

**What are effective program characteristics of
self-management interventions in patients with heart failure?
An individual patient data meta-analysis**

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Supplementary material

DETAILS ON THE SENSITIVITY ANALYSES

Several sensitivity analyses were performed to assess robustness of findings from the primary univariable analysis reported in the manuscript.

First, the univariable approach described in the *Statistical analysis* section in the manuscript did not allow adjustment for other program characteristics, which may introduce confounding by correlation with other characteristics. The number of included studies (N=20) was insufficient for a comprehensive analysis including all characteristics simultaneously in a mixed effects model, as initially intended. To confirm the effects found in the univariable analysis, an observational multivariable analysis was performed as sensitivity analysis. We used the regression models described in the *Statistical analysis* section to estimate treatment effects, but excluded random effects or frailty term. The regression models included all program-specific covariates and a dummy variable indicating study, and were adjusted for sex and age of individual patients.

Second, a complete-case analysis was carried out to assess the effect of imputing data and analyses were repeated by excluding the largest trial. A final sensitivity analysis was performed in which the published main effects of eligible trials that did not provide individual patient data were pooled with the main effects of the individual patient data meta-analysis to assess the impact of missing trials on our findings.

Table S1: Search strategy for PubMed.

(("heart failure"[MeSH Terms] OR CHF[Title/Abstract] OR HF[Title/Abstract] OR "congestive heart failure"[Title/Abstract] OR "chronic heart failure"[Title/Abstract] OR "chronic cardiac failure" [Title/Abstract] OR "congestive cardiac failure"[Title/Abstract] OR "heart failure"[Title/Abstract] OR "cardiac failure"[Title/Abstract] OR "heart decompensation"[Title/Abstract])
AND (self-management[MeSH Terms] OR self-care[MeSH Terms] OR patient-education[MeSH Terms] OR "behavior therapy"[MeSH Terms] OR self-manag*[Title/Abstract] OR self-car*[Title/Abstract] OR self-monitor*[Title/Abstract] OR self-administration[Title/Abstract] OR self-medication[Title/Abstract] OR educate[Title/Abstract] OR educated[Title/Abstract] OR education[Title/Abstract] OR educating[Title/Abstract] OR educational[Title/Abstract] OR instructed[Title/Abstract] OR instruction[Title/Abstract] OR instructions[Title/Abstract] OR instructional[Title/Abstract] OR trained[Title/Abstract] OR "action plan*" [Title/Abstract] OR patient-educat*[Title/Abstract] OR patient-cent*[Title/Abstract] OR patient-focus*[Title/Abstract] OR "behavior therapy"[Title/Abstract] OR "behaviour therapy"[Title/Abstract] OR empowerment[Title/Abstract])
AND ("randomized controlled trial"[MeSH Terms] OR "randomised controlled trial"[MeSH Terms] OR "controlled clinical trial"[MeSH Terms] OR "random allocation"[MeSH Terms] OR "evaluation studies"[MeSH Terms] OR "intervention studies"[MeSH Terms] OR "randomized controlled trial"[Title/Abstract] OR "randomised controlled trial"[Title/Abstract] OR "controlled clinical trial"[Title/Abstract] OR "clinical trial"[Title/Abstract] OR "random allocation"[Title/Abstract] OR intervention[Title/Abstract] OR trial[Title/Abstract] OR trials[Title/Abstract] OR random[Title/Abstract] OR randomized[Title/Abstract] OR randomised[Title/Abstract] OR randomization[Title/Abstract] OR randomisation[Title/Abstract] OR randomizing[Title/Abstract] OR randomising[Title/Abstract] OR randomly[Title/Abstract] OR allocate[Title/Abstract] OR allocated[Title/Abstract] OR allocating[Title/Abstract] OR allocation[Title/Abstract])

Table S2: Missing values for baseline variables and outcomes for each study included in the individual patient data meta-analysis.

