intervention components	Control Description	Quality Applicability
						reliable, non-reliable), quality of life measurement *EuroQoL scale), patient satisfaction with the care received (Catalan Health Department, asking patient about the care and information received and asking patient to score 0 to 10 in an analogical scale).	
Naylor, 2004 USA	12 mo (1997-2001)	239	76/40%	NYHA nd LVEF<45% 86%	A standard orientation and training program guided by a multidisciplinary team of heart failure experts to prepare advanced practice nurse (APN); Use of care management strategies; home visits by APN	Non advanced practice nurse care. Attending physician planned the discharge date, liaison nurses facilitated referrals to home care services in patients' residencies	B Wide
Nucifora 2006 Italy	6 mo (1999-2001)	200	73/62%	NYHA III/IV: 67% LVEF <45%: 58%	Nurse led education including disease and pharmacological treatment, sodium restriction and fluid intake management, Weight control and physical activities, and Other self-care behaviors; facilitated telephone followup; scheduled visits with an internist	Preexisting routine post-discharge care Follow up with their primary care physician as usual	B Wide
Rich 1993 US	3 mo (1988-1989)	98	79/40%	NYHA: mean=2.7	During index hospitalization: Daily education visits by study nurse specialist. Dietician visit with individualized 1.5-2.0 g sodium diet. Medication review by geriatric cardiologist with patient/care givers. Study nurse taught patients about meds and dosing cards. Social worker and home care team visited patient. After discharge: Home care team nurse visited within 48 hrs. 2 more home care team nurse visit in 1 <sup>st</sup> wk. Study nurse phone patient to assess progress.	Conventional medical care determined by patient's physician.	B Mod
Rich 1995 USA	3 mo (1990-1994)	282	79/26%	NYHA mean 2.4 LVEF% 44	Multidisciplinary treatment strategy including inpatient visits by specialist nurse, dietician, medication review by geriatric cardiologist, nurse led education about medications,	Standard treatment and services ordered by primary physician	B Mod

Study, Year, Country	Followup Duration (Intervention y)	Total N Analyzed	Mean Age/% Male	Severity of CHF	Intervention components	Control Description	Quality Applicability
					dosing, and adverse effects; weigh scales, instruction and daily weight charts; social worker and the home care team visits		
Rainville 1999 USA	12 mo (1996-1997)	34	73/50%	NYHA III/IV: 94% LVEF: nd	Before discharge, pharmacist reviewed pathology and treatment of HF, weight monitoring and risk modifications with patient/care giver. Patient given brochure, video, weight log and medication organizer. After discharge, pharmacist phoned within 3 days, at 7, 90 days and 12 months	Routine care and preparation for discharge including: written prescription, physician discharge instructions, nurse review of diet, treatment plans, medications, and drug info sheets	C Mod
Sethares 2004 US	3 mo (1999-2000)	70	76/52%	LVEF%: 41.45 ± 18 SD	Research nurse tailored intervention to perceived benefits and barriers to self-care of HF that were identified by persons with HF at each time period (in hospital, 1 week and 1 month after discharge).	Usual care: discharge teaching by a unit staff nurse and written educational sheets describing the uses, side effects, and frequency of any ordered medications.	B Wide
Stewart 1998 Australia	6 mo (nd)	97	76/45%	NYHA III/IV 51% LVEF%: 38	Before discharge, study nurse counseled treatment regimen compliance and reporting of any sign of clinical deterioration. 1 week after discharge a single home visit by the study nurse and pharmacist. Patients assessed for medication knowledge and compliance. Patients with poor knowledge were offered counseling, a pill remainder container, monitoring by caregivers, medication information and remainder card and referral to a community pharmacist for more regular review. The study nurse coordinated with the primary care physician for any further intensive followup thereafter	Appointments with the primary care physician or cardiologist within 2 weeks of discharge. 27% received home support by domiciliary care or community nurse visits	B Mod
Tsuyuki 2004 USA	6 mo (1999-2000)	276	81/58%	NYHA III or IV: 40% LVEF%: mean EF 32%	Before discharge: Evaluation if dosage of ACE-I was appropriate, all meds were reviewed, recommendations made to optimize other HF therapies and monitored daily thereafter. After discharge: Patient support program covered 5 basic areas: salt and fluid restriction, daily weighing, exercise	General heart disease pamphlet before discharge, but no formal counseling. Followup consisted of monthly telephone contact for a period of 6 mo to ascertain clinical events	B Mod

