RESEARCH ARTICLE

Effectiveness of the European Society of Cardiology/Heart Failure Association website 'heartfailurematters.org' and an e-health adjusted care pathway in patients with stable heart failure: results of the 'e-Vita HF' randomized controlled trial

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Background	Efficient incorporation of e-health in patients with heart failure (HF) may enhance health care efficiency and patient empowerment. We aimed to assess the effect on self-care of (i) the European Society of Cardiology/Heart Failure Association website 'heartfailurematters.org' on top of usual care, and (ii) an e-health adjusted care pathway leaving out 'in person' routine HF nurse consultations in stable HF patients.
Methods and results	In a three-group parallel-randomized trial in stable HF patients from nine Dutch outpatient clinics, we compared two interventions (heartfailurematters.org website and an e-health adjusted care pathway) to usual care. The primary outcome was self-care measured with the European Heart Failure Self-care Behaviour Scale. Secondary outcomes were health status, mortality, and hospitalizations. In total, 450 patients were included. The mean age was 66.8 ± 11.0 years, 74.2% were male, and 78.8% classified themselves as New York Heart Association I or II at baseline. After 3 months of follow-up, the mean score on the self-care scale was significantly higher in the groups using the website and the adjusted care pathway compared to usual care (73.5 vs. 70.8, 95% confidence interval 0.6−6.2; and 78.2 vs. 70.8, 95% confidence interval 3.8− 9.4, respectively). The effect attenuated, until no differences after 1 year between the groups. Quality of life showed a similar pattern. Other secondary outcomes did not clearly differ between the groups.

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Conclusions	Both the heartfailurematters.org website and an e-health adjusted care pathway improved self-care in HF patients on the short term, but not on the long term. Continuous updating of e-health facilities could be helpful to sustain effects.
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Keywords	Telemedicine ● Heart failure ● Self-care ● Mortality ● Hospitalization

Introduction

Heart failure (HF) is a chronic progressive disease, with an increasing prevalence with age. It has a major impact on health status, hospitalizations, and the health care budget.[1–3]

Due to aging of the population and substantial demand on health care resources, e-health interventions to improve relevant patient outcomes, such as self-care, are heavily promoted.[4]

An individual patient data meta-analysis showed that self-management interventions could have a beneficial effect on hospitalization, mortality, and HF-related quality of life.[5] An effect that may act through better adherence to evidence-based treatment.[6,7] These programmes, however, demand considerable human resources, and are time-consuming. Efficient incorporation of electronic health (e-health) blended with existing care by replacing routine consultations could reduce the time investment of HF nurses per patient, creating time for the care of more patients. By monitoring vital signs such as blood pressure, heart rate, and body weight, imminent exacerbations might be timely identified and hospitalizations prevented.[4] Incorporation of e-health may be patient-friendly as it enables self-care activities at a time and place convenient for themselves, and reduces travel time to the hospital.

Earlier studies assessed the effect of e-health tools (mostly telemonitoring) as part of disease management programmes. Some showed promising, but others neutral results in patients with HF.[8,9] These interventions were predominantly evaluated 'on top of' usual care (UC). In view of the anticipated shortage in health care facilities, evaluation of e-health interventions with *replacement* of routine HF outpatient visits seems more relevant.

We created an interactive platform for HF disease management (e-Vita platform) with telemonitoring facilities aimed at replacing routine consultations.

Another e-health tool is the website 'heartfailurematters.org' (HFM website) with information targeted at patients and their family/carers to improve self-care. Although the site is used intensively and translated in several languages, its effect on patient outcomes has never been evaluated.[10]

In our study we evaluated (i) an interactive platform for HF disease management (the e-Vita platform) with telemonitoring facilities, replacing routine consultations, and (ii) the HFM website. Both were compared to UC. The primary outcome was self-care and the secondary outcomes health status, hospitalizations and all-cause mortality.

Methods

Study design

A three-group parallel multicentre randomized pragmatic trial with 1:1:1 group allocation was performed. Patients in group I received UC, in group II UC plus the HFM website,[10] and in group III an e-health adjusted care pathway (EACP) with the e-Vita platform including a link to the HFM website.