	Agren, 2012 ²⁹	Aldamiz, 2007 ³⁰	Aienza, 2004 ³¹	Blue, 2001 ³²	Bruggink, 2007 ³³	DeWalt, 2012 ⁷	Heister, 2013 ³⁴	Jaarsma, 1999 ³⁵	Jaarsma, 2008 ⁶	Leventhal, 2011 ³⁶	Martensson, 2005 ³⁷	Otsu, 2011 ³⁸	PetersKlimm , 2010 ³⁹	Rich, 1995 ⁴⁰	Riegel, 2002 ⁴¹	Riegel, 2006 ⁴²	Sisk, 2006 ⁴³	Smeulders, 2009 ^{44,45}	Stromberg, 2003 ⁴⁶	Tsuyuki, 2004 ⁴⁷
	n=155	n=279	n=338	n=165	n=240	n=605	n=266	n=179	n=1023	n=42	n=153	n=102	n=197	n=282	n=358	n=135	n=406	n=317	n=106	n=276
Baseline characteristics																				
Sex	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Age	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
LVEF	NA	27(9.7%)	30(8.9%)	NA	18(7.5%)	18(3.0%)	NA	0 (0%)	96(9.4%)	1 (2.4%)	NA	NA	26 (13.2%)	60 (21.3%)	154 (43.0%)	29 (21.5%)	NA	NA	NA	94 (34.1%)
NYHA Class	1 (0.6%)	0 (0%)	0 (0%)	2 (1.2%)	1 (0.4%)	0 (0%)	NA	1 (0.6%)	15(1.5%)	1 (2.4%)	0 (0%)	0 (0%)	0 (0%)	3 (1.1%)	5 (1.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.4%)
Years since diagnosis	NA	NA	NA	NA	1 (0.4%)	NA	NA	0 (0%)	1 (0.1%)	NA	NA	NA	44 (22.3%)	NA	NA	NA	NA	7 (2.2%)	NA	NA
Level of education	9 (5.8%)	0 (0%)	11(3.3%)	NA	NA	0 (0%)	1 (0.4%)	NA	30(2.9%)	1 (2.4%)	NA	NA	11 (5.6%)	2 (0.7%)	116 (32.4%)	0 (0%)	2 (0.5%)	4 (1.3%)	NA	NA
Living status	0 (0%)	0 (0%)	5 (1.5%)	0 (0%)	0 (0%)	NA	0 (0%)	NA	NA	0 (0%)	0 (0%)	0 (0%)	24 (12.2%)	0 (0%)	116 (32.4%)	1 (0.7%)	NA	0 (0%)	NA	NA
Clusters of comorbid conditions	NA	0 (0%)	0 (0%)	0 (0%)	18(7.5%)	0 (0%)	NA	0 (0%)	0 (0%)	2 (4.8%)	0 (0%)	NA	1 (0.5%)	3 (1.1%)	2 (0.6%)	0 (0%)	0 (0%)	2 (0.6%)	0 (0%)	0 (0%)
Outcomes																				
HF-related quality of life 6 months	NA	NA	NA	104 (63.0%)	NA	66 (10.9%)	67 (25.2%)	NA	315 (30.8%)	13 (31.0%)	NA	6 (5.9%)	NA	NA	173 (48.3%)	30 (22.2%)	166 (40.9%)	47 (14.8%)	NA	NA
HF-related quality of life 12 months	40 (25.8%)	NA	NA	130 (78.8%)	67 (27.9%)	89 (14.7%)	NA	NA	361 (35.3%)	15 (35.7%)	25 (16.3%)	10 (9.8%)	17 (8.6%)	NA	NA	NA	190 (46.8%)	61 (19.2%)	43 (40.6%)	NA
Mortality - time-to-event	NA	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (1.1%)	NA	1 (0.1%)	0 (0%)	NA	NA	3 (1.5%)	8 (2.8%)	0 (0%)	0 (0%)	NA	NA	0 (0%)	0 (0%)
Mortality 6 months	NA	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	13 (4.9%)	0 (0%)	0 (0%)	0 (0%)	NA	0 (0%)	0 (0%)	7 (2.5%)	0 (0%)	0 (0%)	0 (0%)	NA	0 (0%)	14 (5.1%)
Mortality 12 months	NA	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	23 (8.6%)	NA	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	7 (2.5%)	NA	NA	0 (0%)	NA	0 (0%)	NA
All-cause hospitalization time-to-event	NA	0 (0%)	0 (0%)	0 (0%)	1 (0.4%)	0 (0%)	3 (1.1%)	NA	0 (0%)	0 (0%)	NA	NA	NA	NA	0 (0%)	0 (0%)	NA	NA	0 (0%)	0 (0%)
All-cause hospitalization 6 months	NA	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (1.1%)	0 (0%)	0 (0%)	0 (0%)	NA	NA	NA	NA	0 (0%)	0 (0%)	NA	40 (12.6%)	0 (0%)	0 (0%)
All-cause hospitalization 12 months	NA	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (1.1%)	NA	0 (0%)	0 (0%)	NA	NA	19(9.6%)	7 (2.5%)	NA	NA	0 (0%)	42 (13.2%)	0 (0%)	NA
HF-related hospitalization time-to-event	NA	0 (0%)	0 (0%)	0 (0%)	1 (0.4%)	0 (0%)	NA	NA	0 (0%)	0 (0%)	NA	NA	NA	NA	0 (0%)	0 (0%)	NA	NA	NA	1 (0.4%)
HF-related hospitalization 6 months	NA	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	NA	0 (0%)	0 (0%)	0 (0%)	NA	3 (2.9%)	NA	NA	0 (0%)	0 (0%)	NA	NA	NA	1 (0.4%)
HF-related hospitalization 12 months	NA	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	NA	NA	0 (0%)	0 (0%)	NA	3 (2.9%)	28 (14.2%)	NA	NA	NA	0 (0%)	NA	0 (0%)	NA

