

**Health care professional recruitment of patients
and family carers to palliative care randomised
controlled trials: A qualitative multiple case study**

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I declare that this thesis is my own work and has not been submitted for the award of a higher degree elsewhere.

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Publications and presentations related to this PhD

Journal articles

Dunleavy, L., Walshe, C., Oriani, A., & Preston, N. (2018). Using the 'Social Marketing Mix Framework' to explore recruitment barriers and facilitators in palliative care randomised controlled trials? A narrative synthesis review. *Palliative Medicine*, 32(5), 990-1009.

Oral conference presentations

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Dunleavy, L., Preston, N., Walshe, C. (2020) Can the '6 Ps' of the 'Social Marketing Mix Framework' help inform the recruitment planning and implementation process? A qualitative multiple case study.

15th European Association for Palliative Care World Congress, Madrid, 18th – 20th May

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Dunleavy, L., Walshe, C., Preston, N. (2017) What are the barriers and facilitators to patient and carer recruitment to randomised controlled trials in palliative care? A narrative synthesis review.

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4th International Clinical Trials Methodology Conference and the Society for Clinical Trials

38th Annual Meeting, Liverpool, 7th-10th May 2017

Dunleavy, L., Walshe, C., & Preston, N. (2017). What are the barriers and facilitators to patient and carer recruitment to randomised controlled trials in palliative care? A systematic review with narrative synthesis. *Trials*, 18 (Suppl.).

Glossary

Carer: A person who self-defines as a family member or friend who acts as an unpaid carer for the patient (Froggatt et al., 2018).

Chief Investigator: The individual who takes primary overall responsibility for the design, conduct and reporting of a trial (National Institute for Health Research, 2019b).

Clinical recruitment centre: A clinical setting such as a hospital or hospice where recruitment activity takes place, also referred to as trial or research site in the literature (Bruhn et al., 2019).

Health care professional or clinician: A generic term for medical, nursing and allied health care professionals working in the clinical recruitment centres.

Medical staff or doctor: Medically trained clinicians whose role is to recruit participants to a palliative care trial.

Nurse or nursing staff: A generic term for nurses responsible for recruiting participants to a palliative care trial and includes both research nurses and specialist nurses.

Principal Investigator: The person responsible for the conduct of a trial in a clinical recruitment centre (National Institute for Health Research, 2019b). In the case of a single-centre trial, the Chief investigator and the Principal Investigator will normally be the same person (Health Research Authority, 2018).

Randomised controlled trial or trial: In this thesis, both terms have been used to indicate a randomised controlled trial. Where this is not the case, this has been clearly indicated in the text. An in-depth definition of a randomised controlled trial is provided in chapter one.

Recruiting staff: Health care professionals, both medical and nursing staff, directly involved in recruiting participants to a palliative care trial.

Research nurses: Research nurses work in clinical recruitment centres and their role typically involves; screening and recruitment of participants, ensuring informed consent, operationalising randomisation procedures, collecting and recording data and following participants up during the trial (Spilsbury et al., 2008).

Specialist nurses: Specialist nurses are dedicated to a particular area of nursing such as cancer, palliative care, heart failure or dementia. They provide direct patient care and can play a vital role in educating patients on how best to manage their symptoms, as well as offering support following diagnosis (Liljeroos & Strömberg, 2019; Wallace et al., 2019).

Study Coordinating Centre: Responsible for general oversight of the conduct of the trial and overall data management, monitoring and communication among all of the clinical recruitment centres (John Hopkins Medicine, 2016).

Study coordinating centre staff: A generic term for researchers who work in the trial's study coordinating centre.

Abstract

Introduction: Trial recruitment is an interactional process between health care professionals, patients and carers. There is limited understanding of how health care professionals carry out this role in palliative care trials as well as the reasons why they do or do not recruit eligible participants. The '6 Ps' of the 'Social Marketing Mix Framework' may help guide recruitment planning, but most evidence is anecdotal. The '6 Ps' are; identifying participants, product, price, place, promotion and working with partners.

Aims: To explore how health care professionals undertake recruitment to palliative care randomised controlled trials and the factors that influence the strategies they use and the decisions they make during the recruitment process.

Method: A narrative synthesis of palliative care trial recruitment barriers and facilitators identified in existing trial literature informed the study design. A qualitative multiple case study, using Yin's approach, was conducted. Cases were diverse UK palliative care trials across a variety of settings. Participants included study investigators and research staff involved in the recruitment process from trial coordinating centres and clinical recruitment sites. Data collection included interviews and study documentation. Analysis was informed by developing and refining theoretical propositions, guided by the '6Ps' as an initial analytical framework. Framework Analysis guided within and then cross-case analysis.

Results Three cases were included in the study (n = 3, 9, 7 participants). Cross-case analysis suggests the '6 Ps' are a useful framework for understanding recruitment processes but wider contextual issues also need to be incorporated. These include the 'emotional labour'

of diagnosing dying and communicating palliative and end-of-life care to potential participants and how the recruitment process is influenced by the power relationships and hierarchies that exist among professional groups. These factors can lead to and support paternalistic practices.

Discussion/conclusion Those planning trials need to ensure that trial recruiters, depending on their experience and trial characteristics, have access to training and support to address the 'emotional labour' of recruitment. Consideration also needs to be given to who is primarily responsible for the patient's care when choosing a Principal Investigator.

Chapter one: Background and Introduction

1.1 Introduction

Fewer than 50% of randomised controlled trials achieve their recruitment targets (Treweek et al., 2018) with reports of palliative care trials only reaching their recruitment targets in 37% of cases (Bouça-Machado et al., 2017). Health care professionals play a key role in the recruitment process (Preston et al., 2016), but why they do or do not recruit potentially eligible patients and family carers to palliative care randomised controlled trials is poorly understood. In this study, how health care professionals involved in the recruitment process recruit patients and family carers to palliative care randomised controlled trials, is identified. Why they choose to implement particular recruitment strategies, and the factors that influence their choices, when recruiting to a palliative care trial is also explored.

In this chapter, why palliative care research and more specifically recruitment issues in palliative care randomised controlled trials has been chosen as the focus of this study is discussed. The factors that influence the definition of a palliative care randomised controlled trial are presented as well as the key issues and challenges found in palliative care research. The role of randomised controlled trials in palliative care, their key features and the challenges associated with this study design is examined. How recruitment is defined and why it is challenging to achieve recruitment targets in palliative care trials is explored. Finally, the type of theoretical frameworks that can inform the recruitment process are discussed and why the 'Social Marketing Mix' was chosen as the theoretical framework in this study is outlined.

1.2 My background as a researcher

I am a registered nurse and the majority of my career has been spent in the speciality of palliative care. I have previous experience of working as a specialist palliative care nurse in a hospital and community setting. This role involved managing the complex physical and psychosocial needs of palliative care patients and their carers and working closely with members of the wider multi-disciplinary team. I also have previous experience of working as a palliative care research nurse in a hospice setting. This role involved recruiting patients and carers to palliative care research studies including randomised controlled trials. For example, I was involved in setting up and recruiting to a multi-centre randomised double blind placebo controlled trial of Ketamine for neuropathic pain. The trial was challenging to set up and recruit to and only one patient was recruited from the hospice (Dunleavy et al., 2011).

These experiences strongly influenced the topic and focus of my research as I had some insight into the challenges of palliative care research and more specifically recruiting patients and carers to palliative care trials. During my PhD, I was no longer involved in direct patient care but was working as a research associate on a number of palliative care trials of complex interventions. The issue of reflexivity and how it has been addressed in this study is explored in more detail in chapter four. It is also important to note that my supervisors are also registered nurses who currently work in palliative care research including as senior investigators on palliative care trials. Professor Catherine Walshe has previously worked as a community specialist palliative care nurse and Professor Nancy Preston's background includes experience as an oncology research nurse in a specialist cancer hospital. The issue

of reflexivity, how it has influenced decision making during this study and how it has been addressed is explored across the following chapters.

1.3 What is a palliative care randomised controlled trial?

There is a lack of clarity and consensus surrounding the definition of a palliative care randomised controlled trial in the literature (Bausewein & Higginson, 2012; Gaertner et al., 2016; Sigurdardottir et al., 2014; Van Mechelen et al., 2013; Zafar et al., 2012). This is unsurprising as there is a lack of clarity and consensus surrounding the definition of palliative care outside the field of research. Despite this lack of clarity and consensus, overall, palliative care is associated with providing care with a non-curative intent. A palliative care randomised controlled trial, therefore, typically aims to test the effectiveness of an intervention with a non-curative intent.

The modern hospice movement began in 1967 with the opening of St Christopher's Hospice in London (Radbruch & Payne, 2009) and the term palliative care was first introduced in the mid-1970s with the speciality of palliative medicine being introduced in the UK in 1987 (Pastrana et al., 2008). Terms such as supportive care, hospice care, terminal care and end-of-life care are also used interchangeably in clinical practice, government policy and legislation (Cramp & Bennett, 2013). For example, in the UK the National Institute for Health and Care Excellence has developed quality standards for end-of-life care which they define as those patients who are likely to die within 12 months (National Institute for Health and Care Excellence, 2017). Definitions can also vary between countries, for example, in the

United States hospice care focuses on those patients with a prognosis of 6 months or less (Hui et al., 2013).

This lack of clarity and consensus over terminology can act as a barrier to communication both in clinical practice and in research (Cramp & Bennett, 2013; Hui et al., 2013). Terminal care, end-of-life care and palliative care can be viewed as synonymous terms by patients (Chosich et al., 2020) and the wider public (McIlfatrick et al., 2014). It has been suggested that the term supportive care is less likely to provoke anxiety among patients, carers and clinicians as terms such as hospice care and palliative care are often associated with death and dying (Hui et al., 2013; Siouta et al., 2018; Zimmermann et al., 2016). This use of multiple terms with their associated meanings has implications for the trial recruitment process. It has the potential to influence the acceptability of a palliative care trial to patients, carers and health care professionals and how it is introduced.

1.3.1 Factors that influence the definition of a palliative care randomised controlled trial

There are a number of complex, interlinked factors that need to be considered when attempting to define a palliative care trial. These factors are; who is a palliative care patient; what are palliative care needs; where do palliative care patients receive care and from whom; what is a palliative care intervention and what outcome measures are used in a palliative care trial. These complex interlinked factors are discussed in turn below.

1.3.2 Who is a palliative care patient?

Palliative care populations are heterogeneous as patients can have different diagnoses and comorbidities (Eule et al., 2018; Visser et al., 2015) and as a result, palliative care trial populations can vary widely (Currow et al., 2011). Family carers are also included in a palliative care population and therefore may also be included in a trial population (Hui et al., 2011). The World Health Organisation (2002) recommends that the palliative care approach be introduced as early as possible in the course of any life-threatening illness and not just when the patient is not responding to curative therapy. The World Health Organisation definition also recognises the needs of carers, including those who are bereaved (Sepúlveda et al., 2002);

‘Palliative care is an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.’ (Sepúlveda et al., 2002) (p.94)

The International Association for Hospice and Palliative Care has recently developed an even broader definition. They found it challenging to achieve agreement between those who believe palliative care should be aimed at the relief of all suffering and those who believe it involves the care of those with a very limited remaining life span. This difference of opinion is reflected in their definition;

‘Palliative care is the active holistic care of individuals across all ages with serious health-related suffering due to severe illness and especially of those near the end of

life. It aims to improve the quality of life of patients, their families and their caregivers.’ (Radbruch et al., 2020) (p. 761)

The definition of a palliative care patient chosen for this study reflects an earlier World Health Organisation definition of palliative care (World Health Organization, 1990). This definition is based on the idea that palliative care is aimed at those patients who are not responding to curative therapy, and their family carers. Unlike the original World Health Organisation definition that focused on cancer patients with advanced disease, the palliative care population in this study also includes those patients living with progressive, life threatening non-malignant disease. This decision was influenced by the definition of a palliative care patient proposed in a review of palliative care randomised controlled trials (Van Mechelen et al., 2013). Van Mechelen et al (2013) proposed that the palliative care patient be defined as those living with *‘a progressive, life-threatening disease with no possibility of obtaining remission or stabilisation, or modifying the course of the illness’* (p.197). It was also informed by the definition of a palliative care patient used in Cochrane systematic reviews of palliative care interventions. This example is taken from a Cochrane review of pharmacological treatments for fatigue associated with palliative care;

‘Palliative care patients with fatigue, i.e. patients with an incurable disease (terminal illness) such as advanced cancer, HIV/AIDS, multiple sclerosis, amyotrophic lateral sclerosis, or cardiac, lung or kidney failure.’ (Muecke et al., 2015) (p.4)

A number of strategies are used to operationalise this definition of a palliative care patient in the context of palliative care trials. A trial’s eligibility criteria may include disease staging criteria to help recruiting staff determine that the patient has advanced disease with a limited life expectancy. For example, a Functional Assessment Staging score of 6 or 7 for

those living with advanced dementia (Froggatt et al., 2020), stage iii or iv of the TNM (Tumour, Node, Metastases) classification and staging system for non-small cell lung cancer patients (Rietjens et al., 2016) or a Hoehn and Yahr score of ≥ 4 for those living with Parkinson's disease (Veronese et al., 2017). These type of scores would indicate that the patient has advanced disease with a limited life expectancy.

Symptom assessment scales may also be used as part of a trial's eligibility to define a palliative care patient with advanced disease. For example, a modified Medical Research Council Scale score of 3 or 4, despite optimal management of underlying cause, for patients living with chronic breathlessness with a range of aetiologies (Currow et al., 2019; Ferreira et al., 2020). This may also be achieved by clinicians assessing a patient's prognosis as part of a trial's eligibility assessment (Ferreira et al., 2020; Vanbutsele et al., 2018). In one review of palliative care trials, the estimated prognosis of patients varied between 'less than one week' and 24 months with the most common being 6 months (Bouça-Machado et al., 2017). Validated performance status scales such as the Eastern Cooperative Oncology Group (ECOG) or the Karnofsky scale may be used to estimate survival, both the original or palliative care versions (Abernethy et al., 2005; Chow et al., 2020; Ferreira et al., 2020). Disease specific clinical indicators may be used to inform prognostication as illustrated in a trial of specialist palliative care for those living with advanced neurodegenerative disorders (Veronese et al., 2017).

1.3.3 What are palliative care needs?

Patients living with advanced progressive disease can have a variety of complex physical needs that may affect their quality of life. For example, they may need help managing symptoms such as pain, fatigue, nausea and vomiting, dyspnoea, insomnia, appetite loss and constipation (Carvajalino et al., 2018; Verkissen et al., 2019). They may also have psychological, social and spiritual needs that may affect their quality of life. For example, psychological distress is common in advanced progressive disease (Boakye et al., 2019) with higher rates of distress seen in patients with increased symptom burden (Fitzgerald et al., 2015). Those living with advanced cancer or end stage non-malignant disease may experience different symptoms and illness trajectories (Currow et al., 2011). For example, those living with heart failure, chronic obstructive disease and end stage renal failure were found to have less functionality in their activities of daily living compared to cancer patients on referral to specialist palliative care (Bostwick et al., 2017). Family carers may also have psychosocial and spiritual needs that need to be addressed (Dunleavy et al., 2020; Grande et al., 2017). This holistic focus of care is reflected in the 2002 World Health Organisation definition of palliative care outlined above.

