



# The relationship between self-care, long-term mortality, and heart failure hospitalization: insights from a [AQ2](#) real-world cohort study

Left running head: E. Calero-Molina *et al.*

Right running head: Relationship between self-care, long-term mortality, and HF hospitalization [AQ1](#)

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## Abstract

## Aims

The assumption that improved self-care in the setting of heart failure (HF) care necessarily translates into improvements in long-term mortality and/or hospitalization is not well established. We aimed to study the association between self-care and long-term mortality and other major adverse HF events (MAHFE). [AQ6](#)

## Methods and results

We conducted an observational, prospective, cohort study of 1123 consecutive patients with chronic HF. The primary endpoint was all-cause mortality. We used the European Heart Failure Self-care Behaviour Scale 9-item version (EHFScBS-9) to measure global self-care (overall score) and three specific dimensions of self-care including autonomy-based adherence, consulting behaviour and provider-based adherence. After a mean follow-up of 3.3 years, all-cause death occurred in 487 patients (43%). In adjusted analysis, higher EHFScBS-9 scores (better self-care) at baseline were associated with lower risk of all-cause death [hazard ratio (HR) 0.993, 95% confidence interval (CI) (0.988–0.997),  $P$ -value = 0.002], cardiovascular (CV) death [HR 0.989, 95% CI (0.981–0.996),  $P$ -value = 0.003], HF hospitalization [HR 0.993, 95% CI (0.988–0.998),  $P$ -value = 0.005], and the combination of MAHFE [HR 0.995, 95% CI (0.991–0.999),  $P$ -value = 0.018]. Similarly, impaired global self-care [HR 1.589, 95% CI (1.201–2.127),  $P$ -value = 0.001], impaired autonomy-based adherence [HR 1.464, 95% CI (1.114–1.923),  $P$ -value = 0.006], and impaired consulting behaviour dimensions [HR 1.510, 95% CI (1.140–1.923),  $P$ -value = 0.006] were all associated with higher risk of all-cause mortality.

## Conclusion

In this study, we have shown that worse self-care is an independent predictor of long-term mortality (both, all-cause and CV), HF hospitalization, and the combinations of these endpoints in patients with chronic HF. Important dimensions of self-care such as autonomy-based adherence and consulting behaviour also determine the risk of all these outcomes in the long term.

**Keywords:** Heart failure Self-care Mortality HF hospitalization Outcomes European self-care behaviour scale [AQ7](#)

**Note:** Any change made here needs to be made in the corresponding section at the end of the article.

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### Implications for practice

- We have shown that worse self-care measured with European Heart Failure Self-care Behaviour Scale-9 is an independent predictor of hospitalization mortality and in heart failure patients.
- These results highlight the use self-care evaluation to improve the risk stratification of these patients.
- We must identify patients with poor self-care to especially focus the intervention of the heart failure nurse.

## Introduction

Heart failure (HF) is a devastating syndrome with a very negative impact on mortality, morbidity, and health-related quality of life in patients with this diagnosis. HF also represents a challenge to healthcare systems due to its growing prevalence and the rising medical resource use and expenditure associated with this syndrome.<sup>1–3</sup> Suboptimal self-

care has been identified as a factor that may partially explain the occurrence of major adverse events and limitations in patients with HF.<sup>4–6</sup> Regarding this, in addition to standard HF therapy, new disease management strategies are orientated to address self-care as a therapeutic goal to improve the course of the disease.<sup>5–9</sup> Self-care maintenance, self-care monitoring, and self-care management are the three main building blocks that compose the concept of self-care. [AQ8](#)

The first concept, self-care maintenance, refers to those behaviours that patients incorporate in their daily life; the second, self-care monitoring, refers to the patient's ability to detect warning signs and symptoms of an exacerbation; and the third, self-care management, refers to patient's responses to signs and symptoms.<sup>6,10–12</sup>

One of the most important instruments to assess self-care in patients with HF across the world is the European Heart Failure Self-care Behaviour Scale (EHFScBS).<sup>13,14</sup> In recent years, a new improved version of this scale has been developed. The new 9-item EHFScBS (EHFScBS-9) includes information from nine items of the original scale.<sup>14</sup> Recently, the developers of the original EHFScBS-9 performed a factor analysis of the EHFScBS-9 and described three factors or dimensions of self-care that can be individually assessed using this scale: autonomy-based adherence, consulting behaviour, and provider-based adherence.<sup>15</sup> Measuring self-care with instruments such as the EHFScBS-9 have emerged as key nurse-led interventions to be delivered in comprehensive HF programmes aimed to empower patients in their disease management.<sup>6,8,9,11,16</sup>

However, the assumption that improved self-care necessarily translates into improvements of hard endpoints is not well established.<sup>17,18</sup> Regarding this, previous studies have shown mixed results with no impact on mortality<sup>18</sup> and divergent results in terms of hospitalization.<sup>4,5,17,19</sup> Moreover, none of these studies addressed associations between specific and psychometrically validated dimensions of self-care and clinical events.<sup>4,5,17–19</sup> Limitations in the study design and insufficient modelling of psycho-social determinants of self-care when addressing the impact of self-care on long-term clinical outcomes may have accounted for the divergence in the reported results.<sup>4,5,17–19</sup>

The purpose of the present study was to evaluate the influence of self-care behaviours, evaluated with the EHFScBS-9 and its three dimensions, on the occurrence of major adverse heart failure events (MAHFE). We hypothesized that global self-care (i.e. the EHFScBS-9 total score) and the individual dimensions of self-care (i.e. autonomy-based adherence, consulting behaviour, and provider-based adherence) were associated with increased risk of all-cause death, cardiovascular (CV) death, HF hospitalizations, and the combined MAHFE of all-cause death or HF hospitalizations.

## Methods

Data are available upon request from a third party. Reasonable requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to the corresponding author.

