Clinical effectiveness of telemedicine for chronic heart failure: a systematic review and meta-analysis

Mao-huan Lin, Wo-liang Yuan, Tu-cheng Huang, Hai-feng Zhang, Jing-ting Mai, Jing-feng Wang

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Department of Cardiology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, People's Republic of China

Correspondence to
Dr Wo-liang Yuan, Department of Cardiology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, 107 Yan Jiang West Road, Guangzhou 510120, People's Republic of China; dryuanwl@126.com

M-hL and W-lY, the first two authors, contributed equally to this study.

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ABSTRACT

Telemedicine interventions may be associated with reductions in hospital admission rate and mortality in patients with heart failure (HF). The present study is an updated analysis (as of June 30, 2016) of randomized controlled trials, where patients with HF underwent telemedicine care or the usual standard care. Data were extracted from 39 eligible studies for all-cause and HF-related hospital admission rate, length of stay, and mortality. The overall all-cause mortality (pooled OR=0.80, 95% CI 0.71 to 0.91, p<0.001), HF-related admission rate (pooled OR=0.63, 95% CI 0.53 to 0.76, p<0.001), and HF-related length of stay (pooled standardized difference in means=−0.37, 95% CI −0.72 to −0.02, p=0.041) were significantly lower in the telemedicine group (teletransmission and telephone-supported care), as compared with the control group. In subgroup analysis, all-cause mortality (pooled OR=0.69, 95% CI 0.56 to 0.86, p=0.001), HF-related admission rate (OR=0.61, 95% CI 0.42 to 0.88, p=0.008), HF-related length of stay (pooled standardized difference in means=−0.96, 95% CI −1.88 to −0.05, p=0.039) and HF-related mortality (OR=0.68, 95% CI 0.54 to 0.85, p=0.001) were significantly lower in the teletransmission group, as opposed to the standard care group, whereas only HF-related admission rate (OR=0.64, 95% CI 0.52 to 0.79, p<0.001) was lower in the telephone-supported care group. Overall, telemedicine was shown to be beneficial, with home-based teletransmission effectively reducing all-cause mortality and HF-related hospital admission, length of stay and mortality in patients with HF.

Significance of this study

What is already known about this subject?

- Telemedicine involves telecommunication-based management of patients either by telephone-based care (eg, information/data are collected or distributed by a healthcare provider who calls the patient on a regular basis) or through a home-based teletransmission monitoring system (eg, information/data are automatically transmitted from home to the healthcare provider by internet or a phone line).
- Previous studies have found that telemedicine interventions, including home telemonitoring and telephone-supported care, are variously associated with improvement in all-cause mortality, hospital admission rates and improved quality of life.
- There is insufficient evidence to support use of telephone support with respect to heart failure-related hospitalization and mortality.

What are the new findings?

- Regardless of the type of intervention, telemedicine intervention overall was associated with benefit to the patients with HF-related hospitalization and mortality.
- Home-based teletransmission, a subtype of telemedicine, may significantly reduce all-cause and HF-related mortality.
- Home-based teletransmission may significantly reduce admission rate and shorten the HF-related length of hospital stay.
- Telephone support care, which is usually conducted by a nurse, may significantly reduce HF-related hospital admission rate.

INTRODUCTION

Chronic heart failure (CHF) is a common problem that is associated with a significant clinical and financial burden.[1] Indeed, individuals who experience heart failure (HF) have higher rates of morbidity and mortality, as well as reduced quality of life.[1] From an economic perspective, estimates from the USA indicate that the cost associated with treating HF was in excess of $70 billion per year in recent times.[2] With the increase in aging populations worldwide, HF will remain a significant problem for the foreseeable future, one that will require a concerted effort to optimize management strategies, improve clinical outcomes, and minimize the associated economic burden.

One strategy that has been implemented as an adjunct to conventional medicine in the

Significance of this study

How might these results change the focus of research or clinical practice?

- A home-based teletransmission monitoring system may be recommended in the management of chronic heart failure.
- A combination of home-based teletransmission and nurse-based telephone reinforcement may be encouraged.
- The efficacy of the telemedicine in different populations (eg, patients in either community, remote care or under institutional care) might be investigated.
- The efficacy of telemedicine using an advanced telemonitoring device and newly developed guidelines in the remote monitoring and management of patients with heart failure might be investigated.

management of CHF, in particular to reduce the likelihood of repeat hospital admission, is telemedicine. Telemedicine involves telecommunication-based management of patients and may be active (eg, information/data are collected or distributed by a healthcare provider who calls the patient on a regular basis) or automated (eg, information/data are automatically transmitted to the healthcare provider).[3] The type of information collected or distributed as part of telemedicine-based management of HF is varied, but may include body weight, vital signs, ECGs, education, counseling, etc.[3 4] The advantage of telemedicine is that medical decisions by HF-trained nurses or physicians for the management of patients are made promptly based on the HF-related parameters.[4] Any variation in these vital signs from predefined parameters can trigger an alert suggesting clinical deterioration resulting in a telephone call for further patient assessment.[5] The nurse can take several actions: (1) if the conditions are stable, patients can keep their scheduled appointment, (2) the medications preplanned with the cardiologist or the general practitioner can be reviewed, (3) further investigations or a scheduled cardiological consultation can be arranged.[6]

A number of studies and meta-analyses have reported the effectiveness of telemedicine in the management of CHF. Reports suggest that telemedicine interventions, including teletransmission (a home telemonitoring system) and telephone support, are variously effective in reducing all-cause mortality and hospital admission rates, and improving the quality of life.[7–12] The most recent meta-analysis, reported by Kotb *et al*,[13] included studies published between 1998 and 2011. Given that a number of relevant studies have been published since that time, and that the telemedicine system used in various trials was heterogeneous with inconsistent outcomes, we decided to carry out an up-to-date meta-analysis of the literature on this topic. The aim of our meta-analysis was therefore to comprehensively review the literature and provide an update on the effectiveness of telemedicine (teletransmission system and telephone support care) for treating patients with CHF.

MATERIALS AND METHODS

Search strategy

This meta-analysis was carried out in accordance with the PRISMA guidelines.[14] MEDLINE, the Cochrane Library, EMBASE, and CINAHL Plus were searched (from the date of inception to June 30, 2016) using combinations of the following key words: heart failure, remote, telemedicine, telehealth, health information systems, internet, and monitoring.

Eligibility criteria

Inclusion criteria

Studies were considered for inclusion in the meta-analysis if they met the following criteria: (1) randomized controlled trials (RCTs) involving patients (age≥18 years) diagnosed with CHF; patients had to be hospitalized for HF with New York Heart Association (NYHA) class I–IV, measured at randomization, and received optimized standard medical therapy (ACE inhibitor or angiotensin receptor blocker, and a β-blocker; all medications as tolerated) prior to enrollment. (2) The studies included an intervention group and a control group. In the intervention group, participants received any form of home-based telemedicine (teletransmission or telephone-supported care) combined with the usual standard care. In the control group, patients were required to receive standard care only. (3) End points included length of intervention, hospital admission rate, length of hospital stay and all-cause mortality.

Definitions

Teletransmission consists of a home telemonitoring system. ECG, blood pressure, body weight, and other cardiac-related measurements are sent either wired or wirelessly to a computer-based home HF monitoring system in the patient's home, and the data are linked via a standard phone line to a telemedical center. For some studies, video consultation equipment (video-based telecare) for a two-way video conference was used. The telephone-supported care monitors clinical status and delivers medical management by a conventional telephone call. A telephone-supported care programme usually is a part of a nurse-based care programme after discharge. The vital signs (eg, heart rate, blood pressure, changes in weight) for both groups were collected during regular face-to-face visits or self-reported during the phone interview instead of automatic transfer. Usual care is defined as a guideline-based standard care in addition to the scheduled clinic visits.

Exclusion criteria

Studies were excluded if they were not RCTs, involved patients with acute HF, did not report numerical data for the outcomes of interest, were not published in English, or if they were published in the form of letters, comments, editorials, case reports, or technical reports.

Study selection and data extraction

Studies were identified using the aforementioned search strategy by two independent reviewers (M-hL and W-lY). In cases of uncertainty regarding eligibility, a third reviewer (J-fW) was consulted.

The following information was extracted from studies that met the eligibility criteria: name of the first author, year of publication, patient demographics, type of telemedicine intervention, length of intervention, hospital admission rate, length of hospital stay, and mortality. Data extraction was also performed by the same two independent reviewers who consulted with a third reviewer to resolve any disagreement.

Outcomes

The outcomes of interest were the rates of all-cause and HF-related hospital admission rate, length of hospital stay, and mortality.

Quality assessment

The Cochrane Risk of Bias Tool[15] was used to assess the quality of studies included in the meta-analysis. Quality assessment was performed by two independent reviewers, with consultation of the third reviewer as necessary.

Statistical analysis

The OR and standardized difference in means were calculated for all outcomes for the telemedicine group compared with the usual care (control) group. Subgroup analyses were carried out for teletransmission versus control, and telephone-supported care versus control, groups. Heterogeneity among the studies was assessed by determining the Cochran Q and the I^2 statistic.[16] For the Q statistic, $p<0.10$ was considered to indicate statistically significant heterogeneity. For the I^2 statistic, which indicates the percentage of the observed between-study variability due to heterogeneity rather than chance, no heterogeneity was indicated by an I^2 of 0–25%, moderate heterogeneity was indicated by an I^2 of 25–50%, large heterogeneity was indicated by an I^2 of 50–75%, and extreme heterogeneity was indicated by an I^2 of 75–100%. A random-effects model of analysis was used (the DerSimonian-Laird method) for all pooled ORs and standardized differences in the means of outcomes.[17] A two-sided p value<0.05 was considered to indicate statistical significance. All statistical analyses were performed using the statistical software, Comprehensive Meta-Analysis, V.2.0 (Biostat, Englewood, New Jersey, USA).

RESULTS

Literature search

A total of 911studies were identified in the literature search. Of these, 837were excluded after title and abstract review. Reasons for exclusion are: unrelated to HF, not RCT, unrelated to home-based teletransmission/telephone support care, no outcome of interest, or non-English publications. A total of 74 articles underwent a full-text review. Subsequently, 35 studies were excluded, due to no numerical data for outcomes of interest (n=17), no RCTs (n=9), duplicated publications (n=5), unrelated to HF (n=3), including caregivers in the study (n=1). Finally, a total of 39 randomized, open-labeled, controlled trials were included in the systematic review/meta-analysis.[5 6 18–54] Figure 1 represents the flow chart of studies included in the current meta-analysis.

