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REVIEW

Non-invasive home telemonitoring in patients with decompensated heart failure: a systematic review and meta-analysis

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Abstract

We planned this systematic review and meta-analysis to study an estimate of the effect of non-invasive home telemonitoring (TM) in the treatment of patients with recently decompensated heart failure (HF). A systematic literature search was conducted in the Medline, Cinahl, and Scopus databases to look for randomized controlled studies comparing TM with standard care in the treatment of patients with recently decompensated HF. The main outcomes of interest were all-cause hospitalizations and mortality. Eleven original articles met our eligibility criteria. The pooled estimate of the relative risk of all-cause hospitalization in the TM group compared with standard care was 0.95 (95% CI 0.84–1.08, $P = 0.43$) and the relative risk of all-cause death was 0.83 (95% CI 0.63–1.09, $P = 0.17$). There was significant clinical heterogeneity among primary studies. HF medication could be directly altered in three study interventions, and two of these had a statistically significant effect on all-cause hospitalizations. The pooled effect estimate of TM interventions on all-cause hospitalizations and all-cause death in patients with recently decompensated heart failure was neutral.

Keywords Heart failure; Telemedicine; Telemonitoring; Telerehabilitation; Remote consultation; Mortality; Hospitalization; Quality of life

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Introduction

Heart failure (HF) is a common cardiovascular syndrome causing high mortality and morbidity, with increasing health care costs.[1–5] The expense caused by HF is predominantly due to hospitalization episodes and pharmacological therapies.[1] Optimized medication use has the potential to reduce mortality and morbidity in HF patients with a reduced left ventricular ejection fraction (HFrEF).[6–11] Age-adjusted incidence rates seem to decline particularly in HFrEF compared with HFpEF, although the mortality and hospitalization rates have remained constant and equally high among patients with HFrEF and HFpEF.[3,4] Patients with HFpEF are often multimorbid, and no effective medical treatment has yet been proved to reduce mortality or morbidity.[2]

The European Society of Cardiology (ESC) recommends discharge planning, lifestyle advising, and early follow-up for HF patients.[2] One possible intervention is to monitor HF symptoms and signs from home via telehealth devices using new digital technology. This might enable the prevention of cardiac decompensation. Telemonitoring (TM) is a feasible platform for educating the patient in HF self-management. TM may offer a timely means to up-titrate HF medication and has the potential to improve drug adherence. New easily implementable treatment options are needed to reduce HF morbidity and mortality.[12]

The findings of earlier meta-analyses and large individual studies are incongruous concerning the effect of telehealth interventions in HF.[12–22] The results of earlier systematic reviews and meta-analyses on the potential benefits of home telehealth interventions have been inconclusive for various

reasons.[12,23] Previous meta-analyses and reviews have mostly included various approaches of telehealth interventions among HF patients.[12–14,18–22] Indeed, we found only one previous systematic review and meta-analysis with acutely decompensated HF patients, but this TM study also included patients with implanted heart monitoring devices.[14] Patients with acutely decompensated HF represent a high-risk subgroup of HF patients.

The aim of the present review and meta-analysis was to pool together current knowledge of the effect of non-invasive home TM on re-hospitalization and mortality risk in patients with acutely decompensated HF compared with standard care.

Methods

Study design

The study was designed according to the guidelines included in the PRISMA statement (*Table S7*).[24]

Outcomes

Our main study hypothesis was that TM reduces the risk of all-cause hospitalization or all-cause mortality in patients recently hospitalized for HF decompensation.

Our primary outcomes were all-cause hospitalizations and all-cause mortality. Our secondary outcome was quality of life (QoL) measures.

Eligibility criteria

We included only RCTs comparing TM with standard care in patients with recent HF decompensation (treated in hospital for HF within the previous 1 month) and reporting all-cause mortality or all-cause readmissions as the outcome measure. We define TM as the regular transmission of at least one physical variable at least once weekly from a home setting to the care provider via the telephone system or the internet. The monitoring of physical variables had to be non-invasive. We excluded studies offering telemonitoring to simultaneously treat other diseases. We excluded studies published before 1 January 2004 or in a language other than English. We did not exclude studies offering adjunct interventions to TM and UC groups (disease management programmes/telephone support). The exclusion process was carried out by the main author. In the case of uncertainty concerning inclusion, another author (T. N.) was consulted and consensus reached through discussion.