### Study design, study population, and ethics

This is a secondary analysis of the Definition of the neuro-hormonal Activation, Myocardial function, genOmic expression, and CLinical outcomes in hEart failure patients (DAMOCLES) study, a single-centre, observational, prospective cohort study of 1236 consecutive patients diagnosed with HF recruited between January 2004 and January 2013.

The methodology of the DAMOCLES study has been published previously by our group<sup>16,20–26</sup> Briefly, for inclusion, patients had to be diagnosed with chronic HF according to the European Society of Cardiology diagnostic criteria, had

at least one recent acute decompensation of HF requiring intravenous diuretic therapy (either hospitalized or in the daycare hospital), and had to be in stable condition at the time of study entry. Exclusion criteria were: significant primary valvular disease, clinical signs of fluid overload, pericardial disease, restrictive cardiomyopathy, hypertrophic cardiomyopathy, haemoglobin (Hb) levels  $<8.5$  g/dL, active malignancy, and chronic liver disease. The study was approved by the local committee of ethics for clinical research and was conducted in accordance with the principles of the Declaration of Helsinki. All patients gave written informed consent before study entry.

For the present analysis, all DAMOCLES participants were considered for inclusion. Of them, we excluded patients with missing baseline information on self-care. Thus, for the purposes of the present analysis, the final cohort consisted of 1123 patients.

### **Baseline assessment**

A detailed baseline evaluation was performed for all participants at study entry. This included the collection of information about *demographic* characteristics, exhaustive medical history to gather clinical and disease-related factors such as New York Heart Association (NYHA) functional class, co-morbidities, laboratory information, medical treatments, and the most recent left ventricular ejection fraction (LVEF). Sources of information were the medical history and standardized questionnaires.

### **Evaluation of self-care**

To assess self-care, we used the 9-item European Heart Failure Self-care Behaviour Scale (EHFScBS-9),<sup>14</sup> which is a well-known psychometrically sound instrument that evaluates self-care behaviours in patients with HF (e.g. take medications as prescribed or call the provider in case of dyspnoea). Each item uses a 5-point Likert format for responses from 'I completely agree' to 'I don't agree at all'.

The possible score of the EHFScBS-9 is 9–45, with a lower score indicating better self-care. To improve the clinical interpretability of the results obtained with the EHFScBS-9, the developers of the instrument suggest reversing and standardizing the reported scores from 0 to 100 (higher scores indicate better self-care).<sup>14,15</sup> In this study, we analyse the overall summary score of the EHFScBS-9 to inform on global self-care along with the three dimensions of self-care that can be individually assessed using this scale.<sup>15</sup>

For the purpose of this study, we defined impaired self-care when inverted and standardized individual scores were in the lowest tertile of the 9-item EHFScBS-9 [impaired global self-care ( $<55$  points)] or in the lowest tertile of each individual dimension or factor [impaired autonomy-based adherence ( $<42$  points), impaired consulting behaviour ( $<62$  points), and impaired provider-based adherence ( $<75$  points)].

### **Psycho-social evaluation**

Details on psycho-social evaluation in the DAMOCLES study have been previously reported.<sup>20,21</sup> Briefly, to characterize patients in their psycho-social dimension, baseline prospective information was collected on literacy, marital status, cohabitation with a partner, and the presence and need of a caregiver. Literacy was estimated from the years of education of patients and grouped into two groups for the purpose of this analysis (primary school studies or higher). Likewise, several psychometrically sound and well-validated instruments were administered in order to define important psycho-social aspects. Patient autonomy was evaluated using the Barthel Index and the Lawton and Brody scale<sup>27,28</sup>; cognitive function was determined using the Short Portable Mental State Questionnaire (Pfeiffer) and the mini-mental state examination tests<sup>29,30</sup>; frailty was assessed using the Barber scale<sup>31</sup>; affective status was explored using the short form of the Geriatric Depression Scale (GDS).<sup>32</sup> Caregiver status was obtained directly from the most

recent social evaluation performed before entry into the study.

### Follow-up and major heart failure events ascertainment

Follow-up in DAMOCLES lasted until November 2015. Study participants were followed for a median of 2.93 years (mean 3.3 years). Follow-up was conducted by trained study personnel. Specifically, data on mortality and on the cause of death were obtained from hospital and primary care electronic medical records, and/or by direct interview with the patients' relatives. MAHFE consisted of the occurrence of any of the following: all-cause death, CV death, HF hospitalization, or the composite of all-cause death or HF hospitalization.

The primary endpoint of the study was all-cause death (time to the first event). Key secondary endpoints of the study were CV death, HF hospitalization, and the composite endpoint of two MAHFE: all-cause death or HF hospitalization. Our hypothesis was that global self-care and the individual dimensions of self-care were associated with increased risk of all four MAHFE studied.

### Statistical analyses

Demographic and clinical characteristics, as well as laboratory tests results, were summarized using basic descriptive statistics, both overall and categorized by MAHFE status.

For categorical variables, numbers and percentages were reported, and for continuous variables, mean (standard deviation) or median (inter-quartile range) were used, depending on the distribution of the variables.  $\chi^2$ , Student's *T*, and non-parametric tests were used to compare characteristics across comparison groups.

To evaluate the association between self-care and MAHFE we used both, proportion analyses ( $\chi^2$ ) and unadjusted Cox proportional hazards analyses. We also used generalized additive models (GAM) to explore the associations between self-care and MAHFE. As a result of these analyses, smooth cubic spline curves of the estimated beta coefficients of risk of each event were plotted.