1.3.4 Where does the palliative care patient receive care and from whom?

Patients living with advanced progressive disease are cared for in a variety of clinical settings that includes hospitals, hospices, nursing homes and primary care. Patients may also be cared for in different areas within these settings such as inpatients, outpatients, day care or

home care. The number of patients who will require palliative care is predicted to increase over the coming years because of the ageing population and the number of people living and dying with chronic and complex conditions (Etkind et al., 2017). It has been estimated that end-of-life care provision in care homes and the community needs to double by 2040 to meet this need (Bone et al., 2018).

Palliative care is also provided by generalist or specialist palliative care services. Generalist palliative care is provided by the patient's usual care team and specialist palliative care is provided by professionals specifically trained in palliative care who work full time in this area (Bausewein & Higginson, 2012). How this type of care is provided may differ slightly between countries but generally inpatient specialist palliative care is provided in dedicated palliative care units or hospices (Bausewein & Higginson, 2012). Specialist palliative care teams provide advice and support either in the hospital and/or in the community setting (Bajwah et al., 2020; Bausewein & Higginson, 2012). Specialist palliative care provision may also be the intervention in a palliative care trial as illustrated in a recent Cochrane review of hospital based specialist palliative care (Bajwah et al., 2020).

1.3.5 What is a palliative care intervention?

Defining a palliative care trial intervention can be challenging as terms such as palliative care or best supportive care can also be used to define a control group in an oncology treatment trial (Bausewein & Higginson, 2012; Zafar et al., 2012). Palliative care interventions are interventions that have a non-curative intent. They can be heterogeneous but a typical palliative care intervention would be a complex intervention that reflects a holistic and

multi-disciplinary approach to care or the administration of medication for symptom control (Van Mechelen et al., 2013). Trials may also test non-pharmacological single interventions such as aromatherapy to improve quality of sleep (Kawabata et al., 2020).

Trial interventions may be taken from other patient populations and applied to those living with advanced progressive disease. For example, the use of physiotherapy for fatigue in advanced cancer (Pyszora et al., 2017) or mindfulness to reduce stress in advanced cancer or non-malignant disease (Warth et al., 2020). Interventions may also be developed specifically to meet the needs of those living with advanced progressive disease. For example, the development of the Gold Standard Framework intervention for use in care homes to prevent unnecessary hospital admissions (Kinley et al., 2014) or the implementation of early palliative care telehealth in advanced heart failure (Bakitas et al., 2020). Palliative care interventions, like those in the general trial literature, can be poorly reported, especially in non-pharmaceutical trials (Bausewein & Higginson, 2012). The TIDieR 12 item checklist has been developed to improve the reporting of interventions in trials and therefore potentially their replicability (Hoffmann et al., 2014).

1.3.6 What is a palliative care trial outcome measure?

The main goals of palliative care are to relieve and prevent suffering and improve quality of life as illustrated in the definitions outlined above (Pastrana et al., 2008; Radbruch et al., 2020). In a palliative care trial, the primary outcome is usually quality of life and/or symptom control (Gaertner et al., 2016; Van Mechelen et al., 2013; Vinches et al., 2020) rather than survival or tumour/disease response (Hui et al., 2011). A recent review of

palliative care studies for advanced cancer listed on the clinicaltrials.gov database found the most applied primary outcome measures were efficacy/symptom control (61%), quality of life (14%) and feasibility (12%) (Vinchess et al., 2020). Temel et al (2010) showed an improvement in overall survival as well as quality of life in lung cancer patients who received early palliative care and standard oncology care compared with those who received standard oncology care alone (Temel et al., 2010). As a result, it was suggested that it may be possible for a trial testing a palliative care intervention to use survival as its primary endpoint (Radbruch, 2014). Follow up trials of early palliative care have, however, continued to use quality of life as their primary outcome (Johnsen et al., 2019; Vanbutsele et al., 2018).

1.3.7 The working definition of a palliative care randomised controlled trial used in this study

The working definition of a palliative care randomised controlled trial used in this study is:

A trial aimed at; adult patients with incurable cancer and/or advanced, progressive non-malignant disease and their family carers; that aims to address physical, psychosocial and/or spiritual needs; with an intervention with a non-curative intent; in any setting; by specialist or generalist professionals; and where the primary endpoint is usually symptom control and/or quality of life.

This definition informed the development of the randomised controlled trial definition for the systematic review in chapter two. Both these definitions then subsequently influenced the definition of a randomised controlled trial used in the case study.

Table 1: More detailed explanation of the working definition of a palliative care randomised controlled trial used in this study.

Trial population	Adult patients with incurable cancer and/or advanced, progressive non-malignant disease and their family carers.
Needs of the trial population	A trial that aims to address physical, psychosocial and/or spiritual needs.
Trial setting/services	Hospital, hospice, nursing home and/or primary care. Areas within these settings such as inpatients, outpatients, day care or home care. Palliative care provided by specialist and/or generalist palliative care services/professionals.
Trial intervention	Interventions that have a non-curative intent. Typically, a complex intervention that reflects a holistic and multi-disciplinary approach to care or the administration of medication for symptom control. Trials may also test non-pharmacological single interventions.
Trial outcome measure	Primary endpoint symptom control and/or quality of life. Trials that test an intervention that is clearly a palliative care intervention and the study primary endpoint is survival.

1.4 Palliative care research

There is a call to improve the evidence base in palliative care through the conduct, publication and implementation of high quality research (Higginson, 2016; LeBlanc et al., 2010; Vinches et al., 2020; Visser et al., 2015). Visser et al (2015) warned that *‘despite the growth in published literature, palliative care is not an evidence-based discipline, or at least it is not informed by the level of evidence which most would require to label it such’* (p.198). The majority of treatments, interventions and guidelines commonly used in palliative care have little supporting trial evidence (Higginson et al., 2013; LeBlanc et al., 2010; Watts et al., 2019). For example, the use of benzodiazepines for the relief of breathlessness in advanced

cancer or chronic obstructive pulmonary disease (Simon et al., 2016) or the use of haloperidol for nausea and vomiting in palliative care (Murray-Brown & Dorman, 2015) has little supporting trial evidence.

1.4.1 Palliative care research funding and infrastructure

Palliative care research is historically underfunded in comparison to research into the prevention and cure of life-limiting illnesses (Higginson, 2016). A recent search of the clinicaltrials.gov database found over 69,000 cancer studies, out of those only 514 studies (0.8%) were palliative care studies (Vinches et al., 2020). A bibliometric analysis of European cancer research papers from 2002 to 2013 found only 1.2% of papers focused on palliative care research (Begum et al., 2018). In the United States, fewer than 1% of all grants awarded by large national funders were awarded to investigators performing palliative care research (Brown et al., 2018) and funding for palliative care research was 0.03% of overall heart failure funding by the National Institutes of Health (Xie et al., 2017).

Non hospital settings, where palliative care patients are largely cared for, often lack or have limited research infrastructure. This includes; limited access to research funding, staff with the relevant expertise, protected time for clinicians and the necessary governance structures to facilitate research activity (Dunleavy et al., 2011; Edwards et al., 2019; Moore et al., 2019; Oliver et al., 2020). These contextual factors can make it challenging to carry out research that focuses on the needs of the palliative care population.

1.4.2: The issue of vulnerability in palliative care research

Palliative care patients are viewed as vulnerable and usually present with at least one or several characteristics of vulnerability (see table 2) (Pereira & Hernández-Marrero, 2019). Patients can be frail and have a high symptom burden (LeBlanc et al., 2013) as illustrated in a recent feasibility trial, where 63% of those taking part required help to complete study questionnaires (Lovell et al., 2020). Patients can have a limited life expectancy, be living with prognostic uncertainty and be dealing with many competing demands (LeBlanc et al., 2013). Patients can deteriorate rapidly or die before they are recruited or be too cognitively impaired to consent to a study (Kaiser et al., 2020; Stone et al., 2013). There may need to be the involvement of a consultee or proxy if the patient lacks capacity which can add additional complexity to the research process (Hickman et al., 2012; Kaiser et al., 2020).

Table 2: Characteristics of vulnerability taken from Pereira and Hernandez-Marrero (2019) (p.1)

Cognitive	Does the person have the capacity to understand and make a decision?
Situational	Is the person in a situation in which medical exigency prevents the education and deliberation needed to decide?
Medical	Has the person a serious health-related condition with limited prognosis?
Allocational	Is the person lacking in important social goods that can influence his or her decision?
Social	Does the person belong to a group whose rights and interests have been socially devalued?
Deferential	Is the person's deferential behaviour masking an underlying unwillingness to decide?

Palliative care patients are viewed as particularly vulnerable as they near the end of life (Bloomer, Hutchinson, et al., 2018; LeBlanc et al., 2013). Concerns about vulnerability leads to a preconception that palliative care patients require extra protection from potential exploitation (Abernethy et al., 2014). They can be excluded from taking part in research even when it is available and it has the potential to improve their own as well as future patient care.

1.4.3 Gatekeeping

Fear of potential patient burden and concerns about vulnerability can lead health care professionals (Kaiser et al., 2020; Snowden & Young, 2017), research ethics committees (Gardiner et al., 2010), family carers (Bull et al., 2019; Gysels et al., 2008), management within organisations (Kars et al., 2016) and even study researchers (Coyle et al., 2016; Hickman et al., 2012) to act as gatekeepers. Gatekeeping is when a gatekeeper prevents a potential participant from receiving information about a research study for which they are eligible (Agar et al., 2013; Kars et al., 2016). Assumptions are made that the research is too intrusive or burdensome, that it may be upsetting, give false hope or yield no benefit for the patient (LeBlanc et al., 2013). Clinicians may feel reticent towards research, feel they lack the relevant expertise and worry that the research may over burden the patient's family carers (Kars et al., 2016).

Gatekeeping is not unique to palliative care research (Williams, 2020) but is seen as a particularly challenging issue in this population (Kars et al., 2016; Snowden & Young, 2017; White et al., 2008). Current evidence suggests that patients can value participation in

research and are willing to engage in research even when they are close to death (Bloomer, Hutchinson, et al., 2018; Coyle et al., 2016; Gysels et al., 2013; White et al., 2019). Family carers (Aoun et al., 2017), including those who are bereaved (Barclay et al., 2019), can also value participating in research despite the stress of caring for or losing a close relative. The reasons why gatekeeping occurs in palliative care research, especially health care professional gatekeeping, requires further exploration and research.

1.5 Randomised controlled trials in palliative care research

The concept of randomisation was introduced in agricultural research by Fischer in the 1920s. The first randomised controlled trial in health care that used random number allocation was the Medical Research Council's 1946 streptomycin trial (Friedman et al., 2010; Medical Research Council Streptomycin in Tuberculosis Trials Committee, 1948). In a randomised controlled trial;

'Two or more groups are formed through random allocation; one or more of the groups is exposed to an intervention (experimental group), while the other group(s) receive(s) an alternative treatment or no treatment (comparison or control group). The effects of the intervention are observed by comparing the outcomes of both groups.' (Torgerson, 2008) (p.2)

The role of randomised controlled trials in improving the evidence base in palliative care has been debated in the literature (LeBlanc et al., 2010; Visser et al., 2015). They only make up a small part of the evidence base in palliative care (Eule et al., 2018; Hui et al., 2012; Hui et al., 2011; Rinck et al., 1997; Tieman et al., 2008). In 2005, only 7.22% of published palliative care

and hospice papers were clinical trials (Tieman et al., 2008) while a search of the supportive and palliative oncology literature in the first 6 months of 2004 and 2009, found that randomised controlled trials comprised only 6% of the studies identified (Hui et al., 2011). Even though the minority of studies in palliative care are randomised controlled trials, their numbers are increasing. Of the 107 trials included in a review of therapeutic interventions searched in Medline until February 2015, 13 were published between 1989 and 1999, 49 between 2000 and 2009 and 44 between 2010 and 2015. The majority of these trials focused on oncology and 43% evaluated pharmacological interventions (Bouça-Machado et al., 2017).

1.6 Why randomised controlled trials are important

The early 1990s saw the rise of evidence-based practice in health care with high quality randomised control trials being placed towards the top of the evidence pyramid. Evidence-based practice challenged traditional unsystematic approaches to care which could lead to poor patient outcomes by arguing clinical decisions needed to be based on research evidence (Guyatt et al., 1992). In the UK, randomised controlled trials receive the greatest funding and support from the National Institute for Health Research Clinical Research Network which illustrates their importance in evidence-based practice (see chapter five for further details) (National Institute for Health Research, 2019c). There are various versions of the evidence pyramid but most represent a hierarchy related to the study design's risk of bias (internal validity) (Murad et al., 2016).

The key purpose of randomised controlled trials is to test whether an intervention is effective. This is achieved by assessing and expressing causality between an independent and dependent variable/s. For example, whether a pain control medication, the independent variable, improves the patient's pain scores and quality of life, the dependent variables. A key characteristic of randomised controlled trials is that known and unknown confounding variables (bias) are intended to be distributed equally through the randomisation process. Randomisation does not eliminate confounding variables but distributes such variables equally so reducing the overall bias in the trial (Bennett, 2007). This gives greater confidence that any effects are due to the intervention rather than a result of some other known or unknown variable (Torgerson, 2008) with the treatment effect being the additional change that occurs in the intervention group compared to the control group (King, 2000). This is the reason why randomised controlled trials are placed towards the top of the pyramid in evidence-based practice.

In comparison, quasi-experimental studies such as pre and post-test designs or observational studies are used to identify whether a relationship or association exists between variables rather than a causal effect (Bennett, 2007; Costantini, 2007; Torgerson, 2008). Non randomised study designs are seen to have less internal validity because they can reportedly overestimate treatment/intervention effects (Concato et al., 2000; Torgerson, 2008). This is the reason why they are situated lower down the evidence pyramid.

There have been a number of criticisms of the evidence-based movement and its over reliance on randomised controlled trial methodology. There is often an assumption that trials are of a high quality and there is no risk of bias but this is dependent on how well the

trial is conducted as illustrated by the use of risk of bias tools in systematic reviews of randomised controlled trials (Sterne et al., 2019). Other criticisms include; how trial findings may not be useful for clinical decision making as tightly controlled trial populations are likely to differ from patients in the real world who may have multiple morbidities, how statistically significant benefits may only be minimal in clinical practice and how it ignores the role and value of clinical experience and judgement and individualised patient care. The risk of bias 'quality mark' can also be misused by those with a vested interest, for example, pharmaceutical companies only publishing positive rather than negative trial findings for financial gain (Greenhalgh et al., 2014). The idea that too much trust is placed on the randomised controlled design (Deaton & Cartwright, 2018) and the need for evidence-based practice to be built on a wider range of study types, including qualitative research to explore 'why things work', has been recognised (Greenhalgh et al., 2014).

