Journal of the American College of Cardiology
© 2004 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 44, No. 4, 2004
ISSN 0735-1097/04/$30.00
doi:10.1016/j.jacc.2004.05.055

Multidisciplinary Strategies for the Management of Heart Failure Patients at High Risk for Admission

A Systematic Review of Randomized Trials

Finlay A. McAlister, MD, MSc, FRCPC,* Simon Stewart, PhD, FESC, FAHA,† Stefania Ferrua, MD,‡ John J. J. V. McMurray, MD, FESC, FACC§

Edmonton, Canada; Adelaide, Australia; Torino, Italy; and Glasgow, United Kingdom

OBJECTIVES The aim of this study was to determine whether multidisciplinary strategies improve outcomes for heart failure (HF) patients.

BACKGROUND Because the prognosis of HF remains poor despite pharmacotherapy, there is increasing interest in alternative models of care delivery for these patients.

METHODS Randomized trials of multidisciplinary management programs in HF were identified by searching electronic databases and bibliographies and via contact with experts.

RESULTS Twenty-nine trials (5,039 patients) were identified but were not pooled, because of considerable heterogeneity. A priori, we divided the interventions into homogeneous groups that were suitable for pooling. Strategies that incorporated follow-up by a specialized multidisciplinary team (either in a clinic or a non-clinic setting) reduced mortality (risk ratio [RR] 0.75, 95% confidence interval [CI] 0.59 to 0.96), HF hospitalizations (RR 0.74, 95% CI 0.63 to 0.87), and all-cause hospitalizations (RR 0.81, 95% CI 0.71 to 0.92). Programs that focused on enhancing patient self-care activities reduced HF hospitalizations (RR 0.66, 95% CI 0.52 to 0.83) and all-cause hospitalizations (RR 0.73, 95% CI 0.57 to 0.93) but had no effect on mortality (RR 1.14, 95% CI 0.67 to 1.94). Strategies that employed telephone contact and advised patients to attend their primary care physician in the event of deterioration reduced HF hospitalizations (RR 0.75, 95% CI 0.57 to 0.99) but not mortality (RR 0.91, 95% CI 0.67 to 1.29) or all-cause hospitalizations (RR 0.98, 95% CI 0.80 to 1.20). In 15 of 18 trials that evaluated cost, multidisciplinary strategies were cost-saving.

CONCLUSIONS Multidisciplinary strategies for the management of patients with HF reduce HF hospitalizations. Those programs that involve specialized follow-up by a multidisciplinary team also reduce mortality and all-cause hospitalizations. (J Am Coll Cardiol 2004;44:810–9) © 2004 by the American College of Cardiology Foundation

Heart failure (HF) is the most common discharge diagnosis in elderly patients, accounts for almost a quarter of all cardiovascular hospitalizations, and consumes 1% to 2% of total health care expenditures (1). Although a number of pharmacologic treatments have been shown to improve outcomes in patients with HF (2), the prognosis of these patients remains poor (3). Thus, there is a need for other approaches to management. Although the vast majority of HF research has focused on drug or electrical therapies, programs involving multidisciplinary teams are increasingly touted as a potential strategy for further improving outcomes in HF patients (2). Although some of the purported improvements may arise from better application of the evidence into practice, these multidisciplinary strategies may also better address the complex interplay between medical, psychosocial, and behavioral factors facing patients with HF and their caregivers.

Most initial studies of multidisciplinary interventions were non-randomized, "before and after" case series, raising concerns about their interpretation (4). However, in an earlier systematic review restricted to the 11 randomized trials published up until 1999, we demonstrated that management strategies for patients with HF that involved specialized follow-up by a multidisciplinary team reduced hospitalizations and appeared to be cost-saving (5). These conclusions were reinforced in a recently published systematic review incorporating another seven trials (for a total of 18 trials) (6). However, their effectiveness in improving other clinical outcomes (particularly mortality) was indeterminate in both earlier reviews owing to limited numbers of events. Importantly, the number of studies was also insufficient to allow comparison of the relative benefits of the different types of interventions. In the past five years, several more trials of multidisciplinary strategies for the management of HF have been published.

From the *Division of General Internal Medicine, University of Alberta, Edmonton, Canada; †Division of Health Sciences, University of South Australia, Adelaide, Australia; ‡Divisione Universitaria di Cardiologia Azienda Ospedaliera San Giovanni Battista Corso Dogliotti, Torino, Italy; and §Department of Cardiology, Western Infirmary, Glasgow, United Kingdom. Dr. McAlister is a Population Health Investigator of the Alberta Heritage Foundation for Medical Research and a New Investigator of the Canadian Institutes of Health Research; Dr. Stewart is supported by the National Health and Medical Research Council of Australia and the National Heart Foundation of Australia.

Manuscript received January 20, 2004; revised manuscript received April 8, 2004, accepted May 11, 2004.

Abbreviations and Acronyms

CI = confidence interval
HF = heart failure
NNT = number needed to treat
RR = risk ratio

Thus, we updated our earlier systematic review to incorporate this new evidence and to investigate which types of programs are most efficacious.

METHODS

Identifying relevant studies. We searched for randomized trials in Medline 1966 to 2003, Embase 1980 to 2003, Cinahl 1982 to 2003, Sigle 1980 to 2003, AMED (Allied and Complementary Medicine) 1985 to 2003, the Cochrane Controlled Trial Registry, and the Cochrane Effective Practice and Organization of Care Study Registry. Language restrictions were not applied. The following textword terms and medical subject headings were used: "case management (exp), comprehensive health care (exp), disease management (exp), health services research (exp), home care services (exp), clinical protocols (exp), patient care planning (exp), quality of health care (exp), nurse led clinics, special clinics" and "heart failure, congestive (exp)." Bibliographies of identified studies were hand-searched. We also contacted content experts and authors of the primary studies to identify any studies missed by the electronic searches.

