Home monitoring with IT-supported specialist management versus home monitoring alone in patients with heart failure: Design and baseline results of the SUPPORT-HF 2 randomized trial

SUPPORT-HF 2 Investigators and Committees [1]

Objectives SUPPORT-HF 2 tests the hypothesis that home monitoring with information technology–supported specialist management is more effective in optimizing medical therapy than is home monitoring alone for patients with heart failure.

Methods and results The study was designed as a 2-armed partially blinded parallel randomized controlled trial. Seven sites in the United Kingdom (UK) recruited a total of 202 adults with heart failure at high risk of adverse outcomes and with potential to benefit from remote management (mean age 73 years, 28% female, median left ventricular ejection fraction 37%). Both arms are given a home monitoring and communication kit (Internet-enabled tablet computer, Bluetooth-enabled blood pressure and heart rate monitor, and weighing scale). For each participant, an individualized plan for treatment of heart failure and major comorbidities is developed before randomization. Participants randomized to intervention receive regular feedback to support self-management, and their physicians receive advice on blood investigations and pharmacological treatment from a central specialist heart failure team. Participants in the control arm use the same monitoring system but with no central medical management support. The primary outcome is the use of *recommended medical therapy*, defined as treatment consistent with the guidelines for management of patients with chronic heart failure, and will be measured as a composite opportunity score. The trial data collection ended in October 2017, and results will be reported in 2019. Trial registration: ISRCTN86212709.

Conclusions Preliminary experience suggests that central provision of tailored specialist management using commercially available low-cost monitoring and computing devices, enhanced by customized applications, is feasible. (Am Heart J 2019;208:55-64.)

In many health care systems, patients with chronic heart failure are managed in primary care predominantly by physicians without specialist training for this condition, who often lack sufficient resources to adhere to recommendations on how to achieve target doses of disease-modifying treatments and monitor safety.[1,2] This together with the perceived complexity of disease management for an increasingly multimorbid patient population often leads to reduced quality of care and poor patient outcomes.[2,3]

Innovative models of care delivery that make better use of technological advances, in particular information technology (IT), may help overcome the challenges of chronic disease management for conditions such as heart failure.[4,5] IT can enable automation of repetitive clinical tasks, such as monitoring or patient education, potentially reducing costs. If successful in reducing the frequency of face-to-face interactions with health care professionals, such systems may also provide a more sustainable and scalable alternative to the prevailing labor-intensive and episodic models of care for patients with heart failure. Additionally, analytical techniques based on the recording of large amounts of multimodal information through such systems might be used to improve the early prediction or early detection of clinical deterioration and to stratify treatment according to the patient's profile, ultimately leading to improved outcomes.

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Table I. Eligibility criteria

Inclusion criteria
Participant is willing and able to give informed consent for participation in the trial, and
Male or female, aged 18 y or above, and
Diagnosed with *heart failure*, defined as presence of typical symptoms (eg, breathlessness, ankle swelling, and fatigue) and signs (eg, elevated jugular venous pressure, pulmonary crackles, and displaced apex beat) resulting from an abnormality of cardiac structure or function (as evidenced by cardiac imaging and/or biomarkers such as BNP), and
Potential to benefit from home monitoring and management defined as:
Average self-assessed NYHA class II to IV in the week before randomization; or
BNP >350 pg/mL (100 pmol/L) or NT-pro-BNP >1000 pg/mL (130 pmol/L) in the last 30 d, or
Not on optimal therapy as evidenced by the prerandomization personal management plan suggesting 2 or more treatment targets.
And, high risk of adverse outcomes defined as:
Probability of death within 1 y >10% (MAGGIC integer score 20 or more), or
At least 1 hospital admission related to heart failure in the previous 12 m
Exclusion criteria
No reliable 3G mobile or Wi-Fi network connectivity at home, or
Unable to read or speak English, or
Any other significant disease, including critical unstable or end-stage heart failure, which, in the opinion of the Investigator, may either put the participant at risk because of participation in the trial, or may influence the result of the trial or the participant's ability to participate in the trial.