Study, Year Country	Followup Duration (Intervention y)	Total N Analyzed	Mean Age/% Male	Severity of CHF	Intervention components	Control Description	Quality Applica bility
					<p>alternating with rest periods, proper medication use, early recognition of worsening of symptoms</p> <p>Education material available on website for download. Patients received adherence aids: a medication organizer, medication administration schedule, daily weight log.</p> <p>Telephone followup to reinforce the education for self care behaviors, newsletters, clinical events, physician contact for ACE-I initiation and titration</p>		

**Appendix Table B2: Interventions post discharge**

Study, Year Country	Followup Duration (Intervention y)	No. Analyzed		Mean Age	Severity of CHF	Intervention components	Control description	Quality Applic ability
		Int	Cont	Male%				
Benatar 2003 USA	3 mo (1997-2000)	108	108	67/ 39%	NYHA III or IV: 100% LVEF%: 38.1	Daily home telemonitor through internet monitored by cardiac nurse	Home nurse visits (specialized cardiac nurses): Detailed discussions during first 4 visits: diet, symptom recognition, and compliance with medication regimens Further visits: on patients' symptoms and vital signs with physician notification if needed	B Wide
Blue 2001 Scotland	12 mo (1997-1998)	84	81	74/ 64%	NYHA III or IV:76% LVEF%: nd	Specialist HF nurse visited home within 48 hrs of discharge, with visits every 3 months after 6 week visit. Patient educated about HF and treatment, self-monitoring, medication review and psychological support. Scheduled telesupport every other month.	Patients managed as usual by the admitting physician and then primary care physician	A Wide
Capomolla 2004 Italy	11 mo (2000-2001)	67	66	57/ 93%	NYHA III/IV 49% LVEF% 29	Telemonitoring. Nurse led education about the illness; therapeutic programs, self management of signs and symptoms, diet and fluid recommendations, domestic and activities counseling	Community care. At discharge patients were referred to their community primary care physician and cardiologists or cardiology dept	C Mod
DeBusk 2004 USA	12 mo (1998-2000)	228	234	72/ 48%	NYHA III/IV 50% LVEF %:28%<0.40 and 31% >0.40	Nurse led standardized telephone mediated intervention including initial education session with a videotape, baseline telephone counseling session, nurse initiated followup telephone contacts, pharmacologic treatment management, nurse initiated communication with physicians + usual care	Usual care Instruction on diet, drug adherence, physical activity and response to changing symptoms	B Mod
Doughty 2002 New Zealand	12 mo (1997-1998)	100	97	60%	NYHA III 76% LVEF% 30.6	General practitioner led outpatient review at the heart failure clinic;	<b>Usual care.</b> Continued care of their GP with	A Wide

