Palliative Medicine

Does advance care planning in addition to usual care reduce hospitalisation for patients with advanced heart failure: A systematic review and narrative synthesis.

Journal:	*Palliative Medicine*
Manuscript ID	Draft
Manuscript Type:	Review Article
Date Submitted by the Author:	n/a
Complete List of Authors:	Kernick, Lucy; Hull York Medical School, Wolfson Palliative Care Research Centre Hogg, Karen; Glasgow Royal Infirmary, Department of Cardiology Millerick, Yvonne; Glasgow Caledonian University Murtagh, Fliss; Hull York Medical School, Wolfson Palliative Care Research Centre Djahit, Ayse; Hull York Medical School Johnson, Miriam; University of Hull, Wolfson Palliative Care Research Centre
Keywords:	heart failure, advance care planning, palliative, admissions, readmissions
Abstract:	BACKGROUND: People with advanced heart failure have repeated hospital admissions. Advance care planning can support patient preferences, but studies in people with heart failure have not been assessed. AIM: To evaluate the literature regarding advance care planning and hospitalisation in heart failure. DESIGN: Systematic review and narrative analysis.(PROSPERO CRD42017059190) DATA SOURCES: Electronic databases were searched (1990 to 23.03.2017); MEDLINE(R), Cochrane Library, CINAHL, and Scopus. Four journals were hand searched. Two independent researchers screened against eligibility criteria. One reviewer extracted all data and a sample by a second. Quality was assessed by Cochrane Risk of Bias or the Critical Appraisal Skills Programme Tool for Cohort Studies. RESULTS: 8/1713 articles were included representing 14,357 participants from in/outpatient settings from five countries. Two randomised-controlled trials and one observational study assessed planning as part of a specialist palliative care intervention; one randomised-controlled trial assessed planning in addition to usual cardiology care; one randomised-controlled trial and one observational study assessed planning in an integrated cardiology-palliative care model; one observational study assessed evidence of planning (advance directive) as part of usual care, and one observational study was a secondary analysis of trial participants coded Do Not Attempt Cardiopulmonary Resuscitation. Advance care planning i) reduced hospitalisation(5/7 studies), ii) increased referral/use of palliative services (4/4 studies), iii) supported deaths in the patient-preferred place

	(2/2 studies). CONCLUSIONS: Advance care planning as part of a specialist palliative care care intervention reduces hospitalisation. Preliminary studies of planning integrated into generic care, accessing specialist palliative care support if needed, are promising.

TITLE

Does advance care planning in addition to usual care reduce hospitalisation for patients with advanced heart failure: A systematic review and narrative synthesis.

AUTHORS

Kernick L., Wolfson Palliative Care Research Centre, Hull York Medical School, University of Hull

Hogg K., Glasgow Royal Infirmary, Glasgow University, United Kingdom

Millerick Y., Glasgow Royal Infirmary, Glasgow Caledonian University, United Kingdom

Murtagh F.E.M., Wolfson Palliative Care Research Centre, Hull York University, University of Hull, United Kingdom

Djahit A., Wolfson Palliative Care Research Centre, Hull York Medical School, University of Hull, United Kingdom

Johnson M., Wolfson Palliative Care Research Centre, Hull York Medical School, University of Hull, United Kingdom

CORRESPONDING AUTHOR:

Postal address: Wolfson Palliative Care Research Centre, Hull York Medical School, Cottingham Rd, Hull UK HU6 7RX

Email: lucyk82@hotmail.com

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

PALLIATIVE MEDICINE AUTHOR SUBMISSION CHECKLIST

Please complete this checklist for all papers submitted. Please indicate, very briefly, how this has been addressed. This checklist is a mandatory upload on submission.

Item	Explanation	How this has been addressed (briefly, a sentence will suffice)
Article title	***WHY: Because we want readers to find your work.*** Have you followed our guidelines on writing a good title that will be found by search engines? (E.g. with methods in the title, use of common words for the issue addressed, no country names, and possibly indicating findings). If your study has an acronym is it included in the title?	INCLUDED REVIEW TYPE AND MESH TERMS
Abstract	***WHY: Because structured abstracts have more detail for readers and search engines.*** Have you followed our guidelines on writing your structured abstract? Please remember we have separate abstract structures for original research, reviews and case reports. There should be **no** abbreviations in the abstract, EXCEPT a study acronym which should be included if you have one. If a trial (or other design formally registered with a database) have you included your registration details?	PLEASE SEE Pg1
Key statements	***WHY: Because readers want to understand your paper quickly.*** Have you included our key statements within the body of your paper (after abstract and before the main text is a good place!) and followed our guidelines for how these are to be written? There are three main headings required, and each may have 1-3 separate **bullet** points. Please use clear, succinct, single sentence separate bullet points rather than complex or multiple sentences.	PLEASE SEE Pg2
Keywords	***WHY: Because MeSH headings mean it is properly indexed.*** Have you given keywords for your study? We ask that these are current **MeSH** headings unless there is no suitable heading for use (please give explanation in cover letter). https://meshb.nlm.nih.gov/search	PLEASE SEE Pg2
International relevance	***WHY: We have readers from around the world who are interested in your work.*** Have you contextualised your work for an international audience and explained how your work contributes to an international knowledge base? Avoid drawing from policy from one context only, think how your work could be relevant more widely. Do define terms clearly e.g. hospice has a different	SEE REFERENCES FROM SETTINGS ACROSS THE WORLD, STUDIES ARE DRAWN FROM USA, CANADA, ASIA, EUROPE, UK

	meaning in many countries.	
Publishing guidelines	***WHY: Because clear and robust reporting helps people interpret your work accurately*** Have you submitted a completed checklist for a relevant publishing guideline as a supplementary file? http://www.equator-network.org/ These include CONSORT, PRISMA, COREQ checklists, but others may be more relevant for your type of manuscript. If no published checklist exists please create one as a table from the list of requirements in your chosen guideline. If your study design does not have a relevant publishing guideline please review closest matches and use the most appropriate with an explanation.	YES – PRISMA
Word count	***WHY: Because readers want to find the core information quickly.*** Does your paper adhere to our word count for your article type? Please insert number of words in the box to the right. Remember that tables, figures, qualitative data extracts and references are not included in the word count.	4311
Figures and tables and/or quotations	***WHY: Because readers want to find the core information quickly.*** Have you adhered to our guidelines on the number of tables and figures for your article type? Data (e.g. quotations) for qualitative studies are not included in the word count, and we prefer that they are integrated into the text (e.g. not in a separate table).	Figure – 1 Tables – 4 (in article 1, online 3)
Study registration	***WHY: Because this means readers understand how you planned your study*** Where appropriate have you included details (including reference number, date of registration and URL) of study registration on a database e.g. trials or review database. If your study has a published protocol, is this referenced within the paper?	STUDY REGISTERED WITH PROSPERO SEE Pg4
Other study publications?	***WHY: So readers can understand the full context of your study*** If there are other publications from this study are these referenced within the body of the paper? Please do not reference papers in preparation or submitted, but in-press publications are acceptable.	NO
Scales, measures or questionnaires	***WHY: So readers can understand your paper in the context of this information*** If your study primarily reports the development or testing of scales/measures or questionnaires have you included a copy of the instrument as a supplementary file?	NA

Abbreviations	***WHY: Because abbreviations make a paper hard to read, and are easily misunderstood*** Have you removed **all** abbreviations from the text except for extremely well known, standard abbreviations (e.g. SI units), which should be spelt out in full first? We do not allow abbreviations for core concepts such as palliative or end of life care.	YES
Research ethics and governance approvals for research involving human subjects	***WHY: We will only publish ethically conducted research, approved by relevant bodies*** Have you given full details of ethics/governance/data protection approvals with reference numbers, full name of the committee(s) giving approval and the date of approval? If such approvals are not required have you made it explicit within the paper why they were not required. Are details of consent procedures clear in the paper?	SYSTEMATIC REVIEW – NO ETHICS REQUIRED
Date(s) of data collection	***WHY: So readers understand the context within which data were collected*** Have you given the dates of data collection for your study within the body of your text? If your data are over 5 years old you will need to articulate clearly why they are still relevant and important to current practice.	DATABASE SEARCHES WERE FROM 23/3/17 to 30/6/17 INCLUDED STUDIES FROM 1990 to 30/6/17
Structured discussion	***WHY: So readers can find key information quickly*** Papers should have a structured discussion, with sub headings, summarising the main findings, addressing strengths and limitations, articulating what this study adds with reference to existing international literature, and presenting the implications for practice.	SEE Pg10-13
Case reports	***WHY: So that participants are protected, and its importance made clear*** If your study is a case report have you followed our clear structure for a case report, including highlighting what research is needed to address the issue raised? Have you made clear what consent was required or given for the publication of the case report? Have you provided evidence of such consent as a supplementary file to the editor?	NA
Acknowledgements and declarations	***WHY: So readers understand the context of the research*** Have you included a funding declaration according to the SAGE format? Are there acknowledgements to be made? Have you stated where data from the study are deposited and how they may be available to others? Have you conflicts of interest to declare?	NO FUNDING
Supplementary	***WHY: So the context is clear, but the main paper succinct for the reader***	ONLINE TABLE 3 – MEDLINE

data and materials	Is there any content which could be provided as supplementary data which would appear only in the online version of accepted papers? This could include large tables, full search strategies for reviews, additional data etc.	SEARCH
References	***WHY: So people can easily find work you have referenced*** Are your references provided in SAGE Vancouver style? You can download this style within Endnote and other referencing software.	YES
Ownership of work.	Can you assert that you are submitting your original work, that you have the rights in the work, that you are submitting the work for first publication in the Journal and that it is not being considered for publication elsewhere and has not already been published elsewhere, and that you have obtained and can supply all necessary permissions for the reproduction of any copyright works not owned by you.	YES

TITLE

Does advance care planning in addition to usual care reduce hospitalisation for patients with advanced heart failure: A systematic review and narrative synthesis.

