


Multi-disciplinary palliative care is effective in people with symptomatic heart failure: A systematic review and narrative synthesis

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Abstract

Background: Despite recommendations, people with heart failure have poor access to palliative care.

Aim: To identify the evidence in relation to palliative care for people with symptomatic heart failure.

Design: Systematic review and narrative synthesis. (PROSPERO CRD42016029911)

Data sources: Databases (Medline, Cochrane database, CINAHL, PsycINFO, HMIC, CareSearch Grey Literature), reference lists and citations were searched and experts contacted. Two independent reviewers screened titles and abstracts and retrieved papers against inclusion criteria. Data were extracted from included papers and studies were critically assessed using a risk of bias tool according to design.

Results: Thirteen interventional and 10 observational studies were included. Studies were heterogeneous in terms of population, intervention, comparator, outcomes and design rendering combination inappropriate. The evaluation phase studies, with lower risk of bias, using a multi-disciplinary specialist palliative care intervention showed statistically significant benefit for patient-reported outcomes (symptom burden, depression, functional status, quality of life), resource use and costs of care. Benefit was not seen in studies with a single component/discipline intervention or with higher risk of bias. Possible contamination in some studies may have caused under-estimation of effect and missing data may have introduced bias. There was no apparent effect on survival.

Conclusion: Overall, the results support the use of multi-disciplinary palliative care in people with advanced heart failure but trials do not identify *who* would benefit most from specialist palliative referral. There are no sufficiently robust multi-centre evaluation phase trials to provide generalisable findings. Use of common population, intervention and outcomes in future research would allow meta-analysis.

Keywords

Heart failure, palliative care, hospice, systematic review, quality of life

What is already known about the topic?

- People with advanced heart failure have poorer access to palliative care than people with cancer and the evidence base in support of heart failure palliative care is less developed.

What this paper adds?

- We have drawn together the current literature, both observational and experimental, investigating the use of palliative care in people with symptomatic heart failure.

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Implications for practice, theory or policy

- Our findings support the use of multi-disciplinary palliative care in this patient group, as distinct from single components only, but trials do not identify *who* would benefit most from specialist palliative referral. There are no sufficiently robust multi-centre evaluation phase trials to provide generalisable findings.

Introduction

The great advances in the management of heart failure (HF)¹ brings, as a consequence, more people living to experience advanced disease (New York Heart Association class III and IV)² where response to medical or device therapy is limited.³ People with end-stage disease can have severe symptom burden, poor quality of life⁴ and social isolation. As prognostication is difficult,^{5,6} patients may receive invasive yet futile treatment in hospital during the last days of life, adding to stress for patients, families and the limited healthcare resources.⁷

Palliative care is a multi-disciplinary approach to care for people with life-limiting, progressive illness, aiming to maximise quality of life until death and provide family support through to bereavement.⁸ Evidence supports palliative care *integrated* into management of people with cancer⁹ and other chronic conditions.¹⁰ Benefits include improved symptom burden and quality of life, decreased healthcare utilisation and costs,¹¹ autonomy in care at the end of life and patient satisfaction.¹² Access to palliative care services *alongside* cardiac care for patients with advanced HF is recommended^{13–15} but this is not reflected routinely in practice. Fewer people with HF are placed on the primary care palliative register in the United Kingdom than those with cancer (7% vs 48%),¹⁶ and a similar proportion with advanced heart failure are referred for palliative care during hospital admissions.¹⁷

Barriers to palliative care access include the unpredictable course of heart failure and a conflation of ‘palliative’ and ‘dying’ in the minds of clinicians, patients and the public.^{14,18} Despite the well-established role of palliative care in other areas, this is not so for people with advanced heart failure, for whom heart failure management has one of the strongest evidence bases for any condition; this is likely to be an additional significant barrier in a specialty used to large trials which underpin practice.

The aim of this systematic review is to identify and analyse current available evidence which addresses the question of whether palliative care in people with advanced heart failure is effective with regard to patient-reported outcomes (symptom burden, depression, functional status, quality of life), resource use and costs of cares. The findings are discussed in the context of implications for clinical practice and gaps in knowledge are highlighted to help target future research.

Methods

We conducted a systematic literature review and narrative synthesis. The protocol was registered on PROSPERO (ID = CRD42016029911) and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed. The search was updated to 31 March 2019 using a rapid methodology (single reviewer, simplified search terms, one database (Medline). The methods otherwise describe the original search.

Search strategy

Medline, Cochrane database, CINAHL, PsycINFO, HMC and Care Search Grey Literature were searched using free text and MeSH terms from 1995 to 2017 inclusive. The search strings represented the terms to identify the population (symptomatic heart failure) and the intervention of interest (palliative care) (Supplementary table 1). This was intentionally broad given the nature of the interventions sought. Reference lists and citations of included studies and key review articles were searched. Experts in the field were contacted. There were no language restrictions.

