Using the 'Social Marketing Mix Framework' to explore recruitment barriers and facilitators in palliative care randomised controlled trials? A narrative synthesis review

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Recruitment SR

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Abstract

Background: Effective recruitment to randomised controlled trials is critically important for a robust, trustworthy evidence base in palliative care. Many trials fail to achieve recruitment targets, but the reasons for this are poorly understood. Understanding barriers and facilitators is a critical step in designing optimal recruitment strategies.

Aim: To identify, explore and synthesise knowledge about recruitment barriers and facilitators in palliative care trials using the '6 Ps' of the 'Social Marketing Mix Framework'.

Design: A systematic review with narrative synthesis.

Data sources: Medline, Cinahl, PscyINFO and Embase databases (from Jan 1990 to early October 2016) were searched. Papers included: interventional and qualitative studies addressing recruitment, palliative care randomised controlled trial papers or reports containing narrative observations about the barriers, facilitators or strategies to increase recruitment.

Results: 48 papers met the inclusion criteria. Uninterested participants (Product), burden of illness (Price) and 'identifying eligible participants' were barriers. Careful messaging and the use of scripts/role play (Promotion) were recommended. The need for intensive resources and gatekeeping by professionals were barriers while having research staff on site and lead clinician support (Working with Partners) was advocated. Most evidence is based on researchers own reports of experiences of recruiting to trials rather than independent evaluation.

Conclusions: The 'Social Marketing Mix Framework' can help guide researchers when planning and implementing their recruitment strategy but suggested strategies need to be tested within embedded clinical trials. The findings of this review are applicable to all palliative care research and not just randomised controlled trials.

Keywords: Palliative Care, Palliative Medicine, Terminal Care, Randomized Controlled Trial

Key Messages

What is already known about the topic?

- More randomised controlled trials (RCTs) are required in palliative care to provide the evidence to underpin our clinical practice and care.
- Palliative care RCTs struggle to achieve their recruitment targets.
- The evidence related to the barriers and facilitators to recruitment in palliative care has not yet been synthesised.

What this paper adds

- Uninterested participants (Product), burden of illness (Price), 'identifying eligible participants', the need for intensive resources and gatekeeping by professionals (Working with Partners) are barriers to recruitment.
- Careful messaging, the use of scripts/role play (Promotion), having research staff on site and lead clinician support (Working with Partners) are recommended.

Implications for practice, theory or policy?

- Current evidence about the barriers and facilitators to recruitment to RCTs in palliative care is mostly anecdotal.
- The 'Social Marketing Mix Framework' can help guide researchers when planning and implementing their recruitment strategy.
- More methodological research is needed to help improve recruitment rates to palliative care RCTs.

Recruiting the required number of participants to palliative care research studies is challenging. People can often be 'hard to reach' as they have a diverse range of conditions, are cared for in a wide variety of clinical settings and have unpredictable and complex needs. Recruitment to randomised controlled trials (RCTs) is especially difficult as there are inherent challenges associated with this type of research such as patient[1, 2] or clinician[3] concerns about assignment to a non-preferred treatment arm or to a placebo arm. While recruitment challenges apply to all RCTs, [4, 5] these issues are often heightened in palliative care research as the study population is particularly vulnerable and 'there is often no second opportunity to improve care' (p 70).[6] The difficulty of recruiting participants to palliative care RCTs is reflected in the number of underpowered studies reported in systematic reviews of palliative care interventions.[7-9]

We require adequately powered RCTs to evaluate the safety and effectiveness of health care interventions.This is not only essential to deliver high quality end of life care but is increasingly important as palliative care attempts to justify its role within a complex and resource limited health care system. As an example, an important recent trial finding is that antipsychotic drugs are not beneficial in reducing symptoms of delirium. These findings could be put into practice more rapidly had it not taken over 5 years to reach the target sample size.[10]

Why so many palliative care RCTs struggle or fail to achieve their recruitment targets is an important area of clinical practice that is poorly understood. The use of a memory aid, contact before arrival, cluster consent and 'opt out' consent improved recruitment of people with cancer or organ failure into trials.[11] Strategies that reduce the demand on health care professionals such as a clinical recruiter or automated alert system were seen as the most promising strategies in a review focusing on research studies in general but the studies that were assessed were at high risk of bias.[12] Individuals or organisations prevent eligible patients from entering a palliative care research study because of personal feelings, perceptions and intuitions rather than a formal assessment that involves the patient.[13]

This review is unique as it uses a theoretical framework, the 'Social Marketing Mix Framework', to explore recruitment barriers, facilitators and strategies in palliative care RCTs.[14] Marketing focuses its efforts on meeting the needs of customers by understanding the factors that can influence their decisions to buy a product or sign up to a particular scheme.[15] Social marketing has been used in public health for many years and applies marketing principles to programmes that aim to influence the behaviour of a particular audience to improve their welfare or that of society as a whole.[14] The 'Social Marketing Mix Framework' has been seen as a potentially useful theoretical framework to help organise and plan recruitment activities as well as help to identify factors that can be adjusted to maximise enrollment.[14] It has been applied to trials recruiting the caregivers of patients with Alzheimer's disease[14, 16] and elements of the framework have been used in a successfully recruiting palliative care service delivery trial.[17]

The aim of this review is to identify, explore and synthesise what is known about the recruitment barriers and facilitators in palliative care RCTs using the '6 Ps' of the 'Social Marketing Mix Framework' in order to develop recommendations that can be used to increase recruitment in clinical practice. The '6 Ps' used are: 'Identifying participants' which is defining your target audience, the 'Product' which is the intervention, the 'Price' which is the cost of taking part in the study for participants, the 'Place' is where recruitment activity takes place, 'Promoting the study' is how you reach your target population and 'Working with partners' relates to organisations or individuals who allow access to participants.[14]

Method

Design

Review Question

What can the '6 Ps' of the 'Social Marketing Mix Framework' tell us about the recruitment barriers and facilitators in palliative care RCTs?

Review Design

A narrative approach to synthesis was chosen as this facilitates the incorporation of research and non-research data, to provide new and valuable insights into complex trial recruitment processes.[18] This review has been guided by a narrative synthesis framework made up of four elements[18] as well as the '6 Ps' that make up the 'Social Marketing Mix Framework'. Below is a brief overview of how the four elements of the framework have been applied (see table 1) and further details are discussed within the relevant sections below.

Table 1: Narrative Synthesis Framework[18]

Element 1: The role of theory in evidence synthesis	The 'Social Marketing Mix Framework' was the theory chosen.[14] Theory in a review informs the data extraction process, contributes to the interpretation of findings and is valuable in assessing how widely applicable the findings may be in practice (p12).[18]
Element 2: Developing a preliminary synthesis	Descriptive data about each included study was organised into a table. Relevant sections of included papers were coded line by line using predetermined and open codes. Codes were then organised into categories and refined to develop broader themes.
Element 3: Exploring relationships within and between studies	Tabulation allowed themes to be conceptually mapped within the chosen theoretical framework. This allowed the most common themes across all of the studies to be identified as well as those that apply to the patient, carer

	or health care professional.
Element 4: Assessing the robustness of the synthesis	Under this approach, this involves an overall assessment of the strength of the evidence for drawing conclusions on the basis of the narrative synthesis and being thorough while critical of the methodological approach used to synthesise your findings (p15).[18]

Search Strategy

Embase, Medline, psychINFO and CINAHL databases were searched from the 1st January 1990 until the 8th October 2016 (see figure 1). The search included the terms palliat*, hospice* and ''terminal care'' as they are seen as a robust and valid strategy to identify and retrieve palliative care literature. [19-21] The search terms used within Medline via EBSCO were palliat* or hospice* or terminal care or palliative care/ or palliative medicine/ or terminal care/ (not exploded) and randomi*ed controlled trial* or randomised controlled trial/ (publication and topic). The limits set were human, papers published between 01/01/1990 - 08/10/2016 and randomised controlled trials. The strategy was modified as necessary for the other databases searched. (see supplementary data table 1 for further details of the search terms used). The reference lists of the included studies were also hand searched to identify additional papers specifically focusing on recruitment to palliative care RCTs.

Study Eligibility

The inclusion and exclusion criteria are listed in table 2. Titles and abstracts were screened by a reviewer (LD) to identify potentially eligible papers and another reviewer independently verified 10 % (AO) of this search. One reviewer (LD) screened the remaining full papers to identify the final included papers.

