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Review

The effectiveness of disease management programmes in reducing hospital re-admission in older patients with heart failure: a systematic review and meta-analysis of published reports

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See page 1565 for the editorial comment on this article[†]

KEYWORDS
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Re-admission;
Elderly;
Disease management programmes

Aims To systematically evaluate the published evidence regarding the effectiveness of disease management programmes (DMPs) reducing hospital re-admissions among elderly patients with heart failure (HF).
Methods and Results Computerised search of MEDLINE (1966 to 31 August 2003) and EMBASE (1966 to 31 August 2003). The Cochrane Library was also searched, and reference lists of review articles on the topic, and of all relevant studies identified, were scanned. Search and selection of studies, data-extraction using standardised forms, and assessment of study quality was performed by two reviewers. The end-point was the proportion of persons who underwent hospital re-admission, and pooled relative risks (RR) were used to summarise the effectiveness of DMPs. The meta-analysis included 54 articles, comprising 27 randomised and 27 non-randomised controlled studies. Randomised studies consistently suggested that, in comparison with usual care, DMP reduced the frequency of re-admission for HF or cardiovascular disease by 30% (pooled RR 0.70; confidence interval (CI) 95% 0.62–0.79), all-cause re-admission by 12% (pooled RR 0.88, 95% CI: 0.79–0.97), and the combined event of re-admission or death by 18% (pooled RR 0.82, 95% CI: 0.72–0.94). The results displayed no substantial variation when only DMPs with home visits, out-patient visits to a clinic, or patient follow-up longer than 6 months were included. For DMPs with out-patient clinical visits, however, the reduction in re-admission for HF or cardiovascular disease, and for all causes, did not attain statistical significance. The magnitude of DMP benefits reported by non-randomised studies was more than double that reported by randomised studies. Practically all the non-randomised studies failed to control for confounding factors, such as severity, co-morbidity and drug therapy.

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Conclusion DMPs are effective at reducing re-admissions among elderly patients with HF. Their effectiveness is close to that observed in clinical trials evaluating drugs for HF, such as angiotensin-converting enzyme inhibitors, beta-blockers or digoxin. However, since none of the DMP studies compared different interventions directly, we do not know the relative effectiveness of types of healthcare delivery within the DMP.

Introduction

Heart failure (HF) is the leading cause of hospitalisation among the elderly in developed countries.[1,2] Despite effective treatments to reduce hospitalisations, such as angiotensin-converting enzyme (ACE) inhibitors or beta-blockers, clinical management of these patients remains sub-optimal;[3,4] as a result of this and of the natural history of HF, hospital re-admissions are very frequent. Depending on their age and HF stage, 10–50% of patients are readmitted in the 3–6 months following index hospitalisation.[5–8] Hospitalisations represent the main cost component of HF care.[9]

Elrodt et al.,[10] defined disease management as a multi-disciplinary approach to care for chronic diseases, that co-ordinates comprehensive care along the disease continuum across healthcare delivery systems. Several systematic reviews have shown that disease management programmes (DMPs) are a potentially useful instrument for reducing hospital re-admissions of HF-patients.[11–13] Although DMPs for patients with HF have several components, such programmes always include patient education and support in order to detect signs of decompensation and improve adherence to treatment. Most DMPs rely on nurse participation and include telephone follow-up of patients, yet there is limited knowledge of the influence of the type of healthcare delivery (home medical visits or out-patient visits to a clinic) or the duration of follow-up on the results of DMPs.[14] Many re-hospitalisations of patients with HF are due to causes other than HF.[14] The possible benefits of DMPs in any given area, such as HF, may be accompanied by unexpected effects in other areas, since most HF patients are at an advanced age and suffer from serious comorbidities. It is important, therefore, to ascertain the effectiveness of DMPs on hospitalisations due to cardiovascular causes other than HF and, in particular, on all-cause hospitalisations and death. Lastly, it should be noted that a substantial proportion of DMPs in HF have been assessed using non-randomised before-and-after comparisons.

The aim of this paper was to systematically review the experimental evaluations of DMPs among elderly patients with HF and to ascertain the effectiveness of such programmes on three variables: hospital re-admission for HF or other cardiovascular causes, all-cause re-admission and re-admission or death. In addition, this paper examined the influence of healthcare delivery and of the type of DMP assessment (randomised or non-randomised) on the results of DMPs.

Methods

Search of the literature

A search of MEDLINE (1966 to 31 August 2003) and EMBASE (1966 to 31 August 2003) was undertaken. Because there are numerous terms to name DMP and their use is not standardised in the literature, a very sensitive strategy was pursued to identify the greatest number of papers. The following textual terms and MeSH headings were used: cardiac failure or heart failure was combined with re-admission or re-hospitalisation or hospitalisation or discharge. Language restrictions were not applied. We also searched the Cochrane Library and scanned reference lists of review articles on the topic and of the relevant studies identified. For very recent studies, we completed the information from congress proceedings.

Selection of studies and extraction of data

Studies were included if they met the following criteria: randomised and non-randomised controlled studies assessing DMPs targeted, among others, at patients aged $\geqslant$65 years with principal or secondary diagnosis of HF. Studies were subsequently excluded if: they failed to furnish information to quantify the association between DMPs and re-admission, no evidence of, or <75% of, hospitalisations were re-admissions, <75% of subjects had a diagnosis of HF, <50% of patients were aged over 60 years, or the mean age of patients studied was <60 years; the data supplied were partially reported in another paper already included.

As used by Weingarten et al.,[15] our working definition of DMP was 'an intervention designed to manage HF and reduce hospital re-admissions using a systematic approach to care and potentially employing multiple treatment modalities'. To identify a systematic approach to care, we searched for keywords such as guidelines, clinical pathways, protocols, algorithms, care plans, quality improvement activities, and patient support and education.[15] Indeed, we expected that all DMPs would include teaching and support activities addressed to patients.

For randomised studies, study quality was assessed with the scale developed by Jadad et al.,[16] while for non-randomised studies quality was approximated by the degree of control for confounding factors. The Jadad scale assesses three aspects, namely, randomisation procedure, blinding of the intervention, and patient attrition in the follow-up. The authors advocate that a score of 3 or more on the Jadad scale should be taken to indicate "high quality".[16]

The search and selection of studies, data-extraction (using standardised forms), and assessment of study quality was performed by two reviewers (JG and PGC): disagreements were discussed with a third reviewer (FRA) and settled by consensus.

Statistical analysis

Randomised and non-randomised studies were examined separately. We chose as end-point the proportion of persons readmitted over the follow-up in the DMP and control groups. Studies were eligible for meta-analysis if such an end-point could be ascertained from the published reports. For each study, relative risk (RR) was calculated as the measure of the effect of the intervention. Heterogeneity of the RR across the studies was tested using the χ^2 test. Where the results were homogeneous, RRs were combined using the Mantel—Haenszel fixed-effects model.[17] Where the heterogeneity test was statistically significant but the RRs were nevertheless consistent in their direction (above or below 1), these were combined using Der Simonian and Laird's random effects method.[17]

We produced funnel plots (scatter plots of DMP effects against their standard error across the studies), and looked for the presence of asymmetry as a means of examining the 'small studies effect', including the potential for publication bias. We tested the asymmetry of funnel plots with the method of Egger et al.[18]

We conducted sensitivity analyses, defined a priori, to examine whether the results of the meta-analysis varied with types of organising care within the DMP (home visits, out-patient visits to a clinic, telephone follow-up), duration of follow-up (longer than 6 months), Jadad score, and study size.

All statistical tests were two-sided. The meta-analysis was performed with the RevMan programmeme (Review Manager Version 4.2. Oxford, England: The Cochrane Collaboration, 2000) and the method of Egger et al., was implemented with Stata (Statistics Data Analysis v 7.0. Texas: *Stata Corporation*, 2001).

Results

Studies included and excluded

We identified 5324 papers in EMBASE, 2735 in MEDLINE, and 20 from other sources, chiefly secondary references. After reading the title or abstract of all papers identified, the complete text of 286 was retrieved. Of these, 82 fulfilled the inclusion criteria, but 28 were excluded[19–46] (Table 1). Hence, this review included a total of 54 studies, comprising 27 randomised[47–74] and 27 non-randomised trials.[75–101]

Randomised trials

The studies were published from 1993 through 2003 (Table 2). Of the 27 studies, 13 came from the United States of America. Study size ranged from 34 to 1966, with half of studies not exceeding 200 subjects. Moreover, though the study by Hughes et al.,[61] enrolled 1966 patients, only 30 had HF. Similarly, of the 363 patients included in the study of Naylor et al.,[64] only 60 had HF. Although the success of randomisation among HF subjects was not tested in these two studies, they were nevertheless included since they provided a breakdown of the results for this type of patient. Thus, we decided to consider them as 'independent substudies' specific for heart failure patients. Only 11 studies[47,50,52,53,58,59,63,64,66,69,73] attained a score of 3 on the Jadad scale.

Table 1 Excluded articles

Author (year)	Reason for exclusion
Jerant (2003)[19]	Information shared with Jerant (2001)
Wright (2003)[20]	Association cannot be measured
Avlund (2002)[21]	No information on number of patients with HF
Capomolla (2002)[22]	Mean age of patients: 56 years
Galatius (2002)[23]	No evidence of re-hospitalisations being studied
Chinaglia (2002)[24]	No evidence of re-hospitalisations being studied
Mueller (2002)[25]	No information on age of patients
González (2002)[26]	Association cannot be measured
Riegel (2002)[27]	Information shared with Riegel (Arch. Intern. Med. 2002)
Anonymous (2001)[28]	No information on age of patients
Hershberger (2001)[29]	Only 25% of patients aged 60 years or over
Holst (2001)[30]	Mean age of patients: 54 years
O'Connell (2001)[31]	Mean age of patients: 58 years
Abenhaim (2000)[32]	No information on number of patients with HF
Ramahi (2000)[33]	Association cannot be measured
Civitarese (1999)[34]	No information on age of patients
Cordisco (1999)[35]	Mean age of patients: 58 years
Dahlström (1999)[36]	Association cannot be measured
Knox (1999)[37]	No information on age of patients
Oddone (1999)[38]	Information shared with Weinberger (1996)
Varma (1999)[39]	No evidence of re-hospitalisations being studied
Wilson (1999)[40]	Mean age of patients: 57 years
Dahle (1998)[41]	Mean age of patients: 53 years
Mischke (1998)[42]	No information on age of patients
Fonarow (1997)[43]	Mean age of patients: 52 years
Hanumanthu (1997)[44]	Mean age of patients: 52 years
Lasater (1996)[45]	No information on age of patients
Agustin (1976)[46]	Association cannot be measured

Table 2 Randomised trials evaluating the effect of disease management programmes on hospital re-admission of older patients with heart failure

