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Effect of Moderate or Intensive Disease Management Program on Outcome in Patients With Heart Failure

Coordinating Study Evaluating Outcomes of Advising and Counseling in Heart Failure (COACH)

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Background: Heart failure (HF) disease management programs are widely implemented, but data about their effect on outcome have been inconsistent.

Methods: The Coordinating Study Evaluating Outcomes of Advising and Counseling in Heart Failure (COACH) was a multicenter, randomized, controlled trial in which 1023 patients were enrolled after hospitalization because of HF. Patients were assigned to 1 of 3 groups: a control group (follow-up by a cardiologist) and 2 intervention groups with additional basic or intensive support by a nurse specializing in management of patients with HF. Patients were studied for 18 months. Primary end points were time to death or rehospitalization because of HF and the number of days lost to death or hospitalization.

Results: Mean patient age was 71 years; 38% were women; and 50% of patients had mild HF and 50% had moderate to severe HF. During the study, 411 patients (40%) were readmitted because of HF or died from any cause: 42% in the control group, and 41% and 38% in the basic and intensive support groups, respectively (hazard ratio, 0.96 and 0.93, respectively; $P=.73$ and $P=.52$, respectively). The number of days lost to death or hospitalization was 39 960 in the control group, 33 731 days for the basic intervention group ($P=.81$), and 34 268 for the intensive support group ($P=.49$). All-cause mortality occurred in 29% of patients in the control group, and there was a trend toward lower mortality in the intervention groups combined (hazard ratio, 0.85; 95% confidence interval, 0.66-1.08; $P=.18$). There were slightly more hospitalizations in the 2 intervention groups (basic intervention group, $P=.89$; and intensive support group, $P=.60$).

Conclusions: Neither moderate nor intensive disease management by a nurse specializing in management of patients with HF reduced the combined end points of death and hospitalization because of HF compared with standard follow-up. There was a nonsignificant, potentially relevant reduction in mortality, accompanied by a slight increase in the number of short hospitalizations in both intervention groups.

Clinical Trial Registry: <http://trialregister.nl> Identifier: NCT 98675639

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Author Affiliations are listed at the end of this article.

Group Information: A list of study investigators and participating centers of the Coordinating Study Evaluating Outcomes of Advising and Counseling in Heart Failure is provided at the end of this article.

HEART FAILURE (HF) IS ONE of the largest medical problems of our time, and despite substantial advances in its treatment, morbidity and mortality remain high.^{1,2} In recent years, various disease management programs have been examined, and in some, favorable effects on morbidity (hospitalizations) and even mortality have been reported.³⁻⁶ As a result, in many hospitals, special disease management programs have been implemented such as an HF clinic in which specialized nurses provide additional care.⁷

Although most studies have reported favorable effects of a variety of these disease management programs, not all have shown positive findings.⁸⁻¹⁰ Recent meta-analyses also report effectiveness of HF disease management programs in reducing mortality and hospital readmissions and potential improvements in quality of life and cost savings.^{11,12} Although some factors have been identified as important for a successful program,¹³ it remains largely unclear which components of the programs are primarily responsible for the observed favorable effects and how intensive such programs should be.

The present study was designed to examine the effects of a nurse-led disease management program in a sufficiently large population with an assumed relatively high event rate. The Coordinating Study Evaluating Outcomes of Advising and Counseling in Heart Failure (COACH) was designed to determine the effects of 2 levels of intensity in disease management programs on the combined end points of death and readmission to the hospital. Patients who were eligible for COACH had been hospitalized because of HF and were then randomized to 1 of 3 treatment arms and studied for 18 months.

METHODS

COACH was a multicenter, randomized, open trial with blinded endpoint evaluation, designed to compare basic support and intensive support in patients with chronic HF, with a control group receiving usual care as previously described in detail.¹⁴ Patients were recruited during 28 months (October 23, 2002, to February 2, 2005), and all patients were followed up for a fixed period of 18 months. The medical ethics committee approved the study protocol, and all patients provided written informed consent.