Table 2: Inclusion and Exclusion Criteria

Inclusion	Exclusion
Study Population Cancer ☐ Adult cancer patients with incurable disease (defined by tumour staging) ☐ Non-professional carers of cancer patients with incurable disease ☐ Parents of children with incurable cancer Non-Cancer • Adults with a progressive, life threatening disease (defined by classifications of disease severity such as New York Heart Association Class, NB this would include patients classed in the literature as 'frail elderly' if they were receiving an intervention that was clearly a palliative care intervention. ☐ Non-professional carers of patients with a progressive, life threatening disease ☐ Parents of children with a progressive, life threatening disease **Study Design** The types of papers listed below were included if they contained information about the barriers, facilitators or strategies to recruitment to palliative care RCTs: ☐ Randomised Controlled Trials: Pilot/feasibility studies as well as full scale palliative care RCTs ☐ Intervention studies testing recruitment strategies ☐ Qualitative/observational studies that report barriers, facilitators or strategies to recruitment to palliative care RCTs ☐ Articles reporting narrative opinions and/or observations related to conducting a palliative care RCT	**Study Population** • Adult cancer patients with potentially curable disease • Care of chronic non-life threatening conditions without a curative treatment option • Those studies including patients with both curable and incurable disease if it is impossible to distinguish findings between groups • Primary endpoint of the study is survival or tumour/disease response (NB would be included if the study is testing an intervention that is clearly a palliative care intervention. [22] • Neo adjuvant or adjuvant chemotherapy studies • Palliative care RCTs only recruiting health professionals **Study Design** Non randomised trials

Recruitment SR

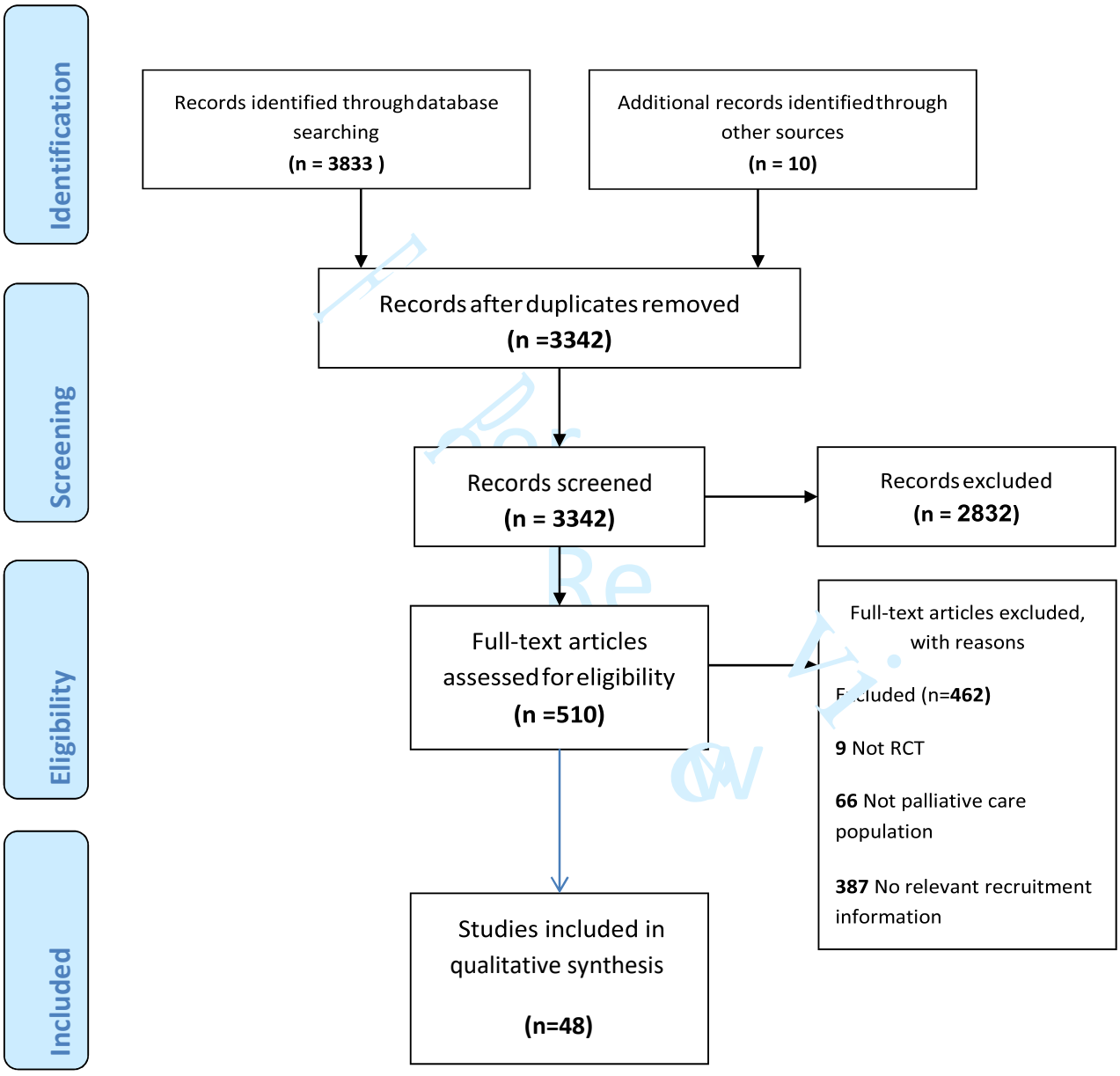

Figure 1: PrismaFlowchart

Data Extraction

NVivo 10 was used to support the data extraction and synthesis process. Descriptive data about each included study was extracted and organised into a table (see table 4). Interview data from patients taking part in a palliative care RCT or professionals involved in recruitment to a RCT and it's subsequent analysis reported in the included qualitative papers was extracted. Data in the form of narrative observations located in the discussion sections of RCT result papers or retrospective reports of researchers' experiences of recruiting to a trial were also extracted. The amount of data extracted was variable across the included studies. Data extraction was carried out by one reviewer (LD) but 10% of the papers were independently verified (AO).

Data Synthesis

Element 2: Developing a preliminary synthesis

Relevant sections of the included papers were initially coded line by line. A mixture of predetermined (priori) codes, the '6 Ps' from the 'Social Marketing Mix Framework' (see table 3) [14] and open codes were used to ensure important aspects of the data were not missed during coding.[23] Initial codes were then organised into the overarching categories barriers, facilitators and strategies in NVivo. Strategies were viewed as interventions that were implemented to support facilitators and overcome barriers. Within these categories codes were merged as appropriate and refined into broader themes. Coding into themes was carried out by one reviewer (LD) but 50 % (AO) of the papers coded were then independently checked by a second reviewer.

Table 3: The '6Ps' of the Social Marketing Mix Framework

Social Marketing Mix Framework (The 6 'Ps') [14]	**Definitions**
Identifying participants	Defining the target audience (p4).
Product <u>Defining the product:</u>	The intervention is the product (its scientific, theoretical basis, does it meet the needs of the target audience?), the product must address a problem that is perceived as serious and amenable to the intervention (p4). The amount of competition for the

<u>The product's competition:</u>	participant's time and energy (p5).
Price	The cost to the potential participant of taking part in the study (e.g. financial, time, physical and emotional effort)**.** Things need to consider: type of costs and how to minimise the costs (p5-6).
Place (Improving accessibility)	'The location where the participant will receive information about, or engage in, the intervention' (p6).
Promoting the study	'Identify the acceptable avenues that reach the target population' (p7).
Working with partners	'Partners are defined as organisations involved with a social change effort or serving as conduits to target audiences' (p8). Things to consider: partner education, partner referrals and recruitment and barriers to partnering.

Element 3: Exploring relationships within and between studies

Tabulation allowed the overarching categories (barriers, facilitators and strategies) and the themes contained within them to be conceptually mapped with the 'Social Marketing Mix Framework' (see supplementary table 3). This allowed for the most common themes across all studies to be identified as well as how they apply to the patient, carer or health care professional. Potential strategies and facilitators that may help address identified barriers identified in the literature can also be visualised.

