Review Article

The role of patient-oriented mHealth interventions in improving heart failure outcomes: A systematic review of the literature

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ABSTRACT

Heart failure (HF) is a debilitating disease with 26 million patients worldwide. Consistent and complex self-care is required on the part of patients to adequately adhere to medication and to the lifestyle changes that the disease necessitates. Mobile health (mHealth) is being increasingly incorporated in patient interventions in HF, as smartphones prove to be ideal platforms for patient education and self-help assistance. This systematic review aims to summarize and report on all studies that have tested the effect of mHealth on HF patient outcomes. Our search yielded 17 studies, namely 11 randomized controlled trials and six non-randomized prospective studies. In these, patients with the assistance of an mHealth intervention regularly measured their blood pressure and/or body weight and assessed their symptoms. The outcomes were mostly related to hospitalizations, clinical biomarkers, patients' knowledge about HF, quality of life (QoL) and quality of self-care. QoL consistently increased in patients who received mHealth interventions, while study results on all other outcomes were not as ubiquitously positive. The first mHealth interventions in HF were not universally successful in improving patient outcomes but provided valuable insights for patient-oriented application development. Future trials are expected to build on these insights and deploy applications that measurably assist HF patients.
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1. Introduction

Heart failure (HF) is a leading cause of morbidity for patients, negatively affecting their quality of life (QoL) and functional status. In the United States, the estimated incidence of HF is 2-5 cases per 1000 person-years.[1] Approximately 64.3 million patients are currently diagnosed with HF worldwide.[2] HF decompensations are frequent and require lengthy hospital stays,[3,4] while the disease's high mortality rate is comparable to those of many types of cancer.[5]

In addition to standard medical treatment, self-care plays a pivotal role in HF patient management. Because of the nature of the disease, there is a constant need for adjustment of medication, especially diuretics to prevent fluid congestion. The goal is to achieve optimal dosing tailored to each patient's health status. Experience often enables patients to make such adjustments by themselves.[6,7] Most patients with HF receive additional medications due to comorbidities, such as diabetes, atrial fibrillation and hypertension.[8] A labyrinth of constantly changing therapeutic regimens is formed, demanding from the patient commitment, self-possession and dedication to the goals being set.[9]

Lifestyle changes are one of the most difficult aspects of HF self-care, but are necessary for managing disease progression. Fluid and salt intake monitoring,[7] daily weighing,[6] physical activity increase[10,11] and vaccinations[12,13] have all been proven to positively affect outcomes in HF patients. Sustaining long-term adherence to the "HF lifestyle" is strenuous and necessitates recurrent

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interventions by a multidisciplinary team consisting of physicians, nurses, exercise physiologists, psychologists and dietitians.[14] Mobile health (mHealth) is arguably the missing link for enabling such multidisciplinary teams to effectively interact with HF patients and vice versa.

mHealth is defined as the use of mobile communications and network technologies for health care.[15] mHealth-based implementations can be designed for use by clinicians,[16] nurses, allied health professionals, caregivers and, importantly, patients themselves.[14,17] Nowadays, modern technologies such as smartphones and tablets are established as the main means for delivering mHealth applications (apps) to their intended audience,[18-35] largely replacing older mobile phone technologies such as automated phone calls and SMS messages. Increasingly, a host of devices including blood pressure monitors, wireless weighing scales and wearables (bands, sensors, etc) are used to collect real-life patient data, which are analyzed and used to augment the quality of mHealth care.[36]

mHealth technology is already used in many patient-oriented interventions, significantly improving QoL and self-care in several chronic diseases for which patient participation is vital, such as diabetes,[37] hypertension[38] and depression.[39] The cornerstone of such interventions is a smartphone-based app that provides patient access to various educational materials (eg, videos, texts), promotes lifestyle changes appropriate for each disease (eg, salt restriction in HF), notifies the patient about actions needed to be taken (eg, medication/vaccination reminders) and enables direct or indirect communication between the patient and their primary caregiver, health care personnel or even other patients with the same disease.[14,18,19,21,40-42] Another important feature is also remote monitoring.[43]

A major target for mHealth-based interventions is chronic HF and the entirety of its complex self-care. Nevertheless, designing a patient-oriented app for HF patients is a process facing many challenges that need to be considered during the inception and development phase, as there is a variety of special needs and obstacles, such as the mild cognitive decline that is very common in HF.[44] The goal of this review is to comprehensively examine the design, implementation and outcomes of smartphone- or tablet-based interventions in HF patients.