PATIENT POPULATION

All patients had been admitted to the hospital with symptoms of HF, New York Heart Association (NYHA) functional classification II to IV.¹⁴ The diagnosis was made on the basis of a combination of typical signs and symptoms for which hospitalization was considered necessary, including the need for intravenously administered medication. All 17 sites were experienced HF centers that had participated in multicenter HF trials. Patients were 18 years or older and had evidence of structural underlying heart disease as shown at cardiovascular imaging. Both patients with impaired left ventricular ejection fraction (LVEF) and those with preserved LVEF could participate. Before discharge from the hospital (ie, before inclusion in the study), patient status had to be stable with standard medication for HF. The decision to enroll a patient in the study was made at the participating center. Major exclusion criteria were concurrent inclusion in another study or HF clinic, inability to complete the questionnaires, invasive procedure or cardiac surgery intervention performed within the last 6 months or such procedure or intervention planned to be performed within the next 3 months, ongoing evaluation for heart transplantation, and inability or unwillingness to give informed consent.

RANDOMIZATION

During hospitalization, patients were randomized to 1 of 3 groups, as follows: basic support, intensive support, or control.¹⁴ The computer-generated randomization scheme used random permuted blocks of 6 patients stratified per center to ensure balanced assignment of patients to each of the 3 groups in each of the 17 participating centers.

INTERVENTION STRATEGIES

The study included 2 types of intervention and a control treatment.¹⁴ **Figure 1** shows the intensity of contacts with the cardiologist and nurse specializing in management of patients with HF (HF nurse) during follow-up. All patients received usual routine management by their cardiologist. This included an outpatient visit less than 2 months after hospital discharge and then every 6 months. Because 17 hospitals were involved, with po-

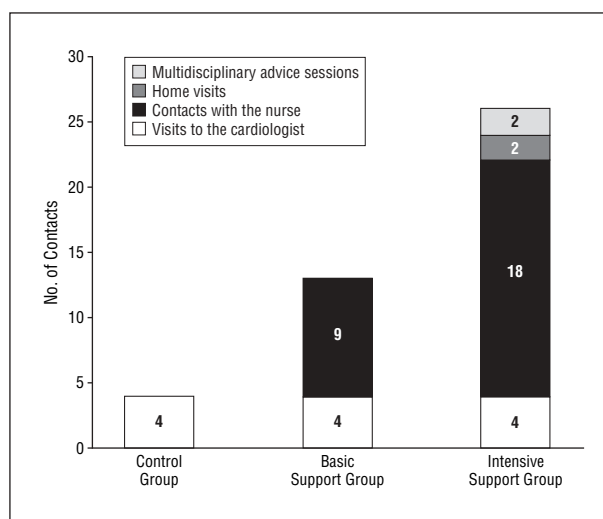


Figure 1. Protocol for contacts with health care providers (cardiologists and specially trained nurses) in the 3 groups.

tential differences in follow-up intensity, a standardized follow-up schedule was developed. Patients in the 2 support groups were visited by an HF nurse during admission, for education and support, and were scheduled for additional visits at the outpatient clinic.

Patients in the basic support group were scheduled for additional visits to the HF nurse at the outpatient clinic. Patients were educated using a protocol, and behavioral strategies were used to improve adherence. In addition, patients were instructed to contact the nurse if there was any change in their condition. Patients in the intensive support group received a similar intervention as used in the basic support group except they had monthly contact with the nurse. In the first month after hospital discharge, weekly telephone contacts were made and the patient was visited at home by the HF nurse. Furthermore, telephone calls, 2 home visits, and multidisciplinary advice given by a physiotherapist, dietician, and social worker were part of the intensive support intervention. In addition to providing information to patients, HF nurses were trained to increase patient self-efficacy. Materials used in the intervention included a patient diary, brochures on HF and its management, and samples of sodium-restricted food seasonings. Patients in both intervention groups were instructed to seek help if symptoms increased or if they gained weight.

Patients in the control group did not receive any treatment other than standard management by their cardiologist. All nurses were trained to increase the self-efficacy of the patients, and the quality of the 2 study interventions was maintained by monthly site visits of the research team to confirm adherence to the protocol.

FOLLOW-UP AND DATA COLLECTION

All patients were examined at hospital discharge and for 18 months thereafter.¹⁴ Data on mortality and number of readmissions to the hospital were collected from medical records and patient interviews. Cause of death, reason for readmission, and date of the event was adjudicated by a central end-point committee whose members were blinded to group assignment.