ABSTRACT

BACKGROUND: People with advanced heart failure have repeated hospital admissions. Advance care planning can support patient preferences, but studies in people with heart failure have not been assessed.

AIM: To evaluate the literature regarding advance care planning and hospitalisation in heart failure.

DESIGN: Systematic review and narrative analysis.(PROSPERO CRD42017059190)

DATA SOURCES: Electronic databases were searched (1990 to 23.03.2017); MEDLINE(R), Cochrane Library, CINAHL, and Scopus. Four journals were hand searched. Two independent researchers screened against eligibility criteria. One reviewer extracted all data and a sample by a second. Quality was assessed by Cochrane Risk of Bias or the Critical Appraisal Skills Programme Tool for Cohort Studies.

RESULTS: 8/1713 articles were included representing 14,357 participants from in/outpatient settings from five countries. Two randomised-controlled trials and one observational study assessed planning as part of a specialist palliative care intervention; one randomised-controlled trial assessed planning in addition to usual cardiology care; one randomised-controlled trial and one observational study assessed planning in an integrated cardiology-palliative care model; one observational study assessed evidence of planning (advance directive) as part of usual care, and one observational study was a secondary analysis of trial participants coded Do Not Attempt Cardiopulmonary Resuscitation. Advance care planning i) reduced hospitalisation(5/7 studies), ii) increased referral/use of palliative services (4/4 studies), iii) supported deaths in the patient-preferred place (2/2 studies).

CONCLUSIONS:

Advance care planning as part of a specialist palliative care care intervention reduces hospitalisation. Preliminary studies of planning integrated into generic care, accessing specialist palliative care support if needed, are promising.

KEY STATEMENTS

What is already known about the topic?

- Advance care planning can support patient care preferences in the event of deterioration
- Studies of advance care planning in people with heart failure have not been assessed.

What this paper adds?

- Studies of advance care planning as part of a specialist palliative care care intervention show benefit with regard to supporting patient-preferred place of care and death and reduction in hospitalisation
- There is only low quality evidence for advance care planning delivered as a single component in this patient group.

Implications for practice, theory or policy?

- Referral of *all* patients with heart failure to specialist palliative care in order to receive advance care planning is non-sustainable and unnecessary
- Findings from studies where advance care planning is integrated into generic care, with access to specialist palliative care support *if needed*, are promising and should be further tested.

KEYWORDS

Heart Failure

Advance Care Planning

Admissions

Readmissions

Palliative

INTRODUCTION

Despite effective treatments, heart failure remains a terminal condition with a high mortality and morbidity.(1, 2) Although there is increasing awareness of the significant symptom burden and palliative care needs of people with advanced heart failure, repeated hospital admissions, emergency department attendance and death in hospital are experienced by many.(3-5) Compared to people with advanced cancer, people living with heart failure have less understanding of their condition, including stage of disease, less involvement in clinical decisions about their care, especially towards the end of life and less access to supportive and palliative care services.(6, 7) An unpredictable illness trajectory with difficult prognostication and fragmented care are cited as reasons for these observations. (8-10) Although integrated services (11) which aim to improve both general and specialist palliative care support to these patients are developing, this is not implemented routinely in all services.

A recent consensus statement defines advance care planning as that which: "… enables individuals to define goals and preferences for future medical treatment and care, to discuss these goals and preferences with family and health-care providers, and to record and review these preferences if appropriate" .(12) Patients can express wishes about their care to their treating team and family members at the time, and assist decision making when they are no longer able to have those conversations themselves.(13) These include simple direct orders such as "do not attempt cardiopulmonary resuscitation" decisions, and complex planning discussions including; treatment goals, ceilings of treatment, and preferences regarding place of care or place of death.

Evidence to date indicates that advance care planning is acceptable with likely benefit to individuals, families and the healthcare system. Although there is no full health economic evaluation there is emerging evidence of cost savings especially for people with diseases associated with high end-of-life healthcare costs. (14, 15) Brinkman-Stoppelenburg's systematic review of 113 papers concluded that advance care planning improved support for patients' end of life wishes, increased hospice use and reduced hospital admission but few papers measured clinical outcomes and none reported any safety measures.(16) A similar issue is apparent in a more recent review of advance care planning in older adults, (17) where most studies did not use a standardised advance care planning, measure impact on quality of life or health service use. People with heart failure have recognised high costs at the end-of-life, mainly driven by hospital admission. Therefore, advance care planning could be an

effective and cost-effective way to support people with advanced heart failure in preferences for care and place of death at the end of life.

Objectives

The primary objective of this study was to assess whether advance care planning, in addition to usual care, reduces the number of hospital admissions for patients with advanced heart failure. The secondary objective was to assess whether advance care planning, in addition to usual care, improves adherence to patient preferences in care, patient-reported outcomes, place of death and satisfaction with care in this patient group.

METHODS

A systematic review was performed using Cochrane methods and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The protocol was registered with PROSPERO, Centre for Reviews and Dissemination, York University (CRD42017059190).

Search strategy

The following databases were searched from 1990 until 23.03.2017: Ovid MEDLINE(R), Cochrane Library; Cochrane Central Register of controlled trials (Central), Methods Studies, CINAHL, and Elsevier Scopus. No language limits were applied. MeSH terms and text words for heart failure and advance care planning and their synonyms were combined. Terms were adapted for each database (see online table 3 for MEDLINE search). Reference lists of retrieved articles were scanned. The contents of the following journals were manually reviewed from 2015 to 2017; Journal of Palliative Medicine, Palliative Medicine, Journal of Pain and Symptom Management, BMJ Supportive and Palliative Care and Circulation. Experts in the field were contacted to ensure important studies included.

Eligibility criteria

Population: Studies included those with participants with all causes and classifications of heart failure (preserved systolic function included). In the absence of an agreed biomarker, advanced heart failure was based on clinical NYHA report (class III or IV). Studies involving paediatric, cardiac transplant and Left Ventricular Devices were excluded.

Intervention: Studies were required to name the intervention as containing; advance care planning/directive, living will, medical directive, resuscitation order/plan, end of life order/plan,

anticipatory care plan or medical treatment plan. Studies addressing 'patient centred care' only, without any of the above terminology or framework were excluded.

Comparator: The comparator was usual care however defined.

Outcome: The primary outcome was hospital admissions including number of hospital admissions (all cause and heart failure cause), number of hospital re-admissions, and rate of hospital admissions. The secondary outcomes were ; health utilisation other than admission to hospital (Emergency department presentation, local doctor, hospice, and community palliative care), place of death, death in preferred location, patient and family satisfaction.

Design: The study design criteria were broadened after initial screening searches due to the limited scope of literature on this area. Study designs included were; randomised control trials, quasi-experimental studies, and single arm observational studies. Due to small number of results, neither the outcome nor the study design were applied to the search.

Study selection

Study abstracts, titles and full texts, where necessary, were screened independently by two reviewers against the inclusion/exclusion criteria. Any discrepancies unresolved by discussion between reviewers were adjudicated by a third reviewer. Studies that matched the selection criteria were retrieved and their full text version analysed.

Data extraction

A standard data extraction tool was piloted on two papers, then used to extract data from the included studies. A second reviewer extracted data using the tool in 25% of studies. Data were extracted in relation to study identifiers, design, setting, population, intervention, control and outcomes. Further information documented included funding, key conclusions, references and any questions to find out from authors. The Cochrane Risk of Bias Tool (18) was used to assess bias in the randomised trails and the Critical Appraisal Skills Programme Tool for Cohort Studies (19) was used to assess bias in the non-randomised trials. Quality was not used as an exclusion criterion, but was taken into account in the analysis of the findings.