Study selection and data abstraction. F.M. and J.M. independently reviewed the results of the search strategy and selected all studies reporting the impact of outpatient-based multidisciplinary management strategies on mortality or hospitalization rates in patients with HF. Studies were excluded if they: appeared in abstract form only, did not report either of the outcomes of interest, employed inpatient interventions only, did not utilize a multidisciplinary approach, or if they enrolled patients with multiple diseases and data for patients with HF were not reported separately or could not be determined after contact with the authors.

F.M. and S.S. independently assigned each reported intervention to one of four a priori defined groups: 1) a. multidisciplinary HF clinic; b. multidisciplinary team providing specialized follow-up but not in a hospital or practice-based clinic; 2) telephone follow-up or telemonitoring and enhanced communication with primary care physician (including advice to deteriorating patients to see their regular physician); or 3) educational programs designed to enhance patient self-care activities. It should be noted that patient education was a key component of all four types of interventions (Table 1). These groupings were reviewed and approved at an ad hoc meeting of HF disease management investigators, including six of the authors of primary studies included in our systematic review (personal communication, Simon Stewart, February 26, 2004). All outcome data were extracted by F.M. and J.M. independently.

Outcomes from each study were assigned according to the intention-to-treat principle, and we accepted the definitions for each outcome used by the investigators in the primary studies. Original investigators were contacted to clarify the published data: authors for 14 of the 20 studies contacted provided further data. We defined "all-cause hospitalization rate" and "heart failure hospitalization rate" as the number of patients in each trial arm who were hospitalized at least once (thus, each patient could only contribute one event to these analyses). We defined "total hospitalizations" and "total heart failure hospitalizations" as the total number of hospitalizations in each trial arm—thus, these end points incorporate multiple re-admissions from the same patient.

Statistical analysis. Analyses were performed using the Meta-Analyst 0.998 software (J. Lau, New England Medical Center, Boston, Massachusetts). As the outcomes of interest were relatively common, we calculated risk ratios. Intention-to-treat analyses were done, and the DerSimonian and Laird random effects model was employed for all analyses. Because of the differences expected between studies (particularly in the usual care arms), a priori we decided to examine for statistical heterogeneity using Cochran's Q test. If the heterogeneity p value was <0.20, we elected not to pool the data but to examine outcomes in the a priori defined intervention groups separately (but only if there was no substantial heterogeneity within the subgroups). Sensitivity analyses, defined a priori, were conducted to look at the effects of duration of intervention, quality of trial (using the Jadad scale) (7), length of follow-up, and year of study completion on the summary risk ratios. We calculated adjusted indirect comparisons to compare different types of interventions according to the method of Song et al. (8).

RESULTS

Study selection and evaluation. Of the 853 citations identified in our search, 76 were eligible for inclusion in this systematic review (Fig. 1, QUOROM flow chart). However, 38 of these studies were excluded as follows: 21 were not randomized, 5 did not report the underlying diagnoses in the enrolled patients (and such data could not be obtained even after contacting authors), 4 did not include the outcomes of interest, 2 evaluated telephone follow-up in lieu of clinic visits rather than a multidisciplinary strategy, 2 did not include a "usual care" control arm, 2 were protocols for ongoing trials, 1 tested an inpatient-based intervention only, and 1 tested patient self-management alone. Of the 29 randomized trials included in this systematic review, 7 reported results in more than one publication (only the main publication from each trial is referenced here) (9–15).

Disagreement among the two reviewers regarding eligibility of the studies occurred on seven occasions for a kappa value of 0.77, and disagreement on type of intervention

Table 1. Description of Studies Included

Study (Year) (Ref.)	Sample Size	Study Population (Location)	Mean Age	Key Components of Intervention	Duration of Intervention
Multidisciplinary heart failure clinic					
Cline et al. (1998) (16)	190	Patients 65–84 yrs with heart failure discharged from hospital (Sweden)	76	Nurse-led patient education, self-management guidelines for patients, and follow-up visits at nurse-run clinic as needed after discharge	12 mos
Ekman et al. (1998) (17)	158	Patients with moderate-severe heart failure discharged from hospital (Sweden)	80	Nurse-led patient education, self-management guidelines for patients, follow-up visits at nurse-run clinic as needed, frequent telephone follow-up	6 mos
Doughty et al. (2002) (14)	197	Patients with heart failure discharged from hospital (New Zealand)	73	Multidisciplinary heart failure clinic with regularly scheduled follow-up, patient education sessions, close liaison with primary care physician	12 mos
Kasper et al. (2002) (18)	200	Patients with heart failure discharged from hospital and having at least one risk factor for readmission (U.S.)	62	Multidisciplinary heart failure clinic (mean 8 visits), primarily nurse-led, with protocol-driven patient assessments and medication adjustments, regular telephone contact (mean 10 calls)	6 mos
Capomolla et al. (2002) (19)	234	Patients discharged from a heart failure unit (Italy)	56	Multidisciplinary heart failure clinic with regularly scheduled telephone contact	12 mos
Stromberg et al. (2003) (20)	106	Patients with heart failure discharged from hospital (Sweden)	78	Nurse-led heart failure clinic, protocol-driven changes in medications, patient education, psychosocial support	12 mos
Ledwidge et al. (2003) (13)	98	Patients with heart failure discharged from hospital (Ireland)	71	Multidisciplinary heart failure clinic with regularly scheduled telephone contact (11 calls)	3 mos
Multidisciplinary team providing specialized follow-up in non-clinic setting					
Hanchett and Torrens (1967) (21)	239	Patients with heart failure attending specialty clinic (U.S.)	60–69 median	Nurse-led patient education, regular telephone contact, regular home/clinic visits	30 mos
Rich et al. (1993) (22)	98	Patients >70 yrs with heart failure discharged from hospital and having clinical features suggesting they were at moderate or high risk for readmission (U.S.)	79	Nurse-led patient education, dietary and social services consultation, review of medications by geriatric cardiologist, and intensive follow-up at home by study team	3 mos
Rich et al. (1995) (9)	282	Patients >70 yrs with heart failure discharged from hospital and having clinical features suggesting they were at high risk for readmission (U.S.)	79	Nurse-led patient education, dietary and social services consultation, review of medications by geriatric cardiologist, and intensive follow-up at home by study team	3 mos
Stewart et al. (1998) (11)	97	Patients with heart failure discharged from hospital with clinical features suggesting they were at high risk for readmission (Australia)	75	Nurse-led patient education, home visit by nurse and pharmacist 7 days after discharge to optimize medications and detect early clinical deterioration; compliance aids given to "at risk" patients	One visit