Study, Year Country	Followup Duration (Intervention y)	No. Analyzed		Mean Age	Severity of CHF	Intervention components	Control description	Quality Applic ability
		Int	Cont	Male%				
						one to one education with the study nurse, education booklet provided; patient diary for daily weights, treatment records, telephone followup with GP, 6 wkly clinic visits, group education session with cardiologist and nurse about disease, monitoring daily weight, action plan for weight changes, medication, exercise, diet	additional follow-up measures as usually recommended by the medical team responsible for their in-patient care.	
Ducharme 2005 Canada	6 mo (1998-2000)	115	115	68/ 73%	NYHA: III or IV LVEF%: 35%	Multidisciplinary care clinic: cardiologists, nurses, dieticians, social worker, etc; Evaluated and observed for up to 5 hrs; Nurse telephone followup 72 hr post discharge and monthly once, or frequently as needed basis; One to one education by study nurse about clinical condition to the patient/ family members complimented with a record maintenance by the patient; Reinforcement of patient education, dietary instructions, interaction of OTC with meds at each subsequent clinic visit	Patients received treatment and appropriate follow-up according to attending cardiologist	B Mod
Ekman 1998 Sweden	5 mo (1994-1996)	79	79	80/ 58%	NYHA mean 3.2 LVEF% 43	Specialist nurse led patient education about their treatment and symptoms of clinical deterioration, tailored care plan with individualized treatment goals, access to clinic nurses during business hours, notebook for daily weight monitoring, treatment and information about clinical deterioration, and nurse initiated telephone followup	The patients were managed in accordance with current clinical practice, i.e., the patient was treated and followed by a general practitioner and visited the emergency room if symptoms worsened.	B Narrow
Holland 2007 UK	6 mo	149	144	78/ 64%	NYHA: III/IV: 67% LVEF%: nd	Community Pharmacist arranged home visit, within 2 weeks of discharge; Educated patient/carer	Usual care not described in the study	A Mod

Study, Year Country	Followup Duration (Intervention y)	No. Analyzed		Mean Age	Severity of CHF	Intervention components	Control description	Quality Applic ability
		Int	Cont	Male%				
						about HF and their drugs; Gave basic exercise, dietary, and smoking cessation advice; Encouraged completing of sign and symptom monitoring diary; Fed back recommendations to GP; Fed back need for drug adherence aid to local pharmacist		
Jerant 2001 USA	6 mo (1998-2000)	13/12	12	67/71: 46%/42%	NYHA (III/IV): 31%/33%  LVEF% 54%/50%	<p><u>Intervn 1:</u> Home telecare with video-conferencing and electronic stethoscope. Nurse telephone support home telecare delivered via a 2-way video-conference device with an integrated electronic stethoscope; received scheduled home telecare visits</p> <p><u>Intervn 2:</u> nurse telephone calls; received scheduled phones calls During all in-person, telecare, and telephone encounters, the study nurse used the Visiting Nurse Association CCHF Care Steps to guide patient assessment: vital signs, ADL, med use, dietary factors etc.</p>	'Usual outpatient care' was not described further	C Narrow
Krumholz, 2002 USA	12 mo (1997-1998)	44	44	76/ 57%	NYHA(III/IV) LVEF% 38	Cardiac nurse led consultation on five sequential care domains including patient knowledge of illness, relation between medication and illness, relation between health behaviors and illness, symptoms and signs of deterioration, nurse initiated scheduled telephone calls	Received all usual care treatments and services ordered by their physicians.	C Mod
Mejhert 2004 Sweden	18 mo (1996-1999)	103	105	76/ 56%	NYHA III or IV: 42% LVEF%: 34%	When patient pays visits to the outpatient program, he/she is encouraged to keep in contact with the nurse. Each visit the nurse: vital signs, weight, lab, ECG	Undergo initial evaluation with their general practitioners and are monitored by a heart failure plan in the primary care	B Mod