However, despite the intuitive appeal of such systems, the evidence for their effectiveness is inconsistent.[6-9] This may be, in part, due to differences in patient-related features, intensity and type of intervention provided, or methodological differences between the clinical trials. To date, most studies have investigated the incremental value of remote monitoring and management of patients who already had medically optimized treatment.[10,11] Furthermore, most trials have focused on remote monitoring per se, with limited or no centralized decision support for specialist care provision. For instance, in the BEAT-HF trial, the nurse-led patient education and self-management intervention did not fully integrate with physician care, which limited recommendations for active drug interventions.[12] However, 2 trials that combined invasive monitoring techniques with rule-based management support showed significant improvements in patient outcomes.[13,14]

Another issue with some of the earlier trials that employed noninvasive monitoring systems was the limited achieved patient adherence to the remote monitoring systems.[12,15] To overcome this critical issue, in an earlier phase of the SUPPORT-HF, we co-designed a user-friendly noninvasive home monitoring system with input from patients and their carers and showed the system to be effective in supporting heart failure patients to monitor their health status regularly, even when IT literacy was low, with little loss of adherence over time.[16,17] Despite no active medical intervention, patients found the system useful mainly because of the reassurance and sense of connectivity that the monitoring system provided.[18] Building on these studies, we designed a trial to evaluate the efficacy of an IT-supported system for remote specialist medical management and patient support. Here we report its design and the baseline characteristics of its participants.

Methods and analysis

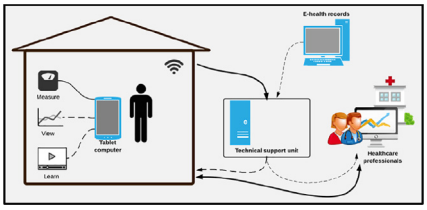
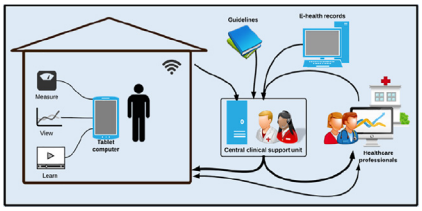
Study design

SUPPORT-HF 2 is a multicenter 2-armed partially blinded parallel randomized controlled trial with a run-in period of up to 2 weeks between screening and randomization. It is testing the hypothesis that, in patients with heart failure, home monitoring with an integrated risk prediction and disease management service, which provides tailored alerts and advice to patients and clinical decision support to health care practitioners (general practitioners, nurses, and hospital cardiologists), is more effective in optimizing medical therapy than home monitoring with the same monitoring equipment but without the use of the integrated data analysis and decision support service. Recruitment was initiated at 7 UK hospital sites, and patient consent and follow-up took place in the participants' homes. Hospitals acted as study sites. However, potentially eligible participants were identified from hospital wards prior to discharge, cardiology outpatient clinics, general practitioners, or community heart failure nurse clinics, or by reviewing the hospital discharge lists and referral lists to community heart failure nurses.

Study eligibility

Adults with a confirmed diagnosis of heart failure, irrespective of its underlying etiology, were eligible for recruitment provided they were judged to have a clear potential to benefit from home monitoring and management and were at high risk of death or hospitalization (see Table I for full eligibility criteria). Patients with either preserved or reduced ejection fraction were eligible, but a recruitment target of a 2:3 ratio of patients with preserved versus reduced ejection heart failure was recommended to each recruiting sites.

Table II. Description of the different elements of intervention by study group

	Enhanced self-management (control)	Supported medical management (intervention)
		