Author, year	Study and participant characteristics[a]	Main components of intervention	O/F[b]	Main findings: Intervention versus (vs) usual care[c]
DIAL, 2003[47,48]	Argentinian Study (JS 3) with 2385 patients initially screened and 1518 patients (64%) finally included: 760 SI, 758 US. Mean age in years 64.8, 71% male. *HF severity*. NYHA Class III–IV (%): 48; Systolic dysfunction 83%. *HF Aetiology*. 44% IHD. *Co-morbidity*. 35% MI, 60% HT, 21% DM, 9% CAD. *Medications*. 80% ACE-inhibitor, 13% Angiotensin receptor blocker, 97% Diuretic, 58% β-Adrenoceptor Antagonist	Frequent telephone follow-up with the objectives of education, counselling, and monitoring to enhance self-control mechanisms, timely medical visits, diet, and drug therapy compliance. Telephone call frequency was determined according to pre-established criteria of clinical status severity assessed at each phone contact	A, B, C (1.2 y)	SI produced a 20% relative risk reduction on the combined end-point (HF hospital re-admission or death, 26.3% vs 31%, $P = 0.02$). SI decreased the number of patients with HF hospital readmission (16.8% vs 22.3%, $P = 0.005$), and the number of patients with any cause hospital re-admission (34.3% vs 39.1%, $P = 0.05$). SI reduced costs ($2.437 vs $2.618 per patient and year). In the subgroup of patients with NYHA Class III–IV, SI saved $1118 per patient and year
Laramee, 2003[49]	USA Study (JS 2) with 589 patients initially screened and 287 patients (49%) finally included: 141 SI, 146 US. Mean age in years 70.7, 54% male. *HF severity*. NYHA functional class mean: 2.34; NYHA Class I, II, III, IV (%): 17, 45, 35, 3. *HF Aetiology*. 71% IHD. *Co-morbidity*. 42% MI, 74% HT, 43% DM, 22% CAD. *Medications*. 82% ACE-inhibitor or angiotensin receptor blocker, 63% β-Adrenoceptor Antagonist	The SI was performed by one HF case manager, with experience in critical care and cardiology. Four major components were: (1) early discharge planning and coordination of care, (2) individualised and comprehensive patient and family HF education, (3) 12 weeks of enhanced telephone follow-up and surveillance, and (4) promotion of optimal HF medications and medication doses based on consensus guidelines. The patient received educational materials, including a 15-page HF booklet	A, B (3 m)	Re-admission rates were equal for both groups (37%). Total inpatient and outpatient median costs and re-admission median cost were reduced 14% and 26%, respectively, for the SI group. Subgroup analysis of patients who lived locally and saw a cardiologist showed a significant decrease in HF readmissions for the SI group ($P = 0.03$)
Strömberg, 2003[50]	Swedish Study (JS 3) with 166 patients initially screened and 106 patients (66%) finally included: 52 SI, 54 US. Mean age in years 77.5, 61% male. *HF severity*. NYHA Class II, III, IV (%): 18, 71, 11. Mean duration of index admission in days 8. *Co-morbidity*. 68% IHD, 40% HT, 24% DM. *Medications*. 87% ACE inhibitor, 41% Digoxin, 100% Diuretic, 19% Long-acting Nitrate, 58% β-Adrenoceptor Antagonist	Nurse-led HF clinic for making protocol-led changes in medications. The first visit was scheduled 2–3 weeks after discharge. All visits lasted for 1h and the nurse evaluated the status and if the HF treatment was optimized, gave education about HF and social support to the patient and his family. The patients could contact the clinic during daily telephone hours and the nurses called patients in order to provide psychosocial support, evaluate drug changes or other actions taken due to deterioration and side effects	B, C (3 and 12 m)	There were fewer patients with the combined end-point (re-admission or death) after 12 months in the SI group compared to the control group (29 vs 40, $P = 0.03$). The SI group had fewer re-admissions (33 vs 56, $P = 0.047$) and days in hospital (350 vs 592, $P = 0.045$) during the first 3 months. After 12 months the SI was associated with a 55% decrease in admissions/patient/month (0.18 vs 0.40, $P = 0.06$) and fewer days in hospital/patient/month (1.4 vs 3.9, $P = 0.02$)
Doughty, 2002[51]	New Zealand Study (JS 2) with 197 patients included: 100 SI, 97 US, no available information about the number of patients initially screened. Mean age in years 73, 61% male, 78% white. *HF severity*. NYHA Class III, IV (%): 24, 75; Mean EF 32%. *Co-morbidity*. 53% IHD, 45% MI, 51% HT, 29% DM, 19% CAD, 32% AF, 20% stroke. *Medications*. 88% ACE-inhibitor, 23% Digoxin, 95% Diuretic	Clinical review early after discharge at a hospital-based HF clinic. Individual and group education sessions given to the patient and patient's carer, a personal diary to record medication and body weight, information booklets and regular clinical follow-up alternating between the general practitioner and HF Clinic. Most visits occurred in HF clinics	A, B, C (1 y)	SI reduced total hospital readmissions and total bed days. The main effect of the intervention was attributable to the prevention of multiple re-admissions (56 vs 95, $P = 0.015$). SI improved quality of life

Table 2 (*continued*)

Author, year	Study and participant characteristics[a]	Main components of intervention	O/F[b]	Main findings: Intervention versus (vs) usual care[c]
Harrison, 2002[52]	Canadian Study (JS 3) with 483 patients initially screened and 192 patients (39%) finally included: 92 SI, 100 US. Mean age in years 76, 55% male. *HF severity*. NYHA Class I, II, III, IV (%): 1, 22, 67, 10. *Co-morbidity*. Mean number of Comorbidities 3.76	Inpatient and outpatient nurse led intervention focused on the transition from hospital-to-home and supportive care for self-management 2 weeks after hospital discharge (including an evidence based education program, phone outreach within 24 h of discharge, phone advice from hospital nurse and an education booklet)	B (3 m)	In the SI group the percentage of patients readmitted was 23 vs 31 in the US group ($P = 0.26$; $n = 157$, 35 patients did not complete the study to 3 m). At 3 m MLHFQ score was better in the SI group
Kasper, 2002[53]	USA Study (JS 3) with 1452 patients initially screened and 200 patients (14%) finally included: 102 SI, 98 US. Mean age in years 63.5, 61% male, 64% white. *HF severity*. NYHA Class II, III (%): 35, 58; 87% EF<45%; Mean EF 27%. *Co-morbidity*. 49% IHD, 67% HT, 40% DM. MLFHQ: 63 (f30, e14); Duke Activity Status 5. *Medications*. 86% ACE-inhibitor, 5% Angiotensin II blocker, 68% Digoxin, 97% Diuretic, 19% Long-acting Nitrate, 5% Hydralazine, 39% β-Adrenoceptor Antagonist	Outpatient multi-disciplinary programme: the intervention team consisted of a cardiologist, an HF nurse, a telephone nurse coordinator and the patient's primary physician. Contact with the patient was on a pre-specified schedule. The HF nurse followed an algorithm to adjust medications	A, B, C (6 m)	SI reduced the Combined endpoint (HF hospital re-admission or death: 43 re-admissions and 7 deaths vs 59 and 13, respectively, $P = 0.09$). The quality-of-life score, percentage of patients on target vasodilator therapy and percentage of patients Compliant with diet recommendations were significantly better in the SI group. Cost per patient was similar in both groups
Krumholz, 2002[54]	USA Study (JS 2) with 390 patients initially screened and 88 patients (23%) finally included: 44 SI, 44 US. Mean age in years 74, 57% male, 74% white. *HF severity*. Mean EF 38%. *Co-morbidity*. 61% MI, 52% DM. *Medications*. 60% ACE-inhibitor, 45% Digoxin, 43% Aspirin, 41% β-Adrenoceptor Antagonist	Outpatient nurse-led education during an hour-long face-to-face in-depth session within two weeks of hospital discharge using a teaching booklet (knowledge of the illness, the relation between health behaviours and illness, knowledge of early signs and symptoms of decompensation and where and when to obtain assistance). Home visits were performed for 45% of SI patients unable to travel to the hospital. Followed by nurse telephone contact on a weekly basis for four weeks, then biweekly for eight weeks, and then monthly. These calls re-inforced care domains but did not modify treatment	A, B, C (1 y)	SI reduced the Combined endpoint (hospital re-admission or death 25 vs 36, relative risk = 0.69, 95%CI: 0.52-0.92; $P = 0.01$). SI obtained a 39% decrease in the total number of re-admissions (49 vs 80, $P = 0.06$). After adjusting for clinical and demographic characteristics, the SI group had a significantly lower risk of re-admission (hazard ratio = 0.56; 95%CI: 0.32–0.96; $P = 0.03$) and hospital re-admission costs of $7515 less per patient

Table 2 (*continued*)

Author, year	Study and participant characteristics[a]	Main components of intervention	O/F[b]	Main findings: Intervention versus (vs) usual care[c]
McDonald, 2002[55]	Irish Study (JS 2) with 337 patients initially screened and 98 patients (29%) finally included: 47 SI, 51 US. Mean age in years 70.8, 66% male. *HF severity*. NYHA Class IV (%): 100. 63% EF$<$45%; Mean EF 37%. Mean duration of index admission in days 14.1. *HF Aetiology*. 47% IHD, 9% HT, 18% Valve Disease, 8% idiopathic. *Medications* ($n = 62$). 97% ACE inhibitor, 82% Digoxin, 95% Diuretic	Inpatient and outpatient specialist nurse led education (daily weight monitoring, disease and medication understanding, and salt restriction) systematically given to the patient and patient's carer, and dietitian consultation (on three or more occasions during index admission). Close clinic follow-up including nurse telephone contact at 3 days after discharge and weekly thereafter (for education and diuretic treatment adjustment as per protocol). At weeks 2 and 6, patient and their next of kin attended the HF clinic to check clinical status and further revise key education issues	A, C (3 m)	SI reduced the combined end-point (HF hospital re-admission or HF death: 4 vs 12, $P = 0.04$). HF re-admission was far less frequent in the SI group (25.5% vs 3.9%)
Riegel, 2002[56]	USA Study (JS 2) with 1145 patients initially screened and 358 patients (31%) finally included: 130 SI, 228 US. Mean age in years 73.9; 49% male. *HF severity*. NYHA Class I, II, III, IV (%): 10, 18, 57, 15. EF ($n = 204$): 54% EF$<$40%, Mean EF 43%. *HF Aetiology*. 65% IHD, 69% HT, 21% myocardiopathy, 10% valve disease. *Co-morbidity*. 42% DM, 36% CAD, 24% AF, 10% stroke. SAS Class I:II:III:IV (%): 10, 18, 57, 15. Charlson comorbidity category Low, Moderate, High (%): 41, 40, 19. *Medications*. 54% ACE-inhibitor, 62% Digoxin, 86% Diuretic	Telephonic case management by a nurse, using a decision-support software program. The patient was telephoned within 5 days after hospital discharge and thereafter at a frequency guided by the software and case manager judgment	A, B (3 and 6 m)	The HF hospitalisation rate was 47.5% lower in the intervention group at 3 months ($P = 0.03$) and 47.8% lower at 6 months ($P = 0.01$). HF hospital days ($P = 0.03$) were significantly lower in the intervention group at 6 months ($P = 0.04$). A cost saving was realised even after intervention costs were deducted. There was no evidence of cost shifting to the outpatient setting. Patient satisfaction with care was higher in the intervention group
Stewart, 2002[57]	Australian Study with 297 patients included: 149 SI, 148 US; it is a pooled analysis over a longer follow-up of 2 cohorts, with interim results reported previously. Mean age in years: 75, 56% male, 29% Non-English speaking. *HF Severity*. NYHA Class II, III, IV (%): 45, 45, 10. Mean EF 38%. *Co-morbidity*. MI 55%, HT 86%, DM 42%, CAD 36%, AF 33%, Charlson 2.9, Dependent for $\geqslant$ 1 activity of daily living 72%. Median duration of index admission in days: 5. *Medications*. 71% ACE inhibitor, 66% Digoxin, 97% Diuretic, 32% β-Adrenoceptor Antagonist	Interventions on a cohort ($n = 97$) reported in Stewart (1998) and on another cohort ($n = 200$) reported in Stewart (1999). In both cohorts, SI patients received a structured home visit within 7 to 14 days of discharge	B, C (4.2 y)	There were significantly fewer unplanned readmissions (0.17 vs 0.29 readmissions per patient per month; $P < 0.05$) and fewer combined end-points (unplanned readmission or death): a mean of 0.21 vs 0.37 events per patient per month ($P < 0.01$). Mean event-free survival was more prolonged (7 vs 3 months; $P < 0.01$). Assignment to intervention was both and independent predictor of event-free survival (RR 0.70; $P<0.01$) and survival alone (RR 0.72; $P < 0.05$). The mean cost of these readmissions was $A325 vs $A660/month ($P < 0.01$)

Table 2 (*continued*)