1.7 Randomised controlled trial study designs and characteristics

Randomised controlled trials can have different designs and characteristics and these are summarised in table 3 with an example from the palliative care literature. This information has been provided to contextualise the recruitment process and its associated challenges.

Table 3: Randomised controlled trial study designs and characteristics with a palliative care exemplar

Trial designs	Definition	Palliative care exemplar
Explanatory randomised controlled trials	Ask whether the intervention can work under ideal conditions (Loudon et al., 2015). Characterised by tightly defined inclusion/exclusion criteria, usually testing drugs with a placebo as a control arm (Torgerson, 2008).	‘Efficacy of oral risperidone, haloperidol, or placebo for symptoms of delirium among patients in palliative care: A randomized clinical trial’ (Agar et al., 2017)
Pragmatic randomised controlled trial	Ask whether the intervention works under usual conditions so aiming to increase the trials applicability in ‘real world’ settings (Loudon et al., 2015). Pragmatic trials frequently include complex interventions. (Ford & Norrie, 2016) with the comparator being usual care (Loudon et al., 2015). <i>*It is important to note that the explanatory/pragmatic trial distinction is a continuum rather than a dichotomy</i> (Loudon et al., 2015).	‘Early palliative care and quality of life of advanced cancer patients: A multi-center randomized clinical trial’ (Franciosi et al., 2019)
Double/single/un-blinded (open) trial	In a double blind trial, the participant, the researchers/clinicians are not aware of the intervention allocation. In a single blinded study generally either the researcher or participant/clinician is not aware. In an un-blinded trial both the participant and the researcher/clinician know the intervention allocation. (Friedman et al., 2010).	Single blinded example (research staff blinded to intervention allocation) Emergency department–initiated palliative care in advanced cancer: a randomized clinical trial (Grudzen et al., 2016)
Placebo/sham trials	Participants are randomly allocated to an active or placebo drug so that patients and researchers/clinicians can be blinded to the group allocation so reducing the Hawthorne/patient preference effect (Torgerson, 2008). The Hawthorne effect is a change in behaviour as a response to observation and assessment (Sedgwick & Greenwood, 2015). Patients can also be given a ‘sham’ intervention (Torgerson, 2008). (see cross over trial example)	‘Oral medicinal cannabinoids to relieve symptom burden in the palliative care of patients with advanced cancer: a double-blind, placebo controlled, randomised clinical trial of efficacy and safety of cannabidiol (CBD)’(Good et al., 2019)

Feasibility/pilot randomised controlled trial	A feasibility trial <i>'asks whether something can be done, should we proceed with it, and if so, how.'</i> A pilot study asks the same questions but incorporates a future study or part of a future study on a smaller scale (Eldridge et al., 2016) (p.1).	'A group intervention to improve quality of life for people with advanced dementia living in care homes: the Namaste feasibility cluster RCT' (Froggatt et al., 2020)
Cross-over trial	Patients are randomised to a sequence of treatments after a 'washout' period. The condition being studied needs to be relatively stable and the intervention short-acting (Hui et al., 2015).	'Transcutaneous electrical nerve stimulation for advanced cancer pain inpatients in specialist palliative care—a blinded, randomized, sham-controlled pilot cross-over trial' (Siemens et al., 2020)
No of 1 trial	A cross-over trial that involves an individual participant being randomised to receive the study interventions in different orders. Sometimes data can be aggregated from multiple patients completing an N-of-1 trial. (Duan et al., 2013). Unit of randomisation is the treatment order. Role in examining rare symptoms in palliative care patients (Hui et al., 2015).	'The effect of methylphenidate on fatigue in advanced cancer: An aggregated N-of-1 trial' (Mitchell et al., 2015)
Wait list/fast track or delayed intervention randomised controlled trials	Patients are randomised to either an early intervention group or a late intervention group that is characterised by an observation period (the control) followed by the study intervention. Often used to examine complex health interventions (Higginson & Booth, 2011; Hui et al., 2015).	How effective are volunteers at supporting people in their last year of life? A pragmatic randomised wait-list trial in palliative care (ELSA) (Walshe et al., 2016)
Parallel cluster randomised controlled trial	A trial where clusters of individuals such as a nursing home or hospital rather than individuals themselves are randomised to different arms (Torgerson, 2008). Popular design in pragmatic trials (Ford & Norrie, 2016). The intervention may be provided at the cluster and/or individual level. Outcomes are measured at the individual cluster member level (Weijer et al., 2012).	'The action study protocol: Advance care planning - An innovative palliative care intervention to improve quality of life in oncology a multi-centre cluster randomized clinical trial' (Rietjens et al., 2016)

Step wedge cluster randomised controlled trial	All clusters receive the new intervention, yet the moment at which they do so is determined by random assignment. Pragmatic constraints may also influence assignment. In cohort stepped-wedge cluster trials, all participants are exposed to both the control and the intervention (Eichner et al., 2019) while in cross-sectional designs, new participants are included after each step (de Hoop et al., 2015).	Cross-sectional design: ‘Assessing the impact of a Carer Support Needs Assessment Tool (CSNAT) intervention in palliative home care: a stepped wedge cluster trial’(Grande et al., 2017)
Factorial design randomised controlled trials	Two or more different interventions are evaluated using the same participant sample (Torgerson, 2008) (p.xii).	Delivery strategies to optimize resource utilization and performance status for patients with advanced life-limiting illness: results from the "palliative care trial" (Abernethy et al., 2013)
Participant preference trial	Participant preferences are taken into account by asking them before randomisation and by only randomising those who do not have a preference so letting those with a preference have their preferred intervention (p. xiv) (Torgerson, 2008).	Advance care planning uptake among patients with severe lung disease: a randomised patient preference trial of a nurse-led, facilitated advance care planning intervention (Sinclair et al., 2017)
Zelen method	Participants are randomised before consent, consent only sought from those receiving the intervention (Torgerson, 2008). Control group participants remain in the study without being informed of the randomisation procedure as they are receiving usual care. Those who refuse consent in the intervention group are reassigned to the control group. (Zelen, 1979).	‘Multi-center randomized controlled trial for advanced cancer patients receiving parenteral nutrition (PN) versus oral feeding (OF): Results of AlimK study’ (Bouleuc et al., 2018)

1.8 The challenges of randomised controlled trials in palliative care

A randomised controlled trial is seen as the 'gold standard' for evaluating the safety and effectiveness of a health and social care intervention because its central tenet is to reduce bias (Torgerson, 2008; Treweek et al., 2013). It has been suggested that randomised controlled trials can often be impractical and may even be unethical in the palliative care population because of the characteristics of the study design (Aoun & Nekolaichuk, 2014; Hadley et al., 2009). Trials can encounter recruitment difficulties, which is discussed in detail in section 1.12, and experience high rates of attrition.

1.8.1 High rates of attrition

Palliative care trials can experience high rates of attrition because of high mortality rates and symptom burden not related to the trial. Statistical power may be reduced or may not be achieved because of patients withdrawing from the study before the evaluation of the main study outcomes due to death, illness or for other reasons (Oriani et al., 2020).

Statistical power relates to the chances of observing any statistically significant difference between the intervention and control group if in fact that difference exists (Torgerson, 2008). Treatment effects may be biased and the generalisability of study findings may be impacted as there may be significant differences between the trials arms because of attrition (Hussain et al., 2016). Attrition can also be an issue in other research designs in palliative care (Harrop, Noble, et al., 2016; Higginson & Booth, 2011) but specific guidance has been produced to help manage attrition reporting and interpretation in palliative care

trials (Preston et al., 2013). This high risk of attrition means it is crucial for palliative care trials to achieve their recruitment targets to try and achieve statistical power.

1.8.2 Internal and external validity

The complex balance between maintaining the internal and external validity of a trial is not a problem unique to palliative care (Ford & Norrie, 2016). In palliative care, multiple interventions or treatments may be implemented to address the patient's diverse and complex needs which can make it difficult to determine the effects of one intervention among many (Visser et al., 2015). Explanatory symptom control trials (see table 3) taking place in specialist centres with narrow eligibility criteria are seen to have good internal validity but poor external validity (Kirkham & Abel, 1997). While concerns about the internal validity of a palliative care trial where there is considerable heterogeneity between patients receiving the same intervention has also been raised (Hadley et al., 2009; Visser et al., 2015). Pragmatic trial designs (see table 3) with broad eligibility criteria testing complex interventions are seen to help address the generalisability concerns of a traditional explanatory randomised controlled trial (Torgerson, 2008). Finding eligible patients may be less challenging in pragmatic designs but they may require a larger sample size to understand any differences between groups in the trial population (Ford & Norrie, 2016). Using qualitative research within these type of trials is recommended (Craig et al., 2008) and has been used to inform intervention content and delivery, trial design, conduct and processes (including recruitment processes), study outcomes and measures and the target condition for the trial (O'Cathain et al., 2013). Qualitative research has been adopted in

trials of complex interventions in palliative care including to explore recruitment issues (Flidner et al., 2019; Froggatt et al., 2020).

1.8.3 Blinding and the use of placebo

In randomised controlled trials, participants may be blinded to the intervention allocation and placebos can also be used (see table 3) which has implications for the recruitment and informed consent process. The use of blinding acknowledges the influence on study outcomes of patient and researcher subjective beliefs and expectations of the treatment under investigation (Sanderson et al., 2013). It may not always be possible to conceal treatment allocation from trial participants as the intervention may be, for example, a clinical service and only the statistician carrying out the analysis may be blinded (Froggatt et al., 2020; Johnsen et al., 2019).

Blinded placebo controlled trials are seen as the gold standard in clinical medicine because they reduce the risk of bias during data collection and assessment and so increase internal validity (Friedman et al., 2010; Torgerson, 2008).

1.8.4 Ethical issues related to randomised controlled trial methodology

Some health care professionals believe it is unethical to carry out randomised controlled trials. This is also an issue in palliative care with some clinicians feeling uncomfortable about randomising palliative care patients, particularly those that are dying, to a control arm. This

is because the control group is excluded from receiving a potentially beneficial intervention. This is in addition to concerns about overburdening palliative care patients with research procedures, such as questionnaire completion or additional tests, at a difficult time in their lives. Patients and carers may share these concerns and worry they are missing out on a potentially beneficial intervention through the randomisation process. Clinical equipoise needs to exist for a randomised controlled trial to be ethically justified, the idea that there is *'uncertainty in the relevant community of experts as to the preferred practice'* (Weijer et al., 2012)(p.7). Clinicians, patients and carers can struggle to understand the concept of clinical equipoise. The challenge of maintaining clinical equipoise during the recruitment process is discussed in detail in section 1.12.2 below.

Whether it is ethically justifiable to carry out and recruit patients to placebo controlled trials in palliative care has been debated in the literature (Hardy, 1997; Kirkham & Abel, 1997). Friedman et al (2010) argue that two situations need to exist to justify the use of a placebo in a trial; participants need to be aware as part of the informed consent process that they may be allocated to a placebo and no standard evidenced based treatment exists. If a proven standard therapy exists, the placebo and the intervention being tested should be used in conjunction with this standard treatment such as the continued use of radiotherapy in a trial of pregabalin versus placebo for cancer related bone pain (Fallon et al., 2016).

Hardy (1997) contended that including palliative care patients in placebo trials was justified because many if not most treatments are based on anecdote and physician preferences and because of the power of the placebo effect. The placebo effect describes *'the phenomenon in which patients' symptoms may improve while receiving an inactive substance in a clinical trial'* (p.722) because of complex psychobiological responses (Sanderson et al., 2013).

Patients may also experience nocebo effects which refers to a situation where the patient experiences adverse effects while receiving a placebo (Sanderson et al., 2013). Placebo trials that show the effectiveness and safety of a symptom control medication despite known high placebo response rates can provide stronger evidence for the treatments use in clinical practice (Currow et al., 2017; Sanderson et al., 2013). Negative results from adequately powered trials can still be viewed as important as they can inform clinical decision making and prevent patients from experiencing unwarranted side effects (Sanderson et al., 2013; Visser et al., 2015). For example, in a placebo controlled trial of Octreotide for inoperable bowel obstruction in advanced cancer, no statistical or clinical significant difference was found between those receiving the placebo and those receiving Octreotide (Currow et al., 2015). Kirkham and Abel (1997) challenged the idea that placebo control trials are the only way to assess how well a symptom control medication works in practice especially given the ethical and practical difficulties of carrying out this type of study in a palliative care population.

Whether trial findings actually influence clinical practice has been discussed in the literature (Campbell et al., 2018; Visser et al., 2015). The continued use of anti-muscarinic drugs for death rattle, upper respiratory tract secretion accumulation with noisy breathing, illustrates the challenges of implementing research findings into clinical practice. They are still used despite evidence suggesting there is no benefit and there is a risk of adverse effects (Visser et al., 2015; Watts et al., 2019).

1.8.5 Alternative randomised controlled trial designs

Alternative randomised controlled trial designs have been suggested to address some of the concerns associated with traditional trial designs that can have a negative impact on the recruitment process. These issues include ethical concerns regarding randomisation and withholding a potentially beneficial treatment or intervention from palliative care patients and their carers (Deutsch et al., 2020). Wait list or fast track trials (see table 3) with short waiting times are seen to have a role in improving recruitment to palliative care trials. It has been proposed that a wait list or fast track trial design may be more acceptable to patients, clinicians and ethics committees as all patients are offered the intervention at some point in time (M. Farquhar et al., 2009; Higginson & Booth, 2011; Torgerson, 2008; Veronese et al., 2017). This is when it would be viewed as unethical to withhold an intervention when previous research has suggested it could potentially be beneficial. In the palliative care context, sufficient patients in the waiting group need to survive long enough to receive the intervention (Higginson & Booth, 2011). Ethical concerns about wait list designs have still been raised as patients may deteriorate or die before they receive the intervention (McWhinney et al., 1994). In cross-over trials of short acting drugs or interventions, all patients also have the option to try all the treatments on offer but may need to be in the study for longer which could influence their decision to participate (Hui et al., 2015).

In the real world, patients may have strong preferences for or against a particular intervention which can influence trial acceptability and therefore the trial recruitment process. If they are not allocated to their preferred trial arm they may experience 'resentful demoralisation' (Torgerson, 2008). This term describes the impact of the person's

disappointment of being randomised to their non-preferred arm on study outcomes (Rebers et al., 2016). Patient preference trials can be used to manage patient expectations that can bias the results of the study and be detrimental to the recruitment process (Torgerson, 2008). A Zelen trial design also aims to deal with preference effects and recruitment challenges (Torgerson, 2008) and their role in the palliative care setting is discussed in the literature review in chapter two.

