



**HAL**  
open science

# Weight telemonitoring of heart failure versus standard of care in a real-world setting: Results on mortality and hospitalizations in a 6-month nationwide matched cohort study

François Roubille, Grégoire Mercier, Guila Lancman, Hélène Pasche, Sarah Alami, Cécile Delval, Antoine Bessou, Jade Vadel, Amayelle Rey, Stéphanie Duret, et al.

## ► To cite this version:

François Roubille, Grégoire Mercier, Guila Lancman, Hélène Pasche, Sarah Alami, et al.. Weight telemonitoring of heart failure versus standard of care in a real-world setting: Results on mortality and hospitalizations in a 6-month nationwide matched cohort study. *European Journal of Heart Failure*, 2024, 26 (5), pp.1201-1214. 10.1002/ejhf.3191 . hal-04495170

**HAL Id: hal-04495170**

**<https://hal.science/hal-04495170v1>**

Submitted on 24 Jul 2024

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

# Weight telemonitoring of heart failure versus standard of care in a real-world setting: Results on mortality and hospitalizations in a 6-month nationwide matched cohort study

François Roubille <sup>1</sup>, Grégoire Mercier <sup>2 3</sup>, Guila Lancman <sup>4</sup>, Hélène Pasche <sup>4</sup>, Sarah Alami <sup>4</sup>, Cécile Delval <sup>4</sup>, Antoine Bessou <sup>5</sup>, Jade Vadel <sup>5</sup>, Amayelle Rey <sup>5</sup>, Stéphanie Duret <sup>5</sup>, Emilie Abraham <sup>5</sup>, Gilles Chatellier<sup># 6 7</sup>, Isabelle Durand Zaleski<sup># 8 9</sup>

<sup>1</sup> Cardiology Department, Hôpital Lapeyronie, PhyMedExp, University of Montpellier, INSERM, CNRS, CHRU, INI-CRT, Montpellier, France.

<sup>2</sup> Economic Evaluation Unit (URME), University Hospital of Montpellier, Montpellier, France.

<sup>3</sup> IDESP, Université de Montpellier, INSERM, Montpellier, France.

<sup>4</sup> Air Liquide Santé International, Bagneux, France.

<sup>5</sup> IQVIA, Courbevoie, France.

<sup>6</sup> Department of Statistics Informatics and Public Health, Université Paris-Cité, Paris, France.

<sup>7</sup> Clinical Research Unit, Groupe Hospitalier Paris Saint Joseph, Paris, France.

<sup>8</sup> Université de Paris, CRESS, INSERM, INRA, URCEco, AP-HP, Hôpital de l'Hôtel Dieu, Paris, France.

<sup>9</sup> Santé Publique Hôpital Henri Mondor, Créteil, France.

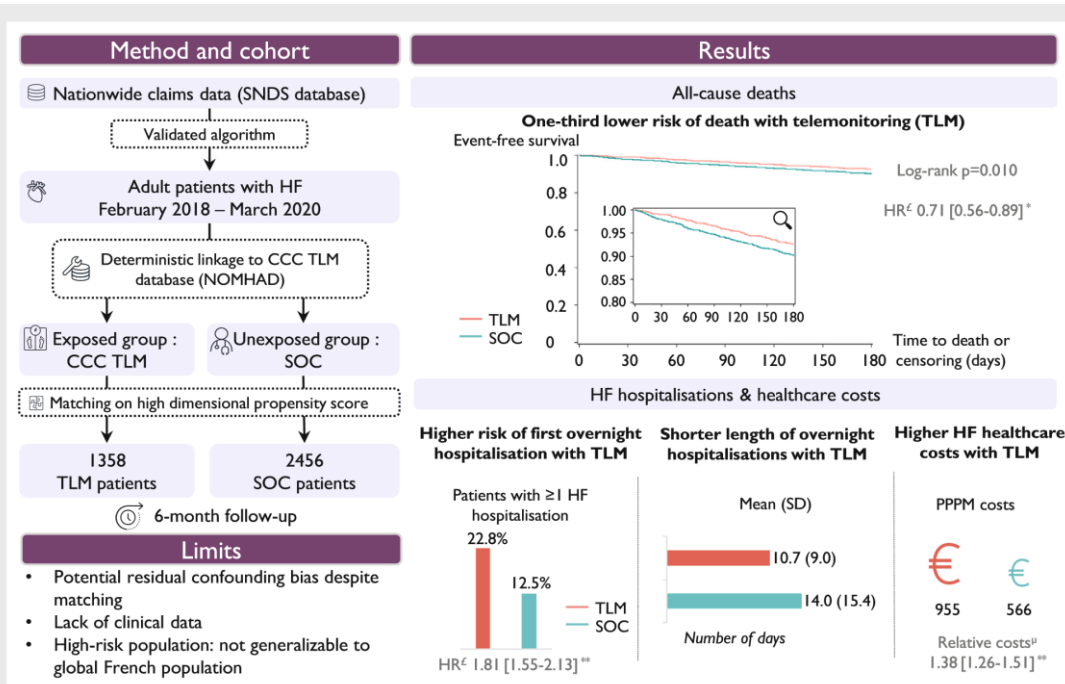
**# Contributed equally.**

## Keywords:

Effectiveness; Heart failure; High-dimensional propensity score; Nationwide; Real-world; Telemonitoring.

\*Corresponding author: Intensive Care Unit, Cardiology Department, University Hospital of Montpellier, 34295 Montpellier, France. Tel: +33 788014136, Email: francois.roubille@gmail.com

† Contributed equally as joint-last authors.



Weight telemonitoring of heart failure versus standard of care in a real-world setting: summary of methods, results on mortality and hospitalizations in a 6-month nationwide matched cohort study. CCC, chronic care connect™; CHF, chronic heart failure; HF, heart failure; SD, standard deviation; SNDS, Système National des Données de Santé; SOC, standard of care; TLM, telemedecine.

## Introduction

Worsening chronic heart failure (HF) is a main cause of hospitalization in Western countries, associated with high morbidity, mortality, and healthcare costs.<sup>1</sup> Repeated and prolonged hospitalizations for HF, often preceded by emergency visits, impair quality of life and result in a significant healthcare system burden. Telemonitoring has emerged as a potential and promising tool to address this challenge. For HF, symptoms and weight can be collected frequently with a non-invasive device to guide patients in maintaining quality of care, optimize rapid access to care, and improve clinical and economic outcomes.<sup>1</sup>

Inconsistent results from randomized controlled trials and observational studies of the medical and economic benefits of non-invasive<sup>2,3</sup> or invasive<sup>4</sup> telemonitoring in HF have led to a weak (class IIb, level of evidence B) recommendation for telemonitoring in the 2021 European Society of Cardiology guidelines.<sup>1,5</sup> The cost of invasive devices and differences in monitoring quality and

methods may explain some of the inconsistencies.<sup>6</sup> In addition, the pathogenesis of HF deterioration can influence the impact of telemonitoring, as has been reported for patients with unstable HF and a recent HF hospitalization, who were at greater risk for a recurrent event.<sup>6</sup>

In 2018, in France, the ETAPES nationwide programme (Experiments in Telemedicine for Improved Patient Pathways) was launched to evaluate the efficiency of telemonitoring in HF patients.<sup>7</sup> Chronic Care Connect™ (CCC), launched in 2017 by CDM e-Health (Air Liquide Healthcare), is among the non-invasive telemonitoring solutions implemented as part of the ETAPES programme (programme details are available in online supplementary *Method S1*).

To gain further evidence on the role of non-invasive telemonitoring in HF management, the objective of this nationwide cohort study was to evaluate the CCC telemonitoring solution compared

with standard of care (SOC) in patients with HF in terms of mortality, HF hospitalizations, and associated costs during a 6-month follow-up.

## Methods

### Study design and data sources

This study was a real-world, comparative, nationwide retrospective cohort study of patients with HF, using the *Système National des Données de Santé* (SNDS). The SNDS, which has been described elsewhere, is the largest claims database in France, covering >99% of the French population.<sup>8,9</sup> It contains individual data for all healthcare expenditures reimbursed by the French National Health Insurance (NHI) fund (French acronym *Caisse Nationale d'Assurance Maladie*, CNAM), with a unique and anonymous identifier for each patient. The SNDS contains socio-demographic data (age, sex, and region), and all healthcare expenses, including outpatient visits, medications, medical procedures, laboratory tests, hospital admissions and procedures, but clinical and biological information are not recorded in SNDS. SNDS also provides registration status from long-term diseases (LTD), defined as potentially life-threatening or disabling diseases requiring regular, costly, long-term care. LTD coverage status guarantees 100% reimbursement for healthcare expenditures related to the LTD for at least 5 years.<sup>10</sup> Online supplementary *Figure S1* describes the various databases included in the SNDS.

To correctly identify HF patients exposed to telemonitoring, a deterministic linkage of the medical registry data from the CCC telemonitoring solution, NOMHAD database, and SNDS was performed. The NOMHAD database contains personal and medical data on HF patients specifically telemonitored by the CCC solution (such as daily body weight, type of HF, symptoms), described in detail in online supplementary *Method S2*.