Clinical management planning	Development of a blinded individualized management plan before randomization. Management plans consist of a selection of treatment opportunities, among 11 clinical treatment targets (including major comorbidities such as hypertension, atrial fibrillation, Table III), that apply to the patient of interest.	
Data collection	Home monitoring: Daily symptom report (NYHA), measurements of weight, blood pressure, and pulse. Periodical assessment of quality of life through validated questionnaires (EQ-5D, MLHFQ). Depression screening at baseline, then 3-monthly (PHQ-2 and PHQ-9).	
	Clinical investigations, events, and medications are collected via linkage to participants' EHR wherever possible. If data integration is not available, the information is collected directly from patients or their physicians and updated every 3 m.	Clinical investigations, events and medications: same as in the control group, with the difference that if EHR linkage is not available, the data are manually updated every 2 wk. Health status: additional information about health status is collected by contacting patients via the tablet PC application, as required.
Usual care	Participants continue to be cared for by their usual-care health professionals. Data collected by participants via the home monitoring system, but not information collected from patients' medical records, are accessible to their usual-care health professionals in their raw format with no ranking or interpretation.	
CCM	Home monitoring and medical records data are accessible to the study team in their raw format with no ranking or interpretation. No recommendations are issued to patients or their healthcare professionals.	CCM team: The core of the intervention is a CCM unit consisting of a cardiologist and heart failure nurses, supported by a clinical decision support system that ranks participants' need for further interaction based on their risk and need for treatment change or monitoring. Clinical decision support: A central clinical decision support platform provides full access to patients' home monitoring data, clinical investigation results, and current medication plan. Patients at high risk of clinical deterioration are flagged for more intensive review of their measurements and adaptation of their medication. Those that are stable but not yet on optimal therapy are flagged for medication uptitration to target doses (or, in the case of diuretics, downtitration) under monitoring of hemodynamic status (blood pressure and heart rate) and renal function according to clinical guidelines. Recommendations: The CCM team reviews the system-generated alerts, decides on the most appropriate actions (such as recommending changes in patients' medication plan and requesting blood tests), and communicates their recommendations to participants as well as their health care professionals.
Patient feedback and management support	Educational material: Participants are able to use the self-management module of the tablet computer, which contains generic educational material such as animations and video clips on heart failure and strategies for managing it. Readings: Participants are able to view their previous readings, displayed in a graphical format. Home monitoring measures that are considered to be clearly abnormal as per current practice guidelines (ie, an increase in weight by 2–3 kg over 2–3 d) are flagged, and participants receive immediate automated feedback via the tablet computer to contact their physician or nurse for further advice. If no such flags are raised, participants receive a message at the end of their session to indicate that their readings are within an acceptable range. Contacting the study team: Participants are also able to contact the technical and administrative team for any study-related questions that they may have by pressing a “request for call back” button. This triggers an email or text message to authorized research staff who usually get back to the participant within 2 working days. Participants are reminded that this system does not replace their usual care and that if they have any health-related questions, they may wish to contact their own physician or nurse.	
	System adherence: Participant's usage record is not monitored.	System adherence: Depending on the participant's usage record, personalized messages are sent electronically to motivate them to engage in self-management activities, according to their need and capacity.

Abbreviations: NYHA, New York Heart Association classification; CCM, Central Clinical Management; EHR, electronic health records; EQ-5D, Euro quality of life questionnaire - 5 dimensions; MLHFQ, Minnesota living with heart failure questionnaire; PHQ, Patient Health Questionnaire.

Comparison groups

Consenting participants enter the study run-in phase and are asked to use the SUPPORT-HF 2 home monitoring system. During run-in, further information for eligibility is obtained. This includes the result of the blood investigations, collection of recent echocardiogram and electrocardiogram reports, and review of 3G mobile or Wi-Fi network connectivity for the participant. During this time, patients' general practitioners, heart failure nurses, and cardiologists (as applicable) are informed about their potential enrolment into the study and its potential implications for further management. Eligible and willing participants are then randomized to the study intervention or control arm by the central research staff using a Web-based randomization program based on a minimization algorithm that stratifies for type of heart failure (reduced vs preserved ejection fraction), patient's estimated risk of death (based on their Meta-Analysis Global Group in Chronic Heart Failure score[19]), and study site. The control group is conceptualized as an attention control, rather than a usual-care control, to reduce placebo and "loser" effect that could systematically change the behavior of participants. In addition, participants are blinded from the actual study hypothesis because positive names are given to both trial groups (ie, "enhanced self-management" for the control group and "supported medical management" for the intervention group). The content of the intervention for each group is described in Table II.

Peer reviewers of the trial funding application made a request for inclusion of a usual-care group. Given the challenges of 3-arm trial, we decided to include patients who drop out during the run-in phase to act as a "usual-care control" nonrandomized group. These patients have no access to study equipment and do not receive any medical intervention from the study team. They were asked for their permission to access their health records and to be contacted by phone every 6 months to obtain additional follow-up information about their quality of life and health status. As we are expecting the clinical characteristics of this nonrandomized group to differ from randomized participants, we will perform adjusted comparisons with the randomized groups. Given the small sample size, analysis will be adjusted for limited numbers of key variables.