Continued on next page

Table 1 Continued

Study (Year) (Ref.)	Sample Size	Study Population (Location)	Mean Age	Key Components of Intervention	Duration of Intervention
Stewart et al. (1999) (25)	200	Patients ≥55 years with heart failure discharged from hospital (Australia)	76	Nurse-led patient education, counselling, exercise regimen, home visit 7–14 days after discharge and assessment re need for medication adjustments as per protocol, and telephone contact at 3 mos and 6 mos	6 mos
Naylor et al. (1999) (12)	363 (108 with heart failure)	Patients ≥65 years discharged from a tertiary care hospital with either coronary disease or heart failure (U.S.)	75	Nurse-led patient education, coordination of home care, at least two home visits, use of a standardized protocol to optimize medications, and weekly telephone contact for 1 month	1 mo
Blue et al. (2001) (27)	165	Patients with heart failure discharged from hospital (U.K.)	75	Nurse-led patient education, initial visit in hospital, home visits and telephone contact as needed, psychological support, protocol-driven titration of medications, liaison with other health care workers	12 mos
Trochu et al. (2004) (37)	202	Patients 65 years or older with heart failure discharged from hospital for a second time (France)	77	Nurse-led patient education, initial visit in hospital, home visit 2 weeks after discharge and monthly telephone contact, psychological support, liaison with other health care workers	12 mos
Telephone follow-up and attendance with primary care physician if deteriorates					
Naylor et al. (1994) (28)	276 (142 with coronary disease or heart failure)	Patients >70 yrs discharged from a tertiary care hospital with either coronary disease or heart failure (U.S.)	76	Comprehensive discharge planning protocol with gerontologic nurse providing education, coordinating care, and maintaining telephone contact for 2 weeks (with modification of treatment plan if appropriate)	0.5 mo
Weinberger et al. (1996) (10)	1,396 (504 with heart failure)	Patients discharged from the general medicine service with heart failure, diabetes mellitus, or chronic obstructive pulmonary disease (U.S.)	63	Primary care nurse provided educational materials and coordinated care between discharge and outpatient clinics, regular telephone follow-up through the course of the study, primary care physician follow-up within 7 days of discharge	6 mos
PHARM (1999) (29)	181	Patients with heart failure being evaluated in cardiology clinic (U.S.)	67	Clinical pharmacist-led medication review, patient education, regularly scheduled telephone contact × 3 to detect clinical deterioration early	6 mos
Rainville (1999) (30)	34	Patients ≥50 years discharged from hospital with heart failure (U.S.)	70	Pharmacist-led medication review, patient education, telephone contact × 2	0.25 mo

Continued on next page

Table 1 Continued

Study (Year) (Ref.)	Sample Size	Study Population (Location)	Mean Age	Key Components of Intervention	Duration of Intervention
Pugh et al. (2001) (26)	58	Patients ≥65 years discharged from hospital with heart failure (U.S.)	77	Nurse-led patient education, regular follow-up via telephone and clinic visits with nurse manager	6 mos
Jerant et al. (2001) (15)	37	Patients ≥40 years discharged from hospital with heart failure (U.S.)	70	Nurse contact via telephone (mean 6 calls) or video-based home telecare (mean 9 calls), patient education, protocol-driven review of symptoms, medication compliance, and medication dosing, with communication to primary care physician if deterioration	2 mos
de Lusignan et al. (2001) (31)	20	Adult patients with heart failure confirmed by cardiologist, identified from the database of an academic general practice (U.K.)	75	Telemonitoring of vital signs and clinical status daily, video consult with study nurse weekly × 3 mos, bi-weekly × 3 mos, then monthly	12 mos
Riegel et al. (2002) (33)	358	Patients discharged from hospital with heart failure (U.S.)	74	Nurse telephone contact (median 14 calls), patient education and counseling, case management guided by computer decision support, liaison with primary care physicians	6 mos
Laramee et al. (2003) (35)	287	Patients discharged from hospital with heart failure and having at least one risk factor for readmission (U.S.)	71	Early discharge planning, patient education, regularly scheduled telephone contact (12 weeks, 9 calls), case manager sent reminders to primary care physician if not on target medications	3 mos
Tsuyuki et al. (2004) (36)	276	Patients discharged from hospital with heart failure (Canada)	72	Early discharge planning with provision of adherence aids, patient education, regularly scheduled telephone contact (24 weeks, 7 calls) with recommendation to see primary care physician if not on target dose ACE inhibitor or deteriorated	6 mos
Enhanced patient self-care activities					
Serxner et al. (1998) (23)	109	Patients discharged from hospital with diagnosis of heart failure (U.S.)	71	Mailed patient education materials to encourage self-management	3 mos
Jaarsma et al. (1999) (24)	179	Patients ≥50 years with heart failure discharged from hospital (Netherlands)	73	Nurse-led patient education, home visit after discharge to reinforce education and self-care plan	0.25 mo
Krumholz et al. (2002) (34)	88	Patients ≥50 years discharged from hospital with heart failure (U.S.)	74	Nurse-led patient education, regular telephone contact to monitor for deterioration (17 calls) but no modifications of treatment by nurse educator	12 mos
Harrison et al. (2002) (32)	192	Patients discharged from hospital with heart failure (Canada)	76	Patient education and counseling, education booklet and map used at home	0.5 mos

ACE = angiotensin-converting enzyme; PHARM = Pharmacist in Heart failure Assessment Recommendation and Monitoring study.