Study, Year Country	Followup Duration (Intervention y)	No. Analyzed		Mean Age	Severity of CHF	Intervention components	Control description	Quality Applic ability
		Int	Cont	Male%				
						workup; optimizes meds if needed; instructs patients to monitor weight, symptoms of deterioration, good compliance of meds, diet advice, and other self care behaviors Information repeated in booklets and computerized educational programs	setting	
Morcillo 2005 Spain	6 mo (2001-2002)	34	36	70/ 64%	NYHA III or IV: 74% LVEF% (mean): 35.4%	One week after discharge the nurse visited patient's home one time for: education of medication, signs and symptoms of the disease and treatment compliance; fluid and diet management and self care habits; discussion of prophylactic vaccinations + identical conventional care as the control group	Conventional care based on best available evidence + scheduled outpatient followup with attending physicians	C Mod
Rieigel 2002 USA	6 mo (nd)	130	228	73/ 49%	NYHA III or IV: 98% LVEF% (mean): nd	Telephonic case management by a RN case manager using decision-support software. RN contact patient at a frequency guided by software and judgment of case manager based on patient's symptoms, needs.	Usual care not described	C Mod
Riegel 2006 USA	6 mo (2002-2004)	69	65	72/ 42%	NYHA III or IV: 82.6% LVEF%: 42.3%	Nurse case manager contacts patient 5 days post-discharge. Software assists nurse in setting priorities for the timing of the next telephone call, content of patient education, and documentation. Nurse case manager assesses poor adherence with meds and diet recommendations	Usual care was not standardized, and before discharge the nurse educated patients about heart failure management typical discharge instructions included medication list, institutional specific discharge instruction sheet and hand written notes to follow a low sodium diet and contact physician if symptoms occur	A Wide
	6 mo	100	100	75/	NYHA III or IV:	Multidisciplinary, home-based	Regular outpatient review	A



Study, Year Country	Followup Duration (Intervention y)	No. Analyzed		Mean Age	Severity of CHF	Intervention components	Control description	Quality Applic ability
		Int	Cont	Male%				
Stewart 1999 Australia	(1997-1998)			62%	88% LVEF mean %: 37%	intervention. Assessed by cardiac nurse 7-14 days after discharge. Assessment of clinical status, understanding of disease and psychological support. Counseling on strategies to improve adherence where necessary	by the cardiologist	Wide
Stromberg 2003 Sweden	12 mo (1997-1999)	52	54	77/ 63%	NYHA III or IV:87% LVEF%: nd	Patients scheduled for first visit 2-3 weeks after discharge. 1 hr visit: nurse evaluated status and optimized treatment; educated patient/family about: heart failure and social support to the patient/family, dietary changes as restricted fluid, sodium and other self care behaviors; monitor symptoms, weight gain and improve patients self care regimen; Psychosocial support by creating a supporting relationship between nurse and patient	Usual care – managed with current clinical practice and received conventional followup with primary health care physician	A Wide
Thompson 2005 England	6 mo (nd)	58	48	73/ 72%	NYHA: III/ IV 76% LVEF%: mean 31%	A nurse led Clinic ( monthly for 6 mo) plus home based intervention. Patients seen by the study specialist nurses prior to discharge and received a home visit within 10 days of hospital discharge; received and educational packet, and a contact card	Usual care patients received standard care by explanation of their condition and prescribed meds by the ward nurse and referral to appropriate post-discharge support	C Mod
Wierchowicki 2006 Poland	12 mo (nd)	80	80	67/ 60%	NYHA: III/IV 84% LVEF%:<45% n=66 (82.5%)	At clinic: assessment by the cardiologist; nurse assessment for medication compliance; weight mgt; signs of CHF; telephone followup; home visits as needed; QOL and self care questionnaires; eucational – one to one education at patient's home or by telephone; physiotherapist's assistance for exercise rehabilitation programme; psychologist's assistance group	Routine care: cared by primary care physicians only. Patient did not participate in any educational or therapeutic activities of the program	C Mod

Study, Year Country	Followup Duration (Intervention y)	No. Analyzed		Mean Age	Severity of CHF	Intervention components  and individual educational activities	Control description	Quality Applic ability
		Int	Cont	Male%				