Digital health system

The SUPPORT-HF 2 digital health system consists of a home monitoring kit for patients and a clinical reporting and management application for clinicians.

The patient home monitoring kit integrates a touchscreen tablet computer, a blood pressure and heart rate monitor, and a weighing scale. A specially designed app allows patients to document their symptoms and automatically records vital-sign readings via Bluetooth. The data are then sent through the internet (mobile or Wi-Fi) to a back-end infrastructure located on secure servers.

The clinical reporting and management application enables secure online access to patients' clinical profile. It presents data collected from patients' home monitoring kits, as well as additional clinical information, such as medications or test results, which is retrieved through linkage to patients' electronic health record wherever possible or else collected from patients or their health care professional.

The clinical application offers enhanced clinical decision-support functionalities for patients in the intervention group. These include alerts for patients at high risk of clinical deterioration and reminders for medication uptitration in patients that are stable but not yet on optimal therapy.

In addition to clinical management, the digital health platform has trial management functionalities, such as automated eligibility assessment, randomized allocation, adverse event reporting, follow-up forms, event reporting, site management, and automated progress reports.

Intervention

The core of the intervention is a central clinical management (CCM) unit consisting of a cardiologist and heart failure nurses. The management plan, established in accordance with clinical guidelines before randomization, and the clinical decision support functionalities from the study's digital health system guide the CCM team in the clinical management of patients. The CCM team reviews patients' clinical profile on a daily basis. Patient data (including blood pressure, weight, blood test results, patient adherence to take his own readings, or risk of clinical deterioration) are automatically color-coded, and abnormal results are highlighted. Treatment management targets are displayed alongside achievement rates, as a reminder of optimal therapy. Patients' health care professionals receive ongoing recommendations for gradual drug titration and blood investigations from the CCM group on behalf of patient's local cardiologist (Table II).

Trial outcomes

The primary outcome is *optimal medical therapy*, defined as prescribed treatment consistent with guidelines for management of patients with chronic heart failure and assessed at the end of last trial follow-up for each participant.

Optimal medical therapy is defined for every patient as the individualized management plan established prerandomization (Table III). Management plans are based on the National Institute for Health and Clinical Excellence guidelines for management of chronic heart failure[20] and complemented with recent European Society of Cardiology guidelines for the use of disease-modifying drugs in heart failure,[21] as well as clinical practice guidelines for management of major comorbidities in patients with

Table III. Treatment targets considered in individualized management plans

Treatment target	Indication	Daily recommended dose
β-Blocker	HFREF	Bisoprolol: 10 mg, carvedilol: 50 mg, metoprolol succinate: 200 mg, nebivolol: 10 mg
ACE-I or ARB or ARN-I	HFREF	ACE-Is: captopril: 150 mg, enalapril: 20 mg, lisinopril: 20 mg, ramipril: 10 mg, trandolapril: 4 mg; ARB: candesartan: 32 mg, losartan: 150 mg, valsartan: 320 mg; ARNI: sacubitril/valsartan: 194 mg
Mineralocorticoid receptor antagonist	HFREF	Eplerenone: 50 mg, spironolactone: 25 mg
Ivabradine	HFREF	-
Hydralazine/nitrate	HFREF	-
Digoxin	HFREF or AF	-
Aspirin	IHD or CVA	-
Oral anticoagulation	AF	-
High-dose statin	IHD or CVA	-
Maintain blood pressure below 130/85 mm Hg*	All	-
Full screening for depression and recommendation for formal diagnosis and treatment by patient's physician*	If responses PHQ-2 questionnaire suggested possible depression	-

Individualized management plans are established prerandomization by the CCM team after reviewing patient's clinical information. Management plans consist of a selection of treatment opportunities (among the 11 treatment targets listed above) that apply to the patient of interest, independently of whether the patient complies to treatment at baseline or not. *HFREF*, heart failure with reduced ejection fraction; *AF*, atrial fibrillation; *IHD*, ischemic heart disease; *CVA*, cerebrovascular accident.
*Blood pressure control and depression screening were included in patients' management plans but excluded from opportunity score calculations

heart failure (atrial fibrillation, ischemic heart disease, hypertension, depression).

