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ORIGINAL RESEARCH ARTICLE

The impact of pharmacist/physician care on quality of life in elderly heart failure patients: results of the PHARM-CHF randomized controlled trial

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Abstract

Aims Patients with heart failure (HF) have impaired quality of life (QoL). The randomized controlled trial PHARM-CHF investigated whether an interdisciplinary intervention consisting of regular contacts with the community pharmacy and weekly dosing aids improves medication adherence in patients with HF. It is unknown how an intervention involving frequent structured pharmacy visits affects QoL. Our aim was to explore adherence to the intervention and effects on QoL.

Methods and results Among 237 patients, *n* = 110 were randomized to pharmacy care and *n* = 127 to usual care. The pharmacy care group received a medication review followed by (bi-)weekly dose dispensing and counselling. The median follow-up was 2.0 years [inter-quartile range (IQR) 1.2–2.7]. Median interval between pharmacy visits was 8.4 days (IQR 8.0–10.3) and the visits lasted in median 14 min (IQR 10–15). Median adherence to the intervention was 96% (IQR 84–100). QoL at 365 days was predefined as a main secondary and at 730 days as another secondary endpoint in PHARM-CHF. QoL was measured by the Minnesota Living with Heart Failure Questionnaire; and for 111 patients (*n* = 47 in the pharmacy care group and *n* = 64 in the usual care group), data were available at baseline, and after 365 and 730 days (mean age 74 years; 41% female). Improvement in QoL was numerically higher in the pharmacy care group after 365 days and was significantly better after 730 days (difference in total scores −7.7 points [−14.5 to −1.0]; *P* = 0.026) compared to the usual care group. In all subgroups examined, this treatment effect was preserved. Improvements in the physical and emotional dimensions were numerically higher in the pharmacy care group after 365 days and were significantly better after 730 days: −4.0 points [−6.9 to −1.2]; *P* = 0.006, and −1.9 points [−3.7 to −0.1]; *P* = 0.039, respectively.

Conclusions A pharmacy-based interdisciplinary intervention was well received by the patients and suggests clinically important improvements in QoL.

Keywords Chronic heart failure; Health-related quality of life; Community pharmacy services; Interdisciplinary care; Randomized controlled trial

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Introduction

Heart failure (HF) is an increasingly prevalent condition, limiting functional capacity associated with impaired quality of life (QoL) and mortality imposing a high burden on health care systems.[1] The QoL of HF patients is independent of the left ventricular ejection fraction (LVEF)[2] and was similar in patients with preserved (HFpEF) and reduced (HFrEF) LVEF in

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contemporary randomized clinical trials (RCTs) after accounting for variation in demographics, functional status, and symptom burden.[3] Poor QoL, measured by the Minnesota Living with Heart Failure Questionnaire (MLHFQ), is associated with increased risk of all-cause death as well as the combined endpoint of cardiac death or hospitalization for worsening HF.[4] QoL of HF patients is more impaired than in age-matched patients without chronic diseases and those with other co-morbidities.[5,6]

Apart from morbidity (hospital readmissions) and mortality, QoL is, therefore, a key target in the management of patients with HF.[7,8] Regulatory agencies are also increasingly recognizing the importance of QoL outcomes in HF, and patient-reported outcomes are increasingly being used as endpoint in clinical trials. Moreover, health technology assessments include QoL as important patient-relevant outcome.[3,9,10]

In the outpatient setting, HF patients have to take care of their own daily therapy, usually without continuous support or surveillance of health care professionals. Pharmacists may provide successful interventions that improve patient outcomes.[11–13] Specifically, pharmacy-based interventions may help HF patients in their medication management.[14,15]

However, randomized evidence on improving medication adherence and QoL of HF patients in the outpatient setting is scarce. The PHARM-CHF RCT found that an interdisciplinary pharmacist/physician intervention (pharmacy care) in comparison with usual care improves adherence to HF medication.[16] The intervention of PHARM-CHF involved very frequent and structured visits to the community pharmacy. It is unknown whether this strategy itself and its effects on medication adherence have positive or negative effects on the QoL. QoL at 365 days was predefined as a main secondary and at 730 days as another secondary endpoint in PHARM-CHF.[17] Our aim was, therefore, to explore adherence to the intervention and effects on QoL after 365 and 730 days.