Author, year	Study and participant characteristics[a]	Main components of intervention	O/F[b]	Main findings: Intervention versus (vs) usual care[c]
Blue, 2001[58]	United Kingdom Study (JS 3) with 801 patients initially screened and 165 patients (21%) finally included: 84 SI, 81 US. Mean age in years 75, 58% male. *HF severity*. NYHA Class II, III, IV (%): 21, 38, 41. 38% severe ventricular dysfunction. *Co-morbidity*. 47% IHD, 53% MI, 47% HT, 17% Valve disease, 18% DM, 25% CAD, 33% AF. Mean duration of index admission in days 8.5. *Medications*. 46% ACE-inhibitor, 19% Digoxin, 74% Diuretic, 25% Nitrate, 13% β-Adrenoceptor Antagonist	Planned nurse home visits of decreasing frequency, supplemented by telephone contact as needed. The aim was to educate the patient about HF and its treatment, optimise treatment, teach self-monitoring and management (especially of early decompensation), monitor electrolyte concentrations, liaise with other health care and social workers, and provide psychological support. Nurses used written protocols on the use of medications. Participants received HF instruction and personal diary booklet	A, B, C (12 m)	SI reduced the combined end-point (HF hospital admission or death, hazard ratio = 0.61, 95% Cl: 0.33, 0.96). There were fewer readmissions for any reason (86 vs 114, $P = 0.018$), fewer admissions for HF (19 vs 45, $P < 0.001$), and fewer days in hospital for HF (mean 3.43 vs 7.46 days, $P = 0.005$)
Jerant, 2001[59]	USA Study (JS 3) with 740 patients initially screened and 37 patients (5%) finally included: 25 SI, 12 US. Mean age in years 70.1, 46% white. *HF severity*. NYHA Class II, III, IV (%): 65, 32, 3. 43% ventricular dysfunction. *Co-morbidity*. 27% IHD, 81% HT, Charlson 1.9; MLHFQ: 60; SF-36 (m, ph): 42, 30.5. *Medications*. 65% ACE-inhibitor, 8% Angiotensin II blocker, 3% Digoxin, 89% Diuretic, 40% Nitrate, 8% Hydralazine, 38% β-Adrenoceptor Antagonist	Outpatient management program: 13 patients were randomized to Home Telecare Nursing Intervention, 12 to Telephone Home Nursing Intervention, and 12 to US. The aim was to educate the patient about HF. Following each encounter a summary letter containing any recommendations was sent to the appropriate primary care provider	A, B (6 m)	Trends favouring both interventions were noted for readmissions for any reason (9 and 5 vs 15, respectively, $P > 0.05$) and for re-admissions for HF (1 and 1 vs 4, respectively, $P > 0.05$). Mean HF related re-admissions costs were 86% lower in the telecare group ($5850) and 84% lower in the telephone group ($7320) than in the US group ($44,479). However, the between-group difference was not statistically significant
McDonald, 2001[60]	Irish Study (JS 2) with 232 patients initially screened and 70 patients (30%) finally included: 35 SI, 35 US. Mean age in years 68.9, 67% male. *HF severity*. NYHA Class IV (%): 100. 71% EF<45%; Mean EF 39%. Mean duration of index admission in days 10.5. *HF Aetiology*. IHD 67%, HT 33%, Idiopathic 13%, Valve Disease 31%. *Medications*. 68% ACE inhibitor, 51% Digoxin, 100% Diuretic	Inpatient and outpatient specialist nurse-led education (daily weight monitoring, disease and medication understanding, and salt restriction) systematically given to the patient and patient's carer, and dietician consultation (on three or more occasions during index admission). Close clinic follow-up including nurse telephone contact at 3 days after discharge and weekly thereafter (for education and diuretic treatment adjustment as per protocol)	B (1 m)	Elimination of 1-month hospital re-admission in both SI and US groups (20% 1-month re-admission rate prior to enrollment in both groups). Both groups obtained an inpatient improvement in HF management
Hughes, 2000[61]	USA Study (JS 2) with 1966 patients included, but only 30 with HF: 14 SI, 16 US. No available descriptive data of HF patients, but results are given separately for this subgroup	Team-Managed Home-Based Primary Care (TM/HBPC), including 24-h contact with patients, TM/HBPC prior approval of hospital readmissions, and TM/HBPC participation in discharge planning	B (6 and 12 m)	Number of re-admissions per patient (HF patients) were 2.2 vs 1.6 ($P = 0.68$) at 6 months, and 3.6 vs 2 ($P = 0.51$) at 12 months ($P = 0.51$)

Table 2 (*continued*)

Author, year	Study and participant characteristics[a]	Main components of intervention	O/F[b]	Main findings: Intervention versus (vs) usual care[c]
Philbin, 2000[62]	USA Study with 10 hospitals included, 5 hospitals were randomly assigned to SI ($n = 762$ during the baseline period, $n = 840$ post-intervention), and 5 hospitals to US ($n = 640$ during the baseline period, $n = 664$ post-intervention). Mean age in years 76, 44% male, 97% white. *HF severity*. NYHA III–IV 89%, Mean EF 38%. *Co-morbidity*. 37% IHD, 15% HT, 13% Myocardiopathy, 11% Valve disease. Charlson 2,9. Duration of index admission in days 7.9. *Medications*. 44% ACE-inhibitor, 43% Digoxin, 70% Diuretic, 35% Nitrate, 15% β-Adrenoceptor Antagonist	Quality improvement intervention attempted to maximize the implementation of an inpatient critical pathway for HF management (time-task matrix) and to improve provider and patient knowledge	A, B (6 m)	There were small and no significant effects on hospital re-admission (−0.8% re-admissions for any reason, −0.2% re-admissions for HF)
Jaarsma, 1999[63]	Netherlands Study (JS 3) with 644 patients initially screened and 177 patients (28%) finally included: 84 SI, 95 US. Mean age in years 73, 58% male. *HF severity*. NYHA Class III, IV (%): 17, 62. Mean EF 34%. *Co-morbidity*. 52% IHD, 59% MI, 23% HT, 23% Myocardiopathy, 30% DM, 24% CAD. Mean duration of index admission in days 13.6. *Medications*. 70% ACE inhibitor, 47% Digoxin, 91% Diuretic, 84% Nitrate	Intensive, systematic, tailored and planned education, and support to the patient and family, by a nurse, on self-care and resource utilisation. Within 1 week after discharge the study nurse telephoned the patient to assess potential problems and to make an appointment for a home visit. The intervention lasted from hospital admission to 10 days after discharge from hospital	A, B (9 m)	There were fewer patients readmitted for any cause (37% vs 50%, $P = 0.06$) and for cardiac causes (29% vs 39%, $P = 0.09$)
Naylor, 1999[64]	USA Study (JS 3) with 363 patients included, but only 60 with HF: 30 SI, 30 US. No available descriptive data of HF patients, but results are given separately for this subgroup	Comprehensive discharge planning by advanced practice-nurse (APN) and home follow-up. Initial APN visit within 48 h of hospital admission, APN visits at least every 48 h during index hospitalisation; at least 2 home APN visits (1 within 48 h after discharge, a second 7–10 days after discharge); additional APN visits based on patient's needs with no limit on number. APN availability 7 days per week (8 AM to 10 PM on weekdays, and 8 AM to noon on weekends); and at least weekly APN-initiated contact with patients and caregivers. The intervention extended from hospital admission through 4 weeks after discharge	B (6 m)	Among patients with HF there were fewer readmissions for any cause (1.48 vs 1.93 per patient per year). Among all study subjects, intervention reduced re-admissions, lengthened the time between discharge and re-admission, and decreased the costs of health care

Table 2 (*continued*)

Author, year	Study and participant characteristics[a]	Main components of intervention	O/F[b]	Main findings: Intervention versus (vs) usual care[c]
Rainville, 1999[65]	USA Study (JS 2) with 377 patients initially screened and 34 patients (9%) finally included: 17 SI, 17 US. Mean age in years 69.8, 50% male. *HF severity*. NYHA Class II, III, IV (%): 14, 68, 18. Mean duration of index admission in days 6.4. *Co-morbidity*. 27.9 Nelson Functional Health Assessment Score (a score of 9 represents the best health and a score of 45 represents the worst health). *Medications*. 88% ACE-inhibitor, 80% Digoxin, 44% β-Adrenoceptor Antagonist	A pharmacist and a clinical nurse specialist identified patient issues that posed potential risk for re-hospitalisation and determined corrective action. The pharmacist reviewed with the patient or caregiver the pathology and pharmacotherapy of HF, weight monitoring, and risk modifications. A patient information brochure, videotape, weight log booklet, and medication organiser were provided. If necessary, the pharmacist recommended medication changes to the physicians	A, B, C (1 y)	SI reduced the combined end-point (death or re-admission): 5 vs 14, $P < 0.05$ and there were fewer patients re-admitted for HF: 4 vs 10, $P < 0.05$. Time to readmission for HF or patient death was significantly longer in SI group ($P < 0.01$). The total number of re-admissions was 20 in the SI group and 26 in US group. The difference was due to the re-admissions for HF, each group had 16 re-admissions for other reasons
Stewart, 1999[66]	Australian Study (JS 3) with 4055 patients initially screened and 200 patients (5%) finally included: 100 SI, 100 US. Mean age in years 75.6, 68% male. *HF severity*. NYHA Class II, III, IV (%): 45, 45, 10. 64% EF<40%. Mean EF 37%. *Co-morbidity*. 78% IHD, 57% MI, 65% HT, 34% DM, 36% CAD, 35% AF. Charlson 3.1; 52% Dependent for ⩾1 activity of daily living, MMSE 29. Mean duration of index admission in days 6.8. *Medications*. 71% ACE-inhibitor, 66% Digoxin, 97% Diuretic, 76% Nitrate, 28% β-Adrenoceptor Antagonist, 23% Warfarin	Structured home visit by a nurse within 7 to 14 days of discharge (physical examination, treatment adherence, education, psychological support, simple exercise regimen, incremental monitoring by family/carers; initiating daily weighing). The nurse co-ordinated efforts to optimise the patient's management and provided a critical link to the appropriate health care if problems arose. Home visits were repeated only if a patient had two or more unplanned re-admissions within 6 months of the index admission. Patients were contacted by telephone at 3 months and 6 months	B, C (6 m)	There were fewer combined end-point events (unplanned re-admission plus out-of-hospital death): 77 vs 129, $P = 0.02$. Event-free survival hazard ratio: 0.66 (CI 95% 0.53–0.79). There were fewer unplanned re-admissions (68 vs 118; $P = 0.03$) and associated days in hospital (460 vs 1173; $P = 0.02$). Hospital-based costs were Aust $490,300 vs Aust $922,600; $P = 0.16$; the mean cost of the interventions was Aust $350 per patient, and other community-based costs were similar for both groups
Stewart, 1999[67]	Australian Study; with 97 patients included: 49 SI, 48 US. It is a subgroup of medical and surgical patients participating in a larger randomised trial, and the same cohort of patients studied in Stewart (1998) but with an 18 month follow-up. Mean age in years 75, 48% male. *HF severity*. NYHA Class II, III, IV (%): 49, 45, 6. Mean EF 38%. *Co-morbidity*. IHD 67%, MI 42%, CAD 36%. Mean duration of index admission in days 7.8. *Medications*. 82% ACE-inhibitor, 67% Digoxin, 100% Diuretic	Single home visit within 1 week after discharge (by a nurse and a pharmacist) to optimise medication management, identify early clinical deterioration, and intensify medical follow-up and caregiver vigilance where appropriate	B (18 m)	There were fewer combined end-point events per patient (unplanned re-admission plus out-of-hospital death): 1.4 ± 1.3 vs 2.7 ± 2.8, $P = 0.03$; and fewer days of hospitalisation per patient: $2.5 \pm 2,7$ vs 4.5 ± 4.8, $P = 0.04$; and once re-admitted, were less likely to experience 4 or more re-admissions: 3/31 vs 12/38, $P = 0.03$. Hospital-based costs were significantly lower (Aust $5100 vs Aust $10,600 per patient, $P = 0.02$)

Table 2 (continued)