Quality Assessment

RCT papers were included to identify recruitment issues rather than assess robustness of findings therefore assessment of the methodological quality of these papers was not carried out. A hierarchy of evidence tool was adapted to assess the level of evidence the identified barriers, facilitators and strategies in the literature were based on (see supplementary data 2).[24] No papers were excluded based on their evidence scoring. This approach was used as the methodology of included papers was mixed and the majority contained non-research evidence. This process allowed judgements to be made about the quality of evidence and the weight that should be given to the extracted data during the synthesis process.[25]

Results

Recruitment SR

This review includes studies testing recruitment strategies (n=3), qualitative explorations of recruitment issues (n=3) and trial reports (n=14) reporting barriers and facilitators to recruitment. Most (n=28) were methodological papers exploring the design of exemplar trial/s. A contextual summary of the included papers with the level of evidence score noted is provided in table 4.[24]

The greatest number of barriers, facilitators and strategies identified could be mapped within the 'working with partners' category and table 3 (see supplementary data) provides a visual overview of how the evidence is weighted within the '6 Ps'.[14]

Recruitment SR

Table 4: Description of Included Studies

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
1 Abernethy et al[26] (US)	A retrospective report of strategies successfully used in a RCT. All of the article.	To evaluate the safety and efficacy of the drug Alvimopan.	RCT, double blinded multi centre	cancer patients hospices, palliative care centres, oncology clinics	N= not stated	N= not stated	Intervention: Alvimopan laxative (2 arms with different doses) Control: placebo	questionnaires and blood samples	2 a
2 Anmari et al[27] (Denmark)	38 39 40	A paper discussing the recruitment strategy and patient reported reasons for non-participation in a RCT. All of the article.	To investigate the effect of a nurse led basic palliative care intervention.	onal interve ntion.	Parallel group RCT multi centre	advanced cancer patients and their carers hospital N=not stated	N= 504 families between October 2011 - February 2013	N=57, not stated	
3 Bakitas et al[28], linked to Bakitas et al[29] (US)		A report of challenges faced during an ongoing RCT. Main section.	To test the efficacy of a psycho-educati		RCT, clinician blinded single centre	advanced cancer patients and carers oncology hospital		N=104 patients, 77 caregivers over 14 months	

Intervention: a 'family and coping-orientated palliative home care intervention' Control: usual care	questionnaire 2 a	
Intervention: weekly telephone sessions with nurse. Optional shared medical appointments with palliative care nurse, physician and other persons living with advanced cancer. Control: usual care	not stated 2 a	

Recruitment SR

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
4 Bakitas et al[29], linked to Bakitas et al[28] (US)	A report of baseline findings and solutions to methodological challenges faced during a RCT. Discussion section.	To test an educational and care management palliative care intervention.	RCT, clinician blinded single centre	advanced cancer patients and carers oncology hospital	N=not stated	N= 322 between Nov 2003 and May 2007	Intervention: a phone-based, nurse-led educational, care coordination palliative care intervention model Control: usual care	questionnaires semi structured interview with a subgroup of participants	2 a
5 Baskin et al[30] (US)	A paper examining barriers to obtaining informed consent by examining the reasons for non-enrolment of eligible patients. Results and discussion section.	To examine the outcomes and acceptability of palliative care approaches compared with usual hospital care.	RCT single centre	advanced dementia patients and their surrogates teaching hospital	N=not stated	N=74 of 146 eligible patients, not stated	Intervention: 'palliative care approaches' Control: usual care	not stated	2 a
6 Bausewein et al[31] (Germany)	A paper reporting the findings from a RCT embedded within a longitudinal study. Discussion section.	To determine the use, acceptance and effectiveness of a hand-held fan to relieve breathlessness, to evaluate recruitment.	Phase II RCT embedded within a longitudinal study multi-centre	advanced lung cancer or COPD hospital, hospice home care and 2 respiratory practices					

N=30 patients in each arm June 2006 to November 2007	N=109 patients were recruited to the main study of which 70 took part in the RCT	Intervention: hand held fan Control: a wristband to serve as a placebo.	interview, post all 2 aquestionnaires

Recruitment SR

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
7 Buss and Arnold[32] (US)	A retrospective report of the experiences of researchers who attempted to set up a RCT. All of the article.	To measure the safety and effectiveness of an anti-nausea agent.	RCT, double blinded single centre	home hospice patients hospice at home	N=Not stated	Failed in set up	Intervention: anti emetic cream Control: placebo	questionnaires	2 a
8 Buss et al[33] (US)	A paper reporting the authors' experiences of recruiting to two related RCTs Discussion section.	To examine the impact of CHESS on caregiver outcomes of affect and QOL.	Longitudinal RCT multi centre	advanced cancer cancer centre	126 patient /carer dyads per arm	Overall, 50% patient/ carer dyads enrolled in the study	Intervention: a web-based information and support system (CHESS) Study 1 CHESS and clinician rapport or CHESS Study 2 CHESS and clinician rapport or control access to computer/internet	survey	2 a
[34] 9 Clark et al (Australia)	39 40	A paper reporting the findings of a phase II RCT. Discussion section.	To assess the feasibility of early consent and a study of hyoscine hydrobromide and octreotide for management of noisy breathing at the end of life.	A pilot phase II randomized, cross-over, double-blinded, controlled efficacy study. single centre	patients in the terminal phase of their illness inpatient palliative unit	N=10 with complete data	N=from April to November 2001, 49 consented 21 randomised	Intervention: Participants while well and their proxies provided written informed consent. If NB were encountered, people were randomized to 200 mcg octreotide or 400 mcg hyoscine hydrobromide subcutaneously. If subsequent treatment was needed, the other medication was administered.	

five point categorical scale	3

Recruitment SR

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
10 Cook et al[35] (UK)	A retrospective report of the experiences of researchers trying to recruit to a RCT. Introduction.	To assess the effects of three potential xerostomia relieving products.	RCT single centre	palliative care unit patients palliative care unit	N= Not stated	N=4 over 5 months	not stated	not stated	2 a
11Currow et al[36], linked to Le Blanc et al[17] and Mitchell and Abernethy[37] (Australia)	A paper describing the approach used in a large RCT and discusses its impact on palliative care research. Discussion section.	To evaluate service-based interventions.	A 2x 2 x 2 factorial cluster RCT single centre	palliative care patients palliative care service	N=not stated	N=461 patients not stated	The 'Palliative Care Trial' evaluated three interventions: case conferences, general practitioner education, and patient education	questionnaires	2 a
12 Daniels and Exley[38] (UK)	38 39 40	A paper reporting the findings of a qualitative study exploring the experiences of specialist nurses involved in recruitment to a RCT. All of the article.	Qualitative Study: To explore the experiences of specialist nurses involved in recruitment to a RCT. Parent Study: a RCT to evaluate the effectiveness of a new community based service.	Qualitative study single centre	hospice home care team specialist nurses and the lead researcher for the RCT hospice	N= 10 nurses and 1 researcher			

N=10 nurses and 1 researcher	n/a semi structured	3	interview and focus group.

Recruitment SR

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
13 Farquhar et al[39] linked to Farquhar et al[40] (UK)	A paper reporting the findings from a RCT. Discussion section.	To test the feasibility of a single-blinded fast track pragmatic RCT for a breathlessness intervention service.	Single-blinded fast track pragmatic RCT (feasibility) single centre	COPD patients and carers community	N= 28 patients to the trial, maximum	N=14 patients 12 carers	Intervention: a breathlessness intervention service immediately for eight weeks or after an eight week period on a waiting list during which time they received standard care.	interviews and questionnaires	2 a
14 Farquhar et al[40] linked to Farquhar et al[39] (UK)	A poster presentation describing and analysing recruitment trajectories and strategies used in a RCT. All of the poster.	To test a breathlessness intervention service for advanced disease.	Phase II pilot single-blind fast track RCT and phase III RCT	Phase II COPD patients only, Phase III cancer and non-cancer	N=not stated	N=not stated	Intervention: a breathlessness intervention service Control: not stated	not stated	2 a
15 Fischer et al[41] (US)	38 39 40	A paper presenting the findings of a pilot RCT. Discussion section.	To determine the feasibility of a patient navigator interventi on to improve palliative	care outcomes for Latino adults with serious illness.	Pilot RCT single centre	Patients with a serious illness who were appropriat e for a palliative approach hospital	N=Not stated	N=64 May 2010-Sept 2011	

All participants received a packet of linguistically matched materials on palliative care. In addition, intervention participants received up to five home visits from the bilingual, bicultural patient navigator.	questionnaire, 2 medical record review	

Recruitment SR

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
16 Fowell et al[42] (UK)	A paper reporting the findings of a feasibility study that explored cluster randomisation and Zelen's design Discussion section.	To explore the feasibility of cluster randomisation and Zelen's design for trials with dying patients.	Feasibility cross over RCT multi centre	dying patients cancer oncology/ palliative care unit	N=not stated	N= 6, all in the cluster arm	Both units used cluster randomisation or randomised consent for three months and then 'crossed over' designs for a further three months.	medical record review	4
17 Goldstein et al[43] (US)	A report outlining challenges faced by researchers while implementing a RCT and solutions introduced. Discussion section.	To evaluate the effect of a communication intervention on ACP and the management of ICDs	Cluster RCT multi Centre	advanced heart failure patients and their caregiver hospital	N= 09/ 2011-08/ 2015, 100 patients at each site (6 sites)	N=not stated	Intervention: aimed at clinicians, interactive educational session, reminders and individualized feedback Control: no specific communication training, feedback or reminders	survey questionnaires/ medical record review	2 a
18 Goodwin et al[44] (Canada)	38 39 40	A paper examining recruitment to a RCT and analysis of recruitment figures.	Discussion section.	To compare the impact on survival of group psycho-	social support combined with educational materials,	to educational materials alone.	RCT multi centre	metastatic breast cancer cancer centres	