Literature search

We searched the Medline, Cinahl, and Scopus databases. The following search was conducted in PubMed: (((telemedic* OR telemedicine OR telemonitoring OR telemonitor*)) AND (cardiomyopathy OR cardiomyop* OR heart failure OR heart* AND fail*)) AND (random* OR randomised OR RCT), using a filter to look only for articles published after 1 January 2004. We used virtually the same terms and filters to search other databases. In Scopus and Cinahl, we used a filter to exclude articles included in Medline. The updated search was conducted on 4 October 2020.

Data extraction of primary studies

Information on participants, methods, interventions, outcomes, and results was extracted onto a data sheet in RevMan 5.3 by the main author (Supporting Information, *Table S1*). For incomplete outcome data, we directly contacted the main author or, if we were unable to reach the main author, another author of the study.

Methods for assessing the risk of bias

The risk of bias was assessed by the main author using the Cochrane risk of bias tool in RevMan 5.3 and the methods presented in the Cochrane handbook.[25] In the case of uncertainty regarding the risk of bias, the matter was decided through discussion with another author (T. N.). We used funnel plots to assess the risk of publication bias in the primary studies (Supporting Information, *Tables S2* and *S3*).

Qualitative synthesis

We separated the primary studies into two groups based on whether there had been a statistically significant effect with the intervention on either of the main outcomes of interest. We presented factors related to the baseline risk of death or re-hospitalization in the primary studies (*Table 1*). We also assessed the methods used in TM interventions in the primary studies (*Table 2*). We then synthesized these data to define possibly effective TM intervention features and a suitable patient population.

Quantitative synthesis

Our primary outcomes of interest were all-cause hospitalizations and all-cause mortality. Our primary outcome measure of interest was risk reduction (RR) for comparisons between the TM and standard care groups. We conducted a meta-analysis of these comparisons using Revman 5.3.

Table 1 Baseline risk (UC group)

Study	Age (years) at baseline (mean ± SD)	% with ACE inhibitor or ARB at baseline	LVEF at baseline (%) (mean ± SD)	% of participants at NYHA class II/III/IV at baseline	All-cause mortality	All-cause hospitalizations
Antonicelli 2008	79 ± 6	Non	37 ± 7	62/31/7	0.17	0.90
Chaudhry 2010	61 (51–73)[a]	67	70[d]	37/51/6	0.23	0.95
Cleland 2005	68 ± 10	83	24 ± 8	36/42/4	0.36	1.23
Comin-Colet 2016	75 ± 11	61	49 ± 16	59/41[e]	0.25	0.93
Dar 2009	72 ± 10	93	Non[f]	Non	0.11	0.86
Dendale 2012	76 ± 10	Non[g]	36 ± 15	3.0 ± 0.5[c]	0.35	1.65
Kotooka 2018	65 ± 16	90	39.2 ± 16.5	72/19/Non	0.11	0.30
Kulshreshtha 2010	70 ± 2	Non	37 ± 18	Non	0.12	Non
Ong 2016	74 (63–82)[a]	55	43 (41.6–44.3)[b]	26/64/10	0.32	1.00
Villani 2014	73 ± 5	Non[h]	32 ± 8	2.9 ± 0.69[c]	0.23	Non
Weintraub 2010	72 (60–78)[a]	83	20 (15–30)[a]	44/46/1	0.17	2.14

All values for UC group. There was no significant difference between groups in baseline characteristics except in Weintraub 2010 (EF greater in intervention group). For all-cause mortality and all-cause hospitalizations values are: number of events/patient years during follow-up in UC group. Non = value not available.
[a](Median (IQR)).
[b](Mean (95% CI)).
[c](Mean ± SD).
[d](% with LVEF <40% in group).
[e](NYHA class I-II/III-IV).
[f](EF measured in 83/91 patients and 33/83 had EF ≥ 40%).
[g]Patients had be on ACE inhibitor or ARB unless contraindicated to fulfil inclusion criteria.
[h]At baseline, 96% of patients on ACE inhibitor or ARB with at least 70% of target dose.

The statistical method used in the meta-analysis was Mantel–Haenszel and the statistical model the random effects model. A *Z*-test was employed to test the null hypothesis, and a *P*-value of <0.05 was interpreted as statistically significant. The presence of heterogeneity was tested with the χ^2 test and its impact with the I^2 statistic. All analyses were performed with the intention-to-treat principle. Sensitivity analyses were performed to calculate the effect estimates using a fixed effects model. We did not plan any subgroup analyses because the sample size was deemed too small for meaningful interpretations. We carried out a sensitivity analysis by recalculating the effect estimates for the main outcomes with a fixed effects model.