Eligibility criteria

Types of participants: Studies were included if participants had symptomatic heart failure (New York Heart Association class III and IV) or other evidence of advanced disease such as left ventricular ejection fraction <40%. Where only a subset were participants with symptomatic heart failure, studies were included if outcome data could be extracted for this subset.

Types of interventions: Any study with a palliative care, or component(s) of, intervention delivered by specialist or generalist services was included apart from advance care planning alone. Specialist palliative care services are those where palliative care is the core business and staff have additional specialist training. Generalist services refer to all other services where basic palliative care may be provided, but palliative care is not their primary purpose, such as primary care or hospital services such as cardiology. For this review, cardiac rehabilitation interventions are considered as ‘rehabilitative’ rather than ‘palliative’ services and were thus excluded.

Types of comparator: There was no restriction on the comparator arm or care setting.

Types of study design: Experimental or quasi-experimental, observational and service evaluations, and

national audits were included. Studies with unclear methods, duplicate publications (except where discreet outcomes were presented), opinion pieces, narrative reviews, editorials, case histories or case series were excluded.

Study selection

One reviewer (S.D.) screened all titles and abstracts against the eligibility criteria and a second reviewer (C.A.V.) independently reviewed a proportion (18%) and both screened retrieved full papers. Any disagreements were resolved by discussion between the two reviewers with access to a third reviewer (M.J.J.) where necessary.

Data extraction

A data extraction spreadsheet was designed and piloted. Two researchers (S.D., C.A.V.) independently extracted the data. Disagreements or discrepancies were resolved by mutual consent or by involvement of a third author (M.J.J.). Study identifiers, study characteristics, information regarding the population, intervention, comparators and outcomes, including results were extracted.

Where data were unreported or ambiguous, attempts were made to contact the authors of the paper.

Risk of bias assessment

S.D. and C.A.V. independently assessed the risk of bias and the disagreements were resolved by discussion and access to M.J.J. as needed. Randomised controlled trials were assessed with the use of the Cochrane Risk of Bias Tool and the Newcastle–Ottawa Quality Assessment Scale was used to judge the risk of bias in cohort and case-control studies.

Synthesis of results

Descriptive narrative synthesis of the study design, the included population, the intervention and comparator are presented in tabular format.

For the purpose of the review, in randomised controlled trials, in accordance with the Medical Research Committee Framework for complex intervention development,¹⁹ the terms 'phase II/III' were not used. Trials were identified as feasibility and pilot phase trials and evaluation trials on the following basis. Studies with a stated aim to assess the efficacy or effectiveness of the intervention were classed as evaluation phase randomised controlled trials. In addition, studies with power calculations aiming to design adequately powered trials to identify the effect of the intervention were also categorised as evaluation phase randomised controlled trials.

Outcomes and results were described; however, a meta-analysis was not conducted due to heterogeneity of outcomes, populations and interventions.

Results

The search process for the included studies is summarised in a flow chart (Figure 1). The original database search identified 7934 records after de-duplication and a further 85 in the rapid update review. Overall, 23 studies met the inclusion criteria.

Study characteristics

Study design and setting. Eight papers reporting seven evaluation phase randomised controlled trials,^{20–27} four feasibility and pilot phase studies/randomised controlled trials,^{28–31} one quasi-experimental study,³² seven cohort studies,^{33–39} two case-control studies^{40,41} and one cross-sectional study⁴² were included. The characteristics of included studies are summarised in Table 1 (interventional studies) and Table 2 (observational studies). Further details including outcomes and results are available in Supplementary table 2. Sixteen studies were community based,^{21,22,25,27–29,35–42} two extended across community and hospitals,^{21,25} three were set in the hospital alone^{24,27,32} and two in hospice.^{33,42}

Sample sizes ranged from 13²⁸ to 16,613.⁴² Six studies^{20–24,26} provided sample size/power calculations. Bekelman et al.,²¹ Brännström and Boman,²² and Hopp et al.²³ achieved adequate power to detect statistically significant differences in outcomes (90%, 80% and 80%, respectively). Aiken et al.,²⁰ Rogers et al.²⁴ and Sidebottom et al.²⁶ were designed to reach adequate power; however, due to difficulty in recruitment and high attrition rate, partly due to death, these studies did not reach their proposed sample size.

Participants. Across 23 studies, 19,891 participants (average age range 52.5–87.5; men = 59.3%) were included. Severity of heart failure was indicated by New York Heart Association classification^{21,22,24,27,28,30,31,36–39,41} (Figure 2), Kansas City Cardiomyopathy Questionnaire,^{21,30,31} recent acute episode resulting in visits to the emergency department, hospitalisation or symptoms of end of life.^{20,22–25,27,30,31,34,35,38} In four studies,^{21,22,24,38} the data on left ventricular ejection fraction were presented in categories – 'normal' (34.6%), 'mild' (19.7%), 'moderate' (24.7%) and 'severe' (21.0%) left ventricular ejection fraction. The average left ventricular ejection fraction of the patients included in seven other studies^{23,27,29–31,36,37,41} was 32%.