Methods

Study design

A full description of the study design has been previously published.[16,17] In brief, PHARM-CHF was an investigator-initiated, prospective multicentre RCT with blinded adjudication of hospitalization events. Patients aged 60 years and older with chronic HF (CHF) defined by HF symptoms, currently treated with a diuretic and hospitalized for HF within the last 12 months or increased BNP (≥350 pg/mL) or N-terminal pro-BNP concentrations (NT-proBNP; ≥1400 pg/mL), were recruited by study physicians. Patients were randomized via a secure web interface tool (www.pharm-chf.de) in a 1:1 ratio to the intervention (pharmacy care) or control group (usual care).

The intervention consisted of the following components: first, patients visited their attending physician for primary assessments (including QoL) and received a current medication list. A comprehensive medication review was performed by pharmacists in the community pharmacy. They compared the physician-documented regimen with the current drug regimen reported by the patient in a brown bag interview. The pharmacist consulted with the attending physician on identified discrepancies and other drug-related problems to consolidate the medication plan.

Pharmacy care continued by (bi-)weekly visits to the community pharmacy including receiving a filled weekly dosing aid, measurement of blood pressure and pulse rate, and counselling. The type of the dosing aid (*dosette,* pill box) was at the discretion of the pharmacist and in agreement with the patient. The interaction in the community pharmacy included questions on the general health and HF symptoms such as shortness of breath, in addition to asking about potential problems with the pharmacotherapy. The intervention has been described in detail in the previously published design paper.[17]

Patients in the usual care group continued to visit pharmacies of their choice to fill prescriptions without further intervention. Usual care mainly consisted of dispensing prescribed medication, including counselling by the pharmacist or pharmacy technician on the safe and appropriate use of the drugs. In Germany, medication review or providing medication in a weekly dosing aid is neither part of usual care nor reimbursed.[16,17]

The PHARM-CHF trial (ClinicalTrials.gov identifier: NCT01692119) was conducted according to the principles stated in the current version of the Declaration of Helsinki, International Conference on Harmonization Good Clinical Practice, and to local and national regulations. Documented approvals from independent ethics committees were obtained for all participating centres and written informed consent from all patients.[16,17]

Outcome measures

Health-related QoL was measured by the MLHFQ. The MLHFQ is one of the best characterized instruments to assess QoL[18] and has been highly rated in systematic reviews.[19–21] The MLHFQ total score ranges from 0 to 105 (0 = best and 105 = worst QoL; minimal clinically important difference 5 points), assessed by the patients at the day of their appointment with their physician at baseline, and after 365 and 730 days. A total score of <24 signifies a good QoL, a score between 24 and 45 signifies a moderate QoL, and a score of >45 signifies a poor QoL. The MLHFQ provides as well scores for the physical (eight items, range 0–40) and

emotional (five items, range 0–25) dimensions.[18,19,22–24] According to the Statistical Analysis Plan as of 10 February 2019, change in MLHFQ overall score between baseline and 365 days was specified as a main secondary outcome and between baseline and 730 days as another secondary outcome.

Statistical analyses

Baseline characteristics are summarized as number of patients (%) for categorical variables and as mean (±SD) or median [inter-quartile range (IQR)] for continuous variables. Changes in MLHFQ scores after 365 and after 730 days to baseline in both study groups were compared by analysis of covariance models adjusted for the baseline value. We analysed patients with data available at baseline, and after 365 and 730 days. We calculated the Pearson correlation coefficients to screen for correlations between variables and the MLHFQ total score. Variation in change of MLHFQ total scores from baseline to 730 days among patients is depicted graphically with a waterfall plot. A *P*-value _x0003C; 0.05 was considered statistically significant. All statistical analyses were performed using SAS® version 9.4 (SAS Institute, Cary, NC, USA).