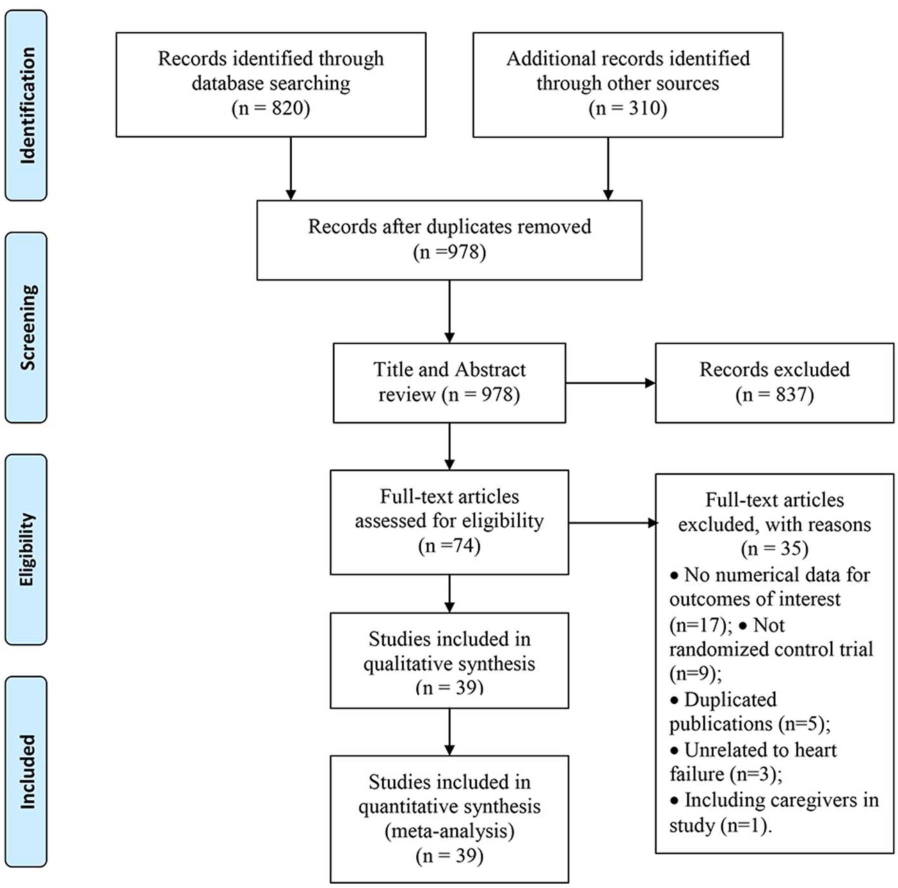


Figure 1 PRISMA flow chart of study selection.

Basic characteristics

Studies were classified into two groups based on the type of intervention(s): teletransmission (n=21)[5 6 18–20 23 25–27 34–36 38 42 44 45 47 49 51 53 54] and telephone-supported care (n=21).[21 22 24 25 28–33 35 37 39 40 41 43 44 46 48 50 51] Please note that three studies[25 35 44] reported outcomes for teletransmission and telephone-supported care. Since the data for different types of intervention were analyzed separately, we included those studies in both groups. The characteristics of the studies included are summarized in table 1 (teletransmission) and table 2 (telephone-supported care). There was a large heterogeneity in sample size and demographic data. The total number of participants was 11 758 (range 20–1653), of which 5935 subjects belonged to the telemedicine groups (range 10–826), while 5823 subjects were in the control group (range 10–827). The

Table 1 Basic characteristics of studies (teletransmission vs usual care) included in the meta-analysis

Author (year)	Comparison	Patient number (N)	Age*	Male (%)	NYHA grade	LVEF (%)*	Follow-up
Lyngå (2012)[42]	Teletransmission (BW)	166	73.7 (9.9)	76	III/IV	<30%: 102 (61.4) 30–39%: 34 (20.5) 40–49%: 30 (18.1)	12 months
	Without monitoring the BW	153	73.5 (10.4)	74		<30%: 80 (52.3) 30–39%: 40 (26.1) 40–49%: 33 (21.6)	
Pekmezaris (2012)[45]	Teletransmission (BP, stethoscope)	83	81 (7)	43	I–IV	NA	30 and
	Usual care	85	83 (7)	33		NA	90 days
Wade (2011)[51]	Teletransmission (BW, BP)	164	75.8 (6.96)	51	NA	NA	12 months
	Usual care	152	77.7 (6.97)	49		NA	
Koehler (2011)[38]	Teletransmission (BW, BP)	354	66.9 (10.8)	81	II/III	26.9 (5.7)	26 months
	Usual care	356	66.9 (10.5)	82		27.0 (5.9)	
Weintraub (2010)[53]	Teletransmission (BW, BP, HR)	95	69.5 (14.2)	63	I–IV	32.1(17.2)	90 days
	Usual care	93	68.5 (12.8)	69		27.2 (15.8)	
Mortara (2009)[44]	Teletransmission (vital signs, stethoscope)	101	59 (11)	84	II–IV	28 (8)	12 months
	Usual care	94	60 (12)	89		29 (7)	
Scherr (2009)[47]	Teletransmission (BW, BP, HR)	66	66 (62, 73)†	70	II–IV	25 (20–38)†	6 months
	Usual care	54	67 (61, 72)†	72		29 (21–36)†	
Giordano (2009)[6]	Teletransmission (ECG)	230	58 (10)	84	II–IV	28 (7)	1 year
	Usual care	230	56 (10)	86		26 (8)	
Dar (2009)[5]	Teletransmission (BW, BP, HR, S/S)	91	70 (12.8)	68	II–IV	>40%: 33/85 (39)	3 and
	Usual care	91	72 (10.4)	65		>40%: 33/83 (40)	6 months
Kashem (2008)[36]	Teletransmission (BW, BP, HR)	24	53 (10)	72	II–IV	25 (3)	1 year
	Usual care	24	54 (11)	76		26 (3)	
Antonicelli (2008)[18]	Teletransmission (ECG, BP, HR, BW)	28	77 (8)	57	II–IV	35 (6)	12 months
	Usual care	29	79 (6)	66		37 (7)	
Balk (2008)[19]	Teletransmission (BW, BP)	101	68 (33, 85)‡	64	I–IV	31 (9, 69)‡	288 days
	Usual care	113	65 (42, 87)‡	75		31 (11, 71)‡	
Soran (2008)[49]	Teletransmission (BW)	160	76.9 (7.1)	31	II–III	24.3 (8.8)	6 months
	Standard care	155	76.0 (6.8)	39		23.8 (8.7)	
Woodend (2008)[54]	Teletransmission (BW, BP, ECG)	62	67 (13)	74	II–IV	NA	1 year
	Usual care	59	66 (11)	70		NA	
Dansky (2008)[26]	Teletransmission (BW, BP, HR, digital stethoscope)	45	78.11 (7.11)	NR	NR	NA	120 days
	Usual care	112	76.88 (10)	NR		NA	
Cleland (2005)[25]	Teletransmission (BW, BP, ECG)	168	67 (13)	80	I–IV	25 (8)	240 days
	Usual care	85	68 (10)	82		24 (8)	
Capomolla (2004)[23]	Teletransmission (BW, BP, HR, S/S)	67	57 (10)	93	II–IV	29 (8)	12 months
	Usual care	66	57 (10)	83		28 (7)	
Goldberg (2003)[34]	Teletransmission (BW)	138	57.9 (15.7)	70	III–IV	21.6 (6.8)	6 months
	Usual care	142	60.2 (14.9)	66		21.8 (6.8)	
Benatar (2003)[20]	Teletransmission (BW, BP, HR, $SatO_2$)	108	62.9 (13.2)	36	III–IV	38.05 (13.70)	12 months
	Usual care	108	63.2 (12.6)	38		38.83 (13.97)	
de Lusignan (2001)[27]	Teletransmission (BW, BP, HR)	10	75.2	n/a	I–IV	NA	12 months
	Usual care	10		n/a		NA	
Jerant (2001)[35]	Teletransmission (digital stethoscope)	13	66.6 (10.9)	46	II–IV	NA	180 days
	Usual care	12	72.7 (11.4)	50		NA	

*Data expressed as mean±SD.
†Data expressed as median (IQR).
‡Data expressed as median (range).
AHA, American Heart Association; BP, blood pressure; BW, body weight; HFSA, Heart Failure Society of America; HR, heart rate; ICD/CRT, implantable cardiac defibrillator/cardiac resynchronization therapy; LVEF, left ventricular ejection fraction; NA, not available; NR, not reported; NYHA, New York Heart Association Grade; RCT, randomized controlled trial; RPM, remote patient monitoring.

