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Telehealth care and remote monitoring strategies in heart failure patients: A systematic review

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Index

ABSTRACT

Background. Heart Failure (HF) is a cardiac clinical syndrome which derive both from cardiac and extra-cardiac conditions. Heart failure is an increasing public health issue and affects a great number of people worldwide. The prevalence of heart failure is generally estimated at 1% to 2% of the general adult population, up to 10% in people aged over 70. Heart failure impacts on patients' living and working abilities, representing a high mortality-related disease. Despite the huge amount of human and economic resources employed, rehospitalization and mortality rates in heart failure patients are still alarming. A tool to safeguard unstable or non-compliant patients from deterioration of their heart failure is remote monitoring. Currently, results of remote clinical management of heart failure patients seem to be effective but not entirely convincing. This study is focused on summarizing data related to the impact of the remote monitoring strategies on heart failure patients.

Objective. To synthesize evidence related to the impact of telemonitoring strategies on mortality and hospital readmissions of heart failure patients.

Methods.

Design. A systematic literature review and meta-analysis were conducted based on the Cochrane Handbook for Systematic Reviews of Interventions and its reporting was checked against the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist.

Data sources. PubMed, Scopus, CINAHL, IEEE Xplore Digital Library, Engineering Source, and INSPEC were searched until August 2021. No further limits or filters were utilized in order to ensure a high sensitivity of the search strategy and adopt a broad approach. No additional search strategy was used to retrieve further data.

Study selection. To be included, available full texts had to be published in English or Italian and involve heart failure patients of any NYHA class, cared with any telecare, remote monitoring, telemonitoring, or telehealth programmes. Also, articles had to collect data about crude incidence rate of mortality and number of patients who underwent rehospitalizations during follow-ups.

Following the inclusion criteria, two raters independently screened titles and abstracts of retrieved references for both eligibility and inclusion in the review, with any disagreement resolved with the involvement of a third researcher.

Synthesis method. To explore the effect of telemonitoring strategies on both one-year mortality and one-year rehospitalizations, studies were synthesized through meta-analyses. The Odds Ratio (OR) or Risk Ratio (when appropriate) was calculated as a principal effect size using the random effects model. Studies not included in the meta-analysis were synthesized narratively.

Results. Sixty-one studies were included in the review. Narrative synthesis of data suggests a trend towards the reduction of deaths among patients who underwent telemonitoring, but number of rehospitalized patients was higher among the monitored ones. Meta-analysis of studies reporting one-year mortality outlined the protective power of care models based on telemonitoring in reducing one-year mortality (OR 0.54, 95% CI = 0.39–0.76). As well as meta-analysis of studies reporting number of rehospitalized patients in one-year outline that telemonitoring strategies are effective in reducing the number of rehospitalized patients when compared with usual care strategies (OR 0.56, 95% CI = 0.40–0.80). Substantial levels of heterogeneity found in the studies suggest to focus future research on the application of homogeneous monitoring strategies, follow-up periods, and outcome reporting.

Conclusion. Evidence from studies included in this review confirms the benefits of telemonitoring in reducing mortality and rehospitalizations of HF patients. Further research is needed to reduce the heterogeneity of the studies.

HEART FAILURE

What is heart failure

Heart Failure (HF) is a cardiac clinical syndrome characterized by signs and symptoms, such as breathlessness, ankle swelling and fatigue, and accompanied by elevated jugular venous pressure, pulmonary crackles and peripheral oedema (1). The main cause is a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress (1). Heart failure is often associated with issues in ejection fraction, leading to an increase in end-diastolic volume and end-diastolic pressure (2). Guidelines use the term "chronic heart failure" to refer to patients already suffering from heart failure (1), but a large number of patients suffering from "acute heart failure" are not considered to be suffering from heart failure, although they may present with a rapid onset of symptoms which, on observation by health professionals, could be recognised as consequence of other pre-existing cardiac pathologies (3).

Aetiology of heart failure

There is no full consensus on the causes of heart failure. However, regarding known causes directly related to cardiac and circulatory conditions, abnormal loading conditions such as hypertension, valvular or structural defects of the heart and blood vessels, pericardial and endocardial pathologies, and arrhythmias are often associated with the onset of heart failure. The onset of heart failure is above all the result of cardiac ischemic problems such as cardiac fibrous tissue after myocardial infarction, coronary pathologies, and endothelial cell dysfunctions (1, 4-6).

Furthermore, according to the guidelines, heart failure can arise as a consequence of a series of conditions that may not even be directly associated with the myocardium (1, 4, 5). In fact, heart failure could be triggered from toxicological damage due to the abuse of alcoholic substances, drugs, and anabolic steroids. Other conditions that could lead to heart failure are immune-mediated, rheumatic heart disease and phlogistic damages deriving from viruses, bacteria, or immune system failure. Furthermore, heart failure may result from infiltrative pathologies such as tumours through metastases or direct infiltration of cancer cells in the heart. Finally,

it can be caused by hormonal metabolic pathologies (e.g., hypercholesterolemia or thyroid pathologies) or nutritional pathologies due to an excess or deficiency of nutrients and genetic causes (1, 4-6).

Categorization and grading of heart failure

Categorization of heart failure is mostly based on Left Ventricular Ejection Fraction (LFEV) values. Measurement of volumes of the ejection fraction of the left ventricle by means of echocardiographic images plays an important role in the management of patients with cardiac diseases, especially heart failure conditions (7). Heart failure is categorized by the volume of the residual ejection fraction after a cardiac primary event. In this regard, three categories of heart failure are recognized: Heart Failure with reduced Ejection Fraction (HFrEF), i.e., when the left ventricular ejection fraction is <40%; Heart failure with mid-range Ejection Fraction (HFmrEF), i.e., when the left ventricular ejection fraction is between 40 and 49%, and Heart Failure with preserved Ejection Fraction (HFpEF), i.e., when the left ventricular ejection fraction is ≥50% (1, 2, 7-10). If the ejection fraction estimates the functional ventricular capacity, the parameter used to estimate the true functional ability of a patient is the New York Heart Association (NYHA) functional class (11). This estimate has been used to describe the severity of symptoms and exercise intolerance (12). Four classes of symptoms are recognized: NYHA I, NYHA II, NYHA III, and NYHA IV (11, 13).

NYHA I	Physical activity is not limited, it does not cause unexpected fatigue, palpitation, and shortness of breath (dyspnoea)
NYHA II	Some limitations of physical activity, the discomfort disappears at rest. Ordinary physical activity results in fatigue, palpitation, and dyspnoea
NYHA III	Profuse limitation of physical activity, absence of discomfort at

	rest and insurgence of fatigue, palpitation, and dyspnoea with less than ordinary activities
NYHA IV	The most severe condition, patients are unable to carry any physical activity without feeling discomfort, symptoms of heart failure are also felt at rest and any physical activity contribute to the increasement of discomfort

Epidemiology of heart failure

Heart failure is an increasing public health issue and affects a great number of people worldwide. Research carried out in the last decade reported that 23 million people suffered from heart failure worldwide (14, 15). Other authors stated that there were at least 38 million people living with heart failure, as reported in a large longitudinal study that considered various pathologies (16). A more recent article estimates that about 64.3 million people live with heart failure worldwide (8). The prevalence of heart failure, despite being influenced by the definition used, is generally estimated at 1% to 2% of the general adult population in developed countries, with an increase up to 10% in people aged over 70 (1, 17, 18). In the USA alone about 5.7 million people live with heart failure, and there are 870.000 new diagnoses every year (4), although another study, carried out in 2014, reports that 5.1 million US citizens live with heart failure, with 550.000 new diagnoses yearly (19). The incidence is estimated at 5.7 cases per 1000 persons/year (2), with significant changes in the rate with aging. In fact, in people <55 years old, the incidence is 0.3 per 1000, while in people ≥85 years old, the incidence is up to 18 per 1000 (19, 20). The National Center for Health Statistics through the National Health and Nutrition Examination Survey estimated the prevalence of heart failure in the USA at 2.5% based on self-reported data (21). As regards Europe, country-specific estimates are rarely reported, but there are statistics related to several European countries. In Germany, the estimated prevalence of heart failure based on

data of over 3 million citizens was 4.0% in both genders. In Belgium, based on primary care data, the prevalence of heart failure in 2015 was 1.2% in men and 1.3% in women. A study on 4 million individuals in the United Kingdom by Conrad and colleagues reported a prevalence of heart failure of about 1.6% (22).

When referring to the outcomes of heart failure both in Europe and worldwide, statistics are more readily available. In Europe, cardiovascular diseases were responsible for 1.83 million deaths in 2016 (36% of all deaths) (23, 24). This represents a remarkable burden for healthcare systems due to frequent rehospitalizations and need for outpatient visits (25). Cardiovascular syndromes amount approximately to 2% of the healthcare expenditure in Europe, which is about 29 billion dollars (26, 27). Other recent European data reporting 12-month all-cause mortality for hospitalized patients and outpatients described 17% and 7% of deaths, with hospitalization rates of 44% and 32%, respectively (1).

Heart failure impacts on patients' living and working abilities, worsening their quality of life, and represents a high mortality-related disease (1, 4, 6, 18, 28). In this regard, despite the huge amount of human and economic resources employed, due to the increasing incidence and better prognosis of its trigger factors, rehospitalization and mortality rates in heart failure patients are still alarming (8, 19). In fact, in general, the first years after infarction are characterized by 40% to 50% mortality within 5 years and 15% to 30% readmission in the first year (15, 29-31). Also, heart failure is associated with the highest 30-day readmission rate among all diagnoses (about 20–25%), and it is estimated that half of the newly diagnosed patients are admitted to hospital within one year from heart failure diagnosis (8, 32, 33). Despite variances in diagnostic criteria and definition (19), most studies and reviews estimate that over half of all heart failure cases are not correctly diagnosed (8). Particularly, 76% of all cases of misdiagnoses occur when patients have a preserved left ventricular ejection fraction (HFpEF) (8, 18). Before symptom establishment, cardiac abnormalities or dysfunctions could act as precursors of heart failure (systolic or diastolic left ventricular dysfunction). The recognition of precursors is important to starting an early treatment that is linked to better patient outcomes (1).

Patients' compliance and quality of life

Some evidence-based guidelines are available at the international level (1, 34) which usually recommend self-management of the disease through fluid restriction, medication, and daily weight measurement in order to keep control of fluid balance (35, 36). Patient compliance with the guidelines is a cornerstone to achieving better health outcomes, but results are often not fully satisfactory (35, 37, 38). Some studies have shown compliance with daily body weight measurement ranging from 12.0% to 75.0%, with the reason for non-compliance ascribed to lack of time and knowledge or little clinical support (38, 39). Furthermore, patients with little adherence are often not promptly connected to clinicians, leading to failed timing for intervention and increased mortality and readmissions (35).

The quality of life is more deeply influenced by heart failure than by any other disease (40, 41). Heart failure is responsible for the progressive deterioration of patients' quality of life, reducing their resilience and ability to deal with the disease (42). In fact, a poor quality of life is not only associated with low resilience and coping but also with worse clinical outcomes, such as an increased risk of rehospitalization and death (40), thus improving the patient's quality of life has become one of the main aims of treatment of heart failure (43).

Caring scenarios

Patients' clinical status could influence diagnoses and outcomes. Therefore, it is recommended to implement caring models that allow wider and targeted patient care to promptly detect signs and symptoms of worsening heart failure and promote long-term health, thereby reducing mortality and rehospitalizations. Patient self-monitoring or self-management of medications, periodic access to outpatient departments, as well as entrusting patients to caregivers, despite being effective, may not be enough to prevent the onset of secondary pathological events (36, 42, 44). In fact, patients usually face difficulties in self-caring that requires both lifestyle and medication changes, as well as proper monitoring of symptoms (36, 45). Difficulties are often not only encountered by patients but also by clinicians that need to tailor caring models to patients' specific situations (36). A tool to safeguard unstable or non-compliant patients right from early detection of

deterioration of their heart failure is remote monitoring (44), which has become one of the most active fields in the management of heart failure (46). With this kind of approach, it is possible to better classify the clinical conditions of patients and, consequently, to better distribute resources among patients who have high risk of worsening heart failure, compared to others with less severe condition, thus making it possible to tailor nursing and medical interventions (44).

Results of remote clinical management of heart failure patients seem to be effective but not entirely convincing. In fact, some prospective trials have not confirmed this hypothesis, because there is not just one type of telemedicine (1). As indicated in a Cochrane Review, despite a significant reduction in all-cause mortality and rehospitalizations in patients subjected to telemonitoring strategies, effects were relatively small and not entirely positive in terms of outcomes (1, 28, 44). Perhaps for this reason no guidelines have recommended large-scale implementation of remote monitoring due to conflicting study results (16, 28, 44, 46). A large number of studies have suggested encouraging results, but it is not yet clear which remote care strategies for heart failure give the best results and to what extent. This review is therefore focused on summarizing useful data on monitoring strategies for heart failure.

AIM

This study aims to synthesize evidence related to the impact of telemonitoring strategies on mortality and hospital readmissions of heart failure patients.

METHODS

An extensive systematic review of the literature was conducted in accordance with relevant criteria described in the ‘Cochrane Handbook for Systematic Reviews of Interventions’ (47) to document the impact of telemonitoring on mortality, rehospitalization, medication compliance, and quality of life.

According to the study aims, only data related to mortality and rehospitalizations were synthesized in this work following the ‘Preferred Reporting Items for Systematic Reviews and Meta-Analyses’ (PRISMA) checklist (48).

Criteria for considering studies for this review

Types of studies

To be included in the review, a study must be primary and quantitative in nature. Also, the study must be available in full text and written in English or Italian.

Types of participants

Eligible participants were all heart failure patients belonging to any of NYHA classes (I, II, III, IV). In studies conducted on mixed samples, i.e., samples that included patients suffering from other main chronic diseases different from heart failure, only data regarding heart failure patients were considered. If it was not possible to distinguish the outcomes of each sample, the study was excluded.

Types of intervention

Eligible methods of care included all available telecare, remote monitoring, telemonitoring, or telehealth programmes.

Types of outcome measures

The first step in this literature review, as stated already, was focused on collecting data about the crude incidence rate of mortality and number of patients who underwent rehospitalizations during follow-ups. Therefore, all articles reporting this kind of outcomes were considered for eligibility.

Search methods for identification of studies

Electronic searches

To identify suitable keywords for the search strategy, a pilot search was performed on PubMed using the following search strings based on the PICO model (49): Population: “Heart failure” OR “cardiac failure” OR decompensation; Intervention: telenursing OR “remote nursing” OR “telehealth nursing” OR “tele health nursing” OR “tele health nursing” OR ((telemedicine OR “remote monitoring" OR "remote patient monitoring" OR telemonitoring) AND nursing); COMPARISON; OUTCOMES: readmission* OR re-hospitalization* OR re-hospitalisation* OR mortality OR death* OR survival OR compliance OR adherence OR ‘quality of life’ (Table 1).

Table 1. Pilot search

P	I	O
“Heart failure” OR “cardiac failure” OR decompensation	telenursing OR “remote nursing” OR “telehealth nursing” OR “tele health nursing” OR “tele health nursing” OR ((telemedicine OR “remote monitoring" OR "remote patient monitoring" OR telemonitoring) AND nursing)	readmission* OR re-hospitalization* OR re-hospitalisation* OR mortality OR death* OR survival OR compliance OR adherence OR ‘quality of life’

Therefore, considering the keywords used in the retrieved studies and the aims of the present study, the following keywords were utilized in the search strategy: ‘heart failure’, ‘telenursing’, ‘telehealth nursing’, ‘Telemetry, nursing’, ‘remote monitoring’, ‘remote patient monitoring’, ‘telemonitoring’, ‘survival rate’, survival, mortality, ‘patient readmission’, ‘Patient Compliance’, ‘Medication Adherence’, ‘Quality of Life’. All these keywords were combined together with the Boolean operator ‘AND’.

The consulted electronic databases were PubMed, Scopus, CINAHL, IEEE Xplore Digital Library, Engineering Source, and INSPEC (Table 2 in Appendix). The

research was performed on August 2021 without time limitations; no further limits or filters were utilized in order to ensure a high sensitivity of the search strategy and adopt a 'broad approach' (47). The full search strings are reported below. All the retrieved references were collected and managed with EndNote X7.8 for Windows (Thomson Reuters, New York).
This first bibliographic research was conducted by three researchers.