Overall, 450 HF outpatients were recruited from nine Dutch HF outpatient clinics between October 2013 and December 2014. Patients were followed up for 1 year. Patients were individually randomized by computerized block randomization (maximum of nine patients per block) to one of the three groups.

Details of the design of the e-Vita HF study have been published elsewhere[11] and a summary of the main design features is presented below.

The study was conducted according to the principles stated in the current Declaration of Helsinki[12] and in accordance with the Dutch law on Medical Research Involving Human Subjects Act (WMO) and approved by the medical ethics committee of the University Medical Centre Utrecht, The Netherlands (number 12/456).

Study population

Heart failure patients were eligible to participate if (i) aged ≥ 18 years, and diagnosed with HF for at least 3 months; (ii) capable to fill out questionnaires, and perform blood pressure measurements and weighing (by standing on a weighing scale); (iii) they had access to internet and e-mail, with basic user skills (or their spouses or carers); and (iv) able to read and understand Dutch.

Written informed consent was obtained during the first study visit at the HF outpatient clinic before any study procedure was undertaken.

Study groups

Usual care group

Allocated patients received UC from one of the nine HF outpatient clinic teams, at least comprising a cardiologist and a HF nurse. UC consisted of on average four routine consultations a year (typically three with the HF nurse, and one with the cardiologist).

'Heartfailurematters.org' website group

Participants received, on top of UC, information and 10 min instruction on the use of the HFM website from the HF nurse at the start of the study. During each routine consultation with the HF nurse, patients were encouraged to use the website, and experienced barriers were explored and solved. Additionally, participants received a leaflet

with useful information, and every 3 months a reminder by e-mail to use the website.

E-health adjusted care pathway group

Participants in this group followed an EACP. They received identical initial information on the use of the HFM website as the participants of HFM group. In addition, the HF nurses instructed the patients and their caretakers on how to use the e-Vita platform with telemonitoring facilities. Patients learned to record body weight, blood pressure and heart rate on a fixed time point everyday (or individually adjusted to a lower frequency if stable). All participants used a standardized weighing scale and blood pressure/heart rate device. The results of the vital parameters were automatically forwarded to the e-Vita platform. At the start of the study, uniform pre-specified alert limits for the values of body weight, blood pressure, and heart rate were set: body weight (+1 kg between two measurements, +2 kg in three consecutive measurements, −3 kg between two measurements, and +2 kg or −2 kg from baseline body weight), systolic blood pressure [average of 140 mmHg (upper limit) and average of 90 mmHg (lower limit) for three consecutive measurements], diastolic blood pressure [average of 100 mmHg (upper limit) and average of 50 mmHg (lower limit) for three consecutive measurements] and heart rate [100 b.p.m. (upper limit) and 50 b.p.m. (lower limit)]. To reduce unhelpful alerts, we encouraged the HF nurses to adjust these limits in shared decision with individual patients, and when necessary after consultation of the cardiologist or general practitioner (GP) of the patient.

If recordings of body weight, blood pressure, and/or heart rate were outside these limits or if measurements were not recorded, the HF nurse received an alert via the e-Vita platform. If deemed necessary, the HF nurse contacted the patient by phone to explore symptoms, and possibly adjusted the individual management, asked the patient to visit the outpatient clinic, or visit the GP practice.

On the e-Vita platform, co-morbidities and medication were kept up to date by the patient, and checked by the HF nurse, who also encouraged the patients to keep it updated. Also, patients received monthly reminders by e-mail. Finally, no routine face-to-face consultations with the HF nurse were scheduled, but if needed the patient could always contact the nurse.

Measurements and outcome parameters

Demographic and disease-specific characteristics were collected at baseline.

Questionnaires were completed by patients at baseline, and after 3, 6 and 12 months, demanding $\approx$ 60 min per time period. Blood tests were performed at baseline, and after 6 and 12 months. Electronic medical files of the HF outpatient clinics and the GP were reviewed after 12 months of follow-up.