Table 2 Basic characteristics of studies (telephone-supported care vs usual care) included in the meta-analysis

Author (Year)	Comparison	Patient number (N)	Age*	Male (%)	NYHA grade	LVEF (%)*	Follow-up
Krum (2013)[39]	Telephone	188	73 (10)	62	II–IV	37.2 (14.14)	12 months
	Usual care	217	73 (11)	64		34.9 (23.48)	
Boyne (2012)[22]	Telephone	197	71.0 (11.9)	58	II–IV	NA	1 year
	Usual care	185	71.9 (10.5)	60		NA	
Domingues (2011)[30]	Telephone	48	62 (12)	67	II–IV	29 (8)	90 days
	Usual care	63	63 (13)	51		29 (9)	
Ferrante (2010)[32]	Telephone	760	64.8 (13.9)	73	II–III	NA	3 years
	Usual care	758	65.2 (12.7)	69		NA	
Chaudhry (2010)[24]	Telephone	826	61 (51, 73)†	57	I–IV	NA	180 days
	Usual care	827	61 (51, 73)†	59		NA	
Mortara (2009)[44]	Telephone	106	60 (12)	86	II–IV	29 (8)	12 months
	Usual care	160	60 (12)	83		30 (7)	
Wakefield (2008)[52]	Telephone	47	71.8 (10.2)	100	II–IV	43.5 (13, 75)‡	90 days
	Videophone	52	69.0 (9.6)	98		38 (6, 73)	
	Usual care	49	67.2 (8.5)	98		43 (12, 81)‡	
Ramachandran (2007)[46]	Telephone	25	43.4 (11.5)	80	I–IV	NA	6 months
	Usual care	25	45.8 (12.5)	76		NA	
Sisk (2006)[48]	Telephone	203	59.6 (13.8)	55	I–IV	NA	12 months
	Usual care	203	59.3 (13.7)	52		NA	
DeWalt (2006)[29]	Telephone	59	63 (9)	58	II–IV	NA	12 months
	Usual care	64	62 (11)	41		NA	
Cleland (2005)[25]	Telephone	173	67 (11)	72	I–IV	25 (8)	240 days
	Usual care	85	68 (10)	82		24 (8)	
Dunagan (2005)[31]	Telephone	76	70.5 (12.7)	41	II–IV	<25%: 29 25–40%: 27 41–50%: 6 >50%: 14	1 year
	Usual care	75	69.4 (13.9)	47		<25%: 36 25–40%: 23 41–50%: 5 >50%: 11	
Tsuyuki (2004)[50]	Telephone	140	71 (12)	58	I-IV	32 (12)	6 months
	Usual care	136	72 (12)	58		31 (11)	
DeBusk (2004)[28]	Telephone	228	72 (11)	48	I–IV	NA	1 year
	Usual care	234		54		NA	
Laramee (2003)[41]	Telephone	141	70.6 (11.4)	58	I–IV	NA	12 weeks
	Usual care	146	70.8 (12.2)	50		NA	
Kasper (2002)[37]	Telephone	102	60.2 (13.8)	65	II–IV	27.1 (13.8)	6 months
	Usual care	98	63.7 (15.0)	56		27.5 (13.9)	
Krumholz (2002)[40]	Telephone	44	75.9 (8.7)	48	NA	38 (17)	1 year
	Usual care	44	71.6 (10.3)	66		37 (16)	
McDonald (2002)[43]	Telephone	51	70.76 (10.37)	63	NA	38.4 (12.9)	3 months
	Usual care	47	70.83 (10.69)	70		37.7 (12.6)	
Blue (2001)[21]	Telephone	84	74.4 (8.6)	64	II–IV	NA	1 year
	Usual care	81	75.6 (7.9)	51		NA	
Jerant (2001)[35]	Telephone	12	71.3 (14.1)	42	II–IV	NA	180 days
	Usual care	12	72.7 (11.4)	50		NA	
Gattis (1999)[33]	Telephone	90	71.5 (60, 77)†	69	I–IV	NA	6 months
	Usual care	91	63.0 (55, 72)†	67		NA	

*Data expressed as mean±SD.
†Data expressed as median (IQR).
‡Data expressed as median (range).
LVEF, left ventricular ejection fraction; NA, not available; NYHA, New York Heart Association Grade.

mean age of patients ranged from 43 to 81 years in the telemedicine groups and from 46 to 83 years in the control groups. The proportion of male patients ranged from 31% to 100% in the telemedicine groups and from 33% to 98% in the control groups. The follow-up period ranged from 90 days (3 months) to 1 year for the teletransmission studies, and from 90 days (3 months) to 3 years for the telephone-supported care studies (tables 1 and 2). A majority of the patients in the included studies had an impairment in the left ventricular ejection fraction (LVEF; defined as LVEF<50% or <40%). The only exceptions were in the study reported by Dar *et al*,[5] where the patients had a preserved left ventricular (LV) systolic function (EF≥40%; table 1) and in Dunagan *et al*'s[31] study, where ~16% of patients had an LVEF>50% (table 2).

Interventions

The types of interventions are described in online supplementary table S1. Teletransmission usually consists of an automated home telemonitoring system to transmit data, like body weight, blood pressure, heart rate, arterial oxygen saturation and/or other vital signs and symptoms via a standard telephone line to a central web server. A two-way video-monitoring system may also be equipped for video conference with the nurse. The telephone support intervention is usually performed during the follow-up period after discharge from the hospital or after the end of the patient education programme. The telephonic monitoring reinforces the instructions received during hospitalization or through educational programmes, and also ensures medication adherence and self-management of symptoms. In most of the studies included in this meta-analysis, the usual care (control group) was defined as a guideline-based standard care in addition to the scheduled clinic visits without any additional intervention.

Data reviewing and treatment

The data collection and related treatment are summarized in online supplementary table S1. In most of the studies, transmitted data from home monitoring were reviewed on a daily basis by an HF nurse. If the patient's data showed abnormality or any alert sign suggesting clinical deterioration, the HF nurse would call the patient to discuss the deviation and to initiate an intervention if necessary. Additional clinic visits were performed whenever needed. Based on the evaluation of all HF-related parameters, the therapeutic regimen was reassessed and altered when necessary. Changes in treatment were only made in consultation with the cardiologist, or by a consultant clinical physiologist. Decision for hospital readmission during follow-up was taken after consulting medical team members according to predefined criteria based on a set of clinical signs and symptoms related to worsening of cardiac insufficiency or its complications. For the telephone-supported care, any suspect data were checked by the monitoring nurse or attending physician. When patients reported symptoms, such as weight gain, after reviewing the reported data, the nurses reinforced the plan of care and made referrals, or contacted the patient's physician for adjustments in the care plan. Most of the studies did not provide specialized nursing assessment, care or medication advice beyond diuretic dosing. During telephone contacts, nurses screened patients for HF exacerbations and administered a standardized screening instrument developed to detect such changes. If there was evidence of an exacerbation, programme nurses recommended that the patient take supplemental diuretics or contact their physician for instructions.

Outcome measurement

Outcome measures are summarized in online supplementary table S2, including all-cause hospital admission rate, length of hospital stay, mortality, and HF-related hospital admission rate, length of hospital stay and mortality. There was remarkable heterogeneity in the data across the studies. For example, the all-cause length of hospital stay ranged from 2.2 to 245 days in the telemedicine groups and from 4.8 to 260 days in the control groups. The HF-related length of hospital stay ranged from 0.67 to 95 days in the telemedicine groups and from 3 to 150 days in the control groups.

Meta-analyses

All-cause hospital admission

A total of 27 studies reported all-cause hospital admission data, including 13 telephone-supported care studies and 14 teletransmission intervention studies (figure 2). There was significant heterogeneity when data from the 27 studies were pooled (Q=90.77, df=27, $p<0.001$, $I^2=71.36\%$). The analysis revealed that there was no significant difference in all-cause hospital admission between the overall telemedicine and control groups (pooled OR=0.92, 95% CI 0.82 to 1.04, Z=−1.29, p=0.196). A subgroup analysis also did not reveal any significant difference between the treatment and control groups (teletransmission, pooled OR=0.90, 95% CI 0.72 to 1.13, Z=−0.89, p=0.376; telephone-supported care, pooled OR=0.93, 95% CI 0.81 to 1.07, Z=−0.98, p=0.329; figure 2).

All-cause length of hospital stay

A total of 13 studies reported all-cause length of hospital stay data, including 7 telephone-supported care studies and 6 teletransmission intervention studies (figure 3). There was significant heterogeneity when data from the 13 studies were pooled (Q=164.64, df=12, $p<0.001$, $I^2=92.71\%$). The analysis revealed that there was no significant difference in all-cause length of hospital stay between the overall telemedicine and control groups (pooled standardized difference in means=−0.15, 95% CI −0.35 to 0.06, Z=−1.42, p=0.155), the teletransmission and control groups (pooled standardized difference in means=−25, 95% CI −0.80 to 0.31, Z=−0.88, p=0.381), or the telephone-supported care and control groups (pooled standardized difference in means=−0.13, 95% CI −0.35 to 0.09, Z=−1.18, p=0.237; figure 3).

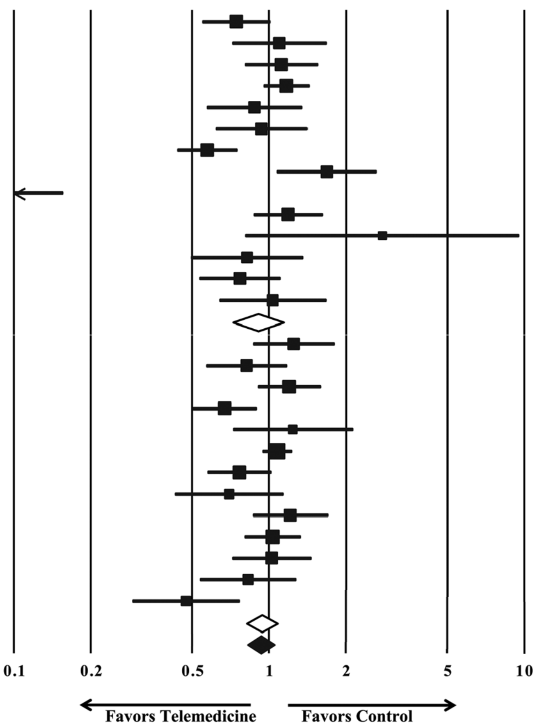
All-cause mortality

A total of 30 studies reported all-cause mortality data, including 17 telephone-supported care studies, and 13 teletransmission intervention studies (figure 4). There was significant heterogeneity when data from the 30 studies were pooled (Q=43.67, df=29, p=0.039, $I^2=33.59\%$). The analysis revealed that all-cause mortality was significantly lower in the overall telemedicine group compared with the control group (pooled OR=0.80, 95% CI=0.71 to 0.91, Z=−3.54, $p<0.001$) and in the teletransmission group compared with the control group (pooled OR=0.69, 95% CI 0.56 to 0.86, Z=−3.43, p=0.001). However, the telephone-supported care group (pooled OR=0.87, 95% CI 0.74 to 1.01, Z=−1.89, p=0.059) showed no significant difference in all-cause mortality as compared with the control group (figure 4).