Search strings

PubMed: "heart failure" [Mesh] AND ("Telenursing" [Mesh] OR "telehealth nursing" OR "Telemetry/nursing"[Mesh] OR "remote monitoring" OR "remote patient monitoring" OR telemonitoring) AND ("survival rate"[Mesh] OR survival [Mesh] OR mortality [Mesh] OR "Patient Readmission"[Mesh] OR "Patient Compliance"[Mesh] OR "Medication Adherence"[Mesh] OR "Quality of Life"[Mesh])

Scopus: (TITLE-ABS-KEY ("heart failure") AND TITLE-ABS-KEY ("Telenursing" OR "telehealth nursing" OR (telemetry AND nurs*) OR "remote monitoring" OR "remote patient monitoring" OR telemonitoring) AND TITLE-ABS-KEY ("survival rate" OR survival OR mortality OR "Patient Readmission" OR "Patient Compliance" OR "Medication Adherence" OR "Quality of Life"))

CINAHL: ("heart failure") AND ("Telenursing" OR "telehealth nursing" OR (Telemetry AND nurs*) OR "remote monitoring" OR "remote patient monitoring" OR telemonitoring) AND ("survival rate" OR survival OR mortality OR "Patient Readmission" OR "Patient Compliance" OR "Medication Adherence" OR "Quality of Life")

IEEE Xplore Digital Library: ("heart failure") AND ("Telenursing" OR "telehealth nursing" OR (Telemetry AND nurs*) OR "remote monitoring" OR "remote patient monitoring" OR telemonitoring) AND ("survival rate" OR survival OR mortality OR "Patient Readmission" OR "Patient Compliance" OR "Medication Adherence" OR "Quality of Life")

Engineering Source: ("heart failure") AND ("Telenursing" OR "telehealth nursing" OR (Telemetry AND nurs*) OR "remote monitoring" OR "remote patient monitoring" OR telemonitoring) AND ("survival rate" OR survival OR mortality OR "Patient Readmission" OR "Patient Compliance" OR "Medication Adherence" OR "Quality of Life")

INSPEC: ("heart failure") AND ("Telenursing" OR "telehealth nursing" OR (Telemetry AND nurs*) OR "remote monitoring" OR "remote patient monitoring" OR telemonitoring) AND ("survival rate" OR survival OR mortality OR "Patient Readmission" OR "Patient Compliance" OR "Medication Adherence" OR "Quality of Life")

Additional search strategies

Since the electronic search was conducted using a 'broad approach' (six databases with inclusive research strings), no additional search strategy was used to retrieve further data.

Data collection and analysis

Selection of studies

Studies were screened for eligibility and inclusion by analysing the titles/abstracts and full texts, respectively. If the abstract was not available, the article was excluded. Two raters independently screened titles and abstracts of retrieved references (eligibility phase). To avoid the exclusion of potentially relevant articles, titles and abstracts had to fulfil the following broad criteria: a) show that the studies were primary and quantitative in nature; b) show that the studies involved heart failure patients who underwent telemonitoring/remote monitoring/remote care; c) show that the studies evaluated the outcomes of heart failure patients, such as mortality, readmission, compliance, and quality of life.

Based on the purpose of this study, full texts were analysed by two raters for inclusion in the review, considering the following criteria: a) the full text was available through the library resources of the University of L'Aquila; b) it was

published in English or Italian; c) it describes a quantitative primary study (randomized controlled trial, prospective study, retrospective analysis, cohort study, or case–control study), d) the study included heart failure patients, and e) the full text reports mortality and number of rehospitalized patients as outcomes. At the end of each step, the first author compared the results of the screening separately with each of the other researchers, and any disagreement was resolved with the involvement of a third researcher.

The following exclusion criterion was considered: If studies were conducted on mixed samples, they were excluded if it was not possible to obtain separate data on patient outcomes. The whole selection and computing processes for the PRISMA flowchart were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). During the inclusion process, any disagreement between the raters was resolved by discussion with a third author until consensus was reached.

Risk of Bias assessment

To evaluate the risk of bias in this review, Joanna Briggs Institute (JBI)'s critical appraisal tools for the evaluation of randomized controlled trials and observational studies were used. The purpose of this appraisal procedure is to assess the methodological quality of a study and determine the extent to which a study has addressed the possibility of bias in its design, conduct and analysis (50). Following the JBI Manual, decisions about the scoring system and cut-off were made in advance and agreed upon by all reviewers before commencement of critical appraisal. Studies were judged for risk of bias according to the following cut-offs: low risk, if the percentage of answers scoring 'yes' was above 70%; moderate risk, if the percentage of 'yes' scores was between 50% and 69%; high risk, if 'yes' scores were below 49%.

Data extraction and management

Data extraction was performed using a previously piloted electronic spreadsheet of Microsoft Excel for Windows. One nursing researcher extracted data and a nursing professor supervised the process and resolved any inconsistency.

For the purposes of this study, the following data were extracted:

a) General information: First author, publication year;

b) Study characteristics: Country, characteristics of the study design (extracted as 'reported by the authors', the setting where the study was conducted, denomination of the remote monitoring programme, main features of the remote monitoring programme, compared care model (control group), sampling methods, sample (N), number of cases (N), number of controls (N), age, NYHA heart failure classification (I, II, III, IV);

c) Data related to the research question of the review: study aim, crude number of deaths, one-year mortality rate for the case and control and its probability, crude number of rehospitalized patients, one-year patients rehospitalized for the case and control and its probability.

For quality of life and medication adherence outcomes, data were extracted but will be reported in a secondary analysis of the database.

Data synthesis

General information, study characteristics, and other data related to the research questions of the review were preliminarily and descriptively synthesized. To explore the effect of telemonitoring strategies on both one-year mortality and one-year rehospitalization, studies were synthesized through meta-analyses, using ProMeta® free software when feasible. The Odds Ratio (OR) or Risk Ratio (when appropriate) was calculated as a principal effect size using the random effects model as a conservative approach to account for different sources of variation between studies. The level of heterogeneity was explored and quantified using the Cochran's Q-test and I^2 test, respectively. A significant Q-test value ($p \leq 0.05$) indicated the presence of heterogeneity, while the threshold for considering heterogeneity as substantial was 50% (47). Subgroup analysis was performed based on the study design to explore heterogeneity. Sensitivity analysis was performed by removing each study from a meta-analysis to determine whether the meta-analysis results were significantly influenced by any single study (47). Data that could not be included in the quantitative synthesis were narratively synthesized. For meta-analyses that included three or more studies, the publication bias was assessed using funnel plots, by testing for the asymmetry of the funnel plots (Begg and

Mazumdar's rank correlation and Egger's linear regression method), and by computing the failsafe number when needed.

Data extraction tool

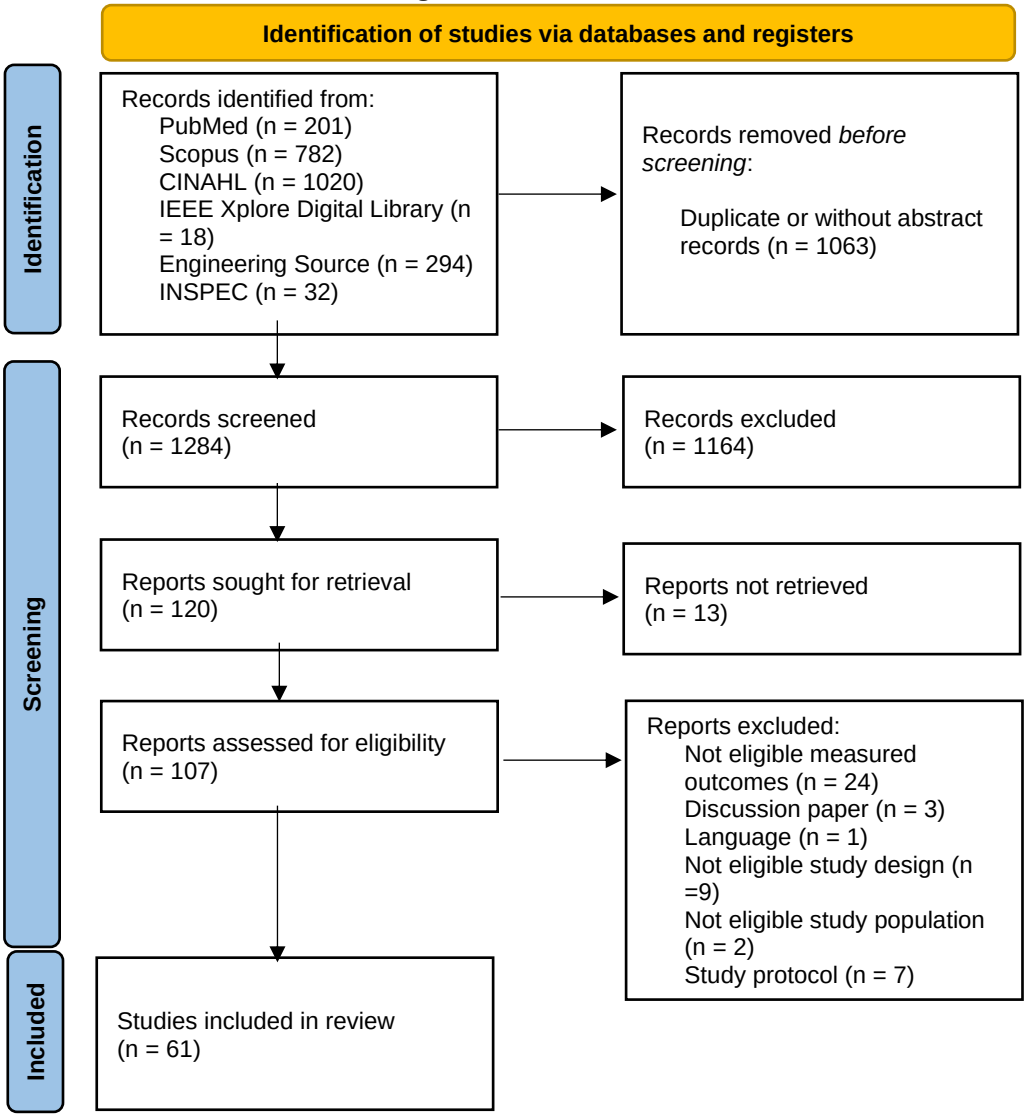
General information	**First author** **Publication year**
Study characteristics	Country Study design "reported by authors" Setting Remote monitoring program Feature of remote monitoring program Control group care model Sampling method Sampling (N) Cases (N) Controls (N) Age of patients NYHA Class
Data related to the research question	Study aim Crude number of deaths One-year mortality rate case One-year mortality rate controls Probability Crude number of patients rehospitalized One-year patients rehospitalized case One-year patients rehospitalized controls Probability

RESULTS

Search results

The electronic search in the scientific databases identified 2347 potentially relevant records. Duplicates and references without abstracts were removed, leaving 1284 titles and abstracts that were assessed for eligibility. One hundred and seven available full texts were then analysed and 61 of them were included in the systematic review, 17 of which were included in the quantitative meta-analytic synthesis (meta-analysis). Detailed information about the search and selection process is reported in the PRISMA flowchart.

Figure 1. PRISMA flow chart



Characteristics of the included studies

As reported in Table 3 in Appendix, the 61 included studies were published from 2004 to 2020 and conducted mainly in the USA (n = 16, 26.2%), Italy (n = 10, 16.4%), the Netherlands (n = 7, 11.5%), Germany (n = 6, 9.8%), and the United Kingdom (n = 4, 6.6%). Regarding the study design as 'stated by the authors', most of the studies were randomized, controlled trials (n = 39, 63.9%), followed by prospective studies (n = 8, 13.1%), and observational retrospective studies (n = 7, 11.5%). Overall, 22198 heart failure patients were involved, with study samples ranging from 20 to 1653. The mean age was reported for 16782 patients, with a range of 52.0 to 81.4 years of age. The median age was reported for 3942 patients, with a range of 61 to 77 years of age. Heart Failure classification based on the NYHA classes was reported for 20249 patients, with 14 studies including 7360 patients with all NYHA classes (I, II, III, IV), 19 studies including 6496 patients with only II, III, and IV classes, and 16 studies including 5205 patients with only I, II, or III classes. In regard to outcomes considered in this study (Table 4 in Appendix):

1) mortality considered as crude number was reported in 29 studies [ID 1, 4, 6, 7, 10, 11, 12, 13, 14, 16, 20, 22, 23, 24, 27, 30, 33, 34, 35, 37, 39, 43, 50, 51, 52, 55, 56, 58, 59];
2) one year mortality was reported in 15 studies [ID 1, 2, 25, 26, 28, 30, 31, 36, 38, 40, 42, 48, 49, 54, 60];
3) crude number of patients rehospitalized was reported in 29 studies [ID 1, 5, 7, 8, 10, 13, 14, 15, 16, 17, 18, 19, 21, 24, 29, 30, 32, 34, 37, 39, 41, 43, 45, 46, 47, 53, 58, 59, 61];
4) one year number of patients rehospitalized was reported in 15 studies [ID 2, 3, 20, 25, 26, 28, 31, 36, 38, 44, 48, 49, 54, 57, 60].

Outcomes of overall mortality and rehospitalized patients in included study

Of the 22198 patients included in the review, 15922 were included in the narrative synthesis. Patients included in telemonitoring or remote care strategies were 7791 (cases), while 7845 were involved in the usual care path for heart failure treatment

(controls). When considering studies that reported the numbers of deaths in patients monitored compared to patients that followed usual care, 1026 deaths were reported among monitored patients while 1106 deaths were reported among controls (Table 5 in Appendix). An overall heterogeneity in follow-up periods was detected. As reported by the authors, these ranged from 0 months to a mean of 1652 days (about 4.5 years). Anyway, some authors found telemonitoring to be effective in reducing mortality during follow-up periods (51-54). In particular, Bogyi and colleagues, in a retrospective observational study conducted in Hungary that included 231 patients, showed a protective effect of telemonitoring on six-month mortality based on daily transmission of pacing impedances, bradycardia, tachycardia, and CRT statistics, mean heart rates, patient activity, and heart rate variability, as well as their instant transmission in case of relevant clinical events (HR 0.368, 95% CI = 0.186-0.72; p=0.004). Also, De Simone and colleague, in a quasi-experimental study conducted in Italy that included 987 patients, showed the protective power of telemonitoring to reduce mortality after at least 12 months of observation based on implanted cardiac devices capable of transmitting heart parameters through mobile phone (HR 0.53, 95% CI = 0.31–0.88; p=0.015). Furthermore, Ong and colleague, in a randomized controlled trial conducted in the USA that included 1437 patients, showed the protective power of telemonitoring to reduce 30-day mortality based on daily transmission of physiological parameters and scheduled telephone coaching calls (RR 0.53; 95% CI = 0.31–0.93; p=0.03). Finally, Sohn and colleagues, in an observational retrospective study conducted in Germany that included 1124 patients, showed a reduction in mortality in patients subjected to telemonitoring based on nurses' telephone calls and recording of blood pressure, pulse, and weight (mortality rates 8.5% versus 13.2%, $p<0.05$) (51-54).

Conversely, most of the studies documented a lack of effectiveness of telemonitoring and remote care models to reduce patient mortality (Table 5 in Appendix).