N=256 over 3 years	N=237 June 1993-December 1997	Intervention: expressive-supportive therapy combined with educational materials and usual care. Control: educational materials and usual care alone.	Not stated 2 a

Recruitment SR

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
19Gorman et al[45] (US)	A paper describing lessons learned during an ongoing RCT. Main section.	To compare the effect of home hospice care with such care supplemented with massage.	RCT single centre	advanced cancer hospice	N= 200 over 4 years	N= 75 patients in two years	Intervention: usual care supplemented by five daily massages Control: usual care	questionnaires and daily logs via a touch screen laptop.	2 a
20 Hanson et al[46] (US)	A paper reporting the findings of a qualitative study. All of the paper.	Qualitative study: To describe barriers and strategies for recruitment during a palliative care RCT. Parent study: a RCT where patients are randomized to discontinue or continue on statins.	Qualitative study Parent study: non blinded multi centre RCT.	Qualitative study: PIs and CRCs from 9 sites Parent study: adults with limited life expectancy	Qualitative study: all eligible site PIs and CRCs Parent study: not stated	Qualitative study: N=18 site PIs and CRCs Parent study: N=381 patients	Intervention: discontinue statins Control: continue statins	Qualitative: study: semi structured telephone interviews at end of recruitment. Review of recruitment rates Parent study: interviews and medical record reviews	3
21 Hardy et al[47](UK)	39 40	A paper reporting the findings from two palliative care RCTs. Discussion section.	To determine the effect of dexamethasone when treating malignant bowel obstruction.	Double blind, placebo-controlled cross over study. single centre	advanced cancer cancer centre	N=not stated	Trial 1: 25 patients over 36 months Trial 2: 14 patients in 24 months, study terminated	Intervention: IV dexamethasone Control: placebo, normal saline if obstruction still present at day 5, the patient was 'crossed over' to the other arm	

Not stated

2 a

Recruitment SR

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
22 Higginson et al[48] (UK)	A paper presenting the findings of a RCT. Discussion section.	To determine whether a new palliative care service improves outcomes. To assess recruitment, compliance and follow-up.	Phase II fast track RCT single centre	patients with MS and specialist palliative care needs and their carers community	N=50 patients	N= 52, one year	Intervention: an innovative palliative care service Control: the above after a > 3 month wait and until then received standard best practice	interviews	2 a
23 Hudson et al[49] (Australia)	A paper discussing the challenges of conducting RCTS with reference to ongoing RCT. Main body	To investigate a support and information programme for lay carers of people receiving palliative care.	RCT multi centre	carers of cancer patients dying at home	N=110	N=106	Intervention: nursing support and information programme Control: standard community palliative care support	questionnaires	2a
24 Hussainy and Marriot[50] (Australia)	A retrospective report discussing the impact of using different recruitment strategies. All of the article.	To compare knowledge of those who had interacted with palliative care trained pharmacists versus control.	RCT single centre	advanced cancer or their carers palliative care service	N=20 patients or carers per month, over 3 months, 30 pharmacies	N=42, 36 pharmacies 14 pharmacies were randomised	Intervention: pharmacists who had extra education in palliative care Control: pharmacists who had no additional education	not stated	2a
25 Jones et al[51] (UK)	37 38 39	40	A paper reporting findings of	a RCT. Discussion section.	To test the acceptabi	lity and feasibility of a patient preference RCT of an ACP intervention.		Phase II patient preference RCT multi centre	

advanced cancer hospital and hospice	N=40 in each arm	N= 77	Intervention: structured ACP Control: usual care	questionnaires 2a

Recruitment SR

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
26 Jones et al[52] (UK)	A paper reporting findings of a RCT. Discussion section.	To test the effectiveness of a rehabilitation intervention.	Two-arm, wait-list control, RCT single centre	advanced cancer hospice day therapy	N=240 patients over one year	N=41 over one year	Intervention: complex rehabilitation intervention plus usual care Control: usual care alone. Those in the control arm joined a wait-list and were offered the intervention three months after randomisation.	questionnaires	2a
27 Jordhoy et al[53](Norway)	A retrospective report of recruitment, attrition and compliance arising from an RCT. Discussion section.	To compare comprehensive palliative care to conventional care.	Cluster RCT multi centre	advanced cancer and care givers community/ districts	N=200 patients in each arm over 2 years	N=434 March 1995-November 1997	Intervention: palliative medicine unit organised care Control: conventional care	questionnaires	2 a
28 Kruse et al[54] (US)	A report outlining challenges faced during an ongoing RCT, solutions and keys strategies implemented. Main body	To determine whether regular video conferencing between informal caregivers and the hospice care team alters caregivers' perceptions of pain management and patients' pain.	Non blinded RCT multi centre	primary caregivers of hospice patients hospice at home	N=Not stated	N=249 caregivers of 233 patients randomised	Intervention: biweekly team meetings through video or phone conferencing Control: usual care	questionnaires and interview	2 a

29	Kutner et al[55]	A paper	To investigate the	RCT	advanced	N=440,	N= 380	Intervention: massage	not stated	2 a

Recruitment SR

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
(US)	describing the strategies and responses to methodological challenges faced during a RCT. Main body.	efficacy of massage therapy for decreasing pain.	multi centre	cancer patients palliative care/ hospice settings	modified to 380	over 36 months	therapy Control: simple touch		
30 Latimer et al[56] (Canada)	A paper reporting the findings from a RCT. Discussion section.	To determine the effectiveness and efficiency of a Patient Care Travelling Record©.	RCT single centre	patients under the palliative care team	N= 90 (45 each arm) over 2 years	N= 46 randomised over 2 years	Intervention: the' Patient Care Travelling Record' Control: usual care	questionnaires	2a
31 Le Blanc et al[17], linked to Currow et al[36] and Mitchell and Abernethy[37] (Australia)	A retrospective report of the recruitment challenges faced during a RCT and how they were approached and overcome. All of the paper.	To test different service delivery models to improve pain control in the palliative setting.	A 2 x2 x 2 factorial RCT single centre	hospital outpatients palliative care service patients (or their legal proxy) and their GP. palliative care service	N= 460 patients over 26 months	N=461 patients over 26 months	Intervention: (1) individualized interdisciplinary case conference with their GP versus control, (2) educational outreach visitation to GPs about pain management versus control, (3) structured educational visitation for patients and caregivers about pain management versus control	not stated	2 a

32	Lee et al[57]	A paper	To assess the	Randomized	advanced	N=20	N=9	Intervention:	questionnaires	2 a

Recruitment SR

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
(New Zealand)	reporting the findings and difficulties encountered during a feasibility RCT. Discussion section.	feasibility of conducting a Phase III RCT investigating the therapeutic value of gastrografin in malignant bowel obstruction.	double-blinded placebo-controlled feasibility study single centre	cancer hospital	patients over 8 months	enrolled	gastrografin Control: placebo		
33 McMillian and Weitzner[58] (US)	A report of the researchers' experiences accruing patients after the first year of a RCT with an analysis of the recruitment data. Discussion section.	Not stated	3 arm RCT single centre	advanced cancer patients and their caregiver hospice home care	N= 846 in 28 months	N= 125 patient/ caregiver dyads over 9 months	Intervention: standard care plus supportive visits or standard care plus teaching of a method of coping with patient symptoms Control: standard care	questionnaires	2 a
34 McWhinney et al[59] (Canada)	38	A report outlining the challenges of carrying out RCTs in palliative care.	To evaluate a palliative care home support team.	RCT with wait list design single centre	advanced cancer patients and their caregiver community	N=110 per group	N=146	Intervention: palliative care home support team Control: received intervention after one month	
		Introduction							

ques tionn	a i	r e	,	2 a	n a	usea and pain diary					
35	Miller and	A letter outlining	Not stated	RCT	ambulatory	N=300 over	N=After 12	Intervention: tool	not stated	2	a