Results

The study was performed at 31 sites including general practitioners, internal medicine specialists, and both office-based and hospital-based cardiologists, and 69 community pharmacies in nine different states of Germany. Among 237 patients, *n* = 110 were randomized to pharmacy care and *n* = 127 to usual care. For 111 patients (*n* = 47 in the pharmacy care group and *n* = 64 in the usual care group), MLHFQ data were available at baseline, and after 365 and 730 days. The remaining patients did not attend the final study visit at 730 days (owing to death, relocation, withdrawal of consent, or other reasons for dropout), or data on QoL were missing at baseline, at 365 days or 730 days' follow-up. At baseline, the mean age of the 111 patients was 74 years (range 60–86), and 41% were female. At baseline, 21% had a LVEF $<$ 40%, 37% a LVEF between 40% and 49%, and 42% a LVEF $\geq$ 50%. At baseline, 49% were in New York Heart Association (NYHA) functional class III and 5% in class IV. Both groups had similar baseline characteristics (*Table 1*). On average, patients suffered from seven co-morbidities, received eight different drugs, and took 10 doses at three different time points per day; 17% of the patients were suspected to currently have depression [nine-item Patient Health Questionnaire (PHQ-9) score $\geq$ 10].[16] Changes in PHQ-9 scores and NYHA functional class were not statistically different between groups at 365 days and 730 days compared to baseline.

Adherence to the intervention

The median follow-up for the 237 patients randomized was 2.0 years (IQR 1.2–2.7). Median adherence to the pharmacy-based intervention (*n* = 110) was 96% (IQR 84–100), and the median interval between pharmacy visits was 8.4 days (IQR 8.0–10.3)[16]; 81% of the patients in the pharmacy care group opted for weekly visits and the remaining 19% for biweekly visits. The median (bi-)weekly visit to the pharmacy lasted 14 min (IQR 10–15).

Health-related quality of life

With a median MLHFQ total score of 37 (IQR 19–52), HF-related QoL of the patients at baseline was moderate (*Tables 1* and *2*). Improvement in QoL was numerically higher in the pharmacy care group, compared with the usual care group, after 365 days and was significantly better after 730 days (difference in MLHFQ total scores −7.7 points [−14.5 to −1.0]; *P* = 0.026) (*Table 2*),[16] with no significant difference between the intention-to-treat and per-protocol populations (data not shown). Interindividual variation in change of MLHFQ total score 730 days to baseline is shown as waterfall plot in *Figure 1*. An improvement in the MLHFQ total score between baseline and 730 days of at least −5 points was observed in 47% of the patients in the pharmacy care group and in 38% of the usual care group [odds ratio (OR) 0.68, 95% confidence interval (CI) [0.32 to 1.46], *P* = 0.33]. A deterioration of the QoL (≥5 points) was observed in 34% and 45% of the patients (OR 1.61, 95% CI [0.74 to 3.50], *P* = 0.23).

Improvement in the MLHFQ physical dimension score was numerically higher in the pharmacy care group, compared with the usual care group, after 365 days and was significantly better after 730 days (−4.0 points [−6.9 to −1.2]; *P* = 0.006). The MLHFQ emotional dimension score after 365 days improved only in the pharmacy care group, and the difference to the usual care group became significant after 730 days: −1.9 points [−3.7 to −0.1]; *P* = 0.039 (*Table* 2).

Sensitivity analyses

In all subgroups pre-specified for the medication adherence endpoints,[17] plus the groups of patients classified as adherent [proportion of days covered (PDC) at least 80% during 365 or 730 days post randomization], the treatment effect for the MLHFQ total score was preserved. A consistent improvement in QoL after 2 years in patients receiving pharmacy care when compared with usual care was demonstrated. For all subgroups, there was no significant interaction (*Figure 2*).