At the final evaluation, the latest treatment plan will be used to calculate the sum of treatment targets achieved for each patient as a binary variable (1 if treatment achieved / 0 otherwise) or, for angiotensin-converting enzyme inhibitor (ACE-I)/angiotensin receptor blocker (ARB)/angiotensin receptor neprilysin inhibitor (ARN-I), β-blocker, and mineralocorticoid receptor antagonist in patients with heart failure and reduced ejection fraction, as the achieved fraction (0, 0.25, 0.5, 1) of the recommended daily dose. The opportunity score will weight each treatment opportunity equally (see **Web Supplement**, Table II).

This method will not take account of the appropriateness of treatment at the end of study. However, in a randomized comparison, we expect that any reasons against usage of medical therapy that may arise during the course of the study will balance between groups and, hence, not be a source of bias.

Co-primary outcomes are the physical functioning subscale of the Minnesota Living with Heart Failure (MLWHF) questionnaire and changes to self-assessed New York Heart Association (NYHA) class to assess the impact of the intervention on physical well-being of participants.

Secondary outcomes, which investigate the biochemical and physiological efficacy of the intervention, are assessed by the validated MAGGIC risk score[19] and blood B-type natriuretic peptide / N-terminal-pro-B-type natriuretic peptide level at the end of the trial for each participant, the proportion of patients in sinus rhythm who have a heart rate between 50 and 70 beat/min, and the proportion of patients with a serum potassium reading in the ideal range for heart failure (4.0-4.9 mmol/L) at the end of trial.

The trial will also report the clinical safety of IT-supported specialist management, as assessed by a composite of all-cause death, total hospital admissions, and unscheduled outpatient visits. Exploratory analysis will investigate cause-specific and heart failure–related outcomes such as cardiovascular death and cardiovascular admissions (including renal failure and hypotensive episodes).

Power calculations

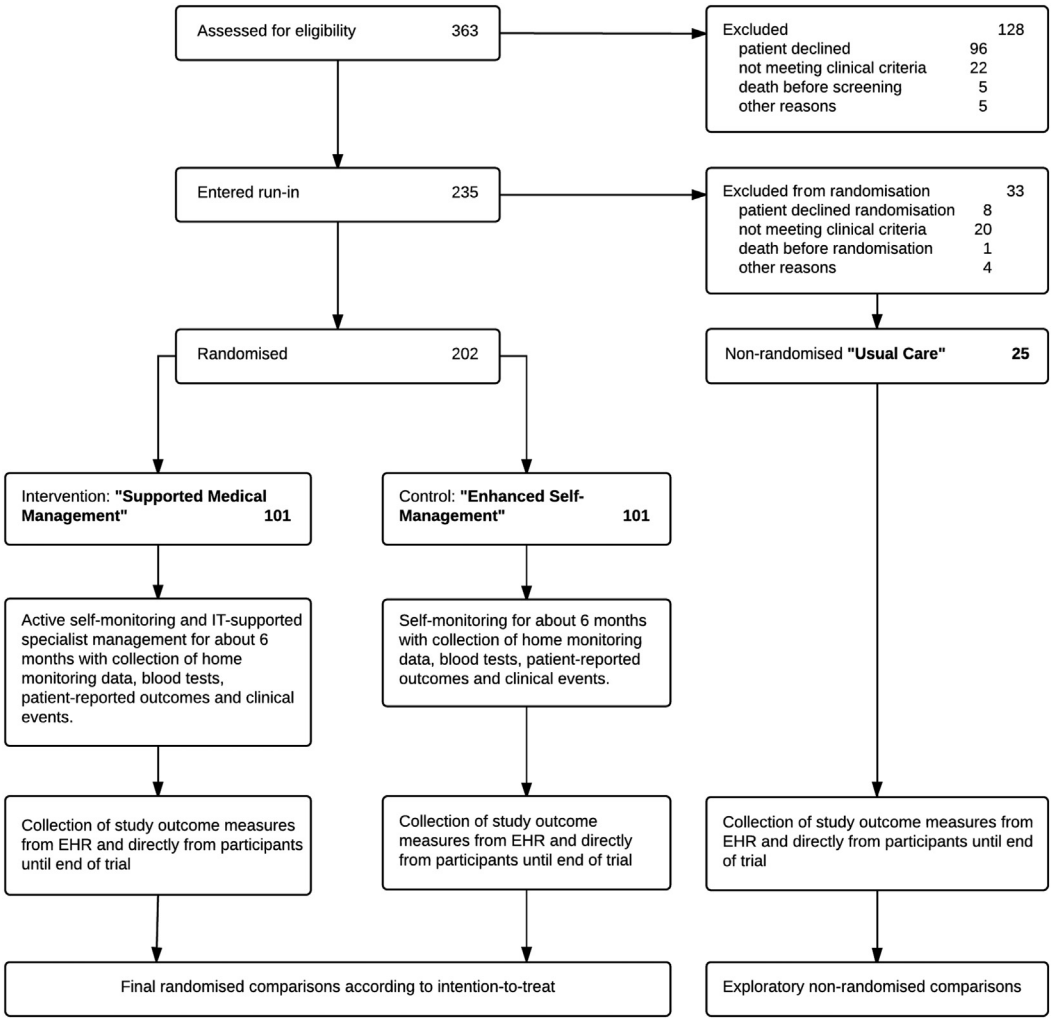
We assumed the opportunity score in the control group at the end of the study to be 0.7 (ie, at the end of the study, participants will have received 70% of the treatment recommendation that they would have been eligible for as assessed at the beginning of the study). We further assumed an absolute 20% difference in the use of appropriate medication between groups to be realistic and important. To detect such a difference with 90% power ($2\alpha = .05$) requires randomization of 82 participants per trial arm. To take account of attrition, we set a target of 200 participants in total.