Recruitment SR

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
Chibnall[60], linked to Miller et al[61] (US)	the researchers' experiences of recruiting to a RCT. All of the letter		multi centre	patients with life threatening illnesses hospital	6 months	months, 98 recruited	designed to help patients prepare for `a good death' Control: not stated		
36 Miller et al[61], linked to Miller and Chibnall[60] (US)	A paper reporting the findings of a RCT. Discussion section.	To evaluate the effects of a program to address psycho-socio-spiritual needs.	randomized pre-test–post-test trial multi centre	patients with a limited life expectancy hospital	N=Not stated	N=98	Intervention: a group intervention entitled 'Life-Threatening Illness Supportive-Affective Group Experience' for reducing patient spiritual, emotional and death related distress. Control-standard care	questionnaires	2 a
37 Mitchell and Abernethy[37] linked to Le Blanc et al[17] and Currow et al[36] (Australia)	38	A retrospective comparative study of two palliative care RCTs. Discussion section.	QCC and PCT: To assess the effect of case conferences that included GPs and the palliative care team.	QCC: RCT PCT: Pragmatic 2x 2x2 factorial cluster RCT QCC: multi centre PCT: single	centre	QCC and PCC: palliative care patients QCC/PCT: palliative care service	QCC N= 220 PCT: N= 460	QCC: N= randomised 159 (72%) of the target July 2001-May 2003 PCT: N= randomized 461 (100%) participants April 2002-June 2004	

QCC Intervention: case conferences conducted at routine palliative care team meetings. GPs participated by teleconference PCT Intervention: Interdisciplinary case conference including GP conducted at patient's home.	QCC: short data 2 collection instrument, data collected by research assistant PCT: data collection by clinical nurse as part of routine care		

38	Noble et al[62]	A paper	To identify the	Feasibility	patients with	N=Stage 1	N= 5	ongoing LMWH	blood tests,	3

Recruitment SR

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
(UK)	reporting the findings of a feasibility study to inform the design of a RCT. Qualitative study results section.	most effective length of anticoagulation for treatment of cancer-associated thrombosis (CAT). To identify the practicalities of conducting a full RCT.	study RCT with embedded qualitative study multi centre	locally advanced or metastatic cancer oncology outpatients	62 patients registered. If at least 15 randomised then stage 2 would occur, until 200 patients had been registered Qualitative study: 40-60 patients 10-15 carers	December 2013-June 2014. Qualitative study: 15 patients 1 carer	treatment for CAT versus cessation of LMWH at 6 months' treatment	diary cards, QOL questionnaires	
39 Philip et al[63] (Australia)	A paper reporting the findings of a RCT. Discussion section.	To examine the effect of oxygen versus air on the relief of dyspnoea.	Randomized, double-blind, crossover trial multi centre	advanced cancer cancer centres, inpatients and outpatients	N=50	N=51 over 5 years	Randomized to receive either air or oxygen via nasal prongs for 15 minutes. Then, following a 30-minute interval without gas, repeat measurements were taken with crossover to the other gas for a further 15 minutes.	questionnaires, oxygen saturation pulse oximetry	2 a

40 Prentice et al[64] (UK)	A paper reporting the	To determine whether topical	Randomized double blind,	hospice cancer	N= 30 patients	N= 31 patients	Intervention: a single application of	pain scales	2 a

Recruitment SR

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
	findings of a RCT. Discussion section.	benzydamine hydrochloride 3% cream is more effective than placebo in reducing pain related to pressure areas.	placebo-controlled trial. multi centre	inpatients with pain related to pressure areas. palliative care units	into each study group.		benzydamine hydrochloride 3% cream to the painful pressure area. Control: placebo cream to the painful pressure area.		
41 Rees and Hardy[65] (UK)	39	A paper detailing a method of obtaining advance consent for a RCT and the interim recruitment results. All of the paper.	A feasibility study of an advance consent process to support a RCT of two anti-muscarinic drugs in the management of noisy respirations.	Feasibility study of an advance consent process embedded within a RCT single	patients admitted to a palliative care ward who may develop "death rattle" palliative care wards in a cancer centre.	N= 75-100 patients a year, complete the study in three years.	From May to November 2002, 58 patients consented Of these, 15 developed death rattle and were randomised N=400 patients /289 caregivers from August 2004 to November 2006	Intervention: to receive either hyoscine or glycopyrronium at the time of death	
42 Riopelle et al[66] (US)		The paper describes the methodological challenges faced during a RCT and the strategies used to overcome them. Main body.	To evaluate a palliative care intervention for Veterans.	Longitudinal RCT single centre	patients with an advanced life-limiting illness and their caregiver hospital	N=not stated		Intervention: palliative care needs evaluation conducted by an interdisciplinary team, followed by ongoing nurse case management Control: usual care	

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pa tie nts :

2 a int er vie ws re

Recruitment SR

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
43 Sampson et al[67] (UK)	A paper reporting the findings of a RCT. Discussion section.	To assess the feasibility of implementing a ACP intervention.	Initially a two-arm feasibility cluster RCT then amended to individual level randomisation single	advanced dementia and an informal carer for proxy consent hospital	N=40 patient/ carer dyads to each study arm.	N=33 patients and carers	Intervention: a palliative care patient assessment which informed an ACP discussion with the carer Control: usual care	questionnaires	2 a
44 Shelby James et al[68] (Australia)		A paper presenting suggestions made during a national clinical research forum. Main body	N/A	14 clinical studies were discussed, 12 of which were double blind RCTs		N/A	N/A	To date, the Australian Palliative Care Clinical Studies Group has randomized more than 500 participants across 12 sites in 8 Phase III studies.	

N/A

N/A

2 b

Recruitment SR

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
45 Storey[69] (US)	A letter outlining the challenges faced by a researcher while trying to recruit to three RCTs. All of the letter.	not stated	1 Placebo RCT 2 RCT 3 RCT multi centre	hospice/ palliative care hospital patients 1 hospices 2 cancer centre and a hospice 3 hospital that specializes in cardiac care	not stated	1 N=not stated 2 screened almost 2000 hospice patients, 21 recruited 3 no patients in a year	1 Intervention: Mexilitine. for severe neuropathic pain Control: Placebo 2 Intervention: psychological intervention to increase forgiveness Control: not stated. 3 Intervention: low dose oxycodone for breathlessness in advanced HF Control: not stated	not stated	2a
46 Vermandere et al[70] (the Netherlands)	A paper reporting the findings of a RCT. Discussion section.	To investigate the effect of a structured spiritual history taking on the spiritual well-being of palliative patients in home care.	Cluster RCT multi centre	incurable, life-threatening disease home care	275 patient–provider dyads.	N= 99 patients, 245 HCPs, April to October 2013	Intervention: health-care providers took a spiritual history on the basis of the 'Ars moriendi' model Control: usual care	questionnaires	2 a
47 Westcombe et al[71] (UK)	This paper examines the challenges encountered in the design and execution of a RCT. Main body	To examine the effectiveness of aromatherapy in improving psychological distress and quality of life.	RCT multi centre	originally advanced cancer then included all stages of cancer cancer centre	N=original target was 508, reduced the number required from 508 to 258.	over 4 years, 75% longer than expected.	Intervention: aromatherapy massage Control: the first was a no-intervention control and the second relaxation therapy. Relaxation therapy arm removed during the trial.	questionnaires	2 a

Recruitment SR

Reference	Type of article and section recruitment was discussed	Aim original study	Method original study	Sample and setting of original study	Target sample over how long	Sample achieved over how long	Type of Intervention /Control	Data Collection	Level of evidence
48 Zambroski et al[72] (US)	A report outlining the challenges of recruiting to a RCT. Discussion section.	To test the feasibility of delivering the COPE psycho educational intervention.	RCT single centre	heart failure patients and caregivers hospice	N= 84 dyads not stated	N=32 not stated	Intervention: psychoeducational intervention for caregivers Control: not stated	questionnaires	2 a

Recruitment SR

1 Identifying participants: Defining the target audience

Barriers: Identifying participants who meet the study inclusion criteria/difficulty predicting prognosis

The challenge of participant identification and complex inclusion criteria were raised as issues. [30, 43, 46, 52, 57, 67, 70, 72] This can relate to the difficulty of predicting prognosis as part of the trial's eligibility assessment, [36, 43, 45, 46, 56, 59] how palliative care is defined in a particular country[70], too narrow and/or ambiguous inclusion criteria[43, 57] and lack of suitable caregiver[72] or surrogate to gain proxy consent. [30, 67]

Facilitator: Broad study eligibility criteria

Including broad study eligibility criteria in your protocol was seen as an aid to recruitment as it ensured a high percentage of patients screened met the study's inclusion criteria.[17, 68]

Strategy: The use of a physician prognostication tool

The use of a physician prognostication tool to help define and identify those patients with an advanced life limiting illness who were likely to die within the next 12 months alongside face to face screening by a clinician was used as successful strategy in a RCT of an interdisciplinary palliative care needs evaluation.[66]

2 Developing the product:

Defining the product:

Barriers: Participants not interested/clinical equipose

A number of papers highlighted high refusal rates as an issue [27, 31, 33, 36, 55, 62, 71] with the lack of clinical equipoise being cited as a possible reason for this, with concerns about being randomised to their non-preferred arm having an influence on whether or not patients agreed to take part.[62, 71] A lack of belief in the intervention,[31, 33] the lack of an acceptable control,[31] the feeling the intervention was not needed at that particular time [27, 33, 62] and competing priorities [55] were also cited as reasons for refusal. These concerns about the intervention, the control and randomisation also apply to health care professionals and may be one of the reasons for their gatekeeping. [38, 52 32, 47, 71 44]

Facilitator: Replicate clinical practice as much as possible

RCTs that replicated clinical practice in recruitment sites as closely as possible were seen to be more likely to be successful.[68] If in recruitment sites clinical practice varied significantly from the processes outlined in the protocol, clinicians were likely to limit the number of participants they approached or avoid approaching altogether.[68]

Facilitator: Offer a desirable and novel intervention

Offering a palliative care symptom control intervention to a group of patients who normally have limited access to such specialist input was suggested as a possible facilitator. [39]

Strategies: Study design

A fast track design RCT with a short lead in time may have increased the response rate in a trial of a breathless intervention service as patients and families knew they were going to get the intervention either straight away or only after a short wait.[39] There were reports of researchers simplifying their study design during the recruitment phase of the trial. They reduced the number of study arms to reduce the number of participants required to ensure statistical power was achieved.[33, 71]

There were strategies specifically suggested to help improve recruitment rates in drug trials. Giving patients the option to enter an extension study after taking part in a placebo controlled symptom control RCT was seen as important as enrolment was delayed for many patients until this was put into place.[26] Clinician's fears that patients will be left with uncontrolled symptoms if they are randomised to the control arm can be reduced with the inclusion of rescue medications in the study design.[68]

The product's competition:

Barrier: Competing services/competing trials

Potential participant's being able to access information or support services similar to those being offered as part of a study in the recruitment centre or local area, was seen as a barrier to recruitment. Patients were able to access similar therapies and support services without having to accept the restriction of randomisation.[44, 71] Competing trials recruiting from a similar patient population was also seen as barrier in one paper. [44]

3 Price: Managing the price

Type of costs:

Barrier: Patient's condition and illness

Patients and caregivers being too burdened by the illness to participate[27, 46, 56, 58, 62] and the reality of having to deal with the unpredictable nature of the patient's disease in the recruitment process[56, 63] were seen as significant barriers. The right time to approach was seen as an issue in one study, [33] with patients citing the time around their initial diagnosis being the wrong time whilst others offered the intervention at the end of treatment would have preferred the intervention earlier.

Barrier: Carer and patient gatekeeping

Gatekeeping by caregivers was also identified as an issue [46, 58, 72] with reports of carers feeling protective towards their loved ones [46, 58, 72] so blocking researcher access to the patient. These findings correspond with a recent review focusing on gatekeeping in palliative care research generally.[13] In addition, this review identified 'gatekeeping' by patients also as an issue in studies that aimed to recruit patient/carer dyads. This took the form of patients refusing to allow their caregivers to be approached[49] or expressing concerns about the additional burden the study would place on their caregivers as well as making a decision that the caregiver would not derive any benefit from being involved in the research.[33]

Minimising the costs

Facilitator: Minimise burden for participants

There was consensus among a group of palliative care trial experts that recruitment success depended on minimising the burden of taking part in a trial for patients, carers and clinical staff.[68] This involved limiting what was required from those participants who agreed to take part in a study.

Strategies: Consent

Strategies to minimise the costs of taking part in the study for participants were related to the informed consent process. Recruitment over the phone using verbal consent procedures was seen as a successful recruitment strategy for enrolling caregivers as they were sometimes unavailable at the time of patient consent. [66] This allowed carers to be contacted and recruited at a later point in time and it prevented the delays which can be associated with face to face consent. The use of advance consent to improve recruitment rates has been used in two feasibility RCTs[34, 65] and was found to be a workable consent process for patients who are unable to give consent at the time of randomisation. The use of Zelen consent (only those randomised to the experimental treatment need to be individually consented) versus cluster consent was tested within a feasibility RCT.[42] The findings suggested cluster randomisation may be a more helpful approach for increasing recruitment rates in trials with dying patients as nurses were reluctant to approach dying patients for consent to change of treatment.

4 Place: Improving accessibility

Barrier: Recruitment setting

The issue of travel was identified as a reason for patients declining a quality of life RCT[71] in an oncology hospital as these types of interventions can often be provided locally while cancer treatment trials are only available in oncology units. Late referral to hospice services was also seen as a barrier to recruitment as patients were often too ill to take part in the study.[69, 72] Hospice catchment areas could also be too small to provide the necessary pool of potentially eligible patients.[72] Attempting to recruit participants during hospitalisation was seen to be challenging as building rapport and

trust with participants during such a stressful time can be difficult.[41, 67] The role of specialist palliative care as a hospital consulting rather than admitting service was a barrier in a trial recruiting patients with malignant bowel obstruction.[57] In contrast, recruiting participants after discharge was seen as more difficult in a couple of papers[46, 58] with the feeling participants can be less receptive.[46] The physical environment and the often complex nature of patient consultations in the outpatient setting are seen to make approaching participants more difficult.[46, 56]

Strategy: Increase the number of recruitment centres

Increasing the number of recruitment sites during the trial to increase the pool of potential participants was a strategy employed by a number studies to improve their recruitment rates.[26, 44, 71] Some studies were set up as multi centre studies but this did not always guarantee recruitment success.[37, 50]

5 Promoting the study

Facilitators: Key/careful messaging/flexibility and persistence

The importance of paying attention to key and careful messaging when discussing a trial with patients, carers and clinical staff to provide reassurance and to address any concerns was seen as important.[17, 26, 39, 45, 46, 55, 68] Recruiting staff also need to ensure they are flexible and demonstrate respectful persistence[46, 66] while developing a rapport with the patient.[66]

Strategy: Role play/scripts

The use of role play and scripts to ensure those involved in the recruitment process use pre-defined key messaging when introducing a study to patients and carers is seen as a useful strategy.[17, 26, 37, 41, 54, 68] One study described how it had refined its recruitment script during its pilot study to avoid introducing terms such as hospice and end-of-life care early on and decided to focus on quality of life instead.[41]

6 Working with partners

This aspect of the 'Social Marketing Mix Framework' is divided into three areas: barriers to partnering, partner education and partner referrals and recruitment.

Barriers to partnering

Barrier: Health care professional gatekeeping

'Gatekeeping' was seen as a barrier to recruitment to RCTs in palliative care with the majority of papers identifying health care professional gatekeeping as the most difficult issue to overcome.[32, 35, 44, 46, 49-52, 55, 56, 61, 64, 70, 71] Gatekeeping in this context is when health care professionals prevent the researcher from approaching eligible patients and/or carers to discuss taking part in a study. This was related to the professionals fear of over burdening patients, [32, 44, 46, 50, 55, 56, 71] lack of belief in

research,[32, 50] seeing patients as being too poorly[35, 38, 46, 64] or emotionally distressed[38, 56] or too stressed to be approached.[49] A lack of belief in the intervention, [44, 61, 71] concerns regarding randomisation,[38, 44, 71] the use of placebo[32, 47, 69] and clinical equipoise, [44, 52, 71] lack of confidence discussing a challenging study[42, 51] and fear of discussing prognosis[52, 53, 70] were also cited as possible reasons.

Barrier: Research ethics committee gatekeeping

Research ethics committees (RECs) play an important role in ensuring ethical standards are met in research and the rights of those taking part are protected. RECs were seen at times not to have a good understanding of palliative care research which led to a misapplication of their gatekeeping role.[73] This resulted in overly paternalistic recruitment procedures being put in place such as face to face consent in the community by a Doctor[32] and insisting patients were informed they had a prognosis of six months or less before they could be approached.[69]

Barrier: Resources

Recruitment to palliative care RCTs is seen as a costly and labour intensive process. A large number of patients have to be screened from a variety of settings in order to find the participants that are eventually recruited to the study and the majority of research staff time is spent screening and consenting rather than carrying out the intervention and collecting data.[34, 38, 46, 58, 72] Not having the necessary staff available due to staff turnover or holidays,[37] clinical staff being too busy[41] or lack of out of hours cover[47, 57] is seen as having an impact on recruitment rates.