Change in MLHFQ total score at 730 days to baseline in patients with signs of depression (PHQ-9 score $\geq$ 10, *n* = 19,

Table 1 Baseline characteristics of the quality of life cohort, according to treatment group

Characteristic	Pharmacy care (n = 47)	Usual care (n = 64)
Age, mean ± SD, years	73.3 ± 6.3	74.5 ± 6.5
Median (IQR)	73.0 (69–78)	75.0 (70–79)
≥75 years, *n* (%)	28 (60)	33 (52)
Female sex, *n* (%)	17 (36)	28 (44)
BMI,[a] kg/m^2, mean ± SD	28.8 ± 4.5	29.4 ± 4.8
LVEF,[b] mean ± SD, %	50.4 ± 14.0	47.1 ± 14.6
LVEF < 40%, *n* (%)	7 (15)	16 (25)
LVEF 40–49%, *n* (%)	18 (38)	23 (36)
LVEF ≥ 50%, *n* (%)	22 (47)	25 (39)
NYHA class, %		
I/II	49	44
III/IV	51	56
Time since last hospitalization for HF, mean ± SD, years	0.36 ± 0.67	0.26 ± 0.28
Within the past 3 months, *n* (%)	19 (42)	25 (41)
Attending DMP CHD, module HF, yes, *n* (%)	15 (32)	20 (31)
Different co-morbidities, mean ± SD	7.5 ± 2.6	6.8 ± 2.2
Medication, *n* (%)		
No. drug packages, mean ± SD	8.3 ± 2.8	8.2 ± 3.0
No. single doses/day, mean ± SD	9.6 ± 3.5	10.3 ± 4.0
No. drug intakes/day, median (IQR)	3.0 (2–3)	3.0 (2–3)
HF-medication,[c] *n* (%)		
ACEi/ARB	39 (83)	54 (84)
Beta-blocker	45 (96)	62 (97)
MRA	14 (30)	27 (42)
MLHFQ[d] total score, mean ± SD	36.4 ± 20.5	37.4 ± 21.5
Good (<24), *n* (%)	13 (28)	21 (33)
Moderate (24–45), *n* (%)	19 (40)	17 (27)
Poor (>45), *n* (%)	15 (32)	26 (41)
Physical dimension, mean ± SD	18.6 ± 9.2	18.5 ± 9.9
Emotional dimension, mean ± SD	6.2 ± 5.8	6.5 ± 5.3
Depression (PHQ-9[e]), mean ± SD	5.5 ± 4.8	6.2 ± 4.3
PHQ-9 score ≥ 10, %	15	19

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CHD, coronary heart disease; CV, cardiovascular; DMP, disease management programme; HF, heart failure; IQR, inter-quartile range; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonists; NYHA, New York Heart Association (functional class); SD, standard deviation.
[a]The body mass index (BMI) is the weight in kilogrammes divided by the square of the height in metres.
[b]According to available chart data for n = 40 in the pharmacy care and n = 53 in the usual care group.
[c]All patients received a diuretic.
[d]Minnesota Living with Heart Failure Questionnaire (MLHFQ); total score 0–105 (0 = best QoL, 105 = worst QoL); a score < 24 signifies a good, a score between 24 and 45 a moderate, and a score > 45 a poor heart failure-related quality of life.
[e]Nine-item Patient Health Questionnaire (score 0–27); patients with a score ≥ 10 are suspected to currently have depression.

Table 2 Heart failure-related quality of life (Minnesota Living with Heart Failure Questionnaire)

MLHFQ	Days post randomization	Pharmacy care Mean ± SD (n = 47)	Usual care Mean ± SD (n = 64)	Intervention effect[a] (95% CI)	P-value
Total score (0–105)	0	36.4 ± 20.5	37.4 ± 21.5	—	0.789
	365	31.4 ± 20.0	37.5 ± 22.1	−5.5 (−12.2 to 1.1)	0.102
	730	32.5 ± 19.3	40.8 ± 19.8	−7.7 (−14.5 to −1.0)	**0.026**
Physical dimension (0–40)	0	18.6 ± 9.2	18.5 ± 9.9	—	0.977
	365	16.6 ± 9.6	19.0 ± 10.0	−2.4 (−5.4 to 0.5)	0.107
	730	15.9 ± 7.7	19.9 ± 8.9	−4.0 (−6.9 to −1.2)	**0.006**
Emotional dimension (0–25)	0	6.2 ± 5.8	6.5 ± 5.3	—	0.799
	365	5.3 ± 5.0	6.4 ± 5.9	−1.0 (−2.9 to 0.9)	0.319
	730	5.6 ± 5.2	7.6 ± 4.9	−1.9 (−3.7 to −0.1)	**0.039**