Multivariate Cox proportional hazards models were developed for each MAHFE. In these models, we evaluated the effect on time to first event probabilities of (i) EHFScBS-9 scores (overall and the three dimension's scores) and (ii) impairment of self-care behaviour (i.e. scoring in the lowest tertile in the overall EHFScBS-9 and/or in any of its dimension). All models were adjusted for covariates associated with the outcomes and these included clinical factors (age, gender, systolic blood pressure, diabetes mellitus, LVEF, renal function, N-terminal pro-B-type natriuretic peptide (NT-proBNP), aetiology of HF, use of disease-modifying drugs, previous HF admission, BMI, iron deficiency, haemoglobin, NYHA functional class, time since diagnosis of HF, co-morbidity burden) and psycho-social factors (dependency for activities of daily livings, geriatric depression scale scores, social support, cognitive function, caregiver status, literacy, and fragility status). Backward conditional stepwise methods were used. To explore the discrimination properties of these models, the c-index was calculated and reported along with *P*-values. Based on these adjusted Cox proportional hazards models, cumulative survival curves exploring the effect of global self-care behaviour on each of the four MAHFE were plotted. Interactions between gender and self-care were also explored in these models. To evaluate the relative dominance on adverse clinical events of each of the three dimensions of self-care behaviour we constructed adjusted Cox proportional hazards models exploring the simultaneous effects of the three dimensions of self-care on the 4 MAHFE over time.

Finally, we explored interactions between key psycho-social factors such as literacy and the primary endpoint on overall EHFScBS-9 scores using age and sex-adjusted general linear models. Age- and sex-adjusted estimated least-square (marginal) means (EEMs/EMMs) and 95% confidence intervals (CIs) of global self-care according to event

status (all-cause death or HF hospitalization) by literacy were plotted. The significance of comparisons of EMMs was evaluated using a Tukey's adjustment and a value of  $\alpha = 0.05$ . [AQ9](#)

All statistical tests and CIs were constructed with a type I error alpha level of 5%, with no adjustments for multiplicity. *P*-values below 0.05 were considered statistically significant. All analyses were performed using SPSS software (version 22.0; IBM, Armonk, NY, USA) and R software (version 4.0.2; R Foundation for Statistical Computing, Vienna, Austria).

## Results

From the total 1236 HF patients included in the DAMOCLES study, only those with information on the EHFScBS were selected ( $N = 1123$ ) for the present analysis.

### Baseline characteristics of patients

Baseline characteristics of the study sample, both overall and according to the occurrence of the composite endpoint of all-cause death or HF hospitalization are presented in [Table 1](#). During follow-up, 652 (58%) patients experienced at least one MAHFE. All-cause death occurred in 487 (43%), CV death in 147 (13%), and HF hospitalization in 384 (34%). In the overall cohort, mean (standard deviation) EHFScBS-9 scores were 69 (28), and impairment of self-care was observed in 349 (31%), 413 (37%), 363 (32%), and 270 (24%) patients for global self-care, autonomy-based adherence, consulting behaviour and provider-based adherence, respectively.

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**Table 1 Baseline characteristics of patients according to the occurrence of major adverse heart failure events (MAHFE)** 

	<i>n</i>	Whole cohort ( <i>n</i> = 1123)	MAHFE+ ( <i>n</i> = 652)	MAHFE- ( <i>n</i> = 471)	<i>P</i> -value
Demographic and clinical factors					
Age, years	1123	72 (11)	75 (10)	69 (12)	<0.001
Sex (female), <i>n</i> (%)	1123	484 (43)	287 (44)	197 (42)	0.502
Systolic blood pressure, mmHg	1121	124 (227)	122 (21)	126 (22)	0.005
NYHA functional class, <i>n</i> (%)					
I–II	661	661 (59)	330 (51)	331 (71)	<0.001
III–IV	454	454 (41)	319 (49)	135 (29)	
HF hospitalization previous year, <i>n</i> (%)	1121	929 (83)	570 (87)	359 (77)	<0.001
HF diagnosis < 1 year, <i>n</i> (%)	1121	696 (62)	373 (57)	323 (69)	<0.001
LVEF, %	1120	44 (17)	45 (17)	44 (16)	0.358

	<i>n</i>	Whole cohort ( <i>n</i> = 1123)	MAHFE+ ( <i>n</i> = 652)	MAHFE- ( <i>n</i> = 471)	<i>P</i> -value
Ischaemic aetiology of HF, <i>n</i> (%)	1123	429 (38)	300 (46)	129 (27)	<0.001
Comorbidities					
Hypertension, <i>n</i> (%)	1123	902 (80)	549 (84)	353 (75)	<0.001
Diabetes mellitus, <i>n</i> (%)	1122	517 (46)	324 (50)	193 (41)	0.004
Previous MI, <i>n</i> (%)	1123	288 (26)	200 (31)	88 (19)	<0.001
Dyslipidaemia, <i>n</i> (%)	1123	624 (56)	382 (59)	242 (51)	0.018
CKD, <i>n</i> (%)	1118	619 (55)	409 (63)	210 (45)	<0.001
Anaemia, <i>n</i> (%)	1122	545 (49)	367 (56)	178 (38)	<0.001
Iron deficiency, <i>n</i> (%)	1103	751 (68)	468 (73)	283 (61)	<0.001
COPD, <i>n</i> (%)	1123	245 (22)	168 (26)	77 (16)	<0.001
Cerebrovascular accident, <i>n</i> (%)	1117	113 (10)	77 (12)	36 (8)	0.027
Osteoarthritis, <i>n</i> (%)	1114	143 (13)	105 (16)	38 (8)	<0.001
Chronic liver disease, <i>n</i> (%)	1117	57 (5)	34 (5)	23 (5)	0.891
Major psychiatric disorder, <i>n</i> (%)	1118	59 (5)	33 (5)	26 (6)	0.787
Treatments (%)					
ACEI or ARBs	1119	824 (74)	453 (70)	371 (79)	<0.001
Beta-blockers	1122	984 (88)	564 (87)	420 (90)	0.167
MRA	1120	422 (38)	231 (36)	191 (41)	0.080
Diuretics	1122	1021 (91)	612 (94)	409 (87)	<0.001
Statins	1122	669 (60)	403 (62)	266 (57)	0.084
Antiplatelet or anticoagulant therapy	1122	923 (82)	752 (88)	351 (75)	<0.001
Laboratory					
Haemoglobin, g/dL	1123	12.6 (2.3)	12.3 (2.5)	13.0 (1.9)	<0.001
eGFR, mL/min/1.73 m <sup>2</sup>	1118	59 (25)	56 (24)	64 (25)	<0.001
NT-proBNP, pg/mL		1582 (685–3723)	1967 (881–4641)	1130 (480–2696)	<0.001
Psycho-social factors					
Dependency for ADL, <i>n</i> (%) <sup>a</sup>	979	387 (40)	282 (48)	105 (27)	<0.001
Dependency instrumental activities, <i>n</i> (%)	1036	80 (8)	37 (6)	43 (10)	0.012
Literacy					
Primary school	701	701 (70)	426 (73)	275 (66)	0.012