The primary outcome was patient's self-care. Self-care was defined as the decision and strategies undertaken by the individual in order to maintain life, healthy functioning and well-being.[13] Self-care was measured with the European Heart Failure Self-care Behaviour (EHFScB) scale.[14] The EHFScB scale includes both self-reported consulting (i.e. 'if shortness of breath increases, leg/feet are more swollen, I gain weight and/or experience fatigue I contact doctor or nurse'), and adherence to regimen behaviours (i.e. 'I weigh myself every day', 'I limit the amount of fluids', 'I exercise regularly', 'I eat a low salt diet', 'I take my medication as prescribed'). It consists of nine items which are scored on a 5-point Likert scale resulting in a standardized score from 0 to 100 with a higher score meaning better self-care.[14,15]

Secondary outcomes were (i) health-related disease-specific quality of life (hrQoL) measured with the Minnesota Living with HF Questionnaire, scoring between 0 and 105 with lower scores meaning better hrQoL,[16] (ii) disease-specific knowledge measured with the Dutch Heart Failure knowledge scale (DHFk), scoring between 0 and 15 with higher scores indicating more knowledge,[17] (iii) patient satisfaction about the HF care measured with a visual analogue scale, scoring between 0 and 100 with higher scores meaning higher satisfaction, (iv) all-cause mortality, (v) cardiovascular-related mortality, (vi) HF-related mortality, (vii) all-cause hospitalizations, (viii) cardiovascular-related hospitalizations, (ix) HF-related hospitalizations, and (x) number of days of HF hospitalizations as captured by hospital and GP registries. The cause of death was assessed by an independent adjudication committee constituting a GP and two cardiologists who were unaware of the patient's allocation.

Statistical analysis

The sample size calculation was based on an overall comparison (with ANOVA) of the three study groups with an expected mean difference of the EHFScB scale score between HFM and UC, and between EAPC and UC of 0.5 and 2.0 points, respectively. These differences were based on previous studies.[11] The estimated mean (standard deviation) EHFScB scale score in HF patients is 20 (5.54), based on unpublished data from a previous study.[18] In addition, an alpha of 0.05 and a power of 80% were used. Based on the aforementioned assumptions, we required at least 414 patients (138 per group) for the study.

We performed an intention-to-treat analysis. Missing values were imputed by the multiple imputation method.[19] The overall difference between the groups in self-care at 3, 6 and 12 months was determined with an ANCOVA. Differences per comparison, between HFM vs. UC and EACP vs. UC were calculated with multiple linear regression models. Results of the crude regression model were presented. If residuals (i.e. an important assumption of a linear regression model) of the model were more sound with adjustment for the baseline values of self-care, the results of the adjusted model were presented as well.

Differences in hrQoL, HF knowledge, and patient satisfaction about HF care, determined after 3, 6 and 12 months were also calculated with multiple linear regression models. Differences in mortality and hospitalizations were analysed with a Cox regression model, and the mean duration of HF hospitalizations with a multiple linear regression model. For all secondary outcomes, results of the crude model were presented.

Analyses were performed with SPSS version 21.0 (IBM Corp., Armonk, NY, USA).