HF-related hospital admission rate

A total of 29 studies reported hospital admission rate data, including 18 telephone-supported care intervention studies and 11 teletransmission intervention studies (figure 5). There was significant heterogeneity when data from the 29 studies were pooled (Q=120.77, df=28, $p<0.001$, $I^2=76.82\%$). The analysis revealed that, in comparison to

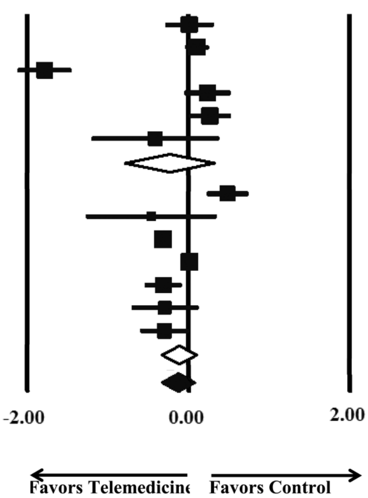
Study name	Comparison	Odds ratio	Lower limit	Upper limit	Z-Value	P-Value	Relative Weight
Lynga (2012)	Tele-transmission vs contro	0.75	0.55	1.02	-1.84	0.065	8.45
Pekmezaris (2012)	Tele-transmission vs contro	1.10	0.72	1.69	0.43	0.664	7.42
Wade (2011)	Tele-transmission vs contro	1.12	0.80	1.56	0.67	0.503	8.28
Koehler (2011)	Tele-transmission vs contro	1.17	0.95	1.44	1.49	0.136	9.25
Weintraub (2010)	Tele-transmission vs contro	0.88	0.57	1.36	-0.58	0.559	7.37
Mortara (2009)	Tele-transmission vs contro	0.94	0.62	1.42	-0.31	0.754	7.54
Giordano (2009)	Tele-transmission vs contro	0.57	0.44	0.75	-3.97	0.000	8.76
Dar (2009)	Tele-transmission vs contro	1.68	1.07	2.64	2.26	0.024	7.21
Antonicelli (2008)	Tele-transmission vs contro	0.05	0.02	0.16	-5.41	0.000	3.21
Soran (2008)	Tele-transmission vs contro	1.19	0.87	1.63	1.08	0.279	8.42
Woodend (2008)	Tele-transmission vs contro	2.78	0.81	9.58	1.62	0.106	2.55
Dansky (2008)	Tele-transmission vs contro	0.82	0.49	1.37	-0.76	0.450	6.69
Cleland (2005)	Tele-transmission vs contro	0.77	0.53	1.12	-1.38	0.168	7.94
Capomolla (2004)	Tele-transmission vs contro	1.04	0.64	1.68	0.14	0.887	6.91
Random		**0.90**	**0.72**	**1.13**	**-0.89**	**0.376**	
Mortara (2009)	Telephone vs control	1.25	0.87	1.81	1.19	0.233	7.23
Cleland (2005)	Telephone vs control	0.82	0.57	1.18	-1.06	0.288	7.24
Boyne (2012)	Telephone vs control	1.20	0.90	1.60	1.26	0.207	9.06
Krum (2013)	Telephone vs control	0.67	0.50	0.90	-2.66	0.008	8.87
Domingues (2011)	Telephone vs control	1.24	0.72	2.14	0.78	0.434	4.54
Chaudhry (2010)	Telephone vs control	1.08	0.94	1.24	1.08	0.281	12.84
Sisk (2006)	Telephone vs control	0.77	0.57	1.03	-1.78	0.075	8.90
Dunagan (2005)	Telephone vs control	0.70	0.43	1.15	-1.42	0.156	5.16
Tsuyuki (2004)	Telephone vs control	1.21	0.86	1.71	1.11	0.266	7.79
DeBusk (2004)	Telephone vs control	1.04	0.80	1.34	0.27	0.790	9.75
Laramee (2003)	Telephone vs control	1.03	0.72	1.47	0.14	0.887	7.43
Blue (2001)	Telephone vs control	0.83	0.54	1.29	-0.84	0.403	5.98
Gattis (1999)	Telephone vs control	0.47	0.29	0.77	-3.00	0.003	5.23
Random		**0.93**	**0.81**	**1.07**	**-0.98**	**0.329**	
Pooled (Random)		**0.92**	**0.82**	**1.04**	**-1.29**	**0.196**	



Heterogeneity test for telephone group: Q = 28.84, df = 12, P = 0.004, I-square = 58.39%
Heterogeneity test for tele-transmission group: Q = 61.60, df = 13, P < 0.001, I-square = 78.90%
Heterogeneity test for overall: Q = 90.77, df = 26, P < 0.001, I-square = 71.36%

Figure 2 Forest plot of all-cause hospital admission for teletransmission and telephone-supported care versus usual care.

Study name	Comparison	Std diff in means	Lower limit	Upper limit	Z-Value	P-Value	Relative Weight
Pekmezaris (2012)	Tele-transmission vs contro	0.01	-0.29	0.31	0.07	0.944	17.20
Koehler (2011)	Tele-transmission vs contro	0.11	-0.04	0.25	1.43	0.152	17.90
Weintraub (2010)	Tele-transmission vs contro	-1.78	-2.12	-1.44	-10.33	0.000	16.99
Dar (2009)	Tele-transmission vs contro	0.24	-0.05	0.53	1.59	0.112	17.26
Cleland (2005)	Tele-transmission vs contro	0.27	0.01	0.53	2.01	0.044	17.42
Jerant (2001)	Tele-transmission vs contro	-0.41	-1.20	0.38	-1.01	0.312	13.23
Random		**-0.25**	**-0.80**	**0.31**	**-0.88**	**0.381**	
Cleland (2005)	Telephone vs control	0.49	0.23	0.75	3.64	0.000	15.30
Jerant (2001)	Telephone vs control	-0.46	-1.27	0.35	-1.11	0.266	5.29
Ferrante (2010)	Telephone vs control	-0.31	-0.42	-0.21	-6.10	0.000	18.88
Chaudhry (2010)	Telephone vs control	0.01	-0.08	0.11	0.28	0.783	18.95
Laramee (2003)	Telephone vs control	-0.31	-0.54	-0.08	-2.62	0.009	16.07
Krumholz (2002)	Telephone vs control	-0.29	-0.71	0.13	-1.36	0.174	11.37
Blue (2001)	Telephone vs control	-0.30	-0.60	0.01	-1.89	0.059	14.16
Random		**-0.13**	**-0.35**	**0.09**	**-1.18**	**0.237**	
Pooled (Random)		**-0.15**	**-0.35**	**0.06**	**-1.42**	**0.155**	



Heterogeneity test for telephone group: Q = 47.20, df = 6, P < 0.001, I-square = 87.29%
Heterogeneity test for tele-transmission group: Q = 115.62, df = 5, P < 0.001, I-square = 95.68%
Heterogeneity test for overall: Q = 164.64, df = 12, P < 0.001, I-square = 92.71%

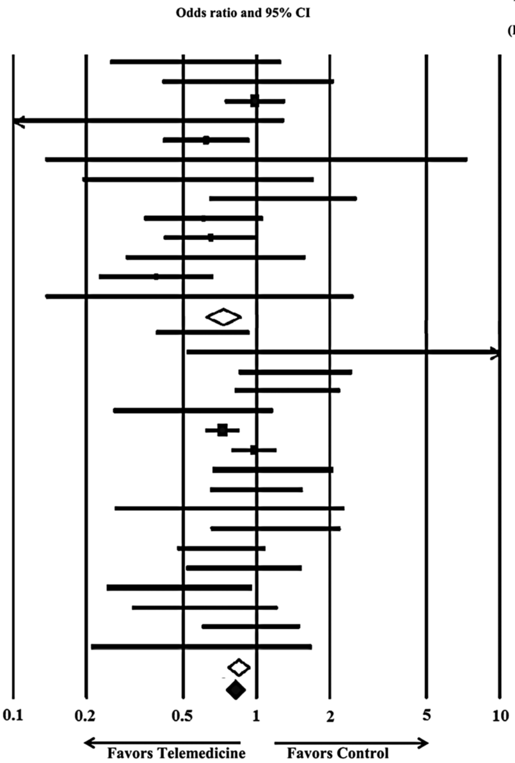
Figure 3 Forest plot of all-cause length of hospital stay for teletransmission and telephone-supported care versus usual care. Std diff in means, standardized difference in means.

the control, the rate of HF-related admission rate was significantly lower in the overall telemedicine group (pooled OR=0.63, 95% CI 0.53 to 0.76, Z=−4.91, p<0.001), in the teletransmission group (pooled OR=0.61, 95% CI 0.42 to 0.88, Z=−2.64, p=0.008), and in the telephone-supported care group (pooled OR=0.64, 95% CI 0.52 to 0.79, Z=−4.15, p<0.001; figure 5).

HF-related length of hospital stay

A total of 11 studies reported HF-related length of hospital stay data, including 5 telephone-supported care studies and 6 teletransmission intervention studies (figure 6). There was significant heterogeneity when data from the 11 studies were pooled (Q=353.45, df=10, p<0.001, I^2=97.17%). The analysis revealed that, in comparison to