	<i>n</i>	Whole cohort ( <i>n</i> = 1123)	MAHFE+ ( <i>n</i> = 652)	MAHFE- ( <i>n</i> = 471)	<i>P</i> -value
Higher than primary school	303	303 (30)	158 (27)	145 (35)	
Barber test, points <sup>a</sup>	1025	2 (1–4)	2 (1–4)	1 (1–3)	<0.001
Moderate or severe cognitive impairment, yes vs. no	906	76 (8)	46 (9)	30 (8)	0.808
Score in the Geriatric Depression Scale (GDS) <sup>a</sup> , points	980	4.0 (5.4)	3 (1–5)	3 (2–5)	0.009
Need caregiver, yes vs. no	798	382 (48)	257 (55)	125 (38)	<0.001
Living with a partner yes vs. no	1078	580 (51.6)	326 (56.3)	253 (43.7)	0.215
Self-care (EHFScBS-9 scores)					
Global self-care	1123	69 (28)	66 (28)	73 (28)	<0.001
Dimension 1, autonomy-based adherence	1123	59 (33)	55(33)	64 (33)	<0.001
Dimension 2, consulting behaviour	1123	70 (36)	67 (37)	75 (35)	<0.001
Dimension 3, provider-based adherence	1123	82 (23)	81 (23.78)	83 (22.92)	0.213

All-cause death or HF hospitalization.

Continuous data are presented as mean (SD).

a For variables with non-parametric distribution, data are presented as median (Q1–Q3), and differences are evaluated using non-parametric tests.

ACEi, angiotensin-converting enzyme inhibitors; ADL, activities of daily living; ADL, dependency instrumental activities, defined as Lawton and Brody  $\leq 8$  in women and  $\leq 5$  in men; Anaemia was defined according to the WHO Criteria; ARBs, angiotensin receptor blockers; CKD, chronic kidney disease, defined as estimated glomerular filtration (eGFR) date  $< 60$  mL/min/1.73m<sup>2</sup>; COPD, chronic obstructive pulmonary disease; Dependency, defined as Barthel Index  $\leq 99$  points; Frailty of the patients was measured by Barber's test; HF, heart failure; LVEF, left ventricular ejection fraction; MAHFE-, patients who did not experience any major adverse heart failure event; MAHFE+, patients who experienced any major adverse heart failure event (all-cause or CV death or HF hospitalization); MI, myocardial infarction; MRA, mineral-corticoid receptor antagonists; NYHA, New York heart Association.

Classical negative prognostic factors such as older age, worse NYHA class, previous hospitalization, co-morbidity burden, and higher levels of NT-proBNP were more prevalent among patients experiencing any MAHFE during follow-up (all *P*-value  $< 0.001$ ). Similarly, psycho-social limitations trended to be more prominent among patients that experienced adverse events over time. Scores of the EHFScBS-9 evaluating overall self-care, autonomy-based adherence, and consulting-behaviour were significantly lower in patients that suffered any MAHFE (all *P*-value  $< 0.001$ ). Provider-based adherence did not differ across groups.

### Association of self-care behaviours with clinical events

Similarly, unadjusted evaluation of the distribution of adverse outcomes according to levels of self-care behaviour

(overall and by dimensions) showed that impaired global self-care, autonomy-based adherence, and consulting behaviour dimensions were associated with a higher risk of any of the four MAHFE (Table 2) but not for provider-based adherence.

**Note:** The table layout displayed in 'Edit' view is not how it will appear in the printed/pdf version. This html display is to enable content corrections to the table. To preview the printed/pdf presentation of the table, please view the 'PDF' tab.


**Table 2 Percentages of adverse outcomes and unadjusted Cox proportional hazards analyses according to levels of self-care (overall and by dimensions)** 