Results

Demographics

From the 1988 invited patients, 450 (23%) consented to participate and were randomized (150 patients per group) (*Figure 1*). Mean age of the participants was 66.8 ± 11.0 years and 74.2% were male. At baseline, 78.8% was classified as New York Heart Association (NYHA) I or II, and the mean left ventricular ejection fraction (LVEF) was 35.7 ± 10.8, and 70.4% had a LVEF ≤ 40% (*Table 1*). Most baseline characteristics did not differ between the three study groups after randomization, although there were more smokers in the UC (19%) than in the HFM and EACP groups (12%, and
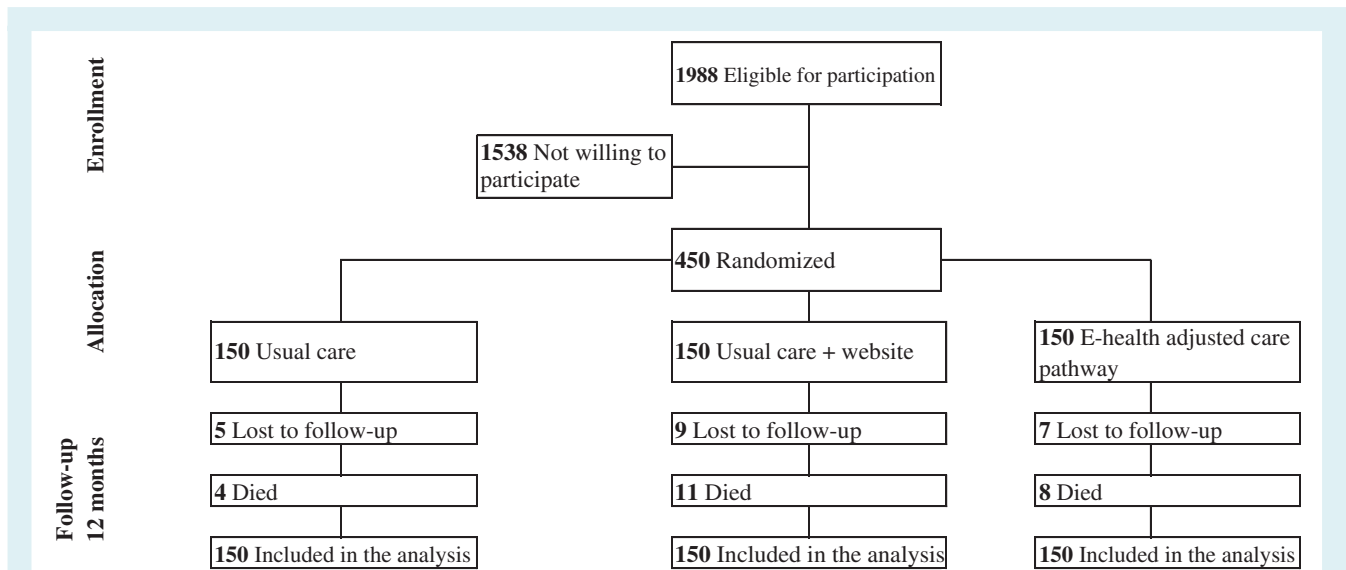
Figure 1 Flow chart of the study patients.

14%, respectively). The proportion of patients in NYHA class I was higher in the EACP (49%) than in the UC and HFM groups (40%).

Primary endpoint (patient's self-care)

At baseline, the mean self-care on the EHFScB scale was 70.6 ± 14.6 in the UC, 69.3 ± 16.4 in the HFM, and 72.0 ± 16.0 in the EACP group. After 3 months, there was a significant (overall $P < 0.001$) difference in self-care between the study groups; HFM vs. UC and EACP vs. UC; mean 73.5 vs. 70.8 [95% confidence interval (CI) 0.6−6.2], and 78.2 vs. 70.8 (95% CI 3.8−9.4), respectively. The significant effect attenuated during the following 9 months, with at 6 months HFM vs. UC mean 74.7 vs. 74.2, and EACP vs. UC 78.6 vs. 74.2, respectively (overall $P = 0.070$), and at 12 months HFM vs. UC mean 72.1 vs. 72.7, and EACP vs. UC 76.1 vs. 72.7, respectively (overall P-value = 0.184) (*Table 2*).

Secondary outcomes

After 3 and 6 months, significant differences were observed in hrQoL between EACP and UC (median EACP 19.0 vs. UC 22.8, $P = 0.029$ and EACP 21.0 vs. UC 24.0, P-value = 0.003), and at 3 months in HF knowledge (median EACP 13 vs. UC 13, $P = 0.014$). This effect attenuated during follow-up, with at 12 months no clear differences between the groups in HrQoL and HF knowledge (*Table 3*).

There was no difference between groups in patient's satisfaction about the received HF care.

Finally, there were no clear differences in all-cause mortality [HFM vs. UC 11 vs. 4, hazard ratio (HR) 2.82 (95% CI 0.90−8.87) and EACP vs. UC 8 vs. 4, HR 2.06 (95% CI 0.62−6.84)], and hospitalizations [HFM vs. UC 66 vs. 66, HR 0.98 (95% CI 0.70−1.38) and EACP vs. UC 57 vs. 66, HR 0.85 (95% CI 0.59−1.21)] between the groups (*Table 4*). Neither was this the case for

disease specific hospitalizations and the duration of HF-related hospitalizations.