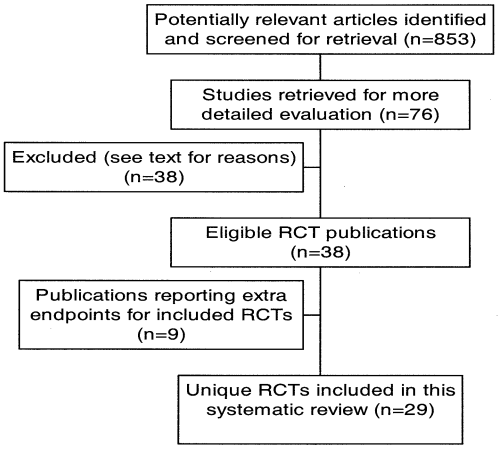

Figure 1. Flow diagram of study selection. RCT = randomized controlled trial.

occurred on four occasions for a kappa value of 0.86. All disagreements were resolved by consensus.

Studies included in the systematic review. Summary data from the 29 randomized trials are presented in Table 1 (9–37). In all trials, the control groups received usual care (which was generally ill-defined).

Quantitative data synthesis. ALL-CAUSE MORTALITY. Two of the 22 trials reporting mortality end points found a significant difference between the intervention and control patients during the pre-specified study periods (Table 2); a third group of investigators (11) subsequently reported a significant difference after 18 months of follow-up (2 deaths in the intervention arm and 9 in the control arm, $p = 0.02$) (38). The summary risk ratio (RR) for all 22 trials (3,781 patients) was 0.83 (95% confidence interval [CI] 0.70 to 0.99); however, although heterogeneity testing was not significant ($p = 0.15$), there was a strong enough trend that we thought the data should not be pooled across all trials. Rather, we examined results within the a priori defined intervention subgroups. Multidisciplinary teams providing specialized follow-up were associated with significant reductions in mortality (RR 0.75 [95% CI 0.59 to 0.96], number needed to treat [NNT] 17), with similar results whether that follow-up was done in HF clinics (RR 0.66, 95% CI 0.42 to 1.05) or not (RR 0.81, 95% CI 0.65 to 1.01). On the other hand, no mortality reductions were seen with those strategies that were based on telephone follow-up with instructions to see regular physician if deteriorating (RR 0.91, 95% CI 0.65 to 1.29) or those programs that emphasized enhanced patient self-care activities (RR 1.14, 95% CI 0.67 to 1.94). The adjusted indirect comparison (8) confirmed that mortality reductions were greater with multidisciplinary teams providing specialized follow-up (whether in HF clinics or non-clinic settings) than programs that relied on enhanced self-care activities alone (adjusted RR 0.66, 95% CI 0.46 to 0.94) or programs that employed regular telephone contact and follow-up with primary care practitioners (adjusted RR 0.82, 95% CI 0.54 to 1.25).

ALL-CAUSE HOSPITALIZATION RATE. Whereas three trials reported a statistically significant reduction in hospitalizations for any reason in patients randomized to the multidisciplinary management strategies, 18 failed to detect any significant difference and 1 reported excess hospitalization rates in the intervention arm (Table 2). Although for the 23 trials (4,313 patients) the summary risk ratio of 0.84 (95% CI 0.75 to 0.93) is consistent with a beneficial impact from the interventions, there was significant heterogeneity in the results ($p < 0.01$).

This statistical heterogeneity again highlights the differences between the intervention categories noted earlier. Those trials evaluating the impact of frequent telephone contact with advice to those patients exhibiting deterioration to see their regular physician demonstrated no impact on all-cause hospitalization rates (RR 0.98, 95% CI 0.80 to 1.20). This is in contradistinction to trials evaluating multidisciplinary teams providing specialized follow-up (RR 0.81 [95% CI 0.71 to 0.92] and NNT 10, with similar results for follow-up in clinic (RR 0.76, 95% CI 0.58 to 1.01) or non-clinic (RR 0.81, 95% CI 0.72 to 0.91) settings, or programs that emphasized enhanced patient self-care activities (RR 0.73, 95% CI 0.57 to 0.93). The adjusted indirect comparison (8) confirmed that, compared with programs that employed regular telephone contact and follow-up with primary care practitioners, all-cause hospitalizations were affected more by programs that emphasized enhanced patient self-care activities (adjusted RR 0.75, 95% CI 0.63 to 0.88) or multidisciplinary teams providing specialized follow-up (adjusted RR 0.81, 95% CI 0.63 to 1.04) compared with telephone contact and follow-up with primary care physician.

HF HOSPITALIZATION RATE. Six of the 19 trials reporting this end point found statistically significant reductions in the need for at least one HF hospitalization with multidisciplinary management strategies, and the pooled effect estimate suggested a substantial impact (RR 0.73, 95% CI 0.66 to 0.82, $p = 0.36$ for heterogeneity, NNT = 11 to prevent 1 patient from being hospitalized for HF) on this outcome (Table 2). Results were similar for specialized follow-up by a multidisciplinary team (RR 0.74, 95% CI 0.63 to 0.87) either in an HF clinic (RR 0.76, 95% CI 0.58 to 0.099) or in a non-clinic setting (RR 0.72, 95% CI 0.59 to 0.87), programs employing telephone follow-up (RR 0.75, 95% CI 0.57 to 0.99), or programs emphasizing enhanced patient self-care activities (RR 0.66, 95% CI 0.52 to 0.83). Given the similarity in the summary estimates, adjusted indirect comparisons were not performed.