2. Materials and Methods

2.1. Search strategy

The search process was based on the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. A thorough search of PubMed Central, Embase, MEDLINE and the Cochrane Database of Systematic Reviews was performed to collect all studies regarding mHealth administered via smartphones or tablets for HF patients in the last 12 years until May 2023. The search strategy included the terms "mHealth", "telemonitoring", "heart failure" and "HF" combined with "OR" and "AND" in all the potentials combinations.

2.2. Inclusion criteria

The criteria used to evaluate studies for eligibility were: (1) original publications reporting on the results of an experimental or semi-experimental trial on HF patients, (2) studies assessing the effect of the use of an mHealth smartphone or tablet app on HF patient outcomes, (3) publications in peer-reviewed journals, (4) publications in the last 12 years and (5) publications written in English. The results of the search strategy were independently screened by two researchers for inclusion in the study on the basis of the title and

abstract. The eligibility of these studies was then determined through careful examination of the full text by the researchers. In cases of disagreement, a third reviewer acted as an arbitrator.

2.3. Study selection

Our search focused on mHealth interventions that used smartphone technology. Therefore, only trials in which the intervention group received a smartphone or tablet app were finally selected through the process. Trials using other forms of mobile technology, such as automated phone calls or SMS messages, were excluded from the final selection.

2.4. Data extraction and quality assessment

Each study selected for inclusion was comprehensively analyzed by the researchers to extract data for the characteristics of the intervention, the size of the study population and primary and secondary end points, with a particular focus on hospitalizations, patients' QoL, their adherence to their medical treatment and the statistics reporting adherence to the mHealth intervention. Additionally, it was investigated whether app validation using recognized validation questionnaires such as the Mobile Application Rating Scale (MARS) or the IMS Institute for Healthcare Informatics Functionality Score was conducted for the apps used in the included studies.

The revised Cochrane risk-of-bias tool for randomized trials (RoB 2) was used to assess the randomized controlled trials (RCTs) for their quality and potential bias.[45] The ROBINS-I (Risk of Bias In Non-randomised Studies - of Interventions) tool was used to assess non-randomized trials for their quality and potential bias.[46]

3. Results

Our search yielded 11 RCTs[18-28] and six prospective studies[29-34] that measured the effect of app-based interventions in HF patients. A detailed presentation of the systematic research is depicted in the PRISMA 2020 flowchart in Fig. 1.