## Description of the Chronic Care Connect™ intervention

Chronic Care Connect™ is a telemonitoring solution for HF management, consisting of a connected scale for daily weight collection and a mobile application for recording of HF symptoms.<sup>11</sup> Input from patients is remotely processed during working hours 5 days a week. Weight gain of  $\geq 3$  kg in 2 days or  $\geq 2$  kg in 5 days generate an alert, as does worsening of at least three symptoms (nocturnal dyspnoea, orthopnoea, cough, oedema, or fatigue) on the same day or at least two symptoms on three consecutive days.<sup>12</sup> One of the CCC's unique features is integration of a new, non-hospital-based stakeholder: a monitoring centre with nurses who are specially trained in HF and telemonitoring and who initially screen incoming alerts.<sup>11</sup> If the alert is regarded as clinically relevant, nurses contact the cardiology department to get involved immediately for the most appropriate medical intervention: urgent teleconsultation, or face-to-face consultation usually ending with diuretic dose adjustment, therapy escalation, or programmed hospitalization. Finally, nurses carry out therapeutic support for patients over the phone, focusing on explaining symptoms and signs of decompensation, the importance of a low-salt diet, physical activity and adherence to medical treatment.

The CCC telemonitoring solution is generally prescribed by a cardiologist or a general practitioner for a 6-month renewable period. The cost of CCC telemonitoring was similar to the cost of other telemonitoring solutions implemented as part of ETAPES for patients with chronic HF. Tariffs were fixed by French authorities for the entire

duration of the programme and corresponded to a care package costing €470 for 6 months. This amount covered €300 for the supplier, €110 for the cardiologist, and €60 for therapeutic support.<sup>7</sup> A description of the CCC telemonitoring strategy is provided in online supplementary *Method S3*.

## Population and study period

Inclusion criteria for the ETAPES programme were worsening chronic HF hospitalization in <30 days prior to reimbursement for a telemonitoring solution or a hospitalization in the last year combined with biologic markers indicating decompensated and poorly controlled HF (online supplementary *Method S1*).<sup>7</sup>

In this study, patients were included from 1 February 2018 to 22 March 2020, if they met the following criteria: (i) age 18 years or more, and (ii) a diagnosis of HF, identified with a validated algorithm developed by the NHI (online supplementary *Method S4*).<sup>13,14</sup> The resulting cohort of patients with HF was stratified into two groups: a telemonitoring group, with patients exposed to the CCC telemonitoring solution within the inclusion period; and the SOC group, comprising a sample of HF patients directly identified in SNDS from a 10% representative sample of HF patients who did not benefit from any telemonitoring (with CCC or any other available solutions).

For telemonitored patients, the index date was defined as the start date of telemonitoring within the inclusion period. For SOC patients, the index date was randomly assigned within the inclusion period, using the index date of a patient from the telemonitoring group who had a similar history of HF (HF hospitalization date and type, or LTD date). SOC patients who did not have any HF hospitalization or LTD date close to at least one telemonitored patient were not included in the SOC group. Patients on chronic dialysis and patients living in a medico-social centre on the index date were excluded from both groups.

A 5-year historical period was used to identify each patient's medical history and comorbidities (including chronic HF). All patients were followed from the index date until the theoretical end of the CCC telemonitoring renewable care package (6 months) or until death, whichever occurred first.

## High-dimensional propensity score matching

To ensure comparability between the telemonitoring and SOC groups, and limit a potential indication bias, groups were matched through a high-dimensional propensity score (hdPS) calculated for each patient. This score reflects the probability that a patient benefits from CCC telemonitoring versus no telemonitoring at all, adjusted for potential confounders.<sup>15</sup> The hdPS was estimated with a logistic regression adjusted for both predefined covariates (listed below) and empirical covariates selected using a data-driven analytic approach (hdPS algorithm). Previous work has shown that covariates empirically selected by the hdPS algorithm improve model performance in comparative studies using SNDS data.<sup>16,17</sup> The selection process of the covariates included in the hdPS and their characteristics are detailed in online supplementary *Method S5*. Predefined covariates were age, gender, the French social deprivation index,<sup>18,19</sup> year and quarter of inclusion to account for HF seasonality, density of general practitioners and cardiologists in the department of residence, cardiac implant (defibrillator/pacemaker) status, time between the last HF hospitalization and the index date (30 days or less and 30 days–1 year), medical history and comorbidities, HF-related drugs (online supplementary *Method S6*), and risk of HF rehospitalization. Risk of HF rehospitalization was used as a proxy

of HF severity and defined from a previous work on HF conducted using the SNDS database.<sup>20</sup> Four categories of HF rehospitalization risk were determined: low (no hospitalization within 36 months prior to the index date), medium (no hospitalization within 12 months and  $\geq 1$  hospitalization between 12 and 36 months prior to the index date), high (one hospitalization within 12 months prior to the index date), and very high ( $\geq 2$  hospitalizations within 12 months prior to the index date).

Patients from the telemonitoring group were then matched with up to two patients from the SOC group based on their hdPS, without replacement, using the Greedy nearest neighbour method with a calliper of 0.20.<sup>21–23</sup> This variable matching ratio (1:2) has been used to increase precision at a small cost bias.<sup>24</sup>

## Study outcomes

The outcomes of interest were all-cause death as a clinical outcome and overnight HF hospitalizations (defined as any HF-related stay of one night or more at the hospital) and all-cause emergency department (ED) visits (whether resulting in HF-related hospitalization or not) as healthcare resource use outcomes. As planned and unplanned hospitalizations cannot be distinguished in the SNDS database, one-day hospitalizations (usually planned hospitalizations) and ED visits before hospitalization (suggesting unplanned hospitalizations) were also described. HF hospitalizations were identified by International Classification of Diseases, tenth revision (ICD-10) codes, as detailed in online supplementary *Method S4*. The cost associated with HF healthcare also was derived, comprising amounts reimbursed for hospital and ambulatory care potentially related to HF management during the follow-up period. Hospital care included hospitalizations with an ICD-10 code for HF (online supplementary *Method S4*) or with HF-related medical device implantation, rehabilitation care following HF hospitalization, and outpatient cardiologist visits. Ambulatory care included consultations with general practitioners and cardiologists, physiotherapy sessions or nursing procedures, HF-related laboratory tests (i.e. creatininaemia, haemogram, ionogram, natriuretic peptides), HF-related medical procedures (i.e. electrocardiogram, echocardiogram, exercise test, cardioversion), and HF-related drugs dispensed in retail pharmacies (online supplementary *Method S6*).

## Statistical analyses

### Baseline characteristics

Patient characteristics (i.e. sociodemographic data, comorbidities, HF features and treatments) at the index date were described before and after hdPS matching. Quantitative variables were reported as mean  $\pm$  standard deviation or median  $\pm$  interquartile range (IQR), and categorical variables as number and percentage. Depending on the variables being considered, Chi-squared or Wilcoxon tests were used to compare the telemonitoring and SOC groups.

### Modelling

For the risk of all-cause death, first overnight HF hospitalization, and first all-cause ED visit occurrence, hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using a Cox proportional hazards regression. Kaplan–Meier survival curves with log-rank tests were also assessed. Regarding the number and cumulative duration of overnight HF hospitalizations, incidence rate ratios and their 95% CIs were estimated using a generalized linear model with negative binomial regression, including the duration of follow-up as an offset variable. Finally, costs associated with HF management were described per patient per

month to account for differences in follow-up time (due to death censoring). A generalized linear model with gamma distribution and log link function was used to estimate relative costs and their 95% CIs. All models were adjusted for covariates that remained unbalanced after hdPS matching, defined as a standardized mean difference (SMD)  $> 10\%$ .<sup>22</sup>

### Stratification

All outcomes of interest were analysed in the following prespecified subgroups: age (18–54, 55–64, 65–74, 75–84, and  $\geq 85$  years), presence of diabetes and/or chronic respiratory diseases, time between the last HF hospitalization and the index date, and the risk of HF rehospitalization.



## Telemonitoring adherence analysis

For the telemonitoring group, we conducted an exploratory analysis on the risk of first overnight HF hospitalization and of all-cause death according to each patient's adherence to body weight measurement, using Kaplan–Meier survival curves and log-rank tests. Telemonitoring adherence was calculated as the number of daily body weights registered into the system divided by expected entries. The expected entries corresponded to the frequency of weighing prescribed by the physician minus the number of days allowed without weighing (including hospitalizations, holidays, death before the end of follow-up). Telemonitored patients with missing weights or weighting prescription data were excluded from this analysis, as were their hdPS matches from the SOC group. Three categories were defined according to terciles of adherence: low (<66.9%), medium (66.9% to 91.3%), and high (>91.3%).<sup>2,25,26</sup>

## Sensitivity analysis

A sensitivity analysis using the hdPS inverse probability of treatment weights (IPTW) was performed on all patients meeting selection criteria, including those excluded after hdPS-matching.<sup>27–29</sup>

All statistical analyses and graphical representations were conducted using SAS<sup>®</sup> Enterprise Guide version 7.15 (SAS Institute, Cary, NC, USA). For all analyses, a 0.05 threshold was used for significance.

## Ethics

In accordance with the French medical data privacy laws, both the Comité Ethique et Scientifique pour les Recherches, les Etudes et les Evaluations dans le domaine de la Santé (CESREES; file number 2821727bis) and the Commission Nationale de l'Informatique et des Libertés (CNIL; file number DR-2021-105) approved this study. All CCC patients were informed of the present study and were given the opportunity to opt out of the use of their data. Concerning patients and data issued from the SNDS database, the French NHI fund, as data controller, is responsible for patient information, and no informed consent was required because these data are anonymous.