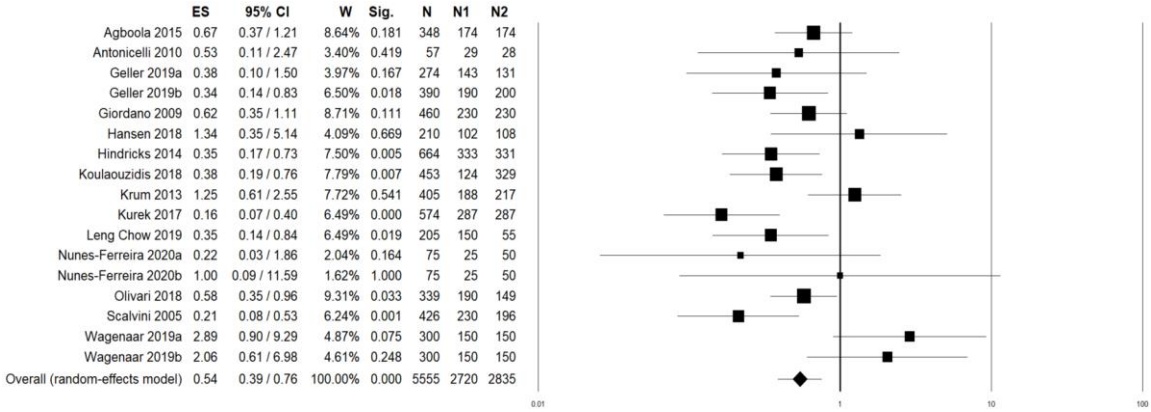
As regards rehospitalizations, the total number of rehospitalized patients included in telemonitoring programmes was 824, while the number of rehospitalized patients during usual care programmes was 764 (Table 6 in Appendix). In particular, Comi'n-Colet and colleagues, in a randomized, controlled trial conducted in Spain that included 188 patients, showed the protective power of telemonitoring to reduce the number of rehospitalized patients within 6 months of follow-up based on

collection of patient biometric data (weight, heart rate and blood pressure) and symptom reporting (HR 0.39 95% CI = 0.19–0.77; p=0.007). Similarly, De Simone and colleague, in a quasi-experimental study conducted in Italy that included 987 patients, showed the protective power of telemonitoring to reduce the number of rehospitalized patients after at least 12 months of observation based on implanted cardiac devices capable of transmitting heart parameters through mobile phone (HR 0.59 95% CI = 0.41–0.86; p=0.006). Also, Hale and colleagues, in a randomized, controlled trial conducted in the USA that included 25 patients, showed the protective power of telemonitoring to reduce the number of rehospitalized patients within 90 days of follow-up based on a remotely monitored electronic pillbox that alerts patients when it is time to take their medications (RR -82%; p=0.04). Finally, Mizukawa and colleagues, in a randomized, controlled trial conducted in Japan that included 57 patients, showed the protective power of telemonitoring to reduce the number of rehospitalized patients within 24 months of follow-up based on self-management education and non-invasive daily measurement of physiological parameters (p=0.048) (52, 55-57). Most of the studies also showed a lack of effectiveness of telemonitoring models in reducing the considered outcome (Table 6 in appendix).

Meta-analyses of the studies that reported results about one-year mortality

All studies reporting one-year mortality outcome values (Table 7 in appendix) were included in the meta-analysis (58-71). The meta-analysis (Figure 2) confirmed the trend demonstrated by some authors (51-54) in supporting the protective power of care models based on telemonitoring in reducing one-year mortality (OR 0.54, 95% CI = 0.39–0.76).

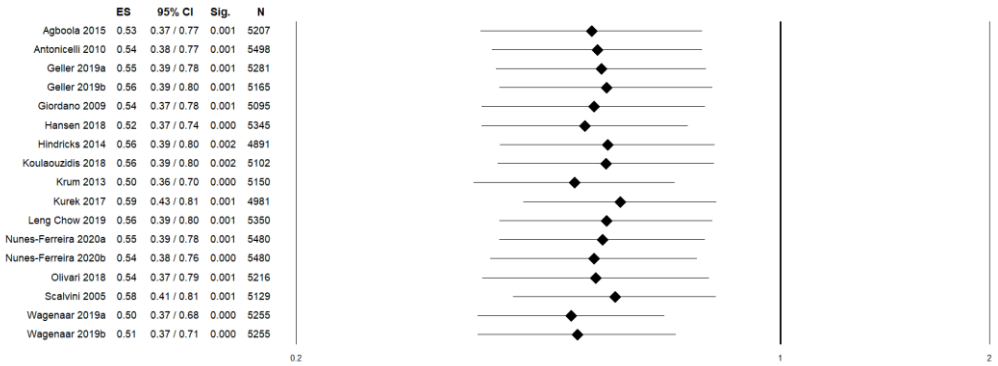
Figure 2. Meta-analysis of studies reporting one-year mortality



ES = Effect size (Odds Ratio), 95% CI = 95% Confidence Interval, W = Weight, Sig. = Statistical significance, N = Total sample, N1 = Case, N2 = Controls; Heterogeneity statistics: Q = 36.69, df = 16, p = <0.05, I^2 = 56.39

Even if the meta-analysis demonstrated a substantial and significant level of heterogeneity (Q test p value = <0.05; I2 = 56.39), the sensitivity analysis performed by removing one study at a time showed stability in the effect size ranging from 0.50 to 0.59, suggesting that the overall result was not significantly influenced by a single study (Figure 3).

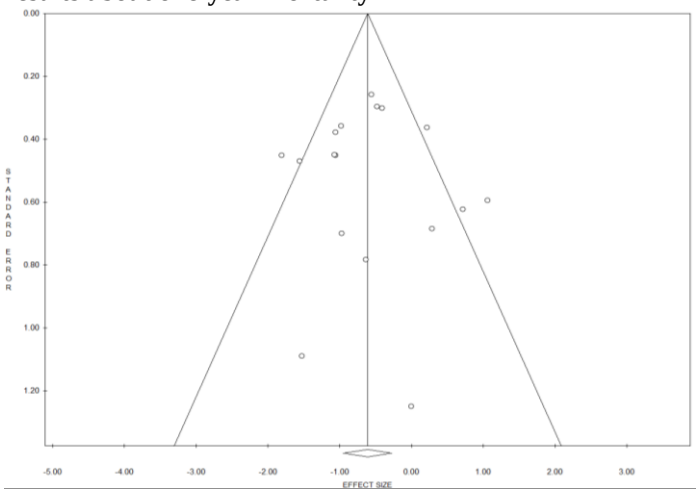
Figure 3. sensitivity analysis of studies reporting one-year mortality



Publication bias analysis

The funnel plot analysis showed no evidence of publication bias (Egger's test, t = 0.18, p= 0.869).

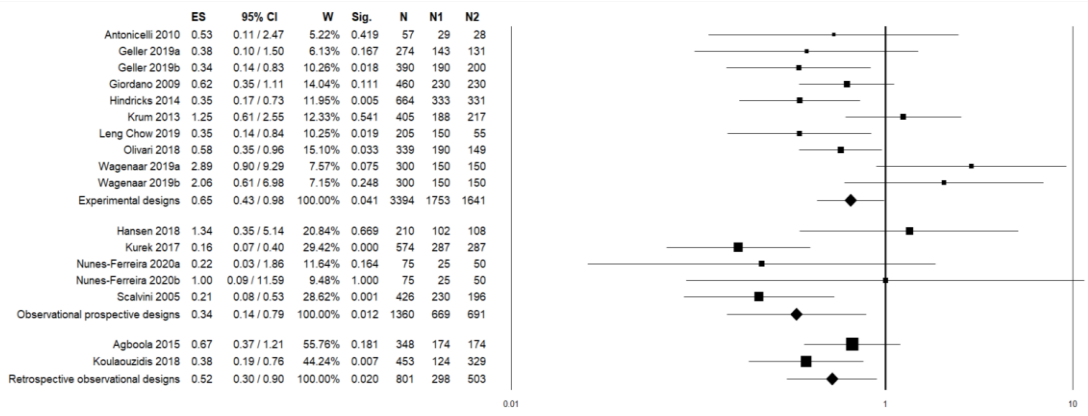
Figure 4. Funnel plot to assess publication bias of meta-analysis of studies reported results about one-year mortality



Egger's linear regression test t= 0.18, p= 0.869. Fail Safe Number = 111

To explore the heterogeneity, a subgroup analysis based on study designs was performed (Figure 5). The analysis showed no significant differences in the effect size obtained using different study designs (ANOVA Q-Test = 1.99; p = 0.37), suggesting that heterogeneity was not affected by this variable.

Figure 5. Subgroup analysis based on study design

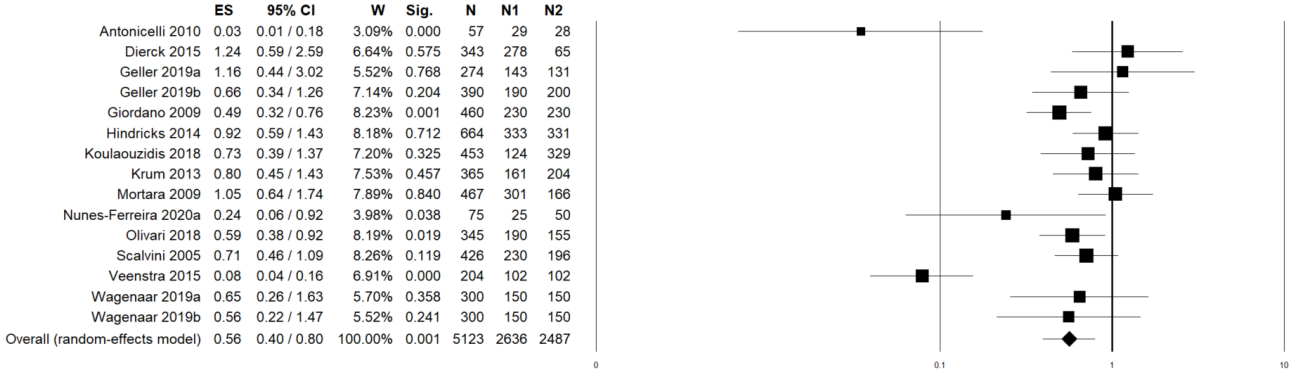


ES = Effect size (Odds Ratio), 95% CI = 95% Confidence Interval, W = Weight, Sig. = Statistical significance, N = Total sample, N1 = Case, N2 = Controls; Heterogeneity statistics: ANOVA Q-Test = 1.99, df = 2, p = 0.37

Meta-analyses of studies that reported results about the number of rehospitalized patients in one year

All studies reporting the number of rehospitalized patients in one year (Table 7 in Appendix) (59-61, 63-65, 68-74) were included in the meta-analysis (Figure 6). Meta-analysis results confirmed the trend demonstrated by some authors (52, 55-57) in supporting the protective power of care models based on telemonitoring to reduce one-year rehospitalization (OR 0.56, 95% CI = 0.40–0.80). A substantial and significant level of heterogeneity was detected (Q test p value = <0.05; I^2 = 77.79).

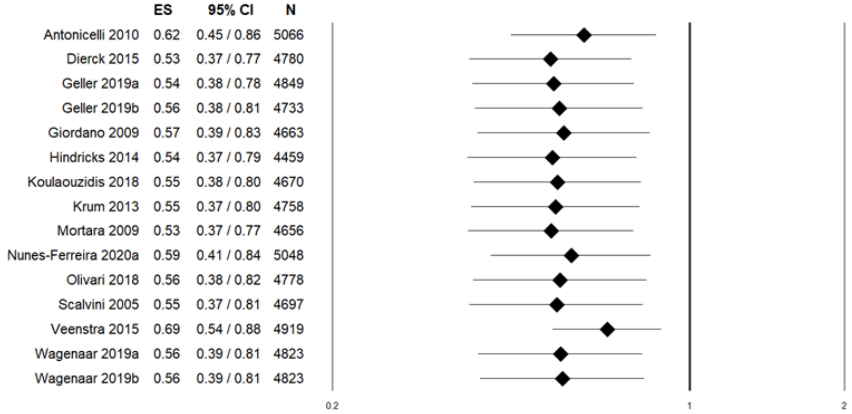
Figure 6. Meta-analysis of studies reporting one-year number of rehospitalized patients



ES = Effect size (Odds Ratio), 95% CI = 95% Confidence Interval, W = Weight, Sig. = Statistical significance, N = Total sample, N1 = Case, N2 = Controls; Heterogeneity statistics: Q = 63.04, df = 14, p = <0.05, I^2 = 77.79

The sensitivity analysis performed by removing one study at time showed a substantial stability in the effect sizes, ranging from 0.53 to 0.69, meaning that the overall result was not significantly influenced by a single study (Figure 7).

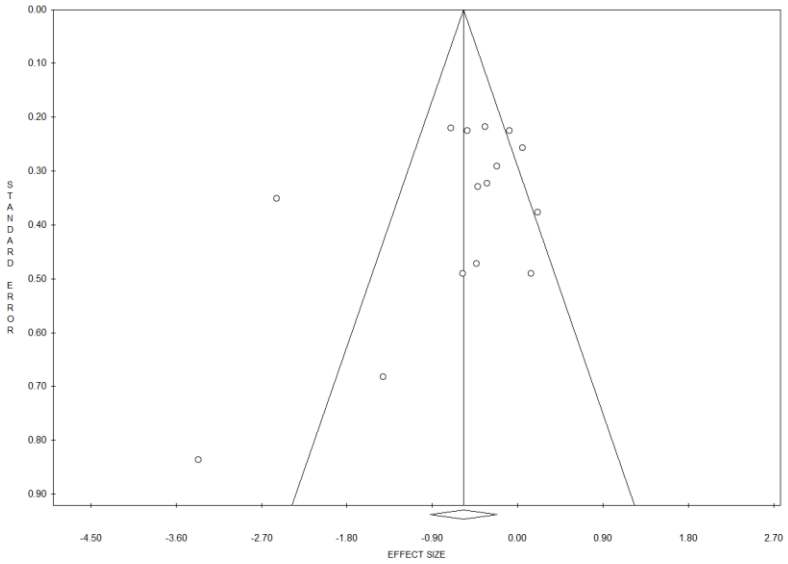
Figure 7. sensitivity analysis of studies reporting one-year number of rehospitalized patients



Publication bias analysis

The funnel plot analysis showed no evidence of publication bias (Egger's t= -1.36, p= 0.198).

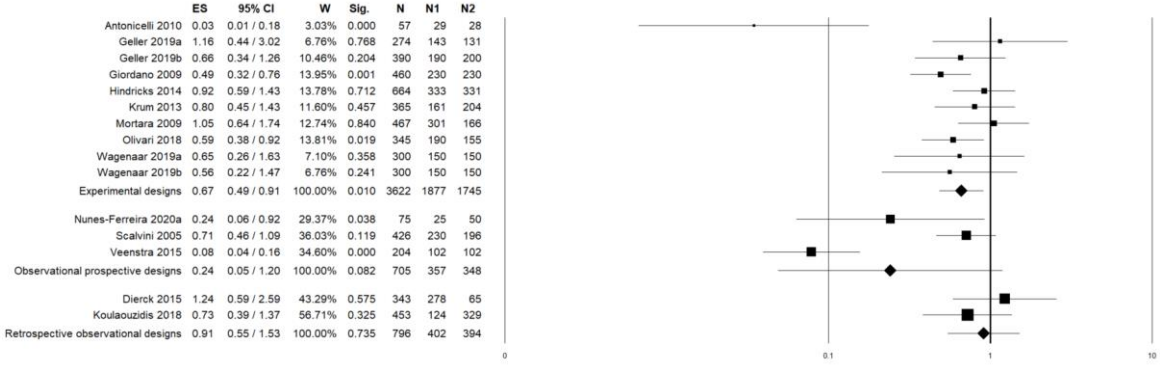
Figure 8. Funnel plot to assess publication bias of meta-analysis of studies reported results about one-year number of rehospitalized patients



Egger's linear regression test t= -1.36, p= 0.198. Fail Safe Number = 145

To explore the heterogeneity, a subgroup analysis based on the study designs was performed (Figure 9). The analysis showed that study designs did not affect heterogeneity (ANOVA Q-Test = 2.83, p = 0.24).

Figure 9. Subgroup analysis based on study design (rehospitalized patients)



ES = Effect size (Odds Ratio), 95% CI = 95% Confidence Interval, W = Weight, Sig. = Statistical significance, N = Total sample, N1 = Case, N2 = Controls; Heterogeneity statistics: ANOVA Q-Test = 2.83, df = 2, p = 0.24

Further explorative analysis

Considering that it was not possible to identify the cause of heterogeneity through the subgroup analysis, it was hypothesized that the content of the telemonitoring care models (Tables 8 and 9 in Appendix), although based on scientific evidence, could have played a crucial role in determining the level of heterogeneity that emerged in the meta-analyses. Therefore, at an exploratory level, a series of meta-analyses were conducted by aggregating the studies in which common interventions were identified among those foreseen in the care model. Meta-analyses were performed as reported in Table 10.