CI, confidence interval; MLHFQ, Minnesota Living with Heart Failure Questionnaire.
[a]Analysis of covariance of change to baseline (adjusted for baseline quality of life).

mean change −15.5, 95% CI [−27.1 to −4.0]) and patients without signs of depression (PHQ-9 score < 10, n = 92, mean change 3.6, 95% CI [−0.5 to 7.7]) is shown as boxplots in *Figure 3*. With the use of the Pearson correlation coefficient, there was a weak correlation between signs of depression and change of MLHFQ total score at 730 days to baseline (r = −0.269, P < 0.002). Correlation coefficients for all other variables were <0.2.

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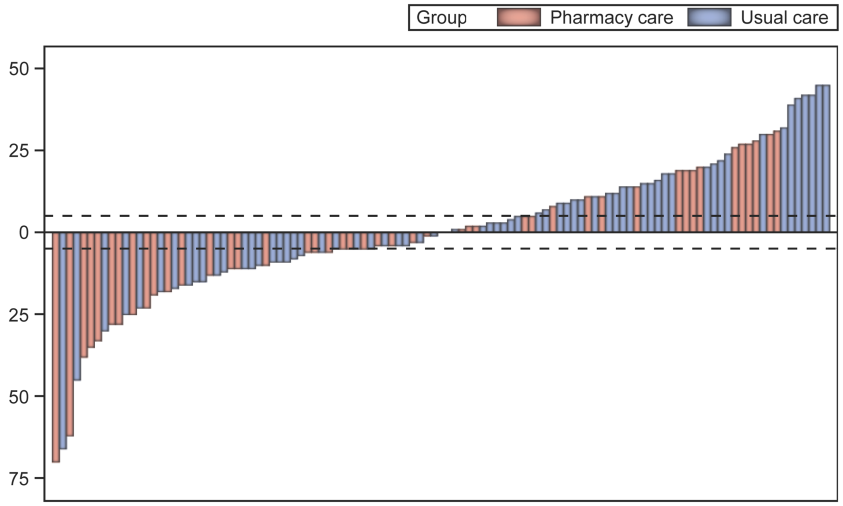
FIGURE 1 Waterfall plot change of the Minnesota Living with Heart Failure Questionnaire (MLHFQ) total score from baseline to 730 days for each patient of the intervention (pharmacy care) and control (usual care) groups. The dotted lines represent the minimal clinically important difference for improvement (−5 points) and worsening (+5 points) of heart failure-related quality of life.



Discussion

The main finding of this analysis suggests that the interdisciplinary intervention involving (bi-)weekly structured visits to the community pharmacy led to long-term and quantitatively important improvements in QoL in elderly patients with CHF. HF patients are often symptomatic and have a poor QoL.[5,25] Improving QoL is acknowledged as a fundamental goal of HF management in the guidelines.[26,27]

Heart failure-specific QoL in our study at baseline was moderate (median score 37) and independent of LVEF, which is, for example, comparable with findings in the CHARM programme with a mean MLHFQ summary score of 41.[2]