## Results

### Patients

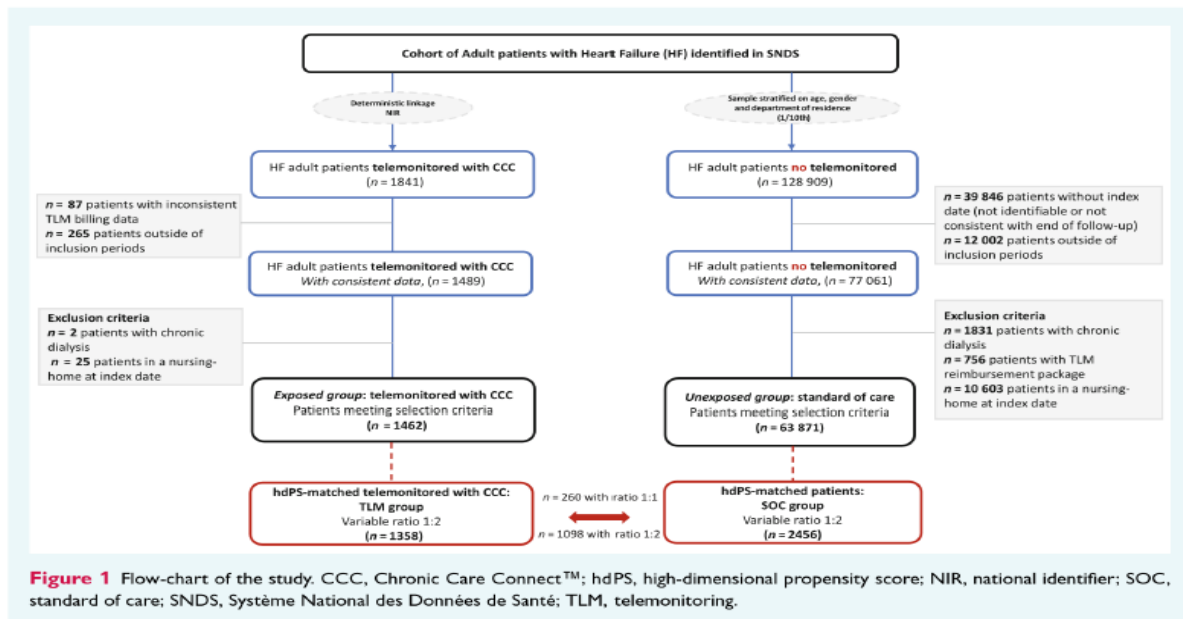
From 1 February 2018 to 22 March 2020, a total of 1462 HF patients using CCC telemonitoring were selected, along with 63 871 HF patients with no reimbursement for any telemonitoring for the SOC group. Ultimately, 1358 telemonitored patients were hdPS-matched to 2456 SOC patients (81% with a 1:2 ratio,  $n = 1098$ ; 19% with a 1:1 ratio,  $n = 260$ ) (Figure 1).

Prior to matching, patient baseline characteristics differed between the telemonitoring and SOC groups. Telemonitored patients were younger (mean age 70.4 vs. 78.5 years for the SOC group), less likely to be female (27.4% vs. 51.8%), and at a higher risk of HF rehospitalization (Table 1). HdPS matching balanced baseline characteristics between the two groups (SMD <0.10), with a satisfying overlap (online supplementary Figures S2–S4), yet the proportion with a cardiac device remained unbalanced (40.9% for telemonitoring vs. 33.3% for SOC; SMD –0.18). After matching, in both groups, the mean age of patients was about 71 years, and less than one-third of patients were women. More than 80% of patients were at high or very high risk of HF rehospitalization, and about half of the patients had a hospitalization for HF within 30 days before the index date. The median time between the last HF hospitalization and index date was 17.0 (IQR: 7.0–66.0) days for the telemonitoring group and 27.0 (IQR: 15.0–70.0) days for the SOC group.

### Clinical outcomes

#### All-cause death

At the end of the 6-month follow-up, the all-cause death rate in the telemonitoring (7.4%) and SOC (9.9%) groups differed significantly ( $p = 0.011$ ). Compared with SOC, telemonitoring was associated with a 29% lower risk of death (HR 0.71, 95% CI 0.56–0.89,  $p = 0.003$ ) (Table 2). Survival curves are presented in Figure 2A.



**Figure 1** Flow-chart of the study. CCC, Chronic Care Connect™; hdPS, high-dimensional propensity score; NIR, national identifier; SOC, standard of care; SNDS, Système National des Données de Santé; TLM, telemonitoring.

## Heart failure hospitalizations and emergency department visits

Heart failure hospitalization outcomes are shown in *Table 2*. Within the 6-month follow-up, 582 HF hospitalizations occurred in the telemonitoring group and 460 in the SOC group. The proportion of patients hospitalized at least once for HF, regardless of the duration of stay, was significantly greater in the telemonitoring group (27.2%,  $n = 369$ ) than in the SOC group (12.9%,  $n = 316$ ;  $p < 0.001$ ). The proportion of patients with at least one overnight HF hospitalization was also significantly greater in the telemonitoring group (22.8%,  $n = 309$ ) than in the SOC group (12.5%,  $n = 306$ ;  $p < 0.001$ ). Furthermore, telemonitoring was associated with a higher risk of first overnight HF hospitalization in comparison with SOC (HR 1.81, 95% CI 1.55–2.13,  $p < 0.001$ ). Survival curves are presented in *Figure 2B*.

The average (standard deviation) length of overnight HF hospitalization, however, was significantly lower in the telemonitoring group than in the SOC group, at 10.7 (9.0) versus 14.0 (15.4) days ( $p < 0.001$ ), respectively. The proportion of overnight HF hospitalizations following an ED visit was also significantly lower in the telemonitoring group (49.9%, 236 hospitalizations out of 473 stays) compared with the SOC group (68.8%, 304 out of 442;  $p < 0.001$ ).

Telemonitoring was associated with a higher proportion of one-day HF hospitalizations among all HF hospitalizations (18.7%, 109 hospitalizations) than SOC (3.9%, 18 hospitalizations;  $p < 0.001$ ).

**Table 1** Baseline characteristics of included patients, before and after matching on high-dimensional propensity score

	Before hdPS matching				After hdPS matching			
	TLM (n = 1462)	SOC (n = 63 871)	SMD	p-value	TLM (n = 1358)	SOC (n = 2456)	SMD	p-value
Age (years), mean (SD)	70.4 (13.0)	78.5 (13.1)	-0.62	<0.001 <sup>c</sup>	71.0 (12.9)	71.7 (14.2)	-0.06	0.015 <sup>c</sup>
Female sex, n (%)	400 (27.4)	33 085 (51.8)	-0.52	<0.001 <sup>d</sup>	389 (28.6)	740 (30.1)	-0.03	0.335 <sup>d</sup>
Risk of HF rehospitalization <sup>a</sup> , n (%)				<0.001 <sup>d</sup>				0.981 <sup>d</sup>
Low	206 (14.1)	28 236 (44.2)	0.70		202 (14.9)	359 (14.6)	-0.01	
Medium	53 (3.6)	7850 (12.3)	0.32		53 (3.9)	102 (4.2)	0.01	
High	743 (50.8)	22 230 (34.8)	-0.33		705 (51.9)	1278 (52.0)	0.00	
Very high	460 (31.5)	5555 (8.7)	-0.59		398 (29.3)	717 (29.2)	0.00	
Time interval between index date and last HF hospitalization <sup>b</sup> , median (IQR)	16.0 (7.0–63.5)	76.0 (25.0–609.0)		<0.001 <sup>c</sup>	17.0 (7.0–66.0)	27.0 (15.0–70.0)		<0.001 <sup>c</sup>
Time interval between index date and last HF hospitalization, n (%)				<0.001 <sup>d</sup>				0.095 <sup>d</sup>
≤30 days	797 (54.5)	12 505 (19.6)	-0.78		720 (53.0)	1224 (49.8)	-0.07	
>30 days–1 year	406 (27.8)	15 280 (23.9)	-0.09		383 (28.2)	771 (31.4)	0.07	
Other (>1 year or no hospitalization)	259 (17.7)	36 086 (56.5)	0.88		255 (18.8)	461 (18.8)	0.00	
Cardiovascular comorbidities, n (%)								
Atrial fibrillation	930 (63.6)	32 649 (51.1)	-0.25	<0.001 <sup>d</sup>	859 (63.3)	1582 (64.4)	0.02	0.476 <sup>d</sup>
Coronary artery disease	845 (57.8)	25 509 (39.9)	-0.36	<0.001 <sup>d</sup>	770 (56.7)	1453 (59.2)	0.05	0.140 <sup>d</sup>
Hypolipemic treatment	777 (53.1)	26 950 (42.2)	-0.22	<0.001 <sup>d</sup>	717 (52.8)	1297 (52.8)	0.00	0.995 <sup>d</sup>
Other comorbidities, n (%)								
Sleep apnoea	296 (20.2)	6781 (10.6)	-0.27	<0.001 <sup>d</sup>	262 (19.3)	463 (18.9)	-0.01	0.740 <sup>d</sup>
Cancer	295 (20.2)	12 992 (20.3)	0.00	0.878 <sup>d</sup>	282 (20.8)	519 (21.1)	0.01	0.790 <sup>d</sup>
Diabetes	509 (34.8)	19 008 (29.8)	-0.11	<0.001 <sup>d</sup>	475 (35.0)	857 (34.9)	0.00	0.959 <sup>d</sup>
Moderate to terminal chronic renal failure (excluding dialysis)	499 (34.1)	16 131 (25.3)	-0.20	<0.001 <sup>d</sup>	467 (34.4)	743 (30.3)	-0.09	0.009 <sup>d</sup>
Hepatic diseases	171 (11.7)	4762 (7.5)	-0.14	<0.001 <sup>d</sup>	147 (10.8)	289 (11.8)	0.03	0.379 <sup>d</sup>
Chronic respiratory diseases (except cystic fibrosis)	398 (27.2)	18 523 (29.0)	0.04	0.136 <sup>d</sup>	372 (27.4)	667 (27.2)	-0.01	0.876 <sup>d</sup>
Thyroid disorders	283 (19.4)	12 585 (19.7)	0.01	0.741 <sup>d</sup>	261 (19.2)	484 (19.7)	0.01	0.716 <sup>d</sup>
Neurotic and mood disorders	48 (3.3)	2973 (4.7)	0.07	0.009 <sup>d</sup>	43 (3.2)	74 (3.0)	-0.01	0.793 <sup>d</sup>
Cardiovascular treatments, n (%)								
Cardiac defibrillator/stimulator	638 (43.6)	9706 (15.2)	-0.66	<0.001 <sup>d</sup>	556 (40.9)	819 (33.3)	-0.18	<0.001 <sup>d</sup>
Angiotensin II receptor blockers	341 (23.3)	11 803 (18.5)	-0.12	<0.001 <sup>d</sup>	311 (22.9)	636 (25.9)	0.07	0.040 <sup>d</sup>
Platelet aggregation inhibitors	476 (32.6)	20 647 (32.3)	0.00	0.851 <sup>d</sup>	439 (32.3)	832 (33.9)	0.03	0.331 <sup>d</sup>
Anti-arrhythmic	307 (21.0)	8616 (13.5)	-0.20	<0.001 <sup>d</sup>	275 (20.3)	486 (19.8)	-0.01	0.733 <sup>d</sup>
Oral anticoagulants	760 (52.0)	25 585 (40.1)	-0.24	<0.001 <sup>d</sup>	694 (51.1)	1268 (51.6)	0.01	0.756 <sup>d</sup>
Beta blockers	866 (59.2)	32 229 (50.5)	-0.18	<0.001 <sup>d</sup>	793 (58.4)	1489 (60.6)	0.05	0.178 <sup>d</sup>
Digoxin	26 (1.8)	2477 (3.9)	0.13	<0.001 <sup>d</sup>	26 (1.9)	48 (2.0)	0.00	0.932 <sup>d</sup>
Angiotensin-converting enzyme inhibitors	389 (26.6)	16 788 (26.3)	-0.01	0.782 <sup>d</sup>	367 (27.0)	685 (27.9)	0.02	0.566 <sup>d</sup>
Ivabradine	49 (3.4)	863 (1.4)	-0.13	<0.001 <sup>d</sup>	39 (2.9)	96 (3.9)	0.07	0.092 <sup>d</sup>
Diuretics	1101 (75.3)	36 781 (57.6)	-0.38	<0.001 <sup>d</sup>	1008 (74.2)	1864 (75.9)	0.04	0.253 <sup>d</sup>