The Ottawa Statement on the Ethical Design and Conduct of Cluster Randomized Trials argues that in cluster trials, those in the usual care arm *'must not be deprived of effective care or programs to which they would have access if there were no study being conducted'* (Weijer et al., 2012) (p.7). Step wedge cluster trials are seen as an option to increase clinician and organisational acceptability of a trial as all organisational clusters receive the intervention sequentially (Grande et al., 2017). Other trial designs have been seen as an attractive option in the palliative care setting as they require smaller sample sizes to reach power such as a cross-over or aggregated N of 1 trials (Hui et al., 2015; Mitchell et al., 2015).

1.8.6 Alternative research methods in the palliative care context

Given the challenges of carrying out and recruiting to randomised controlled trials in palliative care, it has been suggested that other research methods should be considered (Black, 1996; Hadley et al., 2009). The use of existing data sets and secondary analysis to evaluate clinical practice have been recommended, where appropriate, as this approach has the potential to produce information more quickly and cost effectively than a trial (Higginson et al., 2013). High quality prospective observational studies that measure

clinically useful outcomes have been seen as an alternative to randomised controlled trials (Costantini, 2007; Hadley et al., 2009; May et al., 2015). For example, a prospective cohort study compares the experience of patients exposed to a study intervention such as a palliative home care service with other patients not exposed to the intervention with data being collected prospectively, retrospectively or both (Costantini, 2007). Patients are then followed up from intervention exposure to the outcome of interest such as the proportion of home deaths. If the intervention group has a higher or lower frequency of home deaths than the control group, then an association between the palliative home care service and proportion of home deaths is evident (Costantini, 2007). Matching cases and controls for some patient characteristics attempts to reduce the effect of a potential selection bias. The evidence base in palliative care is also deficient of good quality observational studies (Visser et al., 2015).

The use of 'big data' sets such as large healthcare registers linked to multiple data sources are currently being explored in end-of-life care research which may support this type of study design (European Association for Palliative Care, 2020). Using routinely collected data to measure study outcomes may be problematic as, for example, the intensity and prevalence of symptoms may be poorly documented in health care records (Mazzocato et al., 2001). The role of routine clinical data in research needs to be further explored, including its use in randomised controlled trials. For example, how it can be used in trials as outcome data, as a recruitment strategy to target eligible participants, and to improve the incidence of missing data (Mc Cord et al., 2018; Wright-Hughes et al., 2018). In order to increase the evidence base in palliative care, there has been a call for high quality studies that use all the available methodological tools available, including randomisation when possible (Aoun & Nekolaichuk, 2014; Costantini, 2007; Lovell et al., 2020). The

advantages and limitations of each research methodology need to be considered when designing a study to answer a clinical question (Costantini, 2007).

1.8.7 My view of the role of randomised controlled trials in palliative care

My view is that there is a need for evidence-based practice to be built on a wide range of study types, including randomised controlled trials. Trials are increasingly being used in palliative care so there is a need to understand the recruitment process and its associated challenges. As discussed previously, I have worked on a number of trials that have struggled to achieve their recruitment targets and believe if a trial fails to recruit its target then this has ethical implications for patients and carers. Seriously ill patients and their carers will have taken part in a research study where it has not been determined by the end of the trial whether the intervention does more good than harm. This is why my research focuses on trial recruitment issues from the health care professional's perspective, a key barrier to the randomised controlled trials use and implementation in clinical practice.

1.9 Why recruitment is important

Recruiting sufficient numbers of participants is important in all study designs but meeting trial recruitment targets is especially important to ensure the trial is adequately powered to detect a clinical benefit that is statistically significant (Torgerson, 2008). This requirement is reflected in the CONSORT reporting guidelines for randomised controlled trials (Schulz et al., 2010). There are also ethical concerns related to underpowered trials as researchers have

exposed participants to an intervention with uncertain benefit and on study completion may still be unable to determine whether the intervention does more good than harm (Carlisle et al., 2014; Treweek et al., 2018). Struggling to reach estimated recruitment targets also means the trial has the potential to be slow and expensive (Healy et al., 2018; Higginson et al., 2013). One report highlighted that nearly half (45%) of Health Technology Assessment program and UK Medical Research Council funded trials received an extension of some kind (Sully et al., 2013). There are many examples of palliative care randomised controlled trials experiencing slow recruitment rates (Agar et al., 2017; Currow et al., 2019; Johnson et al., 2019) with trials sometimes requiring a change to their study design to try and achieve power (Ferreira et al., 2020; Westcombe et al., 2003) or being abandoned altogether (Bull et al., 2019; Snowden & Young, 2017).

1.10 Definition of recruitment

Recruitment is the enrolment of an individual person meeting specific inclusion criteria into a research study (National Institute for Health Research, 2019c). This definition is an oversimplification of the term and does not reflect the ‘interactional’ nature of recruitment (Donovan et al., 2014). Recruitment is not characterised by a single event and is often a lengthy and complex process. It occurs in real time, in real clinical settings and it can be a difficult activity as it disrupts the usual clinician/patient relationship (Donovan et al., 2014). The process of recruitment typically involves three steps; identifying, approaching and consenting participants. It is usually carried out by health care professionals within clinical recruitment centres (Preston et al., 2016). Clinical recruitment centres are clinical settings,

such as a hospital or a hospice, where recruitment activity takes place. They are also referred to as a trial or research site in the literature (Bruhn et al., 2019). There may be clinicians within the clinical recruitment centres, such as research nurses, whose primary role is to recruit participants to research studies (Spilsbury et al., 2008). Recruitment may also be carried out by researchers directly involved in the trial in conjunction with the patient's usual clinical care team as illustrated in this study of mirtazapine for chronic or refractory breathlessness (Lovell et al., 2020).

Initially, a potential participant will be assessed against the eligibility criteria outlined in the trial's protocol. Once eligibility has been assessed and it has been confirmed the potential participant meets the eligibility criteria, they will be approached or contacted about the trial (Preston et al., 2016). Verbal and written information will be provided about the trial (Donovan et al., 2014). Thirdly, a discussion about a decision to participate in the trial will occur and if the participant wishes to take part they will be usually asked to sign a consent form (Donovan et al., 2014; Preston et al., 2016).

Written informed consent is only legally required in pharmaceutical trials which is reflected in this definition of informed consent outlined in international Good Clinical Practice guidance for the conduct of pharmaceutical trials:

'A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form.' (European Medicines Agency, 2016)(p.10)

For other types of research studies, consent can be written, oral or implied (Health Research Authority, 2020; Preston et al., 2020). The COVID 19 pandemic and its social distancing requirements have led to remote informed consent procedures being implemented that involve the use of verbal and/or electronic consent (Fernandez Lynch et al., 2020).

The Declaration of Helsinki (2013) recommends that participants receive information about the aims, the methods and the benefits and risks of the study as well as what will happen after the study has ended. Information should be given about sources of funding, conflicts of interest and the researcher's institutional affiliations. The potential participant must be informed of the right to refuse to participate in the study and the right to withdraw consent at any time without reprisal (World Medical Association, 2018). In the UK, there is a growing recognition that the amount of information provided to participants when seeking consent should be proportionate to the type of study being offered (Health Research Authority, 2020). There are also wider calls for simplification of participation information sheets and consent processes even in randomised controlled trials (Dal-Ré et al., 2019; O'Sullivan et al., 2020; Valerie et al., 2011).

Ethical guidance on what information should be disclosed to participants taking part in a cluster randomised controlled trial during the informed consent process has been produced but continues to be debated (van der Graaf et al., 2015; Weijer & Taljaard, 2019). Research ethics committees can waiver consent if obtaining informed consent is not feasible and taking part in the study poses only minimal risk (Rebers et al., 2016; Weijer et al., 2012). Participants can be blinded to their allocation status if they are recruited after cluster randomisation if there are concerns about contamination and the study only poses minimal risk (Weijer & Taljaard, 2019). Contamination refers to a situation where control participants

may change their behaviour because they have learnt about the intervention arm so compromising validity (van der Graaf et al., 2015).

1.11 Adults with impaired capacity to consent to research studies

The palliative care population has a high prevalence of cognitive impairment (Currow et al., 2011) with a recent study finding that at least 66% of patients with advanced cancer admitted to a palliative and supportive care unit lacked decision making capacity (Goswami et al., 2020). Evans et al (2020) describe how there is a 'spectrum of capacity' in end-of-life care research that ranges from those who have the potential and are anticipated to lose capacity to those who lack capacity. The legislation, ethical review processes and terminology that governs research involving adults that lack capacity to consent can be complex, variable and jurisdiction specific (Evans et al., 2020; Shepherd, 2020a). Advance consent (Van Esch et al., 2018) and/or proxy/consultee assent (Froggatt et al., 2020) procedures may be used to allow patients to participate in research, even at the end of life, so ensuring patient autonomy is respected (Currow et al., 2011). For example, in England and Wales in non-pharmaceutical trials, advance consent procedures can be used when it is anticipated that patients may lose capacity during a study. Patients are asked if they were to lose capacity in the future whether they would wish to continue in the trial. If so they are asked to nominate a consultee who the researchers can approach to ask their opinion on the patients continued participation in the trial (Department for Constitutional Affairs, 2007; Gysels et al., 2013). In pharmaceutical trials, under European legislation (European Parliament the Council of the European Union, 2014) consent to participate in a study is

presumed to remain legally valid after loss of capacity but consultee review is seen as good practice (Evans et al., 2020). Given the high prevalence of cognitive impairment in the palliative care population, there have been calls for advance consent processes to be extended to all types of palliative care research (Gysels et al., 2013).

1.12 The challenges of recruitment in randomised controlled trials

Recruitment has been identified as one of the prominent challenges in palliative and end-of-life-care research. All types of palliative care studies can experience recruitment challenges (Edwards et al., 2019; Kaiser et al., 2020; Steinhauser et al., 2006; Stone et al., 2013) but recruiting to palliative care randomised controlled trials can be especially difficult (Carrow et al., 2011; Grande & Todd, 2000; Higginson et al., 2013). Achieving recruitment targets to trials can be a struggle in any setting (Treweek et al., 2018) and in the non-palliative care literature, there are many reports of trials struggling to meet their recruitment targets (Carlisle et al., 2014; McDonald et al., 2006; Sully et al., 2013; Walters et al., 2017). In one review of randomised controlled trials funded and published by the UK's National Institute for Health Research Health Technology Assessment Programme, the final recruitment target sample size was achieved in 56% (85/151) of the trials (Walters et al., 2017). In a more recent review, 31% of stepped-wedge cluster trials did not reach their planned recruitment targets (Eichner et al., 2019). Figures can differ between reports and it is estimated that less than half of randomised controlled trials are actually likely to achieve their recruitment targets (Treweek et al., 2018). In the Bouca-Machado et al (2017) review discussed in section 1.5, of the 107 included palliative care trials, only 53.3% of studies reported a

sample size calculation. Of the 57 studies that had reported a sample size calculation, only 36.8% (n=21) reached the estimated target. The challenges of recruiting to palliative care randomised controlled trials is also evident in the number of underpowered studies reported in systematic reviews of palliative care interventions (Haun et al., 2017; Kavalieratos et al., 2016).

1.12.1 Limited pool of eligible participants

In palliative care trials, often large numbers of patients need to be screened against the inclusion and exclusion criteria to identify those who may be eligible to participate. McCaffrey et al (2016) estimated from their experiences of recruitment in four pharmaceutical symptom control trials that approximately 50 specialist palliative care patients need to be referred to the trial for one person to be potentially eligible to participate. This is because thresholds of symptom severity may need to be reached for the patient to be eligible and study criteria related to other assessments and treatments, including disease modifying treatments, may influence eligibility (McCaffrey et al., 2016). This is in addition to the contextual factors that can influence palliative care research generally such as patient frailty, symptom burden, limited life expectancy, prognostic uncertainty, acknowledgement of the patient's mortality, competing demands and gatekeeping (LeBlanc et al., 2013).

1.12.2 Maintaining clinical equipoise

There are also issues associated with randomised controlled trials that are not unique to palliative care that can be magnified in this population because of these underlying contextual factors (Currow et al., 2011). These include patient, carer and health care professional concerns about randomisation, blinding and placebos. As discussed in section 1.8.4, clinical equipoise provides the justification for carrying out randomised controlled trials, the idea that there must be real uncertainty as to whether the new treatment is superior to no treatment or existing treatments (Grande & Todd, 2000). Patients, carers and health care professionals can deny and struggle with the concept of clinical equipoise. In the general literature, there are reports of clinicians holding strong preconceived views about the merits of a particular treatment or service and find balancing the researcher and clinician role challenging (Donovan et al., 2014; Elliott et al., 2018). There are also reports of patients having strong preferences for a particular treatment arm with patients often being keen to receive the new intervention (Harrop, Kelly, et al., 2016; Norris et al., 2019; Paramasivan et al., 2011). This lack of neutrality or clinical equipoise among patients and clinicians in palliative care trials is also raised as an issue in the literature (Deutsch et al., 2020; Grande & Todd, 2000; Harrop, Noble, et al., 2016; LeBlanc et al., 2010). In a non-placebo pharmaceutical trial, 10 patients with advanced cancer were interviewed about their reasons for participating in the trial. Altruism was a secondary motivating factor behind hope of medical benefit (Harrop, Noble, et al., 2016). Research ethics committees can also struggle with the concept of equipoise as illustrated in a recent trial of sustained release morphine for chronic breathlessness. One committee required that all participants

had access to rescue immediate release morphine for symptom control (Ferreira et al., 2020).

1.12.3 Recruitment challenges associated with blinding and placebos

In the general literature, a systematic review of recruitment strategies found open trials rather than blinded, placebo trials improved recruitment (Treweek et al., 2018). There is some evidence in the literature that the use of blinding and placebos can act as a deterrent when recruiting to a palliative care trial. A survey of the views of advanced cancer patients and their relatives towards taking part in hypothetical research found that about one-half were deterred by the concepts of 'randomisation', 'placebo-control' and 'blinding' (White et al., 2008) . A similar survey of palliative care clinicians found less than half of non-medical health care professionals would be willing to refer to blinded or placebo-controlled studies (White et al., 2008). More recently, patients who had taken part in a feasibility placebo controlled trial of mirtazapine for breathlessness in advanced disease were mostly accepting of the fact they may receive the placebo but this was not always the case (Lovell et al., 2020).

1.13 Strategies to facilitate recruitment to trials

What strategies may facilitate recruitment to trials (Boland et al., 2015; Treweek et al., 2018) or to research studies in general (Preston et al., 2016) is hampered by a lack of high-quality evidence. The use of telephone reminders to people who do not respond to a postal

invitation increased recruitment in one review (Treweek et al., 2018). 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 (Boland et al., 2015). 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 (Preston et al., 2016). In a Delphi survey of UK Clinical Trials Units, methods to boost recruitment was identified as the highest priority for trials methodology research (Tudur Smith et al., 2014). More recently, in the UK and Ireland, the Prioritising Recruitment in Randomised Trials Priority Setting Partnership brought together relevant stakeholders, including members of the public, to identify unanswered questions around trial recruitment research (Healy et al., 2018). The top 10 prioritised research questions are outlined in the table below.