Results

Identification of relevant studies

The search of the three databases produced 653 references. After the removal of duplicate publications, we had 522 references (Supporting Information, *Table S4*). We reviewed the titles, then the abstracts and, finally, 28 full articles. After these reviews, 11 articles[15,17,26–34] were included in the final analyses (*Figure 1*). The studies discarded after a review of the headlines and abstracts are listed in the Supporting Information, *Tables S5* and *S6*. For example, after full-article reviews and a discussion among the present authors, three studies were excluded because the TM intervention did not fulfil the inclusion criteria (mode or frequency of data transmission),[35–37] while one was excluded because adequate outcome data were not available[38] and three because it was unclear whether the study patients had suffered a recent decompensation episode.[39–41] After discussion with a senior author (T. N.), one study[28] on patients with HF decompensation 6 weeks previously was included because the patient population was deemed relevant to our review.

Risk of bias assessment

The intervention was not blinded in any of the primary studies. Part of the possible true treatment effect of TM interventions comes from the extra attention paid to the patient in general. The lack of blinding might still introduce performance bias because patients and study/clinical personnel may be more motivated in the context of a research intervention. In two studies,[29,34] even the control group received a research intervention. In both of these studies, the pre-specified endpoint was positive. We judged the risk of performance bias to be unclear in all primary studies.

The overall risk of bias was judged to be high in four primary studies.[17,28,31,32] In three,[17,28,31] there was missing patient data. In one study, the study allocation was not adequately randomized or blinded (*Figure 2*, *Figure S1*).[32]

Funnel plots were drawn for both main outcomes. Both showed evidence of possible publication bias (Supporting Information, *Tables S2* and *S3*). As a sensitivity analysis, effect estimates for the main outcomes were recalculated with a fixed effects model. In this analysis, no significant difference was observed in effect estimates.

Table 2 Interventions

Study	Intervention to both groups	Intervention to TM group	Intervention to UC group	HF medication at the end of follow-up
Antonicelli 2008	-Patients and home caregivers educated during hospital stay (TM group about correct use of equipment) -Decision for hospital re-admission based on consultation with HF team and according to predefined criteria	-Telephone contact at least once a week: symptoms, adherence to medication, HR, BB, weight, 24 h urine output of previous day -Weekly EKG transmission -Clinic visits arranged based on these and telemonitored findings-Medication regularly re-assessed and altered when necessary	-Telephone contact monthly (for outcome data) -Visit at the HF clinic once in every 4 months, and more visits arranged when necessary	-In TM group more beta-blockers, statins and aldosterone antagonists
Chaudhry 2010	-All patients received educational material and a scale	-Education on how to use equipment: scale, Tel-Assurance -system -Every day call to system and answering to questions about HF symptoms (weight, oedema, dyspnoea, dizziness...)-- > possible warning to treating clinician	-Not described	-Not reported
Cleland 2005	-Plan on how to up-titrate heart failure medication	-Weighing scales, BP-meter, a single-lead ECG and instructions on how to use these -Measures 2 times/day-Pre-set limits to values-Guidelines for the management of common scenarios -Pre-set limits broken or trends worrying-- > nurse contacts patient-Short term changes independently by nurse or long-term changes by contacting GP -Management plans implemented-Patients offered chance to contact nurse when needed	-Management plan sent to primary care physician -Follow-up visits every 4 months at research clinic (assessing data relevant to study)	-At 120 days TM group more likely to receive ACE inhibitors and beta-blockers than UC group -At 240 days this difference no longer significant
Comin-Colet 2016	-Both groups take part in multidisciplinary DMP -All management protocols and control intervals same expect TM intervention	-Weight, BP, HR and symptoms (7 HF-related and 1 general question) every day -Alerts viewed by nurse working days/ office hours -Diuretics adjusted-HF specialist consulted if needed	-Institutions to follow same parameters as in TM group-- > contact nurse if measurements out of range	-Not reported
Dar 2009	-Initial home visit by study nurse (advice on self-monitoring)	-Honeywell HomMed telemonitoring system -Every morning system gives verbal instructions to measure weight, blood pressure, heart rate and oxygen saturation -Every morning questions on symptoms -- > answer 'yes' or 'no' -Study nurse reviews data daily (Monday–Friday)	-Each centre had heart failure service -Telephone support during office hours	-Not reported

(*Continues*)

Table 2 (continued)