Analysis

A narrative summary with descriptions, comparisons and limitations of the studies was completed. Meta-analysis of combined data was not possible due to study heterogeneity with regard to population, intervention, comparator and outcome.

RESULTS

Selected studies

Out of 1713 titles, eight papers (four RCTs and four cohort studies), met the eligibility criteria. Figure 1 shows the PRISMA selection flow chart and Table 1 shows the characteristics of included studies.

FIGURE 1: PRISMA Flow sheet

TABLE 1: STUDY CHARACTERISTICS

Setting and Population

Included studies were conducted in USA (3 studies), UK (2 studies), Canada (1 study), Sweden (1 study) and Hong Kong (1 study). Patients were enrolled from the community (2,426 patients) and inpatient (11,931 patients) settings. Overall, studies represented 14,357 participants (mean age 75yrs, total range not provided, men 58%). The median study size was 138 participants (range 72 participants (20) to 8339 (21)). Heart failure was the primary diagnosis in 8 studies, 1 study (22), included patients with acute coronary syndromes *and* heart failure. Five papers gave NYHA class on enrolment; >92% of study participants had class II-IV. The rate of co-morbid chronic disease was high, mean percentage with Diabetes Mellitus across six studies was 38% (range 18% -53%), mean percentage patients with Renal Impairment 53% (range 22% - 77%).

Design

Three of the four RCTs were designed with sufficient power to evaluate effectiveness, (20, 23, 24) one was a feasibility trial (22) and only one was multi-site. (23) Only one recruited from the ambulant patient population. (20) Of the four observational studies, one was secondary analysis of trial data, McAlister (21), two were large retrospective cohorts (25, 26) and one a small two-site prospective cohort. (27)

Types of interventions and Comparators:

Two RCTs (23, 24) and one observational study (25) assessed advance care planning as part of a multi-disciplinary specialist palliative care intervention. One RCT assessed advance care planning in addition to usual cardiology care (22) and one observational study assessed evidence of advance care planning (advance directive documentation) as part of usual medical care (26). Two studies, one RCT (20) and one observational study (27), assessed advance care planning as part of an integrated cardiology-palliative care multi-disciplinary team model. The eigth study was a secondary analysis of

trial data observing the relationship between cardiopulmonary resuscitation code status with clinical outcomes. (21)

In most studies, advance care planning was only one part of a specialist palliative care, or integrated cardiology-palliative care intervention, and was not described specifically. In the feasibility RCT, (22) where advance care planning was the focus of the intervention, a description was provided (duration, timing and number of visits and by whom; production of a future care plan; nurse telephone support as needed) but not in the detail required to identify whether it included the elements recommended by Reitjens *et al* in their (12) consensus statement. In Butler *et al* (26), no detail was given about the process whereby patients had received an advance directive or not. However, it was apparent that patients could receive an advance directive even if they were not under the care of a palliative physician, thus implying this was part of generic practice. No details were given about any other aspect of advance care planning. In the secondary data analysis, (21) detail was given regarding how the DNR orders were classified, but no information was given about the process of identifying goals of treatment.

All four RCTs compared the intervention to usual care, three with a parallel group design and one (22) using a wait-list design. The observational studies used a mixture of comparators including: usual care, and no advance directive or full code status. One (27) had no study comparator but related findings to national data. Usual care descriptions lacked information regarding care received including the discipline of those caring for them, and the likelihood of receiving advance care planning or palliative care involvement as part of usual practice.

Outcome measures

The main study outcomes are described below:

Health service utilisation

Hospital admission/readmission were measured in seven studies. The collection of data differed in both periods measured and whether discrete episodes or 'each night admitted' was the outcome. The time period ranged from 12 weeks, through to 5 years (26). Four studies showed reduction in hospital admission/readmission, including in two of the larger RCTs; mean average readmissions in the advance care planning group at 6 months of 0.42 compared to 1.47 in the control group (p = <0.09), reduced relative risk of readmission in the advance care planning group (0.55, CI 0.35-0.88) (23). Denvir et al (22) found no difference in number of hospital admissions, but nights spent in hospital were fewer in the early intervention group (Early 8.6 (15.3) vs Delayed 11.8 (17.1), p = 0.01).

Amongst the observational studies, two studies (25, 26) found a reduction in hospital admission, but this only reached statistical significance in Butler *et al* (p<0.001 over 5 years).(26)

Two studies reported place of death data; both found increased deaths in preferred location and increased out of hospital deaths (home, nursing home or hospice) with advance care planning than known baseline estimates. (22, 27) Numbers of deaths in Denvir *et al* are too small to draw conclusion, but Johnson *et al* showed preferred place of death achieved in 61%, and hospital deaths in just over 40% compared with national figures of 82%. (27)

Hospice use increased in advance care planning groups in all studies where specialist palliative care services were not part of the intervention anyway. (21, 22, 26) Participants with evidence of advance planning were more likely to have participated in hospice. (21, 25-27) Butler (26) and McAlister (21) showed patients with evidence of advance planning had an increased likelihood of discharge to hospice compared to those without: McAlister (21) (5% vs 1% (p<0.001)), Butler (26) (22.3% vs 6.4% (p<0.001)). (see table 1)

A cost-effectiveness analysis was done as part of the Brannstrom *et al* RCT (28). The intervention arm had a higher staffing cost; mean General Practitioner cost per participant 457 Euro compared with 224 Euro (p=0.00), other medical professional cost 1890 Euro compared with 189 Euro (p=0.00). This was, however, offset by a reduction in emergency hospital and transport costs. Emergency transport cost per participant 98 Euro compared to 418 Euro (p=0.004) and mean hospital cost per participant 1632 Euro compared with 4896 Euro (0.009). The overall net cost analysis was a saving of 49,000 Euro in the intervention group at 6 months.

Patient-report measures

Patient-report measures (quality of life and symptom assessment) were included in the RCTs but varied across the trials thus contributing to heterogeneity. The different tools employed included: McGill quality of life questionnaire-Hong Kong (MQOL-HK), Chronic Heart Failure Questionnaire-Chinese version (CHQ), McGill Quality of heart failure scale (Chinese version), Edmonton Symptom Assessment Scale (ESAS), Kansas City Cardiomyopathy Questionnaire (KCCQ), Functional Assessment of Chronic Illness Therapy Palliative Care Scale (FACIT-pal), Functional Assessment of Chronic Illness Therapy Spiritual Wellbeing Scale (FACIT-Sp), Hospital Anxiety and Depression Score (HADS anxiety and depression), EQ5D heath thermometer and Visual Analogue Scale (VAS) and Essler Questionnaire.

Advance care planning improved QoL although only Rogers *et al* (24) had a sample size estimation solely based on QoL measures as the primary outcome. Rogers *et al* found a clinically and statistically significantly improved KCCQ (9.49 points, 95% CI:0.94 to 18.05, p = 0.030;) and for FACIT–Pal (group difference in favour of intervention; 11.77 points, 95% CI: 0.84 to 22.71, p = 0.035).(24) The clinical important difference for the FACIT-Pal has not been formally evaluated, but is estimated at 9 points. (29, 30) Brannstrom *et al* did not find a significant difference in overall KCCQ-12 score, but the QoL summary score was better in the intervention group (49.5 SD 24.7 *vs* 61.3 SD 26.6 p= 0.047). This team also found greater improvement in age-adjusted delta-value of EQ5D from baseline to 6 months in the intervention group (p=0.02).(20) Wong *et al* found improvement favouring intervention in the McGill QOL (6.16 (0.44) [UC] vs 7.37 (0.29); p<0.001) and total CHFQ scores (4.47 (0.23) [UC] vs 5.26 (0.17) (UC); p<0.001). (23) Both differences are highly statistically significant, but the clinically important difference for the McGill and total CHFQ (unlike for subscales) is unknown.

Symptoms improved in the three larger RCTs. In Wong *et al,* the ESAS summary score improved more with intervention than control (73% vs 41.4% [UC], p<0.05) with statistically and clinically significant improvement in the CHFQ dyspnoea and mastery domains (dyspnoea 4.89 (0.28) (UC) vs 5.82 (0.019), p< 0.001; mastery 4.64 (0.26) (UC) vs 5.36 (0.22, p< 0.001).(23) No statistical difference was found in ESAS measures in Brannstrom *et al* (20) but NYHA class (symptom based) improved for 36% in the intervention group compared with 9% in usual care (p= 0.015). Rogers *et al* did not report KCCQ symptom domains, but depression (–1.94 points; p = 0.020), anxiety (–1.83 points; p = 0.048) and spiritual wellbeing (3.98 points; p = 0.027) improved in the intervention group compared with usual care. (24)

Denvir (22), showed no significant difference between intervention and usual care for symptoms (ESAS) or QoL (EQ5D) but was not designed to show effect for any outcome.