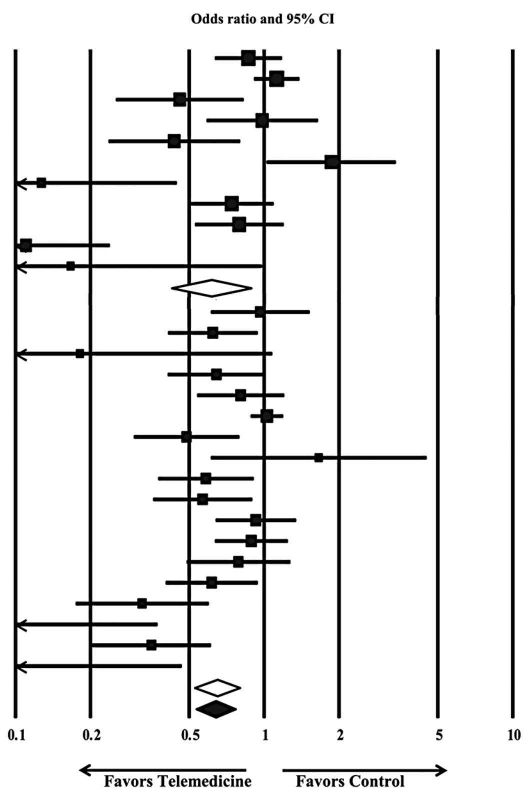
Study name	Comparison	Odds ratio	Lower limit	Upper limit	Z-Value	P-Value	Relative Weight (Random)
Lynga (2012)	Tele-transmission vs control	0.56	0.25	1.27	-1.38	0.167	5.51
Wade (2011)	Tele-transmission vs control	0.92	0.41	2.09	-0.19	0.849	5.51
Koehler (2011)	Tele-transmission vs control	0.99	0.74	1.31	-0.10	0.919	21.03
Weintraub (2010)	Tele-transmission vs control	0.24	0.04	1.30	-1.66	0.098	1.43
Giordano (2009)	Tele-transmission vs control	0.62	0.41	0.94	-2.24	0.025	14.65
Kashem (2008)	Tele-transmission vs control	1.00	0.14	7.40	0.00	1.000	1.05
Antonicelli (2008)	Tele-transmission vs control	0.58	0.19	1.73	-0.98	0.325	3.26
Balk (2008)	Tele-transmission vs control	1.28	0.64	2.59	0.70	0.485	7.05
Soran (2008)	Tele-transmission vs control	0.61	0.34	1.07	-1.73	0.084	9.77
Cleland (2005)	Tele-transmission vs control	0.65	0.42	1.02	-1.89	0.059	13.41
Capomolla (2004)	Tele-transmission vs control	0.68	0.29	1.60	-0.89	0.376	5.09
Goldberg (2003)	Tele-transmission vs control	0.39	0.22	0.67	-3.41	0.001	10.30
de Lusignan (2001)	Tele-transmission vs control	0.58	0.14	2.51	-0.72	0.470	1.92
Random		**0.69**	**0.56**	**0.86**	**-3.43**	**0.001**	
Cleland (2005)	Telephone vs control	0.60	0.38	0.94	-2.23	0.026	7.14
Jerant (2001)	Telephone vs control	5.95	0.51	68.86	1.43	0.153	0.37
Boyne (2012)	Telephone vs control	1.45	0.84	2.49	1.34	0.179	5.52
Krum (2013)	Telephone vs control	1.34	0.81	2.22	1.14	0.255	6.11
Domingues (2011)	Telephone vs control	0.55	0.26	1.17	-1.54	0.122	3.26
Ferrante (2010)	Telephone vs control	0.73	0.62	0.86	-3.84	0.000	15.92
Chaudhry (2010)	Telephone vs control	0.98	0.79	1.21	-0.21	0.835	13.96
Wakefield (2008)	Telephone vs control	1.17	0.66	2.08	0.53	0.600	5.04
Sisk (2006)	Telephone vs control	1.00	0.64	1.56	0.00	1.000	7.26
DeWalt (2006)	Telephone vs control	0.78	0.26	2.31	-0.46	0.648	1.72
Dunagan (2005)	Telephone vs control	1.20	0.65	2.23	0.58	0.563	4.52
DeBusk (2004)	Telephone vs control	0.72	0.47	1.09	-1.54	0.123	7.69
Laramee (2003)	Telephone vs control	0.89	0.51	1.54	-0.42	0.671	5.36
Kasper (2002)	Telephone vs control	0.48	0.24	0.96	-2.06	0.039	3.78
Krumholz (2002)	Telephone vs control	0.61	0.31	1.23	-1.38	0.167	3.78
Blue (2001)	Telephone vs control	0.95	0.59	1.52	-0.22	0.828	6.72
Gattis (1999)	Telephone vs control	0.59	0.21	1.69	-0.98	0.329	1.86
Random		**0.87**	**0.74**	**1.01**	**-1.89**	**0.059**	
Pooled (Random)		**0.80**	**0.71**	**0.91**	**-3.54**	**0.000**	



Heterogeneity test for telephone group: Q = 25.60, df = 16, P = 0.060, I-square = 37.50%
Heterogeneity test for tele-transmission group: Q = 15.85, df = 12, P = 0.198, I-square = 24.29%
Heterogeneity test for overall: Q = 43.67, df = 29, P = 0.039, I-square = 33.59%

Figure 4 Forest plot of all-cause mortality for teletransmission and telephone-supported care versus usual care.

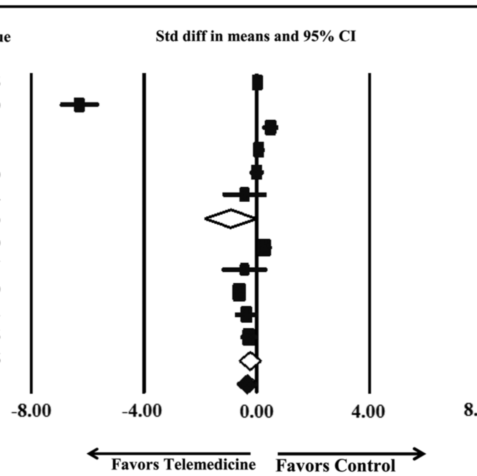
Study name	Comparison	Odds ratio	Lower limit	Upper limit	Z-Value	P-Value	Relative Weight (Random)
Lynga (2012)	Tele-transmission vs control	0.86	0.63	1.18	-0.91	0.362	11.51
Koehler (2011)	Tele-transmission vs control	1.12	0.91	1.39	1.07	0.287	12.05
Weintraub (2010)	Tele-transmission vs control	0.46	0.25	0.83	-2.57	0.010	9.46
Mortara (2009)	Tele-transmission vs control	0.98	0.59	1.65	-0.07	0.946	10.06
Scherr (2009)	Tele-transmission vs control	0.44	0.24	0.80	-2.66	0.008	9.32
Dar (2009)	Tele-transmission vs control	1.86	1.02	3.40	2.02	0.043	9.40
Kashem (2008)	Tele-transmission vs control	0.13	0.04	0.45	-3.22	0.001	5.10
Soran (2008)	Tele-transmission vs control	0.74	0.50	1.09	-1.50	0.133	11.01
Cleland (2005)	Tele-transmission vs control	0.79	0.52	1.20	-1.09	0.276	10.84
Benatar (2003)	Tele-transmission vs control	0.11	0.05	0.24	-5.55	0.000	8.05
Jerant (2001)	Tele-transmission vs control	0.17	0.03	0.98	-1.98	0.048	3.21
Random		**0.61**	**0.42**	**0.88**	**-2.64**	**0.008**	
Mortara (2009)	Telephone vs control	0.96	0.61	1.53	-0.15	0.877	6.45
Cleland (2005)	Telephone vs control	0.62	0.41	0.94	-2.23	0.026	6.82
Jerant (2001)	Telephone vs control	0.18	0.03	1.08	-1.88	0.061	1.19
Boyne (2012)	Telephone vs control	0.64	0.41	1.02	-1.89	0.058	6.49
Krum (2013)	Telephone vs control	0.80	0.54	1.21	-1.05	0.295	6.93
Chaudhry (2010)	Telephone vs control	1.03	0.88	1.20	0.33	0.738	8.96
Wakefield (2008)	Telephone vs control	0.49	0.30	0.80	-2.86	0.004	6.17
Ramachandran (200	Telephone vs control	1.66	0.61	4.52	0.99	0.323	2.96
Sisk (2006)	Telephone vs control	0.58	0.37	0.91	-2.37	0.018	6.58
Dunagan (2005)	Telephone vs control	0.57	0.36	0.90	-2.42	0.016	6.44
Tsuyuki (2004)	Telephone vs control	0.93	0.64	1.35	-0.40	0.690	7.21
DeBusk (2004)	Telephone vs control	0.89	0.63	1.25	-0.68	0.495	7.53
Laramee (2003)	Telephone vs control	0.79	0.49	1.28	-0.96	0.337	6.25
Kasper (2002)	Telephone vs control	0.62	0.40	0.95	-2.21	0.027	6.72
Krumholz (2002)	Telephone vs control	0.32	0.17	0.60	-3.58	0.000	5.15
McDonald (2002)	Telephone vs control	0.07	0.01	0.37	-3.07	0.002	1.24
Blue (2001)	Telephone vs control	0.35	0.20	0.61	-3.69	0.000	5.66
Gattis (1999)	Telephone vs control	0.08	0.01	0.47	-2.82	0.005	1.24
Random		**0.64**	**0.52**	**0.79**	**-4.15**	**0.000**	
Pooled (Random)		**0.63**	**0.53**	**0.76**	**-4.91**	**0.000**	



Heterogeneity test for telephone group: Q = 59.15, df = 17, P < 0.001, I-square = 71.26%
Heterogeneity test for tele-transmission group: Q = 61.03, df = 10, P < 0.001, I-square = 83.61%
Heterogeneity test for overall: Q = 120.77, df = 28, P < 0.001, I-square = 76.82%

Figure 5 Forest plot of heart failure-related admission for teletransmission and telephone-supported care versus usual care.

Study name	Comparison	Std diff in means	Lower limit	Upper limit	Z-Value	P-Value	Relative Weight (Random)
Koehler (2011)	Tele-transmission vs contro	0.03	-0.12	0.17	0.34	0.736	17.33
Weintraub (2010)	Tele-transmission vs contro	-6.29	-6.99	-5.60	-17.69	0.000	15.80
Dar (2009)	Tele-transmission vs contro	0.49	0.20	0.79	3.26	0.001	17.09
Soran (2008)	Tele-transmission vs contro	0.07	-0.15	0.29	0.62	0.535	17.23
Cleland (2005)	Tele-transmission vs contro	0.00	-0.26	0.26	0.00	1.000	17.16
Jerant (2001)	Tele-transmission vs contro	-0.43	-1.23	0.36	-1.07	0.284	15.39
Random		**-0.96**	**-1.88**	**-0.05**	**-2.06**	**0.039**	
Cleland (2005)	Telephone vs control	0.27	0.01	0.53	2.06	0.040	22.97
Jerant (2001)	Telephone vs control	-0.43	-1.24	0.38	-1.04	0.297	12.01
Tsuyuki (2004)	Telephone vs control	-0.62	-0.86	-0.38	-5.02	0.000	23.32
Krumholz (2002)	Telephone vs control	-0.36	-0.78	0.06	-1.68	0.092	19.63
Blue (2001)	Telephone vs control	-0.28	-0.58	0.03	-1.77	0.076	22.07
Random		**-0.27**	**-0.65**	**0.12**	**-1.35**	**0.176**	
Pooled (Random)		**-0.37**	**-0.72**	**-0.02**	**-2.05**	**0.041**	



Heterogeneity test for telephone group: Q = 29.95, df = 4, P < 0.001, I-square = 83.97%
Heterogeneity test for tele-transmission group: Q = 323.93, df = 5, P < 0.001, I-square = 98.46%
Heterogeneity test for overall: Q = 353.45, df = 10, P < 0.001, I-square = 97.17%

Figure 6 Forest plot of heart failure-related length of hospital stay for teletransmission and telephone-supported care versus usual care. Std diff in means, standardized difference in the means.

the control, the HF-related length of hospital stay was significantly lower in the overall telemedicine group (pooled standardized difference in means=−0.37, 95% CI −0.72 to −0.02, Z=−2.05, p=0.041), and in the teletransmission group (pooled standardized difference in means=−0.96, 95% CI −1.88 to −0.05, Z=−2.06, p=0.039). But, no significant difference in HF-related length of hospital stay was observed comparing telephone-supported care group with control group (pooled standardized difference in means=−0.27, 95% CI −0.65 to 0.12, Z=−1.35, p=0.176) (figure 6).