Discussion

We observed an improvement in self-care at 3 months when stable HF patients received the HFM website in addition to UC compared to UC alone (mean score on EHFScBs 73.5 vs. 70.8; difference 2.7, 95% CI 0.6−6.2). An EACP resulted in an even higher improvement when compared to UC (mean 78.2 vs. 70.8; difference 7.4, 95% CI 3.8−9.4). These effects attenuated during the following 9 months, and no clear differences were seen at 12 months between the groups. Secondary outcomes such as hrQoL and HF knowledge showed a similar trend, but mortality and hospitalizations did not clearly differ between the groups.

We are the first to evaluate the health effects of the HFM website. Previously, only the very short-term (2 weeks) effect of a website with HF information was evaluated showing a significant effect on self-care knowledge.[20] In addition, just a few studies evaluated the effect of e-health/telemonitoring interventions on self-care. One of these is the recently published Dutch TEHAF study, also with UC provided by Dutch HF outpatient clinics. The effect of our EACP is in line with this study, reporting significant improvement in self-care on the EHFScB scale for the telemonitoring group vs. UC at 12 months (17.4 ± 4.5) vs. 20.8 ± 5.8), $P < 0.001$).[21] These unstandardized scores correspond with mean standardized scores on the EHFScB scale of 76.7 and 67.3, respectively, which is similar to our EHFScB scale scores at 3 months. The TEHAF study monitored HF symptoms, knowledge, and related behaviour, with the HF nurse intervening when patients gave high-risk (inadequate) responses.[21] Our study monitored just body weight, blood pressure and heart rate, and HF nurses intervened with lifestyle advices or drug treatment adjustments when reported values fell outside the pre-determined limits.

Table 1 Baseline characteristics of the 450 participants in the e-Vita heart failure study

	n	Usual care (n = 150)	Website (n = 150)	E-health adjusted care pathway (n = 150)
Demographics				
Age, years		66.9 ± 11.6	66.7 ± 10.4	66.6 ± 11.0
Male sex		109 (72.7)	112 (74.7)	113 (75.3)
BMI, kg/m^2		28 ± 4.1	28.1 ± 5.1	27.9 ± 5.6
Education level	449	149		
Low		34 (22.8)	31 (20.7)	34 (22.7)
Middle		66 (44.3)	67 (44.7)	59 (39.3)
High		49 (32.7)	52 (34.7)	57 (38.0)
Married or living with a partner		110 (73.3)	123 (82.0)	107 (71.3)
	449	149		
Living with others		111 (74.5)	124 (82.7)	114 (76.0)
Current smoking		29 (19.3)	18 (12.0)	21 (14.0)
	432	145	143	144
Self-care score on EHFSBcB scale		70.6 ± 14.6	69.3 ± 16.4	72.0 ± 16.0
	432	145	143	144
Median HF-related QoL		23.0 ± 32.5	24.0 ± 31.0	23.0 ± 27.8
HF-related characteristics				
Duration of HF in months		40.6 ± 36.0	45.3 ± 42.4	38.5 ± 35.7
	432	142	145	145
LVEF, %		36.2 ± 10.0	35.2 ± 11.1	35.6 ± 11.2
LVEF ≤ 40%		66.7%	73.3%	71.3%
NYHA class[b]	428	143	144	141
I		57 (39.9)	57 (39.6)	69 (48.9)
II		55 (38.5)	53 (36.8)	46 (32.6)
III		24 (16.8)	17 (11.8)	17 (12.1)
IV		7 (4.9)	17 (11.8)	9 (6.4)
Hypertension		70 (46.7)	62 (41.3)	65 (43.3)
Acute coronary syndrome		71 (47.3)	69 (39.3)	72 (48.0)
Stable angina pectoris		28 (18.7)	26 (17.3)	20 (13.3)
Atrial fibrillation		54 (36.0)	68 (45.3)	66 (44.0)
Other heart rhythm disorders		44 (29.3)	44 (29.3)	42 (28.0)
Valvular heart disease		58 (38.7)	66 (44.0)	57 (38.0)
Other co-morbidities				
CVA		20 (13.3)	9 (6.0)	25 (16.7)
Hypercholesterolaemia		43 (28.7)	52 (34.7)	51 (34.0)
Diabetes mellitus		39 (26.0)	36 (24.0)	40 (26.7)
Renal failure		22 (14.7)	23 (15.3)	24 (16.0)
COPD		30 (20.0)	44 (29.3)	36 (24.0)
Medication				
Diuretics[c]		121 (80.7)	115 (76.7)	100 (66.7)
MRA		61 (40.7)	66 (44.0)	59 (39.3)
ACEI/ARBs		122 (81.3)	115 (76.7)	115 (76.7)
Beta-blockers		128 (85.3)	123 (82.0)	121 (80.7)
Oral anticoagulants		71 (47.3)	72 (48.0)	69 (46.0)
Antiplatelet agents		50 (33.3)	49 (32.7)	52 (34.7)
Lipid-lowering drugs		79 (52.7)	81 (54.0)	72 (48.0)