Quality assessment

The four RCTs were of moderate quality with low risk of bias for selection, attrition and reporting biases, but high risk for performance and detecton biases. The sample size, where stated, was reached in all RCTs to reach adequate power. (20, 23, 24) Of note, Denvir *et al* was not designed to assess effectiveness but the Cochrane risk of bias tool does not assess statistical power. The high risk of performance and detection bias was due to non-blinding of participants, providers; unavoidable due to the nature of the intervention. However, the researchers collecting outcome assessments

was unblinded, or unclear. This risks potentially avoidable reporting bias as patient reported outcomes included subjective quality of life and symptom measures.

The observational studies included well recruited cohorts with objective outcomes. The quality, however, was reduced by risk of information bias, insufficient follow up and the impact of potential confounders impacting the results.

The quality assessment details can be found on the online tables 1 and 2.

Generalisability

The population studied was representative of the advanced heart failure population. The patients had symptomatic disease and co-morbidity. Denvir et al (22) also included patients with a recent acute coronary syndrome. The four RCTs were set in the outpatient setting or in conjunction with discharge planning which is a clinically appropriate timeframe. However, only one study was multi-site, hence application across different settings has not been consistently shown. In two RCTs the intervention was completed by one set of facilitators only (nurse practitioner, doctor), hence duplication by different individuals is needed. However, the advance care planning intervention was insufficiently described to apply elsewhere and multi-site data from involving multiple practitioners are needed.

Table 2 depicts outcomes by whether advance care planning was delivered as a single component in general clinical care or as part of a specialist palliative care delivered intervention. Patient-reported measures such as symptom control and quality of life were only measured when advance care planning was delivered as a component of specialist palliative care, apart from the feasbility RCT of advance care planning. In turn, measures specifically relating to the advance care planning component (concurrence with expressed preferences at the end of life, place of death) were not measured in the specialist palliative care trials where the focus was quality of life and symptom control.

DISCUSSION

This systematic review synthesises current evidence to show that, for the population with advanced heart failure, when delivered as part of a specialist palliative care or cardiology-palliative integrated team intervention, advance care planning changes patterns of health service utilisation. Advance care planning increases hospice use, reduces hospital use and supports patients in their preferred place of care and death. This evidence is derived from study populations with high levels of co-

morbidity, consistent with the wider advanced heart failure population, where co-morbidity is common.

Our data also show that advance care planning delivered as part of a specialist palliative care intervention or integrated team improves symptoms and quality of life. However, it is not possible to identify the contribution of the advance care planning component. The studies of advance care planning alone were either not designed to show effectiveness (22), or did not measure patient-reported outcomes (21, 26). Advance care planning as the only additional care component may improve QoL by helping those who wish to, to stay out of hospital, and improve even difficult symptoms indirectly by facilitating access to specialist palliative care. Advance care planning therefore seems well placed as a core skill for *non*-specialist palliative care clinicians, supported by specialist palliative care services for education, training and clinical support as needed. In order to embed advance care planning effectively into routine practice cardiology services may need to be reconfigured and staff trained to conduct advance care planning, become proficient in advanced communication skills and in basic holistic assessment. Referral pathways with specialist palliative care and community services would need to be established. Schellinger *et al* (25) describe the implementation of advance care planning in a large health care system delivered through a specialist palliative care service, but using the model of advance care planning within usual care much can be done within current resource. The interventions used in Brannstrom *et al* (20) and described by Johnson *et al* (27) were integrated models drawing together existing cardiology and palliative care services, for example, in education, training and combined multi-disciplinary team meetings. Across England, pathways of care and mutual education between cardiology and palliative care seem to facilitate development of these required skills for heart failure nurses, and referrals to specialist palliative care if needed. (31)

Advance care planning as part of routine care would help early identification of those who would benefit; careful preparation is needed if a person with a serious illness prefers to live and die at home.(32) A UK based primary care study showed that people with heart failure are much less likely than those with cancer to be registered on the practice palliative care register (a mechanism whereby co-ordinated care for those at the end of life can be facilitated). (33) Of those that were registered, a third were registered in the last week of life; a short timeframe to support death at home if preferred.

Most health costs in advanced heart failure are driven by hospital admission and the use of invasive but futile interventions in the last weeks of life administered in hospital. Hence, place of care and death are financial and quality priorities for patients and the healthcare system alike. Only one study

(advance care planning as part of an integrated cardiology-palliative care intervention) evaluated healthcare costs; favouring intervention. These data are consistent with those from other advanced disease populations where involvement of multi-disciplinary specialist palliative care, which include advance care planning as a component of care, is associated with reduced healthcare costs at the end of life,(32, 34-36) and emerging data for advance care planning as a generic intervention.(15) As transfer of care to the community may have fewer visible costs, careful further financial analysis on interventions is needed, including those affecting family and friends. Health economic evaluation of interventions where advance care planning is used *as a component of cardiology care* rather than specialist palliative care is needed. Although providing less robust data, the included studies of advance care planning as part of usual care, supported by specialist palliative care as needed only, gave promising data. It is likely that the additional cost of the multi-disciplinary palliative care team is needed only those with the most complex and persistent needs, but the benefits of advance care planning would be applicable for all with advanced disease.

Strengths and limitations

This study has a number of limitations regarding the evidence: Firstly, the benefit from advance care planning alone, distinct from delivery as part of a specialist palliative care service cannot be isolated from the most robust data. The details of what elements of advance planning were included, or how it was conducted were not provided. Also, although blinding of participant and clinicians was not possible, those collecting outcome data did not appear to be blinded either which could have led to bias. Although only one trial was multi-site, the risk of contamination was not discussed. The data for advance care planning in routine care are promising, but further testing is needed. Secondly, in the observational studies, many confounders were not addressed. Lastly, although a significant number of patients are represented, there were few studies and meta-analysis was not possible due to the differences in population, intervention, comparator and outcomes

Limitations relating to the systematic review are those inherent with the methods. Despite searching a range of sources we may have missed important papers. Only a proportion of studies had data extracted by two researchers.

Implications for clinical practice

In the light of the emerging evidence base in generic advance care planning studies and encouraging findings in this review advance care planning for people with advanced heart failure seems to be beneficial and possible to implement in routine practice. Advance care planning delivered as part of

specialist palliative care appears to be helpful in terms of hospital use, symptoms and quality of life. However, implementation of advance care planning by cardiology clinicians as part of usual care, but supported by specialist palliative care as needed, is an attractive approach as it would enable *all* patients with advanced heart failure to have the opportunity to have their preferences identified and supported where appropriate and possible. The relatively scarce resource of specialist palliative care would therefore be triaged for patients with complex and persistent concerns. However, issues regarding service configuration, staff training, resources and referral pathways need to be considered and the lack of robust evidence of effectiveness as a stand-alone component recognised. As with any complex intervention which requires ongoing training and support at individual clinician and organisational levels by expert facilitators there are inherent dangers about rolling out at scale. The risk is that the intervention is diminished to a mere document and divorced from the approach to care which provides the context and frame for that documentation. (37)

Implications for research

Given the limitations of the included studies, these data support rather than define a new standard of care for advance care planning for people with advanced heart failure. Multi-centre RCTs which take into account contamination, other confounders, cost-effectiveness and the implications for education, training, and scalability across whole health services should be conducted. Delivery of advance care planning by non-specialist palliative care services seems to be an attractice way forward, but questions regarding effectiveness when delivered as a single component, cost-effectiveness and implementation remain.

For both future research and clinical practice the European Association for Palliative Care's position statement on advance care planning (12) provides a useful framework to ensure core elements are present and important outcome measures, especially those which identify clinical effectiveness in addition to merely noting the presence or absence of advance care planning documentation. In addition, measures of possible advance care planning -related harms should also be included in any trial such as, unresolved distress due to advance care planning, failure for hospital management where this would have been appropriate, beneficial and agreed by the patient, increased carer burden.

CONCLUSIONS

Trials of advance care planning as part of a specialist palliative care care intervention show benefit with regard to supporting patient-preferred place of care and death and reduced hospital admission/time in hospital. Findings from studies where advance care planning is integrated into core cardiology care, with access to specialist palliative care support if needed, are promising and should be tested in future trials.