NA=not applicable since variable in study, hence not analyzed/imputed.

Table S3: Multivariable analysis of effects of characteristics of self-management interventions in patients with heart failure included in the individual patient data meta-analysis.

Outcome	N studies	n patients	Variable	Effect size	Effect	95% CI
<i>HF-related quality of life</i>						
6 months follow-up			No significant characteristic			
12 months follow-up			No significant characteristic			
<i>Mortality</i>						
Time to event	14	4312	Duration (per month) Peer contact	HR	0.95 1.77	(0.92-0.99) (1.13-2.78)
6 months follow-up	17	4985	Intensity (per contact) Peer contact	RR	0.95 2.52	(0.93-0.97) (1.40-4.54)
12 months follow-up			No significant characteristic			
<i>All-cause hospitalization</i>						
Time to first event	12	3833	Standardized training Keeping logs Goal-setting skills	HR	0.95 1.50 1.79	(0.61-1.49) (1.16-1.94) (1.20-2.66)
6 months follow-up	14	4238	Standardized training	RR	1.89	(0.96-3.71)
12 months follow-up	13	4262	Standardized training Keeping logs Goal-setting skills	RR	1.26 1.18 1.62	(0.95-1.67) (0.97-1.44) (1.15-2.28)
<i>HF-related hospitalization</i>						
Time to first event	10	3461	Duration (per month) Standardized training Multidisciplinary team Keeping logs	HR	0.93 0.55 0.91 2.24	(0.90-0.96) (0.29-1.08) (0.64-1.29) (1.40-3.57)
6 months follow-up	12	3741	Duration (per month)	RR	0.85	(0.78-0.92)
12 months follow-up	11	3503	Goal-setting skills	RR	2.02	(1.19-3.43)

HR=hazard ratio; RR=risk ratio.

Results are only presented if program characteristic showed an effect with $P < 0.05$ in the primary analysis.

Table S4: Sensitivity analysis by including published main effects of eligible studies without individual patient data available.

	Individual patient data only				Pooled analysis of individual patient data and published effects		
	Effect	Stu- dies	Pa- tients	Effect size (95% CI)	Stu- dies	Pa- tients	Effect size (95% CI)
<i>HF-related quality of life</i>							
6 months follow-up	SMD	10	3419	0.13 (0.00-0.26)	14	3816	0.15 (0.04-0.26)
12 months follow-up	SMD	11	3356	0.15 (0.00-0.30)	17	4370	0.14 (0.03-0.26)
<i>Mortality</i>							
Time to event	HR	14	4312	0.91 (0.79-1.04)	17	5326	0.89 (0.78-1.01)
6 months follow-up	RR	17	4985	0.83 (0.66-1.05)	20	5999	0.81 (0.66-0.98)
12 months follow-up	RR	14	4204	0.86 (0.72-1.03)	21	5450	0.88 (0.78-1.01)
<i>All-cause hospitalization</i>							
Time to first event	HR	12	3833	0.93 (0.85-1.03)	14	4699	0.93 (0.85-1.00)
6 months follow-up	RR	14	4329	0.92 (0.83-1.01)	17	5279	0.86 (0.66-1.13)
12 months follow-up	RR	13	4266	0.95 (0.87-1.04)	20	5512	0.91 (0.81-1.02)
<i>HF-related hospitalization</i>							
Time to first event	HR	10	3461	0.80 (0.69-0.92)	12	4327	0.79 (0.69-0.90)
6 months follow-up	RR	12	3741	0.81 (0.66-0.99)	14	4607	0.78 (0.66-0.92)
12 months follow-up	RR	11	3503	0.82 (0.64-1.05)	15	4126	0.77 (0.64-0.92)

CI=confidence interval; HF=heart failure; HR=hazard ratio; RR=risk ratio; SMD=standardized mean difference.