Author, year	Study and participant characteristics[a]	Main components of intervention	O/F[b]	Main findings: Intervention versus (vs) usual care[c]
Cline, 1998[68]	Swedish Study (JS 2) with 199 patients included: 56 SI, 79 US, no available information about the number of patients initially screened. Mean age in years 75.6, 53% male. *HF severity*. NYHA mean class 2.6. Mean EF 11%. *Co-morbidity*. 53% IHD, 41% MI, 30% HT, 22% DM, 38% AF, 12% Stroke. *Medications*. 22% ACE-inhibitor, 31% Digoxin, 72% Diuretic, 33% Nitrate, 10% β-Adrenoceptor Antagonist	Education program on HF: two 30 min information visits by a nurse during primary hospitalisation and a 1 h information visit for patients and family two weeks after discharge. Patients received an HF instruction and personal diary booklet. Patients were followed-up at an easy access, nurse directed, outpatient clinic. The nurse was available by telephone during office hours and was able to see patients at short notice. There was only one prescheduled visit by the nurse at eight months after discharge	B (1 y)	Mean time to re-admission was longer (141 vs 106 days; $P < 0.05$) and number of days in hospital tended to be fewer (4.2 vs 8.2 days; $P = 0.07$). There was a trend towards a reduction in health care costs per patient ($2294 vs $3549; $P = 0.7$)
Ekman, 1998[69]	Swedish Study (JS 3) with 1741 patients initially screened and 158 patients (9%) finally included: 79 SI, 79 US. Mean age in years 79, 58% male. *HF severity*. 100% NYHA III—IV. 60% EF<40%. *Co-morbidity*. 54% IHD, 36% MI, 22% DM, 32% AF, 18% Stroke. *Medications*. 29% ACE inhibitor, 32% Digoxin, 73% Diuretic, 18% Nitrate, 24% β-Adrenoceptor Antagonist	Nurse-monitored outpatient-care program aiming at symptom management. The patient was contacted a week after discharge and offered a visit to the HF clinic. Each patient's care was individually planned according to optimal number of visits and specific goals. The nurse was always available by pager during business hours. Patients received a teaching and personal diary booklet of HF	A, B (6 m)	No visits to the nurse occurred in 23 cases among the 79 patients randomised to SI (29%), mainly on account of death or fatigue. The number of hospitalisations (mean difference −0.1, CI 95% −0.5, 0.3 re-admissions) and hospital days did not significantly differ between groups. The difference in mean values of hospital days was 8 days and in the median values 4 days ($P = 0.29$)
Serxner, 1998[70]	USA Study (JS 1) with 109 patients included: 55 SI, 54 US, no available information about the number of patients initially screened. Mean age in years 71, 48% male. Health Status 2.9 (5 point scale)	Patient education mailing program (mailing every three weeks). Patients received an HF instruction and personal diary booklet and a video on HF	A (6 m)	A significant reduction of 44% on number of patients re-admitted one or more times (15 vs 27). Likewise there were half as many total re-admissions (21 vs 43). The intervention represents an $8:$1 return-on-investment to the hospital. The return-on-investment to the healthcare payer would be $19:$1
Stewart, 1998[71]	Australian Study with 97 patients included: 49 SI, 48 US. It is a subgroup of medical and surgical patients participating in a larger randomised trial. Mean age in years 75, 48% male. *HF severity*. NYHA Class II:III:IV (%): 50, 43, 7. Mean EF 39%. *Comorbidity*. IHD 66%, MI 43%, HT 41%, DM 22%, CAD 35%, AF 32%. Charlson 2,2. Mean duration of index admission in days 7.8. *Medications*. 82% ACE inhibitor, 67% Digoxin, 99% Diuretic, 59% Nitrate	Single home visit within 1 week after discharge (by a nurse and a pharmacist) to optimise medication management, identify early clinical deterioration, and intensify medical follow-up and caregiver vigilance where appropriate	B, C (6 m)	There were fewer combined end-point events per patient (unplanned re-admission plus out-of-hospital death):0.8 ± 0.9 vs 1.4 ± 1.8, $P = 0.03$ and fewer days of hospitalisation: 261 vs 452, $P = 0.05$; and once re-admitted, were less likely to experience 3 or more re-admissions for HF ($P = 0.02$). SI was associated with a trend toward reduced risk of unplanned re-admission (OR: 0.4; 95% CI, 0.2—1.1)

Table 2 (*continued*)

Author, year	Study and participant characteristics[a]	Main components of intervention	O/F[b]	Main findings: Intervention versus (vs) usual care[c]
Weinberger, 1996[72]	USA Study: it is a multi-centre trial at nine Veterans Affairs Medical Centers with 1396 patients included, but only 504 HF patients: 249 SI, 255 US. *HF severity*. NYHA Class I, II, III, IV (%): 12, 37, 33, 18. No more available descriptive data about HF patients, but results are given separately for this subgroup. In general, patients had extremely poor quality-of-life scores	Close follow-up by a nurse and a primary care physician, beginning before discharge (including patient education), and continuing for the next six months (including a nurse telephone contact two days after discharge and primary care physician clinic scheduled visits)	B (6 m)	The intervention group had a significantly higher proportion of patients re-admitted (52.2 vs 41.5%), a significantly higher monthly re-admission rate (0.27 ± 0.7 vs 0.15 ± 0.3), and more days of re-admission (11.7 vs 8.3)
Rich, 1995[73]	USA Study (JS 3) with 1306 patients initially screened and 286 patients (22%) finally included: 142 SI, 140 UC. Mean age in years 79, 37% male, 45% white. *HF severity*. NYHA mean class 2.4. Mean EF 42%. *Co-morbidity*. 57% IHD, 43% MI, 65% HT, 28% DM. *Medications*. 59% ACE-inhibitor, 37% Digoxin, 84% Diuretic, 67% Nitrate, 12% β-Adrenoceptor Antagonist	Nurse-directed multi-disciplinary intervention including comprehensive education of the patient and family, a prescribed diet, social-service consultation planning for early discharge, a review of medications by a geriatric cardiologist, and intensive follow-up through the hospital's home care services, supplemented by individualised home visits and telephone contact	A, B, C (3 m)	There were fewer patients re-admitted (risk ratio, 0.56; $P = 0.02$). The number of re-admissions for heart failure was significantly reduced by 56.2 percent, whereas the number of re-admissions for other causes was reduced by 28.5 percent ($P > 0.05$). Fewer patients had more than one readmission (risk ratio, 0.39; $P = 0.01$). There was a non significant reduction in the combined end-point hospital admission or death (−10.5%). The overall cost of care was $460 less per patient
Rich, 1993[74]	USA Study (JS 2) with 261 patients initially screened and 98 patients (38%) finally included: 63 SI, 35 US. Mean age in years 79, 41% male, 50% white. *HF severity*. NYHA mean 2.8. 61% EF<50%. *Co-morbidity*. 24% MI, 65% HT, DM 31%	Nurse-directed multi-disciplinary intervention including comprehensive education of the patient and family, a prescribed diet, social-service consultation planning for early discharge, a review of medications by a geriatric cardiologist, and intensive follow-up through the hospital's home care services, supplemented by individualised home visits and telephone contact	B (3 m)	There were fewer patients re-admitted (33.3% vs 45.7, $P > 0.05$) and fewer days of hospitalisation (4.3 vs 5.7, $P > 0.05$). Recurrent HF was less frequently the primary cause for re-admission (35.0% vs 57.1%)

[a] ACE, Angiotensin converting enzyme; AF, Atrial fibrillation; EF, ejection fraction; CAD, Chronic airways disease; Charlson, Mean Charlson Index of co-morbidity score; DM, Diabetes mellitus; HF, Heart failure; HT, hypertension; IHD, ischaemic heart disease; JS, Jadad Score; MI, myocardial infarction; MLHFQ, Minnesota Living with Heart Failure Questionnaire scores; MMSE, mean Mini-Mental State Examination score; *n*, number of patients included in the study; SAS, Specific Activity Scale scores; SF-36 (m, ph), Medical Outcomes Study SF-36 questionnaire scores (Mental component, Physical component); SI, study intervention; US, usual care.

[b] O/F, Outcome class: A, Heart Failure or cardiovascular re-admission; B, Re-admission for any cause; C, Combined end-point: death or re-admission. Underlined outcomes are those which were included in the meta-analysis. Duration of follow-up is shown in brackets (y, year; m, month).

[c] 95%CI: 95% confidence interval.

With regards to patient characteristics, an average of only 26% (range 5–67%) of initially screened patients was included in the trials. Among the included patients the mean age was over 70 years in most studies. Patients presented with ejection fractions $<$40% in 13 studies, and serious co-morbidity was frequent, principally acute myocardial infarction, arterial hypertension, heart valve disease and diabetes. The majority of patients received ACE-Inhibitor (range 22–97%) and diuretics (range 70–100%); digoxin (range 3–97%) and beta-adrenoceptor antagonists (range 10–63%) were also given to a lesser extent.

Interventions had an important patient education and support component; in many cases, subjects were informed about the nature of HF, alerted to signs of early decompensation, and taught disease management (Table 2). Moreover, in all but 4 studies[49,61,62,70] mention was made of the participation of nurses in the administration or co-ordination of the intervention, and in all but 3 studies,[51,62,70] mention was made of the use of telephone calls as part of the intervention. However, interventions were more variable with regard to place of commencement (in the hospital or after discharge), type of organising care (home visit or out-patient visit to clinic), and duration (ranging from a single home visit or duration of a single week to interventions lasting 12 months).

As the end-point was hospital re-admission, a simple variable obtainable even without contact between investigators and patients (e.g., from administrative sources), loss to follow-up was very small. In all studies the loss was below 5%, with the exception of the study by Laramee where it was 8%.[49] Follow-up of subjects tended to be from 3 to 12 months, though the study by Stewart and Horowitz,[57] reported a median 4.2-year follow-up. Results usually revealed a trend towards improvement in most of the end-points studied: percentage of re-admissions, number of re-admissions per patient and month, re-admission-free time, days of re-admission, etc. (Table 2).

Fig. 1 shows a forest plot of the studies eligible for meta-analysis. With respect to re-admission for HF or cardiovascular cause, six studies reported an homogeneous and significant reduction in re-admission[47,48,54–56,58,60] (Fig. 1(a)). On the basis of the 3160 patients covered, the studies suggest that DMP reduces the frequency of re-admission for HF or cardiovascular cause by 30% (pooled RR 0.70; 95% confidence interval (CI) 0.62–0.79).

With regards to all-cause re-admission, only three studies[48,56,73] reported a significant reduction (Fig. 1(b)). The results of the trials showed certain heterogeneity ($P = 0.012$), due mainly to the study by Weinberger et al.,[72] which reported a statistically significant increase in re-hospitalisations (Fig. 1(b)). A random-effects model based on 4440 patients showed that DMP reduced all-cause re-admissions by 12% (pooled RR 0.88, 95% CI: 0.79–0.97). The study by Weinberger et al.,[72] included patients with an extremely low quality of life; moreover, the intervention simply afforded patients enhanced access to primary-care services, without improving the healthcare delivery structure.[102] Once we excluded this paper, because it dealt with a disease management programme with very limited treatment modalities, the homogeneity of the results across trials rose ($P = 0.31$) and the pooled RR, calculated for 3936 patients, was 0.85, 95% CI: 0.79–0.92. It should be highlighted that the study by Stewart et al.,[57] is not shown in Fig. 2(b) because, despite being the only study with a follow-up of more than 4 years, it embraced subjects from two previous studies[66,71] which had a six-month follow-up and had already been included in Fig. 1. The study by Stewart et al.,[57] was nevertheless incorporated into the sensitivity analysis, with those studies having a follow-up of more than 6 months (see Table 3 below). An earlier study by Stewart et al.,[67] was likewise not included, as it consisted of an 18-month follow-up of patients from another previous study.[71]

For the combined end-point of re-admission or death, four studies[48,54,55,65] reported a statistically significant reduction although three of them had a very small size.[54,55,65] Study results for this end-point were fairly heterogeneous ($P = 0.001$), although more so in terms of the magnitude of the effect measured than in terms of its direction (all studies but one[52] registered an RR of less than 1) (Fig. 1(c)). Based on a total of 2985 patients, DMPs reduced the frequency of this end-point by 18% (pooled RR 0.82, 95% CI: 0.72–0.94). The study by McDonald et al.,[60] was not included in this analysis because it consisted of a one-month follow-up of most of the patients who had been followed up over three months in another, already included, study by the same authors.[55] The study by McDonald et al.,[60] reported the elimination of 1-month hospital re-admission in both regular and multi-disciplinary care. The authors stated that this unexpected result represented a dramatic improvement, both for this patient cohort (20% 30–day pre-enrolment re-admission rate reduced to 0% following index admission in both care groups), and in comparison with available data. Lastly, the only study that examined long-term mortality (4.2 years) observed a marginally significant reduction due to the DMP (56% in the DMP versus 65% in the usual care group; $P = 0.06$).[57]

There was no substantial variation in results when only DMPs with patient follow-up longer than 6 months,[47,50,51,54,57,58,61,63,65,68] home visits,[52,54,57,58,63,64,66,71,73,74] or out-patient visits to a clinic[50,51,53–55,68,69,72–74] were included (Table 3). In the case of DMPs with out-patient visits to a clinic, however, the reduction in the frequency of re-admission for HF or cardiovascular disease, and for all causes, failed to attain statistical significance (Table 3). When only studies with a Jadad score of 3 were selected,[48,50,52,53,58,63,64,66,69,73] the results again did not vary substantially, but they were now homogeneous for the end-points of all-cause re-admission, and re-admission or death (Table 3).