**Appendix Table B3: Interventions on recruited patients in OPD clinic**

Study, Year Country	Followup Duration (Intervention y)	No. Analyzed		Mean / %	Severity of CHF	Intervention components	Control description	ity Appl icab
		Int	Cont	Age Male				
Bouvy 2003 Netherlands	6 mo (1998-2000)	74	78	69/ 72%	NYHA: III/IV: 57% LVEF%: nd	Community pharmacist-led intervention; Pharmacist gave a structured interview to patient on initial visit. Computerized medication history was used to discuss drug use, reasons for non-compliance to reinforce medication compliance. Pharmacist contacted subject monthly. + Usual care.	Patient received medication in a medicine- container with a microchip that recorded the time and date of opening	B Wide
Gattis 1999 USA	6 mo (1996-1997)	90	91	72/ 69%	NYHA III or IV: 33% LVEF%: 30%	Pharmacist led intervention and followup: medication evaluation; therapeutic recommendations; patient education on medication use and compliance; followup telemonitoring	Usual care: patient assessment and education provided by the attending physician and/or physician assistant or nurse practitioner	A Mod
GESICA 2005 Argentina	16 mo (2000-2001)	760	758	65/ 73%	NYHA III or IV: 50% LVEF<40%: 78.6	Recruited from outpatient centers: nurse led telephone followup program + Usual care: education, counseling, and monitoring; adherence to the diet; adherence to the drug treatment; monitoring of symptoms; control of daily weight and edema; daily physical activity	Usual care: followup with cardiologist	A Mod
Murray 2007 USA	12 mo (2001-2004)	122	192	62/ 39%	NYHA: III/IV: 39% LVEF mean %: 49	Pharmacist led intervention to improve medication adherence. Patients recruited from outpatient clinics; pharmacists received training from multidisciplinary team on treatment of heart failure, key concepts for pharmaceutical care of older adults, communication techniques	Usual care: patients received prescription services from pharmacists who had not received the specialized training and did not have patient centered study materials	C Mod
Sisk 2006 USA	12 mo (2000-2002)	203	203	60/ 55%	NYHA III or IV: 57.7% LVEF%: nd	Patients recruited during a scheduled clinic appnts; One nurse per patient: initial onetime	Usual care – received federal consumer guidelines for	A Mod

Study, Year Country	Followup Duration (Intervention y)	No. Analyzed		Mean Age Male	Severity of CHF	Intervention components	Control description	ity Appl icab
		Int	Cont					
						appointment to educate patient about disease, counsel self management, referral to social services, review nurse's future role; Referral to social services if needed; Telephone followup; administering food frequency questionnaire; reinforce self management; Coordinate patient care with patient's clinician	managing systolic dysfunction	
Varma 1999 Northern Ireland	12 mo (nd)	42	41	76/ 51%	NYHA: nd LVEF%:nd	<p>Patients were recruited from both inpatient admissions and outpatient clinic</p> <p>Results of a 2 minute walk test were recorded. Body weight, blood pressure pulse and forced vital capacity were measured.</p> <p>In clinic: Patients received education from a pharmacist on the disease and its treatment, and lifestyle changes that could help control symptoms.</p> <p>Patients instructed on self monitoring, maintaining daily weight in cards, instructed to take an extra dose of diuretic if needed</p> <p>Only physicians and community pharmacists were contacted to assess compliance.</p>	Standard management that excluded all above mentioned interventions	C Mod

Appendix C.1a. Cost among patients with interventions beginning inpatient versus control

Author	Year	Country	Centers	Intervention y	N patients	Followup months	Quality	N-Intervention	Cost_Intervention	N_Control	Cost_Control	Net Diff	P-Value	Comments
Naylor	2004	USA	M	1997-01	239	12		118	7636	121	12481		0.002	US Dollars
Koelling	2005	USA	S	2001-02	223	6		107	5369	116	8292	-2823	0.035	US Dollars
Capomolla	2002	Italy	S		234	12		112	2244	122	2409			Euros
Kasper	2002	USA	M	1996-98	200	6		102	16182	98	8789			NS US Dollars
Laramie	2003	USA	S	1999-00	287	3		141	23054	146	25536			NS US Dollars
Cline	1998	Sweden	S	1991-3	190	12		80	2294	110	3594			NS US Dollars (cost in survivors)
Stewart	1998	Austra	S	nd	97	6		49	3200	48	5400			NS Australian Dollar
Atienza	2004	Spain	M		338	16A		164	2912	174	5417	-2505		Euros
Del Sindaco	2007	Italy	M	2001-02	173	6		86	149660.2	87	248372.3	-98712.1		Euros
Barth	2001	USA	S	nd	34	3		17	401.81	17	124.68			US Dollars
Rich	1995	USA	S	1988-89	98	3		63		35		-460		US Dollars (per patient per month = - \$153)
McDonald	2002	UK	S	1998-00	98	3		51	9974	47	47190	-37216		Euros

Appendix C.1b Combined endpoints of mortality or readmission in the intervention beginning inpatient compared with control group.