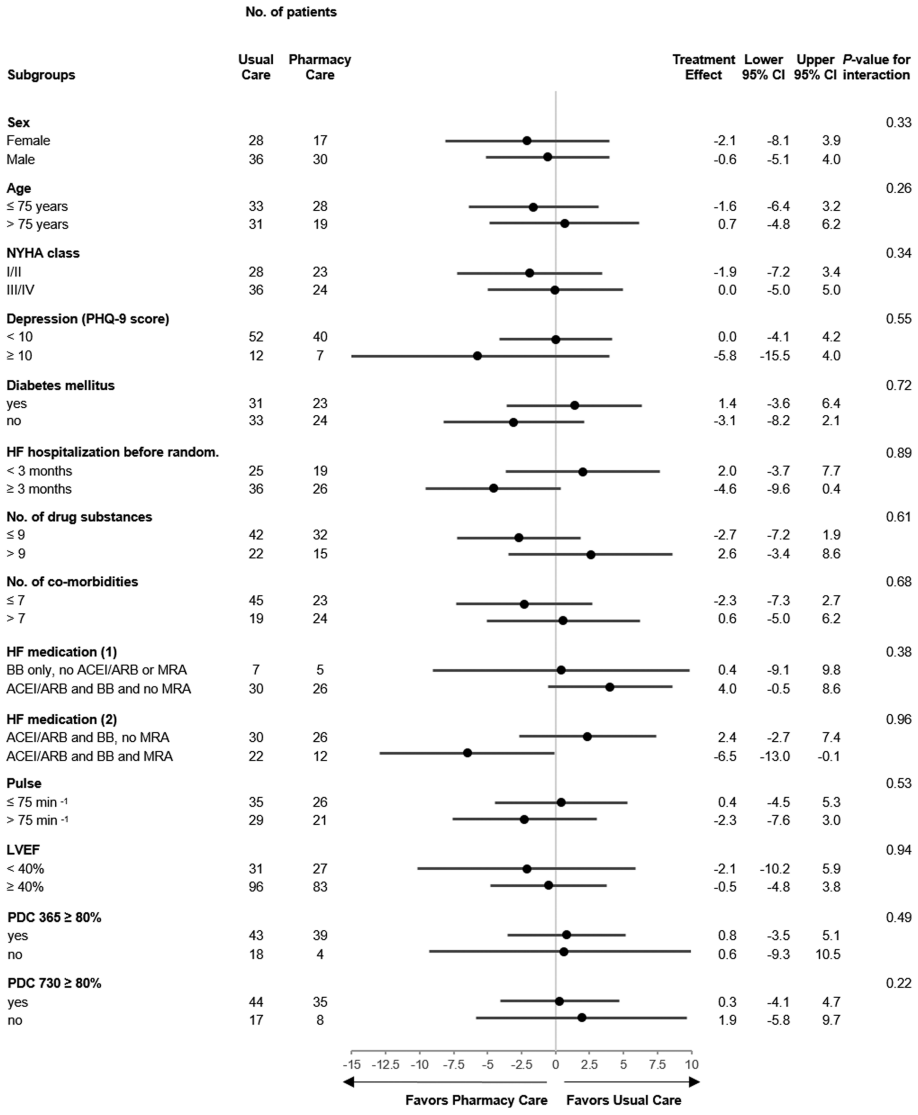
A recent systematic review and meta-analysis included 18 RCTs comparing pharmacist-involved multidisciplinary interventions with usual care. Among the five RCTs measuring QoL, only four studies reported significant improvement and difference. None reported QoL data beyond 12 months.[13] For example, Korajkic *et al*. explored the impact of a 3 months' pharmacist intervention on patient-guided diuretic dose adjustment in ambulatory patients with HF. Seventy-five patients were recruited and 1:1 randomized. QoL measured by the MLHFQ (total score) was significantly lower in the intervention group (38 ± 20) compared with the control group (48 ± 19; P = 0.03). In a comparable pharmaceutical care RCT, n = 104 patients in each group completed the 12 month trial.[15] QoL measured by the MLHFQ improved significantly in the intervention when compared with the usual care group.

Overall, QoL outcomes beyond 12 months in chronic diseases are very rarely available.[6,14,21,28–31] Therefore, it remains unclear whether other interventions without significant between-group differences at 6 months or 1 year may have led to improvements in the long run. In general, however, it seems unlikely that shorter interventions would result in an improved QoL in the long run.

Above all and compared with the generally modest, if significant, improvement of QoL by other HF interventions,[6,21,32,33] including device therapy or telemonitoring,[30,31] the 7.7 points' change in the MLHFQ score in favour of pharmacy care is of significant clinical importance. Of note, patients' QoL improved independent of sex, age, EF, disease severity, burden of illnesses, or pill burden. The data suggest a more pronounced effect of the intervention on the physical compared with the emotional dimension of the MLHFQ. Although in agreement with findings of an RCT exploring the impact of a 3 months' pharmacist intervention on QoL of ambulatory patients with HF in Australia and measured by the MLHFQ,[14] we do not have a conclusive explanation for a significantly different impact on physical compared with emotional components of HF-related QoL.