Intervention. The intervention varied in terms of components and delivery (Supplementary table 3) and details were missing in Connor et al.³³ and Blecker et al.⁴² Most common aspects of palliative care included were symptom management, psychological support and advance care planning. All studies included an assessment of

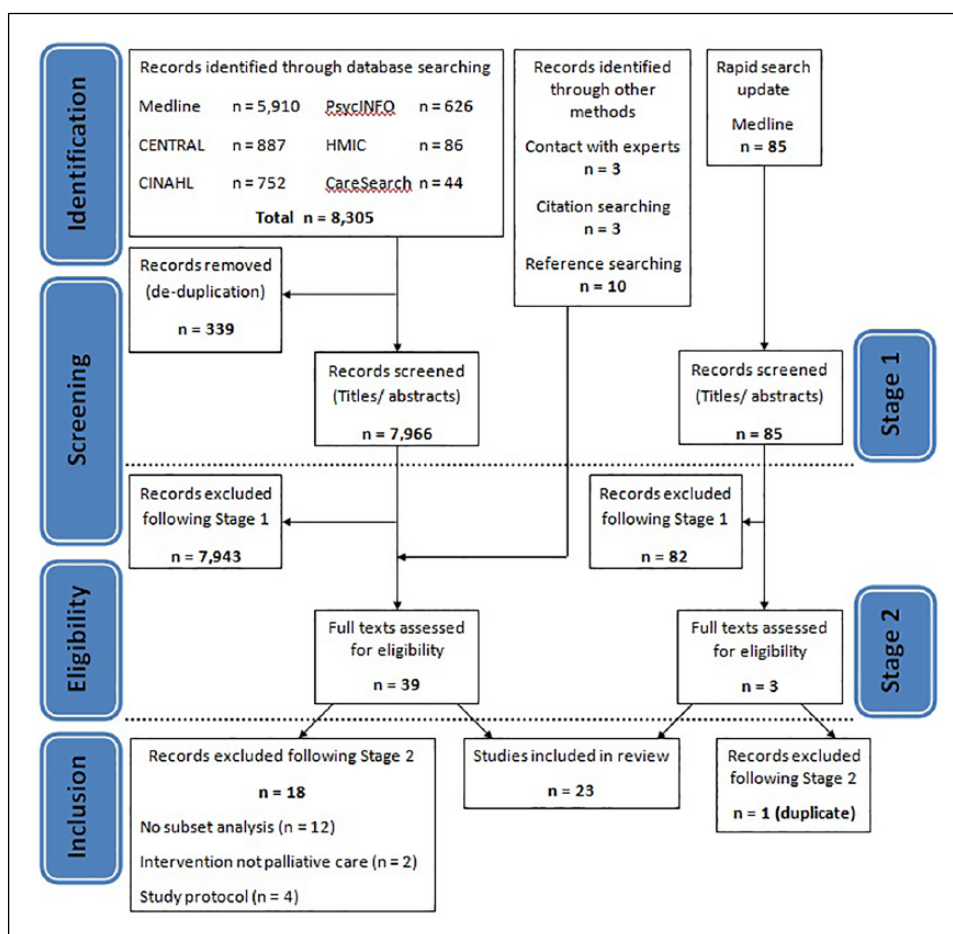


Figure 1. PRISMA flowchart depicting the search process and the study selection.

current medical status and patients' needs and were provided by a multi-disciplinary team.

Comparator. In general, description of the comparator was absent^{22,23,25,26,30,33,35,39–42} or minimal.^{20,21,24,27,28,34} Six of the included studies were single-arm studies, with no comparator,^{29,32,36–39} One feasibility study reported two cohorts,³¹ one from a palliative cardiology clinic and one from usual care, but the study was not designed as quasi-experimental although descriptive comparisons were made. This study is reported as a feasibility study, but as the methods fit best with observational design, the quality was assessed as a cohort study.

Risk of bias

Evaluation phase studies. The risk of bias of the evaluation phase studies is summarised in Supplementary table 4 using the Cochrane Risk of Bias tool. The main source of bias was the lack of blinding, but this was inherently impossible. Three trials attempted to blind outcome assessors.^{20,21,27} There were a number of other issues

relating to risk of bias. Missing data, particularly of patient-reported primary outcomes was significant, but details on pattern of missingness or how this was handled were not provided apart from Rogers et al.²⁴ (used a mixed effects model for the primary outcomes). Wong et al.²⁷ used the generalised estimating equation which is able to take missing data into account, but this was not made explicit as a method of handling missing data.^{20,28} Other biases include the risk of type 1 errors due to multiple statistical testing on small participant samples,²⁰ statistically significant differences in New York Heart Association classes between arms at baseline²⁷ and poor fidelity to allocated arms with some participants accessing palliative care as part of usual care in the comparator arms.^{24,26}

Observational studies – cohort studies. The Newcastle–Ottawa Scale risk of bias assessment for the seven cohort studies is summarised in Supplementary table 5. The four single-arm cohort studies could not be assessed fully as there is no non-exposed group. Most cohort studies had representative samples; however, Taylor et al.³⁸ recruited

Table 1. Characteristics of included interventional studies.