Study	Intervention to both groups	Intervention to TM group	Intervention to UC group	HF medication at the end of follow-up
		-Variation from pre-defined parameters-- > alert-- > phone call to patient-- > life-style advice/advice regarding medication/ recommendation to contact primary care/early review at secondary care		
Dendale 2012	-All subjects: 1 h standard education course in HF -On day of discharge body weight of patients measured -Evaluation at heart failure clinic 2 weeks after discharge	-3 and 6 months follow-up at clinic -All GPs free to ask heart failure specialists advice concerning patient -BP and weight measured every morning -- > if outside pre-specified limits-- > email alert to GP and heart failure clinic-- > GP free to make treatment change-- > in 1–3 days heart failure nurse contacted patient to document changes made	-Patients followed by GP who could refer patients to cardiologist if needed	-Changes in HF medication significantly different between study groups (less down-titration in TM group)
Kotooka 2018		-Pre-defined safety margins for patients -Measurement of BP, HR, body weight and body composition daily at same time-- > nurse monitors results 9–17 7 days a week-- > if threshold broken nurse contacts patients physician-- > management decision left to physicians discretion	-Treated according to national 2010 HF guidelines -Discharge education and request to measure oneself every day	-Not reported
Kulshreshtha 2010		-2 nurse home visits (education, baseline information etc.) -Nurse weekly phone call: additional instruction, monitor adherence -'Vital ranges' defined -Daily measurement of BP, weight, pulse, pulse oximetry and answers to a set of 'symptom-related questions' -- > readings outside limits -- > call to patient -- > nurse recommendation: increase diuretic dose (if physician's order in place)/notify physician or cardiologist/refer to ER/continue monitoring	-Standard care	-Not reported
Ong 2016		-Pre-discharge information -Measurement of weight, BP, HR and answer to 3 symptom questions daily -- > pre-determined threshold exceeded -- > nurse calls patient to assess possible cause -- > if deemed	-Predischarge education and often a postdischarge follow-up telephone call -Treatment otherwise as in routine clinical practise	-Not reported

(*Continues*)

Table 2 (continued)

Study	Intervention to both groups	Intervention to TM group	Intervention to UC group	HF medication at the end of follow-up
		necessary patient encouraged to contact healthcare professional -9 telephone calls over 6 months to all: reinforcing pre-discharge education, reinforce adherence to TM		
Villani 2014	-At 3, 6, 9 and 12 months clinic visits -At 6 and 12 months echocardiography -Before discharge educational session -Patients GP were sent a detailed clinical report	-Weight, BP, HR and ECG (diuresis in some cases) followed: specifics of followed parameters and measuring frequency decided by cardiologist -PDA system makes acoustic alarms: time of measurement, time to take medication -Patients clinical condition and adherence to medication checked daily -Nurse checked telemonitoring results 9–17 Monday to Friday-At pre-defined times cardiologist checked patients results -- > change medication or recommend clinical consultation	-HF medication titrated at 3, 6, 9 and 12 months clinic visits	-Significantly closer to target doses in TM group compared with UC group.
Weintraub 2010	-Both groups in DMP -Nurse home visit -HF medication optimized according to ACCF/AHA 2009 guidelines -Weekly phone call to patient by nurse manager (review of clinical status) -Weekly conference with nurse managers and HF physician to review all patients -Patient has 24/7 telephone access to nurse manager -Nurse manager able to consult HF cardiologist	-Pre-specified safety boundaries (weight, BP, HR, symptoms) -Daily interaction with Health Hubby-- > if safety boundaries broken -- > nurse contacts patient and initiate intervention if necessary	-Not reported	-Not reported

Table 2 (continued)

Study	Quality of Life Scores at the end of follow-up	-Adharence to intervention	Follow-up	Number of patients randomized
Antonicelli 2008	-Significantly better HP-score compared with baseline value and compared with UC	-Not reported	12 months	57
Chaudhry 2010	-Not reported	-14% in TM group never used the system -On final week 55% still using at least 3 times/week	6 months	1653
Cleland 2005	-Not reported	−81% in TM group had >80% compliance with 1 daily measurement -55% in TM group had >80% compliance with 2 daily measurements	240 days	426

Table 2 (continued)