END POINTS

The study had 2 primary end points.¹⁴ The first primary end point was a composite of HF hospitalization or death from any cause. A hospitalization because of HF was defined as an un-

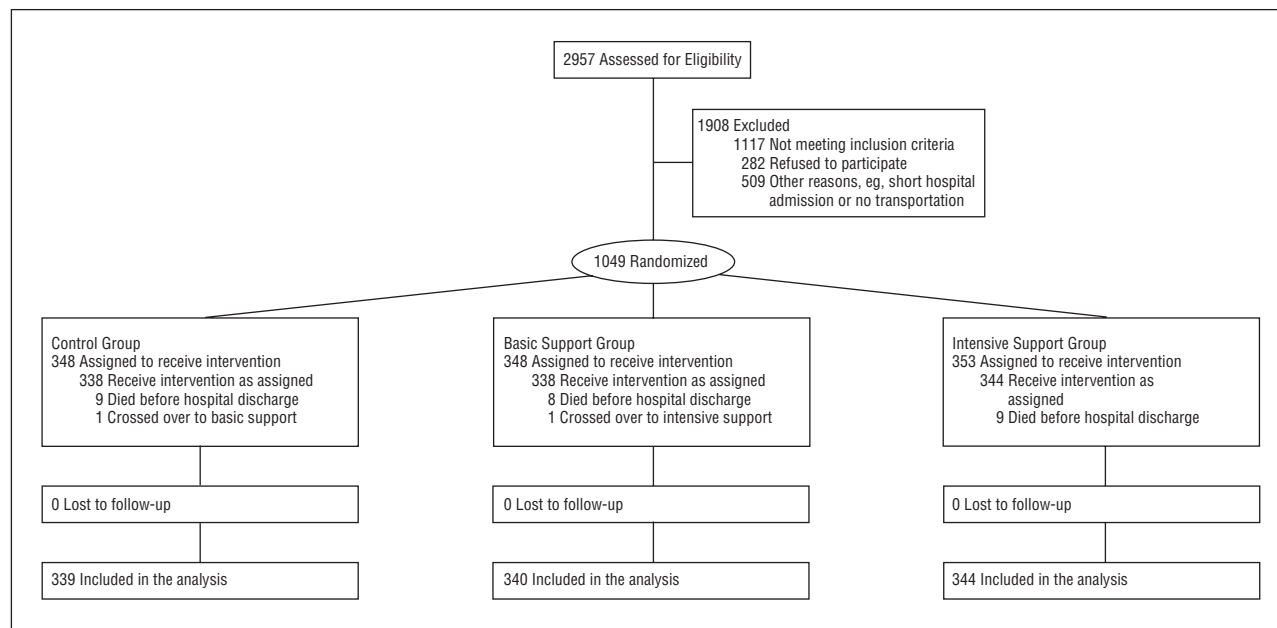


Figure 2. Flow of participants through the trial.

planned overnight stay in a hospital because of progression of HF or as a direct result of HF. Patients had to have typical signs and symptoms, and hospitalizations were classified as HF-related if admission was primarily for treatment of HF or when HF became a major component of the patient's hospital admission according to a predefined *Manual of Operations* for COACH using standard criteria.¹⁵ Evidence of worsening HF was also classified using standard clinical criteria.¹⁵ The second primary end point was the number of "unfavorable days," defined as the number of days lost because of death or hospitalization during the 18 months of follow-up. Major secondary end points were the 2 individual components of the composite end point, that is, death from any cause and hospitalization because of HF, and the number of all-cause hospitalizations per patient. All reported deaths and hospital admissions were referred to and adjudicated by an independent clinical event committee (see "COACH Investigators" section at the end of the article), who were blinded to the allocation of the interventions.

SAMPLE SIZE

We assumed a 40% event rate for the primary end points (death or readmission to the hospital because of HF) in the control group within the first year.¹⁴ A 25% decrease in events in the basic support group was considered both realistic and clinically relevant. With a power of 90% and an α level of .05, 349 patients were required in each of the 3 groups.

STATISTICAL ANALYSIS

All analyses were conducted according to the intent-to-treat principle.¹⁴ There were 2 primary end point comparisons: time to first major event (death or hospitalization because of HF) and the number of days lost because of death or hospitalization. Kaplan-Meier curves were constructed for the different time to event evaluations, and groups were compared using the log-rank test. To estimate the size of the effect, hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated with the use of unadjusted Cox regression models. The number of days lost because of death or hospitalization during the 18 months of follow-up and the number of hospitalizations per patient were

calculated and tested between groups using the Mann-Whitney test. All analyses were prespecified; reported *P* values are 2-sided and have not been adjusted for multiple testing. Dependency of multiple hospitalizations in 1 patient has not been considered in testing differences in incidences of hospitalization because of HF and duration of hospitalizations. $P < .05$ was considered statistically significant. Statistical analyses were performed using commercially available software (SPSS version 12.0; SPSS Inc, Chicago, Illinois, and SAS version 9.1; SAS Institute Inc, Cary, North Carolina).