TOTAL NUMBER OF HOSPITALIZATIONS. Twenty-one trials reported total number of hospitalizations by treatment arm; in 11 of these trials, the intervention arm had significantly fewer total hospitalizations. Pooling the data from all 21 trials revealed a marked reduction in total number of hospitalizations (RR 0.70, 95% CI 0.62 to 0.80), with no appreciable differences between multidisciplinary HF clinics (RR 0.61, 95% CI 0.39 to 0.94), specialized follow-up by

Table 2. Impact of Interventions on All-Cause Mortality, All-Cause Hospitalization Rates, and Heart Failure Hospitalization Rates

Study (Year) (Ref.)	Length of Follow-Up (mos)	All-Cause Mortality (# Events/Total # Pts)			All-Cause Hospitalization Rates (# Re-Admitted at Least Once/ Total # Patients)*			Heart Failure Hospitalization Rates (# Re-Admitted at Least Once/ Total # Patients)*		
		Intervention Arm	Control Arm	Risk Ratio (95% CI)	Intervention Arm	Control Arm	Risk Ratio (95% CI)	Intervention Arm	Control Arm	Risk Ratio (95% CI)
Multidisciplinary heart failure clinic										
Cline et al. (1998) (16)†	12	24/80	31/110	1.06 (0.68, 1.67)	22/56	43/79	0.72 (0.49, 1.06)	NR	NR	NR
Ekman et al. (1998) (17)	6	21/79	17/79	1.24 (0.71, 2.16)	48/79	45/79	1.07 (0.82, 1.38)	36/79	38/79	0.95 (0.68, 1.32)
Doughty et al. (2002) (14)	12	19/100	24/97	0.77 (0.45, 1.31)	64/100	59/97	1.05 (0.85, 1.31)	21/100	23/97	0.89 (0.53, 1.49)
Kasper et al. (2002) (18)	6	7/102	13/98	0.52 (0.22, 1.24)	40/102	42/98	0.92 (0.66, 1.28)	26/102	35/98	0.71 (0.47, 1.09)
Capomolla et al. (2002) (19)	12	3/112	21/122	0.16 (0.05, 0.51)	9/112	37/122	0.26 (0.13, 0.52)	NR	NR	NR
Stromberg et al. (2003) (20)*	12	7/52	20/54	0.36 (0.17, 0.79)	28/52	37/54	0.79 (0.58, 1.07)	17/52	27/54	0.65 (0.41, 1.05)
Ledwidge et al. (2003) (13)	3	3/51	3/47	0.92 (0.20, 4.34)	2/51	12/47	0.15 (0.04, 0.65)	2/51	10/47	0.18 (0.04, 0.80)
Subtotal			0.66 (0.42, 1.05)			0.76 (0.58, 1.01)			0.76 (0.58, 0.99)	
Multidisciplinary team providing specialized follow-up in non-clinic setting										
Hanchett and Torrens (1967) (21)‡	30	NR	NR	NR	NR	NR	NR	NR	NR	NR
Rich et al. (1993) (22)	3	NR	NR	NR	21/63	16/35	0.73 (0.44, 1.20)	NR	NR	NR
Rich et al. (1995) (9)	3	13/142	17/140	0.75 (0.38, 1.49)	41/142	59/140	0.69 (0.50, 0.95)	NR	NR	NR
Stewart et al. (1948) (11)*	6	6/49	12/48	0.49 (0.20, 1.20)	24/49	31/48	0.76 (0.53, 1.08)	12/49	18/48	0.65 (0.35, 1.20)
Stewart et al. (1999) (25)*	6	18/100	28/100	0.64 (0.38, 1.08)	40/100	51/100	0.78 (0.58, 1.07)	21/100	27/100	0.78 (0.47, 1.28)
Naylor et al. (1999) (12)*	6	NR	NR	NR	18/52	26/56	0.75 (0.47, 1.19)	NR	NR	NR
Blue et al. (2001) (27)	12	25/84	25/81	0.96 (0.61, 1.53)	47/84	49/81	0.92 (0.71, 1.20)	12/84	26/81	0.45 (0.24, 0.82)
Trochu et al. (2004) (37)*	12	38/102	42/100	0.89 (0.63, 1.25)	58/95	71/100	0.86 (0.70, 1.05)	47/95	64/100	0.77 (0.60, 0.99)
Subtotal			0.81 (0.65, 1.01)			0.81 (0.72, 0.91)			0.72 (0.59, 0.87)	
Summary for specialized multidisciplinary team follow-up (clinic or non-clinic settings)										
Subtotal			0.75 (0.59, 0.96)			0.81 (0.71, 0.92)			0.74 (0.63, 0.87)	
Telephone follow-up and attendance with primary care physician if deteriorates										
Naylor et al. (1994) (28)*	3	NR	NR	NR	16/72	23/70	0.68 (0.39, 1.17)	NR	NR	NR
Weinberger et al. (1996) (10)*	6	NR	NR	NR	130/249	106/255	1.26 (1.04, 1.52)	NR	NR	NR
PHARM (1999) (29)	6	3/90	5/91	0.61 (0.15, 2.46)	NR	NR	NR	NR	NR	NR
Rainville et al. (1999) (30)	12	1/17	4/17	0.25 (0.03, 2.01)	NR	NR	NR	4/17	10/17	0.40 (0.16, 1.03)
Pugh et al. (2001) (26)	6	NR	NR	NR	NR	NR	NR	9/25	11/30	0.98 (0.49, 1.98)
Jerant et al. (2001) (15)*	6	2/25	0/12	2.50 (0.13, 48.36)	8/25	7/12	0.55 (0.26, 1.16)	2/25	4/12	0.24 (0.05, 1.13)
de Lusignan et al. (2001) (31)	12	2/10	3/10	0.67 (0.14, 3.17)	NR	NR	NR	NR	NR	NR
Riegel et al. (2002) (33)*	6	16/130	32/228	0.88 (0.50, 1.54)	56/130	114/228	0.86 (0.68, 1.09)	23/130	63/228	0.64 (0.42, 0.98)
Laramee et al. (2003) (35)*	3	13/141	15/146	0.90 (0.44, 1.82)	49/134	46/130	1.03 (0.75, 1.43)	18/134	21/130	0.83 (0.46, 1.49)
Tsuyuki et al. (2004) (36)*	6	16/140	12/136	1.30 (0.64, 2.64)	59/140	51/136	1.12 (0.84, 1.50)	37/140	38/136	0.95 (0.64, 1.39)
Subtotal			0.91 (0.67, 1.29)			0.98 (0.80, 1.20)			0.75 (0.57, 0.99)	