hdPS, high-dimensional propensity score; HF, heart failure; IQR, interquartile range; SD, standard deviation; SMD, standardized mean difference; SOC, standard of care; TLM, telemonitoring.

<sup>a</sup>Risk of HF rehospitalization: low (no hospitalization within 36 months prior to the index date), medium (no hospitalization within 12 months and ≥1 between 12 and 36 months prior to the index date), high (one hospitalization within 12 months prior to the index date) and very high (≥2 hospitalizations within 12 months prior to the index date).

<sup>b</sup>Quantitative metrics related to time interval between index date and last HF hospitalization were calculated only for patients with at least one previous HF hospitalization, corresponding to: before matching, 1276 and 40 718 patients for TLM and SOC group, respectively; after matching, 1176 and 2123 patients for TLM and SOC group, respectively.

<sup>c</sup>Wilcoxon test.

<sup>d</sup> $\chi^2$  test.

## Costs associated with heart failure management

Telemonitoring was associated with higher per patient per month HF healthcare costs than SOC (relative costs 1.38, 95% CI 1.26–1.51,  $p < 0.001$ ). Including the cost of telemonitoring (€470 per patient per semester), the total per patient per month costs were €955 in the telemonitoring group versus €566 in the SOC

group. The difference was driven by higher hospital costs in the telemonitoring group (72% of total costs vs. 59% of total costs for the SOC group) (Table 3).

## Stratification analyses

Overall, results of the subgroup analyses were consistent with the general analyses (online supplementary Figure S5). Among

patients at high or very high risk of rehospitalization for HF, telemonitoring was associated with a significant lower risk of death (high risk: HR 0.69, 95% CI 0.49–0.99; very high risk: HR 0.68, 95% CI 0.48–0.96). Likewise, the risk of death was significantly lower among patients who had HF hospitalization within 30 days before the index date (HR 0.60, 95% CI 0.45–0.82) or who had comorbidities (diabetes/chronic respiratory diseases, HR 0.65, 95% CI 0.48–0.88).

In addition, compared with SOC, telemonitoring was associated with a significant lower risk of all-cause ED visits among patients at high risk of rehospitalization or with HF hospitalization within 30 days before the index date or with comorbidities. Healthcare costs according to subgroups are presented in online supplementary Figure S6.

## Adherence to telemonitoring

Adherence to telemonitoring was estimated among the 1154 patients with available information, corresponding to 2076 matched patients of the SOC group, which represented 85% of the study cohort. Patient characteristics are detailed by adherence level category in online supplementary Table S1.

Death rates were significantly lower for highly adherent patients (4.9% vs. 9.1% for medium and low adherence,  $p < 0.001$ ). Likewise,

**Table 2** Outcomes at 6-month follow-up in high-dimensional propensity score-matched groups

	TLM (n = 1358)	SOC (n = 2456)	p-value	HR/IRR (95% CI)	p-value
<b>All-cause death</b>					
Patients with event, n (%)	101 (7.4)	242 (9.9)	0.011 <sup>a</sup>	HR 0.71 (0.56–0.89)	0.003 <sup>c</sup>
Time to event (days), mean ± SD	93.7 ± 50.5	84.9 ± 53.6	0.145 <sup>b</sup>		
<b>HF hospitalizations (all duration)</b>					
Total number of stays, n	582	460			
Number of events per patient, mean ± SD	0.4 ± 0.9	0.2 ± 0.6	<0.001 <sup>b</sup>		
Patients with ≥1 event, n (%)	369 (27.2)	316 (12.9)	<0.001 <sup>a</sup>		
<b>Overnight HF hospitalizations</b>					
Total number of stays, n (%)	473 (81.3)	442 (96.1)	<0.001 <sup>a</sup>		
Length of stay (days), mean ± SD	10.7 ± 9.0	14.0 ± 15.4	<0.001 <sup>b</sup>		
Stays following an ED visit, n (%)	236 (49.9)	304 (68.8)	<0.001 <sup>a</sup>		
Number of events per patient, mean ± SD	0.4 ± 0.8	0.2 ± 0.6	<0.001 <sup>b</sup>	IRR 1.82 (1.59–2.07)	<0.001 <sup>d</sup>
Patients with ≥1 event, n (%)	309 (22.8)	306 (12.5)	<0.001 <sup>a</sup>	HR 1.81 (1.55–2.13)	<0.001 <sup>c</sup>
Time to first event (days), mean ± SD	66.9 ± 51.2	60.8 ± 50.7	0.103 <sup>b</sup>		
Cumulative duration per patient (days), mean ± SD	16.4 ± 15.2	20.3 ± 20.5	0.018 <sup>b</sup>	IRR 0.75 (0.73–0.78)	<0.001 <sup>d</sup>
<b>One-day HF hospitalizations</b>					
Total number of stays, n (%)	109 (18.7)	18 (3.9)	<0.001 <sup>a</sup>		
Number of events per patient, mean ± SD	0.1 ± 0.4	0.01 ± 0.09	<0.001 <sup>b</sup>		
Patients with ≥1 event, n (%)	93 (6.8)	18 (0.7)	<0.001 <sup>a</sup>		
<b>All-cause ED visits</b>					
Number of events per patient, mean ± SD	0.6 ± 1.1	0.6 ± 1.0	0.577 <sup>b</sup>	IRR 0.96 (0.88–1.05)	0.369 <sup>d</sup>
Patients with ≥1 event, n (%)	453 (33.4)	845 (34.4)	0.513 <sup>a</sup>	HR 0.93 (0.83–1.05)	0.234 <sup>c</sup>
Time to first event (days), mean ± SD	70.7 ± 52.1	66.7 ± 52.4	0.127 <sup>b</sup>		

CI, confidence interval; ED, emergency department; HF, heart failure; HR, hazard ratio; IRR, incidence rate ratio; SD, standard deviation; SOC, standard of care; TLM, telemonitoring.

<sup>a</sup> $\chi^2$  test.

<sup>b</sup>Wilcoxon test.

<sup>c</sup>Multivariate Cox regression model.

<sup>d</sup>Multivariate negative binomial regression model.