Table S5: Sensitivity analysis of effects of characteristics of self-management interventions in patients with heart failure included in the individual patient data meta-analysis.

with heart failure included in the individual patient data meta-analysis.						
Outcome	Analysis	Effect measure	OLDER STUDIES (N=10) Effect (95% CI)	P-value hetero- geneity	RECENT STUDIES (N=10) Effect (95% CI)	P-value hetero- geneity
Mortality						
Time to event	Duration (per month)	HR	0.96 (0.94-0.98)	0.001	0.98 (0.94-1.02)	0.504
	Peer contact		NA	--	1.36 (0.68-2.69)	0.334
	No peer contact		0.74 (0.59-0.92)		0.96 (0.80-1.15)	
6 months follow-up	Intensity (per contact)	RR	0.96 (0.94-0.99)	0.014	0.98 (0.95-1.01)	0.157
	Peer contact		NA		1.46 (0.57-3.72)	0.226
	No peer contact		0.80 (0.59-1.08)		0.78 (0.51-1.18)	
12 months follow-up	No significant characteristic					
All-cause hospitalization						
Time to first event	Standardized training	HR	0.85 (0.71-1.03)	0.092	1.10 (0.97-1.26)	0.056
	Heterogeneous training		0.65 (0.50-0.84)		0.79 (0.57-1.08)	
	Keeping logs		1.05 (0.78-1.40)	0.017	1.13 (0.97-1.31)	0.131
	No logs		0.69 (0.58-0.83)		0.92 (0.75-1.14)	
	Goal-setting skills		NA	--	1.26 (0.96-1.66)	0.143
	No goal-setting skills		0.77 (0.66-0.90)		1.00 (0.88-1.15)	
	6 months follow-up	Standardized training	RR	0.91 (0.76-1.09)	0.037	1.03 (0.91-1.16)
	Heterogeneous training		0.66 (0.52-0.84)		0.88 (0.66-1.18)	
12 months follow-up	Standardized training	RR	0.86 (0.73-1.01)	0.417	1.10 (0.97-1.26)	0.084
	Heterogeneous training		0.78 (0.64-0.94)		0.88 (0.71-1.10)	
	Keeping logs		0.90 (0.73-1.11)	0.308	1.13 (0.96-1.34)	0.332
	No logs		0.79 (0.68-0.92)		1.00 (0.84-1.20)	
	Goal-setting skills		NA	--	1.21 (1.02-1.43)	0.024
	No goal-setting skills		0.82 (0.73-0.92)		0.95 (0.85-1.07)	
	HF-related hospitalization					
Time to first event	Duration (per month)	HR	0.94 (0.92-0.96)	<0.001	1.00 (0.99-1.02)	0.664
	Standardized training		0.63 (0.47-0.84)	0.217	1.04 (0.85-1.28)	0.776
	Heterogeneous training		0.47 (0.34-0.67)		0.97 (0.61-1.53)	
	Multidisciplinary team		0.67 (0.29-1.55)	0.654	1.05 (0.82-1.34)	0.851
	Single interventionist		0.55 (0.44-0.69)		1.01 (0.81-1.27)	
	Keeping logs		0.81 (0.54-1.21)	0.031	1.06 (0.85-1.32)	0.686
	No logs		0.47 (0.36-0.62)		0.97 (0.68-1.39)	
6 months follow-up	Duration (per month)	RR	0.93 (0.89-0.97)	0.014	0.99 (0.92-1.04)	0.657
12 months follow-up	Goal-setting skills	RR	NA	--	1.20 (0.78-1.85)	0.664
	No goal-setting skills		0.58 (0.46-0.73)		1.02 (0.55-1.90)	

CI=confidence interval; HR=hazard ratio; NA=not applicable since no studies in category; RR=risk ratio.
 Results are only presented if program characteristic showed an effect with $P < 0.05$ in the primary analysis.