First author, year and country	Study setting	Participants: sample size (N), age (years), sex (%), disease characteristics (NYHA, LVEF)	Intervention	Comparator	Intervention	Comparator
Evaluation phase RCTs						
Aiken ²⁰ 2006 The United States	Community based and hospital based	N = 100 (CHF = 67) Mean Age (SD) = 68 (14) Sex: M = 42.0; F = 58.0			PhoenixCare: Home-based palliative care	Usual care
Bekelman ²¹ 2015 The United States	Community based with outpatient consultations	N = 187 Mean Age (SD) = 68.3 (9.6) Sex: M = 95.2; F = 4.8 NYHA: class I = 16 (8.9%) class II = 77 (42.8%) class III = 82 (45.6%) class IV = 5 (2.8%) LVEF: Normal = 78 (45.6%) Mild = 34 (19.9%) Moderate = 46 (26.9%) Severe = 13 (7.6%)			Patient-centred disease management	Regular care
Brännström ²² 2014 Sweden	Community based with outpatient consultations	N = 36 Mean Age (SD) = 81.9 (7.2) Sex: M = 72.2; F = 27.8 NYHA: class III = 28 (77.8%) class IV = 8 (22.2%) LVEF: 40%–49% = 13 (36.1%) 30%–39% = 16 (44.4%) <30% = 7 (19.4%)			PREFER: Palliative advanced home care and heart failure care	No information
Hopp ²³ 2016 The United States	Hospital based	N = 43 Mean Age (SD) = 67.0 (11.0) Sex: M = 60.5; F = 39.5 Mean LVEF = 36.4% (16.7)			Palliative care consultation	No information
Rogers ²⁴ 2017 The United States	Community based and hospital based	N = 75 Mean Age (SD) = 71.9 (12.4) Sex: M = 56.0; F = 44.0 NYHA: class III = 54 (72.0%) class IV = 15 (20.0%) LVEF: >55% = 21 (28.0%) 40%–55% = 14 (18.7%) 25%–40% = 17 (22.7%) <25% = 23 (30.7%)			PAL-HF: Multi-component palliative care	Usual care
		N = 90 (CHF = 62) Mean Age (SD) = 68 (14) Sex: M = 30.0; F = 70.0				
		N = 197 Mean Age (SD) = 67.9 (10.6) Sex: M = 98.0; F = 2.0 NYHA: class I = 16 (8.5%) class II = 85 (45.0%) class III = 82 (43.4%) class IV = 6 (3.2%) LVEF: Normal = 84 (47.5%) Mild = 34 (19.2%) Moderate = 32 (18.1%) Severe = 27 (15.3%)				
		N = 42 Mean Age (SD) = 68.0 (13.0) Sex: M = 42.9; F = 57.1 Mean LVEF = 38.1% (16.8)				
		N = 75 Mean Age (SD) = 69.8 (13.4) Sex: M = 49.3; F = 50.7 NYHA: class III = 58 (77.3%) class IV = 5 (6.7%) LVEF: >55% = 14 (18.7%) 40%–55% = 19 (25.3%) 25%–40% = 14 (18.7%) <25% = 28 (37.3%)				

(Continued)

Table 1. (Continued)