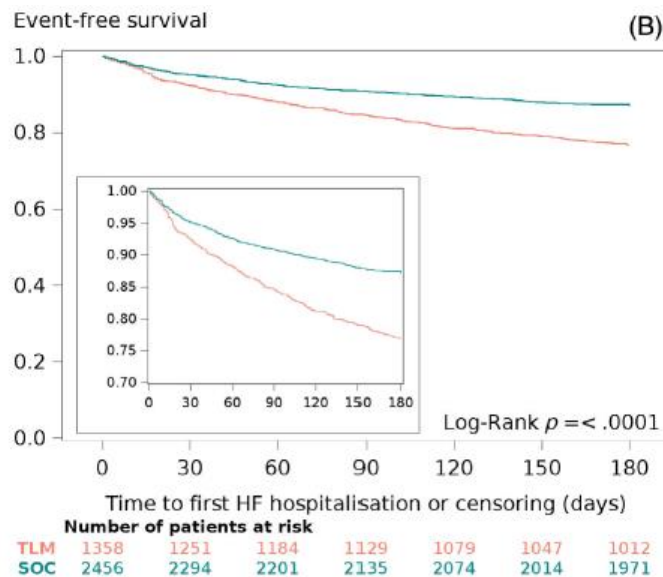
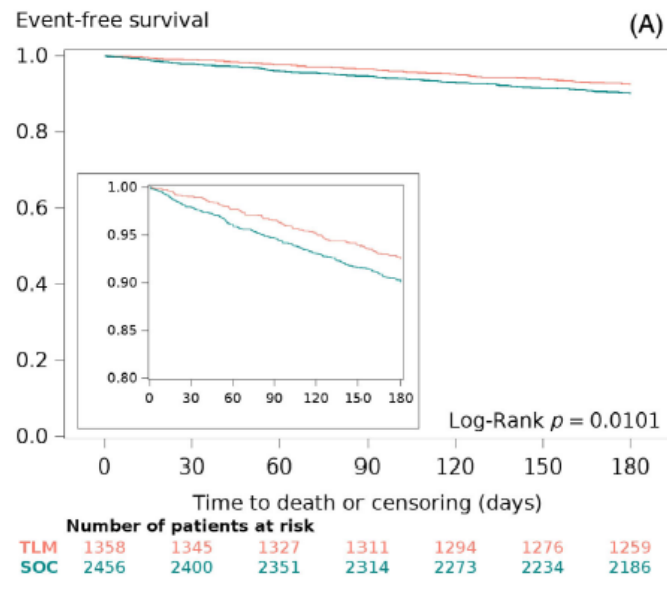
overnight HF hospitalization rates were significantly lower for highly adherent patients (17.5% vs. 24.5% for medium and low adherence,  $p < 0.001$ ) (online supplementary Table S1). Survival curves are presented in Figure 3.

## Sensitivity analyses

Patient characteristics at baseline for the telemonitoring and SOC groups before and after using IPTW method are detailed in online supplementary Table S2. Regarding statistical models, the sensitivity analyses provided consistent results (online supplementary Figure S7). Telemonitoring was associated with a significant lower risk of death (HR 0.68, 95% CI 0.53–0.86) and a significant higher risk of first HF hospitalization (HR 1.81, 95% CI 1.56–2.10) than SOC. The risk of a first all-cause ED visit did not differ significantly between the two groups.

## Discussion

In this French nationwide real-world cohort study, compared with SOC, a non-invasive telemonitoring solution (CCC) was associated with significantly lower all-cause mortality but with a higher risk of first HF hospitalization and higher healthcare costs after an observation period of 6 months (Graphical Abstract).



**Figure 2** Kaplan–Meier curves for all-cause death (A) and first heart failure (HF) hospitalization (B) at 6-month follow-up by group (telemonitoring [TLM] group,  $n = 1358$ ; standard of care [SOC] group,  $n = 2456$ ). The box in the left back side represents the figure with a truncated Y-axis.

## Weight and symptom-based telemonitoring in high-risk patients: reduced mortality but with more hospitalizations for heart failure

Largely because of the ETAPES programme inclusion criteria, half of patients in this study were included in the first 30 days

following a HF-related hospitalization, in the most vulnerable early post-discharge phase.<sup>7</sup> The results observed in this study thus should be considered in the context of high-risk patients, with high event rates and mortality risk.<sup>30</sup> The current findings might have been different in truly stable chronic HF patients, as the greatest telemonitoring-related results have been observed in patients with

severe HF according to New York Heart Association (NYHA) class.<sup>2,6</sup>

Given the nature of our patient management intervention, high-risk patients telemonitored with CCC would be expected to have more frequent contacts with healthcare professionals, leading to closer and more intense management. Indeed, the telemonitoring group had higher rates of 1-day hospitalizations and direct HF hospitalizations without a preceding ED visit, suggesting more planned hospitalizations for these patients. This factor could have limited worsening of their condition before hospitalization and improved prognosis in comparison with SOC patients. Hospitalization, especially of short duration, may reflect early detection of problems and good care rather than an adverse outcome.<sup>31</sup> This possibility is in line with the shorter average length of hospitalizations in the telemonitoring group, as others also have

mentioned.<sup>32</sup> Without this intensive management, cardiac decompensation in SOC patients in the current study might have gone undetected or been detected at such an advanced stage that death was not preventable.<sup>31</sup> In this way, CCC-induced management may have gone hand in hand with better survival among the telemonitored patients. Other studies have reported lower mortality risk with a non-invasive telemonitoring solution based on weight measurement or on multiparameter telemonitoring, compared with SOC.<sup>12,25,33</sup> A smaller trial comparing three groups, including a multiparameter telemonitoring solution and usual care in HF patients, showed concordant results. In that work, 426 patients with a recent admission for HF and left ventricular ejection fraction <40% were assigned randomly to a HF telemonitoring system (twice-daily patient self-measurement of weight, blood pressure, heart rate, and rhythm with automated devices linked to a cardiology centre),



**Table 3** Healthcare costs associated with heart failure management at 6-month follow-up in high-dimensional propensity score-matched groups

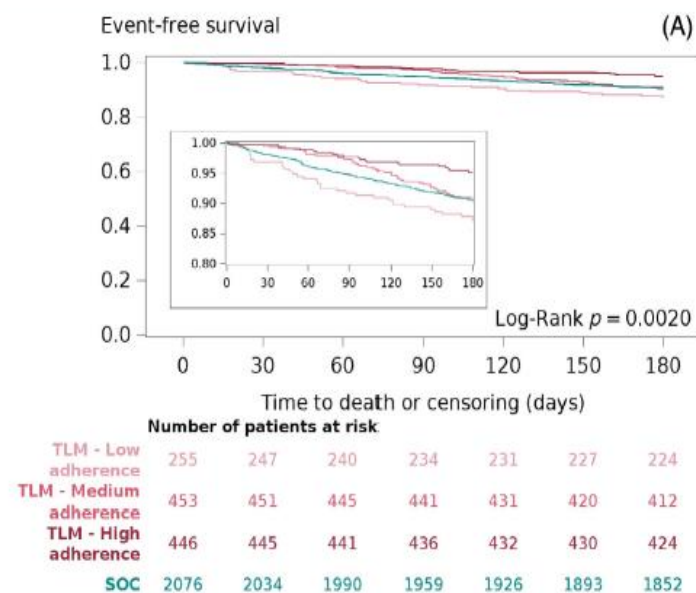
Category	PPPM costs (€)			Relative costs (95% CI) <sup>a</sup>
	TLM (n = 1358)	SOC (n = 2456)	TLM – SOC	
Total costs including telemonitoring solution cost	955	566	+389	1.38 (1.26–1.51) p < 0.001
Total costs excl. telemonitoring solution cost	873 (100%)	566 (100%)	+307	
Hospital costs	626 (72%)	333 (59%)	+294	
HF-related hospitalization				
One-day hospitalizations excluding high-cost drugs and medical devices	10	1	+9	
Overnight hospitalizations excluding high-cost drugs and medical devices	358	204	+154	
Other diagnosis-related hospitalization with HF-related medical device implantation	142	68	+74	
High-cost HF-related medical devices <sup>b</sup>	24	20	+4	
Hospital costs not directly related to HF <sup>b</sup>				
Other high-cost medical devices	52	20	+32	
High-cost drugs	11	5	+6	
Hospitalization in rehabilitation care following hospitalization for HF	23	13	+10	
Outpatient cardiologist visits (± medical procedures)	6	2	+4	
Ambulatory costs	241 (28%)	228 (40%)	+13	
Total physician visits	19	19	0	
General practitioner visits	17	17	0	
Cardiologist visits	2	2	0	
Total other health professional visits	111	128	-17	
Nurse acts and visits	94	110	-16	
Physiotherapist acts and visits	17	18	-1	
Other ambulatory costs	111	81	+30	
HF-related drugs (retail pharmacies)	87	63	+24	
HF-related laboratory tests	17	10	+7	
HF-related medical acts	7	8	-1	
Other costs	6 (0%)	5 (1%)	+1	
Medical transport <sup>c</sup>	6	5	+1	

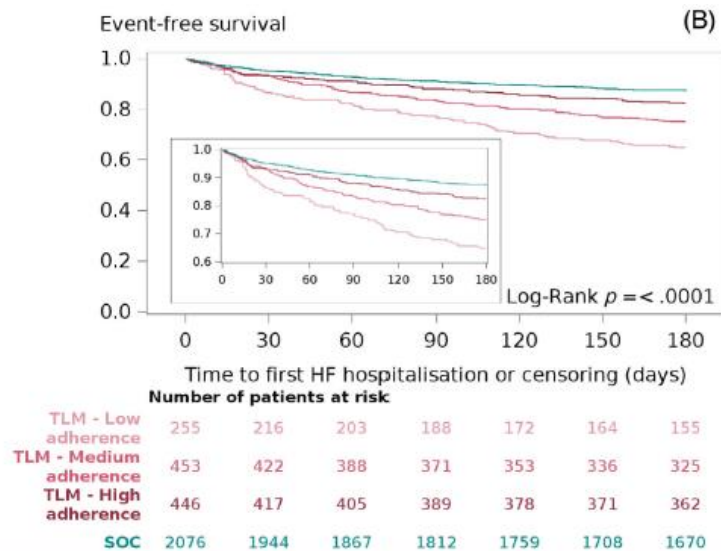
HF, heart failure; PPPM, per patient per month; TLM, telemonitoring; SOC, standard of care.