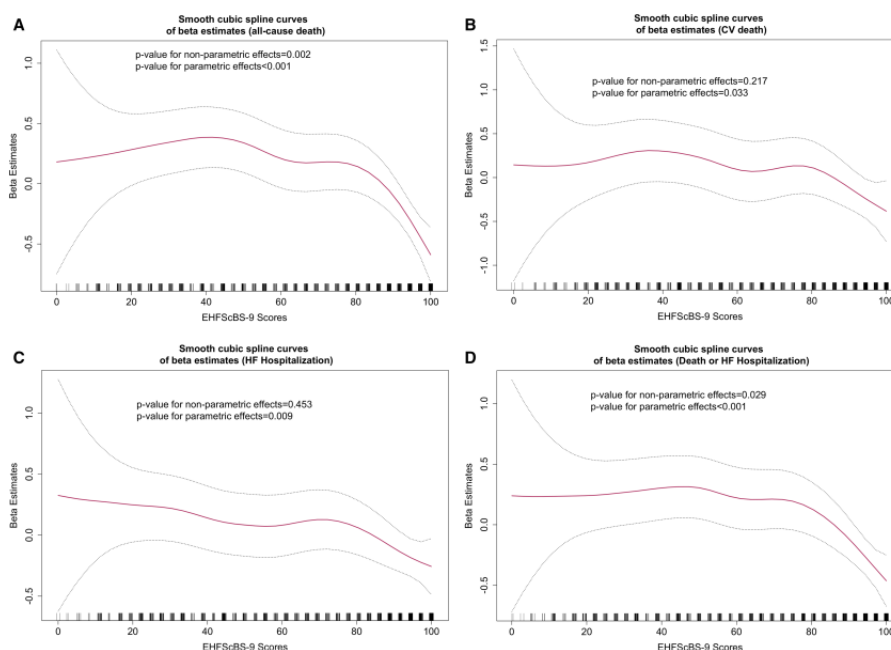
	Cox proportional hazards <sup>a</sup>			Occurrence of MAHFE		
	HR	95% CI	P-value	Impaired self-care, n (%)	Adequate self-care, n (%)	P-value
Dependent variable: major adverse heart failure events	Impaired vs. adequate global self-care					
All-cause death	1.286	1.070–1.547	0.007	185 (53)	302 (39)	<0.001
Cardiovascular death	1.436	1.031–2.001	0.032	59 (17)	88 (11)	0.013
Heart failure hospitalization	1.265	1.026–1.560	0.028	138 (40)	246 (32)	0.012
Combined endpoint (all-cause death or HF hospitalization)	1.239	1.054–1.456	0.009	232 (67)	420 (54)	<0.001
Impaired vs. adequate autonomy-based adherence						
All-cause death	1.172	0.976–1.406	0.089	201 (49)	286 (40)	0.007
Cardiovascular death	1.482	1.069–2.055	0.018	68 (17)	79 (11)	0.013
Heart failure hospitalization	1.258	1.025–1.545	0.028	158 (38)	226 (32)	0.031
Combined endpoint (all-cause death or HF hospitalization)	1.190	1.016–1.395	0.031	260 (63)	392 (55)	0.012
Impaired vs. adequate consulting behaviour						
All-cause death	1.203	1.001–1.446	0.049	186 (51)	301 (40)	<0.001
Cardiovascular death	1.187	0.848–1.661	0.318	55 (15)	92 (12)	0.157
Heart failure hospitalization	1.175	0.954–1.449	0.129	140 (39)	244 (32)	0.037
Combined endpoint (all-cause death or HF hospitalization)	1.151	0.980–1.351	0.087	236 (65)	416 (55)	0.001
Impaired vs. adequate provider-based adherence						
All-cause death	1.050	0.856–1.287	0.638	125 (46)	362 (42)	0.291

	Cox proportional hazards <sup>a</sup>			Occurrence of MAHFE		
	HR	95% CI	<i>P</i> -value	Impaired self-care, <i>n</i> (%)	Adequate self-care, <i>n</i> (%)	<i>P</i> -value
Cardiovascular death	1.069	0.738–1.548	0.725	38 (14)	109 (13)	0.605
Heart failure hospitalization	1.039	0.823–1.310	0.750	95 (35)	289 (34)	0.713
Combined endpoint (all-cause death or HF hospitalization)	1.060	0.888–1.266	0.516	164 (61)	488 (57)	0.322

a Reference category: adequate self-care. Impaired global self-care behaviour was defined as scores in the lowest tertile (<55 points) of the 9-item EHFScBS (inverted and standardized); impaired consulting behaviour was defined as scores of the consulting behaviour dimension in the lowest tertile (<62 points) of the 9-item EHFScBS (inverted and standardized); impaired autonomy-based adherence was defined as scores of the autonomy-based adherence dimension in the lowest tertile (<42 points) of the 9-item EHFScBS (inverted and standardized); impaired provider-based adherence was defined as scores of the provider-based adherence dimension in the lowest tertile (<75 points) of the 9-item EHFScBS (inverted and standardized).


We developed several GAM models to explore linear and non-linear associations between global self-care and clinical events. In [Figure 1](#), smooth cubic spline curves of the beta estimates of the risk of each MAHFE by self-care represented by the overall summary of scores of the EHFScBS-9 are plotted. Significant linear associations between EHFScBS-9 scores and beta estimates of the events were observed for all 4 MAHFE ( $P$ -value < 0.05 in all cases). Moreover, a more prominent descending slope in higher self-care scores for the associations between EHFScBS-9 with all-cause death and the combined endpoint of death or HF hospitalization also produced significant non-parametric  $P$ -values (0.002 and 0.029, respectively).

**Figure 1** Smooth cubic spline curves of the estimates of risk of each MAHFE [all-cause death (A), CV death (B), HF hospitalization (C), and the combined event of all-cause death or HF hospitalization (D)] by self-care represented by the overall summary of scores of the EHFSBS-9. The Y axis represents the estimated beta coefficients of risk of each event. The solid red line depicts the estimated beta coefficient of risk of each event. The dotted line depicts the error standard of the estimated beta coefficient of risk. X axis represents EHFSBS-9 inverted and standardized scores. 



In [Table 3](#), we present adjusted Cox proportional hazards analyses exploring the influence of EHFSBS-9 scores (continuous variable) on MAHFE. Higher EHFSBS-9 overall summary scores, autonomy-based adherence scores, and consulting behaviour scores indicating better self-care were independently associated with a lower risk of all four MAHFE. EHFSBS-9 provider-based adherence score only remained a significant predictor in the model predicting CV death ( $P$ -value = 0.01). Analysis of the c-index demonstrated a moderate model performance in terms of discrimination despite adjustment for significant disease-related and psycho-social modulators of self-care. Regarding this, there were no statistically significant differences in c-statistics between predictive models within each of the 4 outcomes studied (all  $P$ -values for cross comparisons > 0.05).

**Note:** The table layout displayed in ‘Edit’ view is not how it will appear in the printed/pdf version. This html display is to enable content corrections to the table. To preview the printed/pdf presentation of the table, please view the ‘PDF’ tab.