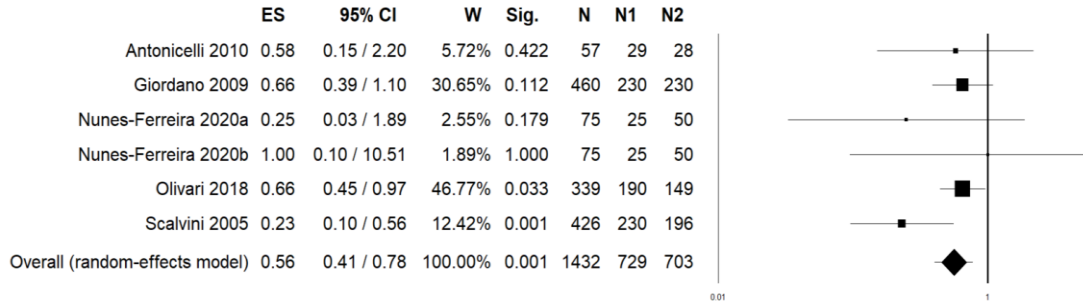
Table 10. Common characteristics among care model of included studies

One-year mortality
• Transmission and evaluation of patients' EKG [ID 3, 29, 50, 51, 56]. • Transmission and evaluation of physiologic parameters (at least blood pressure, heart rate, weight, and blood oxygen saturation) [ID 1, 3, 38, 44, 50, 51, 62]. • Presence of implanted cardiac resynchronization therapy and defibrillator (CRT-D) or implantable cardioverter-defibrillator (ICD) devices [ID 26, 32]. • Telephone monitoring [ID: 1, 3, 29, 40, 56]. • Website-based educational programs [ID 31, 62].
Number of rehospitalized patients in one year
• Transmission and evaluation of patients' EKG [ID 3, 29, 46, 50, 51, 56] • Studies reporting evaluation of relevant physiologic parameters (at least blood pressure, heart rate, weight, and blood oxygen saturation) [ID 3, 21,38, 46, 50, 51, 59, 62] • Telephone monitoring [ID 3, 29, 40, 56]

Care models and one-year mortality

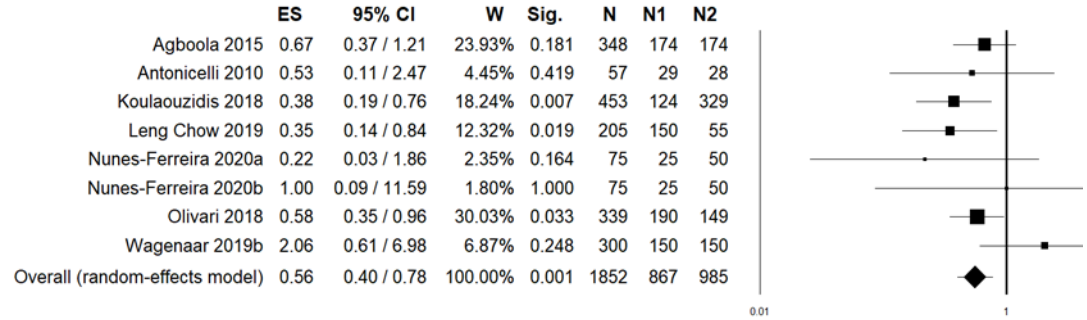
Patients subjected to telemonitoring care models that share the characteristic of electrocardiogram remote transmission reported a reduced probability of one-year mortality (RR = 0.56 95%, CI = 0.41–0.78; Q test p = 0.34, I2 = 10.85). This result emerged also in care models that have the common feature of remote transmission of patient's physiological parameters (OR = 0.56; 95% CI 0.40-0.78; Q test p = 0.33 I2 = 12.26). Finally, aggregating studies providing the remote evaluation of patients with implanted cardiac devices, a reduced probability of death in one year was confirmed (RR = 0.37; 95% CI 0.23–0.61; Q test p = 0.99, I2 = 0.00).

Figure 10. Care models including the remote transmission and evaluation of patients' EKG (one-year mortality)



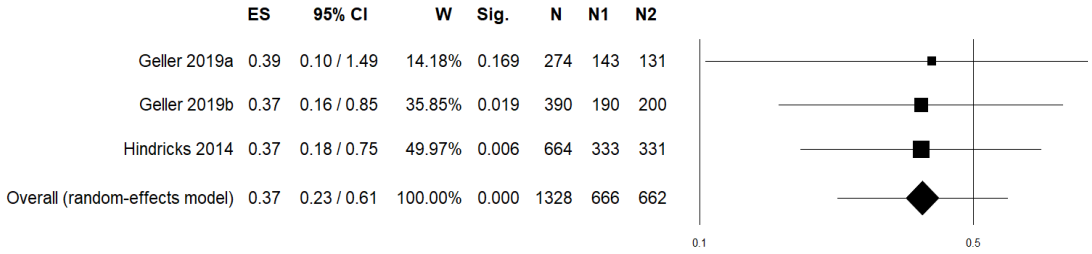
ES = Effect size (Risk Ratio), 95% CI = 95% Confidence Interval, W = Weight, Sig. = Statistical significance, N = Total sample, N1 = Case, N2 = Controls; Heterogeneity statistics: Q = 5.61, df = 5, p = 0.34, I^2 = 10.85

Figure 11. Care model including remote transmission of patient's physiologic parameters (one-year mortality



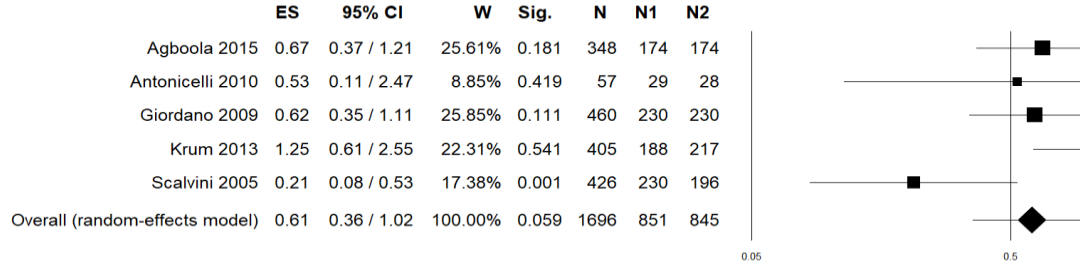
ES = Effect size (Odds Ratio), 95% CI = 95% Confidence Interval, W = Weight, Sig. = Statistical significance, N = Total sample, N1 = Case, N2 = Controls Heterogeneity statistics; Q = 7.98, df = 7, p = 0.33, I^2= 12.26

Figure 12. Figure x. Care model including the presence of implanted cardiac resynchronization therapy and defibrillator (CRT-D) or implantable cardioverter-defibrillator (ICD) devices (one-year mortality)



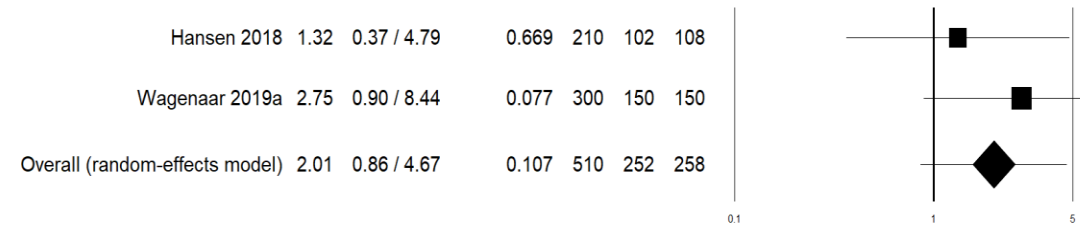
ES = Effect size (Risk Ratio), 95% CI = 95% Confidence Interval, W = Weight, Sig. = Statistical significance, N = Total sample, N1 = Case, N2 = Controls; Heterogeneity statistics: Q = 0.01, df = 2, p = 0.99, I^2 = 0.00

Figure 13. Care models including Telephone monitoring (one-year mortality)



ES = Effect size (Odds Ratio), 95% CI = 95% Confidence Interval, W = Weight, Sig. = Statistical significance, N = Total sample, N1 = Case, N2 = Controls; Heterogeneity statistics: Q = 8.97, df = 4, p = 0.06, I^2 = 55.39

Figure 14. Care model including Website-based educational programs (one-year mortality)



ES = Effect size (Risk Ratio), 95% CI = 95% Confidence Interval, W = Weight, Sig. = Statistical significance, N = Total sample, N1 = Case, N2 = Controls; Heterogeneity statistics: Q = 0.71, df = 1, p = 0.40, I^2 = 0.00

Pooling studies that share telephone monitoring as a common feature of the remote care model, no significant result was detected in reducing the likelihood of one-year mortality (RR = 0.61; 95% CI 0.36–1.02; Q test p = 0.06, I2 = 55.39). When studies in which patients were cared for based on a website educational programme were pooled, the result was not significantly unfavourable for this telemonitoring strategy (RR 2.01 95% CI 0.86–4.67; p = 0.107).

The meta-analyses based on care models did not demonstrate any significant level of heterogeneity except for the care model that used telephone monitoring.

The sensitivity analysis performed by removing one study at a time showed substantial stability in each of the meta-analyses performed except for that related to models that used telephone monitoring, in which the non-significant results was conditioned by the study of Krum and colleagues (65) (Figure 15–19).

Figure 15. Sensitivity analysis of meta-analyses performed on remote transmission and evaluation of patients' EKG (one-year mortality)

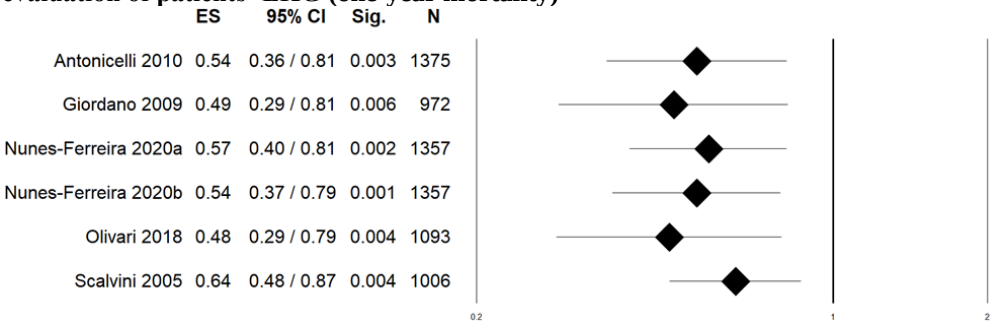


Figure 16. Sensitivity analysis of meta-analysis of study including remote transmission of patient's physiologic parameters (one-year mortality)

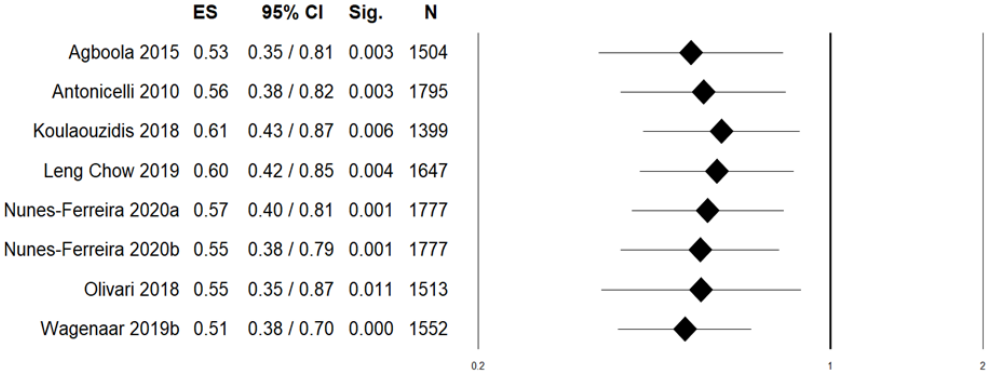


Figure 17. Sensitivity analysis of meta-analysis of study including the presence of implanted cardiac resynchronization therapy and defibrillator (CRT-D) or implantable cardioverter-defibrillator (ICD) devices (one-year mortality)

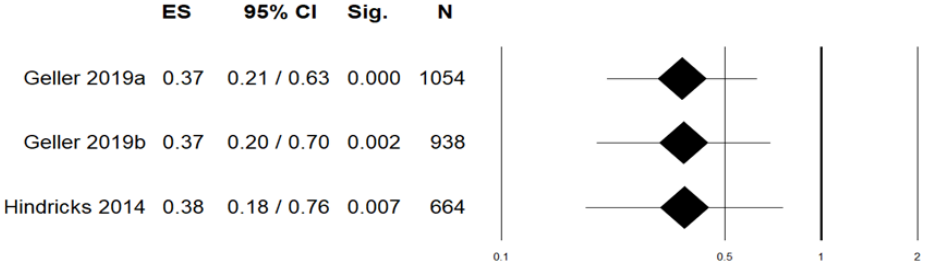


Figure 18. Sensitivity analysis of meta-analysis of studies including Telephone monitoring (one-year mortality)

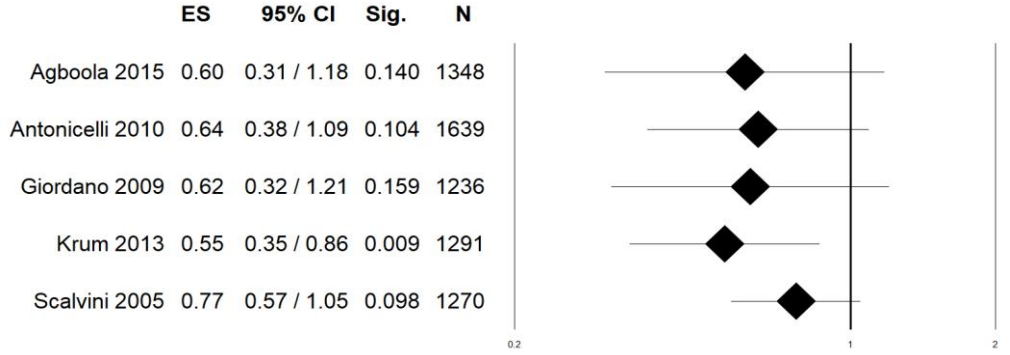
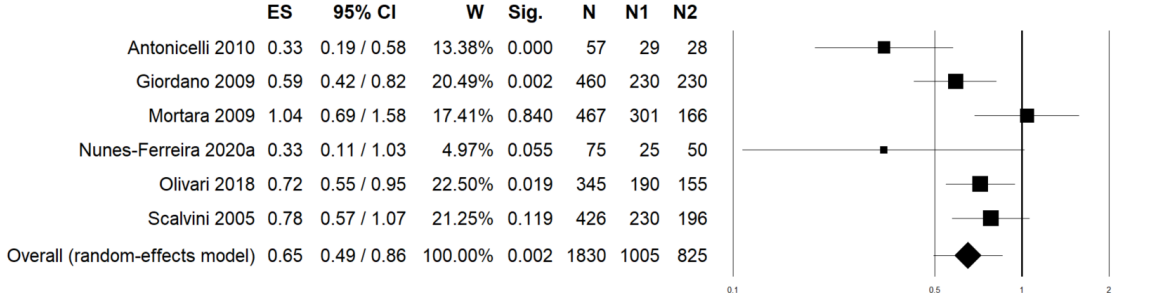


Figure 19. Sensitivity analysis of meta-analysis of studies Website educational programs (one-year mortality)

Care models and number of rehospitalized patients in one year

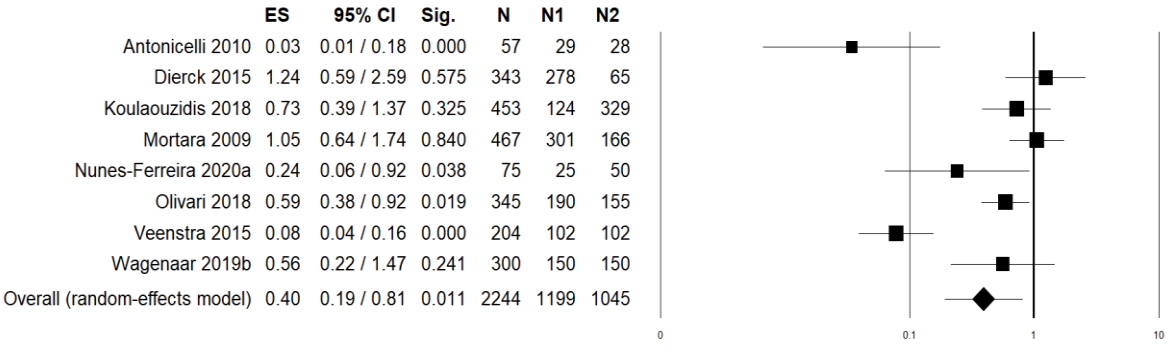
Patients subjected to telemonitoring care models that share the characteristic of electrocardiogram remote transmission reported a reduced number of rehospitalizations in one year (RR = 0.65 95%, CI = 0.49–0.86; Q test p = <0.05, I2 = 63.31). This result emerged also in care models that have remote transmission of patient's physiological parameters as a common feature (RR = 0.40; 95% CI 0.19-0.81; Q test p <0.05, I2 = 87.21). Finally, aggregating studies that used care models based on telephone monitoring, a reduced number of rehospitalized patients in one year was confirmed (RR = 0.62; 95% CI 0.44-0.87; Q test p <0.05, I2 = 63.89).