First author, year and country	Study setting	Participants: sample size (N), age (years), sex (%), disease characteristics (NYHA, LVEF)		Intervention	Comparator	Intervention	Comparator
		Intervention	Comparator				
Sahlen, ²⁵ 2015; Sweden: Details are the same as Brännström et al. ²³							
Sidebottom ²⁶ 2015	Inpatient consultation	N = 116 Mean Age (SD) = 76.0 (11.9) Sex: M = 47.4; F = 52.6	N = 116 Mean Age (SD) = 70.9 (13.6) Sex: M = 57.8; F = 42.2			Palliative care consultation	No information
The United States Wong ²⁷ 2016	Community based	N = 43 Mean Age (SD) = 78.3 (16.8) Sex: M = 43.9; F = 56.1	N = 41 Mean Age (SD) = 78.4 (10.0) Sex: M = 61.0; F = 39.0			Transitional palliative care	Usual care
China		NYHA: class II = 6 (14.0%) class III = 31 (72.0%) class IV = 6 (14.0%) Mean LVEF = 39.0% (14.0)	NYHA: class II = 3 (7.3%) class III = 22 (53.7%) class IV = 16 (39.0%) Mean LVEF = 37.0% (17.0)				
Feasibility and pilot phase RCTs							
Paes ²⁸ 2005	Outpatient consultations	N = 6 Mean Age (SD) = 73.2 (4.2) Sex: M = 100.0; F = 0.0	N = 7 Mean Age (SD) = 78.0 (7.0) Sex: M = 80.0; F = 20.0			Palliative care consultation	Regular care
The United Kingdom		NYHA: class III = 3 (50.0%) class IV = 3 (50%)	NYHA: class III = 3 (60.0%) class IV = 2 (40%)				
Bakitas ²⁹ 2017	Community based with outpatient consultations	N = 61 Mean Age (SD) = 70.59 (10.7) Sex: M = 50.8; F = 49.2				Single-arm study ENABLE CHF-PC: Early palliative care intervention	
The United States		NYHA: class I = 1 (1.6%) class II = 3 (4.9%) class III = 43 (70.5%) class IV = 12 (19.7%) Unknown = 2 (3.3%) Mean LVEF = 37.86% (16.3)					
O'Donnell ³⁰ The United States	Inpatient and/or recent discharged to community from admission for acute decompensated heart failure	N = 26 Mean Age (SD) = 74.7 (11.2) Sex: M 53.9, F = 46.1 NYHA class 1 or 2 = 10 (38.5%) NYHA class 3 or 4 = 16 (61.5%) Mean LVEF = 30% ¹⁴	N = 24 Mean Age (SD) = 69.2 (10.2) Sex: M = 62.5, F = 37.5 NYHA class 1 or 2 = 8 (33.3%) NYHA class 3 or 4 = 16 (66.7%) Mean LVEF = 36% ¹⁷			Social worker consultation for care planning Palliative care physician consultation	Usual care and printed materials about palliative care and advance care planning

Table 1. (Continued)

First author, year and country	Study setting	Participants: sample size (N), age (years), sex (%), disease characteristics (NYHA, LVEF)	Intervention	Comparator	Intervention	Comparator
Johnson ³¹ The United Kingdom	Community based with outpatient consultations	Cohort 1: palliative cardiology N = 43 Mean Age (SD) = 75.8 (12.3) Sex: M 55.8, F = 44.2 NYHA: class I = 0 class II = 0 class III = 40 (93.0) class IV = 3 (7.0)	Cohort 1: palliative care clinic conducted by consultant cardiologist with special interest and heart failure nurse consultant	Cohort 2: usual care N = 34 Mean Age (SD) = 78.4 (11.3) Sex: M 50.0, F = 50.0 NYHA: class I = 0 class II = 3 (8.8) class III = 30 (88.2) class IV = 1 (2.9)	Cohort 1: palliative care clinic conducted by consultant cardiologist with special interest and heart failure nurse consultant	Cohort 2: usual care
Quasi-experimental study Tadwalkar ³² 2014 The United States	Inpatient visits	N = 14 Mean Age (SD) = 58 (11) Sex: M = 42.9; F = 57.1	Religious support	N = 9 Mean Age (SD) = 57 (10) Sex: M = 55.6; F = 44.4	Religious support	Non-religious support

NYHA: New York Heart Association; LVEF: left ventricular ejection fraction; CHF: congestive heart failure; SD: standard deviation; RCT: randomised controlled trial.

male veterans only and the second cohort in Johnson et al.³¹ used a convenience sample only. None of the included studies measured the outcome of interest at baseline, but these were expected to improve or worsen based on exposure rather than appear or disappear. Comparability could be assessed through the baseline characteristics of the included participants, but analyses did not control for confounding factors. The primary objective for Johnson et al.³¹ was to test the feasibility of a subsequent trial with regard to recruitment, attrition and data quality from these two settings and was not designed to compare the two groups in any way other than descriptively.

Observational studies – case-control studies. The Newcastle–Ottawa Scale risk of bias assessment for the two case-control studies is summarised in Supplementary table 6. The case definition, case representativeness and selection of controls was appropriate in both studies; however, the controls are poorly defined. The comparison groups were matched for age, sex and race. Evangelista et al.⁴¹ provided no information on how the exposure was measured and neither study provided information on non-response rates.

Observational studies – cross-sectional study. Cross-sectional design has inherent flaws, for example, the exposure and outcome are measured at the same time period. The summary quality rating for Blecker et al.⁴² is fair, but the sample is not justified, no weight is given to level of exposure to intervention or repeat exposure in the analysis and the outcome measurement relied significantly on coding.

Outcomes

The salient results of the outcomes from the included studies are summarised in Table 3.

Patient-centred outcomes. Symptom burden was measured with the use of Edmonton Symptom Assessment Scale^{22,26,27,31,36,37,41} and Memorial Symptom Assessment Scale.^{20,29,32} Five^{26,29,36,37,41} out of the nine studies investigating the change in symptom burden found significant improvement in symptoms such as breathlessness, pain and fatigue. Participants in the intervention arm of Aiken et al.²⁰ experienced significantly higher symptom distress than their counter-parts in the control arm, and in Johnson et al.³¹ symptoms improved more in the usual care cohort. Nine studies investigated depression using the Patient Health Questionnaire-9,^{21,26,30,41} Hospital Anxiety and Depression Scale^{24,25,29,31} and Quick Inventory of Depressive Symptomatology.³² Five studies^{21,24,25,30,41} found significant improvement in depression with the intervention. There was a significant improvement in New York Heart Association classes from baseline following the

Table 2. Characteristics of included observational studies.