REFERENCES

1. Dunderdale K, Thompson DR, Miles JNV, Beer SF, Furze G. Quality-of-life measurement in chronic heart failure: do we take account of the patient perspective? European Journal of Heart Failure. 2005;7(4):572-82.
2. Kane PM, Murtagh FEM, Ryan K, Mahon NG, McAdam B, McQuillan R, et al. The gap between policy and practice: a systematic review of patient-centred care interventions in chronic heart failure. Heart Failure Reviews. 2015;20(6):673-87.
3. British Heart Foundation Cardiovascular Statistics Compendium 2017 Oxford, United Kingdom2017 [cited 2017 29 November]. Available from: https://www.bhf.org.uk/research/heart-statistics/heart-statistics-publications/cardiovascular-disease-statistics-2017.
4. Lyons P, Verne J. Pattern of hospital admission in the final year of life. BMJ Supportive & Palliative Care. 2011;1(1):81.
5. Gheorghiade M, Vaduganathan M, Fonarow GC, Bonow RO. Rehospitalization for Heart Failure: Problems and Perspectives. Journal of the American College of Cardiology. 2013;61(4):391-403.
6. Jaarsma T, Beattie JM, Ryder M, Rutten FH, McDonagh T, Mohacsi P, et al. Palliative care in heart failure: a position statement from the palliative care workshop of the Heart Failure Association of the European Society of Cardiology. European Journal of Heart Failure. 2009;11(5):433-43.
7. Gadoud A, Jenkins S, Hogg K. Palliative Care for people with heart failure: Summary of current evidence and future direction. Palliative medicine. 2013;27(9):822-8.
8. Bekelman DB, Rumsfeld JS, Havranek EP, Yamashita TE, Hutt E, Gottlieb SH, et al. Symptom Burden, Depression, and Spiritual Well-Being: A Comparison of Heart Failure and Advanced Cancer Patients. Journal of General Internal Medicine. 2009;24(5):592-8.
9. Lewin WH, Schaefer KG. Integrating palliative care into routine care of patients with heart failure: models for clinical collaboration. Heart Failure Reviews. 2017:1-8.
10. Living and Dying with advanced heart failure: a palliative care approach. March 2008 www.palliative.care.scotland.org.uk: Scotland Partnership for Palliative Care; [cited 2017 27-02-2017]. Available from: https://www.palliativecarescotland.org.uk/content/publications/HF-final-document.pdf.
11. Johnson M, Houghton T. Palliative care for patients with heart failure: description of a service. Palliative medicine. 2006;20(3):211-4.
12. Rietjens JAC, Sudore RL, Connolly M, van Delden JJ, Drickamer MA, Droger M, et al. Definition and recommendations for advance care planning: an international consensus supported by the European Association for Palliative Care. The Lancet Oncology.18(9):e543-e51.
13. Detering KM, Hancock AD, Reade MC, Silvester W. The impact of advance care planning on end of life care in elderly patients: randomised controlled trial. BMJ. 2010;340:c1345.

14. Dixon J, Matosevic T, Knapp M. The economic evidence for advance care planning: Systematic review of evidence. Palliat Med. 2015;29(10):869-84.
15. Klingler C, in der Schmitten J, Marckmann G. Does facilitated Advance Care Planning reduce the costs of care near the end of life? Systematic review and ethical considerations. Palliative Medicine. 2016;30(5):423-33.
16. Brinkman-Stoppelenburg A, Rietjens JA, van der Heide A. The effects of advance care planning on end-of-life care: a systematic review. Palliat Med. 2014;28(8):1000-25.
17. Weathers E, O'Caoimh R, Cornally N, Fitzgerald C, Kearns T, Coffey A, et al. Advance care planning: A systematic review of randomised controlled trials conducted with older adults. Maturitas. 2016;91:101-9.
18. Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343.
19. CASP. Critical Appraisal Skills Programme: Cohort Checklist. [online] Available at: http://www.casp-uk.net/checklists 2017 [
20. Brännström M, Boman K. Effects of person-centred and integrated chronic heart failure and palliative home care. PREFER: a randomized controlled study. European Journal of Heart Failure. 2014;16(10):1142-51.
21. McAlister FA, Wang J, Donovan L, Lee DS, Armstrong PW, Tu JV. Influence of Patient Goals of Care on Performance Measures in Patients Hospitalized for Heart Failure: An Analysis of the Enhanced Feedback for Effective Cardiac Treatment (EFFECT) Registry. Circulation: Heart Failure. 2015;8(3):481-8.
22. Denvir MA, Cudmore S, Highet G, Robertson S, Donald L, Stephen J, et al. Phase 2 Randomised Controlled Trial and Feasibility Study of Future Care Planning in Patients with Advanced Heart Disease. Scientific Reports. 2016;6.
23. Wong F, Yuet K. Effects of a transitional palliative care model on patients with end-stage heart failure: a randomised controlled trial.: Heart; 2016. p. 1100.
24. Rogers JG, Patel CB, Mentz RJ, Granger BB, Steinhauser KE, Fiuzat M, et al. Palliative Care in Heart Failure: The PAL-HF Randomized, Controlled Clinical Trial. Journal of the American College of Cardiology. 2017;70(3):331-41.
25. Schellinger S, Sidebottom A, Briggs L. Disease Specific Advance Care Planning for Heart Failure Patients: Implementation in a Large Health System. Journal of Palliative Medicine. 2011;14(11):1224-30.
26. Butler J, Binney Z, Kalogeropoulos A, Owen M, Clevenger C, Gunter D, et al. Advance directives among hospitalized patients with heart failure. JACC: Heart Failure. 2015;3(2):112-21.
27. Johnson M, Nunn A, Hawkes T, Stockdale S, Daley A. Planning for end-of-life care in heart failure: Experience of two integrated cardiology-palliative care teams. British Journal of Cardiology. 2012;19(2):71-5.
28. Sahlen K-G, Boman K, Brännström M. A cost-effectiveness study of person-centered integrated heart failure and palliative home care: Based on a randomized controlled trial. Palliative Medicine. 2016;30(3):296-302.
29. Kavalieratos D, Corbelli J, Zhang D, Dionne-Odom JN, Ernecoff NC, Hanmer J, et al. Association between palliative care and patient and caregiver outcomes: a systematic review and meta-analysis. Jama. 2016;316(20):2104-14.
30. Ringash J, O'sullivan B, Bezjak A, Redelmeier DA. Interpreting clinically significant changes in patient-reported outcomes. Cancer. 2007;110(1):196-202.
31. Johnson MJ, MacCallum A, Butler J, Rogers A, Sam E, Fuller A, et al. Heart failure specialist nurses' use of palliative care services: a comparison of surveys across England in 2005 and 2010. European Journal of Cardiovascular Nursing. 2012;11(2):190-6.
32. Isenberg SR, Lu C, McQuade J, Chan KKW, Gill N, Cardamone M, et al. Impact of a New Palliative Care Program on Health System Finances: An Analysis of the Palliative Care Program

Inpatient Unit and Consultations at Johns Hopkins Medical Institutions. Journal of Oncology Practice. 2017;13(5):e421-e30.
33. Gadoud A, Kane E, Macleod U, Ansell P, Oliver S, Johnson M. Palliative Care among Heart Failure Patients in Primary Care: A Comparison to Cancer Patients Using English Family Practice Data. Plos One. 2014;9(11).
34. Morrison RS, Dietrich J, Ladwig S, Quill T, Sacco J, Tangeman J, et al. Palliative Care Consultation Teams Cut Hospital Costs For Medicaid Beneficiaries. Health Affairs. 2011;30(3):454-63.
35. Morrison RS, Penrod JD, Cassel JB, Caust-Ellenbogen M, Litke A, Spragens L, et al. Cost savings associated with US hospital palliative care consultation programs. Archives of internal medicine. 2008;168(16):1783-90.
36. Isenberg SR, Lu C, McQuade J, Razzak R, Weir BW, Gill N, et al. Economic evaluation of a hospital-based palliative care program. Journal of oncology practice. 2017;13(5):e408-e20.
37. Seymour J, Clark D. The Liverpool Care Pathway for the Dying Patient: a critical analysis of its rise, demise and legacy in England. Wellcome Open Research. 2018;3.