Figure 20. Care models including the remote transmission and evaluation of patients' EKG (number of rehospitalized patients)



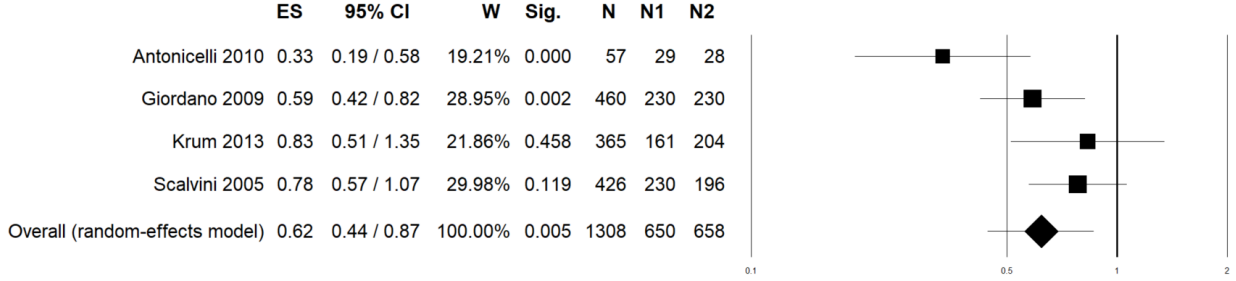
ES = Effect size (Risk Ratio), 95% CI = 95% Confidence Interval, W = Weight, Sig. = Statistical significance, N = Total sample, N1 = Case, N2 = Controls; Heterogeneity statistics: Q = 13.63, df = 5, p = <0.05, I^2 = 63.31

Figure 21. Care model including remote transmission of patient's physiologic parameters (number of rehospitalized patients)



ES = Effect size (Odds Ratio), 95% CI = 95% Confidence Interval, W = Weight, Sig. = Statistical significance, N = Total sample, N1 = Case, N2 = Controls; Heterogeneity statistics: Q = 54.71, df = 7, p = <0.05, I^2 = 87.21

Figure 22. Care models including telephone monitoring (number of rehospitalized patients)



ES = Effect size (Risk Ratio), 95% CI = 95% Confidence Interval, W = Weight, Sig. = Statistical significance, N = Total sample, N1 = Case, N2 = Controls; Heterogeneity statistics: Q = 8.31, df = 3, p = <0.05, I^2 = 63.89

Even for studies that had common care models, the heterogeneity remained substantial. Therefore, the protective effect of care models based on the transmission of patient's EKG and physiological parameters, together with telephone intervention, was confirmed, although the result was influenced by high heterogeneity.

The sensitivity analysis performed by removing one study at time showed substantial stability in each of the meta-analyses performed except for that related to models that used telephone monitoring, in which the non-significant results were conditioned by the study of Giordano and colleagues (61) (Figures 23–25).

Figure 23. Sensitivity analysis of study including remote transmission and evaluation of patients' EKG (number of rehospitalized patients)

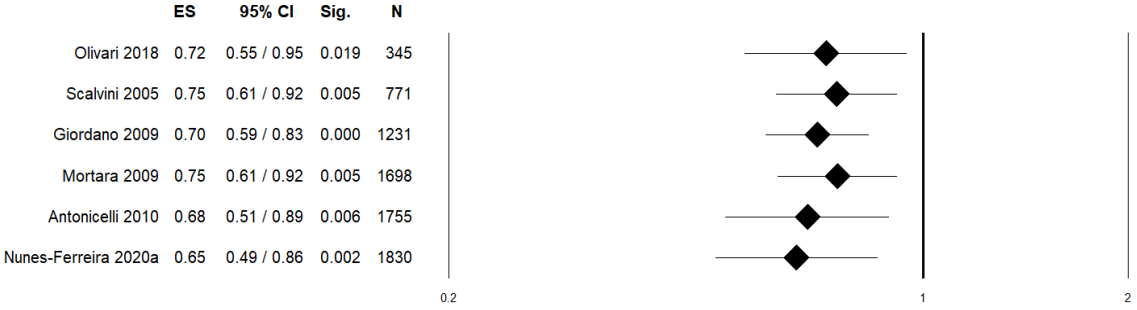


Figure 24. Sensitivity analysis of study including transmission of patient's physiologic parameters (number of rehospitalized patients)

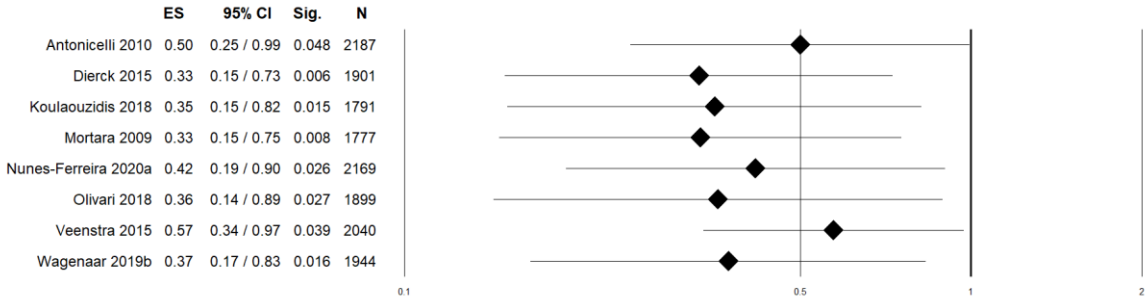
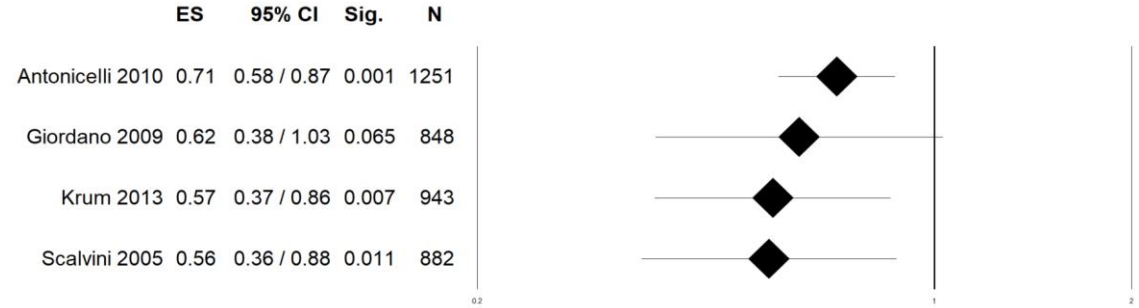


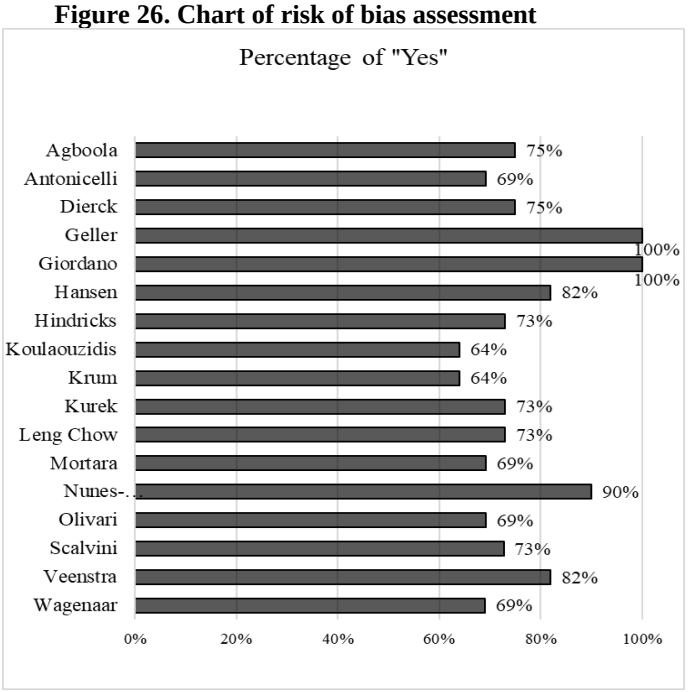
Figure 25. Sensitivity analysis of study including Telephone monitoring (number of rehospitalized patients)



Risk of bias

Studies included in the meta-analysis were analyzed by Joanna Briggs Institute's critical appraisal tools specific to each study design (50). Judgement of risk of bias based on author's cut-offs showed an average of 76% for "yes" (Figure 26). Specifically, six manuscripts showed a moderate risk of bias (50%–69%) and eleven showed a low risk of bias (> 70%).

Figure 26. Chart of risk of bias assessment



DISCUSSION

Characteristics of the included studies

The included studies were published from 2004 to 2020, and they highlight how the topic has developed recently both in regard to the growing advancement in technologies and the need to provide tailored nursing and medical interventions for patients (36, 44). It is interesting how European countries lead the number of published articles compared to the USA and other nations. More than half of the included studies are randomized, controlled trial, thus representing a high level of scientific evidence. Since, as stated in a few of the studies (1, 28), there is need to strengthen available evidence, more high-quality studies should be undertaken to better delineate the magnitude of the effects of telemonitoring on patient outcomes. In all, the studies included over 20.000 heart failure patients with average ages ranging from about 52 to 82 years, representing a wide range of people. Despite the fact that outcomes in the studies were not usually adjusted for NYHA condition, this classification was usually reported as baseline characteristics of included patients. However, it is desirable for the NYHA Class to be reported more homogeneously in future studies including patients from all four classes. This will make it possible to adjust outcomes based on the NYHA Class, in order to not only understand fully whether remote care models can significantly impact the health of patients and at what level but also to better distribute resources based on the clinical condition of patients (44).

Overall mortality and rehospitalized patients

Narrative synthesis included the greatest part of patients involved in the review, about 72% of the overall number. In regard to patients included in telemonitoring compared to usual care groups, the numbers were well balanced. The total numbers of deaths were quite similar among the two compared groups. Four studies (51-54) depicted a reduced risk of death in heart failure patients subjected to telemonitoring based on the daily transmission of vital signs and heart parameters through an implanted device. All four studies shared the feature of daily recording and transmission of parameters related to heart and cardiovascular condition. However, patients

in these studies were followed up for heterogeneous periods, so these results cannot be generalized for the entire population. In fact, a study that observed a 30-day reduction in mortality did not observe the same result at the 180-day time point, making the effectiveness of telemonitoring strategies in reducing mortality doubtful (53). In addition, the differences in outcome-reporting modalities (HR, OR, mean differences, percentages, and p-values only) suggest a trend towards the reduction of deaths among patients who underwent telemonitoring, but it is difficult to make inferences on larger populations.

Meta-analysis of studies reporting one-year mortality confirms the hypothesis that telemonitoring strategies are effective in reducing mortality when compared with usual-care strategies (OR 0.54, 95% CI = 0.39–0.76). Heterogeneity result suggests that, despite the effectiveness of the model, some factors among the studies influenced the results, but the sensitivity analysis depicts that all the studies weighed in a balanced way on the total result, confirming the robustness of the result.

To explore heterogeneity, stratification for study design was performed, and this demonstrated that the heterogeneity was not related to the research designs, which, in fact, were not statistically different in effect sizes. Furthermore, no publication bias was detected in the funnel plot analysis and Egger's test, thus making the overall result of the meta-analysis reliable. To further explore heterogeneity, other meta-analyses were carried out by pooling the studies based on some common characteristics of the telemonitoring models. Hence, studies were aggregated based on transmission and evaluation of patient's EKG, transmission and evaluation of physiological parameters, use of implantable devices, telephone monitoring, and use of web-based educational programmes. Surprisingly, the meta-analyses based on care models did not demonstrate any significant level of heterogeneity except for the care model that used telephone monitoring. These results highlighted, on the one hand, that the effect sizes of each study included in the meta-analysis mainly followed the same direction as the overall effect size and, on the other hand, that the potential role of care models is based on the remote transmission and evaluation of patient's EKG and

physiological parameters and use of implanted devices data in determining patient outcomes.

Unlike the mortality data, the total number of rehospitalized patients who underwent telemonitoring was higher than those who underwent usual care. In regard to studies that reported significant reduction in rehospitalized patients (52, 55-57), three out of four used a telemonitoring strategy based on transmission of patient's physical and heart parameters. One of these three studies used an electronic pillbox capable of notifying patients in time to take their medication. Despite the fact that some studies obtained significant reductions in the number of rehospitalized patients, many others did not, making the effectiveness of telemonitoring doubtful.

The absolute higher number of rehospitalizations among the monitored compared to the unmonitored patients could suggest that patients who underwent remote monitoring received timely assistance in the event of alteration of the monitored parameters. As a result, precautionary early hospitalizations could have taken place in the monitored patients, thereby preventing the worsening of their heart failure, while in patients of the usual-care group physiological alterations were not detected early and hospitalizations were avoided or delayed. The meta-analysis of the studies reporting the number of rehospitalized patients in one year confirms the hypothesis that telemonitoring strategies are effective in reducing the number of rehospitalized patients when compared with usual care strategies (OR 0.56, 95% CI = 0.40–0.80). Probably the early detection of monitored patients' physiological alterations made tailored care interventions outside the hospital possible while reducing rehospitalizations (1). Also, the heterogeneity result suggests that some factors among the studies could have influenced the results even if, again, the sensitivity analysis confirms the strength of the result. Stratification based on study design once again demonstrated that the heterogeneity was not related to the research designs. Finally, no publication bias was detected in the funnel plot analysis and Egger's test, thus making the overall result of the meta-analysis reliable. As was done for the mortality outcome, for the number of rehospitalized patients in one year, studies were aggregated based on common characteristics of monitoring strategies such as transmission and evaluation of patients' EKG and physiological parameters

and telephone monitoring. Meta-analyses of these studies showed a substantial level of heterogeneity despite confirmation of the effectiveness of monitoring strategies stratified for common characteristics. The reason for heterogeneity in these studies is unclear, and therefore it could be associated with patients' clinical characteristics and differences in patient management. Heterogeneity emerged in the application of intervention, actually reducing the reliability of results, hence it is advisable a standardization of application methodologies, adhering to guidelines, to fully understand their effectiveness. Finally, given that the meta-analytic results indicate that the effect of the intervention could change depending on the technologies involved and the characteristics of the telemonitoring strategy, the suggestion is to focus the research on the application of homogeneous monitoring strategies, follow-up periods, and outcome reporting.

Before tailoring a care strategy based on the characteristics of a patient, it is necessary to understand which is the most effective composition of the monitoring strategy capable of providing the best results among all other strategies.

Moreover, studies included in the review described applied strategies that are not harmful to patients and have no ethical issue. Therefore, the composition of an innovative monitoring intervention would not represent a clinical and ethical problem. Understanding what features are needed when building a monitoring intervention would help ensure economic sustainability and optimize resource consumption related to the issue of heart failure, which is still a priority health matter globally (8, 14, 15). Finally, once the evidence of a standardized intervention to be applied has been obtained, it would be useful to expand the number of cost–benefit analyses.

Risk of bias

The overall low risk of bias is a factor that further strengthened the results obtained in the meta-analyses, demonstrating their reliability. The low risk of bias was due to the presence of randomized controlled trials among the included studies that qualitatively raised the level of evidence. In addition, the other studies did not present a substantial risk of bias.

Limitation

One limitation of this literature review concerns the non-inclusion of additional research modalities such as citation search and contact with authors, however including various databases (together with non-clinical ones), in order to maximize the chances of finding relevant primary studies, represents a strenght of this study. The exploratory meta-analytic approach based on the identification of common features in telemonitoring strategies allowed only to understand the potential role of interventions in determining reduction in negative outcomes. However, it is still necessary to provide and investigate standardized care strategies to clarify their effectiveness and magnitude of their outcomes.