3.1. RCT studies

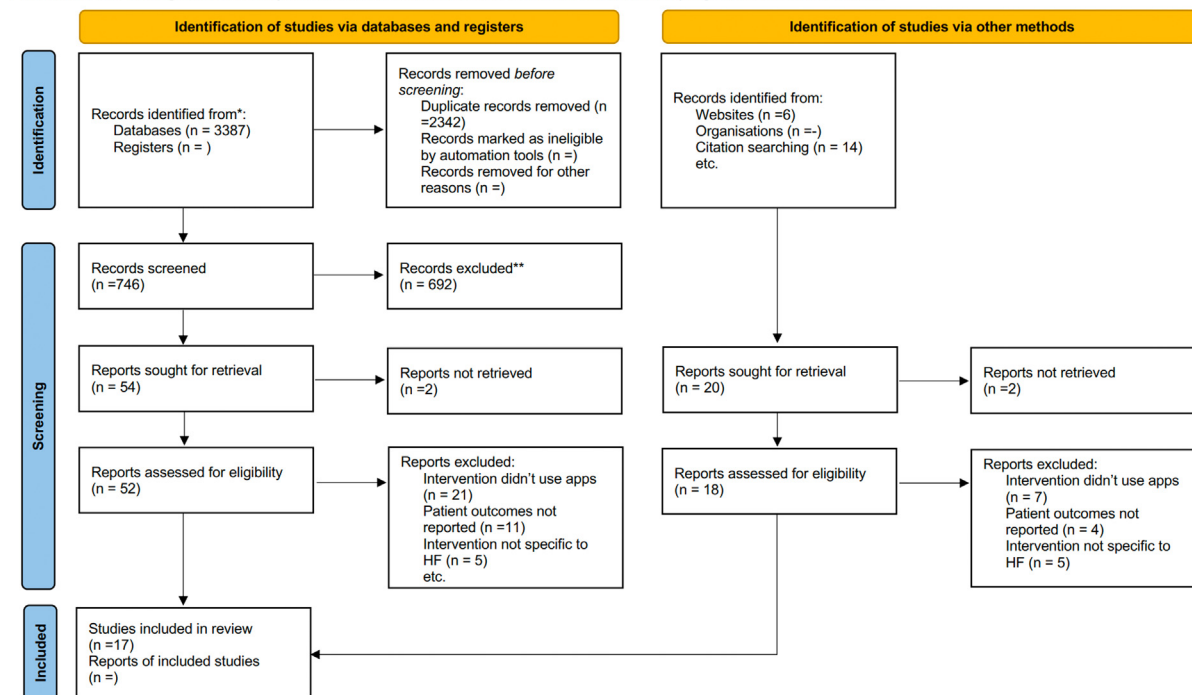#### 3.1.1. Main study characteristics

Sample sizes were modest in all RCTs, varying from 18 (Athilingam et al.[21]) to 100 (Seto et al.[18]) and consisting of both male and female participants. The studies were published in the period from 2012 to 2022. Among them, most were conducted in the United States (5/11, 45.6%) and Europe (4/11, 36.4%), while one was conducted in Australia and one in Asia. The duration of intervention varied from 1-6 months, and was 3-6 months in most studies (9/11, 81.8%).

Regarding app validation, five out of 11 (45%) studies did not use validated apps,[19,20,23,26,28] while only three (27%) used apps that had undergone quantitative validation using validated questionnaires.[21,22,24] The remaining three (27%) studies used app-based interventions that had only undergone qualitative validation.[25,27]

3.1.2. Type of mHealth interventions

All studies used an mHealth app; these were smartphone-based in most studies (9/11, 81.8%), whereas two studies provided the patients with a tablet-based mHealth app. Given that the cornerstone of HF management is monitoring of vital signs, fluid status and symptoms, the interventions aimed to regularly assess these parameters. Blood pressure and body weight measurements were inserted in the app either with Bluetooth-connected devices (4/11,

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources

Figure 1. The PRISMA 2020 flow diagram.

36.4%) or manually (6/11, 54.5%). One study (Johnson et al.[28]) did not monitor the vital signs or weight of the enrolled participants, as app feasibility and patient satisfaction were primarily evaluated. Furthermore, patients were able to report or assess their HF-related symptoms through the app in 10 out of the 11 included RCTs, allowing physicians to remotely survey their clinical status. Remarkably, educational content along with medication tracers or reminders was available in most studies.

Additional mHealth interventions were used in five studies. In Seto et al., patients who did not have an implantable cardioverter-defibrillator were provided with a single-lead electrocardiographic recorder.[18] A chest harness (Zephyr BioHarness 3.0, Medtronic) monitoring heart rate and activity was used in Athilingam et al.[21] Moreover, patients enrolled in the HeartMan trial used the Heart-Man Wristband, including a photoplethysmographic sensor, that provided information on the heart rate and beat-to-beat intervals, a tri-axial accelerometer, and a temperature sensor.[24] Lastly, a Fitbit physical activity monitor (Fitbit Charge 2) and a fitness band (Xiaomi Mi Band 2) were used in Dorsch et al. and Indraratna et al., respectively.[26,27]

3.1.3. Study outcomes

The outcomes measured were similar among studies, including the patients' QoL and quality of self-care, the number and length of hospital admissions and the level of adherence to medication.

The impact of the mHealth interventions on the participants' QoL was assessed in all studies but one, using mainly the Minnesota Living with Heart Failure Questionnaire (5/11, 45.5%) and the Kansas City Cardiomyopathy Questionnaire (4/11, 36.4%). Although in most studies there was no statistically significant difference between intervention and control groups (6/11, 54.5%), in four studies the use of an mHealth app appeared to improve the QoL of HF patients.

Regarding hospitalizations, seven out of 11 studies investigated the effect of the intervention on HF decompensations requiring inpatient care. The results indicated that the mHealth intervention failed to reach a statistically significant difference between the two groups in most of these studies (5/7, 71.4%).

Conversely, we noticed a remarkable trend toward improvement in self-care and patient education of participants using an mHealth app, which reinforced the significance of medication adherence in the management of their chronic and progressive cardiac disease.

A complete overview of the studies included in this review is presented in Table 1. The results of a complete risk of bias assessment for RCTs with the use of RoB 2 are also shown in Fig. 2.

3.2. Non-randomized studies

In addition to RCTs, there is a plethora of non-randomized prospective studies, six of which met our inclusion criteria.[29-34] Most interventions tested were designed similarly to those described above, including daily measurement of body weight, blood pressure and vital signs, symptoms assessment, educational material, hospitalization monitoring and questionnaires, mainly about QoL and self-care. Those studies had a duration from 6 weeks to 6 months and varied significantly in sample size (8-315 patients). We expound further on two studies below: one for its strong evidence base and the other for its large sample size. A complete overview of the six studies is presented in Table 2. The results of a complete risk of bias assessment with the use of the ROBINS-I tool are also shown in Fig. 3.