STUDY ID	DESIGN/ SETTING	POPULATION	STUDY AIM	INTERVENTION	COMPARATOR	OUTCOMES	FINDINGS
Randomised Controlled Trials: *Sample size calculated to achieve 80% power at a significance level of 0.05 #Feasibility study, not powered for effect							
Wong et al 2016	* RCT Multi-site Hong Kong Post DC	N = 84 INT = 43 CONT = 41 NHYA III-IV: 89.3% Age: Mean 78.3 SD 16.8 Male 56% Mean DM 41% Mean CKD 52%	To examine the effects of home-based transitional PC program for patients with ESHF post hospital DC	12 wk program post DC; Integrated SPC model, support from MDT **ACP involves discussion of EOL issues and treatment preferences** FU: 12months (reported to 12wk) *SPC based intervention*	UC: SPC medical clinic, DC advice and referral PRN	*Primary outcome* 4 wk adm *Secondary outcomes: measured over 4 and 12 wk, results for 12 wk,* Adm Symptoms (ESAS), QOL (McGill, CHQ)	**Admissions:** *4 wk adm rate:* INT 0.21 vs CONT 0.41 p=0.10 *12 wk adm rate:* INT 0.42 vs CONT 1.10 p=0.001 *RR of adm:* INT 4wk 0.81 (CI 0.51-1.27) INT 12 wk 0.55 (0.35-0.88) **Symptoms** *Depression* improved ESAS INT 45.9% vs CONT 16.1% p<0.05 *Dyspnoea* improved ESAS INT 62.2% vs CONT 29% p<0.05 Total improved ESAS INT 73% vs CONT 41.4% p>0.05 **QOL** McGill: 6.16 SD 0.44 vs 7.37 SD 0.29 (UC); p<0.001 CHQ: 4.47 SD 0.23 vs 5.26 SD 0.17 (UC); p<0.001
Rogers et al 2017	*RCT Single-site USA Pre-Post DC	N = 150 INT =75 CONT = 75 NYHA III-IV 88% Age: Mean 71yrs SD not given Male 53% Mean DM 53% Mean CKD 77%	To assess impact of ITP intervention on HF-related, and overall QOL in advanced HF	Multicomponent, interdisciplinary, SPC intervention, with HF management Protocol driven physical symptom management, psychosocial and spiritual care, **end of life preparation. ACP communication education for NP and discussion and documentation of AD (ongoing)** FU: 3monthly for 4 years *SPC based intervention*	UC: Cardiology driven MDT, standard HF management. PC consult PRN. HFN/Cardiology and GP FU	*Primary Outcome* QOL (KCCQ, FACIT-Pal) *Secondary Outcomes* Caregiver satisfaction, Cost utilisation Spiritual wellbeing (FACIT-Sp) Symptoms: (HADS)	**QOL** *KCCQ*: change from baseline at 24wk 9.49 point diff (CI 0.94-18.05) p=0.03, *FACIT-Pal:* change from baseline at 24wk 11.77 point diff (CI 0.84-22.71)p-0.035 change at 12wk not given for either score but trend for less diff on graph *FACIT-Sp*: greater improvement in INT group at 24w - diff 3.98 (CI 0.46-7.50)p=0.027 **Symptoms** *HADS-Dep*: reduction greater in INT group at 24w difference -1.94 (CI -3.57-0.31)p=0.020 *HADS-Anx*: reduction greater in INT group at 24w difference -1.83 (CI-3.64—0.02)p=0.048 **Admissions/mortality:** No statistical difference in 6m mortality hospital adm rate

Denvir et al 2016	Phase 2# RCT/ Wait-list design Single-site UK Pre-post DC	N =100 E =50 D =50 Elderly (>70), advanced heart disease (HF & ACS no NYHA data) Age: Mean 81yrs SD not given Male 60% Mean DM 38% Mean CKD 62%	Assess the feasibility and acceptability of FCP in patients with advanced heart disease	FCP: initial OPD with cardiologist and TN (trained in FCP principles) then 2 HV with TN over 12 wk. **Aim is to discuss and prepare FCP**. Record is given to patients, GP and after hours EHR. Focus on communication with service providers, patients and teams. (**ACP = FCP)** All patients received FCP either 1st 12wk or 2nd FU: 24wk *Cardiology based intervention*	DELAYED 'D' group had UC 1st 12 wks, then FCP 2nd 12wks EARLY 'E' group had FCP 1st 12wk, then UC 2nd 12 wk UC not stated	*Primary Outcome* HQRL at 12wk (EQ5D) Symptoms (ESAS), Psychological distress (Kessler questionnaire) *Secondary Outcome-* Healthcare usage Place of death and carer outcomes between 2 groups	**QOL** *EQ5D:* no significant mean diff between 2 groups 12wk (-0.01 CI -0.16,-0.13 p=0.86) or 24wk (-0.07 CI -0.25,0.11p=0.44) EQ5D VAS: no diff between 2 groups at 12 or 24wk **Symptoms** ESAS: no statistical mean diff between 2 groups at 12wk (0.62 CI -8.34,9.58, p0.89) or 24wk (3.18 CI -6.90 13.26 p0.52) **Admissions** Significant diff in number of nights in hospital at 12wk E 2.7 (SD5.5) vs D 5.4 (SD9.4) p=<0.01 and 24wk E 8.6(SD15.3) vs D 11.8(17.1) p=<0.01 No diff in mean adm at 12wk E 0.5(SD0.9) vs D 0.4(SD0.6) p=0.6 or 24w E 0.8(SD1.3) vs D 0.7(SD0.7) p=0.54 **Mortality** No difference in mortality at 12 or 24wk **Place of death** E: hospital 3/4(75%), home 1(25%) D: hospital 1/3(33%) hospice 1(33%), care home 1 (33%), home 0 No diff in carer distress scores between 2 groups.
Brannstrom et al 2014	*RCT Single-site SWEDEN OUTPT Home	N=72, PREFER = 36 UC =36 HF NYHA III-IV 100% Age: INT Mean 81.9 SD 7.2 CONT Mean 76.6 SD10.2 P=0.012 Male 78.8% Mean DM =	Evaluate outcomes of PREFER with regards to symptoms, HQRL and hospitalisation compared with UC	PREFER: integrated interdisciplinary home based model combining community PC and cardiology teams to provide patient centred care. Team approach initially with physician and specialist nurse At 6m hand back to regular provider with management plan. **ACP based on ESC principles, enrolment on PC registry, plan back to providers**	UC: GP or Medicine-Geriatric clinic FU	*Primary outcome:* Symptom burden (ESAS), QOL (KCCQ-12, EQ-5D) and functional classes (NYHA) *Secondary outcome:* Hospitalisations and days spent in hospital	**QOL** EQ-5D PREFER increased at 6m. The between group age-adj delta-value of HRQL baseline to 6m better for PREFER vs UC (p=0.02) **Symptoms** ii) KCCQ-12 Symptom summary scores were better in PREFER (55.9 SD 20.6 vs 65.8 SD 25.8, p=0.041) ESAS: no significant diff were found between groups. Numerical improvements were observed in 8/9 items in PREFER vs 4/9 in UC, Nausea improved PREFER 2.3 SD 2.7 and not in UC 1.2 SD 1.7 (p0.0) NYHA improved at 6m PREFER 36% vs UC 9% (p0.015)

		18% Mean CKD = 65%		FU: 6months *Combined SPC and Cardiology intervention*			**Admissions** Mean hospitalisations less PREFER 0.42 SD0.60 UC 1.47 SD 1.81 (p<0.009), Mean no days in hospital lower in PREFER 2.9 SD 8.3 vs UC 8.5 SD 12.4 (p0.011) **Costs** Cost analysis: GP increased 16,468 euro for 296hr PREFER vs 8075 euro for 144hr UC Emergency transport decreased 3525 for 11 trips PREFER vs 15061 for 47 trips UC Other medical professionals increased 68103 for 2381hr PREFER vs 6807 for 238hrs UC. Hospital care decreased 58793euro for 103 days PREFER vs 176357euro for 309 days UC
Observational studies							
Schellinger et al 2011	Retrospective Cohort Multi site USA OUTPT	N=1894 DSACP =602 No DSACP = 1292 NYHA not reported Age = 81% >65y Male 49% Mean DM = 43% Mean CKD = 42%	Describe the initial outcomes for the 1st 2 yrs implementing DS-ACP for HF in a large health system	DS-ACP: in-depth planning discussion for patients with advanced chronic illness, their chosen health agent +/-family. Proactive intervention to explore understanding of illness/fears gaps in information. **ACP:Planning for complications and decision making with preparation of Statement of Treatment form as well as Advance Directives**. *FU: 2 years* *SPC based intervention*	Not stated	*Primary Outcome:* ACP documentation on EHR. Inpatient or ED admission within 30 or 60 days of referral *Secondary outcomes:* For those that died; hospice use, hospice LOS, Characteristics of those completing DS-ACP	**ACP documentation** Health Directives: DS-ACP 94% vs no DS-ACP 24.8% p<0.001 POLST: documented in DS-ACP 3.8% vs no DS-ACP 0% Statement of Treatment: DS-ACP only 84.8% vs 0% p<0.001 **Admissions** Hospital Readm: Those who completed DS-ACP with 30days of DC had reduced adm at 30 and 60 days vs those completed within 60days and no ACP. (Not statistically significant) ED Adm: no observable diff in ED attendance **Hospice use** Increased hospice use in DS-ACP 56.1% vs no DS-ACP 37.3% p<0.002, No diff in hospice LOS OR for DS-ACP for hospice use 2.21 CI 1.3-3.7 p=0.03 Type of referral was associated with participation in DS-ACP p>0.001 Referrals from physicians/clinic (DSACP 40% vs 25.4%) or NCM (DSACP 30% v14.4%) compared with DC order (DSACP 23.9% vs 54.7%)