There was some indication of asymmetry in the funnel plots for the three outcomes considered, in that there was a gap in the right bottom side of the graphs. The asymmetry was statistically significant for heart failure or cardiovascular re-admission, and for re-admission or death (Fig. 2). Therefore the results were compatible

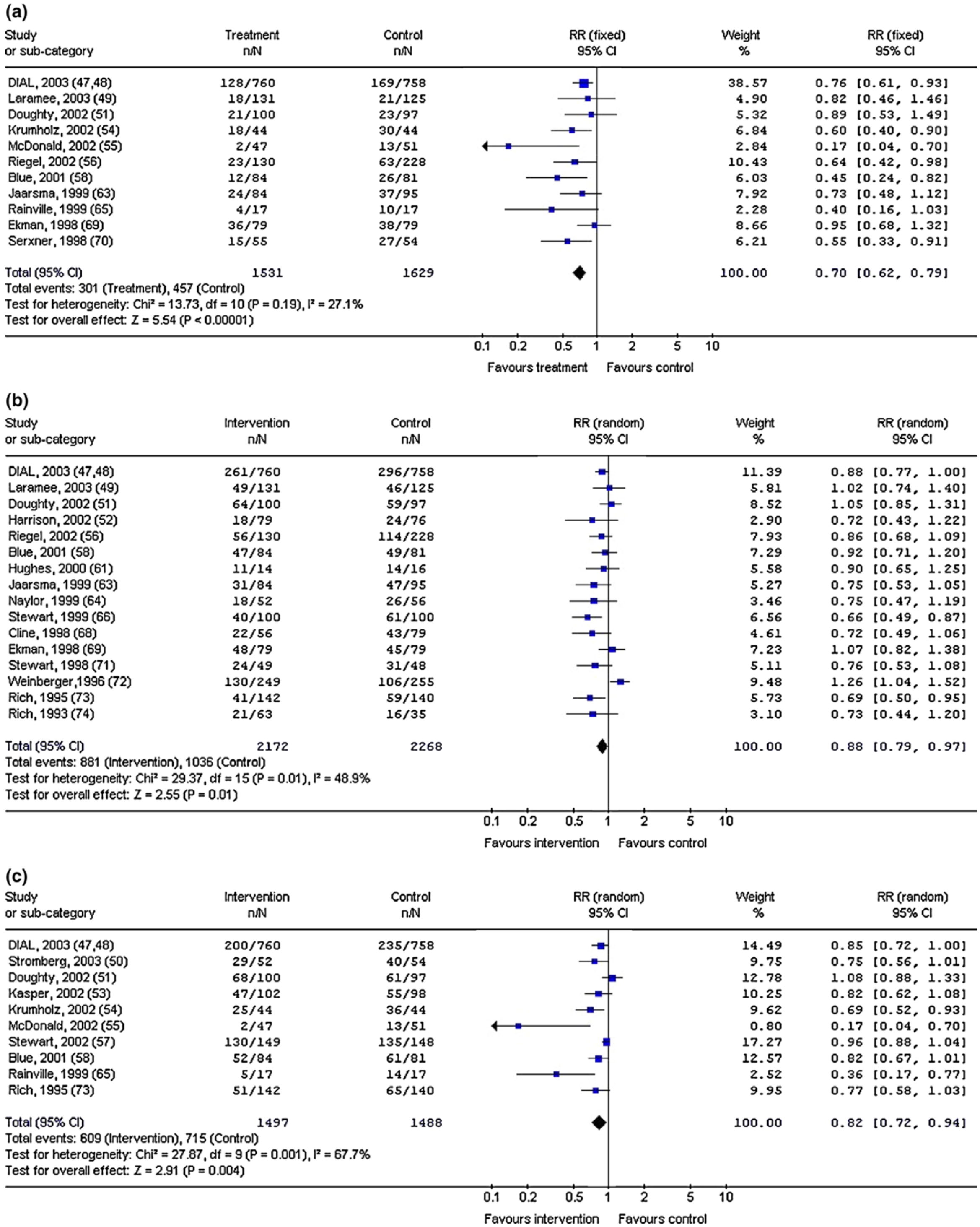

Fig. 1 Meta-analysis of the effectiveness of disease management programs on three outcomes among older patients with heart failure. Randomised studies. (a) Heart failure or cardiovascular readmission, (b) all cause readmission, (c) readmission or death.

with certain publication bias. However, if such bias really exists, its magnitude is likely to be small, because sensitivity analyses showed that pooled RR for the three outcomes did not vary significantly when small studies (e.g., less than 100 subjects) were excluded (Table 3).

A number of studies reported that DMPs has a greater effect reducing multiple versus first re-hospitalisations.[51,54,56,73] In addition, Stewart et al.,[67] and Rich et al.,[74] found that in the subgroup of patients with a worse clinical situation, DMPs increased re-hospitalisation.

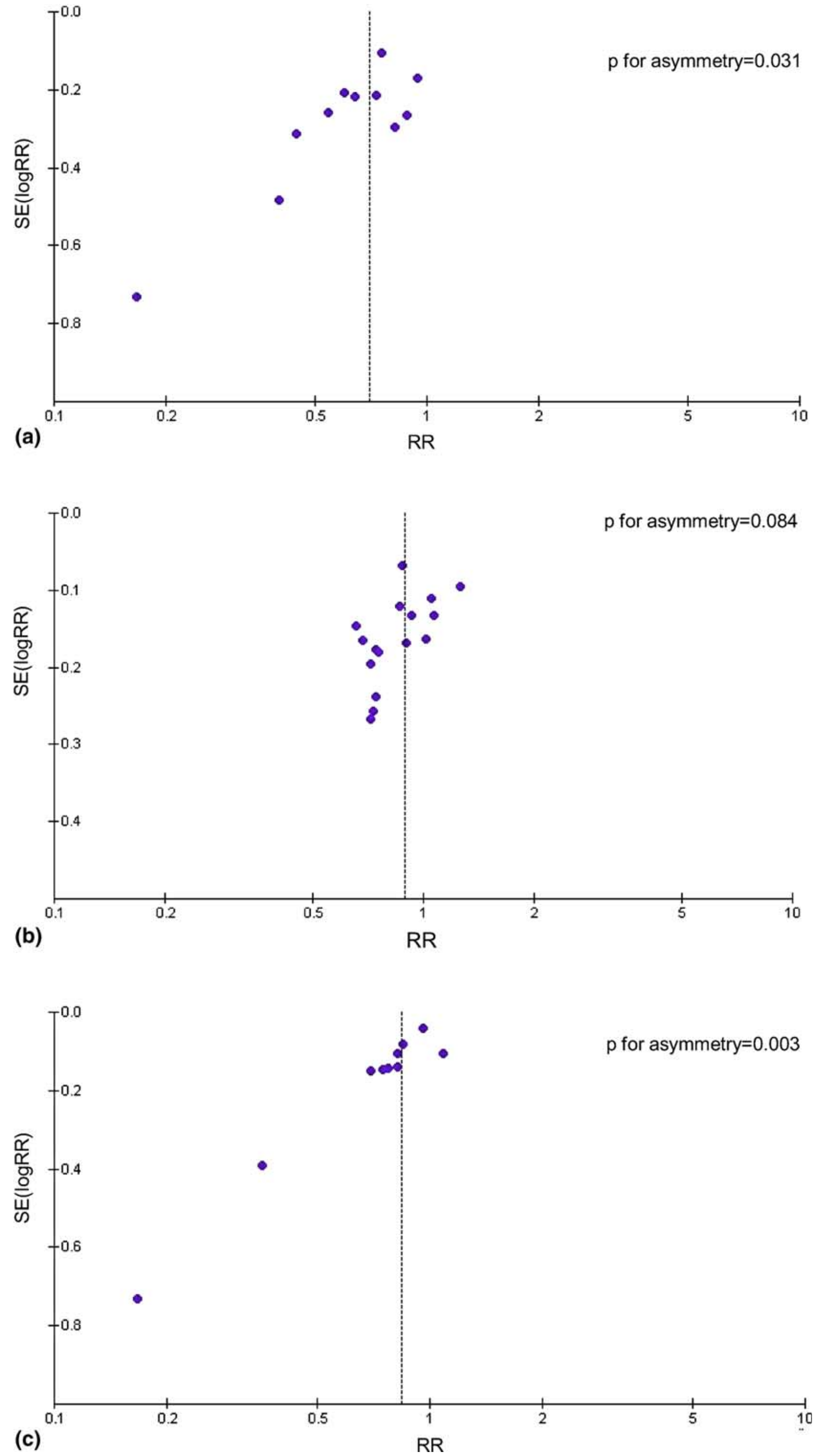

Fig. 2 Funnel plots for the three outcomes among older patients with heart failure. The vertical line in the graphs corresponds to the pooled relative risk across studies. (a) Heart failure or cardiovascular readmission, (b) all cause readmission, (c) readmission or death.

Of the 27 studies included in the review, 13 assessed the cost of DMP versus that of usual HF management. Two of these studies[61,64] were not considered because they did not report data specifically for subjects with HF and their patients were mostly elderly subjects with other diseases. Ten studies[48,49,54,56,59,66–68,70,73] estimated that the implementation of a DMP reduced costs and only one study[53] reported similar costs in the DMP and usual-care groups. Lastly, an economic analysis of the data from the trial by McDonald et al.,[55] published subsequently, suggested that intervention was cost-effective.[103] Similarly, Stewart et al.,[104] carried out an

Table 3 Effectiveness of a disease management program (DMP) in reducing hospital re-admissions or death in older patients with heart failure, by DMP characteristics and duration of follow-up

	Number of studies	Number of subjects	Test for heterogeneity (*P*-value)	Pooled relative risk (95% CI)	*P*-value
Re-admission for heart failure or other cardiovascular disease					
All studies[48,49,51,54,55,56,58,63,65,69,70]	11	3160	0.19	0.70 (0.62–0.79)	<0.0001
Follow-up >6 months[48,51,54,58,63,65]	6	2181	0.37	0.71 (0.61–0.83)	<0.0001
Home visits[54,58,63]	3	432	0.41	0.61 (0.46–0.79)	0.0003
Visits to a clinic[51,54,55,69]	4	541	0.052	0.71 (0.47–1.08)[a]	0.11
Jadad score = 3[48,58,63,69]	4	2020	0.19	0.75 (0.64–0.80)	0.0003
More than 100 subjects[48,49,51,56,58,63,69,70]	8	2307	0.25	0.76 (0.65–0.89)	0.0008
All-cause re-admission					
All studies[48,49,51,52,56,58,61,63,64,66,68,69,71,72,73,74]	16	4440	0.01	0.88 (0.79–0.97)[a]	0.01
Follow-up >6 months[48,51,58,61,63,68]	6	2224	0.46	0.88 (0.80–0.97)	0.010
Home visits[52,58,61,63,64,66,71,73,74]	9	1314	0.77	0.75 (0.66–0.85)	<0.0001
Visits to a clinic[51,68,69,72,73,74]	6	1374	0.0077	0.94 (0.76–1.15)[a]	0.53
Jadad score = 3[48,52,58,63,64,66,69,73]	8	2765	0.21	0.83 (0.76–0.91)	<0.0001
More than 100 subjects[48,49,51,52,56,58,63,64,66,68,69,72,73]	13	4215	0.006	0.89 (0.79–0.99)[a]	0.04
Re-admission or death					
All studies[48,50,51,53,54,55,57,58,65,73]	10	2985	0.001	0.82 (0.72–0.94)[a]	0.004
Follow-up >6 months[48,50,51,54,57,58,65]	7	2405	0.0043	0.85 (0.74–0.97)[a]	0.02
Home visits[54,57,58,73]	4	832	0.018	0.83 (0.69–1.00)[a]	0.05
Visits to a clinic[50,51,53,54,55,73]	6	971	0.017	0.80 (0.65–0.98)[a]	0.04
Jadad score = 3[48,50,53,58,73]	5	2271	0.95	0.82 (0.74–0.91)	0.0003
More than 100 subjects[48,50,51,53,57,58,73]	7	2765	0.07	0.87 (0.81–0.94)	0.0006

[a] Random-effects model.

economic analysis of DMP in HF based on data yielded by previous trials, and concluded that DMP, particularly those including nurse-coordinated home visits, were very effective.