CONCLUSION

Evidence from studies included in the narrative analysis partially confirm the effectiveness of telemonitoring in reducing mortality and the number of rehospitalized patients during the various follow-up periods investigated. Meta-analyses related to one-year follow-up studies reinforce the protective trend of telemonitoring strategies towards mortality and the number of rehospitalized patients. Heterogeneity detected in meta-analysed studies needs to be overcome by undertaking studies that contemplate the application of similar monitoring strategies and care interventions in similar patient populations.

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APPENDIX

Table 2. Research strings and results

Database (Platform)	Query	Records retrieved
PubMed	"heart failure"[Mesh] AND ("Telenursing"[Mesh] OR "telehealth nursing" OR "Telemetry/nursing"[Mesh] OR "remote monitoring" OR "remote patient monitoring" OR telemonitoring) AND ("survival rate"[Mesh] OR survival [Mesh] OR mortality [Mesh] OR "Patient Readmission"[Mesh] OR "Patient Compliance"[Mesh] OR "Medication Adherence"[Mesh] OR "Quality of Life"[Mesh])	02/08/21 201 results
Scopus	(TITLE-ABS-KEY ("heart failure") AND TITLE-ABS-KEY ("Telenursing" OR "telehealth nursing" OR (telemetry AND nurs*) OR "remote monitoring" OR "remote patient monitoring" OR telemonitoring) AND TITLE-ABS-KEY ("survival rate" OR survival OR mortality OR "Patient Readmission" OR "Patient Compliance" OR "Medication Adherence" OR "Quality of Life"))	02/08/21 782
CINAHL	("heart failure") AND ("Telenursing" OR "telehealth nursing" OR (Telemetry AND nurs*) OR "remote monitoring" OR "remote patient monitoring" OR telemonitoring) AND ("survival rate" OR survival OR mortality OR "Patient Readmission" OR "Patient Compliance" OR "Medication Adherence" OR "Quality of Life")	1020 (02/08/21)
IEEE Xplore Digital Library	("heart failure") AND ("Telenursing" OR "telehealth nursing" OR (Telemetry AND nurs*) OR "remote monitoring" OR "remote patient monitoring" OR telemonitoring) AND ("survival rate" OR survival OR mortality OR "Patient Readmission" OR "Patient Compliance" OR "Medication Adherence" OR "Quality of Life")	18 (02/08/21)
Engineering Source	("heart failure") AND ("Telenursing" OR "telehealth nursing" OR (Telemetry AND nurs*) OR "remote monitoring" OR "remote patient monitoring" OR telemonitoring) AND ("survival rate" OR survival OR mortality OR "Patient Readmission" OR "Patient Compliance" OR "Medication Adherence" OR "Quality of Life")	294 (02/08/21)
INSPEC	("heart failure") AND ("Telenursing" OR "telehealth nursing" OR (Telemetry AND nurs*) OR "remote monitoring" OR "remote patient monitoring" OR telemonitoring) AND ("survival rate" OR survival OR mortality OR "Patient Readmission" OR "Patient Compliance" OR "Medication Adherence" OR "Quality of Life")	32 (02/08/21)

Table 3. Characteristics of included studies (n=61)

ID	Author	Year	Country	Study design	Aim	Setting	Care model case	Care Model Control	Sampling
1	Agboola	2015	USA	Observational retrospective	To evaluate the effect of a heart failure telemonitoring program, Connected Cardiac Care Program (CCCP), on hospitalization and mortality.	Massachusetts General Hospital	Cccp	Usual care	Convenience
2	Antonicelli	2010	ITA	RCT	To explore adherence to prescription of b-blockers over time in elderly CHF patients undergoing home telemonitoring compared with those receiving standard care from a specialized CHF management team and to determine if there were any differences in mortality and rate of re-admission to hospital between these two groups.	Centre of Telemedicine of the Italian Research Centre on Aging in Ancona and the Italian Institute for Auxology in Milan, Italy	Telemonitoring	Contacted monthly by telephone, seen in the CHF outpatient clinic every 4 months	Randomized
3	Antonicelli	2008	ITA	Prospective study	To explore whether, as compared to standard care from a specialized CHF management team, the addition of home telemonitoring to an integrated CHF patient care system may reduce mortality and rate of re-admission to hospital in elderly CHF patients.	Italian National Research Centre on Ageing Hospital	Telemonitoring	Usual care	Convenience
4	Balk	2008	NL	RCT	To evaluate the effects of guidance provided by the MOTIVA system, in patients with chronic heart failure.	8 Dutch hospitals	Motiva system	Usual care	Randomized
5	Blum	2014	USA	RCT	To address a number of shortcomings of the early studies of home telemonitoring. As one of the projects, we hypothesized that centrally monitoring weight, blood pressure, and heart rate, and being able to act on that information quickly, would prevent many hospitalizations related to fluid overload. Furthermore, we looked at the effect of home monitoring on 30-day readmission rates, mortality, and health-related quality of life measures.	University of Maryland Medical Center	Remote monitoring	Usual care	Randomized
6	Bogyi	2019	HUN	Observational retrospective	To investigate the effects of remote monitoring on mortality in an optimally treated heart failure patient population undergoing CRT-D implantation	Medical Centre of the Hungarian Defence Forces	Remote monitoring	The control group consisted of CRT-D recipients, who were followed up in our outpatient device clinic without remote monitoring.	Convenience
7	Boriani	2017	ITA	RCT	To evaluate whether RM may be of higher clinical and/or economic value compared with standard follow-up strategies.	Europe and Israel	Carelink monitor	the Standard arm received only in-office visits every 4 months.	Randomized
8	Bowles	2009	USA	Prospective study	To compare the effects of evidence-based disease management guidelines delivered to patients with HF and diabetes using three different modalities: in-person visits alone (Control), in-person visits and telephone intervention (Telephone) and in-person visits and telemonitoring (Telemonitoring).	Four agencies in Pennsylvania	(Sentry III, Honeywell hommed, Inc. And vitelcare Turtle, Visual Telecommunications Network, Inc.). The third monitor (Aviva 1010, American telecare Inc.) Provided this plus a digital stethoscope and videoconferencing	All patients, regardless of group assignment, received home nursing guided by the appropriate evidence-based disease-management protocol for HF, diabetes or both	Randomized

9	Boyne	2014	NL	RCT	To analyze the effects of telemonitoring on disease specific knowledge, self-efficacy, self-care and adherence.	Outpatient clinic of one of three hospitals in the South of the Netherlands	Health Buddy system	Usual care	Randomized
10	Boyne	2012	NL	RCT	There is a need for innovative strategies to reduce heart failure hospitalizations.	Three hospitals in The Netherlands	The patients in the intervention arm received a device, with a liquid crystal display and four keys, connected to a landline phone.	Usual care	Randomized
11	Capomolla	2004	ITA	RCT	To evaluate the outcomes of this approach and compare them with those of the usual program of care after discharge from an HFU.	NA	Telemonitoring	Usual care	Randomized
12	Chaudhry	2010	USA	RCT	Determine whether telemonitoring would reduce the combined end point of readmission or death from any cause among patients recently hospitalized for heart failure.	33 cardiology practices across the US	Telemonitoring	Usual care	Randomized
13	Cleland	2005	UK	RCT	We sought to identify whether home telemonitoring (HTM) improves outcomes compared with nurse telephone support (NTS) and usual care (UC) for patients with heart failure.	Germany, the Netherlands, UK	Nurse telephone support + home telemonitoring	Usual care	Randomized
14	Comi´n-Cole	2015	ESP	RCT	To evaluate the impact of adding telemedicine to a multidisciplinary HF programme	Hospital del Mar Research Institute	Tele health	Usual care	Randomized
15	Dar	2009	UK	RCT	To determine if home telemonitoring of the signs and symptoms of typical heart failure patients recently discharged from hospital could reduce the risk of all-cause re-hospitalization, when compared with usual specialist care (UC).	Three acute hospitals in urban, multi-ethnic North West London	Honeywell hommedtm		Randomized
16	De Simone	2015	ITA	Quasi-experimental	Test the hypothesis that remote monitoring can reduce death from any cause and cardiovascular hospitalizations in HF patients who receive ICD/CRT-D.	25 Italian centres	Remote monitoring	Usual care	Convenience
17	Delaney	2010	USA	Pre–post study	The primary aim of this pilot study was to gather preliminary information regarding the feasibility of a nurse-directed multicomponent home care intervention using evidence-based protocols designed in previous trials to teach HF self-management and to prevent/reduce depression and a telemonitoring (TM) system in preparation for a larger randomized trial. The secondary aim of this study was to investigate the possibility that such an Intervention might improve quality of life (QOL), prevent/reduce depressive symptoms, and reduce hospitalizations	Large multibranch Medicare certified non-profit home care agency in Connecticut	The HEART program	Usual care	Convenience
18	Delaney	2013	USA	RCT	To examine the influence of an Intervention combining telemonitoring (TM) and self-care education on the frequency hospitalization in adults with HF following home care. Secondary outcomes included quality of life (QOL) and HF knowledge.	Large multibranch home care agency in Connecticut.	Telemonitoring	Usual care	Randomized
19	Delaney	2014	USA	Quasi-experimental	The purpose of this study was to develop, implement, and test the efficacy and feasibility of the Home Care Education, Assessment, Remote-	A large multibranch home care agency with two urban and two suburban offices	Home care education, Assessment, Remote-monitoring, Therapeutic activities	Usual care	Convenience

					Monitoring, and Therapeutic Activities (HEART) program				
20	Dierck	2015	UK	Observational retrospective	The aim of the present analysis was to investigate the impact of HTM compared to usual care on prescription rates of guideline HF medication, hospitalisation rates and all-cause mortality	National (UK) Health Service	Htm	Usual care	Convenience
21	Ding	2020	AUS	RCT	This study aimed to examine whether the ITEC-CHF program improved patient compliance with weight monitoring as well as other self-management behaviors and health outcomes	Two trial sites in Australia: one in Victoria (VIC) and one in Western Australia (WA).	Itec-chf	Usual care	Randomized
22	Domingues	2011	BRA	RCT	To compare two nursing intervention groups among patients hospitalized due to decompensated HF	Tertiary university hospital in Porto Alegre, Brazil.		Usual care	Randomized
23	Frederix	2018	BEL	RCT	Whether an initial six-month CHF telemonitoring programme could induce long-term health benefits and cost savings once the tele intervention stopped.	Belgium.	Telemonitoring	Usual care	Randomized
24	Galinier	2020	FRA	RCT	To assess the effect of a telemonitoring programme vs. standard monitoring in preventing all-cause deaths or unplanned hospitalisations over 18months of follow-up in patients with HF	France	Telemonitoring	Usual care	Randomized
25	Geller	2019 a	GER	RCT	The present IN-TIME subanalysis explores difference between ICD and CRT-D patients in the endpoint rate and in the benefit of telemonitoring.	Heart Center Leipzig, Germany. 36 investigational sites in seven countries	Lumax ® dual-chamber ICD or Lumax ® CRT-D capable of automatic daily multiparameter telemonitoring	Usual care	Randomized
26	Geller	2019 b	GER	RCT	The present IN-TIME subanalysis explores difference between ICD and CRT-D patients in the endpoint rate and in the benefit of telemonitoring.	Heart Center Leipzig, Germany. 36 investigational sites in seven countries	Lumax ® dual-chamber ICD or Lumax ® CRT-D capable of automatic daily multiparameter telemonitoring	Usual care	Randomized
27	Gingele	2017	NL	Observational retrospective	To investigate potential long-term effects of telemonitoring	Three hospitals in the Netherlands (Maastricht, Heerlen, Sittard)	Health Buddy system	Control patients had four personal contact moments with a HF specialist.	Convenience
28	Giordano	2009	ITA	RCT	To determine whether a multidisciplinary home-based tele management programme would reduce hospital readmission rate and costs in CHF patients	Cardiovascular rehabilitation departments of "Salvatore Maugeri" Foundation	Home-based telemanagement (HBT)	Usual care	Randomized
29	Hale	2016	USA	RCT	The primary goal of this randomized controlled pilot study is to compare the MedSentry medication monitoring system versus usual care in older HF adults in patients who recently completed a HF telemonitoring program	Massachusetts General Hospital (MGH) or Brigham and Women's Hospital (BWH)	The medsentry Medication Management System	Usual care	Randomized
30	Hansen	2018	GER	Prospective study	We aimed to provide more evidence that quarterly automated follow-ups are non-inferior to follow-ups which involve personal physician contact in HF patients with recently implanted ICD/CRT-D devices over 12 months. Secondly, we aimed to determine whether the type of physician contact affected outcomes.	17 sites across Germany	Telemetry Merlin@home transmitter.	phone or visit	Randomized

31	Hindricks	2014	GER	RCT	We did the fluence of home moniToring on mortality and morbidity in heart failure patients with IMpaired lEft ventricular function (IN-TIME) trial to evaluate the incremental benefit of automatic multiparameter telemonitoring for patients with heart failure treated with an ICD or a CRT-D	36 tertiary clinical centres, in Australia (1), Europe (33), and Israel (2)	Telemonitoring	Usual care	Randomized
32	Hoban	2013	USA	Prospective study	The purpose of this research study was to determine if there is a difference in hospital readmission rates, patient's perception of quality of life, and self-care behaviors, in HF patients who were telemonitored and those who were not.	large, not-for profit HHA, which services five counties in the Philadelphia area	Telemonitoring	Usual care	Randomized
33	Kalter-Leibovi	2017	ISR	RCT	We aimed to evaluate the long-term effect of a countrywide comprehensive disease management program among patients with chronic heart failure	Heart failure centers	Disease management	Usual care	Randomized
34	Koehler	2011	GER	RCT	to investigate whether RTM would reduce mortality and hospitalizations in ambulatory chronic HF patients compared with usual care	Clinical Trial Center Leipzig	Remote monitoring	Usual care	Randomized
35	Kotooka	2018	JPN	RCT	NA	A total of 27 centers participated in this study: 3 outpatient clinics, 4 provincial hospitals, 6 general hospitals in urban areas, 1 national center, and 13 university hospitals in Japan.	Telemonitoring	Usual care	Randomized
36	Koulaouzidis	2018	UK	Observational retrospective	We hypothesised that the patients at high risk, and, Hence, potentially with most to benefit, were those who had recently been diagnosed with HF, and we therefore assessed the effects of TM in patients who were recently diagnosed with HF with reduced ejection fraction (HFrEF) and had New York Heart Association (NYHA) class II–III symptoms.	Kingston-upon-Hull,	Motiva system	Usual care	Convenience
37	Kraai	2016	NL	RCT	The aim of this study is to assess the effect of telemonitoring on top of an ICT-guided-DMS with an CDSS in patients with worsening HF on the combined endpoint of death, readmission and HR-QoL, compared to patients treated with ICT-guided-DMS and CDSS alone.	Ten Dutch hospitals	Telemonitoring	ICT-guided-DMS	Randomized
38	Krum	2013	AUS	RCT	The aim of this study was therefore to determine whether an automated telephone support system would improve quality of life and reduce death and hospital admissions for rural and remote heart failure patients.	Rural and remote areas of Australia	Usual care + intervention	Usual care	Randomized
39	Kulshreshtha	2010	USA	Pilot study	The objective of this pilot study was (1) to determine whether RM could be successfully implemented in non-homebound HF patients, (2) to assess satisfaction with RM among ambulatory HF patients, and (3) to obtain preliminary estimates of the 6-month hospital readmission rate between non-homebound patients who participated in an RM program and patients who either declined (non-participants) or were not offered the opportunity to participate (control).	Massachusetts General Hospital (MGH)	Remote monitoring	Usual care	Randomized