Depression is common in HF and associated with adverse clinical outcomes.[34,35] The PHQ-9 is a commonly used instrument facilitating not only diagnosis but also estimation of severity of depressive symptoms.[36] Depression as assessed by the PHQ-9 was shown to independently predict health care use and mortality in patients with HF.[35] The 21-item MLHFQ focuses on the burden of HF in individuals' well-being.[37,38] A signal for an improved QoL from baseline to 730 days in patients with compared with patients without signs of depression was observed. However, this subgroup of patients was rather small. Although there was no significant difference in the primary medication adherence outcomes for patients with and without suspected depression in PHARM-CHF,[16] the potential impact on QoL of patients with HF and depression should be explored in a specifically designed trial.

FIGURE 2 Forest plot of sensitivity analyses for the MLHFQ total score. Shown are data of baseline-adjusted changes after 730 days, using analyses of covariance with each subgroup as a covariate, and treatment and the interaction between treatment and subgroup as covariates. The point estimate and the 95% confidence intervals (CIs) are stated for each subgroup. The *P*-values of the interaction term (treatment and subgroups) are presented. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BB, beta-blocker; LVEF, left ventricular ejection fraction; MLHFQ, Minnesota Living with Heart Failure Questionnaire; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; PDC, proportion of days covered; PHQ-9, nine-item Patient Health Questionnaire; random., randomization.



Whether the MLHFQ is sensitive to detect differences in QoL on the basis of the change in level of adherence to medication remains unclear. Recently, Chambela *et al*. suggested a relationship of an improvement in QoL, measured by the MLHFQ with an increase in medication adherence. This RCT compared pharmaceutical care with standard care in 81 patients with Chagas disease and HF.[39] Uchmanowicz and colleagues concluded that with an increasing QoL, the level of adherence to therapeutic recommendations among elderly hypertensive patients increases.[40] Further findings support an association between medication adherence and QoL among patients with hypertension (and/or diabetes).[41] Whether this association holds true for CHF patients remains unclear. Our data do not suggest a significantly different effect of the intervention on HF-related QoL between patients with high (PDC $\geq$ 80%) compared with low adherence to HF medications (PDC $<$ 80%), both during 365 and 730 days post randomization.

Our study design and the intervention applied are difficult to compare with those of the literature. Previous RCTs applied different, interdisciplinary or multidisciplinary interventions for usually $<$1 year, in different settings.[14,15,42–46] In

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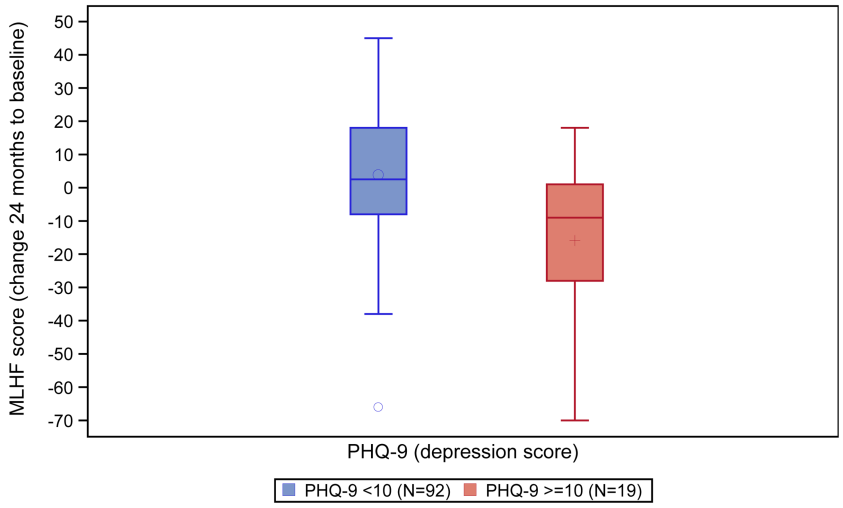
FIGURE 3 Boxplots of the changes of the Minnesota Living with Heart Failure (MLHF) Questionnaire scores 730 days to baseline in the subgroup of patients without [nine-item Patient Health Questionnaire (PHQ-9) score < 10, *n* = 92] and with (PHQ-9 score ≥ 10, *n* = 19) signs of depression.