Non-randomised trials

Table 4 summarises the 27 non-randomised trials included in the review. Patient characteristics and type of intervention were similar to those of randomised studies. In the great majority of studies DMP were also associated with favourable results for several of the end-points considered.

No study adjusted for confounding factors as important as co-morbidity or type of drug treatment, and only one was adjusted for disease severity.[79] In 14 studies[75,78,79,82,86,88,91–93,95,97–99,101] before-and-after comparisons were made using the same subjects, so that both sex and (as the follow-up period was relatively short) age were deemed to be adjusted. Some studies matched control subjects for sex and age,[81] functional status, co-morbidity and age,[87] and sex and medical claims.[90]

Of the 12 studies that furnished information on re-admissions for HF, five were eligible for meta-analysis (Fig. 3(a)). Three studies[78,92,97] reported a significant reduction ($P < 0.05$) in re-hospitalisations in the intervention groups, and the other 2 showed a trend to reduce hospitalisations. However, there was heterogeneity in the magnitude of the benefit across studies ($P < 0.001$). Based on a total of 1875 patients, the pooled RR was 0.38; 95% CI: 0.16–0.93. Favourable results for DMPs even improved (pooled RR 0.2; 95% CI: 0.09–0.64) after exclusion of two trials in which the interventions (HF observation unit in hospital emergency ward[78] and use of a clinical pathway to reduce hospital stay)[80] were somewhat different to those in the remaining studies.

Of the 16 studies that reported data on all-cause re-admission (Fig. 3(b)), eight were meta-analysed. Only three studies[82,84,85] showed a significant reduction ($P < 0.05$) in re-hospitalisations, and the pooled RR ($n = 1599$ patients) across all studies was 0.50, 95% CI: 0.34–0.74. These results were not substantially modified (pooled RR 0.41; 95% CI: 0.30–0.79) by exclusion of the study by Luzier et al.,[85] which differed from the remaining DMP, in that it consisted of optimization of ACE-inhibitor dosage by a clinical pharmacist. Lastly, only two studies[76,77] supplied information on the combined end-point of re-hospitalisation or death, and both suggested that DMPs had a favourable effect (pooled RR 0.37; 95% CI: 0.24–0.58) (Fig. 3(c)).

Of the 27 studies reviewed, only 12 assessed the cost of DMPs versus that of usual HF management.[79,81–83,85–87,89–91,94,101] All concluded that there was a reduction in cost with DMP, though in two studies[85,87] costs increased in two subgroups of patients.

Table 4 Non-randomized trials evaluating the effect of disease management programs on hospital readmission of older patients with heart failure

Author, year	Study and participant characteristics[a]	Main components of intervention	O/F[b]	Main findings: Intervention versus (vs) usual care[c]
Vavouranakis, 2003[75]	Greek Study, $n = 33$, analysis as paired comparison of patient's pre-enrollment vs post-enrolment values. Mean age in years 65.4. Male sex 13% *HF severity*. NYHA Class III, IV (%): 61, 39. Mean EF 26.9%. *HF Aetiology*. 67% IHD, 3% HT, 21% Myocardiopathy, 6% Valve Disease. *Medications*. 82% ACE inhibitor, 61% Digoxin, 100% Diuretic, 67% Nitrate	Intensive home surveillance of patients, including frequent home visits associated with laboratory tests and telephone contacts to implement standard therapy, treat early symptoms and provide psychological support	A (1 y)	The cardiovascular readmission rate decreased (1.25 ± 1 vs 2.14 ± 1.1 hospitalisations per patient-year, $p < 0.01$)
Akosah, 2002[76]	USA Study, $n = 101$, (38 SI, 63 US). Mean age in years 68 SI vs 76 US ($P < 0.05$). Male sex 71% SI vs 43% US ($P < 0.05$) *HF severity*. Mean EF 29% SI vs 39% US ($p < 0.05$). *Co-morbidity*: 62% IHD, 55% HT, 36% DM, 19% CAD, Dysrhythmias 65% SI vs 43% US ($P < 0.05$). *Medications*. ACE-inhibitor 82% SI vs 65% US	Disease management in a short-term aggressive intervention in a HF clinic following hospital discharge. Multi-speciality team, medication titration, intensive patient education. Mean time of enrolment in the clinic was 3 months. Timing of follow-up visits was flexible and individualised	B, C (1 m, 3 m, and 1 y)	Study intervention reduced the combined re-admission and mortality rate at 3 months (10% vs 30%, $P < 0.01$) and 1 year (21% vs 43%, $p < 0.02$). There was a 77% relative risk reduction for 30-day hospital re-admission (3% vs 13%, $P = 0.08$), and a statistically lower rate of re-admissions at 3 months (5% vs 23%, $P < 0.02$), and 1 year (16% vs 31%, $P < 0.03$). Time to hospital re-admission also tended to be longer (192 vs 104 days, $P = 0.08$). Multiple re-admission rates were also lower
Azevedo, 2002[77]	Portuguese Study, $n = 339$ (157 SI, 182 US). Mean age in years: 69.3 SI vs 65.0 US ($p < 0.05$). Male sex: 60% SI vs 45 % US ($p < 0.05$) *HF severity*. NYHA Class III–IV (%): 74% SI vs 82% US ($P = 0.07$). 72% SI vs 61% US had EF<40% ($P = 0.04$). *Co-morbidity*: 52% SI vs 42% US had IHD ($P = 0.06$), 21% SI vs 16.5% US had DM ($p = 0.2$), 30% SI vs 44.5% US had AF ($P = 0.006$). *Medications (SI)*. 93% ACE-inhibitor, 95.5% furosemide, 37% of patients with systolic dysfunction beta-blockers	Outpatient management at a multi-speciality HF clinic including systematic diagnostic assessment. Patients had their regular appointments, and unscheduled visits or phone consultations whenever needed	C (1 m)	The risk of the combined end-point (re-admission or death) was significantly lower (adjusted odds ratio 0.23; 95%CI: 0.12–0.46; adjustment variables were not specified, but certainly they did not include gender and NYHA functional class)
Peacock, 2002[78]	USA Study, $n = 154$, comparison against outcome for 9 months prior to programme implementation. Mean age in years 67.9, 60% male	Emergency department observation unit treatment protocol for HF exacerbation. This included diagnostic and therapeutic algorithms, cardiology consultation, close monitoring, patient education, and discharge planning	A (3 m)	HF re-admission rate decreased 64% (50% vs 77%; $P = 0.007$)
Constantini, 2001[79]	USA Study, outcomes were compared between 173 patients before SI implementation, 283 SI and 126 concurrent US patients. There were no differences between groups in age: Mean age in years 70.8; and sex distribution: 44% male. *HF severity*. Moderate-Severe Left ventricular dysfunction (%): 68 SI, 43 US, 62 baseline patients	A faculty cardiologist and a nurse care manager at an academic medical center reviewed each patient's data and made guideline-based recommendations	B (1 m)	There were small non-significant differences in 30-day hospital re-admissions (6% of SI patients, 4.8% of US patients, 6.4% of baseline patients). Hospital length of stay was lower as were costs of hospitalisation (median, $2934, $4830, and $3209; respectively; $P < 0.01$). These differences persisted after adjustment for severity of illness

Table 4 (*continued*)

Author, year	Study and participant characteristics[a]	Main components of intervention	O/F[b]	Main findings: Intervention versus (vs) usual care[c]
Lanzieri, 2001[80]	USA Study, $n = 73$, (39 SI, 34 US). Mean age in years 68 SI vs 65.7 US. Male sex: 68% SI vs 60% US. *HF severity*. Mean EF 36%SI vs 40%US. *Co-morbidity*: Both groups were similar for the presence of IHD, HT, and DM. *Medications*. 62% ACE-inhibitor, 60% Digoxin, 74% Diuretic, 22% β-Adrenoceptor Antagonist, 49% Nitrate	Use of a clinical care multi-disciplinary action plan to decrease length of stay and limit resource utilisation including: target length of hospital stay, projections for daily improvements based on intervention guidelines for diagnostic studies and medical therapy, early identification of patients with special discharge needs, and intensive patient education	A (6 m)	Shorter length of stay for patients in the SI group. No impact on HF re-admission rates (25.6% vs 32.4%, $P = 0.52$)
Vaccaro, 2001[81]	USA Study, 52 SI patients, 638 US patients included in the control group, matched for sex and age. 75% of patients 65 years old or more, 56% male	Interactive telephone support program, the patient is provided with coaching, education, and re-inforcement of self-care management skills. Patients are given a personal information appliance to receive and respond to daily sessions of questions, and educational information sent from their care manager	B (6 m)	Re-admissions were reduced 49.6% ($P < 0.001$). Costs were reduced for hospitalisations and emergency room visits in 50.6%, and return on investment was approximately 200%
Whellan, 2001[82]	USA Study, $n = 117$, analysis as paired comparison of patient's pre enrolment vs post enrolment values. Mean age in years 62, 62% male, 55% white. *HF severity*. NYHA Class II, III, IV (%): 50, 30, 20. Mean EF 23%. *Medications*. 77% ACE-inhibitor, 49% β-Adrenoceptor Antagonist	Protocols for management of medications, protocols for exacerbations, patient education manual which included a daily diary for weights and diet. An inpatient consultation service and an outpatient CHF clinic	B (5 m)	The re-admission rate decreased (1.5 vs 0 hospitalizations per patient-year, $P < 0.01$). The Health System saved a median of $8751 per patient-year
Bull, 2000[83]	USA Study, $n = 158$, before-and-after non-equivalent control group design. Mean age in years 73.7, 27% male, 94% white	A professional—patient partnership model of discharge planning which included: an educational program for nurses and social workers on discharge planning, elders and caregivers viewed a videotape on preparing to leave the hospital, a brochure on how to access community services	B (0.5 and 2 m)	Although there were no statistically significant differences, the intervention group was re-admitted less often (4% vs 6.7% at 2 weeks, 3.2% vs 17% at 2 months). The average cost saving per person was approximately $4300
Dahl, 2000[84]	USA Study, $n = 1192$, analysis before ($n = 583$) and after ($n = 609$) the implementation of SI. Mean age in years 75(SI), 96% white (SI)	Inpatient multi-disciplinary program managed by nurses which included a clinical pathway, social worker and dietician, education sessions toward patients and family members. A home health care plan was also developed and incorporated in the discharge plan when appropriate	A, B (0.5, 1 and 3 m)	Patients were re-admitted less frequently for HF, cardiac causes and all causes, but this difference was not statistically significant at 0.5 month of follow-up. However, it was statistically significant at 1 month for HF re-admissions, and for the three outcomes at 3 month follow-up

Table 4 (*continued*)