Study	Quality of Life Scores at the end of follow-up	-Adharence to intervention	Follow-up	Number of patients randomized
Comin-Colet 2016	-MLHFQ significantly better in TM group at 6 months	- < 1% of daily transmissions missed in TM group	6 months	188
Dar 2009	- MLwHF, EQ 5D: no difference between groups	-Not reported	6 months	182
Dendale 2012	-Not reported	–83% of all the recordings made by the patients measured and received correctly	6 months	160
Kotooka 2018	-No difference in QOL-measurements between study groups (GSES, MLHFQ, PHQ-9)	-Adherence at 1, 6, and 12 months 96.2%, 90.4%, and 90.9%	Mean 15 months (range 0–31 months)	183
Kulshreshtha 2010	-Not reported	-Not reported	6 months	150
Ong 2016	-MLHFQ significantly better in TM group	-TM (percentage of days transmitting any type of data): 51.7% -Telephone coaching (percentage of protocol-required phone calls that were completed): 68.0%	180 days	1437
Villani 2014	-Symptom and QoL scores significantly better in TM group (STAI-6, PHQ-9, PGWBI, MMAS)	- > 80% of the planned contacts performed	1 year	80
Weintraub 2010	-Not reported	-Not reported	90 days	188

Qualitative analysis of primary studies

All-cause hospitalizations

In two studies, the all-cause hospitalization rate was significantly lower in the TM group than in the standard care group.[27,29] The proportion of patients with HFpEF seemed particularly high in one[29] of these two studies, although a comparison was difficult to draw due to non-uniform definitions of HF subtypes. In the other,[27] the population was slightly older than in the included studies as a whole (*Table 1*).

The two studies with a low hospitalization rate in the intervention groups[27,29] offered the possibility to directly alter the HF medications of the patients in the TM group. In the first[27] of the two, patients in the TM group used more beta-blockers, statins and aldosterone antagonists at the end of follow-up than the patients receiving standard care. Adherence to the intervention was not reported.[27] The medication rate at the end of follow-up was not reported in the latter study,[29] but the adherence to the intervention was good (*Table 2*).