Assuming a mean score of 25 (SD 10) on the physical subscale of the MLWHF in the control group,[22] randomization of 200 patients will also have 90% power at 2-sided $\alpha = .5$ to detect a 5-point difference in the MLWHF physical subscale between the 2 groups at the end of the study or 75% power to detect a 4-point difference in the subscale.

Statistical analysis

Key variables at baseline were summarized, in each of the 3 study arms (management groups plus usual care),

Figure 1



Consort diagram.

using means and SDs for continuous variables, or medians (interquartile intervals [IQIs] if highly skewed) and number (percentage) for categorical variables.

A detailed statistical analysis plan for the trial is provided in the **Web Supplement.**

Results

Between October 2015 and June 2017, 363 patients were identified from 7 UK centers and assessed for eligibility (Figure). Of these, 128 were ineligible at the screening visit, and a further 33 were ineligible following full eligibility assessment after the run-in period.

The characteristics of study participants at baseline are shown in Table IV. One hundred one were randomized to "enhanced self-management" and 101 to "supported medical management." Of those ineligible for randomization, 25 agreed to be followed up as the "usual-care group."

Randomized groups were similar in age and sex distribution, comorbidities, and level of competency in using digital technologies. About half of the participants reported very limited or no prior experience in the use of digital technologies such as smartphones and touch-screen tablet computers.

There was no material difference between the groups in their physical measurements, left ventricular ejection fraction, functional status, quality of life, or medication use at baseline. Mean left ventricular ejection fraction was 37% (SD 12.0%), and 66% of patients were classified as having heart failure with reduced ejection fraction. At baseline, 72% of patients were receiving loop diuretics, 78% an ACE-I or angiotensin receptor blocker, 77% a β-blocker, and 51% an aldosterone antagonist, with some imbalances between groups (Table IV). Median MAGGIC