Table 4: The top 10 research questions from the Prioritising recruitment in Randomised trials study (PRioRiTy) (Healy et al, 2018)

1. How can randomised trials become part of routine care and best utilise current clinical care pathways?
2. What information should trialists communicate to members of the public who are being invited to take part in a randomised trial in order to improve recruitment to the trial?
3. Does patient/public involvement in planning a randomised trial improve recruitment?
4. What are the best approaches for designing and delivering information to members of the public who are invited to take part in a randomised trial?

5. What are the barriers and enablers for clinicians/healthcare professionals in helping conduct randomised trials?
6. What are the key motivators influencing members of the public's decisions to take part in a randomised trial?
7. What are the best approaches to ensure inclusion and participation of under-represented or vulnerable groups in randomised trials?
8. What are the best ways to predict recruitment rates to a randomised trial and what impact do such predictions have on recruitment?
9. What are the best approaches to optimise the informed consent process when recruiting participants to randomised trials?
10. What are the advantages and disadvantages to using technology during the recruitment process?

How the recommendations above fit with this study's research question, methodology and findings is discussed in the following chapters.

1.14 Theoretical frameworks to inform the trial recruitment process

In the general trial literature, it has been suggested that theoretical frameworks may improve our understanding of complex recruitment processes. Tramm et al (2013) argue that the Medical Research Council's Complex Intervention Framework can be applied to the trial recruitment context (Craig et al., 2013; Tramm et al., 2013). This framework was not used in this study as the aim of this PhD was not to develop and evaluate a recruitment intervention.

There have been calls to use theoretical concepts from the marketing and business world to address trial recruitment challenges (Francis et al., 2007; Galli et al., 2014; McDonald et al., 2011). Marketing focuses on meeting customers' needs by understanding the factors that influence customer purchasing decisions (Galli et al., 2014). It has been proposed that running a trial can be like running a business so applying marketing principles to trial recruitment processes may lead to improvements in recruitment rates (Francis et al., 2007; McDonald et al., 2011). Using marketing theory to inform trial recruitment processes would appear to clash with the altruistic principles of health care (McDonald et al., 2011), particularly in the context of palliative and end-of-life care. This is because the purpose of commercial marketing is to make a profit by encouraging, with some even arguing manipulating, customers into purchasing goods and services that are on offer. Giving palliative care patients and carers the 'hard sell' and convincing them to take part in a trial they may not wish to take part in would clearly be unethical in the context of health care and therefore would not be an appropriate approach to follow.

1.14.1 'Social Marketing Mix Framework'

Social marketing has been used in public health for many years and applies commercial 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 rather than for financial gain (Grier & Bryant, 2005; Nichols et al., 2004). The 'Social Marketing Mix', adopted from commercial marketing, is a key concept within social marketing and is viewed as '*central to the planning and implementation of an integrated marketing strategy*' (Grier & Bryant,

2005) (p. 322). Social marketing has traditionally focused on applying the four 'Ps' of marketing: product, price, place and promotion (Gordon, 2012).

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 enrolment. There are different versions used in the trial recruitment literature (Galli et al., 2014; Tompkins et al., 2019) but the version chosen for this study was that outlined by Nichols et al (2004) which uses '6 Ps' (see table 5). These are; Identifying participants, Product, Price, Place, Promoting the study and Working with Partners. This framework was chosen for a number of reasons. This study focuses on the key role that health care professionals play in the recruitment process and this framework recognises the importance of 'Working with Partners'. Peplau's theory of interpersonal relations has been used to understand the nurse-patient relationship during the trial recruitment and retention process. This theoretical framework was not chosen as this study does not focus purely on the nursing workforce or explore the issue of trial retention (Penckofer et al., 2011).

The 'Social Marketing Mix Framework' was also chosen as it has the potential to offer a patient centred approach to the trial recruitment process. Nichols et al (2004) challenge the idea that applying marketing principles to the trial recruitment process in health care is controversial. They argue that it actually puts the patient or carer at the centre of the research process as it requires the researcher to focus on *'the needs, wants, and preferences of the target audience'* (Nichols et al., 2004)(p.10). For example, has the researcher considered whether the intervention or 'Product' being trialled is what the patient or carer wants and have they minimised the 'Price' of taking part in the trial for participants. The

purpose of social marketing is to facilitate voluntary rather than coercive behaviour change, ideally by involving consumers in the design, implementation and evaluation process (Grier & Bryant, 2005).

There are limited theories of trial recruitment available with the 'Social Marketing Mix Framework' being the only one used in a similar population. It has been applied to trials recruiting the carers of patients with Alzheimer's disease (Etkin et al., 2012; Nichols et al., 2004; Schulz et al., 2003) so aligning more closely with the palliative care population. In addition, elements of this framework have been used in a successfully recruiting palliative care service delivery trial (LeBlanc et al., 2013). On a personal level, this approach 'made sense' to me as a palliative care researcher and previous palliative care research nurse. The business model approach to trial recruitment developed by Francis et al (2007) was another possible theoretical framework. This approach was not chosen as it has been applied to trauma and smoking cessation trials and the characteristics of these studies are quite different to palliative care trials which is reflected in their framework.

Using the principles of community based participatory research to recruit 'hard to reach populations', such as dementia caregivers and/or ethnic minority groups, is another approach suggested in the literature (Grill & Galvin, 2014). This framework was not chosen as it was expected, given the patient population, that recruitment would largely take place via health care settings rather than community organisations.

Table 5: The '6 Ps' of the 'Social Marketing Mix Framework'

Elements	Definitions
Identifying participants	Defining the target audience (p.4).
Product <i>Defining the product:</i> <i>The product's competition:</i>	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 (p.4). The amount of competition for the participant's time and energy (p.5).
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 (p.5-6).
Place (Improving accessibility)	'The location where the participant will receive information about, or engage in, the intervention' (p.6).
Promoting the study	'Identify the acceptable avenues that reach the target population' (p.7).
Working with partners	'Partners are defined as organisations involved with a social change effort or serving as conduits to target audiences' (p.8). Things to consider: partner education, partner referrals and recruitment and barriers to partnering.

1.15 Stakeholder engagement

I recognise the importance of and have personal experience of engaging public and professional stakeholders in the planning, ongoing management and dissemination activities of palliative randomised controlled trials (Froggatt et al., 2020; Korfage IJ, 2020). The research question in this thesis required health care professional stakeholders with experience of palliative care trials. The decision was made not to engage additional health

care professional stakeholders in the development, ongoing management or analysis stage of this study. This approach was taken, as I, along with my supervisors, have relevant palliative care clinical and research experience. Given the small number of palliative care professionals involved in trial recruitment, recruiting stakeholders with relevant experience may have limited the already small pool of eligible participants. Health care professionals can be time poor and difficult to engage so this may have caused study delays. This study also had no funding to cover the cost of stakeholder engagement. The limitations of this approach are discussed in chapter seven.

1.15 Conclusion

There is a need to increase and improve the evidence base that underpins clinical practice in palliative care. High quality adequately powered randomised controlled trials can play a role in addressing this deficit by being the optimal method for assessing whether palliative care interventions are effective. The trial recruitment process is complex and is made up of a number of interconnected stages. Randomised controlled trials in palliative care, like those outside palliative care, can experience recruitment difficulties. Some of the recruitment challenges are not unique to palliative care but can be amplified in this vulnerable patient population. The barriers to recruitment in palliative care randomised controlled trials and the potential facilitators and strategies that may help to overcome them needs further exploration.

Chapter two: Literature review

2.1 Introduction

In the previous chapter, the need for more high quality adequately powered randomised controlled trials to improve the evidence base in palliative care was highlighted. Why so many palliative care trials struggle or fail to achieve their recruitment targets is an important area of clinical practice that is poorly understood. The aim of this literature review is to identify, explore and synthesise what is known about recruitment issues in palliative care randomised controlled trials. This review is unique as it uses the 'Social Marketing Mix Framework', the chosen theoretical framework for this study, to explore recruitment barriers and facilitators in palliative care randomised controlled trials. This review has been peer reviewed and published (Dunleavy et al., 2018), presented at the 15th European Association for Palliative Care World congress in Madrid (oral presentation) (Dunleavy, 2017) and the 4th International Clinical Trials Methodology Conference in Liverpool (poster presentation) (Dunleavy et al., 2017). The findings of the review informed the research question by identifying gaps in the current evidence base.

2.2 Literature review methods

A systematic approach is used in this literature review as it was guided by a review question and how the literature was identified, selected, appraised and synthesised are explicitly described (Jesson et al., 2011).

2.2.1 Aim of the review

The aim of this review is to identify, explore and synthesise what is known about the recruitment barriers and facilitators in palliative care randomised controlled trials using the '6 Ps' of the 'Social Marketing Mix Framework'.

2.2.2 Review question

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

2.3 Literature review design

2.3.1 Narrative synthesis

The literature review is guided by Popay et al's (2006) narrative synthesis framework as this approach facilitates the incorporation of research and non-research data. Initial searches indicated that the data to support the review question was likely to be narrative observations made by authors about recruitment issues rather than primary research data. This review is based on the premise that narrative observations can provide valuable insights into what the barriers and facilitators are to patient and carer recruitment to palliative care randomised controlled trials and the strategies that have been implemented to overcome them.

Narrative synthesis uses a textual approach to synthesis so that ‘*studies addressing a different aspect of the same phenomenon can be narratively summarised and built up to provide a bigger picture of that phenomenon*’ (Booth et al., 2012)(p.146). Popay et al (2006) developed a general framework made up of four elements to guide the process of narrative synthesis. They suggest it does not need to be followed in a linear fashion and is an iterative process (Popay et al., 2006). Table 6 provides an overview of how the four elements of the framework have been applied within this study. The process is discussed in more detail within the relevant sections below.

Table 6: Narrative Synthesis Framework (Popay et al 2006)

<i>Element 1: The role of theory in evidence synthesis</i>	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 (p.12).The ‘6 Ps’ of the ‘Social Marketing Mix Framework’ was the chosen theory in this study.
<i>Element 2: Developing a preliminary synthesis</i>	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.
<i>Element 3: Exploring relationships within and between studies</i>	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.
<i>Element 4: Assessing the robustness of the synthesis</i>	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 (p.15).

2.4 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 concepts were palliative care and randomised controlled trials. 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 (Sigurdardottir et al., 2014; Sladek et al., 2006; Tieman et al., 2008). 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. A start date of 1990 was chosen for the search as two key palliative care trial methodological papers were published in the 1990s. It was felt that it was important to capture these two papers in the search strategy (McWhinney et al., 1994; Rinck et al., 1997). These papers highlighted that there were only a handful of palliative care randomised controlled trials carried out prior to 1990. The strategy was modified as necessary for the other databases searched (see appendix 1). The reference lists of the included studies were also hand searched to identify additional papers specifically focusing on recruitment to palliative care randomised controlled trials.

2.4.1 Study Eligibility

The inclusion and exclusion criteria are listed in table 7. Titles and abstracts were screened by myself to identify potentially eligible papers and another reviewer independently verified 10% of this search. I screened the remaining full papers to identify the final included papers. Any discrepancies when screening titles and abstracts were resolved through discussion and by obtaining the full text of the article for further clarification if necessary.

Table 7: Inclusion and exclusion criteria

Inclusion	Exclusion
<p>Study Population</p> <p>Cancer</p> <ul style="list-style-type: none"> • 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 <p>Non-Cancer</p> <ul style="list-style-type: none"> • Adults with a progressive, life threatening disease (defined by classifications of disease severity such as the New York Heart Association Functional Classification. 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. 	<p>Study Population</p> <ul style="list-style-type: none"> • 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 (Radbruch, 2014). • Neo adjuvant or adjuvant chemotherapy studies • Palliative care randomised controlled trials only recruiting health professionals

<ul style="list-style-type: none"> • Non-professional carers of patients with a progressive, life threatening disease • Parents of children with a progressive, life threatening disease <p>Study Design</p> <p>The types of papers listed below were included if they contained information about the barriers, facilitators or strategies to recruitment to palliative care randomised controlled trials:</p> <ul style="list-style-type: none"> • Randomised controlled trials (pilot/feasibility studies as well as full scale palliative care trials) • Intervention studies testing recruitment strategies • Qualitative/observational studies that report barriers, facilitators or strategies to recruitment to palliative care randomised controlled trials. • Articles reporting narrative opinions and/or observations related to conducting a palliative care randomised controlled trial. 	<p>Study Design</p> <p>Non randomised trials</p>
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2.5 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 8). Interview data from patients taking part in a palliative care randomised controlled trial or professionals involved in recruitment to a trial and its subsequent analysis reported in the included qualitative papers was extracted. Data in the form of narrative observations

located in the discussion sections of randomised controlled trial 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 myself but 10% of the papers were independently verified by another reviewer. This was to improve the rigor of the review by a second reviewer checking understanding and interpretation of the data and for any data extraction errors (Campbell et al., 2019). The same double coder, a medical professional, was used for screening titles and abstracts and data extraction. Any discrepancies in the data extraction process were resolved through discussion and there was no requirement to consult an independent arbiter.

2.6 Data Synthesis

2.6.1 Element 2: Developing a preliminary synthesis

Following Popay et al's approach, relevant sections of the included papers were initially coded line by line. A mixture of predetermined (piori) codes, the '6 Ps' from the 'Social Marketing Mix Framework' and open codes were used to ensure important aspects of the data were not missed during coding (Gale et al., 2013). 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 myself but 50 % of the papers

coded were then independently checked by a second reviewer. This was to improve the rigor of the review by verifying the interpretation of the findings (Campbell et al., 2019).

2.6.2 Element 3: Exploring relationships within and between studies

As recommended by Popay et al, 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 table 9). 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.

2.7 Quality Assessment

Trial 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. Reflecting Popay et al's approach, 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 appendix 2)(Eagar et al., 2007). 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 (Aveyard et al., 2016).