Regarding app validation, only one study used an app that had undergone no validation,[32] while three study apps had undergone quantitative validation using reliable questionnaires[29,31,33] and a further two had only undergone qualitative validation.[30,34]

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Table 1
An overview of the 11 RCTs included in the systematic review.

Studies S: Smartphone T: Tablet	Population and study characteristics	App validation	Application characteristics and collective data	Outcomes	Other comments
Seto et al. 2012[18], S	50/50, 6 months	Qualitative, physician only	-Daily morning blood pressure and body weight (5-min duration) -Once a week one lead ECG if available -Report symptoms if present	QoL: -ML-HFQ used -Improved in IG vs CG (p = 0.05) Hospitalization: no difference observed between groups (p = 0.1) Other outcomes: IG patients had higher percentage of prescriptions with aldosterone antagonists (p = 0.02)	-Obsolete smartphone technology -Disproportionate increase in HF clinic visits and nurse workload to outcomes
Vuorinen et al. 2014[19], S	47/47, 6 months	None	-Blood pressure, pulses, body weight -Symptomatology assessment (dizziness, dyspnea, palpitations, weakness, edema)	QoL: N/A Hospitalization: no difference observed between groups (p = 0.351) Other outcomes: -Wider medication variation in IG vs CG (medication increased p = 0.042, decreased p = 0.026) -IG required significantly greater medical staff's (nurses) time vs CG (p < 0.001)	-No difference between groups regarding NT-proBNP, LVEF and other clinical variables
Hägglund et al. 2015[20], T	40/32, 3 months	None	-Body weight via wirelessly connected scale, symptomatology -Diuretics titration	QoL: -KCCQ and SF-36 used -Significant improvement in KCCQ observed in the IG vs CG (p < 0.05) Hospitalization: 2.2 reduction to days of HF-related hospitalization per patient for IG vs CG (RR = 0.38, p < 0.05) Other outcomes: N/A	-Tablet hard drive used for data collection and storage -The intervention included patient education and advices regarding self-care in adherence to the guidelines for HF (eg, consult for increase in diuretics if body weight gain detected)
Athilingam et al. 2018[21], S	9/9, 1 month	Yes, using self-validated questionnaire	-Daily body weight and symptoms assessment -Heart rate and acceleration data via connected (BioHarness 3.0) chest strap -Medication tracer and reminder -Patient education, 10 available circuits -Exercise: deep breathing and walking exercises	QoL: -KCCQ used -No statistical difference Hospitalization: N/A Other outcomes: -Self-care management (p = 0.01) and self-care confidence (p = 0.03) of IG showed significant improvement vs CG, as appraised by the Self-Care of Heart Failure Index	-Small sample size -Only 72% of the patients concluded the 30-day follow-up -Patients stated their preference for the use of a smartphone app alone or combined with a wrist-wearable tracker over the chest strap
Rahimi et al. 2020[25], T	101/101 6 months	Yes, qualitative	-Daily weight, blood pressure and heart rate measurement -Daily report of physical symptoms -Educational context	QoL: -ML-HFQ used -No statistical difference Hospitalization: no statistical difference Other outcomes: N/A	-Both CG and IG used the application -Study purpose is one step further, as it tested the effect of specialized support
Davoudi et al. 2020[22], S	60/60 3 months	Yes, MARS and IMS Institute for Healthcare Informatics functionality scale	-Daily weight and vital signs measurement -Daily recording of physical and psychological symptoms -Educational content -Medication reminder	QoL: -ML-HFQ used -ML-HFQ showed significantly better QoL in IG vs CG (p < 0.001) Hospitalization: N/A Other outcomes: N/A	-Medication errors were identified
Wei et al. 2021[23], S	15/13 2 months	None	-Daily weight measurement, symptoms survey, reports on diet (salt intake) and physical activity -Interactive lessons -Feedback messages and direct messaging between patient and physician	QoL: -KCCQ used -KCCQ showed improvement in QoL (ρ = 0.63, p = 0.03) Hospitalization: N/A Other outcomes: increased duration of app use was correlated with improved HF knowledge (ρ = 0.59, p = 0.04), improved QoL (ρ = 0.63, p = 0.03) and weight loss (ρ = 0.40, p = 0.19)	-Small sample size -Differences between IG and CG (IG had only NYHA I and II patients)
Luštrek et al. 2021[24], S	38/23 3-6 months	UTAUT questionnaire	-Medication reminder -Daily report of symptoms, weight and blood pressure measurement -Vital signs record -Physical activity and daily mood tracking -Environmental factors measurement (temperature, humidity) -Nutrition advice	QoL: -ML-HFQ used -No statistical difference Hospitalization: N/A Other outcomes: -Self-care maintenance (SCHFI) showed significant improvement in IG vs CG (p < 0.05) -Depression (BDI II) and both anxiety dimensions (STAI) showed significant improvement in IG vs CG (p < 0.001)	-Intervention made no significant changes in patients' illness perception (IPQ) and in the level of self-care confidence (SCHFI) -A custom wristband sensor, blood pressure monitor, pill organizer, weight scale and smartphone were provided