Table IV. Baseline characteristics by treatment allocation1

	Randomized comparisons		Non-randomized usual care group (n=25)
	Enhanced self-management (control) (n=101)	Supported medical management (intervention) (n=101)	
Number of participants	101	101	25
Age (y), mean (SD)	70.4 (11.9)	72.8 (11.1)	73 (13.5)
Sex, female, n (%)	31 (31%)	26 (26%)	8 (32%)
Co-morbidities, n (%)			
Hypertension	48 (48%)	46 (46%)	15 (60%)
Ischaemic heart disease	55 (54%)	52 (51%)	9 (36%)
Stroke/transient ischaemic attack	13 (13%)	14 (14%)	4 (16%)
Atrial fibrillation	63 (62%)	65 (64%)	14 (56%)
Chronic kidney disease	14 (14%)	16 (16%)	9 (36%)
Diabetes mellitus	30 (30%)	34 (34%)	7 (28%)
Chronic obstructive lung disease	21 (21%)	14 (14%)	3 (12%)
Asthma	6 (6%)	10 (10%)	5 (20%)
Previous venous thromboembolism	4 (4%)	6 (6%)	2 (8%)
Level of competency in use of digital technologies			
Very limited or none, n (%)	47 (47%)	41 (41%)	12 (48%)
Competent, n (%)	46 (46%)	51 (50%)	13 (52%)
Expert, n (%)	8 (8%)	9 (9%)	0 (0%)
Left ventricular ejection fraction (%), mean (SD)	36.7 (12.4)	36.7 (11.6)	39.2 (14.6)
Systolic blood pressure (mmHg), mean (SD)	122.6 (18.2)	127.5 (21.7)	130.5 (6.4)
Diastolic blood pressure (mmHg), mean (SD)	73.7 (10.3)	73.7 (10.8)	91.0 (12.7)
Heart rate (beats per minute), mean (SD)	71.9 (13.1)	69.7 (11.7)	74.5 (13.2)
Body mass index (kg/m^2), mean (SD)	28.6 (7)	28.3 (5.9)	28.4 (9.2)
BNP (pg/ml), median (IQI)	187.1 (81.4; 456.7) (n=68)	257.0 (141.2; 386.0) (n=55)	158.3 (47.6; 333.2) (n=14)
NT-pro-BNP (pg/ml), median (IQI)	1141.5 (642.0; 1852.0) (n=36)	1570.0 (596.0; 3819.0) (n=49)	2746.0 (1215.0; 3712.0) (n=9)
Creatinine (µmol/L), median (IQI)	101.0 (84.0; 133.0)	110.0 (87.0; 134.0)	99.5 (82.0; 124.5) (n=24)
Urea (mmol/L), median (IQI)	8.8 (6.1; 12.0)	8.7 (6.6; 11.5) (n=100)	8.8 (7.3; 10.2) (n=24)
Potassium (mmol/L), mean (SD)	4.5 (0.6)	4.5 (0.5)	4.4 (0.6)
Haemoglobin (g/dl), median (IQI)	13.6 (11.9; 14.3) (n=99)	13.5 (11.5; 14.2) (n=95)	12.9 (11.8; 15.2) (n=22)
NYHA class*			
Class 1	32%	33%	100%
Class 2	24%	32%	0%
Class 3	37%	26%	0%
Class 4	8%	10%	0%
MAGGIC risk score, mean (SD)	22.6 (7.6)	22.1 (6.6)	20.2 (7.9)
Medications			
ACE-I or ARB	80 (79%)	75 (74%)	13 (52%)
Beta-blocker	77 (76%)	76 (75%)	14 (56%)
Aldosterone antagonist	55 (54%)	44 (44%)	11 (44%)
Digoxin	19 (19%)	18 (18%)	5 (20%)
Ivabradine	4 (4%)	2 (2%)	2 (8%)
Hydralazine/nitrate	9 (9%)	3 (3%)	2 (8%)

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Table IV (*continued*)

	Randomized comparisons		Non-randomized usual care group (n=25)
	Enhanced self-management (control) (n=101)	Supported medical management (intervention) (n=101)	
Loop diuretics	71 (70%)	76 (75%)	12 (48%)
Aspirin	32 (32%)	33 (33%)	5 (20%)
Oral anticoagulation	47 (47%)	38 (38%)	9 (36%)
Statin	65 (64%)	61 (60%)	9 (36%)
Calcium channel blocker	5 (5%)	17 (17%)	0 (0%)
Quality of life and well-being			
MLWHF Overall [max: 105], mean (SD)	36.2 (24.9)	35.2 (24.8)	-
MLWHF Physical [max: 40], mean (SD)	18.8 (12.3)	17.8 (11.8)	-
MLWHF Social [max: 40], mean (SD)	9.9 (8.6)	10.3 (8.8)	-
MLWHF Emotional [max: 40], mean (SD)	7.5 (6.8)	7.2 (7)	-
EQ5D score [max: 20], mean (SD)	5.0 (3.4)	4.9 (3.9)	-
Opportunity score, mean (SD)	0.37 (0.24)	0.36 (0.25)	0.29 (0.26)

*Mean self-reports over 7 days prior to randomization.

risk score was 23 in the control group and 22 in the intervention group, indicating a predicted 1-year probability of death of 14% and 12%, respectively.