**Table 3** Adjusted Cox proportional hazards analyses exploring the influence of scores of the EHFSBS-9 in predicting major adverse heart failure events (MAHFE) including all-cause and CV mortality, HF admission and combination of all-cause death or HF admission in patients with chronic HF (stepwise backward methods) 


Cox proportional hazards				Concordance		
HR	95% CI	$P$ -value	C-index	95% CI	$P$ -value	

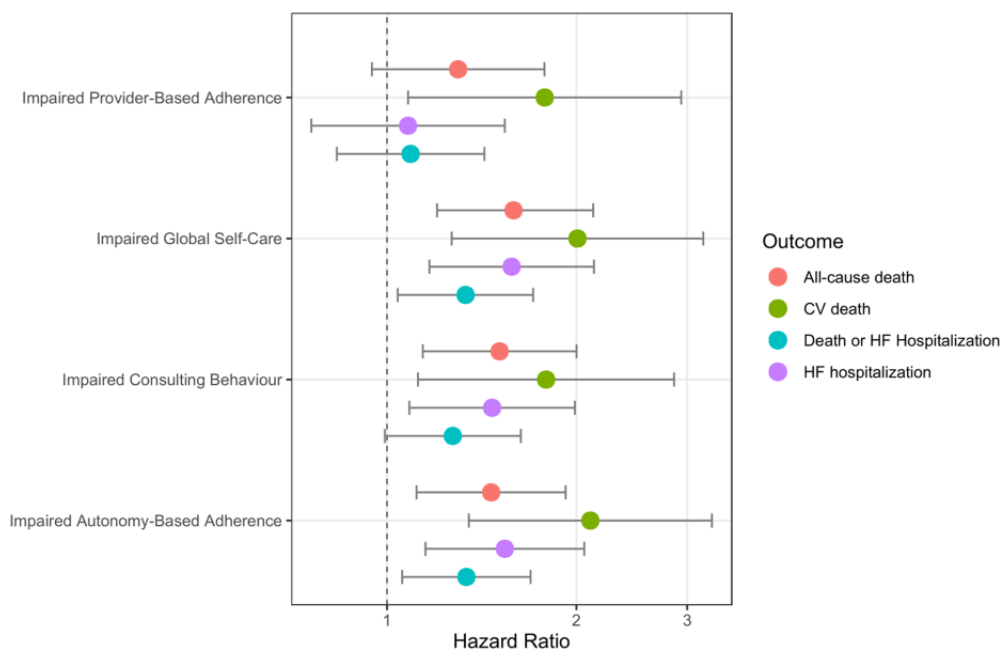
	Cox proportional hazards			Concordance		
	HR	95% CI	P-value	C-index	95% CI	P-value
Outcome: all-cause death						
EHFScBS-9 Overall summary score	0.993	0.988–0.997	0.002	0.752	0.723–0.781	<0.001
EHFScBS-9 Autonomy-based adherence score	0.994	0.990–0.998	0.005	0.752	0.723–0.781	<0.001
EHFScBS-9 Consulting behaviour score	0.995	0.991–0.998	0.002	0.750	0.721–0.780	<0.001
EHFScBS-9 Provider-based adherence score	0.994	0.987–1.001	0.076	0.750	0.721–0.780	<0.001
Outcome: CV death						
EHFScBS-9 Overall summary score	0.989	0.981–0.996	0.003	0.782	0.735–0.829	<0.001
EHFScBS-9 Autonomy-based adherence score	0.993	0.987–1.000	0.047	0.788	0.741–0.834	<0.001
EHFScBS-9 Consulting behaviour score	0.992	0.987–0.998	0.011	0.785	0.737–0.833	<0.001
EHFScBS-9 Provider-based adherence score	0.987	0.978–0.997	0.011	0.788	0.741–0.835	<0.001
Outcome: HF hospitalization						
EHFScBS-9 Overall summary score	0.993	0.988–0.998	0.005	0.712	0.678–0.747	<0.001
EHFScBS-9 Autonomy-based adherence score	0.994	0.990–0.998	0.005	0.713	0.679–0.747	<0.001
EHFScBS-9 Consulting behaviour score	0.995	0.991–0.999	0.007	0.711	0.676–0.747	<0.001
EHFScBS-9 Provider-based adherence score	0.996	0.990–1.003	0.295	0.709	0.674–0.744	<0.001
Outcome: all-cause death or HF hospitalization						
EHFScBS-9 Overall summary score	0.995	0.991–0.999	0.018	0.699	0.671–0.728	<0.001
EHFScBS-9 Autonomy-based adherence score	0.996	0.993–0.999	0.022	0.703	0.675–0.731	<0.001
EHFScBS-9 Consulting behaviour score	0.996	0.993–1.000	0.024	0.698	0.669–0.726	<0.001
EHFScBS-9 Provider-based adherence score	0.996	0.991–1.002	0.206	0.697	0.668–0.725	<0.001


a Reference category: adequate self-care. Impaired global self-care behaviour was defined as scores in the lowest tertile (<55 points) of the 9-item EHFScBS (inverted and standardized); impaired consulting behaviour was defined as scores of the consulting behaviour dimension in the lowest tertile (<62 points) of the 9-item EHFScBS (inverted and standardized); impaired autonomy-based adherence was defined as scores of the autonomy-based adherence dimension in the lowest tertile (<42 points) of the 9-item EHFScBS (inverted and standardized); impaired provider-based adherence was defined as scores of the provider-based adherence dimension in the lowest tertile (<75 points) of the 9-item EHFScBS (inverted and standardized).