RESULTS

During the study, 2957 patients were hospitalized because of symptomatic HF and structural underlying heart disease (**Figure 2**). A total of 1908 patients were excluded. Of these, 1117 patients did not meet the inclusion criteria because they were already enrolled in the HF clinic or another trial ($n=336$); were unable to follow the study protocol owing to dementia, other psychiatric illness, or deafness ($n=328$); had a planned or recent invasive procedure or surgery ($n=292$); had a terminal illness or were receiving palliative treatment ($n=125$); or died before randomization ($n=36$). An additional 282 patients refused to participate, and 509 were excluded because of other, usually logistic, reasons. Patients who participated were, on average, 4 years younger and more often male (63% vs 51%) compared with non-participants. A total of 1049 patients were randomized during hospitalization because of HF, of whom 1023 were discharged alive and were followed up for 18 months; this latter group forms the present study population.

BASELINE CHARACTERISTICS

The baseline characteristics of the 3 groups were comparable. Mean age was 71 years (age range, 23-93 years), 62% were men, and 61% were married (**Table 1**).

Table 1. Baseline Patient Characteristics at Hospital Discharge According to Assigned Treatment

| Characteristic | No. (%) | | | |
|--|-----------------------|-----------------------|-----------------------------|---------------------------------|
| | All Patients (N=1023) | Control Group (n=339) | Basic Support Group (n=340) | Intensive Support Group (n=344) |
| Age, mean (SD), y | 71 (11) | 72 (11) | 71 (11) | 70 (12) |
| Female sex | 384 (38) | 136 (40) | 115 (34) | 133 (39) |
| LVEF, mean (SD) | 34 (14) | 34 (14) | 34 (14) | 33 (15) |
| NYHA functional class ^a | | | | |
| II | 513 (50) | 177 (54) | 171 (51) | 165 (48) |
| III | 461 (46) | 139 (42) | 159 (47) | 163 (48) |
| IV | 34 (4) | 13 (4) | 8 (3) | 13 (4) |
| Blood pressure, mean (SD), mm Hg | | | | |
| Systolic | 118 (21) | 119 (22) | 118 (20) | 117 (21) |
| Diastolic | 68 (12) | 68 (12) | 69 (13) | 68 (12) |
| Heart rate at hospital discharge, mean (SD), beats/min | 75 (14) | 75 (14) | 75 (13) | 74 (14) |
| Previous hospital admission because of HF, No. (%) of patients | 334 (32) | 120 (35) | 108 (32) | 106 (31) |
| Comorbidities | | | | |
| Hypertension | 439 (43) | 157 (46) | 152 (45) | 130 (38) |
| Atrial fibrillation | 372 (36) | 121 (36) | 122 (36) | 129 (37) |
| Diabetes | 289 (28) | 103 (30) | 98 (29) | 88 (26) |
| Stroke | 105 (10) | 37 (11) | 35 (10) | 33 (9) |
| COPD | 268 (27) | 84 (25) | 87 (26) | 97 (28) |
| History of MI | 436 (43) | 149 (44) | 144 (42) | 143 (42) |
| Index hospital stay, median (range), d | 10 (7-16) | 11 (7-16) | 10 (7-16) | 10 (7-17) |
| Living alone | 396 (39) | 139 (42) | 136 (41) | 121 (35) |
| Body mass index, mean (SD) ^b | 27 (5) | 27 (5) | 27 (5) | 27 (5) |
| Duration of disease, median (range), y | 1 (0-34) | 1 (0-34) | 1 (0-29) | 1 (0-22) |
| eGFR, mean (SD), mL/min/1.73 m ² | 55 (21) | 52 (20) | 57 (19) | 57 (23) |
| Medication | | | | |
| ACEI or ARB | 847 (83) | 277 (82) | 290 (85) | 280 (81) |
| β-Blockers | 677 (66) | 221 (65) | 239 (70) | 217 (63) |
| Diuretics ^c | 980 (95) | 325 (96) | 330 (97) | 325 (95) |
| Digoxin | 309 (30) | 100 (30) | 108 (32) | 101 (29) |
| Calcium antagonists | 162 (16) | 60 (18) | 57 (17) | 45 (13) |
| Nitrates | 324 (32) | 109 (32) | 101 (30) | 114 (33) |
| Statins | 388 (38) | 126 (37) | 141 (42) | 121 (35) |
| Laboratory values | | | | |
| BNP, median (IR), pg/dL | 493 (730) | 530 (986) | 478 (657) | 478 (634) |
| NT-proBNP, median (IR), pg/dL | 2528 (4291) | 2677 (5251) | 2404 (3903) | 2505 (4274) |
| Serum sodium, mean (SD), mEq/L | 139 (4) | 139 (4) | 139 (4) | 139 (4) |
| Hemoglobin, mean (SD), g/dL | 13.2 (1.9) | 12.9 (1.9) | 13.2 (2.1) | 13.2 (1.9) |