2.8 Results

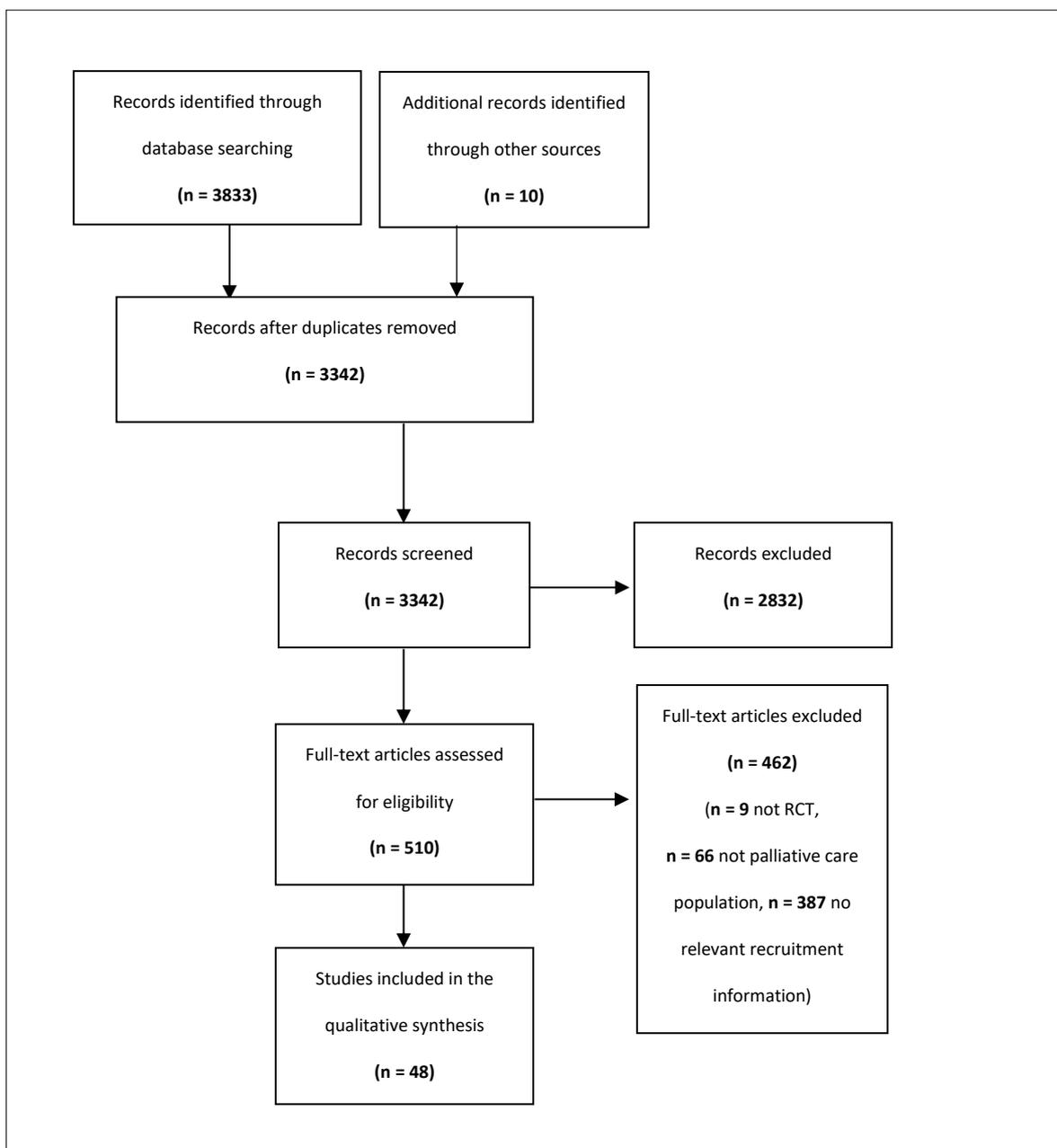


Figure 1: PRISMA flowchart

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 8. The barriers, facilitators and strategies are mapped within the '6 Ps' of the 'Social Marketing Mix Framework' in the narrative below. The greatest number of barriers, facilitators and strategies identified could be mapped within the 'Working with Partners' category and table 9 provides a visual overview of how the evidence is weighted within the '6 Ps'.

Table 8: Description of included studies

Author/date/ country	Article type & data extraction point	Aim original study	Method original study	Sample & setting	Target sample	Time to recruit sample	Type of Intervention /Control	Data Collection	LoE*
1 Abernethy et al (2010) (US)	Retrospective report of successful strategies 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 Ammari et al (2015) (Denmark)	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.	Parallel group RCT multi centre	advanced cancer patients and their carers hospital	N= 504 families between October 2011 - February 2013	N=57, not stated	Intervention: a 'family and coping-orientated palliative home care intervention' Control: usual care	questionnaire	2 a
3 Bakitas et al (2006), linked to Bakitas et al(2009) (US)	A report of challenges faced during an ongoing RCT. Main section.	To test the efficacy of a psycho- educational intervention.	RCT, clinician blinded single centre	advanced cancer patients and carers oncology hospital	N=not stated	N=104 patients, 77 caregivers over 14 months	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

Author/date/country	Article type & data extraction point	Aim original study	Method original study	Sample & setting	Target sample	Time to recruit sample	Type of Intervention /Control	Data Collection	LoE*
4 Bakitas et al(2009), linked to Bakitas et al (2006) (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 November 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 (1998) (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 (2010) (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 recruited to the main study, 70 took part in the RCT	Intervention: hand held fan Control: a wristband to serve as a placebo.	interview, postal questionnaires	2 a

Author/date/country	Article type & data extraction point	Aim original study	Method original study	Sample & setting	Target sample	Time to recruit sample	Type of Intervention /Control	Data Collection	LoE*
7 Buss and Arnold (2004) (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 (2008) (US)	A paper reporting the authors' experiences of recruiting to two related RCTs Discussion section.	To examine the impact of CHES 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 (CHES) Study 1 CHES and clinician rapport or CHES Study 2 CHES and clinician rapport or control access to computer/internet	survey	2 a
9 Clark et al (2008) (Australia)	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 (NB) at the end-of-life.	A pilot phase II randomised, 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 randomised 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

Author/date/ country	Article type & data extraction point	Aim original study	Method original study	Sample & setting	Target sample	Time to recruit sample	Type of Intervention /Control	Data Collection	LoE*
10 Cook et al (2002) (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 (2006), linked to LeBlanc et al (2013) and Mitchell and Abernethy (2005) (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 (2001) (UK)	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 interview and focus group.	3

Author/date/country	Article type & data extraction point	Aim original study	Method original study	Sample & setting	Target sample	Time to recruit sample	Type of Intervention /Control	Data Collection	LoE*
13 Farquhar et al (2009) linked to Farquhar et al (2011) (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 (2011) linked to Farquhar et al (2009) (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 (2015) (US)	A paper presenting the findings of a pilot RCT. Discussion section.	To determine the feasibility of a patient navigator intervention to improve palliative care outcomes for Latino adults with serious illness.	Pilot RCT single centre	Patients with a serious illness who were appropriate for a palliative approach hospital	N=Not stated	N=64 May 2010-September 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, medical record review	2 a

Author/date/ country	Article type & data extraction point	Aim original study	Method original study	Sample & setting	Target sample	Time to recruit sample	Type of Intervention /Control	Data Collection	LoE*
16 Fowell et al (2006) (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 (2014) (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 Implantable Cardioverter Defibrillators.	Cluster RCT multi Centre	advanced heart failure patients and their caregiver hospital	N= September 2011- August 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 (2000) (Canada)	A paper examining recruitment to a RCT and analysis of recruitment figures. Discussion section.	To compare the impact on survival of group psychosocial 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

Author/date/country	Article type & data extraction point	Aim original study	Method original study	Sample & setting	Target sample	Time to recruit sample	Type of Intervention /Control	Data Collection	LoE*
19 Gorman et al (2008) (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 (2014) (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 randomised to discontinue or continue on statins.	Qualitative study Parent study: non blinded multi centre RCT.	Qualitative study: Principal Investigators (PIs) and clinical research coordinators (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	Semi structured telephone interviews at end of recruitment, review of recruitment rates. Parent study: interviews and medical record reviews	3
21 Hardy et al (1998) (UK)	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

Author/date/ country	Article type & data extraction point	Aim original study	Method original study	Sample & setting	Target sample	Time to recruit sample	Type of Intervention /Control	Data Collection	LoE*
22 Higginson et al (2008) (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 (2001) (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 (2009) (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 (2011) (UK)	A paper reporting findings of a RCT. Discussion section.	To test the acceptability 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

Author/date/ country	Article type & data extraction point	Aim original study	Method original study	Sample & setting	Target sample	Time to recruit sample	Type of Intervention /Control	Data Collection	LoE*
26 Jones et al (2013) (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 (1999)(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 (2013) (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

Author/date/ country	Article type & data extraction point	Aim original study	Method original study	Sample & setting	Target sample	Time to recruit sample	Type of Intervention /Control	Data Collection	LoE*
29 Kutner et al (2010) (US)	A paper describing the strategies and responses to methodological challenges faced during a RCT. Main body.	To investigate the efficacy of massage therapy for decreasing pain.	RCT multi centre	advanced cancer patients palliative care/ hospice settings	N=440, modified to 380	N= 380 over 36 months	Intervention: massage therapy Control: simple touch	not stated	2 a
30 Latimer et al (1998) (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 hospital outpatients	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 LeBlanc et al (2013), linked to Currow et al(2006) and Mitchell and Abernethy (2005) (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	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

Author/date/ country	Article type & data extraction point	Aim original study	Method original study	Sample & setting	Target sample	Time to recruit sample	Type of Intervention /Control	Data Collection	LoE*
32 Lee et al (2013) (New Zealand)	A paper reporting the findings and difficulties encountered during a feasibility RCT. Discussion section.	To assess the feasibility of conducting a Phase III RCT investigating the therapeutic value of gastrografin in malignant bowel obstruction.	Randomised double-blinded placebo-controlled feasibility study single centre	advanced cancer hospital	N=20 patients over 8 months	N=9 enrolled	Intervention: gastrografin Control: placebo	questionnaires	2 a
33 McMillan and Weitzner (2003) (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(1994) (Canada)	A report outlining the challenges of carrying out RCTs in palliative care. Introduction	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	questionnaire, nausea and pain diary	2 a

Author/date/ country	Article type & data extraction point	Aim original study	Method original study	Sample & setting	Target sample	Time to recruit sample	Type of Intervention /Control	Data Collection	LoE*
35 Miller and Chibnall (2003), linked to Miller et al (2005) (US)	A letter outlining the researchers' experiences of recruiting to a RCT. All of the letter	Not stated	RCT multi centre	ambulatory patients with life threatening illnesses hospital	N=300 over 6 months	N=After 12 months, 98 recruited	Intervention: tool designed to help patients prepare for 'a good death' Control: not stated	not stated	2 a
36 Miller et al (2005), linked to Miller and Chibnall (2003) (US)	A paper reporting the findings of a RCT. Discussion section.	To evaluate the effects of a program to address psycho- socio-spiritual needs.	randomised 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 (2005) linked to LeBlanc et al (2013) and Currow et al (2006) (Australia)	A retrospective comparative study of two palliative care RCTs (QCC and PCT). 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/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= randomised 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 collection instrument, data collected by research assistant PCT: data collection by clinical nurses as part of routine care	2 a

Author/date/ country	Article type & data extraction point	Aim original study	Method original study	Sample & setting	Target sample	Time to recruit sample	Type of Intervention /Control	Data Collection	LoE*
38 Noble et al (2015) (UK)	A paper reporting the findings of a feasibility study to inform the design of a RCT. Qualitative study results section.	To identify the most effective length of anticoagulation for treatment of cancer- associated thrombosis (CAT). To identify the practicalities of conducting a full RCT.	Feasibility study RCT with embedded qualitative study multi centre	patients with locally advanced or metastatic cancer oncology outpatients	N=Stage 1 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	N= 5 December 2013-June 2014. Qualitative study: 15 patients 1 carer	Ongoing Low Molecular Weight Heparin (LMWH) treatment for CAT versus cessation of LMWH at 6 months' treatment	blood tests, diary cards, QOL questionnaires	3
39 Philip et al (2006) (Australia)	A paper reporting the findings of a RCT. Discussion section.	To examine the effect of oxygen versus air on the relief of dyspnoea.	Randomised, double-blind, crossover trial multi centre	advanced cancer cancer centres, inpatients and outpatients	N=50	N=51 over 5 years	Randomised 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

Author/date/ country	Article type & data extraction point	Aim original study	Method original study	Sample & setting	Target sample	Time to recruit sample	Type of Intervention /Control	Data Collection	LoE*
40 Prentice et al (2004) (UK)	A paper reporting the findings of a RCT. Discussion section.	To determine whether topical benzydamine hydrochloride 3% cream is more effective than placebo in reducing pain related to pressure areas.	Randomised double blind, placebo- controlled trial. multi centre	hospice cancer inpatients with pain related to pressure areas. palliative care units	N= 30 patients into each study group.	N= 31 patients	Intervention: a single application of benzydamine hydrochloride 3% cream to the painful pressure area. Control: placebo cream to the painful pressure area.	pain scales	2 a
41 Rees and Hardy (2003) (UK)	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	Intervention: to receive either hyoscine or glycopyrronium at the time of death	not stated consent checked on each admission	3
42 Riopelle et al (2011) (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	N=400 patients /289 caregivers from August 2004 to November 2006	Intervention: palliative care needs evaluation conducted by an interdisciplinary team, followed by ongoing nurse case management Control: usual care	patients: interviews caregivers: Interviews	2 a

Author/date/ country	Article type & data extraction point	Aim original study	Method original study	Sample & setting	Target sample	Time to recruit sample	Type of Intervention /Control	Data Collection	LoE*
43 Sampson et al (2011) (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 (2012) (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 randomised more than 500 participants across 12 sites in 8 Phase III studies.	N/A	N/A	2 b
45 Storey (2004) (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	not stated	1 N=not stated 2 screened almost 2000 hospice patients, 21 recruited	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	not stated	2a

Author/date/country	Article type & data extraction point	Aim original study	Method original study	Sample & setting	Target sample	Time to recruit sample	Type of Intervention /Control	Data Collection	LoE*
				2 cancer centre and a hospice 3 hospital that specializes in cardiac care		3 no patients in a year	advanced heart failure Control: not stated		
46 Vermandere et al (2016) (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 (2003) (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.	N= 289 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
48 Zambroski et al (2014) (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

* LoE= Level of evidence ACP= advance care planning QOL= quality of life

2.8.1 Identifying participants: defining the target audience

The challenge of participant identification and complex inclusion criteria were raised as issues in the literature (Baskin et al., 1998; Goldstein et al., 2014; Hanson et al., 2014; Jones et al., 2013; Lee et al., 2013; Sampson et al., 2011; Vermandere et al., 2016; Zambroski et al., 2014). This can relate to the difficulty of predicting prognosis as part of the trial's eligibility assessment (Currow et al., 2006; Goldstein et al., 2014; Gorman et al., 2008; Hanson et al., 2014; Latimer et al., 1998; McWhinney et al., 1994), how palliative care is defined in a particular country (Vermandere et al., 2016), too narrow and/or ambiguous inclusion criteria (Goldstein et al., 2014; Lee et al., 2013) and lack of suitable carer (Zambroski et al., 2014) or surrogate to gain proxy consent (Baskin et al., 1998; Sampson et al., 2011).

Including broad study eligibility criteria in your protocol was seen as a facilitator to recruitment as it ensured a high percentage of patients screened met the study's inclusion criteria (LeBlanc et al., 2013; Shelby-James et al., 2012). 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 trial of an interdisciplinary palliative care needs evaluation (Riopelle et al., 2011).