First author, year and country	Study setting	Participants: sample size (N), age (years), sex (%), disease characteristics (NYHA, LVEF)	Intervention	Comparator	Intervention	Comparator
Cohort studies						
Connor ³³ 2007 The United States	Hospice care (Retrospective)	N = 2095 (CHF = 83) Mean Age = 73.5 Sex: M = 55; F = 45			Hospice care	No claims for hospice care
Enguidanos ³⁴ 2005 The United States	Community based with outpatient consultations (Prospective)	N = 159 (CHF = 31) Mean Age (SD) = 70 (13.92) Sex: M = 49.1; F = 50.9			Home-based palliative care programme	Standard health care
Pattenden ³⁵ 2013 The United Kingdom	Community based (Prospective)	N = 99 Mean Age (SD) = 81.7 Sex: M = 60.6; F = 39.4			'Better Together' intervention: education and palliative nursing	'Convenience sample' – historical
Evangelista ³⁶ 2014 The United States	Outpatient consultations (Prospective)	N = 29 Mean Age (SD) = 53.3 (7.3) Sex: M = 75.9; F = 24.1 NYHA: class II = 20 (69.0%) class III = 9 (31.0%) Mean LVEF = 23.1% (4.3)			Single-arm study Palliative care consultations: 'Intervention group'	Participants receiving >2 palliative care consultations 'Comparator group'
Evangelista ³⁷ 2014 The United States	Outpatient consultations (Prospective)	N = 29 Mean Age (SD) = 54.1 (8.4) Sex: M = 75.9; F = 24.1 NYHA: class II = 20 (69.0%) class III = 9 (31.0%) Mean LVEF = 25.9% (5.3)			Participants receiving ≤1 palliative care consultations Single-arm study Palliative care consultations: 'Intervention group'	Participants receiving ≤1 palliative care consultations Single-arm study Palliative care consultations: 'Comparator group'
Taylor ³⁸ 2017 The United States	Community based (Retrospective)	N = 32 Age Range (Median) = 48–94 (70) Sex: M = 100; F = 0 NYHA: class III = 2 (6.7%) class IV = 28 (93.3%) 23 patients had HFpEF (LVEF < 30%); 7 had HFpEF			Participants receiving palliative care consultation and follow up. 'Comparator group'	Participants receiving initial palliative care consultation only. Single-arm study Home delivered palliative care

Table 2. (Continued)

First author, year and country	Study setting	Participants: sample size (N), age (years), sex (%), disease characteristics (NYHA, LVEF)		Intervention	Comparator
		Intervention	Comparator		
Wong ³⁹ 2013 Singapore	Community based (Prospective)	N = 44 Mean Age (SD) = 79 (9) Sex: M = 38.6; F = 61.4 NYHA: class III = 31 (70.0%) class IV = 13 (30.0%)		Single-arm study Home palliative care programme	
Case-control studies					
Brian Cassel ⁴⁰ 2016 The United States	Community based (Retrospective)	N = 174 Mean Age (SD) = 87.5 (6.6) Sex: M = 44.3; F = 55.7	N = 499 Mean Age (SD) = 87.1 (6.4) Sex: M = 43.7; F = 56.3	Transitions: Concurrent medical and palliative care	No information
Evangelista ⁴¹ 2012 The United States	Outpatient consultation (Prospective)	N = 36 Mean Age (SD) = 53.9 (8.0) Sex: M = 72.2; F = 27.8 NYHA: class II = 25 (69.4%) class III = 11 (30.6%) Mean LVEF = 25.4% (5.2)	N = 36 Mean Age (SD) = 53.3 (8.7) Sex: M = 69.4; F = 30.6 NYHA: class II = 26 (72.2%) class III = 10 (27.8%) Mean LVEF = 26.0% (6.2)	Palliative care consultation	No information
Cross-sectional study					
Blecker ⁴² 2011 The United States	Hospice care	N = 6436 Mean Age (SD) = 85.0 (7.6) Sex: M = 39.5; F = 60.5	N = 10,177 Mean Age (SD) = 83.6 (7.9) Sex: M = 44.5; F = 55.5	Hospice care	No claims for hospice care

NYHA: New York Heart Association; LVEF: left ventricular ejection fraction; CHF: congestive heart failure; HFpEF: heart failure with preserved ejection fraction; HFREF: heart failure with reduced ejection fraction.

intervention,^{22,38} but no change in functional status measured by Palliative Performance Scale²⁷ or Australian-modified Karnofsky Performance Scale.³¹