Values are presented as n (%) or mean ± standard deviation, if not specified.

ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident (including transient ischaemic attack); HF, heart failure; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; QoL, quality of life.

[a]LVEF was < 40% in patients first diagnosed at admission to hospital, on average 3 years before participation in the trial.

[b]Patient-reported NYHA classes.

[c]Includes loop diuretics and thiazides.

Table 2 Overall effect and effect per comparison of a website and an e-health adjusted care pathway on patient self-care after 3, 6, and 12 months unadjusted and adjusted for self-care at baseline

	Mean	Model 1		Model 2	
		Unadjusted	Overall effect between the groups	Adjusted for self-care at baseline	Overall effect between the groups
		95% CI	P-value	95% CI	P-value
3 months			<0.001		<0.001
Usual care	70.8	ref		ref	
Website	73.5	(−0.61 to 6.14)		(0.60 to 6.22)	
E-health[a]	78.2	(4.05 to 10.80)		(3.80 to 9.43)	
6 months			0.034		0.070
Usual care	74.2	ref		ref	
Website	74.7	(−3.08 to 4.21)		(−2.08 to 4.38)	
E-health[a]	78.6	(0.81 to 8.10)		(0.48 to 6.94)	
12 months			0.082		0.184
Usual care	72.7	ref		ref	
Website	72.1	(−4.45 to 3.21)		(−3.71 to 3.44)	
E-health[a]	76.1	(−0.39 to 7.27)		(−0.74 to 6.41)	

CI, confidence interval.
[a] E-health adjusted care pathway.

Table 3 Effect of a website and an e-health adjusted care pathway on secondary outcomes after 3, 6, and 12 months

Outcomes	3 months		6 months		12 months	
	Median (n = 150)	95% CI of the difference between the groups	Median n = 150)	95% CI of the difference between the groups	Median (n = 150)	95% CI of the difference between the groups
Patient satisfaction about their HF care (0 = no satisfaction, 100 = maximal satisfaction)						
Usual care	75.7	ref	75.5	ref	75.3	ref
Website	76.1	−6.33 to 7.39	75.2	−7.03 to 6.48	71.5	−12.32 to 1.79
E-health[a]	77.8	−1.32 to 12.39	80.5	−0.19 to 13.32	71.7	−10.65 to 3.46
HF-related QoL[b] (0 = best QoL, 105 = worst QoL)						
Usual care	22.8	ref	24.0	ref	26.5	ref
Website	26.5	−4.42 to 4.81	26.0	−5.70 to 3.80	28.3	−3.63 to 6.08
E-health[a]	19.0	−9.76 to −0.53[*]	21.0	−11.90 to −2.40[*]	25.5	−7.90 to 1.81
Disease-specific knowledge[c] (0 = most insufficient knowledge, 15 = most sufficient knowledge)						
Usual care	13.0	ref	13.0	ref	13.0	ref
Website	13.0	−0.18 to 10.49	13.0	−0.19 to 0.50	13.0	−0.28 to 0.39
E-health[a]	13.0	0.09 to 0.75[*]	13.0	−0.06 to 0.63	13.0	−0.14 to 0.53

CI, confidence interval; HF, heart failure; QoL, quality of life.
[a] E-health adjusted care pathway.
[b] Measured with the Minnesota Living with Heart Failure Questionnaire.
[c] Measured with Dutch Heart Failure knowledge (DHFk) scale.
[*] Significant.