<sup>a</sup>Multivariate gamma model comparing PPPM costs, excluding hospital costs not directly related to HF.

<sup>b</sup>Within HF-related hospitalizations, i.e. with HF diagnosis or for HF-related medical device implantation.

<sup>c</sup>Occurring the same day as a cardiologist visit or as HF-related hospital admission.





**Figure 3** Kaplan–Meier curves for all-cause death (A) and first heart failure (HF) hospitalization (B) by adherence level category for telemonitored patients matched to standard of care (SOC) patients (telemonitoring [TLM] group,  $n = 1154$ ; SOC group,  $n = 2076$ ). Telemonitored patients with missing adherence data and their matched SOC patients were not retained for this analysis. Adherence levels were defined according to deciles: low  $< 66.9\%$ ; medium  $66.9\text{--}91.3\%$ ; and high  $> 91.3\%$ . The box in the left back side represents the figure with a truncated Y-axis.

to a nurse-centred management system, or to a usual-care system centred on the general practitioner. Patients randomly assigned to receive usual care had higher 1-year mortality compared to other groups (45%,  $p = 0.032$ ). Of note, that study was conducted about 20 years ago, in a different context from the current study regarding HF, and in a multinational system, so that many factors

and heterogeneities in health systems likely are in play.<sup>31</sup> The common key explanation for the benefits of telemonitoring on clinical outcomes, including CCC, is the quickness, quality, and efficiency of response to high-level alerts.<sup>1,12</sup> Indeed, the results of the TIM-HF2 trial, based on a non-invasive multiparameter telemonitoring associated with an appropriate immediate intervention

by the cardiologist, led the 2019 Heart Failure Association expert consensus report to consider non-invasive telemonitoring similar to the one used in TIM-HF2 for management of HF.<sup>34,35</sup>

Nevertheless, in this particular population of high-risk worsening HF patients, physiological features such as daily weight changes or increased symptoms could provide inadequate warning of impending decompensation.<sup>36</sup> Even if symptoms often are perceived as sudden, Zile *et al.*<sup>37</sup> showed a consistent pattern of

slowly rising cardiac filling pressures for about 3 to 4 weeks before HF hospitalizations. Assessment of symptoms in the aftermath of an episode of severe decompensation thus could be unreliable if patients with worsening HF and severe cardiac dysfunction report few or no symptoms.<sup>31</sup> The CCC telemonitoring solution seems to apply late in the evolution of worsening chronic HF, when hospitalizations for emergency treatment usually can no longer be avoided. Consequently, we found a higher number of HF hospitalizations in the telemonitoring group than in the SOC group. The results observed in telemonitored patients could be explained by the lack of multiparameter collection and the short follow-up period. On one hand, inclusion of multiple parameters could allow for earlier detection of HF decompensation than telemonitoring based on weight and symptoms, and thus reduce HF hospitalizations.<sup>38,39</sup> The recent MONITOR-HF study demonstrated that haemodynamic-guided monitoring techniques tracking congestion with cardiac filling pressures or pulmonary impedance changes in asymptomatic patients can identify early worsening of HF, enabling rapid specific treatment and helping to avoid HF hospitalizations.<sup>40</sup> On the other hand, in their meta-analysis, Umeh *et al.*<sup>32</sup> showed that prolonged telemonitoring ( $\geq 12$  months) was associated with decreased HF hospitalization, unlike the shorter duration ( $\leq 6$  months) telemonitoring. In our study, the 12.9% rehospitalization rate found at 6 months in the SOC group is comparable to the annual rate of HF rehospitalizations ranging from 15% to 20% reported in a large French retrospective study conducted between 2002 and 2012 (i.e. before the deployment of telemonitoring in France).<sup>41</sup> The slightly lower difference may be due to the improved management of HF patients, such as the guideline-directed medical therapy for patients with reduced ejection fraction HF.

The increased number of HF hospitalizations observed in the telemonitoring group resulted in higher costs. Given differences in reimbursement systems among countries, comparability in terms of healthcare costs is limited.<sup>42</sup>

## Optimizing Chronic Care Connect™ performance

The results of telemonitoring based on weight measurements could be improved by optimizing care structures using CCC to limit the observed high number of HF hospitalizations. Considering that the study period included the very beginning of using telemonitoring dedicated to HF in France as well as overlapping with the COVID-19 pandemic, modification in the behaviour and organizational structure of most cardiology departments using telemonitoring is expected. Alami *et al.*<sup>11</sup> showed that cardiology departments in France progressively changed their organization upon or shortly after the implementation of CCC, for instance by admitting patients

directly (i.e. avoiding the need to attend the ED). Nevertheless, some practical limitations may be an obstacle to the optimization of CCC, such as the need for cardiology staff investment and compatibility with the current healthcare system.<sup>43</sup>

## Place of weight telemonitoring in heart failure management

Although telemonitoring of weights and symptoms did not decrease worsening HF hospitalizations, the detection still helped to identify the steps needed to achieve effective monitoring programmes.<sup>39</sup> This study provided support for the incorporation of CCC telemonitoring in the late acute phase of worsening HF in high-risk patients. As telemonitoring is not a treatment *per se*, the CCC solution could offer physician an opportunity to adapt interventions early, including diuretics and guideline-recommended treatments.<sup>1</sup> However, the added value of CCC can be improved. By combining weight measurement, symptoms, and haemodynamic parameters, alerts from CCC could happen even earlier, saving hospitalizations and healthcare costs. As non-invasive telemonitoring appears simpler and less costly than invasive telemonitoring, the non-invasive interventions could be prescribed to a greater proportion of patients, and invasive telemonitoring could be reserved for very high-risk patients requiring more intensive monitoring.<sup>6</sup>

A tailored therapy with built-in adaptation over time could maximize the benefits of telemonitoring, for example, by intensifying during unstable phases of HF and attenuating when the patient is stable, leading to higher adherence during prolonged follow-up.<sup>39</sup> Adherence to weight measurement has been associated with clinically important benefits and identified as a key factor for telemonitoring programme with symptom assessment success.<sup>2,25,26,33</sup> Our results support this finding as the best results of CCC were found in adherent patients. Education of patients through partnership, self-care, and motivation support is surely an elementary condition to the success of telemonitoring solutions.

Finally, artificial intelligence-based analysis has the potential to play an important role in early prediction of clinical deterioration in HF patients by creating trustworthy hospitalization prediction algorithms and possibly preventing costly hospitalization.<sup>44,45</sup> If included in telemonitoring algorithms, artificial intelligence could help to adapt the telemonitoring system to variations in the population benefiting from it (e.g. new guidelines, new drugs) and at the individual level.

## Strengths and limitations

To conduct this large real-world study, we used the SNDS, which provides representative data on overall routine clinical care for HF in France in private and public hospital settings, and the NOMHAD database, which ensures correct identification of a patient's exposure to CCC telemonitoring and provides data on patient adherence. Nevertheless, administrative databases present several limitations. First, the level of detail needed for correct HF phenotyping and the level of patient risk (e.g. NYHA class and ejection fraction) were not available in the SNDS database. Thus, we used

the NHI algorithm to identify HF patients, which is based only on ICD-10 codes. Second, we approached the HF condition with the risk of HF rehospitalization and with the time interval between index date and last HF hospitalization to better identify patients at highest risk.<sup>20</sup> These variables could be insufficient to address the very significant changes in risk across the first 12 months after HF-related hospitalizations. Third, the results on mortality should be interpreted with caution as no information regarding in-hospital guideline-directed medical therapy was available, and identification of in-hospital co-infections worsening prognosis is unreliable in the SNDS. Finally, data available from the NOMHAD database did not include telemedical intervention information such as the number of alerts, the proportion of alerts leading to an ED visit, HF hospitalization, or a change in medication without an ED visit. This lack of information precluded further interpretation of the results observed.

Our real-world study reflects the actual use of telemonitoring in a clinical setting and helps to address some of the external validity limitations in randomized controlled trials.<sup>46</sup> However, the lack of randomization in real-world studies needs to be accounted for with an appropriate methodology. In the present study, hdPS matching was used to reduce the strong indication bias highlighted by the large baseline differences between the telemonitoring and SOC groups. Although hdPS algorithm is expected to identify proxies for unobserved confounders,<sup>47,48</sup> unmeasured clinical variables may remain unbalanced after hdPS matching, which can lead to residual confounding bias.<sup>49</sup> Remaining differences show that the choice of index date for the SOC group did not completely succeed to generate fully comparable periods at risk. To limit the impact, the 'risk of rehospitalization' and 'time between index date and last HF hospitalization' variables were included in the hdPS matching. Finally, given the absence of data such as medical vital statistics, clinical markers, or socioeconomic status, which is an inherent bias of medico-administrative databases, the results of our study should be interpreted with caution. Moreover, matching methods led to the exclusion of patients, especially SOC patients, from the analyses, which reduces the external validity of the study. Indeed, the matched sample reflects patients for whom the telemonitoring was prescribed, that is, the younger, more privileged, and male patients. The health benefits found in this matched population may not be reproduced in the broader population of all-comer HF patients.