2.8.2 Product: defining the product

A number of papers highlighted high refusal rates as an issue amongst potential trial participants (Ammari et al., 2015; Bausewein et al., 2010; Buss et al., 2008; Currow et al., 2006; Kutner et al., 2010; Noble et al., 2015; Westcombe et al., 2003). The lack of clinical equipoise was cited as a possible reason for this, with concerns about being randomised to their non-preferred arm, which could be the intervention or control arm, having an influence on whether or not patients agreed to take part (Noble et al., 2015; Westcombe et al., 2003). A lack of belief in the intervention (Bausewein et al., 2010; Buss et al., 2008) and the lack of an acceptable control (Bausewein et al., 2010) were reasons for patients declining to take part. 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 as discussed in section 2.8.8.1 below. The feeling the intervention was not needed at that particular time (Ammari et al., 2015; Buss et al., 2008; Noble et al., 2015) and competing priorities (Kutner et al., 2010) were also cited as reasons for patient refusal. Intervention and control arms that replicated clinical practice in recruitment sites as closely as possible were seen to be more likely to be successful (Shelby-James et al., 2012). 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 them altogether (Shelby-James et al., 2012). Offering a palliative care symptom control intervention to a group of patients who normally have limited access to such specialist input was suggested as another possible facilitator (M. C. Farquhar et al., 2009).

A number of study design strategies were seen to help address recruitment barriers. A fast track design with a short lead in time may have increased the response rate in a trial of a breathless intervention service by addressing the issue of clinical equipoise and patient preferences. All patients and families knew they were going to get the intervention either straight away or only after a short 8 week wait (M. C. Farquhar et al., 2009). 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 (Buss et al., 2008; Westcombe et al., 2003). There were strategies specifically suggested to help improve recruitment rates in drug trials. Giving patients the option to enter an open label extension study after taking part in a placebo controlled symptom control trial was seen as important as enrolment was delayed for many patients until this was put into place (Abernethy et al., 2010). An extension study follows the main trial and allows an unlicensed drug to be continued to be prescribed to all of those enrolled in the extension study (Taylor & Wainwright, 2005). 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 (Shelby-James et al., 2012).

2.8.3 Product: The product's competition

A barrier to recruitment was potential participants 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. Patients were able to access similar therapies and support services without

having to accept the restriction of randomisation (Goodwin et al., 2000; Westcombe et al., 2003). Competing trials recruiting from a similar patient population was also seen as barrier in one paper (Goodwin et al., 2000).

2.8.4 Price: Type of costs

Patients and carers being too burdened by the illness to participate in the trial was a substantial barrier to recruitment (Ammari et al., 2015; Hanson et al., 2014; Latimer et al., 1998; McMillan & Weitzner, 2003; Noble et al., 2015). The reality of having to deal with the unpredictable nature of the patient's disease in the recruitment process was also a barrier to recruitment (Latimer et al., 1998; Philip et al., 2006). The right time to approach patients and carers about the trial was seen as an issue in one study (Buss et al., 2008), 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. Carers feeling protective towards their loved ones could lead to gatekeeping with reports of carers blocking researcher access to the patient (Hanson et al., 2014; McMillan & Weitzner, 2003; Zambroski et al., 2014). These findings correspond with a review focusing on gatekeeping in palliative care research generally (Kars et al., 2016). 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 carers to be approached about the study (Hudson et al., 2001). They could also express concerns about the additional burden the study would place on their carer as well as making a decision that the carer would not derive any benefit from being involved in the research (Buss et al., 2008).

2.8.5 Price: Minimising the costs

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 (Shelby-James et al., 2012). This involved limiting what was required from those participants who agreed to take part in a study such as minimising the number of questionnaires to be completed and using routine clinical data where possible. Strategies to minimise the burden 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 carers as they were sometimes unavailable at the time of patient consent (Riopelle et al., 2011). 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 trials (Clark et al., 2008; Rees & Hardy, 2003). It 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 trial (Fowell et al., 2006). 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.

2.8.6 Place: Improving accessibility

The type of setting where recruitment took place could act as a barrier to recruitment. The issue of travel was identified as a reason for patients declining to take part in a quality of life trial in an oncology hospital as these types of interventions can often be provided locally while cancer treatment trials are only available in oncology units (Westcombe et al., 2003). 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 (Storey, 2004; Zambroski et al., 2014). Hospice catchment areas could also be too small to provide the necessary pool of potentially eligible patients (Zambroski et al., 2014). 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 (Fischer et al., 2015; Sampson et al., 2011). The role of specialist palliative care as a hospital consulting rather than admitting service was a barrier to recruitment in a trial recruiting patients with malignant bowel obstruction (Lee et al., 2013). In contrast, recruiting participants after discharge was seen as more difficult in a couple of papers (Hanson et al., 2014; McMillan & Weitzner, 2003) with the feeling participants can be less receptive (Hanson et al., 2014). The physical environment and the often complex nature of patient consultations in the outpatient setting are seen to make approaching participants more difficult (Hanson et al., 2014; Latimer et al., 1998).

Increasing the number of clinical recruitment centres during the trial to increase the pool of potential participants was a strategy employed by a number of studies to improve their recruitment rates (Abernethy et al., 2010; Goodwin et al., 2000; Westcombe et al., 2003).

Some studies were set up as multi centre studies but this did not always guarantee recruitment success (Hussainy & Marriott, 2009; Mitchell & Abernethy, 2005).

2.8.7 Promoting the study

The importance of paying attention to key and careful messaging when discussing a trial with patients, carers and clinicians to provide reassurance and to address any concerns was seen as important (Abernethy et al., 2010; M. C. Farquhar et al., 2009; Gorman et al., 2008; Hanson et al., 2014; Kutner et al., 2010; LeBlanc et al., 2013; Shelby-James et al., 2012). This includes, for example, using the term study rather than trial, stressing to patients they can withdraw from the trial at any time without negatively affecting their care, using standardised wording to explain the concept of randomisation and blinding to patients (Abernethy et al., 2010; LeBlanc et al., 2013) and explaining to clinicians the benefits of taking part in research for patients (Abernethy et al., 2010; Shelby-James et al., 2012). 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 (Abernethy et al., 2010; Fischer et al., 2015; Kruse et al., 2013; LeBlanc et al., 2013; Mitchell & Abernethy, 2005; Shelby-James et al., 2012). 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 (Fischer et al., 2015). Recruiting staff also need to ensure they are flexible and demonstrate respectful persistence (Hanson et al., 2014; Riopelle et al., 2011) while developing a rapport with the patient (Riopelle et al., 2011) when promoting a trial.

2.8.8 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.

2.8.8.1 Barriers to partnering

'Gatekeeping' was seen as a barrier to trial recruitment with the majority of papers identifying health care professional gatekeeping as the most difficult issue to overcome (Buss & Arnold, 2004; Cook et al., 2002; Goodwin et al., 2000; Hanson et al., 2014; Hudson et al., 2001; Hussainy & Marriott, 2009; Jones et al., 2013; Jones et al., 2011; Kutner et al., 2010; Latimer et al., 1998; Miller et al., 2005; Prentice et al., 2004; Vermandere et al., 2016; Westcombe et al., 2003). This was related to the professionals fear of over burdening patients (Buss & Arnold, 2004; Goodwin et al., 2000; Hanson et al., 2014; Hussainy & Marriott, 2009; Kutner et al., 2010; Latimer et al., 1998; Westcombe et al., 2003), lack of belief in research (Buss & Arnold, 2004; Hussainy & Marriott, 2009), seeing patients as being too poorly (Cook et al., 2002; Daniels & Exley, 2001; Hanson et al., 2014; Prentice et al., 2004) or emotionally distressed (Daniels & Exley, 2001; Latimer et al., 1998) or too stressed to be approached (Hudson et al., 2001). Lack of confidence discussing a challenging study (Fowell et al., 2006; Jones et al., 2011) and fear of discussing prognosis (Jones et al., 2013; Jordhøy et al., 1999; Vermandere et al., 2016) were cited as possible reasons for health care professional gatekeeping.

Concerns regarding randomisation (Daniels & Exley, 2001; Goodwin et al., 2000; Westcombe et al., 2003), the use of placebo (Buss & Arnold, 2004; Hardy et al., 1998; Storey, 2004), a lack of belief in the intervention (Goodwin et al., 2000; Miller et al., 2005; Westcombe et al., 2003) and in clinical equipoise (Goodwin et al., 2000; Jones et al., 2013; Westcombe et al., 2003) were also highlighted as possible reasons for health care professional gatekeeping.

Gatekeeping by research ethics committees could also be an issue. Research ethics committees play an important role in ensuring ethical standards are met in research and the rights of those taking part are protected. They were seen at times not to have a good understanding of palliative care research which led to a misapplication of their gatekeeping role (Lee & Kristjanson, 2003). This resulted in overly paternalistic recruitment procedures being put in place such as face to face consent in the community by a Doctor (Buss & Arnold, 2004) and insisting patients were informed they had a prognosis of six months or less before they could be approached (Storey, 2004).

Recruiting to a palliative care trial 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. The majority of research staff time is spent screening and consenting rather than carrying out the intervention and collecting data (Clark et al., 2008; Daniels & Exley, 2001; Hanson et al., 2014; McMillan & Weitzner, 2003; Zambroski et al., 2014). Not having the necessary staff available due to staff turnover or holidays (Mitchell & Abernethy, 2005), clinical staff being too busy (Fischer et al., 2015) or lack of out of hours cover (Hardy et al., 1998; Lee et al., 2013) is seen as having an impact on recruitment rates.

2.8.8.2 Partner education

Personal and repeated contact with referral sources was seen as crucial strategy to create and maintain enthusiasm and motivation throughout the life of the study as well as address any concerns that may develop (Daniels & Exley, 2001; Jordhøy et al., 1999; LeBlanc et al., 2013; Mitchell & Abernethy, 2005; Prentice et al., 2004). The approaches used included presentations, regular meetings and involvement of clinical staff in the study design and procedure development (LeBlanc et al., 2013). Identifying an enthusiastic study champion to assist access to potential participants and help promote the study among patients and clinicians was also seen as a valuable strategy (Hanson et al., 2014; Kutner et al., 2010; Miller & Chibnall, 2003; Westcombe et al., 2003).

2.8.8.3 Partner referrals and recruitment

Having research staff on site to provide logistical and practical support to enhance study recruitment is the strategy discussed most frequently in the literature (Abernethy et al., 2010; Bakitas et al., 2009; Bakitas et al., 2006; Currow et al., 2006; Farquhar et al., 2011; Hanson et al., 2014; Jordhøy et al., 1999; Kruse et al., 2013; Kutner et al., 2010; LeBlanc et al., 2013; Miller & Chibnall, 2003; Mitchell & Abernethy, 2005; Westcombe et al., 2003). Some authors have seen this intervention as the one that had the greatest impact on their recruitment rates (Abernethy et al., 2010; Farquhar et al., 2011). It can be seen to relieve the excessive burden of recruitment on busy clinical staff (Abernethy et al., 2010; Currow et al., 2006; Farquhar et al., 2011; Jordhøy et al., 1999; LeBlanc et al., 2013), help address the

issue of gatekeeping (Bakitas et al., 2009; Bakitas et al., 2006; Mitchell & Abernethy, 2005), support relationship building (Abernethy et al., 2010; Farquhar et al., 2011; Kruse et al., 2013), help keep a trial visible (Westcombe et al., 2003), allow direct access to participants (Hanson et al., 2014) and provide consistency (LeBlanc et al., 2013). 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 (Cook et al., 2002). 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 (Ammari et al., 2015).

Having the support of lead clinicians is seen as a facilitator to recruitment as this enhanced patient acceptance of the trial (Bakitas et al., 2006; Buss et al., 2008; M. C. Farquhar et al., 2009; Fischer et al., 2015; Goodwin et al., 2000; Hanson et al., 2014; Higginson et al., 2008) and promoted a research culture in the recruitment sites (Goodwin et al., 2000). Financial incentives for study site staff were used as a strategy in one study to attempt to improve sluggish recruitment with mixed results across sites (Kutner et al., 2010). Monthly recruitment progress reports sent to individual sites were also used in one study and it was felt this encouraged 'healthy competition and camaraderie' (Kutner et al., 2010).

Identifying and finding potential participants is one of the most significant recruitment challenges in palliative care trials 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 (Abernethy et al., 2010) or those who are on specific medication rather than relying purely on clinical notes (Hanson et al.,

2014). Reviewing clinical lists or notes which may include electronic database searches if the facilities are available (Hanson et al., 2014; Kutner et al., 2010; Zambroski et al., 2014).

Other strategies included incorporating the screening process into the regular palliative care service triage process (LeBlanc et al., 2013; Mitchell & Abernethy, 2005), using a screening algorithm (Abernethy et al., 2010) and simplifying and minimising the screening process for clinicians (LeBlanc et al., 2013).

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 (Hanson et al., 2014)

Table 9: Barriers and facilitators to recruitment identified from the literature review conceptually mapped within the ‘6 Ps’ of the ‘Social Marketing Mix Framework’.