Table 4 Effect of a website and an e-health adjusted care pathway on mortality and hospitalization

Outcomes	n	HR	95% CI of the difference between the groups
All-cause mortality			
Usual care	4	ref	ref
Website	11	2.82	0.90 to 8.87
E-health[a]	8	2.06	0.62 to 6.84
HF-related mortality			
Usual care	3	ref	ref
Website	7	2.39	0.62 to 9.24
E-health[a]	3	1.03	0.21 to 5.11
All-cause hospitalizations			
Usual care	66	ref	ref
Website	66	0.98	0.70 to 1.38
E-health[a]	57	0.85	0.59 to 1.21
HF-related hospitalizations			
Usual care	12	ref	ref
Website	8	0.65	0.27 to 1.60
E-health[a]	7	0.57	0.23 to 1.45

CI, confidence interval; HF, heart failure; HR, hazard ratio.
[a]E-health adjusted care pathway.

The fact that the adjusted care pathway in our study also increased HF knowledge after 3 months is not surprising as HF knowledge is strongly related to self-care.[11] The positive effect on hrQoL after 3 and 6 months of follow-up we found was also observed in previous telemonitoring studies.[22,23]

Our study was designed and powered for the primary outcome self-care. We also recorded mortality and hospitalizations, but our sample size was insufficient (underpowered) to formally compare these outcomes between the groups. There were no significant differences between the study groups in all-cause mortality or HF-related mortality, neither in all-cause hospitalizations or HF-related hospitalizations (*Table 4*).

A large previous study also executed in the Netherlands evaluated a disease management programme in patients from the HF outpatient clinics, powered on death and HF hospitalization, and showed a non-significant beneficial effect on mortality and HF hospitalizations.[24] A systematic review of 41 studies on e-health in HF could show a clear significant beneficial effect on both mortality and HF hospitalizations of e-health on top of UC.[23] Compared to other studies, we included a high percentage of NYHA class I patients in the e-Vita HF study. This might partly be due to the fact that NYHA class was self-reported, not clinician-reported. Self-reporting may lead to an over-optimistic assessment of the NYHA class as patients adapt to the their clinical situation. In contrast, clinicians tend to assign a less favourable NYHA class, because they not only use patient-reported symptoms, but also information from medical history, and results from clinical tests.[25] Regarding generalization of our results, the mild severity of HF (79% NHYA class I or II) should be acknowledged. We assume that effects of the studied interventions are larger in patients with more severe

HF, and in settings with a lower level of care as usual for HF as in the Netherlands.

Both HFM and EACP point to a short-term effect on self-care. Both e-health tools, although, very different in nature, seem to address but not sustain the components necessary to maintain self-care as measured with the EHFScB scale consisting of two components: self-care maintenance (e.g. 'I exercise regularly') and self-care management (e.g. 'if I gain weight I contact a doctor or nurse'). Adding monitoring of shortness of breath and providing interactive learning functionalities like the pre-set questions and dialogues in the TEHAF study (about symptoms, knowledge, and behaviour) enhance the sustainability of the effect given that the effect in the TEHAF study lasted over 12 months.[21] Also, pro-active e-signals, for example 'triggers' and 'push messages' (i.e. any notification from an app while not actively in use) could be helpful to improve sustainability.[26] In addition, incorporation of behavioural models in e-health could be helpful for sustaining the effect on self-care.[27]

The purpose of our study was to report on the effect of a website and the platform on several clinically relevant outcomes, not on actual use or uptake of the tools. How the adjusted care pathway affects usage of care, workload and costs in comparison to UC and the HFM website group will be reported in the cost-effectiveness analysis of the e-Vita HF study. We were able to include the number of patients as needed based on our sample size calculations, which allows us to draw robust conclusions regarding our primary outcome of self-care.

Limitations

A participation rate of 23% is low, but rather comparable to previous telemonitoring studies that reported these rates.[23] Low participation rates may impede generalizability, but are not a methodological problem, i.e. a flaw in design or bias. The low participation in our study is a realistic representation of the proportion actually willing to use e-health, when in stable HF, which is valuable information for future use. We did not register the reasons for not participating, and therefore do not know how many patients refused because of a lack of reliable internet access.