Table 1 (*continued*)

Studies S: Smartphone T: Tablet	Population and study characteristics	App validation	Application characteristics and collective data	Outcomes	Other comments
Dorsch et al. 2021[26], S	42/41 3 months	None	-Medication reminder -Daily report of symptoms, weight -Nutrition and activity advice -Educational content	-Decrease in sexual problems ($p < 0.05$) QoL: -ML-HFQ used -No statistical difference at 3 months Hospitalization: no statistical difference Other outcomes: self-care maintenance (SCHFI) showed no significant improvement in IG vs CG	-Open-label study, participants knew in which group they were included
Indraratna et al. 2022[27], S	81/83 (18/18 patients with HF) 6 months	Likert scale	-Daily report of heart rate, weight and blood pressure measurement -Vital signs record -Physical activity tracking -Educational content	QoL: EQ-5D-5 L used -No difference between groups Hospitalization: reduction in hospital readmission in IG vs CG ($p = 0.02$) Other outcomes: -Medical adherence was increased in IG vs CG ($p = 0.002$) -Higher rate of cardiac rehabilitation in IG vs CG ($p = 0.03$)	-Few patients with heart failure (36/164) -No significant parameters were measured regarding QoL -Physical parameter data loss due to COVID-19 pandemic
Johnson et al. 2022[28], S	16/15 3 months	None	-Daily symptoms check -Educational context -Feedback messages and direct contact between patient and physician -Medication reminder	QoL: -KCCQ used -No statistical difference at 3 months Hospitalization: no statistical difference Other outcomes: N/A	-Small sample size

Abbreviations: CG, Control group; IG, Intervention group; HF, Heart failure; ML-HFQ, Minnesota Living with Heart Failure Questionnaire; LVEF, Left ventricular ejection fraction; KCCQ, Kansas City Cardiomyopathy Questionnaire; SF-36, 36-Item Short Form Survey; SCHFI, Self-Care of Heart Failure Index; BDI II, Beck Depression Inventory II; STAI, State-Trait Anxiety Inventory; NYHA, New York Heart Association Functional Classification; EQ-5D-5 L, European Quality of Life 5-Dimension 5-Level Version; MARS, Mobile Application Rating Scale; UTAUT, Unified Theory of Acceptance and Use of Technology.

Bakogiannis et. al.[29] designed and conducted an evidence-based patient-oriented mHealth app whose impact on the QoL of HF patients was evaluated in a single center prospective study. The study had 30 participants using the application for a period of 3 months. Measurements of weight and blood pressure and reporting of potential symptoms were conducted by patients daily. Patients also received education in HF in the form of weekly questionnaires. The app included a gamification feature rewarding patients for being active in the app with medals in order to enhance patient adherence. There was no significant improvement in QoL, but a
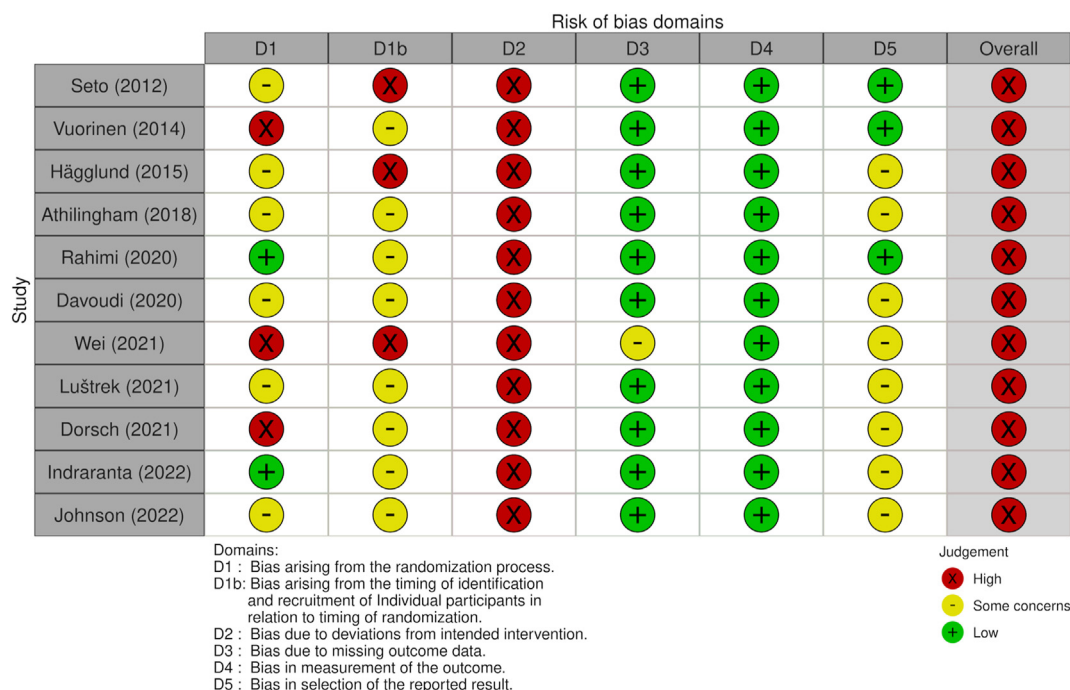