Various measures were used to assess quality of life, including Kansas City Cardiomyopathy Questionnaire and

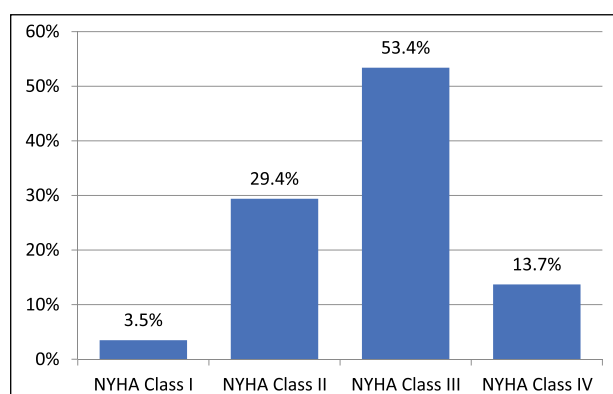


Figure 2. Distribution of participants across the NYHA classes reported in 13 studies; reported here for the 12 studies where all four classes are reported separately.

EuroQol-5D. Some studies used a combination to assess disease- or intervention-specific and health-related quality of life. Seven^{24–27,29,30,41} out of 11 studies found significant improvement in quality of life, with one other²² noting a significant improvement in health-related quality of life but not in disease-specific quality of life. Five studies investigated the effect on survival, while others^{20,24,27,29–31} commented on attrition due to death. Four studies^{22,23,26,31} found no significant difference in mortality between the intervention and comparator arm. There were significantly fewer deaths in the intervention arm in Bekelman et al.²¹ and the participants survived significantly longer in Connor et al.³³

Resource use. Thirteen studies evaluated use of resources in different ways. Seven^{22,27,31,35,39,40,42} out of 10 studies found significant reduction in hospitalisations and readmissions, and five^{29,31,34,40,42} out of six studies had significant reduction in length of stay in hospital or service use. There was no significant difference in hospice use among the participants. Patients in the intervention arm were more likely to complete advance care planning^{26,30,31} and less likely to die in hospital.^{34,40} Three studies^{34,35,40}

Table 3. Summary of salient outcome results.

Study	Patient-centred outcomes					Resource use				
	Symptom burden	Depression	Quality of life ^a	Functional status	Mortality	Hospital visits	Length of service use	Hospice care	Place of death and ACP	Costs
Aiken ²⁰	☒					◇				
Bekelman ²¹		✓	◇		✓	◇				
Brännström ²²	◇		✓◇	✓	✓	✓				
Hopp ²³					◇			◇		
Rogers ²⁴		✓	✓							
Sahlen ²⁵			✓							◇
Sidebottom ²⁶	✓	✓	✓		◇	◇		◇	✓	
Wong ²⁷	◇		✓✓	◇						
Paes ²⁸		◇	◇							
Bakitas ²⁹	✓	◇	✓				✓	◇		
Tadwalkar ³²	◇	◇	◇							
O'Donnell ³⁰		◇	◇		◇				✓	
Johnson ³¹	☒	◇	◇	◇	◇	✓			✓	✓
Connor ³³					✓					
Enguidanos ³⁴							✓	◇	✓	✓
Pattenden ³⁵						✓	◇			✓
Evangelista ^{†36}	✓	✓								
Evangelista ^{a,37}	✓									
Taylor ³⁸				✓						
Wong ³⁹						✓				
Brian Cassel ⁴⁰						✓	✓		✓	✓
Evangelista ⁴¹	✓		✓							
Blecker ⁴²						✓	✓			☒

✓: results significantly in favour of intervention, ☒: results significantly in favour of control, ◇: no significant difference. ACP: advance care planning.
^aNote that the quality of life assessment was conducted separately in some studies for disease-specific/health-related/palliative care-specific data, therefore may have multiple entries.

[†]*P* = 0.05 taken as the the level of sufficient statistical significance.

found a statistically significant drop in costs in the intervention arm, one feasibility study found preliminary cost savings in the intervention group³¹; however one found no significant difference and the expenditure of the intervention arm in Blecker et al.⁴² was significantly higher when adjusted for covariates.

Discussion

This review collated the current body of evidence from a range of countries examining the effects of palliative care on patients with advanced heart failure with the intent to guide future clinical and research priorities for this population.

The results from evaluation phase studies support the use of multi-component, multi-disciplinary palliative care interventions. Benefits were improvement in patient-centred outcomes including symptom burden, depression, quality of life, functional status, and reduced use of healthcare resources and costs of care.

Findings were inconsistent across all studies, likely due to the significant clinical and methodological heterogeneity between studies, across all aspects: study design, study population and setting, components of the intervention and control and choice of outcome measures.

Limitations of the included studies

Although we searched the international literature, 16 out of 23 studies were conducted in the United States which may limit generalisability.