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BNP, B-type natriuretic peptide; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; HF, heart failure; IR, interquartile range; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NT-proBNP, N-terminal prohormone B-type natriuretic peptide; NYHA, New York Heart Association.

SI conversion factors: To convert sodium to millimoles per liter, multiply by 1.0; hemoglobin to grams per liter, multiply by 10.0.

^aClass II indicates mild (slight limitation of physical activity; comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnea); III, moderate (marked limitation of physical activity; comfortable at rest, but less than ordinary activity causes fatigue, palpitation, or dyspnea); and IV, severe (unable to carry out any physical activity without discomfort; symptoms of cardiac insufficiency at rest; if any physical activity is undertaken, discomfort is increased).

^bCalculated as weight in kilograms divided by height in meters squared.

^cIncludes loop diuretics, thiazides, and aldosterone antagonists.

Whereas at admission to the hospital, virtually all patients had NYHA functional class III or IV disease, at discharge, 50% were classified as having NYHA class II disease and 50% as having NYHA III or IV disease. Both patients with decreased LVEF and preserved LVEF were included, and the mean LVEF was 34%.

INTERVENTION

There was a substantial difference in contacts with the study cardiologists and the specially trained nurses in all 3 groups compared with the planned protocol (Figure 1). Control patients were supposed to visit the cardiologist

only 4 times and to have no contact with an HF nurse. According to this schedule, 858 visits to the cardiologist should have taken place, but an actual total of 1144 visits to the cardiologist were made (286 additional visits, or 33% more). In the basic support group, 2347 visits and telephone calls were planned, but 3302 visits or telephone calls (40% more) were actually made. In the intensive support group, 5868 visits and telephone calls were planned and 6469 (10% more) were made. The estimated time investment of nurses in the basic support group was 20 hours per patient, and in the intensive intervention group was 40 hours per patient. Two patients crossed over to another group, 1 patient from the