Figure 2. Risk of bias assessment of the randomized control studies with the modified risk of bias Cochrane collaboration tool (RoB 2).

Table 2
An overview of six prospective studies included in the systematic review.

Studies S: Smartphone T: Tablet	Population and study characteristics	App validation	Application characteristics and collective data	Outcomes	Other comments
Rahimi et al. 2015[34], T	−52 patients -non-interventional cohort study −6 months	Yes, qualitative	-Daily weight, blood pressure and heart rate measurement -Daily report of physical symptoms -Educational context	QoL: -ML-HFQ used -No significant changes observed QoSC: N/A Hospitalization: 15 patients had a minimum of 1 HF-related hospitalization	-The study tested only usability (no feasibility)
Alnosayan et al. 2017[33], S	−8 patients -pilot study −6 months	Yes, SUS	-Symptoms assessment -Motivational and educational messages -Medication reminder -Weight, blood glucose and blood pressure measurement	QoL: -ML-HFQ used -ML-HFQ showed an improvement in QoL with a decrease of 3.6 QoSC: N/A Hospitalization: 15 patients had a minimum of 1 HF-related hospitalization	-Disadvantages include the necessity of wireless weight scale, wireless blood pressure monitor and a Bluetooth-enabled blood glucose meter
Werhahn et al. 2019[31], S	−10 patients -prospective feasibility trial −2 months	Yes, SUTAQ	-Daily blood pressure and weight measurement -Medication reminder -Report of symptoms -app-based 6MWT	QoL: -ML-HFQ and KCCQ used -ML-HFQ showed a decrease between baseline and 2-month follow-up (−16.77) and KCCQ an increase between baseline and 2- month follow-up (−24.7) QoSC: N/A Hospitalization: N/A	-Smartwatch necessary at all times (expect sleeping) -Mean daily step count used as measurement for daily physical activity
Ware et al. 2020[30], S	−315 patients -pretest-posttest pragmatic study −6 months	Qualitative, physician only	-Daily weight, blood pressure and heart rhythm measurements -Daily report of physical symptoms -Self-care feedback messages	QoL: -ML-HFQ and EQ-5D-5 L used -ML-HFQ showed a significant decrease of 9.8 points relative to baseline (p < 0.001) -EQ-5D-5 L showed no significant change QoSC: −SCHFI used -SCHFI showed an increase of 7.8, 8.5 and 2.5 for maintenance, management and confidence, respectively Hospitalization: −50% reduction of HF-related hospitalization between baseline and 6-month follow-up (p < 0.001)	-Not all patients complete the 6- month follow-up
Heiney et al. 2020[32], S	−12 patients -quasi-experimental pilot study −4 week	None	-Daily weight, measurements -Symptoms quantification (dyspnea) -Questions about salt restriction -Educational and inspirational messages	QoL: -HRQOL 14 used −1.46 decrease in unhealthy days −0.75 decrease in days experiencing limitation in daily activity QoSC: −SCHFI used -Management subscale was not scored -No significant differences on other subscales Hospitalization: 1 patient reported admission to the hospital	-Limitation due to small sample size and quasi-experimental type of study
Bakogiannis et al. 2021[29], S	−14 patients -single-center prospective study −3 months	Yes, PSSUQ and MARS	-Daily blood pressure and weight measurements -Quantification of potential symptoms (dyspnea, edema, mood, heart rhythm) -Medication reminder -Patient education via weekly quiz	QoL: -KCCQ and EQ-5D-5 L used -Nonsignificant improvement QoSC: -EHFScBs used -Significant improvement from baseline score of 4.4% (SD 7.2%, p = 0.002) Hospitalization: 1 patient hospitalized	-Evidence-based intervention -Long-term adherence via gamification of features and reward motivation