Continued on next page

Table 2 Continued

Study (Year) (Ref.)	Length of Follow-Up (mos)	All-Cause Mortality (# Events/Total # Pts): Intervention Arm	All-Cause Mortality: Control Arm	All-Cause Mortality: Risk Ratio (95% CI)	All-Cause Hospitalization Rates (# Re-Admitted at Least Once/Total # Patients)*: Intervention Arm	All-Cause Hospitalization: Control Arm	All-Cause Hospitalization: Risk Ratio (95% CI)	Heart Failure Hospitalization Rates (# Re-Admitted at Least Once/Total # Patients)*: Intervention Arm	Heart Failure Hospitalization: Control Arm	Heart Failure Hospitalization: Risk Ratio (95% CI)
Enhanced patient self-care activities										
Serxner et al. (1998) (23)*	6	NR	NR	NR	NR	NR	NR	15/55	27/54	0.55 (0.33, 0.91)
Jaarsma et al. (1999) (24)*	9	22/84	16/95	1.56 (0.88, 2.76)	31/84	47/95	0.75 (0.53, 1.05)	24/84	37/95	0.73 (0.48, 1.12)
Harrison et al. (2002) (32)*	5	6/92	5/100	1.30 (0.41, 4.13)	21/92	31/100	0.74 (0.46, 1.19)	18/92	24/100	0.82 (0.47, 1.40)
Krumholz et al. (2002) (34)*	12	9/44	13/44	0.69 (0.33, 1.45)	16/44	23/44	0.70 (0.43, 1.13)	18/44	30/44	0.60 (0.40, 0.90)
Subtotal				1.14 (0.67, 1.94)			0.73 (0.57, 0.93)			0.66 (0.52, 0.83)
Total				0.83 (0.70, 0.99)			0.84 (0.75, 0.93)			0.73 (0.66, 0.82)

*Further data provided by authors. †The hospitalization data in this study were reported only for those patients who did not die during follow-up. ‡This study reported total number of hospitalizations (all-cause and heart failure) and was included in those analyses.
CI = confidence interval; NR = not reported; PHARM = Pharmacist in Heart failure Assessment Recommendation and Monitoring study; pts = patients.

multidisciplinary team (RR 0.68, 95% CI 0.56 to 0.83), telephone follow-up (RR 0.77, 95% CI 0.63 to 0.95), or enhanced patient education and self-care activities (RR 0.68, 95% CI 0.54 to 0.87).

TOTAL HF HOSPITALIZATIONS. The frequency of multiple re-admissions for HF was particularly affected by the multidisciplinary strategies, such that total HF hospitalizations were markedly reduced (20 trials, RR 0.57, 95% CI 0.49 to 0.67). There were no appreciable differences between types of interventions: RR 0.67 (95% CI 0.53 to 0.83) for multidisciplinary HF clinics, RR 0.47 (95% CI 0.36 to 0.61) for specialized follow-up by multidisciplinary team, RR 0.65 (95% CI 0.49 to 0.85) for telephone follow-up, and RR 0.60 (95% CI 0.41 to 0.88) for enhanced patient education and self-care activities.

OTHER END POINTS. Six (9,16,18,20,29,37) of the 10 trials (10,13,14,27) that assessed the use of proven efficacious medications demonstrated significantly higher prescribing rates (or dosing) in those patients randomized to the multidisciplinary strategies. Five (18,23,24,31,35) of the six (36) trials that examined patient compliance reported significantly higher adherence rates to medications and dietary/fluid restrictions in patients exposed to the multidisciplinary interventions. Nine (9,14,18,19,23,25,32,33,37) of the 18 trials (10,12,16,17,28,30,31) that assessed patient quality of life or functional status demonstrated significantly better outcomes in the intervention arms (another two trials [13,26] reported a nonsignificant trend toward better quality of life scores). Finally, although none of these trials included formal cost-effectiveness analyses, 15 (9,11–13,15,16,19,22,23,25,28,33,34,36,37) of the 18 trials describing the costs of the intervention reported that it was cost-saving (the other three trials [18,26,35] reported their interventions to be cost-neutral).

SENSITIVITY ANALYSES. Analyses did not reveal any significant effects of year of publication, duration of intervention, Jadad score, sample size, or length of follow-up on our results.

DISCUSSION

In summary, pooling the data from the 29 randomized trials of multidisciplinary management strategies for patients with HF reveals that these programs are associated with a 27% reduction in HF hospitalization rates (NNT = 11) and a 43% reduction in total number of HF hospitalizations. Those strategies that incorporate specialized follow-up by a multidisciplinary team or in a multidisciplinary HF clinic also reduce all-cause mortality by approximately one-quarter (NNT = 17) and all-cause hospitalizations by one-fifth (NNT = 10). The beneficial effects of these multidisciplinary strategies compare favorably with established drug treatments for HF (for example, angiotensin-converting enzyme inhibitors reduce mortality by 20% [NNT = 19] and HF hospitalization rates by 33% [NNT = 16] in similar patient populations) (39) and suggest that the current

enthusiasm for these programs is not misplaced. Further, although none of these trials incorporated formal cost-effectiveness analyses, 15 of the 18 trials reported that their multidisciplinary interventions were cost-saving (the other three trials reported cost neutrality), and recent analyses in the U.K. and U.S. have shown that when applied on a national basis, multidisciplinary management strategies have the potential to deliver substantial cost savings (6,40).

In our earlier systematic review (5), we were unable to draw any conclusions about which elements of these multidisciplinary strategies were most efficacious in patients with HF. Incorporating the trials published over the past five years, enhanced patient self-care, follow-up monitoring by specially trained staff, and access to specialized HF clinics appear to be the most efficacious approaches. Although telephone follow-up programs that advise deteriorating patients to see their regular physician do reduce HF hospitalizations, they have no impact on mortality or all-cause hospitalizations. Of note, while this conclusion is based on the 10 trials (1,897 patients) of telephone support programs published thus far, it is also consistent with the preliminary report from the DIAL Trial Investigators (1,518 patients from 51 centers) presented at the 2002 American Heart Association Meeting (41).

Whereas the specific elements to be included in any multidisciplinary disease management program should take into account those features unique to each health region (including prevalence, local barriers to optimal care, and local resources), we believe that three elements are crucial to the success of these programs. First, specially trained HF nurses should be key components of any intervention. Second, efforts should be made to educate patients and their caregivers about HF, precipitating factors, and the need for compliance with medication and dietary advice (particularly because most HF re-admissions are caused by factors that patients can be taught to recognize and avoid) (42). Finally, there must be ready access to clinicians trained in HF.