the majority of studies, QoL did not differ between groups.[42–46] For example, the HeartMed RCT utilized community pharmacists to provide two home visits 2 to 8 weeks after discharge including a drug review and self-management and lifestyle advice to 149 intervention patients for 6 months. Eligible patients were adults, admitted as an emergency in which 'heart failure was an important ongoing clinical condition'. The investigators found no difference in hospitalizations or self-reported adherence. MLHFQ was completed by 78 intervention patients and 80 control patients at 6 months (66% of surviving intervention patients and 67% of surviving controls). Whereas intervention patients' scores increased (worsened) slightly, those for control patients decreased (improved) slightly.[46]

A recent systematic review on disease management interventions for HF found that QoL was generally poorly reported (median follow-up was 6 months), with high attrition. Low-quality evidence indicated that clinic-based interventions may result in little or no difference in QoL.[21]

Nine of 11 structured telephone support studies, and five of 11 telemonitoring studies reported significant improvements in QoL.[47] For example, Ferrante *et al.* found a 4.4-point difference in the MLHFQ total score by a telephone intervention vs. usual care.[48] The recent TIM-HF II telemonitoring RCT found no significant differences in the changes in the MLHFQ total score between baseline and 12 months.[31]

In general, previous HFpEF and HFrEF RCTs have observed only a modest improvement of QoL by pharmacotherapy.[3,6,29] A recent systematic review and meta-analysis identified nine trials reporting drug treatment effects on QoL measured by the MLHFQ.[49] Overall estimate showed that pharmacotherapy resulted in better, although modestly improved, QoL scores (−1.63 points, 95% CI [−2.94 to −0.31], *P* = 0.001). For example, in the TOPCAT trial studying symptomatic HFpEF patients, use of spironolactone was associated with a modest improvement in QoL. Adjusted mean changes measured by the Kansas City Cardiomyopathy Questionnaire (KCCQ), for the spironolactone group, were significantly better than those for the placebo group at 4-month (1.54; *P* = 0.002), 12-month (1.35; *P* = 0.02), and 36-month (1.86; *P* = 0.02) visits.[29] As for the MLHFQ, the minimal clinically important difference in the KCCQ score is 5 points.[50]

In the recent PARAGON-HF trial studying symptomatic HFpEF patients, between baseline and month 8, there was a mean decrease (hence, worse QoL) in the KCCQ clinical summary score of 1.6 points in the sacubitril–valsartan group and 2.6 points in the valsartan group (between-group difference, 1.0 point; 95% CI [0.0 to 2.1]).[33]

Limitations

The findings of this study should be interpreted in consideration of the following potential limitations. First, patients were not blinded to the intervention, and this may have biased their reports of their health status. The significant differences in the changes in QoL scores to baseline between 365 and 730 days do not suggest a relevant bias, however. Second, the statistical analysis plan did neither pre-specify the subgroups with regard to QoL nor report any sensitivity analysis to impute scores for patients who died or with missing values. Third, QoL information was not available for all patients at all three time points. However, the rates of missing MLHFQ values were similar for both groups, and the number of deaths was not significantly different.[16] Fourth, the number of patients in the intervention and the control groups is relatively small. Hence, especially the subgroup analyses

should be interpreted with caution. Finally and given that HF-specific QoL after 365 days was a main outcome and after 730 days another secondary outcome in PHARM-CHF, our findings have to be considered exploratory, warranting future randomized studies.

Conclusions

A pharmacy-based interdisciplinary intervention, when compared with usual care, not only improved adherence to HF medication[16] but also suggested long-term clinically important improvements in HF-related QoL. Patients' adherence to the intervention was high.

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Conflict of interest

None to declare.

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