Abbreviations: ML-HFQ, Minnesota Living with Heart Failure Questionnaire; 6MWT, Six Minute Walk Test; KCCQ, Kansas City Cardiomyopathy Questionnaire; HFSPS, Heart Failure Somatic Perception Scale; NYHA, New York Heart Association Functional Classification; EQ-5D-5 L, European Quality of Life 5-Dimension 5-Level Version; SCHFI, Self-Care of Heart Failure Index; HRQOL 14, Health Related Quality Of Life Scale 14; EHFScBs, European Heart Failure Self-care Behaviour scale; SUS, System Usability Scale; SUTAQ, Service User Technology Acceptability Questionnaire; MARS, Mobile Application Rating Scale; PSSUQ, Post-Study System Usability Questionnaire.

statistically significant increase was observed in quality of self-care (p = 0.002) when compared with baseline. HF-related hospitalization was reported at 3% in the period of the study.

Ware et al.[30] presented results of a pragmatic study aiming to evaluate the effect of an mHealth program in patients with HF. The study included 315 patients, who used the mobile-based monitoring app over a period of 6 months. The intervention app allowed for logging of daily body weight, blood pressure and heart rate measurements and reports of physical symptoms by patients. Self-care feedback messages were also displayed to patients. Study results showed 50% reduction of HF-related hospitalization between baseline and 6-month follow-up (p < 0.001) and statistically significant improvements in QoL (p < 0.001) and in self-maintenance (p < 0.001). Regarding

Figure 3. Risk of bias assessment of the non-randomized studies with the ROBINS-I (Risk of Bias in Non-randomised Studies - of Interventions) tool.

clinical outcomes, a statistically significant decrease (59%) in brain natriuretic peptide was observed between baseline and 6 months (p < 0.001).

4. Discussion

After thorough literature research, 17 studies assessing apps' effects on patient outcomes met the inclusion criteria, of which 11 were RCTs. The vast majority of original publications on the subject were usability studies and study protocols. This observation implies that many mHealth-based interventions are currently in earlier stages of development with potentially promising results in the future.

All studies used a similar type of intervention, asking that patients weigh themselves, measure their blood pressure and regularly assess their symptoms, logging all results in an app. As expected, some variation was present, for example in the frequency at which patients were requested to interact with the apps. Some interventions even used Bluetooth-enabled peripherals that automatically logged the data, which significantly improves the user experience. Many apps incorporated medication reminders, whereas patient education modules were also present in some studies. Patients found most features subjectively helpful. With the currently available evidence, it is difficult to ascertain whether some modules were more useful than others in improving patient education and self-care.

Although the importance of using validated apps in app-centered mHealth interventions has been repeatedly highlighted, notably in a review of commercially available patient-centered apps for HF by Mortara et al.,[47] most RCT studies and several non-randomized trials included in this systematic review did not use validated apps in their intervention arms. Thankfully, a trend can be observed of more recent studies being more likely to use quantitative validation methods in the development of the mHealth apps.

Regarding outcomes, QoL was significantly improved by various app-based interventions.[18,20-23,30-33] The reports on other outcomes, including quality of self-care, number and duration of hospitalizations and the apps' effect on medication adherence, were not as uniformly positive. Nonetheless, a trend can be observed regarding the benefit of app use,[18,19,21] indicating that evidence-based and cutting-edge apps have the potential to improve a traditional "hard" outcome in HF.

The conclusions that can be drawn from these studies will certainly assist in future design and preparation of RCTs on mHealth-based interventions. As an example, Athilingam et al. surmised that the use of a chest harness for vital signs measurement quite negatively affected patients' adherence to the intervention, in part because of its mediocre battery capacity.[21] Less restrictive wearables are suggested as a more efficient alternative for combination with apps. Personalized medicine is theoretically ideal for HF care, where no two patients are the same, each with different background, comorbidities, disease phenotype and often, acute changes in their health status. All these factors indicate the importance of continuous personalized treatment for the particularities of each patient. Although this study does not indicate significant improvements in the outcomes of the personalized treatment arm, it demonstrates the current standard of remote care and monitoring capabilities in HF and provides a glimpse into the future.