Author, year	Study and participant characteristics[a]	Main components of intervention	O/F[b]	Main findings: Intervention versus (vs) usual care[c]
Luzier, 2000[85]	USA Study, $n = 110$ (51 SI, 28 Positive Controls = patients considered to be appropriately treated, 31 Negative Controls = patients whose physicians declined recommendations). Mean age in years 73, 58% male. *HF severity*. NYHA Class I–II, III, IV (%): 5, 83, 20; Mean EF 28%. *Co-morbidity*. 92% IHD, 33% MI, 57% HT, 47% DM, 15% CAD. *Medications*. 100% ACE-inhibitor, 10% Angiotensin II blocker, 85% Digoxin, 92% Diuretic, 5% Hydralazine/nitrate, 5% β-Adrenoceptor Antagonist	Optimisation of ACE-inhibitor doses by a clinical pharmacist	B (6 m)	Negative controls had an increased risk of re-admission at 3 months (29%, $P = 0.02$) compared with positive controls (14%) and Study Intervention patients (19%). The increased re-admission rate of negative controls became even more significant 6 months after discharge ($P < 0.007$). Many re-admissions in negative controls occurred early, between 1 and 2 months after discharge. The increased rate of re-admission of negative controls was associated with higher cost
Paul, 2000[86]	USA Study, $n = 15$, before-and-after design. 6 men, 9 women. Mean age in years: 62	Nurse-managed multidisciplinary outpatient heart failure clinic	B (6 m)	The number of hospital readmissions (19 vs 38), hospital days (72 vs 151), and mean length of stay (3.8 vs 4.2) were reduced. Mean inpatient hospital charges decreased ($5893 vs $10,624 per patient admission)
Riegel, 2000[87]	USA Study, $n = 240$ (120 SI, 120 US controls matched on pre-admission functional status, co-morbidity, and age). Mean age in years 72.6, 45% male. *HF severity*. NYHA Class I, II, III, IV (%): 0, 11, 52, 37. Mean EF ($n = 102$) 44.6%. *HF Aetiology*. 40.8% IHD, 21.4% HT, 26.7% Myocardiopathy, 11.2% Valve Disease. *Co-morbidity*. 27% DM, 34% CAD, 34% AF. 10% Stroke. SAS Class I:II:III:IV (%): 22, 22, 43, 12. Charlson co-morbidity category Low, Moderate, High (%): 56, 33, 11. *Medications*. 53% ACE-inhibitor, 59% Digoxin, 17% Diuretic	A multi-disciplinary team of clinicians implemented a disease management program designed to promote self-management. The program used educational materials, in-hospital counselling by pharmacists and dieticians, discharge assessment by social worker, outpatient support groups, physician collaboration, home visits by a HF-specialty team of nurses, and telephonic case management by registered nurses with expertise in HF.	A,B (3 and 6 m)	No significant differences were evident at 3 or 6 months in re-admissions for any cause and HF re-admissions. When data were examined by pre-admission functional status, any cause re-admission rates were 17.6% lower (37.5% vs 45.5%), and total cost was 68% lower, in those intervention group patients who reported minimal functional compromise (SAS class II, $n = 54$); and any cause re-admission rates were 68% higher (34.8% vs 20.7%), and total cost 288% higher, in patients with perceived normal functional ability (SAS class I, $n = 52$)
Branch, 1999[88]	USA Study, $n = 23$, comparison against outcomes for 3 months prior to implementation. Mean age in years 66, 51% male. *HF severity*. 100% NYHA Class III–IV	Multi-disciplinary outpatient HF clinic. The clinic combines intensive patient and family education with aggressive follow-up: regular office visits, 24-h access to medical staff, and telephone tracking	A, B (3 m)	There was a mean reduction of 0.7 re-admissions for any cause and a mean reduction of 5.2 inpatient days of re-admission for any cause per patient at 3 months. Similarly, there was a mean reduction of 0.8 re-admissions for HF, and a mean reduction of 4 inpatient days of re-admission for HF per patient at 3 months. All four reductions were statistically significant
Cardozo, 1999[89]	USA Study, $n = 295$ (95 SI: all are over the age of 65; 200 US: random sample of patients treated before the implementation of the pathway). Male 28%SI vs 39%US, $P = 0.08$. *HF severity*. NYHA Class I–II, III–IV (%): 14, 86	Implementation of a 5-day clinical pathway which includes diagnostic procedures, discharge planning and patient education	B (1 m)	Re-admission rates at 1 month showed a significant increase, from 9.25% to 13.5%, but also patients on the pathway had significant reductions in length of stay and cost of care as well as more effective delivery of process of care

Table 4 (*continued*)

Author, year	Study and participant characteristics[a]	Main components of intervention	O/F[b]	Main findings: Intervention versus (vs) usual care[c]
Heidenreich, 1999[90]	USA Study, $n = 154$, (68 SI, 86 US controls matched to the intervention group on sex and medical claims during the preceding year). Mean age (SI) in years 73, 53% male (SI). *HF severity (SI)*. 100% NYHA Class II–III; 55% moderate systolic dysfunction. *Co-morbidity (SI)*. 44% MI, 57% HT, 32% DM. *Medications (SI)*. 75% ACE-inhibitor or hydralazine, 57% Digoxin, 88% Diuretic	Multi-disciplinary home monitoring system including: patient education, daily self-monitoring, and physician notification of abnormal weight gain, vital signs, and symptoms	B (7 m)	Compared with the prior year medical claims per year decreased in the intervention group ($7400 vs $8500), whereas they increased in the control group (18,800 vs $9200). Similar differences were observed for readmissions and total hospital days
Rauh, 1999[91]	USA Study; analysis before ($n = 407$, control group) and after ($n = 347$) the implementation of the SI. Mean age in years 75.8 (SI), 42% male (SI). *HF severity (SI)*. Mean EF 37.9%. *Co-morbidity (SI)*. 41% MI, 33% CAD. *Medications (SI)*. 59% ACE-inhibitor, 61% Digoxin, 77% Diuretic, 38% Nitrates, 4% Hydralazine, 12% β-Adrenoceptor Antagonist	Inpatient and outpatient multi-disciplinary approach which included: intensive education program focusing on diet, treatment compliance, and symptom recognition. Use of out-patient infusions and aggressive pharmacological treatment for patients with advanced HF. All patients had follow-up telephone contacts on a weekly basis for 1 month and every other week thereafter for a minimum of 3 months after discharge	A (3 m)	There was a significant reduction in the 3 month HF re-admission rate (13% vs 18%, $P = 0.05$). The mean cost per admission decreased 17%, and it was noted a 77% ($718,468) net reduction in non re-imbursed (lost) hospital revenue
Cacciatore, 1998[92]	Italian Study, $n = 435$, comparison against outcome for 1 year prior to implementation. Mean age in years 62, 74% male. *HF severity*. NYHA Class I–II, III–IV (%): 56, 44. Mean EF 36%. *HF Aetiology*. 42% IHD, 13% HT, 35% Cardiomyopathy. *Comorbidity*. 21% AF. *Medications*. 70% ACE-inhibitor, 70% Digoxin, 87% Diuretic, 6% β-Adrenoceptor Antagonist	Outpatient management programme, which includes adjustment of medical therapy, patient education and visits timed according to the patient's status	A (5y)	There were fewer HF re-admissions (8.5% of patients/year vs 54.4% of patients/year, p<0.05)
Shah, 1998[93]	USA Study, $n = 27$, analysis comparing the outcomes during the equivalent period before and after the program patient by patient. Mean age in years 62. *HF severity*. NYHA Class II, III–IV (%): 37, 63.33% EF<20%. *HF Aetiology*. 63% IHD. *Co-morbidity*. 15% DM. *Medications*. 89% ACE-inhibitor, 93% Digoxin, 100% Diuretic	Interactive home monitoring program including: patient education materials, automated reminders for medication compliance, self-monitoring of daily weights and vital signs, and facilitated telephone communication with a nurse-monitor	A (8.5 m)	The number of re-admissions for cardiovascular diagnoses and hospital days was reduced from 0.6 to 0.2 ($P = 0.09$) per patient year of follow-up and from 7.8 to 0.7 days per patient per year ($P < 0.05$), respectively. Re-admissions for all causes fell from 0.8 to 0.4 per patient per year ($P =$ not significant), and hospital days for all causes were reduced from 9.5 to 0.8 days per patient per year ($P < 0.05$)
Tilney, 1998[94]	USA Study, analysis before ($n = 3401$ control group) and after ($n = 1915$) the implementation of the SI. Mean age in years 73.5(SI), 50.5% male (SI). *Co-morbidity* (SI, $n = 219$): 43% IHD, 71% HT, 30% DM, 17% CAD, 18% Arrhythmia	MULTIFIT (Cardiac solutions, Ralin Medical): A physician-supervised, nurse-mediated, home-based system for HF management that implements consensus guidelines for pharmacologic and dietary therapy using a nurse manager to enhance dietary and pharmacological adherence and to monitor clinical status by frequent telephone contact	B (13 m)	Hospital re-admissions for all diagnoses dropped 60%, and total hospital days were reduced 58%. Inpatient costs for HF re-admissions dropped 78%, while inpatient costs for all other admissions fell by 50%

Table 4 (*continued*)

Author, year	Study and participant characteristics[a]	Main components of intervention	O/F[b]	Main findings: Intervention versus (vs) usual care[c]
Roglieri, 1997[95]	USA Study, $n = 149$, analysis before and after the implementation of the SI. Mean age in years 75.4, 59% male (SI). *HF severity*. Mean EF 36.4%	Telemonitoring (weekly phone call), post-hospitalization patient education (home visit by a nurse, educational mailing) and physician education (mailings and phone calls).	A (5.3 m)	The 30-day and 90-day cardiovascular re-admission rate decreased 50% and 38%, respectively
Shipton, 1997[96]	USA Study ($n = 24$, 12 SI, 12 UC). Mean age in years 77.8(SI) vs 76.5 (UC), 5 men (SI) vs 6 men (UC)	Systematic educational program in the home setting given by nurses and initiated within 48 h after discharge. Nurses used a manual to instruct patients in basic survival skills, HF pathophysiology, reportable signs and symptoms, diet and medication	B (6 m)	There were fewer re-admissions (5 vs 7) and fewer total days in hospital for re-admissions (22 vs 52)
Smith LE, 1997[97]	USA Study, $n = 20$, comparison against outcome for 6 months prior to enrolment into the clinic. Mean age in years 61, 100% male. *HF severity*. Mean NYHA class 2.6. *Co-morbidity:* 60% IHD, 40% HT, 25% DM, 20% CAD, 25% AF. *Medications*. 95% ACE inhibitor, 40% Nitrate, 40% Aspirin, 20% Warfarin	Care delivered in a cardiomyopathy clinic: the frequency of visits was individualised. Patients were followed by a nurse practitioner and a cardiologist with maximisation of standard treatment. A nurse was available by telephone to respond to any concerns	A (6 m)	There were 86% (14 to 2, $P = 0.017$) and 100% (8 to 0, $P = 0.002$) reductions in the number of HF re-admissions and emergency visits
West, 1997[98]	USA Study, $n = 51$, comparison against outcome for 1 year prior to implementation. Mean age in years 66, 71% male, 80% white. *HF severity*. NYHA Class I, II, III, IV (%): 22, 38, 28, 12. *Co-morbidity*: 71% IHD, 63% MI, 59% HT, 29% DM, 26% CAD, 26% AF. *Medications*. 76% ACE-inhibitor, 100% Diuretics, 36% Nitrate	MULTIFIT (Cardiac solutions, *Ralin Medical*): A physician-supervised, nurse-mediated, home-based system for HF management that implements consensus guidelines for pharmacological and dietary therapy using a nurse manager to enhance dietary and pharmacologic adherence and to monitor clinical status by frequent telephone contact	A, B (5 m)	Re-admission rates for HF and for all causes decreased 87% and 74%, respectively
Kornowski, 1995[99]	Israeli Study, $n = 42$, comparison against outcome for 1 year prior to implementation. Mean age in years 78, 57% male. *HF severity*. 100% NYHA Class III–IV. *Co-morbidity:* 95% IHD, 67% MI, 36% HT, 28% DM, 24% CAD, 26% AF, 9% Valve Disease. *Medications*. 67% ACE-inhibitor, 100% Diuretics, 57% Digoxin, 76% Nitrate, 38% Aspirin, 19% Anticoagulants	Intensive home-care surveillance: patients were examined at least once a week at home by internists from the district hospital and by a trained paramedical team	A, B (1 y)	Mean total readmission rate was significantly reduced (a 62% reduction, $P < 0.001$). Cardiovascular re-admissions showed a significant reduction (a 72% rate reduction, $P < 0.001$). Similarly, re-admission duration was significantly reduced for total and cardiovascular admissions (a 77% $P < 0.001$ and an 83% $P < 0.001$ reduction, respectively)
Schneider, 1993[100]	USA Study, $n = 54$, (26 SI, 28 US, assignment was done by flipping a coin for a random start and then assigning subjects to each group alternatively). Mean age in years 72.2, 58% (SI) vs 43% (UC) male	Medication discharge planning and nurse-led inpatient education	B (1 m)	There was a significant reduction in re-admissions (7.7% vs 28.6%)

Table 4 (*continued*)

Author, year	Study and participant characteristics[a]	Main components of intervention	O/F[b]	Main findings: Intervention versus (vs) usual care[c]
Cintron, 1983[101]	Puerto Rico Study, $n = 15$, for each patient an equal period before and after de SI was used for analysis. Mean age in years 65. *HF severity.* NYHA Class III: IV (*n*): 3, 12. *Co-morbidity (n).* 12 MI, 2 Valve Disease	Nurse practitioner HF clinic	B (1 y)	There was a significant 60% reduction in the number of re-admissions and 85% reduction in the mean number of hospitalised days. There was an estimated savings of $8009 per patient

[a] ACE, Angiotensin converting enzyme; AF, Atrial fibrillation; EF, ejection fraction; CAD, Chronic airways disease; Charlson, Mean Charlson Index of comorbidity score; DM, Diabetes mellitus; HF, Heart failure; HT, hypertension; IHD, ischaemic heart disease; MI, myocardial infarction; MLHFQ, Minnesota Living with Heart Failure Questionnaire scores; MMSE, mean Mini-Mental State Examination score; n, number of patients included in the study; SAS, Specific Activity Scale scores; SF-36 (m, ph), Medical Outcomes Study SF-36 questionnaire scores (Mental component, Physical component); SI, study intervention. US, usual care.
[b] O/F, Outcome class: A, Heart Failure re-admission; B, Re-admission for any cause; C, Combined end-point: death or re-admission. Underlined outcomes are those which were included in the meta-analysis. Duration of follow-up is shown in brackets (y, year; m, month).
[c] 95% CI: 95% confidence interval.