The baseline characteristics of the nonrandomized usual-care group are also similar to the randomized groups although data was missing or number of cases too small to enable reliable comparisons for several measures.

Discussion

How best to design and evaluate service delivery interventions in the complex and dynamic healthcare environment for heart failure (and other chronic diseases) has been subject to much debate.[5-7,15,23] In designing the SUPPORT-HF 2 trial, we considered the need for flexibility of the intervention to adapt iteratively to changing environments (eg, availability of newer technologies) as well as the need for a study design that is capable of detecting modest causal effects. This was partly achieved by making a clear distinction between a formative evaluation that allows continuous improvement of the home monitoring and management system during the course of the trial and a summative evaluation that focuses on the core of the intervention and compares the outcomes between randomized groups at the end of the trial. By enabling the adaptation of the peripheral components of the intervention (eg, type of hardware chosen) while keeping core components fixed (eg, centralized decision support), a system is created that is resilient to technological innovation while being subject to rigorous randomized evaluation.

In a trial of home monitoring and management, it is difficult to fully blind participants and study staff to treatment allocation, and this might bias effect estimates toward the intervention. In SUPPORT-HF 2, we elected to have an attention control group rather than a usual-care group. By partially blinding participants and their health care professionals (in addition to trial staff) to treatment allocation, we aimed to reduce the risk of "false-positive" findings as a result of greater attention given to study participants in the active arm (even without the remote monitoring intervention). This design is one of the most rigorous approaches possible in open-label trials to achieve an unbiased estimate of treatment effects and, in our study, provides further advantages, such as simplification of acquiring consent and more efficient processes for collection of study outcomes. However, the monitoring that participants in the control group receive might lead to dilution of treatment effects, in particular for subjective outcomes such as quality of life. Another disadvantage is that findings of a trial that has no usual-care group might be less relevant to policy makers. To address this latter issue, we introduced a third nonrandomized arm group which can help with the estimation of resource implications in a typical clinical scenario. The current report shows that key baseline features of those who were included in the usual-care group are broadly similar to the randomized groups in terms of their clinical features and demographics, but they had poorer quality of life.

Given that integrated digital health care is likely to be most useful in contexts where quality of care is (on average) suboptimal, with substantial unwarranted variability at the provider level,[24] we restricted recruitment

to patients with some potential for benefit from more intensive and regular monitoring and management. However, patients were still relatively well treated, which might limit the willingness of nonspecialists to follow the guidance provided for further uptitration or change in patient's treatment.

To inform a stratified risk-based management of patients, we intended to link participants' home monitoring data to their electronic health records (EHRs) mainly to obtain laboratory results, update the list of prescribed medications in real time, and capture information about health service use and outcomes. However, with the exception of one site, we were unable to achieve data integration. Therefore, all relevant test results and outcomes had to be entered manually by research staff into the trial IT system. The main issues brought forward by IT departments were perceived issues relating to data governance and insufficient capacity or funding to set up the linkage.

The SUPPORT-HF 2 has reached its recruitment target, and participant follow-up was completed in October 2017. Our preliminary experience shows that central provision of tailored specialist management support with the use of commercially available, low-cost devices enhanced by customized applications is feasible.

Ethics and dissemination

The trial has been registered at ISCRTN (ISRCTN86212709), and ethics approval was obtained from the medical research and ethics committee (approval date August 28, 2014; reference 14/SS/1025).

Patient recruitment for this trial closed in July 2017, and follow-up and data collection period was completed in October 2017. Trial results will be reported in 2019 according to the statistical analysis plan presented in the **Web Supplement**.

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Declarations of interest

Investigators have no conflicts of interest to declare. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper, and its final contents.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ahj.2018.09.007.

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