40	Kurek	2017	POL	Prospective study	This study aimed to analyze the impact of RM on mortality and hospitalization rate using an all-comers prospective observational registry from a high-volume cardiovascular center.	NA	The RM group included the following devices: carelinktm (Medtronic, Minneapolis, merlintm MN, USA): 5.1% (St. Jude Medical, St. Paul, MN, Monitoringtm USA): 72% and Home (Biotronik, Berlin, Germany): 22.9%.		Convenience
41	Lehmann	2006	USA	Pilot study	To measure the impact of managing CHF patients via telehealth technology on overall healthcare utilization, including physician visits, ED visits, and hospital readmissions	Centers for Medicare and Medicare Services			Randomized
42	Leng Chow	2019	SGP	Quasi-experimental	Our study aimed to compare the effectiveness of telemonitoring over structured telephone support in reducing heart failure-related healthcare utilization	Changi General Hospital (CGH)	Telemonitoring	structured telephone support (STS),	Convenience
43	Mizukawa	2019	JPN	RCT	The purpose of the present study was to compare the effectiveness of CM and SM with usual care in improving psychosocial status (as assessed by QOL, self-efficacy, and self-care behavior scores) among patients who experienced hospitalization for HF. We also compared their effectiveness in reducing rehospitalization and all-cause mortality within 24 months.	Five acute care hospitals in Hiroshima Prefecture, Japan	Collaborative management (cm)	Usual care / Self-Management (SM)	Randomized
44	Mortara	2009	ITA	RCT	The objectives were as follows: (i) to evaluate the feasibility of this system in patients with HF; (ii) to compare the efficacy of HT vs. usual care to reduce the cardiac events in HF patients at high risk of re-admission; (iii) to define the prevalence and the clinical relevance of home breathing disorders and abnormalities of heart rate variability.	Eleven centres in three European countries (UK, Italy, and Poland).	Telemonitoring		Randomized
45	Myers	2006	USA	Prospective study	We implemented a home telemonitoring intervention among recently discharged patients with class III or IV CHF that consisted of daily patient self-monitoring and a daily phone call to the patient. We then compared use outcomes to a similar cohort of usual care patients within the same health care system.	Partners Home Care, Boston Massachusetts.	Home telemonitoring	Usual care	Convenience
46	Negarandeh	2019	IRN	RCT	The aim of this study was to assess the effects of monitoring through telephone (tele-monitoring) on self-care behaviors and readmission of patients with HF after discharge.	The Grand Hospital of Dezful	Telemonitoring	Usual care	Randomized
47	Nouryan	2018	USA	RCT	The purpose of the present study was to attempt to isolate the effects of telemonitoring by enrolling patients in the outpatient setting, after completion of home care, when their condition was no longer being closely followed by a nurse monitor.	Biostatistic Department	Telemonitoring	Usual care	Randomized
48	Nunes-Ferreira	2020	PRT	Prospective study	To assess the feasibility and effectiveness of a telemonitoring (TM) programme in reducing hospitalization and mortality in a population with HF and reduced ejection fraction.	Tertiary hospital (Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal)	Patients followed up prospectively with the support of non-invasive TM facilities	Usual care	Convenience
49	Olivari	2018	ITA	RCT	we aimed to explore the effectiveness of remote monitoring in elderly patients with heart failure, in	Veneto Region	Telemonitoring	Usual care	Randomized

					Italy and Greece, early after hospital discharge.				
50	Ong	2016	USA	RCT	The objective of the Better Effectiveness After Transition– Heart Failure (BEAT-HF) study was to evaluate the effectiveness of a care transition intervention using remote patient monitoring in reducing 180-day all-cause readmissions	Six academic medical centers in California	Telemonitoring	Usual care	Randomized
51	Pedone	2015	ITA	RCT	The current study was planned to evaluate whether a telemonitoring system providing information directly to the physician in charge of individuals' care and including telephone support could prevent hospital readmissions and death in elderly adults with HF.	Geriatric acute care ward of a teaching hospital, and outpatient clinic of the same hospital.	Telemonitoring	Usual care	Randomized
52	Piotrowicz	2020	POL	RCT	To determine whether potential improvements in functional and quality of- life outcomes after a 9-week training period translate into improvement in clinical outcomes during the extended follow-up of 12 to 24 months, compared with usual care (UC).	Five centers in Poland: the Institute of Cardiology in Warsaw (coordinating center), the Silesian Center for Heart Diseases in Zabrze (site 2), Medical University of Gdansk (site 3), Medical University of Lódz (site 4), and Medical University of Warsaw (site 5)	Hybrid comprehensive telerehabilitation HCTR	Usual care	Randomized
53	Radhakrishnan	2013	USA	Observational retrospective	We have investigated the associations between the characteristics of patients with HF and re-hospitalization during a 60-day period of telemonitoring after discharge from hospital	New England	Tele health		
54	Scalvini	2005	ITA	Prospective study	The aim of the present study was to analyse the costs of a home-based intervention with a telecardiology system in CHF patients.		Home-based telecardiology (HBT)	Usual care	Convenience
55	Seto	2012	CAN	RCT	The objective of our randomized controlled trial was to perform an in-depth investigation of the effects of a highly automated and user-centered mobile phone-based telemonitoring system on self-care and clinical management, with the aim of improving heart failure outcomes	University Health Network (UHN) Heart Function Clinic in Toronto, Ontario	Telemonitoring	Usual care	Randomized
56	Sohn	2012	GER	Observational retrospective	The aim of this article was to perform a health economic cost–cost analysis by comparing an intervention group of program participants with a matched control group.	Germany	Telemedicine for the Heart	Usual care	
57	Veenstra	2015	NL	Pre–post study	The first objective of this study was to assess the impact of telehealth-based disease management on unplanned admissions, disease severity and quality of life in CHF patients.	CHF outpatient unit of a local community hospital in the north of the Netherlands	Motiva system		Convenience
58	Vuorinen	2014	FIN	RCT	The objective of this study was to investigate whether the multidisciplinary care of HF patients could be improved with telemonitoring at the Cardiology Outpatient Clinic of Helsinki University Central Hospital (HUCH), primarily in terms of reducing HF-related hospitalizations.	Cardiology Outpatient Clinic of HUCH	Telemonitoring	Usual care	Randomized
59	Wade	2011	USA	RCT	The goal was to assess impact on outcomes and quality of life, and also to assess the feasibility of	Aetna Medicare Advantage	Tele health	Usual care	Randomized

					utilizing an Internet-based telemonitoring technology to facilitate CM in an elderly HF population with multiple comorbidities				
60	Wagenaar	2019	NL	RCT	In our study we evaluated (i) an interactive platform for HF disease management (the e-Vita platform) with telemonitoring facilities, replacing routine consultations, and (ii) the HFM website. Both were compared to UC. The primary outcome was self-care and the secondary outcomes health status, hospitalizations and all-cause mortality.	Nine Dutch HF outpatient clinics	'Heartfailurematters.org' website group + E-health adjusted care pathway group	Usual care	Randomized
61	Yanicelli	2020	ARG	RCT	To validate the HTS for the first time in a real setting, its effectiveness to improve self-care and treatment adherence of HF patients		Telemonitoring	Usual care	Randomized

Table 4. Outcomes considered in studies

		Sample			Mortality Absolute frequency		One-year Mortality Absolute frequency		Patient rehospitalized Absolute frequency		One-year patients rehospitalized Absolute frequency	
Author	**Year**	**Sample**	**Case**	**Control**	**Telemonitoring**	**Usual care**	**Case**	**Control**	**Case**	**Control**	**Case**	**Control**
Agboola	2015	348	174	174	75	97	22	31	75	97		
Antonicelli	2010	57	29	28			3	5			9	26
Antonicelli	2008	57	28	29			3	5			9	26
Balk	2008	214	101	113	9	8						
Blum	2014	203	102	101					80	74		
Bogyi	2019	231	62	169	10	53						
Boriani	2017	865	437	428	40	34			63	60		
Bowles	2009	303	93+98	112					17% + 16%	10%		
Boyne	2014	382	197	185								
Boyne	2012	382	197	185	18	12			18	25		
Capomolla	2004	133	67	66	4	7						
Chaudhry	2010	1653	826	826	92	94						
Cleland	2005	426	341	85	27+28	20			34+40	24		
Comi´nCole	2015	188	88	100	12	5			32	11		
Dar	2009	182	91	91					17	10		
De Simone	2015	987	499	488	25	35			49	65		
Delaney	2010	24	12	12					2	3		
Delaney	2013	100	50	50					3	7		
Delaney	2014	50	26	24					4	6		
Dierck	2015	333	278	55	13%	16%					51	10
Ding	2020	148	67	81					15	8		
Domingues	2011	120	57	63	6	13						
Frederix	2018	160	80	80	57	54						
Galinier	2020	990	507	483	91	89			141	160		
Geller	2019a	274	143	131			3	7			10	8
Geller	2019b	390	190	200			7	20			17	26
Gingele	2017	382	197	185	97	82						
Giordano	2009	460	230	230			9%	14%			43	73
Hale	2016	25	14	11					1	4		
Hansen	2018	210	102	108	5	6	4.60%	3.60%	10	13		
Hindricks	2014	664	333	331			10	27			44	47
Hoban	2013	80	40	40					8	12		
KalterLeibovi	2017	1360	682	678	232	218						
Kao	2016											
Koehler	2011	710	354	356	54	55			64	74		
Kotooka	2018	181	90	91	10	13						
Koulaouzidis	2018	453	124	329			10	62			14	49
Kraai	2016	177	94	83	14	10			25	23		
Krum	2013	405	188	217			17	16			23/161	35/204

Kulshreshtha	2010	150	42	108	4	7			4	13		
Kurek	2017	574	287	287			6	33				
Lehmann	2006	20	10	10					5	7		
Leng Chow	2019	205	150	55			12	11				
Mizukawa	2019	57	20	19	3	4			4	11		
Mizukawa	2019	57	20	18	3	3			4	5		
Mortara	2009	461	301	160							53	28
Myers	2006	166	83	83					18	24		
Negarandeh	2019	80	40	40					7	19		
Nouryan	2018	89	42	47					33.3%	27.7%		
NunesFerreira	2020	125	25	100			1	10			12%	36%
Olivari	2018	339	190	149			36	43			60	62
Ong	2016	1437	715	722	100	114						
Pedone	2015	96	50	46	3	7						
Piotrowicz	2020	850	425	425	54	52						
Radhakrishnan	2013	590	403						73			
Scalvini	2005	426	230	196			6	22			56	61
Seto	2012	100	50	50	3	0						
Sohn	2012	1124	281	843	24	111						
Veenstra	2015	102	102	102							32	132
Vuorinen	2014	94	47	47	0	0			8	13		
Wade	2011	316	164	152	6	6			57	49		
Wagenaar	2019	450	150+150	150			11+8	4			8+7	12
Yanicelli	2020	40	20	20					2	0		

Table 5. Narrative synthesis of mortality

		Sample			Mortality Absolute frequency		Follow-up	Results
Author	**Year**	**Sample**	**Case**	**Control**	**Telemonitoring**	**Usual care**		
Balk	2008	214	101	113	9	8	From 2 to 537 days	Seventeen patients died, 8 in the Control group and 9 in the Intervention group
Bogyi	2019	231	62	169	10	53	3 to 6 months	HR 0.368, (0.186-0.727); p=0.004
Boriani	2017	865	437	428	40	34	2 years	HR 1.13 (0.71–1.80); p=0.594
Boyne	2012	382	197	185	18	12	Mean of 12 months	P=0.34
Capomolla	2004	133	67	66	4	7	10 ± 6 months of follow-up	-
Chaudhry	2010	1653	826	826	92	94	6 months	HR 0.97 (0.73-1.30)
Cleland	2005	426	341	85	27+28	20	240 days	-
Comi´nColet	2015	188	88	100	12	5	6 months	HR 0.68 (0.23–2.00); p=0.485
De Simone	2015	987	499	488	25	35	At least 12 months	HR 0.53 (0.31–0.88); p=0.015
Domingues	2011	120	57	63	6	13	3 month period	RR 0.61 (0.25 to 1.48); p=0.38
Frederix	2018	160	80	80	57	54	6 months	$\chi 2$=0.26; p=0.61
Galinier	2020	990	507	483	91	89	18 months	-
Gingele	2017	382	197	185	97	82	Mean 1652 days	-
KalterLeibovici	2017	1360	682	678	232	218	Mean lenght 2.67 years	adjusted HR, 0.997 (0.820 to 1.213)
Koehler	2011	710	354	356	54	55	Minimally 12 months and maximally 28 months	HR 0.97 (0.67–1.41); p=0.87
Kotooka	2018	181	90	91	10	13	0–31 months	HR 0.809 (0.354–1.847); p=0.614
Kraai	2016	177	94	83	14	10	9 months	CI 95% −0.14 +0.07; p=0.27
Kulshreshtha	2010	150	42	108	4	7	6 months	-
Mizukawa	2019	57	20	19	3	4	range 1.4-24 months	p=0.859
Mizukawa	2019	57	20	18	3	3	range 1.4-24 months	p=0.859
Ong	2016	1437	715	722	100	114	6-month	adjusted HR for 30-day all-cause mortality 0.53 (0.31-0.93); p=0.03 adjusted HR for 180-day all-cause mortality 0.85 (0.64-1.13); p=0.26
Pedone	2015	96	50	46	3	7	6-month	incidence rate 13/100 person-years (5–39) Vs incidence rate 37/100 person/years, (18–76)
Piotrowicz	2020	850	425	425	54	52	12 to 24 months	HR 1.03 (0.70-1.51)
Seto	2012	100	50	50	3	0	6 months	-
Sohn	2012	1124	281	843	24	111	retrospective	8.5% versus 13.2%, p<0.05
Vuorinen	2014	94	47	47	0	0	6 months	-
Wade	2011	316	164	152	6	6	6 months	OR 1.030 (0.321, 3.305); p=0.96

Table 6. Narrative synthesis of patients rehospitalized

		Sample			Patient rehospitalized Absolute frequency		Follow-up	Results
Author	**Year**	**Sample**	**Case**	**Control**	**Telemonitoring**	**Usual care**		
Blum	2014	203	102	101	80	74	-	p = 0.51
Boriani	2017	865	437	428	63	60	2 years	IRR 0.97 (0.74–1.29); p=0.846
Bowles	2009	303	93+98	112	17% + 16%	10%	60 days	p-value = non-significant
Boyne	2012	382	197	185	18	25	Mean of 12 months	HR 0.65, (0.35–1.17)
Cleland	2005	426	341	85	34+40	24	240 days	-
Comi´nCole	2015	188	88	100	32	11	6 months	HR 0.39 (0.19–0.77); p=0.007
Dar	2009	182	91	91	17	10	6 months	-
De Simone	2015	987	499	488	49	65	minimum of 12 months	HR0.59 (0.41–0.86); P=0.006
Delaney	2010	24	12	12	2	3	90 days	p = 0.74
Delaney	2013	100	50	50	3	7	90 days	p-value = non-significant
Delaney	2014	50	26	24	4	6	60 days	p-value = non-significant
Ding	2020	148	67	81	15	8	6 months	HR 1.98; p=0.24
Galinier	2020	990	507	483	141	160	18 months	-
Hale	2016	25	14	11	1	4	90 days	RR -82%; p=0.04
Hoban	2013	80	40	40	8	12	90 days	p-value = non-significant
Koehler	2011	710	354	356	64	74	Median 26 months	HR 0.84 (0.60–1.18); p=0.32
Kraai	2016	177	94	83	25	23	9 months	CI 95% −0.12 +0.14 P=0.87
Kulshreshtha	2010	150	42	108	4	13	6 months	Mean diff. 0.19±0.45 vs 0.38±1.06; p=0.56
Lehmann	2006	20	10	10	5	7	6 months	p = 0.38
Mizukawa	2019	57	20	19	4	11	range 1.4-24 months	p = 0.048
Mizukawa	2019	57	20	18	4	5	range 1.4-24 months	p = 0.048
Myers	2006	166	83	83	18	24	2 months	p = 0.21
Negarandeh	2019	80	40	40	7	19	3 months	p = 0.06
Nouryan	2018	89	42	47	33.3%	27.7%	6 months	p-value = non-significant
Radhakrishnan	2013	590	403		73		60 days	-
Vuorinen	2014	94	47	47	8	13	6 months	IRR 0.812, (0.525-1.256); p =0.351
Wade	2011	316	164	152	57	49	6 months	OR 1.164 (0.722-1.875); p=0.53
Yanicelli	2020	40	20	20	2	0	90 days	p=0.5