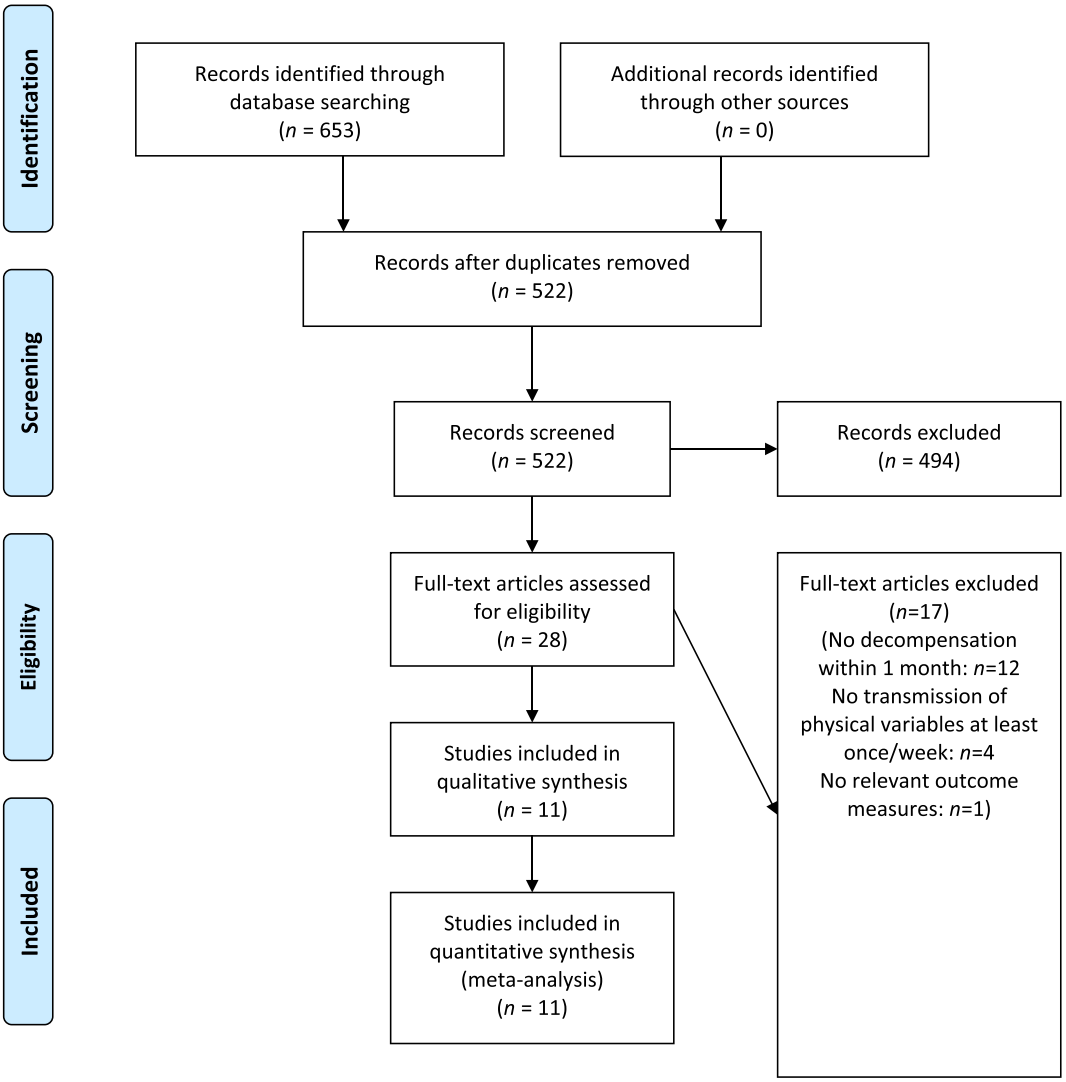
All-cause mortality

In one study, all-cause mortality rate was statistically significantly lower in the TM group than the standard care group (4 vs. 14 deaths).[30] Markers of the baseline risk of adverse CV events seemed similar compared with the other studies (*Table 1*). This study also had several other noteworthy features: there was a relatively high number of hospitalizations and deaths per patient year in the standard care group during follow-up. The TM intervention personnel could not directly alter HF medication use, but a general practitioner was informed of any changes in the measured parameters by e-mail notifications and could also consult an HF specialist through a website. The general practitioners were instructed to alter the medication at their own discretion. There was significantly less down-titration of HF medication in the TM group during follow-up compared with the standard care group. The adherence to the intervention was good (*Table 2*).

Heart failure medication management

In four studies, study personnel could alter diuretic doses when deemed necessary.[27–29,32] In three studies, the study personnel or equipment informed a physician of a possible need for changes in the overall HF medication.[15,30,31] The patient was asked to inform the treating physician in a similar situation in one study.[17] There were also studies in which the treatment process was not adequately described.[26,33,34] The study personnel could directly alter the doses of other HF medications in three studies,[27,29,33] and there was a higher level of target HF medication at the end of the follow-up period in the TM group when compared with the standard care group in three studies.[27,30] HF medication at the end of follow-up was not reported in seven studies[15,17,26,29,31–34] (*Table 2*).

Figure 1 Flow diagram.



Quality of life measures

Four studies demonstrated an improvement in QoL metrics during follow-up in the TM group as compared with the standard care group.[17,27,29,33] Only one study reported a neutral effect on QoL (*Table 2*).

Clinical heterogeneity

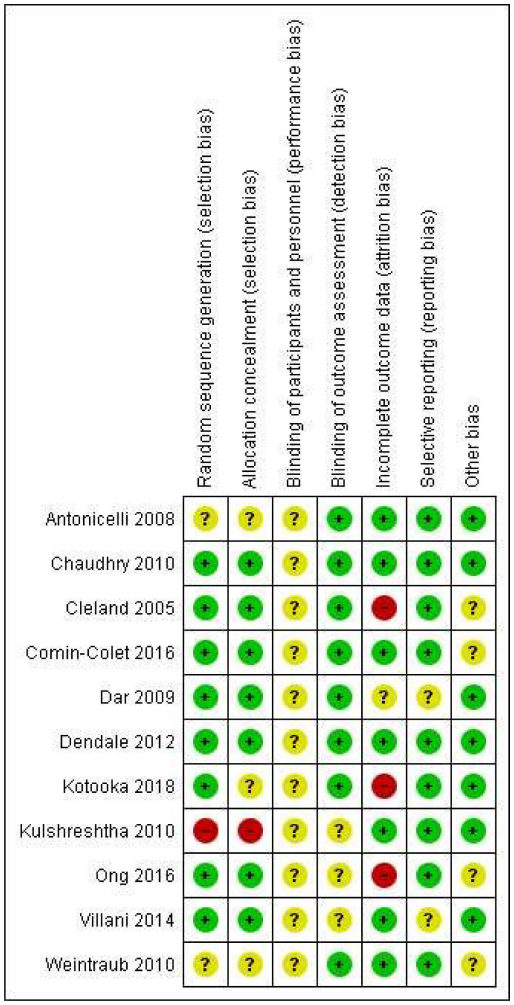
The baseline characteristics of patient populations, the rate of adverse events in the control group, the number of patients screened, and the withdrawal rate and adherence to the intervention differed considerably among the studies (*Tables 1* and *2*). There was a significant clinical heterogeneity among the included studies. The two largest studies with neutral effects offered no direct way to alter the HF medication of patients within the TM intervention.[15,17] This aspect of the TM intervention varied among the other studies, and the results were insufficiently reported[26,33,34] (*Table 2*).