Discussion

This review provides evidence that DMPs reduce re-admissions for HF or cardiovascular cause, all-cause re-admissions, and the frequency of the combined end-point of re-admission or death among older patients with heart failure. These results were observed regardless of the type of healthcare delivery within DMPs, such as being home-based or clinic-based, and the duration of follow-up. In addition, these results were obtained in heterogeneous groups of patients, with different degrees of morbidity and severity, and in settings with diverse healthcare systems ranging from publicly funded systems of the type found in the UK to other, fundamentally privately funded systems like that of the USA.

The benefits of DMPs are of a magnitude close to that observed in clinical trials evaluating drugs for HF, such as ACE-inhibitors,[105–107] beta-blockers[108–110] or digoxin.[111] Furthermore, there is evidence that the programmes can be cost-effective and even lead to financial savings.[13] However, since none of the DMP studies compared different interventions directly, we do not know the relative effectiveness of types of organising care within the DMP. Accordingly, clinical trials should be conducted to compare these directly (e.g., either by comparing tele-management with home visit care,[112] or by comparing interventions in which nurses change drug therapy according to protocols with interventions in which patients are referred to a physician for this purpose, etc.).

Why should different interventions in relatively heterogeneous patients and settings all yield favourable results? Although the data in this review do not allow for a definitive answer, it is possible to speculate on two possibilities. First, rather than residing in what most differentiates some DMPs from others, such as the mode of delivering care, the key elements of success lie in what is common to all of them: programme content, in particular patient education to increase self-efficacy in managing their disease. Second, trial patients tend to be strictly selected: of those who are initially screened, the percentage of subjects finally included does not reach 50% in the majority of randomised trials (Table 2). This suggests that in each study, researchers have chosen those patients who can benefit most from the intervention (e.g., patients who have a high risk of re-admission or display a considerable degree of ignorance of the nature of the disease and its management), or that patients refuse to participate in interventions which they perceive as uncomfortable or for which they are not prepared (e.g., fatigued patients refuse to participate in programmes that require visits to a clinic). Future studies must clarify these points and, in particular, ascertain which specific type of intervention is best suited to each type of patient.

What does our study add to previous reviews on this topic? A meta-analysis of randomised clinical trials of DMPs in HF was published in 2001.[11] The review, which included 11 studies published up to 1999, concluded that DMP for the care of HF-patients which involved multi-

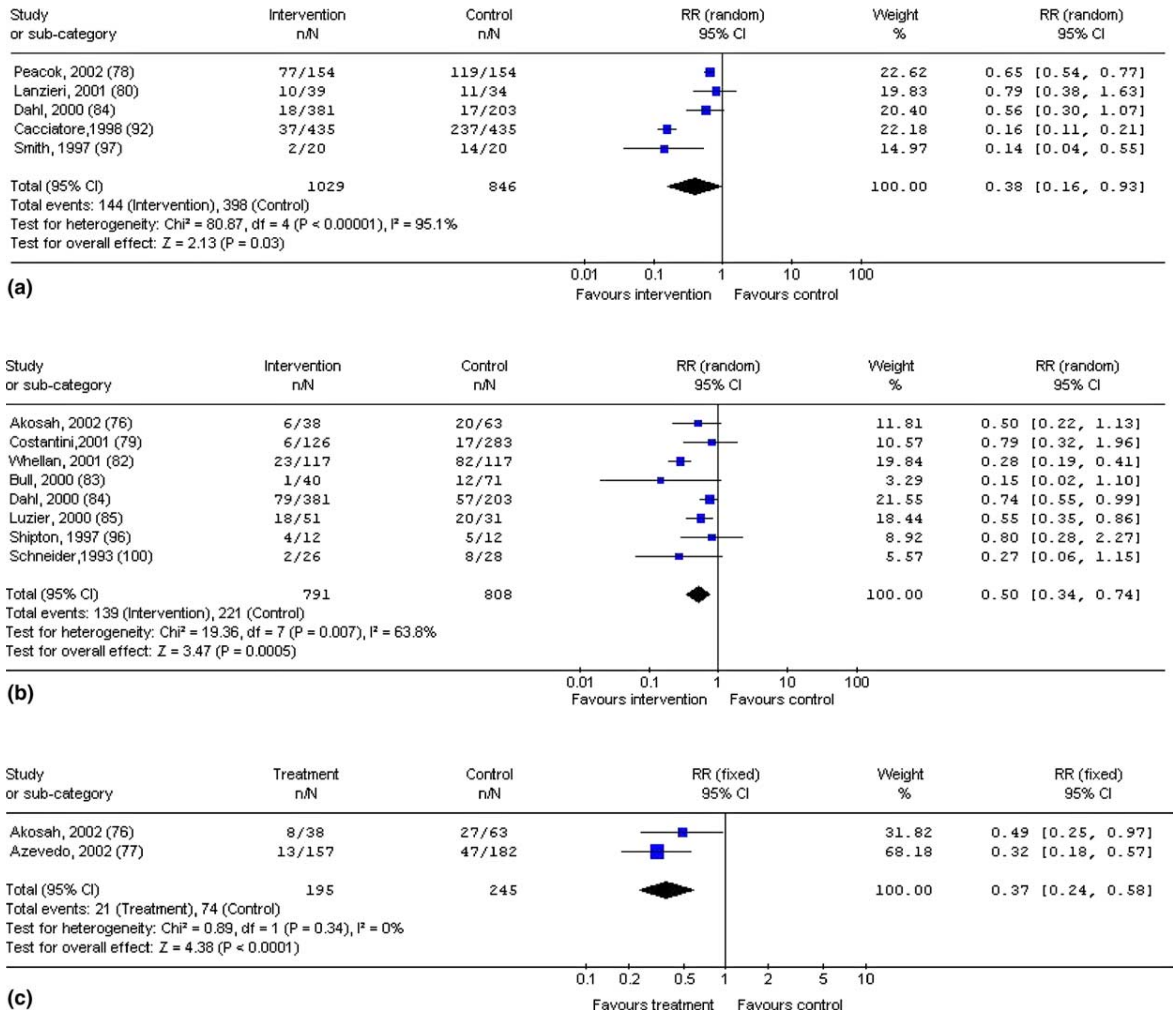

Fig. 3 Meta-analysis of the effectiveness of disease management programs on three outcomes among older patients with heart failure. Non-randomised studies. (a) Heart failure or cardiovascular readmission, (b) all cause readmission, (c) readmission or death.

disciplinary teams, reduced hospitalisations and appeared to be cost saving. From 1999 through August 2003, a further 16 randomised trials have been published. Moreover, the review did not include non-randomised trials. Another systematic review on this topic was published in 2003.[12] The review included 32 randomised and non-randomised studies published up to March 2002. By August 2003, however, a total of 54 studies (randomised and non-randomised) on DMPs in HF had been published. This recent review[12] made excessive emphasis on "vote counting", a technique whereby the number of studies with positive results for a number of outcomes are counted as effective. This technique yields no estimate of effect size, and does not directly assess homogeneity of effect across studies. Most importantly, it weights studies of all sizes and effects of all magnitudes equally. "Vote counting" should be restricted to situations where effect measures are not presented and cannot be obtained,[17] which is not the case for most studies evaluating DMP in HF. Lastly, another review has been published in 2004,[13] after our manuscript was submitted for publication. This study evaluated interventions described as comprehensive discharge planning plus post-discharge support for inpatients with HF and mean age $\geqslant 55$ years. This review did not consider non-randomised trials but covered 3304 patients from 18 randomised trials published from 1966 to October 2003. The review yielded results for DMPs that are even more favourable than those obtained by us. In fact, Phillips et al.,[13] estimated a 25% reduction in all-cause readmission (pooled RR 0.75, 95% CI: 0.64–0.88) while we only observed a 12% reduction.

For the correct interpretation of our results, some features of the studies must be commented upon. Firstly, the Methods section often provides insufficient information to judge the quality of the interventions, their intensity or duration. In most instances where patient education is provided, insufficient information is given to understand how the educational process was carried out and how to replicate it. Furthermore, the descriptions supplied do not allow for clear comprehension of the key elements for success of any given programme (e.g., improvement in patient education and support, or improvement and optimization of treatments). This is probably due to the space constraints imposed on manuscripts. Thus, it might be useful to create a repository of detailed descriptions of DMP, so that these could be reproduced and compared.

Secondly, such dearth of information is particularly marked for the groups who underwent so-called "usual care". This is a key aspect, because the effectiveness of any intervention diminishes with the quality of care dispensed in the group assigned to usual care. Hence, a possible explanation for the modest results observed in the trial by Laramee et al.,[49] is that patients in the usual-care group also received medication and CHF education by staff nurse. Furthermore, these patients received nurse home-visits with the same frequency as did the DMP group.

Thirdly, with the single exception of the recent DIAL study,[47,48] the size of randomised trials is moderate at best, limiting the statistical power to show relevant reductions (e.g., 15–20%) in hospital re-admissions. Furthermore, only one study reports on the effectiveness of DMP beyond one year follow-up,[57] and it requires confirmation. Hence, future studies should have a larger size and duration; interventions should perhaps also have a wide spectrum, being targeted, not merely at HF, but rather at better management of all co-morbidities,[57] since many re-admissions in patients with HF are due to causes other than HF.

Fourthly, randomised studies are inevitably non-blinded. This allows for a certain degree of co-intervention by healthcare staff, other care-givers or the patients themselves to compensate for not being in the DMP group, or to optimise the situation of the intervened subjects and better illustrate the effectiveness of DMP. Thus, it is not easy to anticipate the effect of non-blind design on study results. Furthermore, many of the trials did not state whether the randomisation sequence was concealed until allocation of patients to trial groups. Although failure to do so could lead to overestimation of the benefit of the intervention,[113] no such overestimate was observed in our review when the results of studies with a Jadad score of 3 were compared against the results of all the randomised trials (Table 3).

Fifth, approximately half the studies reviewed were non-randomised and had a very low degree of adjustment for confounding factors. The magnitude of DMP benefits as reported by non-randomised trials were more than double that reported by randomised trials. Yet the consistence in the direction of the results in the two types of studies lends the non-randomised studies a certain degree of credibility.

Lastly, some decisions we made in our review also call for comment. First, the studies which evaluate DMPs usually assess several end-points; thus, there is a reasonably high likelihood of achieving statistical significance in one or more of the many comparisons made. Consequently, we confined ourselves to studying hospital re-admission, which is an easily understandable, clinically and socially relevant variable. In addition, procedures to measure re-admission are widely standardised, rendering this end-point easily combinable. Second, fairly different interventions have been combined; this is inevitable due to the very definition of DMPs, which accepts multiple treatment modalities and, because in all likelihood, no two DMPs are alike. In an attempt to mitigate this limitation, DMP who share some types of healthcare delivery were grouped in the sensitivity analysis. Third, the use of scores to assess the quality of studies included in the meta-analysis is controversial; although they are appropriate for comparing groups of trials, as we did, their results depend on the choice of the scale and some of them give more weight to quality of reporting than to actual methodology. In fact, the latter is one of the common criticisms of the Jadad score. We have tried to overcome this problem by indicating specific components of quality, supported by both empirical and theoretical evidence, such as blinding of outcome assessment or control for confounders. Lastly, since the quality of the economic assessments was not a principal objective of our review, this aspect was not evaluated. Nevertheless, it should be pointed out that, in most trials, the cost analyses did not include all the relevant components of cost. It is possible, as Ekman and Swedberg suggest,[14] that a potential saving stemming from a reduction in re-admissions may conceivably lead to an increase in costs in other categories of care, such as hip surgery or cataract operations, because the target population are elderly and closer follow-up by healthcare staff may well facilitate the provision of such services.

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