There are a few important caveats with this systematic review. First and foremost, all but two of these trials tested programs in high-risk HF patients (i.e., those who had been recently discharged from hospital), and all programs were administered by specially trained staff from academic health centers in urban areas. Whether the same benefits could be obtained in lower risk patients or if the programs were delivered by staff without special training is uncertain, but seems unlikely. Second, these trials were relatively short in duration, raising questions about their long-term effectiveness. However, the median survival of patients with HF after hospital discharge is only 18 to 24 months (3,43). Thus, interventions that demonstrate substantial benefits so quickly in HF are particularly welcome. In addition, preliminary evidence suggests that the benefits from at least one of these programs were maintained over a further five years of follow-up (44). Although concerns may be raised that attendance at a specialized HF clinic may improve the provision of effective HF therapies at the expense of other needed medications (45), we chose all-cause mortality as our primary outcome and all-cause hospitalizations as one of our secondary outcomes for this very reason. Further, our evaluation of the incremental benefits of the various components of each intervention is hampered by the lack of direct comparisons. For example, a recent trial reported that daily nurse-supervised telemonitoring of HF patients was more efficacious and less costly than home visits by nurses who were not specially trained in HF (46). However, adjusted indirect comparisons such as those we present in this systematic review have been shown to provide reasonable estimates of the relative efficacy of different interventions when the control arms are similar (8). Finally, few of these trials reported on prescribing rates for angiotensin-converting enzyme inhibitors or beta-blockers, preventing us from examining whether the benefits of these programs are merely attributable to improved prescribing patterns or patient compliance, or whether the benefits are additive to optimal medical therapy.

In conclusion, a wide variety of multidisciplinary strategies to manage patients with HF reduce HF hospitalizations. Strategies that incorporate follow-up monitoring by specially trained staff and/or access to specialized HF clinics also reduce mortality and all-cause hospitalizations. Indeed, the benefits and cost-effectiveness of these programs compare favorably with established drug treatments for HF. The question is no longer whether these programs work, but rather which of these programs work best. Our systematic review suggests that patient education to enhance self-care, follow-up monitoring by specially trained staff, and access to specialized HF clinics are the most efficacious approaches. These conclusions are based on adjusted indirect comparisons, and direct comparisons of different types of interventions (and/or different intensities) in head-to-head trials should be the next frontier for research in this field. The challenge for policymakers is to incorporate this evidence into future health care planning to deal with the current epidemic of HF patients being discharged from acute care institutions throughout North America.

Acknowledgments

The authors thank the following study investigators who kindly provided further data from their studies: Drs. Jaarsma, Krumholz, Laramee, Harrison, Jerant, Riegel, Stromberg, Stewart (two studies), Naylor (two studies), Gattis, Trochu, and Tsuyuki.

Reprint requests and correspondence: Dr. Finlay A. McAlister, 2E3.24 WMC, University of Alberta Hospital, 8440 112 Street, Edmonton, Alberta, Canada T6G 2R7. E-mail: Finlay.McAlister@ualberta.ca

REFERENCES

1. Stewart S, Jenkins A, Buchan S, McGuire A, Capewell S, McMurray JJV. The current cost of heart failure to the National Health Service in the UK. Eur J Heart Fail 2002;4:361–71.