Johnson et al 2012	Prospective Cohort study 2 sites UK OUTPT	N=126 Site 1(S1)=46 Site 2(S2)=79 NHYA II-IV = 100% Age Mean = 78yrs SD10.7 Gender Male 62 (DM and CKD data not given)	Describe care received by patients with advanced HF in two integrated teams with regard to place of death and evidence of advance planning	**Assessed both services for recognition of advanced HF close to death, evidence of EOLC in relation to POD, supportive and palliative care services accessed** Site 1: MDT(Cardiology, PC), 24/7 phone support, hospice, hospital beds, minimal nursing at home for dying patients Site 2: no formal MDT, back up cardiology/PC support, (increased services for dying patients at home) FU: 12 months *Combined SPC and cardiology intervention*	National data And between two sites	*Primary Outcome:* Evidence of recognition of advanced HF in people who died within 12m of referral Evidence of planning for EOLC, Supportive and PC services	**Recognition of those within 12 months of death** Time from adm to service -> death longer in S2 206 days vs 50 days S1 Surprise question -> death longer in S2 171 vs 36 days S1; Surprise question agreed in 70%, 89% died in 12/12 **Evidence of ACP** PPD known S1 78% S2 55% S2 higher PPD and actual POD home 25/39 vs S1 10/30 (ACT/PREF) **Hospice/palliative care service use** SPC to death 77days S2 vs 29 days S1, Hospice deaths higher in S1 15/7 vs S2 6/5 hospital deaths S2 32/2 vs S1 9/1 SPC used in 72% in S1 and 34% S2
McAlister et al 2015	Retro-cohort Multi-site CANADA INPT	N=8339 DNR = 2112 CPR = 6227 HF = 85% NYHA II-IV Age Mean =77yrs SD not recorded Male 51% Mean DM = 34% CKD: % eGFR <30 mL/min = 22	Explore the associations between DNR designations, quality of care and outcomes	Used patient data from the EFFECT trial to perform chart review comparing **those with DNR designation to those for full resuscitation (CPR)** EFFECT: Enhanced Feedback For Effective Cardiac Treatment Population Cluster Randomised trial involving 86 hospitals with acute admissions for AMI or acute HF. *Use of secondary trial data*	Comparison between DNR and CPR	*Primary Outcome:* Examine the DNR order in hospitalised HF pts Examine the association between DNR orders and and outcomes *Secondary Outcome:* Difference in quality of care between DNR and CPR	N=6227, 1220 DNR on admission, 892 changed to DNR during admission **Characteristics of those with DNR** DNR older 85yrs SD8 vs 74yrs SD 12 p<0.001, more likely to be female 68% vs 57% p<0.001, live in aged facility 49% vs 5% p<0.001, have Dementia 32% vs 5% p<0.001 **Service use** DNR > DC to continuing care or palliative care unit 5%vs 1%, or aged facility 41% vs 6% p<0.001 Medications as measure of ideal treatment less frequent in DNR group ED visit at 30 days same **Mortality** DNR Higher 30 day mortality 15% vs 3% p0<0.001, 6m mortality 37% vs 13% <0.001 and 12m mortality 49% v 21% p<0.001 **Admissions** All cause readmission at 30 days, 6m, 12m same

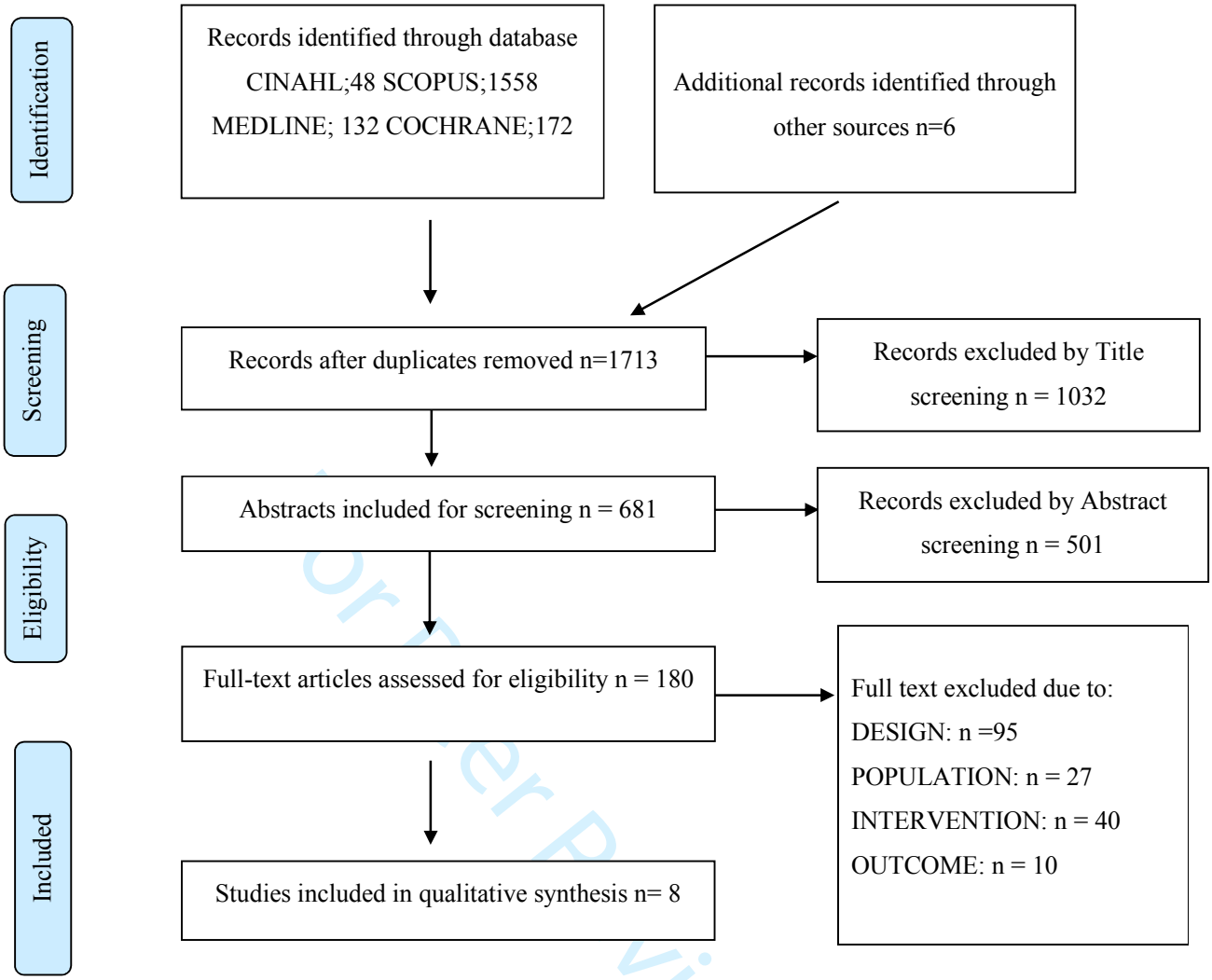
Butler et al 2015	Retro-cohort Single – centre USA INPT	Primary diagnosis HF 3592; with AD 413, no AD 3179 Primary or comorbid HF NYHA not reported Age Mean 63.9yrs SD 15.9 Male 56% DM not stated CKD: creat>2.75mg/dl 15.6%	Assess frequency and correlates of documented AD among hospitalised HF patients	Retrospective case file review of all patients admitted to 2 hospitals with primary or secondary diagnosis of **HF to assess presence of AD.** The 2 units shared online medical record, which recorded AD and full medical history. Follow up 5 years *Intervention based on usual medical care*	No AD	*Primary Ouctome:* Prevalence of AD in EHR during or before adm *Secondary Outcomes:* Time to creation of AD, Characteristics of those with AD Mortality Admissions	Primary HF patient analysis only used: **Prevalence of AD** 11.5% had AD documented **Patient characteristics** AD less common in African American descent 42.9% vs white 56.1% p<0.01 Increased rate of AD in more affluent 42.4% vs 28.6% lowest p<0.001 **Mortality** Higher in-hospital mortality in AD 9.9% vs 4.5% p<0.001 **Hospice use** Higher rate DC to hospice AD 22.3% vs 6.4% p<0.001 **Admissions** No of readm over 5 years: Initially *reduction* year 1: AD 37.7% vs 58%, Years 2-3 *increase*: AD 40.4% vs 27.4% Then *reduction* years 4-5: AD 26.9% vs 14.6% (p<0.001)
Overall: N = 14,357, Age (Mean) 75yrs, Male = 58%, mean DM = 38%, estimated average CKD = 53%							