Partner education

Strategy: Personal repeated contact with referral sources

Personal and repeated contact with referral sources was seen as crucial to create and maintain enthusiasm and motivation throughout the life of the study as well as address any concerns that may develop.[17, 37, 38, 53, 64] The approaches used included presentations, regular meetings and involvement of clinical staff in the study design and procedure development.[17] Identifying an enthusiastic study champion to assist access to potential participants and help promote the study among patients and clinical staff was also seen as a valuable strategy.[46, 55, 60, 71]

Partner referrals and recruitment

Facilitators: Support of lead clinicians/the usefulness of a trials cooperative

Support of lead clinicians is seen as a facilitator as this enhanced patient acceptance of the trial along[33, 46 28, 39, 41, 44, 48] with promoting a research culture in the recruitment sites.[44] The usefulness of a national palliative care clinical trial's cooperative made up of experts in the field of palliative care trial research was

recognised in one study. This resource was seen to help improve recruitment as it facilitated team based support, the sharing and dissemination of best practices and the opportunity to learn from each other.[46]

Strategy: Screening strategies

From the literature it would appear identifying and finding potential participants is one of the most significant recruitment challenges in palliative care RCTs with the approaches used dependent on local resources and systems. A number of screening strategies are suggested which include 'active questioning' to identify patients with a particular symptom[26] or those who are on specific medication rather than relying purely on clinical notes[46] and reviewing clinical lists or notes which may include electronic database searches if the facilities are available.[46, 55, 72] Other strategies included incorporating the screening process into the regular palliative care service triage process,[17, 37] using a screening algorithm[26] and simplifying and minimising the screening process for clinicians.[17]

Strategy: Financial incentives/recruitment progress reports

Financial incentives for study site staff were used in one study to attempt to improve sluggish recruitment with mixed results across sites.[55] Monthly recruitment progress reports sent to individual sites were used in one study and it was felt this encouraged 'healthy competition and camaraderie'.[55]

Strategy: Research staff on site

Having research staff on site to provide logistical and practical support to enhance study recruitment is the strategy discussed most frequently in the literature.[17, 26, 28, 29, 36, 37, 40, 46, 53-55, 60, 71] Some authors have seen this intervention as the one that had the greatest impact on their recruitment rates.[26, 40] It can be seen to relieve the excessive burden of recruitment on busy clinical staff,[17, 26, 36, 40, 53] help address the issue of gatekeeping,[28, 29, 37] support relationship building,[26, 40, 54] help keep a trial visible,[71] allow direct access to participants[46] and provide consistency.[17]

But it is important to note that in some trials this does not always appear to be the case and the issue of gatekeeping remained a problem despite the presence of a research nurse.[35] The issue of research staff not being available at the 'right time' to approach potential participants was sometimes seen as a problem with patients being discharged or transferred to another department before they were able to be approached.[27]

Discussion

Main findings/results of the study:

This review has shown that the barriers to recruitment and the potential strategies that may help to overcome them described in the literature are largely based on

anecdotal evidence. There are likely to be issues to consider for most studies, such as the need to pay attention to key and careful messaging, plan for adequate resources to find your participants, ensuring you have the support of the lead clinician and gatekeeping by health care professionals, but the lack of evidence highlights the need for more methodological studies to be embedded within trials including nested trials of recruitment strategies.

Using a marketing approach in palliative care could appear to be controversial but it could be argued that it actually puts the patient or carer at the centre of the process as it requires the researcher to focus on 'the needs, wants, and preferences of the target audience' (p10).[14] Recruitment is a complex process and needs careful planning before the study is started. The 'Social Marketing Mix Framework' may help researchers better understand the processes underpinning recruitment and influence the design of their recruitment plan and how they implement this plan in practice.[14] The framework can help those involved in trials apply general recruitment principles while acknowledging the need to take trial specific and local circumstances into account. For example, one of the challenges identified in the literature was the issue of high refusal rates and this was not always related to the patient's condition. Their refusal sometimes appeared to be related to their concerns about the 'product' which in social marketing terms relates to the intervention that is being offered in the study. A lack of belief in the intervention or the control, the feeling the intervention was not needed or having a particular preference for a certain treatment arm were discussed as reasons for refusal. Under the 'Social Marketing Framework' ensuring the 'product' meets the needs of the target audience is a key consideration when designing a study which in practice is reflected in the increasing requirement for patient and public involvement to be involved in the study design process. [74]

The role of health care professionals in recruitment to palliative care RCTs is fundamental and a plan of a how a study will work with its partners to meet its recruitment goals is crucial. 'Working with partners' with its focus on 'partner education', 'partner referrals and recruitment' and 'barriers to partnering' is a key aspect of the marketing framework applied in this review and is linked to the concepts of 'Place' and 'Promotion'. For example, this refers to the location where recruitment activity takes place as well as the way in which the health care professional presents the study to the patient.

However, 'Product' and 'Price' are applied to the patient and/or carer and not the partner under this framework which may not fully capture the complexities of recruitment in palliative care. For example, clinicians struggling to accept the intervention or randomisation and feeling the emotional costs of approaching a patient or carer at a difficult time in their lives, making it hard for them to balance the costs of taking part in the study with the potential benefits the study may have for participants.

Strengths and weaknesses/limitations of the study:

To the authors knowledge this is the first review to synthesise the evidence related to the barriers and facilitators to recruitment to RCTs in palliative care. The search strategy and approach used was thorough in this review, however, the authors do not claim to have identified and reviewed all published palliative care RCTs papers for reported barriers and facilitators to recruitment. The review findings are largely based on researcher anecdotal evidence so should be interpreted with caution. This is however, the level of evidence that is currently underpinning our understanding of recruitment issues in palliative care RCTs.

What this study adds:

This review is unique in this field as it uses a theoretical framework, the 'Social Marketing Mix Framework', to explore the barriers and facilitators to recruitment to RCTs in palliative care. Using theory in the review process can help the reviewer and reader assess how applicable and generalisable the findings of a review can be in practice. This review builds upon the findings of a recent qualitative review into gatekeeping in palliative care research and provides an insight into the some of the factors that may be at play during the trial recruitment process.[13] This review can help those involved in recruitment identify the factors they should consider when planning and implementing a recruitment strategy for any palliative care research study and not just a RCT. Reviews that focus purely on 'tested' recruitment strategies or interventions are important but their findings can be complemented by work that adopts a more qualitative approach as they have the potential to 'elicit and identify the hidden challenges' that make up this important clinical activity.[75]

Implications for research and clinical practice

There is a need for more methodological research focusing on recruitment to palliative care RCTs. There are clearly themes mentioned more frequently in the literature that would suggest they are significant in clinical research but without the research to explore or address these issues further it is likely palliative care RCTs will continue to struggle to reach their recruitment targets. The benefits of using qualitative research to address recruitment related issues such as patient and recruiter concerns regarding randomisation in the early stages of trial development have been seen in the field of cancer treatment trials. [76] This approach appears to be increasingly incorporated into the design of palliative care feasibility RCTs. [62, 77] Feasibility studies have the potential 'to design out' any issues that may negatively impact on a trials recruitment success or demonstrate that a study is in fact not feasible before progressing to a more costly full scale RCT. The use of embedded clinical trials to test recruitment strategies is another approach that is being developed in the field of trial methodology [78] and has the potential to be used within palliative care research along with the growing recognition of the importance of patient and public involvement when designing a study. [74]

Conclusion

The 'Social Marketing Mix Framework' can help guide researchers when planning and implementing their recruitment strategy but more methodological research is

needed to help address the issue of poor recruitment to palliative care RCTs. The findings of this review are applicable to all palliative care research and not just randomised controlled trials.

Conflict of Interest: 'The Author(s) declare(s) that there is no conflict of interest'.

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Declarations:

Authorship:

Lesley Dunleavy is the main author of this paper and has produced this paper as part of her PhD in Health Research at Lancaster University.

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Supplementary Data Table 1: Search Strategy

	Search strategies
Medline via EBSCOhost	- palliat* or - hospice* or - terminal care or - terminal care/ (not exploded) or - palliative care/ or - palliative medicine/ and - randomi*ed controlled trial* or - randomised controlled trial/ (publication and topic) - limits: human, 01/01/1990 to 08/10/2016 , Randomised Controlled Trials
PsycINFO via EBSCOhost	- palliat* or - hospice* or - terminal care or - palliative care/ or - terminally ill patients/ or - terminal cancer/ and - clinical trials/ or - randomi*ed controlled trial* - limits 01/01/1990 to 08/10/2016, clinical trial, human.
CINHAL via EBSCOhost	- palliat*or - hospice* or - terminal care or - palliative care/ or - terminal care/ (not exploded), and - Randomi*ed Controlled Trial*, or - Clinical Trials/ (exploded), or - randomised controlled trial/ - limits 01/01/1990 to 08/10/2016, human and exclude Medline
Embase via Ovid	- palliat* or - hospice* or - terminal care or - exp palliative therapy/ or - terminal care/ and - randomi*ed controlled* or - randomized controlled trial/ - limits human, RCTs, 01/01/1990 to 08/10/2016

Supplementary Data 2: A hierarchy of evidence tool (adapted for the purposes of this review).[24]

7 Very well supported evidence: barriers/facilitators/strategies evaluated with a systematic review, meta-analysis (this section has been added for the purposes of this review).