Author	Year	N patients	Followup months	N-Interventions	Combined events	N control	Combined events	RR	P-Value	Primary endpoint
Del Sindaco	2007	173	6	86	40	87	56	0.36	<0.001 RRR 0.167-0.509	yes
Ledwidge	2005	130	3	62	4	68	12	0.37	0.04OR = 0.07 - 0.84	yes
Atienza	2004	338	16	164	0.7	174	1.17	0.47	<0.01 Patient per year	yes
Stewart	1998	97	6	49	0.8	48	1.4	0.56	0.03Patient per year	yes
Koelling	2005	223	6	107	50	116	74	0.65	0.0180.45-0.93	yes
Kasper	2002	200	6	102	50	98	72	0.67	NS P=0.03, Poisson model	yes
Dunagan	2005	151	12	76	53	75	57	0.69ns	0.47-1.01	No
Linne	2006	230	6	122	58	108	55	0.93ns		yes
Cline	1998	190	12	80	56	110	79	0.97	NS	No
Nucifora	2006	200	6	99	95	101	90	1.08	NS	yes

Appendix C2a. Cost incurred among interventions post discharge versus control group

Author	Year	Country	N patients	Followup months	N-Intervention	Cost intervention	N control	Cost control	Difference	P-Value	Comments
Stewart	1999	Australia	200	6	100	490300	100	922600	-432300.00	ns	Australian \$
Krumholz	2002	USA	88	12	44	14420	44	21935	-7515.00	0.02	
Riegel	2006	USA	134	6	69	10015	69	13967	-3952.00	nd	
Morcillo	2005	Spain	70	6	34	314.8	36	1505.6	-1190.80	<.001	Euro
Riegel	2002	USA	358	6	130	1192	228	2186	-994.00	ns	Inpatient Heartfailure cost
Jerant	2001				12	28888	12	21595	7293.00	ns	Group telesupport vs usual care
Jerant	2001	USA	37	6	13	29701	12	21595	8106.00	ns	Home telecare vs usual care
Benatar	2003	USA	216	12	108	677710	108	500343	177367.00	ns	Home Nurse Visit vs. Nursetelemanagement

Appendix C2b. Combined endpoints of mortality or death among interventions post discharge versus control group

<b>Author</b>	<b>Year</b>	<b>Followup months</b>	<b>N-Intervention</b>	<b>CombEvents Intervention</b>	<b>N Control</b>	<b>CombEvents Control</b>	<b>RR</b>	<b>P-Value</b>	<b>Quality</b>
Thompson	2005	6	58	15	48	21	0.59 <sup>nd</sup>		C
Stewart	1999	6	100	77	100	129	0.60	0.02	A
Krumholz	2002	12	44	25	44	36	0.69	0.01	B
Stromberg	2003	12	52	29	54	40	0.75	0.03	A
Doughty	2002	12	100	68	97	61	1.08 <sup>ns</sup>		C



Appendix C3. Combined end points and costs incurred in patients beginning intervention in the outpatient clinic versus control group

Author	Year	Country	Centers	Intervention y	N patients	Followup months	N-Intervention combined_Interventio n	N_Control combined_Control	RR	P-Value	Comments	
Sisk	2006	USA	M	2000-02	406	12	203	203	#DIV/0!			
GESICA	2005	Argentina	M	2000-01	1518	16	760	299	758	339	0.88	0.057
Bouvy	2003	Netherlands	M	1998-00	152	6	74	19	78	19	1.05	ns
Murray	2007	USA	M	2001-04	314	12	122		192		#DIV/0!	Mean Difference - \$2960 per patient (-\$7603 to \$1388)