ACP = advance care planning, ACS = recent acute coronary syndrome, ACT = actual, AD = advance directive, adm = admission/ admitted, , AMI = acute myocardial infarct, Brad = Bradford and Airedale HFNS, CHQ = chronic heart failure questionarie – Chinese version, CI = confidence interval, CKD = Chronic Kidney Disease, CONT = control, creat = creatinine, CPR = cardiopulmonary resuscitation, D = delayed or control group, DC = discharge, diff = difference, DM = diabetes , DNR = do not resuscitate, DS-ACP = Disease Specific Advance Care Planning, E = Early or Intervention group, ED = emergency department, eGFR = estimated glomerular filtration rate, EHR = Electronic Health Record, EOL = end of life, EQ5D = EQ5D quality of life scale, EQ5D VAS = EQ5D visual analogue scale, ESAS = Edmonton Symptom Assessment Scale, ESC = European Society Cardiology, ESHF= end stage heart failure, FACIT-Pal = Functional Assessment of Chronic Illness Therapy Palliative Care Scale, FACIT-Sp = Functional Assessment of Chronic Illness Therapy Spiritual Wellbeing Scale, FCP = future care planning, FU = follow up, GP = general practitioner, HADS- Anx = Hospital Anxiety Score, HADS – Dep = Hospital Depression Score, HF = heart failure, HQRL = health related quality of life, hr = hours of practice, HV = home visit, INPT = inpatient, INT = intervention, ITP = interdisciplinary palliative care, KCCQ = Kansas City Cardiomyopathy Questionnaire, LOS = length of stay, m = months, McGill = McGill Quality of Life questionnaire;Hong-Kong, MDT = multidisciplinary team, med = medication, mx = management, N = total number participants, NYHA = New York Heart Association rating of heart failure, OPD = outpatients department review, OR = Odds Ratio, OT= occupational therapist, OUTPT = outpatient, NCM = nurse care manager , NP = nurse practitioner, PC = palliative care, , p/c = phone call or telephone follow up, POD = place of death, POLST = Physician Orders for Life Sustaining Treatment, PPD = preferred place of death, PREF = preferred, PRN = as required, Prov = provider(s), PT = physiotherapist, QOL = quality of life, Readm = readmissions, RCT = randomised control trial, RR = relative risk, Scar = Scarborough HFNS, SD = standard deviation, SPC = specialist palliative care, TN = trial nurse, UC = usual care, UK = United Kingdom, USA = United States of America, wk = weeks, yrs = years

Table 2. Outcomes by model of ACP delivery

STUDY ID	Hospital admissions	Specialist palliative care use	Symptoms	Quality of Life	Concurrence with end of life preferences
MODEL: ACP delivered as part of a specialist palliative care intervention					
Wong et al 2016 RCT	DECREASED	NOT MEASURED	IMPROVED	IMPROVED	NOT MEASURED
Rogers et al 2017 RCT	UNCHANGED	NOT MEASURED	IMPROVED	IMPROVED	NOT MEASURED
Schellinger et al 2011 Observational	DECREASED	INCREASED	NOT MEASURED	NOT MEASURED	INCREASED
MODEL: ACP delivered as part of an integrated cardiology-specialist palliative care intervention					
Brannstrom et al 2014 RCT	DECREASED	NOT MEASURED	IMPROVED	IMPROVED	NOT MEASURED
Johnson et al 2012 Observational	NOT MEASURED	IMPROVED	NOT MEASURED	NOT MEASURED	IMPROVED
MODEL: ACP delivered as part of cardiology or general medical care					
Denvir et al 2016 Feasibility RCT	DECREASED	INCREASED	NO DIFFERENCE	NO DIFFERENCE	NO DIFFERENCE
McAlister et al 2015 Observational	NO DIFFERENCE	INCREASED	NOT MEASURED	NOT MEASURED	NOT MEASURED
Butler et al 2015 Observational	DECREASED	IMPROVED	NOT MEASURED	NOT MEASURED	NOT MEASURED

ACP = Advance care plan; RCT= randomised controlled trial;



Online Table 1. Quality assessment randomised controlled trials

STUDY	SELECTION BIAS/ ALLOCATION BIAS	PERFORMANCE BIAS	DETECTION BIAS	ATTRITION BIAS	REPORTING BIAS	OTHER
Wong, 2016	LOW Randomisation by "Research Randomiser"	HIGH Neither subjects nor providers blinded due to structure of design	HIGH Neither providers nor researchers blinded due to structure of design	LOW All subjects accounted for	LOW All pre-specified outcomes reported	Sample Size Sample size reached
Rogers, 2017	LOW Complete randomisation schedule	HIGH Neither subjects nor providers blinded due to structure of design	HIGH Neither providers nor researchers blinded due to structure of design	LOW All subjects accounted for	LOW All pre-specified outcomes reported	Sample size Sample size reached
Denvir, 2016	LOW crossover design 1:1 Random permuted blocks	HIGH Neither subjects nor providers blinded due to structure of design	UNCLEAR Not stated who recorded/collected data	LOW All subjects accounted for	LOW All pre-specified outcomes reported	Sample size Sample size reached Only 2 providers (1x cardiologist 1x NP)
Brannstrom, 2014	LOW Envelopes in blocks of 20	HIGH Neither subjects nor providers blinded due to structure of design	HIGH Neither providers nor researchers blinded due to structure of design	LOW All subjects accounted for	LOW All pre-specified outcomes reported	Sample size Sample size reached

Online Table 2. Quality appraisal observational studies

STUDY	COHORT RECRUITED IN ACCEPTABLE WAY?	EXPOSURE MEASURED TO DECREASE BIAS?	OUTCOME MEASURED TO DECREASE BIAS?	IDENTIFIED ALL CONFOUNDERS ?	RESULTS?	GENERALISABLE ?
Schellinger et al, 2011	YES Multiple pathways	YES Documented discussions	YES Objective measures	NO ACP done in usual care, contribution of co-morbidity etc.	Reduced significance likely due to short follow up. Increased use hospice strong	YES Shows achievable model Agrees with other data
Johnson et al, 2012	YES All referrals to HFNP	YES Defined each service	YES Objective measures	NO ACP skills of GP, role of co-morbidities	Results comparisons between two groups.	YES Shows two practice models. Follow up/lack of data may have reduced statistical significant results
McAlister et al, 2015	NO Selection limited by eligibility criteria for EFFECT trial so may not be representative of patient population	YES All classified by set DNR criteria, although rudimentary and lacks further categorisation	YES Objective measures	NO Role of different teams to engage in ACP Community supports Admissions to other hospitals	Results good Narrow CI, Odds ratio for 30 day mortality from time of admission	NO Selection restricted by EFFECT trial eligibility However, supports other data
Butler et al, 2015	YES However, coding errors for HF could occur	YES ACP not on E.H.R found to be minimal	YES Objective measures	NO Many confounders discussed, but other include co-morbidity, home services	Increased discharge to hospice strong data	YES Cohort generalizable Supports other data Low uptake ACP

Online Table 3: OVID MEDLINE SEARCH: (23/3/17)

Search	Searches	Results	Annotation
#1	exp Heart Failure/	103111	
#2	Systolic heart failure.mp or Heart Failure, Systolic/	2137	
#3	Diastolic heart failure.mp or exp Heart Failure, Diastolic/	1429	
#4	Ventricular Dysfunction.mp or exp Ventricular Dysfunction/	39694	
#5	Ventricular dysfunction left.mp or exp Ventricular Dysfunction, Left/	26558	
#6	Ventricular dysfunction right.mp or exp Ventricular dysfunction, Right/	4750	
#7	Cardiac failure.mp	10507	
#8	CCF.mp	1099	
#9	HF.mp	25569	
#10	exp Defibrillators	15821	
#11	ICD.mp	23607	
#12	LHF.mp	76	
#13	RHF.mp	404	
#14	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13	186604	POPULATION
#15	Advance care planning.mp or exp Advance care planning/	8324	
#16	Resuscitation orders.mp or exp Resuscitation orders/	3545	
#17	Anticipatory care plan*.mp	15	
#18	Living will.mp or exp Living Wills/	2017	
#19	Advance directive.mp or exp Advance directives/	7034	
#20	Medical directive.mp	53	
#21	End of life plan.mp	134	
#22	End of life discussion.mp	43	
#23	Medical treatment order.mp	2	
#24	15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23	11674	INTERVENTION
#25	14 and 24	211	
#26	Limit 25 to “all adult (19 plus years)”	135	