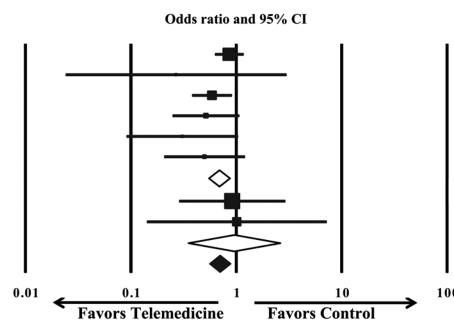
HF-related mortality

A total of eight studies reported HF-related mortality data, including two telephone intervention studies and six teletransmission intervention studies (figure 7). There was no significant heterogeneity when data from the eight studies were pooled (Q=6.02, df=8, p=0.538, I^2=0%). The analysis revealed that, in comparison to the control, HF-related mortality rate was significantly lower in the overall telemedicine group (pooled OR=0.69, 95% CI 0.55 to 0.86, Z=−3.24, p=0.001) and in the teletransmission group (pooled OR=0.68, 95% CI 0.54 to 0.85, Z=−3.30, p=0.001). However, no difference in the telephone-supported care group was observed as compared with the control group (pooled OR=0.94, 95% CI 0.34 to 2.57, Z=−0.12, p=0.904; figure 7).

Sensitivity analysis

The results of meta-analyses using the leave-one-out approach to assess sensitivity of fixed-effect models are summarized in online supplementary figure S1, including all-cause hospital admission (A), all-cause length of hospital stay (B), all-cause mortality (C), HF-related hospital admission (D), HF-related length of hospital stay (E), and HF-related mortality (F). The direction and magnitude of the pooled estimates did not vary considerably, indicating that the meta-analyses had good reliability. The removal of Chaudhry *et al*'s[24] study caused the pooled standard difference in means to become significant in the overall meta-analysis of all-cause length of hospital stay (p=0.039, see online supplementary figure S1B). The removal of Weintraub *et al*'s[53] study caused the pooled standard difference in means to become non-significant for the overall meta-analysis of HF-related length

Study name	Comparison	Odds ratio	Lower limit	Upper limit	Z-Value	P-Value	Relative Weight (Random)
Koehler (2011)	Tele-transmission	0.86	0.62	1.18	-0.94	0.350	51.91
Scherr (2009)	Tele-transmission	0.27	0.02	3.00	-1.07	0.286	0.91
Giordano (2009)	Tele-transmission	0.59	0.38	0.92	-2.35	0.019	27.12
Soran (2008)	Tele-transmission	0.52	0.25	1.08	-1.76	0.078	9.80
Capomolla (2004)	Tele-transmission	0.31	0.09	1.05	-1.88	0.060	3.53
Goldberg (2003)	Tele-transmission	0.50	0.21	1.22	-1.53	0.126	6.73
Random		**0.68**	**0.54**	**0.85**	**-3.30**	**0.001**	
McDonald (2002)	Telephone	0.92	0.29	2.95	-0.15	0.884	74.02
Gattis (1999)	Telephone	1.01	0.14	7.26	0.01	0.991	25.98
Random		**0.94**	**0.34**	**2.57**	**-0.12**	**0.904**	
Pooled (Random)		**0.69**	**0.55**	**0.86**	**-3.24**	**0.001**	



Heterogeneity test for telephone group: Q = 0.01, df = 1, P = 0.933, I-square = 0%
Heterogeneity test for tele-transmission group: Q = 5.63, df = 5, P = 0.344, I-square = 11.13%
Heterogeneity test for overall: Q = 6.02, df = 7, P = 0.538, I-square = 0%

Figure 7 Forest plot of heart failure-related mortality for teletransmission and telephone-supported care versus usual care.

of hospital stay (p=0.468, see online supplementary figure S1E).

Publication bias

Publication bias was assessed by constructing funnel plots by Egger's test.[55] The absence of publication bias was indicated by data points forming a symmetric funnel-shaped distribution and one-tailed significance level p>0.05. Funnel plots to detect publication bias are shown in online supplementary figure S2. There was no significant evidence of publication bias for all-cause hospital admission (t=1.481, df=25, p=0.076, see online supplementary figure S2A), all-cause length of hospital stay (t=0.448, df=11, p=0.332, see online supplementary figure S2B), all-cause mortality (t=0.386, df=28, p=0.351, see online supplementary figure S2C), HF-related length of hospital stay (t=1.713, df=9, p=0.060, see online supplementary figure S2E), or HF-related mortality (t=1.521, df=6, p=0.090, see online supplementary figure S2F) as determined by Egger's test. However, there was significant evidence of publication bias for the HF-related admission rate (t=5.285, df=27, p<0.001, see online supplementary figure S2D). The observed studies in HF-related admission are shown as white circles. The observed point estimate of OR is shown as a white rhombus at 0.63 (95% CI 0.53 to 0.76). Duval and Tweedie's trim and fill method was used to adjust for the effect of publication bias[56] and the 10 theoretically imputed studies are shown as black circles in online supplementary figure S2D. Incorporating these imputed studies, the adjusted point estimates of OR are shown as a black rhombus at 0.85 (95% CI 0.69 to 1.04).

Quality assessment

The results of the quality assessment are summarized in figure 8, including the potential risk of individual studies (8A) and the overall risk (8B). Overall, the studies had a low risk of attrition and reporting bias. In addition, the majority of studies included analyses based on an intention-to-treat population. Overall, the studies had a high risk of performance and detection bias, and a low to unclear risk of selection bias.

DISCUSSION

Telemedicine involves telecommunication-based management of patients with chronic diseases either by telephone-based care (eg, information/data are collected or distributed by a healthcare provider who calls the patient on a regular basis) or through a home-based teletransmission monitoring system (eg, information/data are automatically transmitted to the healthcare provider by internet or a phone line). In this systematic review and meta-analysis, we performed an up-to-date assessment of the effectiveness of telemedicine for the management of patients with CHF. A total of 39 RCTs, comparing two different types of telemedicine (telephone-supported care and teletransmission) with usual care, were included in our analyses. Telemedicine intervention, overall, was shown to be beneficial in patients with HF-related hospitalization and mortality regardless of the type of data retrieval system. The home-based

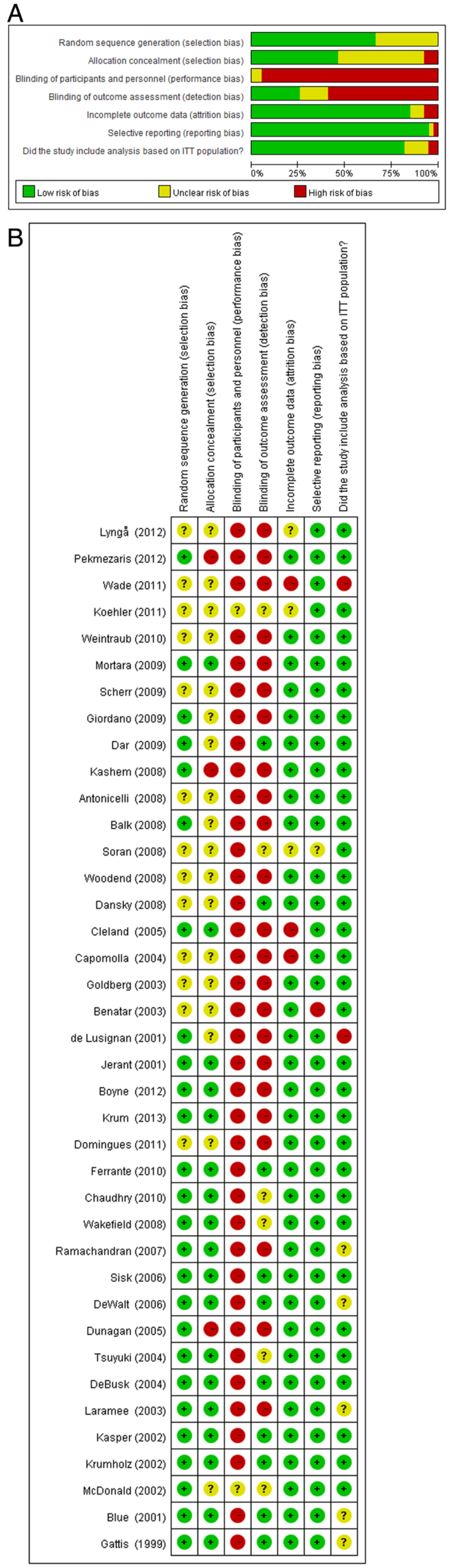


Figure 8 The results of quality assessment. (A) Risk of bias for each study; (B) the summary of bias of the included studies. ITT, intention-to-treat.

teletransmission monitoring system was effective in improving the clinical outcomes, particularly reducing all-cause mortality and HF-related outcomes (admission rate, length of stay and mortality). Telephone-based monitoring (telephone-supported follow-up care) appears to provide little benefit except for reducing the HF-related admission rate.

In a recent network meta-analysis of 30 RCTs by Kotb *et al*,[13] teletransmission was found to reduce the odds of mortality as well as the HF-related hospitalizations compared with the standard care. In addition, structured telephone support reduced the odds of HF-related mortality and hospitalizations, while ECG monitoring reduced the odds of HF-related hospitalizations.[13] Our systematic review and meta-analysis differs from the previous studies for the following reasons: (1) our meta-analysis of 39 randomized, open-labeled, controlled trials provide additional data to the field with an updated literature search up to June 2016; (2) it provides a more comprehensive systematic review in terms of patient characteristics (tables 1, 2); intervention procedures and follow-up care (see online supplementary table S1); and numerical data of outcome measurements (see online supplementary table S2); (3) our meta-analysis does not fully support the use of telephone-based monitoring (telephone-supported care) in patients with HF.