We explicitly aimed to include stable outpatients, and the use of e-health as a replacement of routine face-to-face contacts. Then, non-invasive e-health is most feasible and may safely (and cost-effective) reduce routine control visits. This aim resulted, as could be expected, in a relatively young and healthy study population (on average 3.4 years known with HF, mean age 67 ± 11) years).[28] Straightforward applicability to all outpatients with HF is not possible, and also not justified. In addition, participants had relatively low percentages of co-morbidities. The aforementioned implies that cardiologists and HF nurses should realize that our results constrain to stable HF outpatients with a low NYHA class.

The low number of events, e.g. mortality and HF hospitalizations, in our study was due to the fact that we only included stable HF patients from the HF outpatient clinic, and the majority of these patients had NYHA class I–II. We therefore had (on purpose) no participants who were just discharged from hospital (including

those who die within a few months), or patients who were unstable/in NYHA class III and IV.

Missing data (20% of the participants did not complete all questionnaires) was imputed by multiple imputation, allowing us to analyse the entire dataset. A method that results in more credible outcomes as was shown by simulation studies.[29] We also imputed values on self-care for the patients who died during the follow-up. To exclude accompanying bias, we performed a sensitivity analysis excluding those patients (5.1%), which revealed similar results.

In our study we registered the medication use at the start and end of the study. We do not have longitudinal data and cannot assess if changes in drug use affected the results. Importantly, however, an item of the EHFScB scale is 'intake of prescribed medication', and we showed a significant improvement on this self-care scale in the first 3 months, with a persisting but non-significant trend over the following 9 months in the EACP. Because the scale consists of multiple items, it is however impossible to assess which items were most important.

Of notice, the care delivered by HF outpatient clinics, the Netherlands is intensive compared to many other European countries with on average three to four routine consultations a year.[24,30] Therefore, it is a challenge to surpass the effect of UC on self-care and other outcomes with the interventions and effects of the studied interventions may be (much) larger in more deprived areas.[31]

Although the interpretability of the EHFScB scale was recently evaluated,[32] it remains difficult to assess a clinically relevant difference in scores.

In addition, our results might suggest that replacement of routine care as performed in our study was safe. However, we can only conclude that we identified no clear safety concerns. To formally prove safety of an intervention in a study would require a non-inferiority design instead of a superiority design. The former would imply a non-inferiority trial, which in general requires a much larger sample size if events related to safety do not occur frequently.[33]

Finally, the HFM website is freely accessible since 2012 and even though we explicitly instructed the HF nurses not to encourage this, patients in the UC group may have visited the site themselves, which could have resulted in a smaller effect (i.e. difference) between the intervention groups and UC. Indeed, according to a patient reported questionnaire filled out at the end of the study, 21% of the patients in the UC group had visited the HFM website once or more often. In the HFM and EACP, where patients were stimulated to use the HFM website, 57%, and 66% respectively visited the website once or more often.

In conclusion, we showed that both the HFM website and e-health platform improved self-care in HF patient on the short term, but this effect attenuated during the following 9 months. Continuous updating of e-health facilities to help sustain effects over longer time should be considered for evaluation.

Implications for clinical practice

Our primary outcome was a patient relevant outcome measure. The shortcoming of applying the EHFScB scale is that the clinical relevance is unclear of the significance difference on the scale we found in the first 3 months for both HFM and EAPC. There is yet no consensus on which change in this score is clinically meaningful. Our study may provide key information that is helpful to define such clinical meaningfulness with the help of future studies evaluating the EHFScB scale. Our results on the secondary outcomes of all-cause and HF-related mortality and hospitalizations are useful for updating the individual patient data systematic review on e-health in HF. Nevertheless, based on our study results, the use of the HFM website may be recommended to educate HF patients. The website may positively effects self-care, is freely accessible, and the use by patients or their relatives followed by discussion with the HF nurse does not require serious changes in the infrastructure of the health care system. To decide on implementation of an EACP, further research on sustainability of the effect and cost-effectiveness would be needed.

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