6 Well supported evidence: barriers/facilitators/strategies evaluated with a prospective randomised controlled trial.

5 Supported evidence: barriers/facilitators/strategies evaluated with a control group and reported in a peer-reviewed publication.

4 Promising evidence: barriers/facilitators/strategies evaluated with a comparison group.

3 Acceptable evidence: barriers/facilitators/strategies evaluated with an independent assessment of outcomes, but no comparison group (e.g. pre and post testing, post testing only or qualitative methods) or historical comparison group (e.g. normative data).

2 Emerging evidence: (this section has been divided into two for the purposes of this review)

- 2 a Barriers/facilitators/strategies evaluated without an independent assessment of outcomes (e.g. formative evaluation, service evaluation conducted by host organisation).
- 2 b Suggested as a possible barrier/facilitator/strategy by a group of expert health care professionals e.g. through a consensus exercise (stronger evidence than single author/research team opinion).

1 Expert opinion: (this section has been divided into three for the purposes of this review)

- 1a Expert opinion unsupported by evidence (Professional opinion):suggested as a possible barrier/facilitator/strategy by health care professionals
- 1b Expert opinion unsupported by evidence (Researcher opinion): suggested as a possible barrier/facilitator/strategy by researchers
- 1c Expert opinion unsupported by evidence (Participants opinion): suggested as a possible barrier/facilitator/strategy by research participant

Supplementary Data Table 3: A table of the barriers and facilitators to recruitment conceptually mapped with the 'Social Marketing Mix Framework'.[14]

Social Marketing '6 Ps'	Themes from the literature	Patient	Carer	Partners
1 Identifying participants	**Barriers**			
	Lack of participants who meet the study inclusion criteria	Goldstein et al,[43] Zambroski et al,[72] Jones et al,[52] Hanson et al,[46] Lee et al,[57] Vermandere et al[70]	Baskin at al,[30] Sampson et al,[67] Zambroski et al[72]	
	Difficulty predicting prognosis	Currow et al,[36] Goldstein et al,[43] Gorman et al,[45] Latimer et al,[56] Hanson et al,[46] McWhinney et al[59]		
	Facilitator			
	Broad study eligibility criteria	Le Blanc et al,[17] Shelby James et al[68]		
	Strategies			
	Prognostication tool alongside face to face screening by clinicians	Riopelle et al[66]		
2 Product	**Barriers**			
Defining the Product	Participants not interested	Currow et al,[36] Kutner et al,[55] Westcombe et al,[71] Bausewein et	Buss et al[33]	

		al,[31] Noble et al,[62] Buss et al,[33] Anmari et al[27]		
	Clinical equipose	Noble et al,[62] Bausewein et al,[31] Westcombe et el[71]		Buss and Arnold,[32] Goodwin et al,[44] Westcombe et al,[71] Hardy et al,[47]Jones et al,[52] Daniels and Exley[38]
	Facilitator			
	Trial replicates clinical practice as much as possible			Shelby James et al[68]
	Offer a desirable and novel intervention	Farquhar et al[39]		
	Strategies: Study Design			
	Fast track RCT	Farquhar et a[39]	Farquhar et al[39]	
	Simplify design	Westcombe et al,[71] Buss et al[33]		
	Extension study	Abernethy et al[26]		Abernethy et al[26]
	Rescue medication	Shelby James et al[68]		Shelby James et al[68]
The Product's competition	**Barriers**			
	Competing services	Goodwin et al,[44] Westcombe et al[71]		
	Competing trials	Goodwin et al,[44]		

3 Price	**Barriers**			
	Patient's condition/illness	McMillan and Weitzner,[58] Latimer et al,[56] Philip et al,[63] Hanson et al,[46] Buss et al,[33] Anmari et al,[27] Noble et al[62]		
	Gatekeeping	Buss et al,[33] Hudson et al[49]	McMillan and Weitzner,[58] Zambroski et al,[72] Hanson et al[46]	
	Facilitator			
	Minimise study burden	Shelby James et al[68]	Shelby James et al[68]	Shelby James et al[68]
	Strategies			
	Verbal consent		Riopelle et al[66]	
	Advanced consent	Rees and Hardy,[65] Clark et al[34]	Clark et al[34]	
	Cluster consent	Fowell et al[42]		Fowell et al[42]
4 Place	**Barriers**			
	Type of Recruitment setting	**Cancer centre:** Westcombe et al[71] **Hospice:** Storey,[69] Zambroski et al[72] **Hospital Inpatients:** Fischer et al,[41] Sampson et al,[67] Lee et al[57] **Community:** Hanson et al,[46]	**Hospital Inpatients:** Sampson et al[67] **Hospice:** Zambroski et al[72] **Hospital Outpatients:** Latimer et al[56]	

		McMillan and Weitzner[58] **Hospital Outpatients:** Latimer et al,[56] Hanson et al[46]		
	Strategy			
	Increase number of recruitment centres	Abernethy et al,[26] Goodwin et al,[44] Mitchell and Abernethy,[37] Hussainy and Marriott,[50] Westcombe et al[71]	Hussainy and Marriott[50]	
5 Promoting the study	**Facilitator**			
	Key/careful messaging	Abernethy et al,[26] Gorman et al,[45] Le Blanc et al,[17] Farquhar et al,[39] Hanson et al,[46] Kutner et al[55]	Abernethy et al,[26] Kutner et al,[55] Le Blanc et al[17]	Abernethy et al,[26] Gorman et al,[45] Kutner et al,[55] Le Blanc et al,[17] Shelby James et al[68]
	Flexibility and persistence	Riopelle et al,[66] Hanson et al[46]		
	Rapport between researcher and participant	Riopelle et al[66]		Riopelle et al[66]
	Strategy			
	Role play/scripts			Fischer et al,[41] Abernethy et al,[26] Kruse et al,[54] Le Blanc et al,[17] Mitchell and Abernethy,[37] Shelby James et al[68]

6 Working with partners	**Barriers:** Barriers to partnering			
	Health care professional gatekeeping			Buss and Arnold,[32] Cook et al,[35] Goodwin et al,[44] Hussainy and Marriott,[50] Kutner et al,[55] Westcombe et al,[71] Jones et al,[51] Latimer et al,[56] Miller et al,[61] Daniels and Exley,[38] Hanson et al,[46] Prentice et al,[64] Jones et al,[52] Fowell et al,[42] Hudson et al,[49] Vermadere et al,[70] Hardy et al,[47] Storey,[69] Jordhoy et al[53]
	Gatekeeping by research ethics committee			Buss and Arnold,[32] Storey[69]
	Resources: labour intensive			McMillan and Weitzner,[58] Clark et al,[34] Hanson et al,[46] Daniels and Exley,[38] Zambroski et al[72]
	Resources: Research or clinical staff availability			Mitchell and Abernethy,[37] Fischer et al,[41] Lee et al,[57] Hardy et al[47]
	Strategies: Partner			

	education			
	Personal repeated contact with referral sources			Jordhoy et al,[53] Le Blanc et al,[17] Mitchell and Abernethy,[37] Prentice et al,[64] Daniels and Exley[38]
	Study champion			Hanson et al,[46]Kutner et al,[55] Westcombe et al,[71] Miller et al[60]
	Facilitator: Partner referrals and recruitment			
	Support of lead clinicians			Bakitas et al,[28] Goodwin et al,[44] Buss et al,[33] Fischer et al,[41] Higginson et al,[48] Farquhar et al,[39]Hanson et al[46]
	Support of a palliative care clinical trials cooperative			Hanson et al[46]
	Strategies: Partner referrals and recruitment			
	Active questioning			Abernethy et al,[26] Hanson et al[46]
	Review clinic/hospital lists/clinical notes			Kutner et al,[55] Hanson et al,[46] Zambroski et al[72]
	Clinical triage nurse			Le Blanc et al,[17] Mitchell and

				Abernethy[37]
	Screening algorithm			Abernethy et al[26]
	Minimal screening for clinicians			Le Blanc et al[17]
	Financial incentives			Kutner et al[55]
	Recruitment progress reports			Kutner et al[55]
	Research staff on site			Abernethy et al, [26] Anmari et al,[27] Bakitas et al,[28] Bakitas et al,[29]Cook et al,[35] Currow et al,[36] Farquhar et al,[40]Jordhoy et al,[53] Kruse et al,[54] Kutner et al,[55] Le Blanc et al,[17] Miller et al,[60] Mitchell and Abernethy,[37] Westcombe et al,[71] Hanson et al[46]