Patients in randomised controlled trials were randomised individually and intervention was delivered in the same site as the control arm; therefore, there is a risk of control group contamination.^{20,21,26,30,41} Also, some patients did not receive the prescribed intervention either due to limited availability of providers²⁶ or limited access to care if patients deteriorated rapidly.³⁵ Meanwhile, other patients received palliative care despite allocation to control in response to clinical need.^{24,26} Therefore, the effect of the intervention may be under-estimated. Furthermore, in one study,²⁰ heart failure participants were a subgroup only. Baseline differences in symptom distress (higher in the intervention group) were therefore not adjusted for, which may have affected the findings.

Conclusions from the non-randomised trials³² and observational studies regarding the precise impact of the intervention should be cautious due to risk of selection bias and effect of confounders which were either not reported, or, if they were, adjusted findings were not presented.

Eleven studies^{20–25,27,28,32,35,39} included only patients with New York Heart Association class III and IV, consistent with the population most likely to benefit from palliative care. Other studies did not provide New York Heart

Association classification or also included patients with New York Heart Association class I and II but without subgroup-analysis. This may have led to an underestimation of effects.

Palliative care is a multi-component intervention but was variably delivered across included studies. Studies investigating the effects of limited aspects of palliative care^{23,32} found no significant difference in outcomes between the intervention and the comparator, unlike studies investigating a more comprehensive intervention. Two studies^{26,41} assessed the effect of a single palliative care consultation – which does not represent usual palliative care practice. Hopp et al.²³ chose completed 'do not resuscitate' orders as the primary outcome which is inconsistent with the defined aim of palliative care (improvement in quality of life and symptom control).⁸

Apart from the risk of contamination, the quality of the studies designed to evaluate effectiveness^{20–27} was good, accepting that blinding was not possible. However, as expected with palliative care studies, there were missing data in patient-reported primary outcomes at levels associated with bias. Rogers et al.²⁴ addressed this explicitly for their primary outcomes using a linear mixed model with an indicator variable for the treatment group and Wong et al.²⁷ used generalised estimating equations. As with previously noted poor reporting of missing data,⁴³ neither described the pattern of missingness to confirm that this approach was appropriate.⁴⁴ However, Rogers et al.²⁴ did note the significant levels of missing data and made the reasonable comment that bias should be limited because the attrition was similar in both arms.

Strengths and limitations of the review

This review was not restricted to randomised controlled trials, to allow an understanding of the breadth and gaps in the published literature relating to palliative care for people with heart failure. However, as with any systematic review, some studies with potential for inclusion may have been missed. Due to the clinical and methodological heterogeneity between the included studies, we were unable to conduct a meta-analysis. This heterogeneity reflects the variation in palliative care implementation around the world.

Implications for clinical practice and research

Palliative care delivered as comprehensive intervention with regular assessments of patients' needs and a tailored management appears to be beneficial for patients with symptomatic heart failure. However, in practice, referral of all patients with New York Heart Association III and IV heart failure to specialist palliative care seems both unnecessary and unsustainable.

Current recommendations^{5,13–15,45} support an integrated approach where usual care teams (in cardiology, elderly care or primary care) provide general palliative care for identified needs but involve specialist palliative care for complex or persistent concerns.⁴⁶ Although the study of a palliative care intervention led by the cardiology team was not designed to show effectiveness,³¹ it demonstrates that it is possible to deliver in clinical practice.

Future trials of specialist palliative care should focus on the patients with heart failure most likely to benefit from specialist intervention. A recent cohort study of people admitted to hospital for heart failure identified that those most likely to have specialist palliative care needs (defined as those with ‘persistently severe impairment of any patient reported outcome’) as those with a Kansas City Cardiomyopathy Questionnaire summary score of <29 on admission.⁴⁷ This moves away from the question of ‘when is the right time to refer’, which assumes proximity to death as the primary criterion.

Well-designed studies which minimise contamination (e.g. cluster design) are also needed to test the effectiveness and cost-effectiveness of interventions whereby the usual care team provides most palliative care, supported by specialists as needed. Consensus around core components of palliative care, configuration of palliative care teams, the most effective model of service provision to ensure tailored generalist and/or specialist palliative care, core outcome sets and careful thought and agreement about how to both minimise and manage missing data would facilitate both quality of results and the ability to conduct meta-analysis.

Conclusion

Multi-component, multi-disciplinary palliative care interventions appear to provide patient-centred benefit and reduce use of healthcare resources and costs. However, there are no sufficiently robust multi-centre evaluation phase trials to provide generalizable findings. Consensus is needed for core intervention components, study population, outcome sets, management strategies for missing data and optimum design to inform multi-centre trials for use in future meta-analysis.

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Author contributions

S.D. and M.J.J. conceived the question; S.D., M.J.J. and A.H. designed the protocol; S.D. conducted the search; S.D. and C.A.V. selected the studies and extracted data; S.D. wrote the first draft; all authors contributed to critical revision and agreed the final manuscript.

Data sharing

All data are presented in this manuscript.

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Supplemental material

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