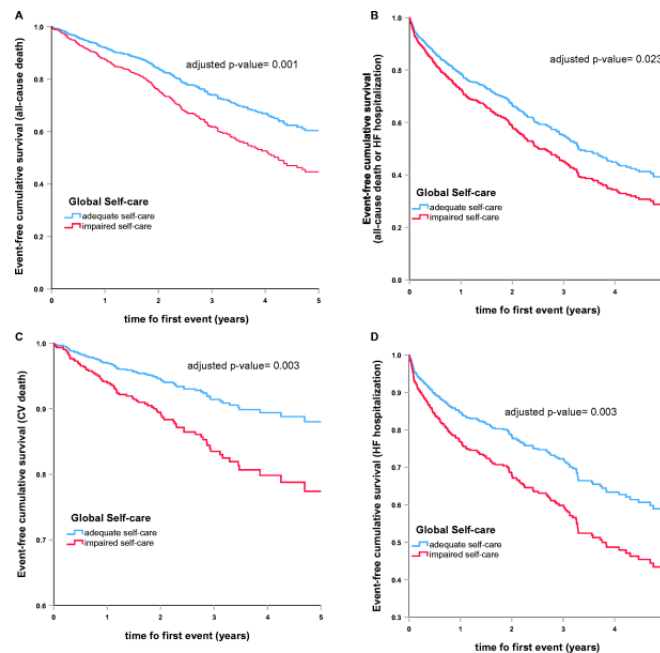
MAHFE+, patients who experienced any major adverse heart failure event (all-cause or CV death or HF hospitalization); MAHFE-, patients who did not experience any major adverse heart failure event. Model performance (discrimination) was evaluated by means of the C-statistic of each model after adding significant disease-related and psycho-social modulators of self-care.

These findings were confirmed in additional adjusted Cox proportional hazards models (*Figures 2 and 3, Supplementary material online, Table S1*). In multivariable models, impaired global self-care, impaired autonomy-based adherence, and impaired consulting behaviour dimensions were associated with a higher risk of any of the four MAHFE (time to the first event). Impaired provider-based adherence only showed a significant association with events risks for CV death but not for all-cause death, HF hospitalization, or the combination of death or HF hospitalization. The strongest associations were observed between CV death and impaired global self-care [hazard ratio (HR) 2.0, 95% CI (1.3–3.2),  $P$ -value = 0.003] and impaired autonomy-based adherence [HR 2.1, 95% CI (1.3–3.3),  $P$ -value = 0.001]. [AQ10](#)

**Figure 2 Adjusted Cox proportional hazards models exploring the effect of global self-care and its three dimensions on the four MAHFE over time.** 



**Figure 3** Cumulative survival curves exploring the effect of global self-care behaviour on each of the four MAHFE. Curves are based on Cox proportional hazards models adjusted for covariates. (A) All-cause death event-free survival; (B) CV death event-free survival; (C) HF hospitalization event-free survival; (D) combined endpoint of all-cause death or HF hospitalization event-free survival. 



To further evaluate the interplay between the three self-care dimensions, we fitted four predictive adjusted Cox proportional hazards models to explore the simultaneous effects of autonomy-based adherence, consulting behaviour, and provider-based adherence on MAHFE over time. As shown in [Supplementary material online, Figure S1](#), autonomy-based adherence dominated the significant association between self-care and CV death, HF hospitalization, or the combined endpoint of death or HF hospitalization. Interestingly, consulting behaviour resulted in the dominant component of self-care associated with all-cause death.

### Interaction effects on self-care between clinical events and gender or psycho-social determinants

To complete the association analyses, we explored potential interactions between gender and self-care using Cox proportional hazards models. In unadjusted analyses, the interaction term gender by impaired global self-care was not significant for any of the MAHFE (all  $P$ -value  $> 0.05$ ).

Among psycho-social factors, we observed that higher levels of literacy were associated with reduced risk of the combined endpoint all-cause death or HF hospitalization [HR 0.905, 95%CI (0.839–0.975),  $P$ -value = 0.004]. In [Supplementary material online, Figure S2](#), we present the least-square means of EHFScBS-9 according to event status (combined event) by the level of literacy. Interestingly, there was a significant interaction between these two terms for the overall self-care score ( $F = 2.814$ ,  $P = 0.024$ ), mainly driven by the hospitalization events ( $F = 3.453$ ,  $P$ -value = 0.008). Interestingly, we observed significant divergent results of EMMs of EHFScBS-9 scores in patients with advanced university studies according to event-free status (interaction term:  $F = 8.189$ ,  $P$ -value = 0.004).

## Discussion

In this study, we have shown that self-care is an independent predictor of long-term mortality (both, all-cause and CV), HF hospitalization, and the combination of these endpoints in patients with chronic HF. We also have shown

that important factors of self-care such as autonomy-based adherence and consulting behaviour determine the risk of all these four MAHFE in the long term. Interestingly, the influence of global self-care, autonomy-based adherence, and consulting behaviour on hard endpoints was observed despite adjustment for important clinical prognostic factors and relevant psycho-social determinants. Importantly, we have also demonstrated that the impact of self-care status on the four MAHFE measured can be considered clinically meaningful: patients with poor global self-care had an absolute risk increase of 14%, 5%, 8%, and 18% in all-cause death, CV death, HF hospitalization, and the combined endpoint of death or HF hospitalization respectively. On the other hand, patients with adequate self-care experienced large relative risk reductions (RRRs) in MAHFE compared to patients with poor global self-care: 32% RRR in CV death, 26% RRR in all-cause death, 25% in the combined endpoint, and 20% reduction in HF hospitalization. We present unique and original data since this is, to the best of our knowledge, the first study that demonstrates (i) a significant association between self-care and long term mortality (all-cause and CV) in patients with chronic HF, (ii) the long-term prognostic impact of specific metrically validated dimensions of self-care measurable with the EHFSBS-9.<sup>14,15</sup>