Quantitative analysis

The pooled estimate of the effect of telemonitoring on all-cause hospitalization in comparison with standard care was neutral in a combined analysis with 4291 patients (RR 0.95, 95% CI 0.84–1.08, *P* = 0.43) (*Table 3*). We performed sensitivity analyses for both main outcome effect estimates by excluding studies with a high risk of bias that has no significant effect on the main results.

The pooled estimate of the effect of telemonitoring on all-cause mortality as opposed to standard care was neutral (RR 0.83, 95% CI 0.63–1.09, *P* = 0.17) (*Table* 4). This analysis

Figure 2 Risk of bias summary.



Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

+: Low risk of bias

-: High risk of bias

?: Unclear risk of bias

included the data of 11 studies and 4521 patients. We conducted a *post hoc* sensitivity analysis by excluding one study[26] with an effect considerably different from the others. After the exclusion of this study, the effect estimate reached statistical significance in favour of TM (0.83, 95% CI 0.69–0.99, $P = 0.04$).

Assessment of heterogeneity in pooled effect estimates

In the comparison of all-cause hospitalization in TM versus standard care, there was evidence of substantial heterogeneity in the effect estimates ($P = 0.0003$, $I^2 = 73\%$) (*Table 4*). In the comparison of all-cause mortality in TM versus standard care, there was non-significant evidence of moderate heterogeneity in the effect estimates (*Table 3*).

Discussion

Main findings

Our meta-analysis demonstrated that non-invasive home TM had a neutral effect on the all-cause hospitalization rate and all-cause mortality in patients with decompensated HF. These

Table 3 All-cause mortality (TM vs. UC)

Study or subgroup	TM Events	TM Total	UC Events2	UC Total2	Weight	Risk ratio M-H, Random	Risk ratio CI Start	Risk ratio CI End
Antonicelli 2008	3	28	5	29	3.62	0.62	0.16	2.36
Chaudhry 2010	92	826	94	827	21.89	0.98	0.75	1.28
Cleland 2005	28	168	20	85	14.06	0.71	0.42	1.18
Comin-Colet 2016	5	81	12	97	5.84	0.50	0.18	1.36
Dar 2009	17	91	5	91	6.29	3.40	1.31	8.83
Dendale 2012	4	80	14	80	5.27	0.29	0.10	0.83
Kotooka 2018	10	92	13	91	8.59	0.76	0.35	1.65
Kulshreshtha 2010	7	82	4	68	4.42	1.45	0.44	4.75
Ong 2016	100	715	114	722	22.69	0.89	0.69	1.13
Villani 2014	5	40	9	40	5.83	0.56	0.20	1.51
Weintraub 2010	1	95	4	93	1.48	0.24	0.03	2.15
Total	272	2298	294	2223	100.00	0.83	0.63	1.09
Heterogeneity					Test for overall effect			
Tau^2	χ^2	*df*	*P*	I^2	*Z*	*P*		
0.069	17.742	10	0.059	43.637	1.365	0.172		

Table 4 All-cause hospitalizations (TM vs. UC)

Study or subgroup	TM Events	TM Total	UC Events2	UC Total2	Weight	Risk ratio M-H, random	Risk ratio CI start	Risk ratio CI end
Antonicelli 2008	9	28	26	29	3.89	0.36	0.21	0.62
Chaudhry 2010	407	826	392	827	17.24	1.04	0.94	1.15
Cleland 2005	155	168	69	85	16.76	1.14	1.02	1.27
Comin-Colet 2016	20	81	45	97	5.56	0.53	0.34	0.82
Dar 2009	44	91	39	91	8.36	1.13	0.82	1.55
Dendale 2012	64	80	66	80	15.09	0.97	0.84	1.13
Kotooka 2018	27	92	34	91	5.99	0.79	0.52	1.19
Ong 2016	363	715	355	722	17.09	1.03	0.93	1.15
Weintraub 2010	51	95	49	93	10.01	1.02	0.78	1.33
Total	1140	2176	1075	2115	100	0.95	0.84	1.08
Heterogeneity					Test for overall effect			
Tau^2	χ^2	*df*	*P*	I^2	*Z*	*P*		
0.02	29.31	8	0.0003	73	0.78	0.43		

findings differ from previous meta-analyses that have combined data on both recently decompensated and stable HF patients.[12–14,18–22]