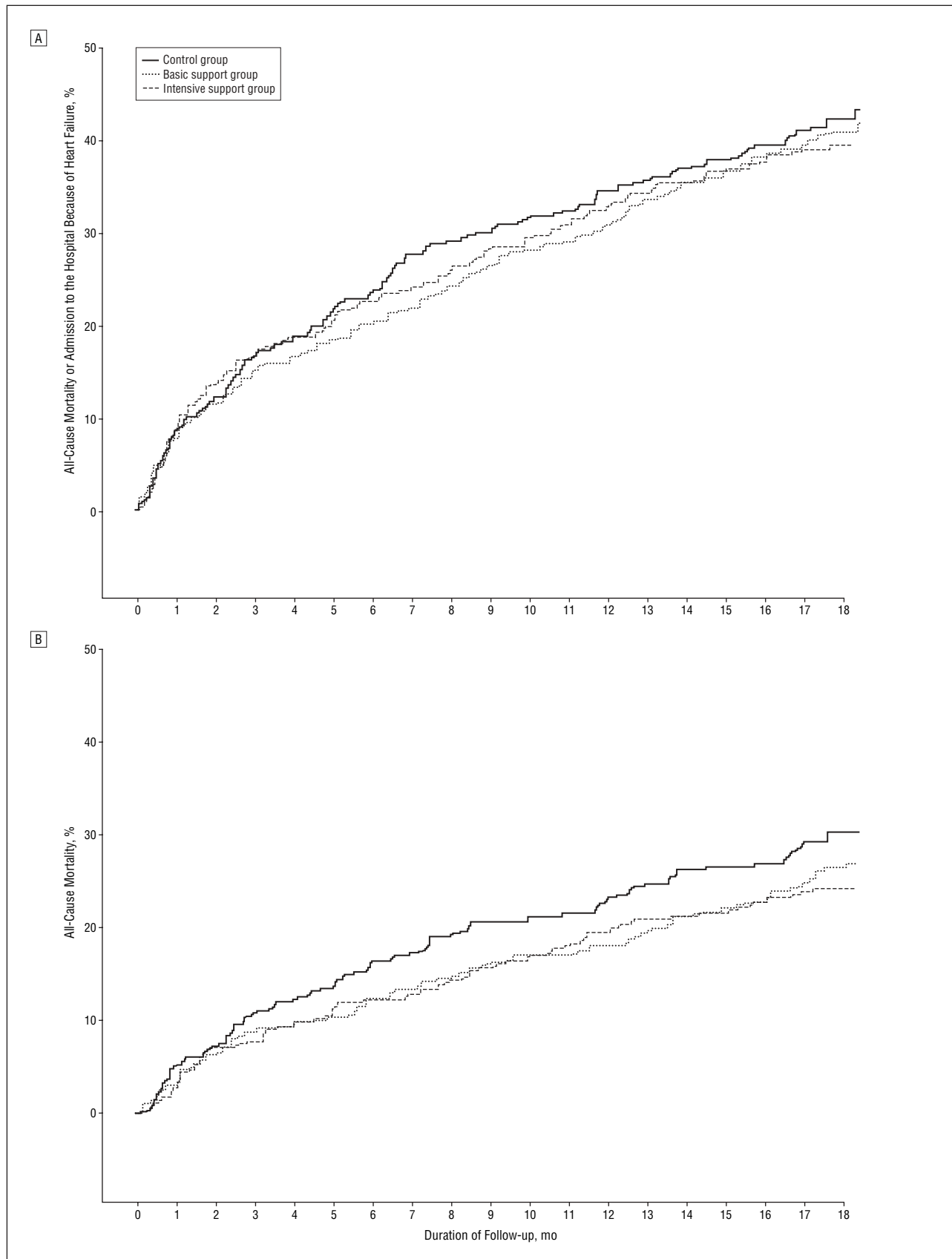


Figure 3. End points. A, Kaplan-Meier curve for time to death or first hospitalization because of heart failure (primary end point). B, Kaplan-Meier curve for all-cause mortality (major secondary end point).

basic support group to the intensive support group and 1 patient from the control group to the basic support group. These patients were analyzed as randomized (intent-to-treat principle).

OUTCOMES

PRIMARY END POINTS

During the 18 months of the study, 411 of 1023 patients (40%) reached the primary end point (death or hospitalization because of HF): 141 patients (42%) in the control group, 138 patients (41%) in the basic support group, and 132 patients (38%) in the intensive support group. Analysis of the time to first event showed HRs of 0.96 (95% CI, 0.76-1.21; $P=.73$) and 0.93 (95% CI, 0.73-1.17; $P=.53$) for the composite end point of death and hospitalization because of HF in the basic and intensive support groups, respectively, vs the control group (**Figure 3A**).

The total number of days lost because of death or all-cause hospitalization during the 18-month study (the other primary end point) was 39 960 days in the control group compared with 33 731 days in the basic support group and 34 268 in the intensive support group (**Figure 4**). Per patient, the median number of days lost was 12 in the control group (25th and 75th percentiles, 0.0 and 173.0 days), 9 in the basic support group (25th and 75th percentiles, 0.0 and 88.0 days; $P=.81$ vs control group), and 7½ in the intensive support group (25th and 75th percentiles, 0.0 and 86.5 days; $P=.49$ vs control group).

SECONDARY END POINTS

Mortality

The all-cause mortality rate was 29% in the control group, 27% in the basic support group, and 24% in the intensive support group (Figure 3B). The 12% and 19% reductions in mortality rate during the 18 months were not statistically significant, with HR of 0.88 (95% CI, 0.66-1.18; $P=.39$) and HR of 0.81 (95% CI, 0.60-1.08; $P=.15$). For the 2 intervention groups combined, the HR was 0.85 (95% CI, 0.66-1.08; $P=.18$).

Hospitalizations

Of all patients, 55% were hospitalized at least once for any cause during the 18 months, for a total of 1161 hospitalizations (**Table 2**). A total of 64% (746) of these hospitalizations were considered related to cardiovascular disorders, but only 32% (375) were related to HF. There were slightly more hospitalizations because of HF in the intensive support group compared with the control group (134 vs 120). Considering a total cumulative follow-up of 429.02 years for the intensive support group and 409.27 years for the control group, incidence rates of 0.31 and 0.29 per follow-up year were calculated for the intensive support and control groups, respectively, with an incidence rate ratio of 1.07 (95% CI, 0.83-1.37; $P=.62$). However, the median duration of admissions to the hospital because of HF in both support groups (8.0