Table 7. Study who underwent meta-analysis

			Sample			One-year Mortality Absolute frequency		One-year patients rehospitalized Absolute frequency	
ID	**Author**	**Year**	**Sample**	**Case**	**Control**	**Case**	**Control**	**Case**	**Control**
1	Agboola	2015	348	174	174	22	31		
2	Antonicelli	2010	57	29	28	3	5	9	26
20	Dierck	2015	333	278	55			51	10
25	Geller	2019a	274	143	131	3	7	10	8
26	Geller	2019b	390	190	200	7	20	17	26
28	Giordano	2009	460	230	230	9% 21	14% 32	43	73
30	Hansen	2018	210	102	108	4.60%(5)	3.60% (4)		
31	Hindricks	2014	664	333	331	10	27	44	47
36	Koulaouzidis	2018	453	124	329	10	62	14	49
38	Krum	2013	405	188	217	17	16	23/161	35/204
40	Kurek	2017	574	287	287	6	33		
42	Leng Chow	2019	205	150	55	12	11		
44	Mortara	2009	461	301	160			53	28
48	NunesFerreira	2020a	75	25	50	1	8	3	18
48	NunesFerreira	2020b	75	25	50	1	2		
49	Olivari	2018	339	190	149	36	43	60	62
54	Scalvini	2005	426	230	179	6	22	56	61
57	Veenstra	2015	102	102	102			32	87
60	Wagenaar	2019a	300	150	150	11	4	8	12
60	Wagenaar	2019b	300	150	150	8	4	7	12

Table 8. characteristics of monitoring strategy of study who described mortality

ID	Author	Care Model
1	Agboola	CCCP is a 4-month home telemonitoring and education program designed to improve self-management in heart failure patients at risk for hospitalization within the Partners HealthCare network of hospitals. Participants monitor relevant physiologic parameters (blood pressure, heart rate, weight, and blood oxygen saturation) and answer questions on heart failure–related symptoms on a touch-screen computer on a daily basis (Figure 1). The remote monitoring equipment included ViTel Net and devices approved by the Food and Drug Administration: a UA 767PC Turtle 400 monitor, a Life-Source digital weight scale, an A&D blood pressure cuff and meter, and a BCI pulse oximeter device (UC-321PBT). Measurements and responses to symptom questions are transferred securely to a remote monitoring database where the records are reviewed by telemonitoring nurses. participants also receive structured biweekly telephone-based education sessions over an 8-week period. Patient education covered a variety of topics including diet, physical activity, importance of daily measurements, recognizing symptoms of disease decompensation, and medication adherence. In addition to the structured educational sessions, they received “just-in time” teaching, that is, unscheduled education done to intervene when the remote monitoring nurses observe that measurements fall outside the set baseline range customized for each participant by their physicians or at the onset of new symptoms.
3	Antonicelli	In the TM group, patients (or one of their relatives) were contacted by telephone at least once a week by the CHF team to obtain information on symptoms and adherence to prescribed treatment, as well as blood pressure, heart rate, bodyweight and 24-hour urine output data for the previous day. A weekly ECG transmission was also required.
26	Geller	Recently implanted Lumax ® dual-chamber ICD or Lumax ® CRT-D capable of automatic daily multiparameter telemonitoring. The role of this unit was to ensure the awareness of investigational sites for pre-defined medical events such as ventricular and atrial tachyarrhythmia episodes, low percentage of biventricular pacing, increase in the frequency of ventricular extrasystoles, decreased patient activity, and abnormal intracardiac electrograms transmitted in conjunction with detected arrhythmias.
29	Giordano	"Home-based telemanagement is a multidisciplinary care approach referring to medical/nursing interventions made over the telephone, with the possibility to transmit an ECG trace to a workstation at each investigator site through a single Call Center. Patients assigned to the HBT strategy, received before hospital discharge a portable device (Card-Guard 2206) transferring by a fixed or mobile telephone, a one-lead trace to a receiving station, where a nurse or doctor were available 24 h, 7 days/week."
31	Hansen	Automated follow-up via Merlin.net only
32	Hindricks	"Patients received a commercially available Lumax dual-chamber ICD or CRT-D (Biotronik SE & Co. KG, Berlin, Germany), equipped with a Biotronik Home Monitoring function. At a set time every day (typically 0300 h) or on detection of tachyarrhythmia, the devices transmitted cumulative and last-saved diagnostic data. A small portable patient device receives the data and relays them automatically over mobile telephone links to the Biotronik Home Monitoring Service Center (Berlin, Germany). Data from all countries were processed automatically and posted on a secure internet site accessible to patients’ physicians. In the telemonitoring group, transmitted data were reviewed by study investigators according to their clinical routine. In parallel, transmitted data were reviewed by a central monitoring unit composed of trained study nurses and supporting physicians, located at the Heart Center Leipzig (Germany)."
38	Koulaouzidis	TM is performed with the use of the commercial system, Motiva Telemonitoring System (Philips Healthcare, Amsterdam, Netherlands) This includes a secure broad band home television channel providing educational material, reminders of medication, health-related surveys and motivational messages to encourage the prescribed lifestyle regimen. Individuals were given automated devices for taking daily measurements of blood pressure, heart rate and weight at home; they were asked to obtain the measurements at the same time of day, preferably in the morning, half an hour after taking their tablets"
40	Krum	"In addition to UC, the usual care plus intervention (UC+I) group received ongoing support by touchtone telephone using the TeleWatch system. The TeleWatch system is a telephone based automated telemedicine system developed by Johns Hopkins Biomedical Engineering in conjunction with their clinical heart failure group. This telemedicine system was required to be dialed into by the patient on an at least a monthly basis at which time questions were asked with regard to heart failure clinical status, medical management of their condition, and social questions relevant to their heart failure status. Specific questions are summarized in Table 1. Alerts were set up within the TeleWatch system, alerting the CHAT nurse via the Patient Watch Screen to follow up patients who reported prespecified signs or symptoms warranting intervention."
42	Kurek	"The Central Remote Monitoring Office is situated in our center and supervised by 2 physicians (a cardiology resident and a cardiology consultant) and 2 electrophysiology nurses, who daily analyze data derived from RMonline systems and undertake adequate actions if indicated."
44	Leng Chow	"The TM enhanced programme comprise of the three components: (a) TM; (b) tele-education; and (c) tele support. TM entailed daily measurement by patients of body weight, blood pressure and heart rate using bluetooth enabled devices. These measurements were wirelessly transmitted via a central console that had a built-in SIM card to a back-end monitoring platform for viewing by the nurses as well as the patients’ tablet device for self-monitoring by the patient. The platform used was Motiva and was configured to send advice to patients such as to repeat blood-pressure measurements while at rest and tasks to nurses for follow-up if hospital determined thresholds were breeched."
50	Nunes-Ferreira	Patients assigned to the TM programme (TM group) were provided with home--monitoring devices to evaluate blood pressure, heart rate, peripheral oxygen saturation, body weight, total body water content, body temperature, daily walking steps, and three -lead electrocardiogram (ECG).

51	Olivari	"The RM group, patients were equipped with a Personal Health System, composed of a wearable Wrist Clinic device and a digital weight scale for clinical data collection. The delivery of the devices and monitoring of the data were performed by a single Regional Center for all patients enrolled at the eight participating hospitals. When consigning the device at the patient's home, the Regional Center's operator gave the instructions for the appropriate use of the equipment. The patients, either on their own or with the help of a caregiver, measured their heart rate, blood pressure, 1-lead ECG and pulse-oximetry with the Wrist-Clinic device, and their weight with the digital weight scale. These data were transmitted on a daily basis, 5 days/week, to the eHealth regional center, and were processed automatically in order to identify potential alarm values based on a personalised telemonitoring plan, set up by the clinician at enrolment. The operators verified the alarms and, if necessary, informed the clinicians on an elective basis"
56	Scalvini	HBT programme consisted of trans-telephonic follow-up and ECG monitoring, followed by visits from the paramedical and medical team only if necessary. The patients received a portable device, transferring data by a mobile or fixe telephone line. A one-lead ECG recording was transmitted to a receiving station, where a nurse was available for reporting and interactive teleconsultation. The patient could call the centre when assistance was required (teleassistance), while the team could call the patient for scheduled appointments (telemonitoring).
62	Wagenaar	Heartfailurematters.org' website group Participants received, on top of UC, information and 10min instruction on the use of the HFM website from the HF nurse at the start of the study. During each routine consultation with the HF nurse, patients were encouraged to use the website, and experienced barriers were explored and solved. Additionally, participants received a leaflet. E-health adjusted care pathway group Participants in this group followed an EACP. They received identical initial information on the use of the HFM website as the participants of HFM group. In addition, the HF nurses instructed the patients and their caretakers on how to use the e-Vita platform with telemonitoring facilities. Patients learned to record body weight, blood pressure and heart rate on a fixed time point everyday (or individually adjusted to a lower frequency if stable). All participants used a standardized weighing scale and blood pressure/heart rate device. The results of the vital parameters were automatically forwarded to the e-Vita platform

Table 9. characteristics of monitoring strategy of study who described number of rehospitalized patients

ID	Author	Care Model
3	Antonicelli	In the TM group, patients (or one of their relatives) were contacted by telephone at least once a week by the CHF team to obtain information on symptoms and adherence to prescribed treatment, as well as blood pressure, heart rate, bodyweight and 24-hour urine output data for the previous day. A weekly ECG transmission was also required.
21	Dierck	"The Motiva HTM system (Philips, Amsterdam, The Netherlands) is a television-based platform that can deliver educational videos to the patient and transmit daily symptom questionnaires and measurement data (i.e., weight, heart rate and blood pressure) from the patient's home via a broadband internet connection to a secure server. The system consists of bluetooth connected weighing scales and an automated sphygmomanometer. Clinical alerts are generated by worsening symptoms of HF, and/or when vital signs fall outside of the individually predefined 'normal range'"
26	Geller	Recently implanted Lumax ® dual-chamber ICD or Lumax ® CRT-D capable of automatic daily multiparameter telemonitoring. The role of this unit was to ensure the awareness of investigational sites for pre-defined medical events such as ventricular and atrial tachyarrhythmia episodes, low percentage of biventricular pacing, increase in the frequency of ventricular extrasystoles, decreased patient activity, and abnormal intracardiac electrograms transmitted in conjunction with detected arrhythmias.
29	Giordano	"Home-based telemanagement is a multidisciplinary care approach referring to medical/nursing interventions made over the telephone, with the possibility to transmit an ECG trace to a workstation at each investigator site through a single Call Center. Patients assigned to the HBT strategy, received before hospital discharge a portable device (Card-Guard 2206) transferring by a fixed or mobile telephone, a one-lead trace to a receiving station, where a nurse or doctor were available 24 h, 7 days/week."
32	Hindricks	Patients received a commercially available Lumax dual-chamber ICD or CRT-D (Biotronik SE & Co. KG, Berlin, Germany), equipped with a Biotronik Home Monitoring function. At a set time every day (typically 0300 h) or on detection of tachyarrhythmia, the devices transmitted cumulative and last-saved diagnostic data. A small portable patient device receives the data and relays them automatically over mobile telephone links to the Biotronik Home Monitoring Service Center (Berlin, Germany). Data from all countries were processed automatically and posted on a secure internet site accessible to patients' physicians. In the telemonitoring group, transmitted data were reviewed by study investigators according to their clinical routine. In parallel, transmitted data were reviewed by a central monitoring unit composed of trained study nurses and supporting physicians, located at the Heart Center Leipzig (Germany)."
38	Koulaouzidis	TM is performed with the use of the commercial system, Motiva Telemonitoring System (Philips Healthcare, Amsterdam, Netherlands) This includes a secure broad band home television channel providing educational material, reminders of medication, health-related surveys and motivational messages to encourage the prescribed lifestyle regimen. Individuals were given automated devices for taking daily measurements of blood pressure, heart rate and weight at home; they were asked to obtain the measurements at the same time of day, preferably in the morning, half an hour after taking their tablets"
40	Krum	"In addition to UC, the usual care plus intervention (UC+I) group received ongoing support by touchtone telephone using the TeleWatch system. The TeleWatch system is a telephone based automated telemedicine system developed by Johns Hopkins Biomedical Engineering in conjunction with their clinical heart failure group. This telemedicine system was required to be dialed into by the patient on an at least a monthly basis at which time questions were asked with regard to heart failure clinical status, medical management of their condition, and social questions relevant to their heart failure status. Specific questions are summarized in Table 1. Alerts were set up within the TeleWatch system, alerting the CHAT nurse via the Patient Watch Screen to follow up patients who reported prespecified signs or symptoms warranting intervention."
46	Mortara	"The patients enrolled in HT strategies 2 and 3 transmitted weekly records of the following data to the coordinating centre via an automated interactive voice response (IVR) system: (i) weight; (ii) heart rate; (iii) systolic arterial pressure; (iv) dyspnoea score (1–10); (v) asthenia score (1–10); (vi) oedema score (1, feet swell in the morning; 2, in the evening; 3, always swollen); (vii) changes in therapy; and (viii) blood results.Patients in HT strategies 2 and 3 were also given a portable device (a solid-state lightweight Holter-style recorder with built-in signal pre-processing, FM, Monza, Italy), which continuously recorded ECG, respiration, and physical activity over 24 h at home. The recorders (managed by the patients) automatically transmitted data by a telephone, through a dedicated modem (Appel Electronica srl, Torino, Italy), for analysis by the coordinating centre. A 24 h answering machine allowed each patient to contact his/her reference hospital at any time and leave a message requesting help or advice (all HT groups)."
50	Nunes-Ferreira	Patients assigned to the TM programme (TM group) were provided with home--monitoring devices to evaluate blood pressure, heart rate, peripheral oxygen saturation, body weight, total body water content, body temperature, daily walking steps, and three -lead electrocardiogram (ECG).
51	Olivari	"The RM group, patients were equipped with a Personal Health System, composed of a wearable Wrist Clinic device and a digital weight scale for clinical data collection. The delivery of the devices and monitoring of the data were performed by a single Regional Center for all patients enrolled at the eight participating hospitals. When consigning the device at the patient's home, the Regional Center's operator gave the instructions for the appropriate use of the equipment. The patients, either on their own or with the help of a caregiver, measured their heart rate, blood pressure, 1-lead ECG and pulse-oximetry with the Wrist-Clinic device, and their weight with the digital weight scale. These data were transmitted on a daily basis, 5 days/week, to the eHealth regional center, and were processed automatically in order to identify potential alarm values based on a personalised telemonitoring plan, set up by the clinician at enrolment. The operators verified the alarms and, if necessary, informed the clinicians on an elective basis"

56	Scalvini	HBT programme consisted of trans-telephonic follow-up and ECG monitoring, followed by visits from the paramedical and medical team only if necessary. The patients received a portable device, transferring data by a mobile or fixe telephone line. A one-lead ECG recording was transmitted to a receiving station, where a nurse was available for reporting and interactive teleconsultation. The patient could call the centre when assistance was required (teleassistance), while the team could call the patient for scheduled appointments (telemonitoring).
59	Veenstra	The telemonitoring system was used to obtain and check patient vital sign measurements (blood pressure, pulse, weight) on a daily basis. All members of the cardiology department had access to the telemonitoring system, allowing them to check vital sign measurements at every moment and react accordingly. The Motiva telehealth system (Philips Healthcare, Best, the Netherlands) was used and included a secured broadband home TV channel providing educational material, reminders of medication, health-related surveys and motivational messages to encourage the prescribed lifestyle regimen. Patients were given automated devices for daily measurements of blood pressure, heart rate and weight at home. A nurse practitioner evaluated the measurements every day using a dedicated clinical user interface. With tailored alarm settings, the nurse practitioner could identify which patients exceeded the alarm limits and needed extra attention. The situation was evaluated with a phone call or extra visit and if necessary the nurse practitioner altered the treatment
62	Wagenaar	Heartfailurematters.org' website group Participants received, on top of UC, information and 10min instruction on the use of the HFM website from the HF nurse at the start of the study. During each routine consultation with the HF nurse, patients were encouraged to use the website, and experienced barriers were explored and solved. Additionally, participants received a leaflet. E-health adjusted care pathway group Participants in this group followed an EACP. They received identical initial information on the use of the HFM website as the participants of HFM group. In addition, the HF nurses instructed the patients and their caretakers on how to use the e-Vita platform with telemonitoring facilities. Patients learned to record body weight, blood pressure and heart rate on a fixed time point everyday (or individually adjusted to a lower frequency if stable). All participants used a standardized weighing scale and blood pressure/heart rate device. The results of the vital parameters were automatically forwarded to the e-Vita platform