## Conclusion

The investigation of different telemonitoring systems in a real-world setting is essential in the field of digital cardiology, in particular with the worldwide expansion of telemonitoring reimbursement. The results of this nationwide cohort study highlight a role for telemonitoring solutions such as CCC in the management of high-risk HF patients. However, for telemonitoring solutions based on weight and symptoms, consideration should be given to implement additional methods of assessment to recognize imminent worsening of HF, such as impedance changes, as a way to reduce mortality risk and the need for HF hospitalizations. Further research is warranted to confirm these results, to identify

which patients might benefit from telemonitoring and to explore long-term effects.

## Acknowledgements

The authors would like to thank the French 'Caisse Nationale d'Assurance Maladie' (CNAM), and its staff involved in the project for providing the data. The authors acknowledge the help of Soline Leblanc, who was involved in data management and analysis, as well as the help of Amandine Gouverneur, who assisted with the development of the manuscript, both from IQVIA. The authors also thank the supportive teams from Air Liquide Santé International, including Corinne Laurelli, Gisèle Al-Hamoud, Juan-Fernando Ramirez, and Laurent Lecourt, and from CDM e-Health, including Pierre-Emmanuel Augustin, Max René, Sébastien Brouard, and the nurses, for their contributions to this study.

## Funding

This research was funded by CDM e-Health (Jouy-en-Josas, France), affiliate of Air Liquide Healthcare (France).

**Conflict of interest:** G.L., H.P., S.A. and CD are employees of Air Liquide Santé International and shareholders in Air Liquide. A.B., J.V., A.R. and E.A. are employees of IQVIA, with which Air Liquide Santé International contracted to support data acquisition and analysis for this study. S.D.'s affiliation changed (from IQVIA to Novartis) during the completion of the manuscript. F.R., G.M, G.C. and I.D.Z. received consulting fees from Air Liquide Santé International.

## References

1. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). With the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail* 2022;24:4-131. <https://doi.org/10.1002/ejhf.2333>
2. Galinier M, Roubille F, Berdague P, Brierre G, Cantie P, Dary P, et al.; OSICAT Investigators. Telemonitoring versus standard care in heart failure: A randomised multicentre trial. *Eur J Heart Fail* 2020;22:985-994. <https://doi.org/10.1002/ejhf.1906>
3. Inglis SC, Clark RA, Dierckx R, Prieto-Merino D, Cleland JG. Structured telephone support or non-invasive telemonitoring for patients with heart failure. *Cochrane*

4. Radhoe SP, Veenis JF, Brughts JJ. Invasive devices and sensors for remote care of heart failure patients. *Sensors* 2021;21:2014. <https://doi.org/10.3390/s21062014>
5. Dierckx R, Inglis SC, Clark RA, Prieto-Merino D, Cleland JGF. Telemedicine in heart failure: New insights from the Cochrane meta-analyses. *Eur J Heart Fail* 2017;19:304-306. <https://doi.org/10.1002/ejhf.759>
6. Scholte NTB, Gürgöze MT, Aydin D, Theuns DAMJ, Manintveld OC, Ronner E, et al. Telemonitoring for heart failure: A meta-analysis. *Eur Heart J* 2023;44:2911-2926. <https://doi.org/10.1093/eurheartj/ehad280>
7. Arrêté du 11 octobre 2018 portant cahiers des charges des expérimentations relatives à la prise en charge par télésurveillance mises en œuvre sur le fondement de l'article 54 de la loi n° 2017-1836 de financement de la sécurité sociale pour 2018 - Légifrance. 2023. (accessed 6 February 2024). Available from: <https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000037533105>
8. Bezin J, Duong M, Lassalle R, Droz C, Pariente A, Blin P, et al. The national healthcare system claims databases in France, SNIIRAM and EGB: Powerful tools for pharmacoepidemiology. *Pharmacoepidemiol Drug Saf* 2017;26:954-962. <https://doi.org/10.1002/pds.4233>
9. Scailteux LM, Droitcourt C, Balusson F, Nowak E, Kerbrat S, Dupuy A, et al. French administrative health care database (SNDS): The value of its enrichment. *Therapie* 2019;74:215-223. <https://doi.org/10.1016/j.therap.2018.09.072>
10. Pergeline J, Lesuffleur T, Rey S, Fresson J, Rachas A, Tuppin P. Long-term chronic diseases and 1-year use of healthcare services by children under 18 years of age during 2018-2019: A French nationwide observational study. *Arch Pédiatr* 2023;30:48-58. <https://doi.org/10.1016/j.arcped.2022.11.014>
11. Alami S, Courouve L, Lancman G, Gomis P, Al-Hamoud G, Laurelli C, et al. Organisational impact of a remote patient monitoring system for heart failure management: The experience of 29 cardiology departments in France. *Int J Environ Res Public Health* 2023;20:4366. <https://doi.org/10.3390/ijerph20054366>
12. Galinier M, Itier R, Matta A, Massot M, Fournier P, Galtier G, et al. Benefits of interventional telemonitoring on survival and unplanned hospitalization in patients with chronic heart failure. *Front Cardiovasc Med* 2022;9:943778. <https://doi.org/10.3389/fcvm.2022.943778>
13. Méthodologie médicale de la cartographie des pathologies et des dépenses, version G9 (années 2015 à 2020, Tous Régimes). 2022. Available from: [https://assurance-maladie.ameli.fr/sites/default/files/2022\\_methode-repe...](https://assurance-maladie.ameli.fr/sites/default/files/2022_methode-repe...) (accessed 6 February 2024)
14. Feldman SF, Lesuffleur T, Olié V, Gastaldi-Ménager C, Juillièrè Y, Tuppin P. Outpatient healthcare utilization 30 days before and after hospitalization for heart failure in France: Contribution of the national healthcare database (Système national des données de santé). *Arch Cardiovasc Dis* 2020;113:401-419. <https://doi.org/10.1016/j.acvd.2019.11.011>
15. Schneeweiss S, Rassen JA, Glynn RJ, Avorn J, Mogun H, Brookhart MA. High-dimensional propensity score adjustment in studies of treatment effects using health care claims data. *Epidemiology* 2009;20:512-522. <https://doi.org/10.1097/EDE.0b013e3181a663cc>



16. Payet C, Polazzi S, Obadia JF, Armoiry X, Labarère J, Rabilloud M, et al. High-dimensional propensity scores improved the control of indication bias in surgical comparative effectiveness studies. *J Clin Epidemiol* 2021;130:78-86. <https://doi.org/10.1016/j.jclinepi.2020.10.003>
17. Blin P, Dureau-Pournin C, Bénichou J, Cottin Y, Mismetti P, Abouelfath A, et al. Comparative real-life effectiveness and safety of dabigatran or rivaroxaban vs. vitamin K antagonists: A high-dimensional propensity score matched new users cohort study in the French National Healthcare Data System SNDS. *Am J Cardiovasc Drugs* 2020;20:81-103. <https://doi.org/10.1007/s40256-019-00359-z>
18. Temam S, Varraso R, Pernet C, Sanchez M, Affret A, Jacquemin B, et al. Ability of ecological deprivation indices to measure social inequalities in a French cohort. *BMC Public Health* 2017;17:956. <https://doi.org/10.1186/s12889-017-4967-3>
19. Barry Y, Le Strat Y, Azria E, Gorza M, Pilkington H, Vandentorren S, et al. Ability of municipality-level deprivation indices to capture social inequalities in perinatal health in France: A nationwide study using preterm birth and small for gestational age to illustrate their relevance. *BMC Public Health* 2022;22:919. <https://doi.org/10.1186/s12889-022-13246-1>
20. Constantinou P, Pelletier-Fleury N, Olié V, Gastaldi-Ménager C, Juillère Y, Tuppin P. Patient stratification for risk of readmission due to heart failure by using nationwide administrative data. *J Card Fail* 2021;27:266-276. <https://doi.org/10.1016/j.cardfail.2020.07.018>
21. Stuart EA. Matching methods for causal inference: A review and a look forward. *Stat Sci* 2010;25:1-21. <https://doi.org/10.1214/09-STS313>
22. Austin PC. Using the standardized difference to compare the prevalence of a binary variable between two groups in observational research. *Commun Stat Simul Comput* 2009;38:1228-1234. <https://doi.org/10.1080/03610910902859574>
23. Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. *Pharm Stat* 2011;10:150-161. <https://doi.org/10.1002/pst.433>
24. Rassen JA, Shelat AA, Myers J, Glynn RJ, Rothman KJ, Schneeweiss S. One-to-many propensity score matching in cohort studies: One-to-many matching in cohort studies. *Pharmacoepidemiol Drug Saf* 2012;21:69-80. <https://doi.org/10.1002/pds.3263>
25. Sabatier R, Legallois D, Jodar M, Courouve L, Donio V, Boudevin F, et al. Impact of patient engagement in a French telemonitoring programme for heart failure on hospitalization and mortality. *ESC Heart Fail* 2022;9:2886-2898. <https://doi.org/10.1002/ehf2.13978>
  
26. Haynes SC, Tancredi DJ, Tong K, Hoch JS, Ong MK, Ganiats TG, et al.; Better Effectiveness After Transition-Heart Failure (BEAT-HF) Research Group. Association of adherence to weight telemonitoring with health care use and death: A secondary analysis of a randomized clinical trial. *JAMA Netw Open* 2020;3:e2010174. <https://doi.org/10.1001/jamanetworkopen.2020.10174>
27. Curtis LH, Hammill BG, Eisenstein EL, Kramer JM, Anstrom KJ. Using inverse probability-weighted estimators in comparative effectiveness analyses with observational databases. *Med Care* 2007;45:S103-S107. <https://doi.org/10.1097/MLR.0b013e31806518ac>