Considering the relatively limited data from the studies, we observed quite a high degree of heterogeneity in the effect estimates for all-cause hospitalizations. Thus, we have placed more weight on the qualitative analysis. The two largest original studies[15,17] reported a neutral effect on the main outcomes. However, these studies did not include the possibility to directly alter HF medication through the TM intervention. Adherence to the TM intervention was also poor in these studies. Three studies[27,29,30] with a positive effect of the TM intervention on either of the main outcomes reported quite a good adherence rate. In these studies, there was evidence of a higher level of prescribed HF medication at the end of follow-up in the TM group[27,30] or direct way for TM intervention to affect HF medication.[29]

A recent review of HF medication studies found that the majority of HF patients are prescribed guideline-directed medications: 92% receive an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) and 93% receive a beta-blocker.[42] However, the doses were mostly suboptimal, with only 29% of ACEI and 18% of beta-blocker users at target doses, although 50–60% of the patients in randomized controlled trials (RCT) achieved target doses of these drugs.

It seems plausible that the most potential treatment effect of TM comes from a more optimal use of diuretics and the up-titration of HF medication. It is possible that the absolute treatment effect is greater in HF patients with more advanced cardiac disease and the highest risk of rehospitalization and death. It seems that patient adherence to TM interventions is higher with interventions that are relatively simple and easy to use. Based on previous analyses,[12,13,18–22] it is likely that non-invasive home TM in recently decompensated HF has provided proof of concept, but the most feasible system and environment for implementing a TM intervention remain to be established.

It is likely that the treatment effect of a TM intervention depends on the details of the intervention and on how the general health care system has been included in the study setup. The results of our analysis seem to partly reflect the

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dilemma of determining the treatment effect of TM interventions in various countries.[12,23,43] Due to existing research gaps in TM studies on HF, it is preferable to conduct an RCT with appropriate statistical power to show the potential treatment effect with a simple and clinically applicable TM intervention that includes a mechanism for altering the HF medication in a timely fashion for patients with a high risk of future adverse HF events. In addition, TM interventions should be tailored to the local health care environment.

Study limitations

The number of published studies was limited, which decreases the accuracy of the pooled estimates and the power to detect a true treatment effect. The included studies were clinically heterogeneous: some study interventions offered general lifestyle and treatment advice, while others focused on detailed HF medication adjustments. The baseline characteristics of study populations, withdrawal rates, the adherence to the study intervention, and the number of adverse events in the standard care group varied between the studies. There was evidence of substantial statistical heterogeneity in the effect estimates for all-cause hospitalizations in the primary studies, which increases the risk of bias in our pooled estimates. In addition to possible differences in the TM intervention, the content of standard care may have been slightly different between the TM studies. The lack of accurately reported outcomes for all-cause hospitalizations in two studies[32,33] increases the risk of bias. In the funnel plots of the study main outcomes, there was asymmetry in favour of a TM intervention.

Conclusions

Published trials on non-invasive home TM interventions in recently decompensated HF patients are scarce. The current systematic review and meta-analysis of existing data showed that non-invasive home TM had no effect on all-cause hospitalizations or mortality in recently decompensated HF patients. The neutral effect emerging from the included trials may be partly explained by a large amount of clinical heterogeneity between TM trials.

Conflict of interest

The authors declare no conflict of interest.

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Author contributions

T.D. and T.N. contributed to the conception or design of the work. T.D. contributed to the acquisition, analysis, or interpretation of data for the work. T.N. contributed to the acquisition and interpretation of data for the work. T.D., T.N., and J.L. drafted the manuscript. T.D., T.N., and J.L. critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Risk of bias graph
Table S1. Data sheets of primary studies (web addenda)
Table S2. Funnel plot on all-cause mortality (TM vs. UC)
Table S3. Funnel plot on all-cause hosps (TM vs. UC)
Table S4. After duplicates removed
Table S5. After headlines screened
Table S6. After abstracts screened
Table S7. PRISMA checklist

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