Our study complements other studies that did not report mortality as individual endpoint<sup>5,19</sup> and it rebuts previous works that did not demonstrate a clear association between self-care and mortality.<sup>4,17,18</sup> Those factors that contributed to the disparities in the results observed between previous studies included limitations in the study design such as time of follow-up, limited sample size, reduced number or terminal events,<sup>5,19</sup> exclusion of significant segments of patients such as individual older than 80 years old<sup>18</sup> or patients with LVEF > 40%,<sup>5,18</sup> or evaluation of self-care using instruments other than EHFSBS.<sup>5,19</sup> Besides, predictive models used in these studies did not include analysis of specific validated dimensions of self-care and were not adequately balanced for important psychosocial determinants of self-care.<sup>4,5,17,18</sup> In contrast with previous research, our study, first, addressed the prognostic effect of self-care on a broad-spectrum real-world cohort of 1123 patients recruited regardless of age or LVEF second, evaluated the prognostic impact of each of the component factors of self-care as described by the developers of the EHFSBS-9<sup>14,15</sup> and third, analysed the effect of self-care in the context of a comprehensive psycho-social evaluation of study participants.<sup>20,21</sup>

We used the EHFSBS-9 to assess self-care. The optimal psychometric properties of the EHFSBS-9 regarding validity and reliability have been recently confirmed in a systematic review.<sup>6,14,15</sup> The factor structure of the EHFSBS-9 was further investigated by the developers of the instrument.<sup>15</sup> They re-evaluated the psychometric properties of the EHFSBS-9 in a large cohort of patients using confirmative factor analysis, factor score determinacy along other metric evaluations. To improve the clinical interpretability of the results obtained with the EHFSBS-9, the developers of the instrument introduced reversion of scores and its standardization from 0 to 100 so that a higher score meant better self-care.<sup>15</sup> In this study, three well-fitting factors with adequate psychometric properties were identified: consulting behaviour, autonomy-based adherence, and provider-based adherence. Upon their findings, the authors suggested that the EHFSBS-9 scores could be used to compute the 3 sub-scales to allow more detailed evaluations and individualized interventions to improve self-care.<sup>15</sup>

The mechanisms behind the effect of self-care behaviour on clinical outcomes have been addressed previously.<sup>4,5,11,19</sup> Briefly, empowered patients with optimal self-maintenance behaviours may be able to effectively self-monitor, and self-manage in response to changes in health status. These behaviours may translate in substantial benefits, for instance, early detection of worsening, prevention of drug-related adverse events, prevention of hospitalization, and achievement of more optimized disease-modifying drug regimes compared to patients with sub-optimal self-care. As a consequence, patients with poor self-care may have an increased risk of disease progression and a higher risk of death. The association between global self-care and outcomes was observed for autonomy-based adherence and

consulting-behaviour; however, it was not confirmed for provider-based adherence (except for its association with CV death when this factor was evaluated as a continuous variable). The item composition of these factors may allow explaining these associations. First, autonomy-based adherence summarizes important self-maintenance actions such as self-weighing every day, fluid restriction, and daily exercise. Likewise, consulting-behaviour summarizes important self-management skills that empower patients to adequately seek help when patients experience worsening of symptoms, develop oedema, or experience rapid weight gain as an indicator of fluid retention. On the other hand, provider-based adherence was not clearly associated with outcomes. Its factor structure (only represented by two items) and its metric properties (ceiling effect)<sup>15</sup> may have compromised the granularity of the information obtained within this factor resulting in a less reliable capture of this particular self-care behaviour.

Our data strongly supports self-care evaluation using the EHFSCBS-9 item questionnaire as a powerful tool to stratify event risk and tailor interventions in patients with HF. Given the association of specific self-care dimensions with hard-endpoints, granular information obtained regarding autonomy-based adherence and consulting behaviour should also become a key element in self-care evaluation in HF managed care. Our study emphasizes the improvements in the follow-up of these patients in different healthcare models. Knowing the consequences of poor self-care in patients with HF can lead to a more intensive attitude at all levels of care in HF programmes, including cardiac rehabilitation programmes, primary care, and HF specialist nurses. The use of this scale in risk stratification and intervention design complements the already described value of this instrument to provide insights on self-care of patients and guide significant educational interventions in patients with chronic HF aimed to modify the clinical course of the disease and improve patient-reported outcomes. Future research is needed to (i) define the complex interplay between self-care, psycho-social determinants and outcomes (clinical and patient-reported), (ii) confirm the prognostic role of self-care in other healthcare (community HF, advanced HF care, home-based care) and socio-cultural contexts, and (iii) continue research focused not only on self-care globally but also on each of its components to individualize patient care.

## **Limitations**

Our study has some limitations by design that need to be commented on. First, self-care was measured only at baseline thus information on self-care trajectories was not available for this analysis. It is likely that some patients may have experienced improvement or deterioration of self-care that were not captured in our study. However, there is data suggesting that self-care tends to be stable over time.<sup>33</sup> Second, self-care was reported by patients and caregivers, thus limitations such as recall may limit the accuracy of the measures of self-care.<sup>34</sup> However, evaluation of the psychometric properties of the scale suggests that the reliability of these measures is optimal.<sup>6</sup> Third, in our study, we have defined poor self-care when patients were in the first tertile of the test score. This cut-off point had not been used in previous studies, among other reasons because this is the first article that has modified the score from 0 to 100 to simplify its understanding. It is reasonable to consider that those patients with a self-care score in the first tertile are patients with poor self-care, and this allows us to easily compare them with those patients with better self-care. And finally, an additional limitation is related to selection bias as this occurs in all studies that based recruitment of samples on specific selection criteria like in our study.

## **Conclusions**

This is the first study that demonstrates that global self-care and specific dimensions of self-care measured with the EHFScBS-9 are significant determinants of long-term all-cause mortality and CV mortality in patients with HF and that these associations are independent of traditional HF prognostic predictors and other important psycho-social determinants. In line with previous studies, we have also shown an independent association between impaired self-

care and HF hospitalization and the combination of these endpoints in patients with chronic HF. Our results give support to the use of global and factor self-care evaluations to allow better stratification of risk of events in patients with HF and guide tailored interventions to improve their self-efficacy.

## Supplementary material

Supplementary material is available at *European Heart Journal – Cardiovascular Pharmacotherapy* online.

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**Conflict of interest:** none declared. [AQ13](#)

## References [AQ14](#) [AQ15](#)

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