28. Bosco-Lévy P, Debouverie M, Brochet B, Guillemin F, Louapre C, Maillart E, et al. Comparative effectiveness of dimethyl fumarate in multiple sclerosis. *Br J Clin Pharmacol* 2022;88:1268-1278. <https://doi.org/10.1111/bcp.15071>
29. Chesnaye NC, Stel VS, Tripepi G, Dekker FW, Fu EL, Zoccali C, et al. An introduction to inverse probability of treatment weighting in observational research. *Clin Kidney J* 2022;15:14-20. <https://doi.org/10.1093/ckj/sfab158>
30. Harjola V, Follath F, Nieminen MS, Brutsaert D, Dickstein K, Drexler H, et al. Characteristics, outcomes, and predictors of mortality at 3 months and 1 year in patients hospitalized for acute heart failure. *Eur J Heart Fail* 2010;12:239-248. <https://doi.org/10.1093/eurjhf/hfq002>
31. Cleland JGF, Louis AA, Rigby AS, Janssens U, Balk AHMM; TEN-HMS Investigators. Noninvasive home telemonitoring for patients with heart failure at high risk of recurrent admission and death: The Trans-European Network-Home-Care Management System (TEN-HMS) study. *J Am Coll Cardiol* 2005;45:1654-1664. <https://doi.org/10.1016/j.jacc.2005.01.050>
32. Umeh CA, Torbela A, Saigal S, Kaur H, Kazourra S, Gupta R, et al. Telemonitoring in heart failure patients: Systematic review and meta-analysis of randomized controlled trials. *World J Cardiol* 2022;14:640-656. <https://doi.org/10.4330/wjc.v14.i12.640>
33. Rabbe S, Blankart CR, Franz WM, Hager L, Schreyögg J. Impact of a telemonitoring intervention in patients with chronic heart failure in Germany: A difference-in-difference matching approach using real-world data. *J Telemed Telecare* 2023;29:365-373. <https://doi.org/10.1177/1357633X20984024>
34. Koehler F, Koehler K, Deckwart O, Prescher S, Wegscheider K, Kirwan BA, et al. Efficacy of telemedical interventional management in patients with heart failure (TIM-HF2): A randomised, controlled, parallel-group, unmasked trial. *Lancet* 2018;392:1047-1057. [https://doi.org/10.1016/S0140-6736\(18\)31880-4](https://doi.org/10.1016/S0140-6736(18)31880-4)
35. Seferovic PM, Ponikowski P, Anker SD, Bauersachs J, Chioncel O, Cleland JGF, et al. Clinical practice update on heart failure 2019: Pharmacotherapy, procedures, devices and patient management. An expert consensus meeting report of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 2019;21:1169-1186. <https://doi.org/10.1002/ejhf.1531>
36. Ong MK, Romano PS, Edgington S, Aronow HU, Auerbach AD, Black JT, et al.; Better Effectiveness After Transition-Heart Failure (BEAT-HF) Research Group. Effectiveness of remote patient monitoring after discharge of hospitalized patients with heart failure: The Better Effectiveness After Transition-Heart Failure (BEAT-HF) randomized clinical trial. *JAMA Intern Med* 2016;176:310-318. <https://doi.org/10.1001/jamainternmed.2015.7712>
  
37. Zile MR, Bennett TD, St John Sutton M, Cho YK, Adamson PB, Aaron MF, et al. Transition from chronic compensated to acute decompensated heart failure: Pathophysiological insights obtained from continuous monitoring of intracardiac pressures. *Circulation* 2008;118:1433-1441. <https://doi.org/10.1161/CIRCULATIONAHA.108.783910>
38. Nunes-Ferreira A, Agostinho JR, Rigueira J, Aguiar-Ricardo I, Guimarães T, Santos R, et al. Non-invasive telemonitoring improves outcomes in heart failure with reduced ejection fraction: A study in high-risk patients. *ESC Heart Fail* 2020;7:3996-4004. <https://doi.org/10.1002/ehf2.12999>

39. Stevenson LW, Ross HJ, Rathman LD, Boehmer JP. Remote monitoring for heart failure management at home. *J Am Coll Cardiol* 2023;81:2272-2291. <https://doi.org/10.1016/j.jacc.2023.04.010>
40. Brugts JJ, Radhoe SP, Clephas PRD, Aydin D, Van Gent MWF, Szymanski MK, et al. Remote haemodynamic monitoring of pulmonary artery pressures in patients with chronic heart failure (MONITOR-HF): A randomised clinical trial. *Lancet* 2023;401:2113-2123. [https://doi.org/10.1016/S0140-6736\(23\)00923-6](https://doi.org/10.1016/S0140-6736(23)00923-6)
41. Gabet A, Juillièrè Y, Lamarche-Vadel A, Vernay M, Olié V. National trends in rate of patients hospitalized for heart failure and heart failure mortality in France, 2000-2012. *Eur J Heart Fail* 2015;17:583-590. <https://doi.org/10.1002/ejhf.284>
42. Reinhold T, Brüggengjürgen B, Schlander M, Rosenfeld S, Hessel F, Willich SN. Economic analysis based on multinational studies: Methods for adapting findings to national contexts. *J Public Health* 2010;18:327-335. <https://doi.org/10.1007/s10389-010-0315-0>
43. Desnos M, Jourdain P. Télémedecine: une solution d'avenir pour l'insuffisance cardiaque? *Bull Acad Natl Med* 2020;204:817-825. <https://doi.org/10.1016/j.banm.2020.07.034>
44. Croon PM, Selder JL, Allaart CP, Bleijendaal H, Chamuleau SAJ, Hofstra L, et al. Current state of artificial intelligence-based algorithms for hospital admission prediction in patients with heart failure: A scoping review. *Eur Heart J Digit Health* 2022;3:415-425. <https://doi.org/10.1093/ehjdh/ztac035>
45. Barrett M, Boyne J, Brandts J, Brunner-La Rocca HP, De Maesschalck L, De Wit K, et al. Artificial intelligence supported patient self-care in chronic heart failure: A paradigm shift from reactive to predictive, preventive and personalised care. *EPMA J* 2019;10:445-464. <https://doi.org/10.1007/s13167-019-00188-9>
46. Dreyer NA, Tunis SR, Berger M, Ollendorf D, Mattox P, Gliklich R. Why observational studies should be among the tools used in comparative effectiveness research. *Health Aff (Millwood)* 2010;29:1818-1825. <https://doi.org/10.1377/hlthaff.2010.0666>
47. Schneeweiss S, Eddings W, Glynn RJ, Patorno E, Rassen J, Franklin JM. Variable selection for confounding adjustment in high-dimensional covariate spaces when analyzing healthcare databases. *Epidemiology* 2017;28:237-248. <https://doi.org/10.1097/EDE.0000000000000581>
48. Guertin JR, Rahme E, LeLorier J. Performance of the high-dimensional propensity score in adjusting for unmeasured confounders. *Eur J Clin Pharmacol* 2016;72:1497-1505. <https://doi.org/10.1007/s00228-016-2118-x>
49. Austin PC, Wu CF, Lee DS, Tu JV. Comparing the high-dimensional propensity score for use with administrative data with propensity scores derived from high-quality clinical data. *Stat Methods Med Res* 2020;29:568-588. <https://doi.org/10.1177/0962280219842362>

# Abstract

## **Aims:**

Evaluating the benefit of telemonitoring in heart failure (HF) management in real-world settings is crucial for optimizing the healthcare pathway. The aim of this study was to assess the association between a 6-month application of the telemonitoring solution Chronic Care Connect™ (CCC) and mortality, HF hospitalizations, and associated costs compared with standard of care (SOC) in patients with a diagnosis of HF.

## **Methods and results:**

From February 2018 to March 2020, a retrospective cohort study was conducted using the largest healthcare insurance system claims database in France (Système National des Données de Santé) linked to the CCC telemonitoring database of adult patients with an ICD-10-coded diagnosis of HF. Patients from the telemonitoring group were matched with up to two patients from the SOC group based on their high-dimensional propensity score, without replacement, using the nearest-neighbour method. A total of 1358 telemonitored patients were matched to 2456 SOC patients. The cohorts consisted of high-risk patients with median times from last HF hospitalization to index date of 17.0 (interquartile range: 7.0-66.0) days for the telemonitoring group and 27.0 (15.0-70.0) days for the SOC group. After 6 months, telemonitoring was associated with mortality risk reduction (hazard ratio [HR] 0.71, 95% confidence interval [CI] 0.56-0.89), a higher risk of first HF hospitalization (HR 1.81, 95% CI 1.55-2.13), and higher HF healthcare costs (relative cost 1.38, 95% CI 1.26-1.51). Compared with the SOC group, the telemonitoring group experienced a shorter average length of overnight HF hospitalization and fewer emergency visits preceding HF hospitalizations.

## **Conclusion:**

The results of this nationwide cohort study highlight a valuable role for telemonitoring solutions such as CCC in the management of high-risk HF patients. However, for telemonitoring solutions based on weight and symptoms, consideration should be given to implement additional methods of assessment to recognize imminent worsening of HF, such as impedance changes, as a way to reduce mortality risk and the need for HF hospitalizations. Further studies are warranted to refine selection of patients who could benefit from a telemonitoring system and to confirm long-term benefits in high-risk and stable HF patients.