2. Jessup M, Brozena S. Medical progress: heart failure. N Engl J Med 2003;348:2007–18.
3. MacIntyre K, Capewell S, Stewart S, et al. Evidence of improving prognosis in heart failure: trends in case fatality in 66,547 patients hospitalized between 1986 and 1995. Circulation 2000;102:1126–31.
4. Philbin EF. Comprehensive multidisciplinary programs for the management of patients with congestive heart failure. J Gen Intern Med 1999;14:130–5.
5. McAlister FA, Lawson FME, Teo KK, Armstrong PW. A systematic review of randomized trials of disease management programs in congestive heart failure. Am J Med 2001;110:378–84.
6. Phillips CO, Wright SM, Kern DE, et al. Comprehensive discharge planning with postdischarge support for older patients with congestive heart failure: a meta-analysis. JAMA 2004;291:1358–67.
7. Jadad AR. Assessing the quality of reports of randomized clinical trials: is blinding necessary. Control Clin Trials 1996;17:1–12.
8. Song F, Altman DG, Glenny AM, Deeks JJ. Validity of indirect comparison for estimating efficacy of competing interventions: empirical evidence from published meta-analyses. BMJ 2003;326:472–7.
9. Rich MW, Beckham V, Wittenberg C, Leven CL, Freedland KE, Carney RM. A multidisciplinary intervention to prevent the readmission of elderly patients with congestive heart failure. N Engl J Med 1995;333:1190–5.
10. Weinberger M, Oddone EZ, Henderson WG, for the Veterans Affairs Cooperative Study Group on Primary Care and Hospital Readmission. Does increased access to primary care reduce hospital readmissions? N Engl J Med 1996;334:1441–7.
11. Stewart S, Pearson S, Horowitz JD. Effects of a home-based intervention among patients with congestive heart failure discharged from acute hospital care. Arch Intern Med 1998;158:1067–72.
12. Naylor MD, Brooten D, Campbell R, et al. Comprehensive discharge planning and home follow-up of hospitalized elders: a randomized clinical trial. JAMA 1999;281:613–20.
13. Ledwidge M, Barry M, Cahill J, et al. Is multidisciplinary care of heart failure cost-beneficial when combined with optimal medical care? Eur J Heart Fail 2003;5:381–9.
14. Doughty RN, Wright SP, Pearl A, et al. Randomized, controlled trial of integrated heart failure management. The Auckland Heart Failure Management Study. Eur Heart J 2002;23:139–46.
15. Jerant AF, Azari R, Nesbitt TS. Reducing the cost of frequent hospital admissions for congestive heart failure: a randomized trial of a home telecare intervention. Med Care 2001;39:1234–45.
16. Cline CMJ, Israelsson BYA, Willenheimer RB, Broms K, Erhardt LR. Cost effective management programme for heart failure reduces hospitalisation. Heart 1998;80:442–6.
17. Ekman I, Andersson B, Ehnfors M, Matejka G, Persson B, Fagerberg B. Feasibility of a nurse-monitored, outpatient-care programme for elderly patients with moderate-to-severe chronic heart failure. Eur Heart J 1998;19:1254–60.
18. Kasper EK, Gerstenblith G, Hefter G, et al. A randomized trial of the efficacy of multidisciplinary care in heart failure outpatients at high risk of hospital readmission. J Am Coll Cardiol 2002;39:471–80.
19. Capomolla S, Febo O, Ceresa M, et al. Cost/utility ratio in chronic heart failure: comparison between heart failure management program delivered by day-hospital and usual care. J Am Coll Cardiol 2002;40:1259–66.
20. Stromberg A, Martensson J, Fridlund B, et al. Nurse-led heart failure clinics improve survival and self-care behaviour in patients with heart failure. Eur Heart J 2003;24:1014–23.
21. Hanchett E, Torrens PR. A public health home nursing program for outpatients with heart diseases. Pub Health Reports 1967;82:683–8.
22. Rich MW, Vinson JM, Sperry JC, et al. Prevention of readmission in elderly patients with congestive heart failure: results of a prospective, randomized pilot study. J Gen Intern Med 1993;8:585–90.
23. Serxner S, Miyaji M, Jeffords J. Congestive heart failure disease management study: a patient education intervention. Congestive Heart Failure 1998;4:23–8.
24. Jaarsma T, Halfens R, Huijer Abu-Saad H, et al. Effects of education and support on self-care and resource utilization in patients with heart failure. Eur Heart J 1999;20:673–82.
25. Stewart S, Marley JE, Horowitz JD. Effects of a multidisciplinary, home-based intervention on unplanned readmissions and survival among patients with chronic congestive heart failure: a randomised controlled study. Lancet 1999;354:1077–83.
26. Pugh LC, Havens DS, Xie S, Robinson JM, Blaha C. Case management for elderly persons with heart failure: the quality of life and cost outcomes. MEDSURG Nursing 2001;10:71–8.
27. Blue L, Lang E, McMurray JJV, et al. Randomised controlled trial of specialist nurse intervention in heart failure. BMJ 2001;323:715–8.
28. Naylor M, Brooten D, Jones R, Lavizzo-Mourey R, Mezey M, Pauly M. Comprehensive discharge planning for the hospitalized elderly. Ann Intern Med 1994;120:999–1006.
29. Gattis WA, Hasselblad V, Whellan DJ, et al. Reduction in heart failure events by the addition of a clinical pharmacist to the heart failure management team. Arch Intern Med 1999;159:1939–45.
30. Rainville EC. Impact of pharmacist interventions on hospital readmissions for heart failure. Am J Health Syst Pharm 1999;56:1339–42.
31. de Lusignan S, Wells S, Johnson P, Meredith K, Leatham E. Compliance and effectiveness of 1 year's home telemonitoring: the report of a pilot study of patients with chronic heart failure. Eur J Heart Fail 2001;3:723–30.
32. Harrison MB, Browne GB, Roberts J, et al. Quality of life of individuals with heart failure. Med Care 2002;40:271–82.
33. Riegel B, Carlson B, Kopp Z, et al. Effect of a standardized nurse case-management telephone intervention on resource use in patients with chronic heart failure. Arch Intern Med 2002;162:705–12.
34. Krumholz HM, Amatruda J, Smith GL, et al. Randomized trial of an education and support intervention to prevent readmission of patients with heart failure. J Am Coll Cardiol 2002;39:83–9.
35. Laramee A, Levinsky SK, Sargent J, et al. Case management in a heterogeneous congestive heart failure population: a randomized controlled trial. Arch Intern Med 2003;163:809–17.
36. Tsuyuki RT, Fradette M, Johnson JA, et al. Multicentre disease management program for hospitalized patients with heart failure: the Review of Education on ACE inhibitors in Congestive heart failure Treatment (REACT) Study. J Card Fail 2004. In Press.
37. Trochu JN, Baleynaud S, Mialet G, et al. Efficacy of a multidisciplinary management of chronic heart failure patients: one year results of a multicentre randomized trial in French medical practice. Eur Heart J 2004. In Press.
38. Stewart S, Vandenbroek AJ, Pearson S, Horowitz JD. Prolonged beneficial effects of a home-based intervention on unplanned readmissions and mortality among patients with congestive heart failure. Arch Intern Med 1999;159:257–61.
39. Flather MD, Yusuf S, Kober L, et al. Long-term ACE inhibitor therapy in patients with heart failure or left ventricular dysfunction: a systematic overview of data from individual patients. Lancet 2000;355:1575–81.
40. Stewart S, Blue L, Walker A, Morrison C, McMurray JJ. An economic analysis of specialist heart failure nurse management in the UK: can we afford not to implement it? Eur Heart J 2002;23:1369–78.
41. Grancelli H, Varini S, Ferrante D, et al. Randomized trial of telephone intervention in chronic heart failure (DIAL): study design and preliminary observations. J Card Fail 2003;9:172–9.
42. Tsuyuki RT, McKelvie RS, Arnold JM, et al. Acute precipitants of congestive heart failure exacerbations. Arch Intern Med 2001;161:2337–42.
43. Senni M, Tribouilloy CM, Rodeheffer RJ, et al. Congestive heart failure in the community: trends in incidence and survival in a 10-year period. Arch Intern Med 1999;159:29–34.
44. Stewart S, Horowitz JD. Home-based intervention in congestive heart failure: long-term implications on readmission and survival. Circulation 2002;105:2861–6.
45. Steinbrook R. Patients with multiple chronic conditions—How many medications are enough? N Engl J Med 1998;338:1541–2.
46. Benatar D, Bondmass M, Ghitelman J, Avitall B. Outcomes of chronic heart failure. Arch Intern Med 2003;163:347–52.