The included non-RCT studies share the same idea with the RCTs but have protocols that are easier to implement in real-world conditions. This enables researchers to deploy mHealth interventions faster and with fewer expenses, but at the cost of greatly reducing the quality of evidence. As described in our systematic review, non-RCT studies used a greater variety of tools to measure different parameters, such as QoL or quality of self-care, with great variation in sample size. A major point raised by the present systematic review is that high-quality evidence of the effect of mHealth-based interventions in HF is very limited. Therefore, all future research on this subject should avoid quasi-experimental study designs, which inherently carry a higher risk of bias compared with RCTs.

As for the resources needed for such interventions, only the study by Indraratna et al. performed a cost-effectiveness analysis, but given that most patients suffered from a recent acute coronary syndrome, it does not reflect the true situation regarding the use of mHealth apps in patients with HF and therefore is not relevant for this review.[27] No other RCT performed this type of analysis. However, a clear divide can be observed between interventions that require no input from health care professionals and those that do. Interventions featuring data surveillance by HF nurses and physicians unanimously reported increased workload despite the organizational benefits, which should be a consideration for this design decision (Table 1). Seto et al. suggested that physician workload was significantly increased, as they were tasked with appropriately responding to each alert created

by patients' apps.[18] In the study by Vuorinen et al., HF nurses' time allocated per patient increased significantly, as did the number of visits to HF clinic.[19] Given that hospitalizations incur most of the health costs for HF patients, even modest decreases in their frequency and duration would justify the implementation of such resource-intensive app-based interventions. Apps that do not convey patient data and instead autonomously provide guidance and patient education are very promising because of the limited resources necessary, but this strategy's impact on patient safety and outcomes is uncertain. Hägglund et al. used such an intervention with reasonable success, but larger trials are necessary to prove such apps' safety and efficacy.[20]

Medication adherence is another aspect of HF patient care with great potential for improvement with mHealth app use. Apps featuring push notifications for pill and refill reminders have the capacity to improve adherence to medication. Pill reminders were implemented in many of the presented studies' mHealth apps.[21,22,24,26,28-31] Moreover, only Athilingam et al. used a validated tool, specifically the Morisky Medication Adherence Scale, to evaluate medication adherence.[21] However, the results of this small study will need to be corroborated by those of larger trials.

We consider that the future of mHealth interventions in HF patients seems promising, especially since the COVID-19 pandemic has facilitated an enormous acceleration in the role of telehealth. However, despite the growing patient engagement with telehealth technologies, personalized mHeatlh interventions have not yet been optimized. Future research is needed on developing patient-centered mHealth apps integrated into established HF clinical pathways. According to our view, more comprehensive evaluation of patient feedback could assist in developing the appropriate mHealth app features, which could ultimately improve compelling end points in RCTs involving sizeable and heterogeneous HF populations.

5. Conclusions

HF is a chronic disease for which consistent and complex self-care is required to achieve good outcomes. According to the results of our systematic review, there is limited experience concerning the design and implementation of app-based interventions in HF. Despite trends indicating patient benefits from HF apps, several of the included mHealth interventions failed to improve important outcomes such as QoL and number of hospitalizations. We believe that larger and longer-lasting trials, using apps updated after careful examination of the shortcomings of past efforts, are needed to definitively assess the extent of benefit that smartphone apps can offer to HF patients. Indeed, research on the subject is far from over, as several trial protocols involving app-based interventions are yet to be published.

6. Limitations

This systematic review was limited by the small number of included trials, the small mean sample size and the high risk of bias found in many studies, especially those without a control sample and/or with non-randomized methodology. Furthermore, the heterogeneity of the interventions meant that a meta-analysis would have provided limited actionable insight. The authors believe that as interest in app-based interventions for HF grows and standardization of apps occurs, larger studies with comparable apps will greatly improve the quality of evidence regarding this subject.

Author contributions

Conceptualization, C.B., D.M. and A.T.; methodology, C.B., D.M. and A.T.; writing—original draft preparation, C.B., D.M., A.T., A.C.M. and C.L.; writing—review and editing, V.P.V., A.C.M., E.A., A.B., P.K. and C.E.P.; visualization, C.B.; supervision, V.P.V., E.A., A.B., P.K. and C.E.P.

Institutional review board statement

Each study included in our review was review by an institutional review board.

Informed consent statement

Each of the included studies complied with the Declaration of Helsinki. An informed consent form was mandatory in all included studies.

Declaration of competing interest

The authors declare no conflict of interest.

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