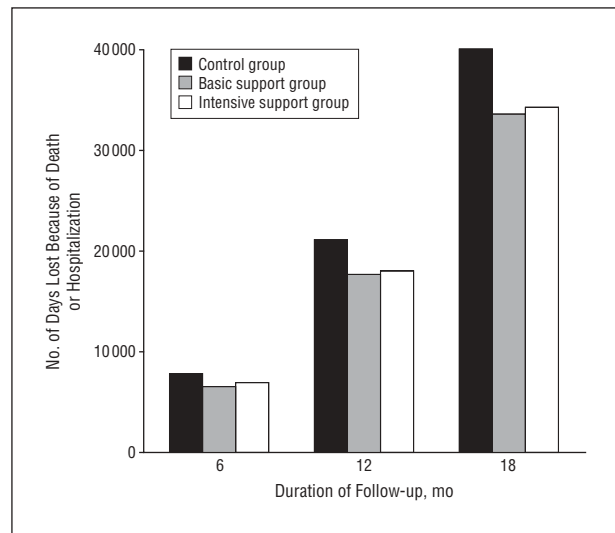


Figure 4. Number of days lost because of death or hospitalization during 18 months of follow-up (composite primary end point).

days in the basic support group and 9.5 days in the intensive support group) was shorter compared with the control group (12.0 days; basic support group vs control group, $P=.01$, and intensive support vs control group, $P=.29$ (Table 2). There was no difference between groups with respect to the proportion of patients who had multiple readmissions to the hospital because of HF.

COMMENT

The primary findings of this randomized controlled study, which, to our knowledge, is one of the largest to date in the field of HF disease management, do not support the concept that adding either a basic or an intensive nurse-led management program to standard care of a cardiologist reduces the combined end point of death or rehospitalization because of HF. We did, however, observe a nonsignificant but potentially clinically relevant 15% decrease in all-cause mortality, which was accompanied by a slight increase in (shorter) hospitalizations in both intervention groups.

Disease management programs are implemented on a large scale in many countries, and recent guidelines advocate the use of an organized system of specialist HF care to improve symptoms and reduce hospitalizations (class IA) and to increase survival (class IB).^{1,2} In the present large study in 17 centers, we did not find an effect on the composite end point of death and hospitalization because of HF. Given the existing data, this finding is unexpected and will affect the role of disease management programs for HF and HF guidelines. It is, therefore, important to identify factors that may have led to this outcome.

The 2 most obvious explanations for the absence of a difference in the event rate between the control and intervention groups are that either patients in the control group were managed well enough already, thus making it difficult to further improve outcomes, or the quality of the intervention did not improve treatment. We believe that the first explanation, in particular, may have an important role in the present study because of a lower-than-

Table 2. Outcomes in Patients According to Intervention Strategies

| Outcome | No. (%) | | | |
|--|----------------------------|--------------------------|-----------------------------------|---------------------------------------|
| | Total Patients (N=1023) | Control Group (n=339) | Basic Support Group (n=340) | Intensive Support Group (n=344) |
| Primary end points | | | | |
| Death or hospitalization because of HF | 411 (40) | 141 (42) | 138 (41) | 132 (38) |
| No. of days lost in 18 months | 107 959 | 39 960 | 33 731 | 34 268 |
| No. of days lost per patient, median (25th and 75th percentiles) | 10.0 (0.0-109.0) | 12.0 (0.0-173.0) | 9.0 (0.0-88.0) | 7.5 (0.0-109.0) |
| Other events | | | | |
| Hospitalization | | | | |
| All causes | 567 (55) | 181 (53) | 192 (57) | 194 (56) |
| Cardiovascular disease | 433 (42) | 143 (42) | 143 (42) | 147 (43) |
| HF | 260 (25) | 84 (25) | 84 (25) | 92 (27) |
| No. of hospitalizations | | | | |
| All causes | 1161 | 376 | 377 | 408 |
| Cardiovascular disease | 746 | 255 | 236 | 255 |
| HF | 375 | 120 | 121 | 134 |
| Death | | | | |
| All causes | 272 (27) | 99 (29) | 90 (27) | 83 (24) |
| Cardiovascular disease | 219 (21) | 72 (21) | 76 (22) | 71 (21) |
| Noncardiovascular disease | 38 (4) | 19 (6) | 10 (5) | 9 (3) |
| Unknown cause | 15 (2) | 8 (2) | 4 (1) | 3 (1) |
| Duration of hospitalization because of HF, median (25th and 75th percentiles), d | 9.0 (5.0-17.0) | 12.0 (5.0-19.5) | 8.0 (4.0-14.0) | 9.5 (5.0-17.0) |