Notably, the home-based teletransmission monitoring system was associated with a significantly lower rate of all-cause mortality and HF-related mortality. Previous meta-analyses had also shown that teletransmission (often referred to as telemonitoring) is associated with improved survival outcomes, although most have focused on all-cause, rather than HF-related, outcomes.[7 8] Likewise, Clarke *et al*[11] reported a decreased risk of all-cause mortality with telemonitoring, in addition to a reduction in the rate of HF-related hospital admission. In a Cochrane Collaboration Review published in 2010, Inglis *et al*[9] found that telemonitoring significantly reduced the risk of all-cause mortality and HF-related hospitalization. In another systematic review and network meta-analysis published in 2013, Pandor *et al*[12] found that the telemonitoring intervention with medical support during office hours was associated with a reduction in all-cause mortality as compared with the usual care. However, in contrast to the finding of our meta-analysis, Pandor *et al*'s meta-analysis reported that there was no effect of telemonitoring on the rate of HF-related hospital admission. The reason for this difference is not readily apparent, although we do note that Pandor *et al*'s[12] meta-analysis included both RCTs and observational cohort studies (vs only RCTs in our meta-analysis). In addition, the meta-analysis conducted by Pandor *et al*'s research group only searched the literature from 2008 to January 2012. Two recent related RCTs published in 2013[57] and 2014[58] supported the Pandor *et al*'s report that telemonitoring of in-home patients with HF and/or chronic lung disease (CLD) reduced the percentage of patients with hospital admissions, but no effect on the length of stay and HF-related admission.[57] Furthermore, the telemonitoring system did not result in lower costs, decreased 30-day readmission rates, reduced length of stay, improved symptoms, or improved 180-day mortality.[58] We did not include Martín-Lesende's RCT in our meta-analysis since 72% of patients in this study had chronic lung disease. We also did not include Blum's RCT, since the main objective of this study was to evaluate the medical cost and health-related quality of life. Overall, we believe that there is strong and consistent evidence that teletransmission (telemonitoring) can improve the survival rate as well as hospital admission in patients with CHF. As such, when feasible, we recommend the implementation of teletransmission-based monitoring in patients with CHF.

The telephone support intervention is usually performed during the follow-up period after the discharge from the hospital or after the end of the patient education programme. HF-related hospital admission rate was the only outcome that was significantly decreased compared with usual care. Other meta-analyses have reported similar findings, where structured telephone support care showed no significant reduction in all-cause mortality. However, it was associated with reduced HF-related hospitalization.[9 11 12] A recently published RCT of a nurse-implemented transitional care programme (a predischarge visit, two home visits, and then regular telephone calls over 9 months) also found that the patients in the intervention group had a lower hospital readmission rate at 6 weeks, with no significant differences in the event-free survival and mortality.[59] We did not include this study in meta-analysis since the results were affected by the attrition rate.

The inconsistent outcomes of the telephone-supported care programme may be due to the lack of consensus protocol, or guideline for conducting a telephone-supported care. Telephone-supported care is a part of the nurse-based care programme after discharge. The purpose of a telephone interview may range from improving diet and treatment compliance, to regular monitoring of the HF-related symptoms, and self-management. The telephone contact also aims to reinforce the instructions received during the hospitalization or as a part of the patient education programme. The reason why remarkably different outcomes were found between home-based teletransmission monitoring and telephone-supported care remains uncertain. However, many automated home monitoring systems are designed for transmission of body weight, blood pressure, and heart rate via a standard telephone line or network system to a central server (refer to online supplementary table S1). It may be helpful to monitor the real-time clinical condition of the patients for early treatment. However, for the telephone-supported care programme, intervention patients were usually scheduled to receive telephone calls once a week or a month, generally from a designated nurse (refer to online supplementary table S1). In a recently published large sample size RCT (n=1437), patients were scheduled to receive only nine telephone calls over a 6-month period. The vital signs (eg, heart rate, blood pressure, changes in weight) were collected during regular face-to-face contacts or were self-reported during the phone interview instead of automatic transfer.[60] It is intriguing that the combination of teletransmission (telemonitoring) and telephone-supported care interventions found no differences in 30-day readmission or 180-day mortality between the intervention and the control groups.[60 61]

We realize that HF may occur in the presence of a normal LVEF, and patients with preserved ejection fraction (HFpEF) may represent up to half of the HF population.[62]

HFpEF represents a complex and heterogeneous clinical syndrome with a poor outcome, and a preserved systolic LV function, with LVEF>50%.[62] One of the inclusion criteria in studies included in this meta-analysis was the impaired LVEF, defined as LVEF<50%. Most of the studies comprised patients with reduced LVEF, <40%; thus, our patients were mostly reduced ejection fraction (HFrEF), and not HFpEF. The only exceptions were studies by Dar *et al*,[5] which consisted of patients with EF≥40%, and Dunagan *et al*,[31] where ~16% of patients had LVEF>50% (tables 1 and 2). Therefore, the study reported by Dar *et al*[5] may be the only one that relates to HFpEF.

Our study has a number of limitations that warrant mention. Although we found that telemedicine was associated with a number of improved patient outcomes, we did not perform a comprehensive assessment of outcomes relevant to patients with CHF. Other outcomes, not assessed but relevant, include emergency department visits, treatment costs, and quality of life. Quality of life is a particularly important measure in the context of CHF and a considerable improvement in the quality of life by telemedicine has been reported.[7–9] Regarding the quality of the studies included in our meta-analysis, all were randomized, open-labeled, controlled trials. A double-blind design is not feasible for these types of studies. Nevertheless, the lack of double-blinding does introduce the possibility of bias and the Hawthorne effect.[63] Furthermore, the presence of heterogeneity among the studies (I^2 of 50–75%) may affect the validity of our conclusion. However, we analyzed the data by the random-effects model. The meta-analysis can be done using a random-effects model if there is heterogeneity among the studies.[16 17] Therefore, the conclusion of our study is valid. The random-effects model assumes that the effects being estimated in the different studies are not identical, but the studies included in the meta-analysis constitute a random selection of studies from this hypothetical population.[17] Another limitation is the detection of publication bias in the analysis of the HF-related hospital admission rate. These results must therefore be interpreted with caution. Further research is warranted to determine the optimal means of monitoring, particularly in the category of teletransmission.

In conclusion, the results of this meta-analysis support the use of teletransmission monitoring for improving patient outcomes after HF. Specifically, the home-based teletransmission monitoring system was associated with lower rates of HF-related hospital admission, all-cause mortality and HF-related mortality, and can thus be recommended in the management of CHF. In contrast, nurse-based telephone-supported care appears to provide little benefit, and only a reduction in the rate of HF-related admission was noted as compared with the control group. However, a combination of home-based teletransmission and a nurse-based telephone reinforcement may be encouraged. We suggest that telemedicine is only one component of managing CHF and does not/should not replace face-to-face consultations between healthcare providers and patients. Nevertheless, telemedicine clearly has the potential to improve patient outcomes by encouraging better self-management and early intervention. The efficacy of telemedicine using an advanced telemonitoring device and newly developed guidelines in the remote monitoring and management of patients with HF should be investigated.

Contributors W-lY is the guarantor of integrity of the entire study. W-lY and J-fW were involved in study design. M-hL and T-cH were involved in definition of intellectual content; manuscript preparation; manuscript editing. H-fZ and J-tM were involved in literature research and statistical analysis. J-tM was involved in data acquisition. M-hL and W-lY were involved in manuscript review.

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REFERENCES

1. Krum H, Abraham WT. Heart failure. *Lancet* 2009;373:941–55.
2. National Center for Health Statistics. Health, United States 2005 With Chartbook on Trends in the Health of Americans. http://www.cdc.gov/nchs/data/hus/hus05.pdf (accessed 06 Nov 2014).
3. Kashem A, Cross RC, Santamore WP, *et al*. Management of heart failure patients using telemedicine communication systems. *Curr Cardiol Rep* 2006;8:171–9.
4. Anker SD, Koehler F, Abraham WT. Telemedicine and remote management of patients with heart failure. *Lancet* 2011;378:731–9.
5. Dar O, Riley J, Chapman C, *et al*. A randomized trial of home telemonitoring in a typical elderly heart failure population in North West London: results of the Home-HF study. *Eur J Heart Fail* 2009;11:319–25.
6. Giordano A, Scalvini S, Zanelli E, *et al*. Multicenter randomised trial on home-based telemanagement to prevent hospital readmission of patients with chronic heart failure. *Int J Cardiol* 2009;131:192–9.
7. Clark RA, Inglis SC, McAlister FA, *et al*. Telemonitoring or structured telephone support programmes for patients with chronic heart failure: systematic review and meta-analysis. *BMJ* 2007;334:942.
8. Polisena J, Tran K, Cimon K, *et al*. Home telemonitoring for congestive heart failure: a systematic review and meta-analysis. *J Telemed Telecare* 2010;16:68–76.
9. Inglis SC, Clark RA, McAlister FA, *et al*. Structured telephone support or telemonitoring programmes for patients with chronic heart failure. *Cochrane Database Syst Rev* 2010;(10):CD007228.
10. Inglis SC, Clark RA, McAlister FA, *et al*. Which components of heart failure programmes are effective? A systematic review and meta-analysis of the outcomes of structured telephone support or telemonitoring as the primary component of chronic heart failure management in 8323 patients: Abridged Cochrane Review. *Eur J Heart Fail* 2011;13:1028–40.
11. Clarke M, Shah A Sharma U. Systematic review of studies on telemonitoring of patients with congestive heart failure: a meta-analysis. *J Telemed Telecare* 2011;17:7–14.
12. Pandor A, Gomersall T, Stevens JW, *et al*. Remote monitoring after recent hospital discharge in patients with heart failure: a systematic review and network meta-analysis. *Heart* 2013;99:1717–26.
13. Kotb A, Cameron C, Hsieh S, *et al*. Comparative effectiveness of different forms of telemedicine for individuals with heart failure (HF): a systematic review and network meta-analysis. *PLoS ONE* 2015;10:e0118681.
14. Liberati A, Altman DG, Tetzlaff J, *et al*. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Ann Intern Med* 2009;151:W65–94.
15. Higgins JPT, Green S, Cochrane Collaboration. *Cochrane handbook for systematic reviews of interventions*. Chichester, England: Hoboken, NJ: Wiley-Blackwell, 2008.
16. Higgins JP, Thompson SG, Deeks JJ, *et al*. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557–60.
17. Schroll JB, Moustgaard R, Gøtzsche PC. Dealing with substantial heterogeneity in Cochrane reviews. Cross-sectional study. *BMC Med Res Methodol* 2011;11:22.
18. Antonicelli R, Testarmata P, Spazzafumo L, *et al*. Impact of telemonitoring at home on the management of elderly patients with congestive heart failure. *J Telemed Telecare* 2008;14:300–5.
19. Balk AH, Davidse W, Dommelen PV, *et al*. Tele-guidance of chronic heart failure patients enhances knowledge about the disease. A multi-centre, randomised controlled study. *Eur J Heart Fail* 2008;10:1136–42.
20. Benatar D, Bondmass M, Ghitelman J, *et al*. Outcomes of chronic heart failure. *Arch Intern Med* 2003;163:347–52.
21. Blue L, Lang E, McMurray JJ, *et al*. Randomised controlled trial of specialist nurse intervention in heart failure. *BMJ* 2001;323:715–18.

22 Boyne JJ, Vrijhoef HJ, Crijns HJ, *et al*. Tailored telemonitoring in patients with heart failure: results of a multicentre randomized controlled trial. *Eur J Heart Fail* 2012;14:791–801.
23 Capomolla S, Pinna G, La Rovere MT. Heart failure case disease management program: a pilot study of home telemonitoring versus usual care. *Eur Heart J Suppl* 2004;6(Suppl 6):F91–8.
24 Chaudhry SI, Mattera JA, Curtis JP, *et al*. Telemonitoring in patients with heart failure. *N Engl J Med* 2010;363:2301–9.
25 Cleland JG, Louis AA, Rigby AS, *et al*. Noninvasive home telemonitoring for patients with heart failure at high risk of recurrent admission and death: the Trans-European Network-Home-Care Management System (TEN-HMS) study. *J Am Coll Cardiol* 2005;45:1654–4.
26 Dansky KH, Vasey J Bowles K. Impact of telehealth on clinical outcomes in patients with heart failure. *Clin Nurs Res* 2008;17:182–9.
27 de Lusignan S, Wells S, Johnson P, *et al*. Compliance and effectiveness of 1 year's home telemonitoring. The report of a pilot study of patients with chronic heart failure. *Eur J Heart Fail* 2001;3:723–30.
28 DeBusk RF, Miller NH, Parker KM, *et al*. Care management for low-risk patients with heart failure: a randomized, controlled trial. *Ann Intern Med* 2004;141:606–13.
29 DeWalt DA, Malone RM, Bryant ME, *et al*. A heart failure self-management program for patients of all literacy levels: a randomized, controlled trial [ISRCTN11535170]. *BMC Health Serv Res* 2006;6:30.
30 Domingues FB, Clausell N, Aliti GB, *et al*. Education and telephone monitoring by nurses of patients with heart failure: randomized clinical trial. *Arq Bras Cardiol* 2011;96:233–9.
31 Dunagan WC, Littenberg B, Ewald GA, *et al*. Randomized trial of a nurse-administered, telephone-based disease management program for patients with heart failure. *J Card Fail* 2005;11:358–65.
32 Ferrante D, Varini S, Macchia A, *et al*. Long-term results after a telephone intervention in chronic heart failure: DIAL (Randomized Trial of Phone Intervention in Chronic Heart Failure) follow-up. *J Am Coll Cardiol* 2010;56:372–8.
33 Gattis WA, Hasselblad V, Whellan DJ, *et al*. Reduction in heart failure events by the addition of a clinical pharmacist to the heart failure management team: results of the Pharmacist in Heart Failure Assessment Recommendation and Monitoring (PHARM) Study. *Arch Intern Med* 1999;159:1939–45.
34 Goldberg LR, Piette JD, Walsh MN, *et al*. Randomized trial of a daily electronic home monitoring system in patients with advanced heart failure: the Weight Monitoring in Heart Failure (WHARF) trial. *Am Heart J* 2003;146:705–12.
35 Jerant AF, Azari R, Nesbitt TS. Reducing the cost of frequent hospital admissions for congestive heart failure: a randomized trial of a home telecare intervention. *Med Care* 2001;39:1234–45.
36 Kashem A, Droogan MT, Santamore WP, *et al*. Managing heart failure care using an internet-based telemedicine system. *J Card Fail* 2008;14:121–6.
37 Kasper EK, Gerstenblith G, Hefter G, *et al*. A randomized trial of the efficacy of multidisciplinary care in heart failure outpatients at high risk of hospital readmission. *J Am Coll Cardiol* 2002;39:471–80.
38 Koehler F, Winkler S, Schieber M, *et al*. Impact of remote telemedical management on mortality and hospitalizations in ambulatory patients with chronic heart failure: the telemedical interventional monitoring in heart failure study. *Circulation* 2011;123:1873–80.
39 Krum H, Forbes A, Yallop J, *et al*. Telephone support to rural and remote patients with heart failure: the Chronic Heart Failure Assessment by Telephone (CHAT) study. *Cardiovasc Ther* 2013;31:230–7.
40 Krumholz HM, Amatruda J, Smith GL, *et al*. Randomized trial of an education and support intervention to prevent readmission of patients with heart failure. *J Am Coll Cardiol* 2002;39:83–9.
41 Laramee AS, Levinsky SK, Sargent J, *et al*. Case management in a heterogeneous congestive heart failure population: a randomized controlled trial. *Arch Intern Med* 2003;163:809–17.
42 Lynga P, Persson H, Hagg-Martinell A, *et al*. Weight monitoring in patients with severe heart failure (WISH). A randomized controlled trial. *Eur J Heart Fail* 2012;14:438–44.
43 McDonald K, Ledwidge M, Cahill J, *et al*. Heart failure management: multidisciplinary care has intrinsic benefit above the optimization of medical care. *J Card Fail* 2002;8:142–8.
44 Mortara A, Pinna GD, Johnson P, *et al*. Home telemonitoring in heart failure patients: the HHH study (Home or Hospital in Heart Failure). *Eur J Heart Fail* 2009;11:312–18.
45 Pekmezaris R, Mitzner I, Pecinka KR, *et al*. The impact of remote patient monitoring (telehealth) upon Medicare beneficiaries with heart failure. *Telemed J E Health* 2012;18:101–8.
46 Ramachandran K, Husain N, Maikhuri R, *et al*. Impact of a comprehensive telephone-based disease management programme on quality-of-life in patients with heart failure. *Natl Med J India* 2007;20:67–73.
47 Scherr D, Kastner P, Kollmann A, *et al*. Effect of home-based telemonitoring using mobile phone technology on the outcome of heart failure patients after an episode of acute decompensation: randomized controlled trial. *J Med Internet Res* 2009;11:e34.
48 Sisk JE, Hebert PL, Horowitz CR, *et al*. Effects of nurse management on the quality of heart failure care in minority communities: a randomized trial. *Ann Intern Med* 2006;145:273–83.
49 Soran OZ, Pina IL, Lamas GA, *et al*. A randomized clinical trial of the clinical effects of enhanced heart failure monitoring using a computer-based telephonic monitoring system in older minorities and women. *J Card Fail* 2008;14:711–17.
50 Tsuyuki RT, Fradette M, Johnson JA, *et al*. A multicenter disease management program for hospitalized patients with heart failure. *J Card Fail* 2004;10:473–80.
51 Wade MJ, Desai AS, Spettell CM, *et al*. Telemonitoring with case management for seniors with heart failure. *Am J Manag Care* 2011;17:e71–9.
52 Wakefield BJ, Ward MM, Holman JE, *et al*. Evaluation of home telehealth following hospitalization for heart failure: a randomized trial. *Telemed J E Health* 2008;14:753–61.
53 Weintraub A, Gregory D, Patel AR, *et al*. A multicenter randomized controlled evaluation of automated home monitoring and telephonic disease management in patients recently hospitalized for congestive heart failure: the SPAN-CHF II trial. *J Card Fail* 2010;16:285–92.
54 Woodend AK, Sherrard H, Fraser M, *et al*. Telehome monitoring in patients with cardiac disease who are at high risk of readmission. *Heart Lung* 2008;37:36–45.
55 Egger M, Davey Smith G, Schneider M, *et al*. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–34.
56 Duval S, Tweedie R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* 2000;56:455–63.
57 Martín-Lesende I, Orruño E, Bilbao A, *et al*. Impact of telemonitoring home care patients with heart failure or chronic lung disease from primary care on healthcare resource use (the TELBIL study randomised controlled trial). *BMC Health Serv Res* 2013;13:118.
58 Blum K, Gottlieb SS. The effect of a randomized trial of home telemonitoring on medical costs, 30-day readmissions, mortality, and health-related quality of life in a cohort of community-dwelling heart failure patients. *J Card Fail* 2014;20:513–21.
59 Yu DS, Lee DT, Stewart S, *et al*. Effect of nurse-implemented transitional care for Chinese individuals with chronic heart failure in Hong Kong: a randomized controlled trial. *J Am Geriatr Soc* 2015;63:1583–93.
60 Ong MK, Romano PS, Edgington S, *et al*. Effectiveness of remote patient monitoring after discharge of hospitalized patients with heart failure: the Better Effectiveness After Transition—Heart Failure (BEAT-HF) randomized clinical trial. *JAMA Intern Med* 2016;176:310–18.
61 Black JT, Romano PS, Sadeghi B, *et al*. A remote monitoring and telephone nurse coaching intervention to reduce readmissions among patients with heart failure: study protocol for the Better Effectiveness After Transition—Heart Failure (BEAT-HF) randomized controlled trial. *Trials* 2014;15:124.
62 van Heerebeek L, Paulus WJ. Understanding heart failure with preserved ejection fraction: where are we today? *Neth Heart J* 2016;24:227–36.
63 Thokala P, Baalbaki H, Brennan A, *et al*. Telemonitoring after discharge from hospital with heart failure: cost-effectiveness modelling of alternative service designs. *BMJ Open* 2013;3:e003250.