Abbreviation: HF, heart failure.

expected event rate in the control group, which is often noted in clinical trials. In earlier studies, patients in the control group did not receive any structured specialized follow-up, which might be associated with higher rates of mortality and hospitalization.^{11,12} In our study, however, control patients were seen by a cardiologist, which constitutes usual care in the health care system in the Netherlands. Moreover, the 339 patients in the control group had an additional 286 visits to their cardiologist, often because of an increase in symptoms. It is likely that these visits “upgraded” the control group and led to better adherence to medication, which is known to be associated with a better outcome.¹⁶ Although patients in the 2 intervention groups also had more visits than planned, it is conceivable that this surplus of visits had the largest effect in the control group. Although specific measures were taken during the study to avert extra contacts¹⁴ and we discouraged local investigators to have these unplanned visits, we often could not prevent them because in patients whose condition deteriorated, the cardiologist intensified contacts. The alternative explanation for the absence of a contrast between the groups might be that the additional support in the 2 intervention groups was not successful enough in educating and counseling patients. Although this cannot be proved, we believe that this latter explanation is not likely inasmuch as substantial time and effort was spent by specially educated and experienced workers to improve knowledge about HF and its treatment, which is well known to be important in this population.¹⁷

A comparable increase in the number of hospital admissions in combination with a decrease in mortality has been reported previously with intervention programs in HF.^{9,18} Cleland et al¹⁸ reported the highest percentage of

days spent in the hospital in patients who were monitored most intensively (by nurse visits and telephone calls). Health care providers might be forced to realize that readmissions to the hospital because of HF are part of the need in these severely ill patients and should not always be considered negative. The present study showed that a one-size-fits-all model of disease management does not reduce readmissions in every hospital, and institutions may differ substantially in their organization and expertise in the treatment of HF.

While the number of hospitalizations in the present study was not favorably affected, there was a 15% (non-significant) reduction in mortality that was consistent throughout the follow-up and confirms findings of previous meta-analyses.^{11,12} This reduction is comparable to proved pharmacologic interventions in this population, and although the study was not powered to examine mortality, it is substantial. We found that the separate components of the composite end point moved in opposite directions, reflected by a higher readmission rate and a lower mortality rate. Patients in both intervention groups may have had low-threshold access to the care providers, resulting in relatively easy admission to the hospital. For this reason, hospitalizations being part of the primary end point may not have been ideal and we might have powered the study for mortality alone. Also, while hospitalizations may possibly be affected by subjective factors, such an effect is unlikely when assessing mortality, and the present finding may, thus, be genuine.

Most, if not all, previous studies that evaluated the effect of programs in a similar (clinical) setting as COACH were relatively small and conducted primarily in 1 or only a few sites.^{11,12} While COACH is the largest study in this

clinical setting, there are 2 even larger studies, but both had a completely different design and examined the effect of (additional) telephone intervention.^{19,20} Galbreath et al¹⁹ studied 1069 patients with HF in a single center and showed that initial weekly and later monthly telephone intervention led to a borderline statistically significant reduction in all-cause mortality during an 18-month study. In another study from Argentina,²⁰ 1518 outpatients with HF were enrolled, and the investigators found a statistically significant 29% reduction in hospital admissions because of HF but no effect on mortality. Two other studies, which were more similar to COACH and reported the most pronounced favorable effects, were conducted in only 2 or 3 dedicated and experienced hospitals.^{4,21} Favorable effects observed in other studies may also be attributed to the other components in the programs, but also to direct involvement of the researchers conducting the study in delivering care. It also cannot be ruled out that studies with positive findings were published more often than studies with negative findings, leading to publication bias.

COMMENT

The findings of the present large study, at first glance, seem to be in contrast to those of earlier similar studies, but we believe that they should not lead to abandoning the concept of disease management programs for HF; rather, they must lead to more precise definitions of how such programs should be implemented. These data will contribute to the discussion of optimal design and execution of disease management in patients with HF and indicate that one model does not fit all patients or all health care systems.

Hospital admissions contribute substantially (60%-70%) to costs of treating patients with HF, and in our study, the threshold may have been too low to admit patients to the hospital. Organizing these short hospitalizations effectively is one of the major challenges in the future. The observed effect on mortality, albeit not statistically significant, is promising because mortality is a pivotal clinical end point in patients with HF. It suggests that this non-pharmacologic intervention may have been successful in preventing progression of the disease.

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