The ‘6 Ps’	Themes from the literature and how they relate to the patient, carer or partner	
1 Identifying participants: defining the target audience	Barrier	
	Identifying participants who meet the study inclusion criteria	Patient : Goldstein et al (2014), Zambroski et al (2014), Jones et al (2013) Hanson et al (2014), Lee et al (2013), Vermandere et al (2016), Carer : Baskin at al (1998), Sampson et al (2011), Zambroski et al (2014)
	Difficulty predicting prognosis	Patient : Currow et al (2006), Goldstein et al (2014), Gorman et al (2008), Latimer et al (1998), Hanson et al (2014), McWhinney et al (1994)
	Facilitator	
	Broad study eligibility criteria	Patient : LeBlanc et al (2013), Shelby James et al (2012)
	Strategy	
Physician prognostication tool	Patient: Riopelle et al (2011)	
2 Product	Barrier	
Defining the Product	Participants not interested	Patient : Currow et al (2006), Kutner et al (2010) , Westcombe et al (2003), Bausewein et al (2010), Noble et al (2015), Buss et al (2008), Ammari et al (2015) Carers: Buss et al (2008)
	Clinical equipoise	Patient : Noble et al (2015), Bausewein et al (2010), Westcombe et el (2003), Buss et al (2008) Partners : Buss and Arnold (2004), Goodwin et al (2000), Westcombe et al (2003), Hardy et al (1998), Jones et al (2013), Daniels and Exley (2001)

<i>The Product's competition</i>	Facilitator	
	Trial replicates clinical practice as much as possible	Partners: Shelby James et al (2012)
	Offer a desirable and novel intervention	Patients: Farquhar et al (2009)
	Strategy	
	Fast track randomised controlled trial	Patients: Farquhar et al (2009) Carers: Farquhar et al (2009)
	Simplify design	Patients: Westcombe et al (2003), Buss et al (2008)
	Extension study	Patients: Abernethy et al (2010), Partners: Abernethy et al (2010)
	Rescue medication	Patients: Shelby James et al (2012), Partners: Shelby James et al (2012)
	Barrier	
	Competing services	Patients : Goodwin et al (2000), Westcombe et al (2003)
Competing trials	Patients: Goodwin et al (2000)	
3 Price	Barrier	
<i>Type of costs</i>	Patient's condition/illness	Patients : McMillan and Weitzner (2003) Latimer et al (1998), Philip et al (2006), Hanson et al (2014), Buss et al (2008), Ammari et al (2015), Noble et al (2015)

Minimising the costs	Gatekeeping	Patients : Buss et al (2008), Hudson et al (2001), Carers : McMillan and Weitzner (2003), Zambroski et al (2014), Hanson et al (2014)
	Facilitator	
	Minimise study burden	Patients : Shelby James et al (2012), Carers : Shelby James et al (2012), Partners : Shelby James et al (2012)
	Strategy	
	Verbal consent	Carers : Riopelle et al (2011)
	Advance consent	Patients : Rees and Hardy (2003), Clark et al (2008), Carers : Clark et al (2008)
	Cluster consent	Patients : Fowell et al (2006), Partners : Fowell et al (2006)
4 Place	Barrier	
	Type of recruitment setting	Patient : Cancer centre : Westcombe et al (2003), Hospice : Storey (2004), Zambroski et al (2014), Hospital Inpatients : Fischer et al (2015), Sampson et al (2011), Lee et al (2013)· Community : Hanson et al (2014), McMillan and Weitzner (2003), Hospital Outpatients : Latimer et al (1998), Hanson et al (2014) Carer : Hospital Inpatients : Sampson et al (2011), Hospice : Zambroski et al (2014), Hospital Outpatients : Latimer et al (1998)
	Strategy	
Increase number of clinical recruitment centres	Patient : Abernethy et al (2010), Goodwin et al (2000), Mitchell and Abernethy (2005), Hussainy and Marriott (2009), Westcombe et al (2003) Carer : Hussainy and Marriott (2009)	

5 Promoting the study	Facilitator	
	Key/careful messaging	Patient : Abernethy et al (2010), Gorman et al (2008), LeBlanc et al (2013), Farquhar et al (2009), Hanson et al (2014), Kutner et al (2010), Carer : Abernethy et al (2010), Kutner et al (2010), LeBlanc et al (2013), Partner : Abernethy et al (2010), Gorman et al (2008), Kutner et al (2010), LeBlanc et al (2013), Shelby James et al (2012)
	Flexibility and respectful persistence	Patient : Riopelle et al (2011), Hanson et al (2014)
	Rapport between researcher and participant	Patient: Riopelle et al (2011), Partner: Riopelle et al (2011)
	Strategy	
	Role play/scripts	Partner : Fischer et al (2015), Abernethy et al (2010), Kruse et al (2013) LeBlanc et al (2013), Mitchell and Abernethy (2005), Shelby James et al (2012)
6 Working with partners <i>Barriers to partnering</i>	Barrier	
	Health care professional gatekeeping	Partner: Buss and Arnold (2004), Cook et al (2002), Goodwin et al (2000), Hussainy and Marriott (2009), Kutner et al (2010), Westcombe et al (2003), Jones et al (2011), Latimer et al (1998), Miller et al (2005), Daniels and Exley (2001), Hanson et al (2014), Prentice et al (2004), Jones et al (2013), Fowell et al (2006), Hudson et al (2001), Vermadere et al (2016), Hardy et al (1998), Storey (2004), Jordhoy et al (1999)
	Gatekeeping by research ethics committee	Partner: Buss and Arnold (2004), Storey (2004)

Partner education	Resources: labour intensive	Partner : McMillan and Weitzner (2003), Clark et al (2008), Hanson et al (2014), Daniels and Exley (2001), Zambroski et al (2014)
	Resources: research or clinical staff availability	Partner: Mitchell and Abernethy (2005), Fischer et al (2015), Lee et al (2013), Hardy et al (1998)
	Strategy	
	Personal repeated contact with referral sources	Partner: Jordhoy et al (1999), LeBlanc et al (2013), Mitchell and Abernethy (2005), Prentice et al (2004), Daniels and Exley (2001)
	Study champion	Partner : Hanson et al (2014), Kutner et al (2010), Westcombe et al (2003), Miller and Chibnall (2003)
Partner referrals and recruitment	Facilitator	
	Support of lead clinicians	Partner: Bakitas et al (2006), Goodwin et al (2000), Buss et al (2008), Fischer et al (2015), Higginson et al (2008), Farquhar et al (2009), Hanson et al (2014)
	Support of a palliative care clinical trials cooperative	Partner: Hanson et al (2014)
	Strategy	
	Active questioning	Partner : Abernethy et al, (2010) Hanson et al (2014)
	Review clinic/hospital lists/clinical notes	Partner : Kutner et al (2010), Hanson et al (2014), Zambroski et al (2014)
	Clinical triage nurse	Partner : LeBlanc et al (2013), Mitchell and Abernethy (2005)

	Screening algorithm	Partner : Abernethy et al (2010)
	Minimal screening for clinicians	Partner : LeBlanc et al (2013)
	Financial incentives	Partner : Kutner et al (2010)
	Recruitment progress reports	Partner: Kutner et al (2010)
	Research staff on site	Partner: Abernethy et al (2010), Ammari et al (2015), Bakitas et al, (2006), Bakitas et al (2009), Cook et al (2002), Currow et al (2006), Farquhar et al (2011), Jordhoy et al (1999), Kruse et al (2013), Kutner et al (2010), LeBlanc et al (2013), Miller and Chibnell (2003), Mitchell and Abernethy (2005), Westcombe et al (2003), Hanson et al (2014)

2.9 Discussion

The findings of this review have shown that the barriers to recruitment and the potential facilitators and strategies that may help to overcome them described in the literature are largely based on anecdotal evidence. The majority of evidence that currently informs our understanding of the palliative care trial recruitment process is based on trial reports or methodological papers that explore the design of exemplar trial/s rather than primary research data. The review findings suggest that there are likely to be issues to consider for most palliative care trials but further methodological research is needed. These issues include; the need to pay attention to key and careful messaging when promoting a trial; the need to plan for adequate resources to find eligible participants, ensuring you have the support of the lead clinician and having research staff on site.

The greatest number of barriers, facilitators and strategies identified within the literature could be mapped within the 'Working with Partners' category. This highlights the fundamental role that health care professionals play in the recruitment process. Their key role has also been recognised in the general trial recruitment literature (Fletcher et al., 2012). Health care professional gatekeeping was identified as the most difficult issue to overcome in the majority of papers. This review builds upon the qualitative review carried out by Kars et al (2016) into gatekeeping in palliative care research.

The findings also indicated that the 'Social Marketing Mix Framework' may help researchers better understand the processes underpinning recruitment to palliative care trials. 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, as discussed previously, relates to the intervention that is being offered in the study. As discussed in chapter one, the lack of clinical equipoise and the influence of patient preferences on decision making can also act as a barrier to recruitment in trials outside palliative care (Harrop, Kelly, et al., 2016; Norris et al., 2019; Paramasivan et al., 2011).

Under the 'Social Marketing Mix Framework' ensuring the 'product' meets the needs of the target audience is a key consideration when designing a study. This is reflected in the increasing requirement for patient and public involvement representatives to be involved in the study design process (Crocker et al., 2018). Patient and public involvement has been defined as research that is carried out 'with' or 'by' members of the public which includes patients and carers (National Institute for Health Research-INVOLVE, 2019). Patient and public involvement may improve the acceptability of a trial (Crocker et al., 2018). This may have a positive impact on trial recruitment rates but further research is required to explore its impact both in (Chambers et al., 2019) and outside the context of palliative care (Healy et al., 2018).

'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. 'Product' and 'Price' are applied to the patient and/or carer and not the 'partner' under this framework. The findings of this review suggest that this may not fully capture the complexities of recruitment in palliative care. For example, clinicians may struggle to accept the intervention or randomisation and

may feel the emotional costs of approaching a patient or carer at a difficult time in their lives. This may make it hard for them to balance the costs of taking part in the study with the potential benefits the study may have for patients and carers.

This review has highlighted the need for more methodological research focusing on recruitment issues in palliative care randomised controlled trials, including the role of health care professionals in the recruitment process. This priority for research has been subsequently reflected in the PRioRiTy study recommendations (see table 4) as discussed in the previous chapter (Healy et al., 2018). Whether and how the 'Social Marketing Mix Framework' applies to the palliative care trial recruitment process also needs further exploration.

2.9.1 Strengths and limitations of the review

To the authors knowledge this was the first review to synthesise the evidence related to the barriers and facilitators to recruitment to randomised controlled trials in palliative care. This review is unique in palliative care as it uses a theoretical framework to explore the barriers and facilitators to trial recruitment. Using theory in the review process can help the reviewer and reader assess how applicable and generalisable the findings of the review are to clinical practice. 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 (Donovan et al., 2014). This has been illustrated in a recent Cochrane qualitative synthesis review exploring the complexity

of factors that influence a person's decision whether to participate in a trial (Houghton et al., 2020). The search strategy and approach used was thorough in this review, however, I do not claim to have identified and reviewed all published palliative care randomised controlled trial papers for reported barriers and facilitators to recruitment. Initial searches of the literature identified that including non-randomised controlled clinical trials in the search strategy created too many 'hits' for a single researcher to review. By limiting the focus of the search to randomised controlled trials may have meant important barriers and facilitators to palliative care clinical trial recruitment may have been missed. Unfortunately, funding was not available in this study for two independent reviewers to extract data from the full data set. This may have meant data related to the barriers and facilitators to palliative care trial recruitment may have been missed. The review findings are largely based on researcher anecdotal evidence so should be interpreted with caution. This is the level of evidence that is currently underpinning our understanding of recruitment issues in palliative care randomised controlled trials.

The review has not been updated following the initial search because examining large numbers of trial papers only identified a small number of papers that included descriptions of recruitment issues. Following the review, a number of strategies have been used to keep up to date with the current recruitment literature. These include monthly email updates from Pub Med and relevant journals, citation tracking of papers, checking the reference lists of papers and following the work of key authors. The current trial recruitment literature is explored in this thesis particularly in the discussion chapter.

2.10 Conclusion

Most of the evidence related to the barriers and facilitators to recruitment in palliative care randomised controlled trials is anecdotal. There can be multiple reasons for why a trial may struggle to reach its recruitment targets, including patient related factors such as patient preferences. This review has highlighted, as in the general trial literature, the key role that health care professionals play in the recruitment process. More methodological research is needed to explore trial recruitment issues in palliative care. This includes, as also recognised in the general trial literature, research that captures the perspectives of health care professionals involved in the recruitment process.

Without further methodological research it is likely palliative care trials will continue to struggle to reach their recruitment targets. The findings of the review suggest that the 'Social Marketing Mix Framework' can help guide researchers when planning and implementing their recruitment strategy but whether and how the framework applies to the palliative care trial setting also needs further exploration.

Chapter three: Choice of research methods

3.1 Introduction

In this chapter, the research question and the aims of the study are outlined. The types of research design and methods available to address the research question are discussed. Why the chosen approach was identified as the most suitable to answer the research question is outlined. The key features of the chosen research design are described along with how they reflect the epistemological and ontological stance taken in this study. How the chosen research methods were operationalised in practice is examined in the next chapter.

3.2 Research question and study aims

As highlighted in the previous two chapters, health care professionals play a crucial role in the recruitment of patients and carers to research studies and the reasons why they do or do not identify and approach potential participants is complex (Preston et al., 2016). There is little understanding of the process of recruitment in randomised controlled trials and the influence recruiters may have on it (Donovan et al., 2014) and this is especially so in the field of palliative care. This is illustrated by the findings of the literature review in the previous chapter which found the current evidence base to be largely anecdotal. In this study, the aim is to develop a better understanding of which health care professional related factors may influence recruitment to randomised controlled trials in palliative care.

Research Question

How do health care professionals recruit patients and their family carers to palliative care randomised controlled trials and why do they use certain strategies during the recruitment process?

Study Aims

- To identify how health care professionals involved in the recruitment process undertake the recruitment of patients and family carers to palliative care randomised controlled trials.
- To explore why health care professionals involved in the recruitment process choose to implement particular recruitment strategies, and the factors that influence their choices, when recruiting to palliative care randomised controlled trials.

The research question aligns with the priorities set by the Prioritising Recruitment in Randomised Trials study as discussed in chapter one (Healy et al., 2018; Hennessy et al., 2018). Most notably priorities 5 and 7:

5. 'What are the barriers and enablers for clinicians/healthcare professionals in helping conduct randomised trials?'

7. 'What are the best approaches to ensure inclusion and participation of under-represented or vulnerable groups in randomised trials?'

Clinicians attitudes towards participation in palliative care research and why, for example, they may act as gatekeepers has also been highlighted as an area of clinical practice that requires further research (Gysels et al., 2013).

3.3 Study design

3.3.1 Choosing an appropriate study design

Once the research question has been developed, the next phase of the research process is to decide on the most appropriate study design to address the research question posed. Bryman (2012) argues that a decision about an appropriate study design is based on the importance attached to a number of priorities. These priorities include; whether there is a need to express causality between variables; generalise beyond the study population; understand behaviours and their meanings in their social context and/or the need to study phenomena and their interconnections over time (Bryman, 2012). As illustrated in table 10, there are a number of research designs that can be used to answer research questions related to recruitment issues in palliative care trials.

Table 10: An overview of research designs and research strategies (adapted from Bryman (2012))

Research Designs	Research strategies (typical forms)	Types of trial recruitment research questions the research designs/strategies can address.
Experimental	Randomised controlled trial	Could be used to understand if an intervention aimed at recruiting staff, such as a training programme, <i>affects</i> recruitment rates.
Quasi experimental	E.g. Non-randomised controlled trials, controlled and uncontrolled before and after (pre-post) and time-series designs	Could be used to understand if an intervention aimed at recruiting staff, such as a training programme, is <i>associated</i> with increased recruitment rates.
Cross-sectional (data collected at single time point)	<p>Quantitative strategies: surveys, structured observation, content analysis</p> <p>Qualitative strategies: interviews, focus groups, content analysis</p>	<p>A survey, for example, could be used to explore recruiting staff's views and experiences of recruiting to a palliative care trial.</p> <p>Interviews or focus groups, for example, could be used to explore in more depth, recruiting staff's views and experiences of recruiting to a palliative care trial.</p>
Longitudinal (mapping change)	<p>Quantitative strategies: surveys on a sample more than once (includes cohort studies), documentary content analysis focusing on different time periods</p> <p>Qualitative strategies: interviews more than once, documentary content analysis focusing on different time periods, ethnography</p>	<p>A survey could be used, for example, to explore at more than one time point recruiting staff's views and experiences of recruiting to a palliative care trial.</p> <p>Interviews or focus groups, for example, could be used to explore in more depth at more than one time point recruiting staff's views and experiences of recruiting to a palliative care trial.</p>

A non-experimental approach was the most appropriate to follow in this study as there was no intervention to be tested. As a result, there was no requirement to assess and express causality between an independent and dependent variable. Quantitative surveys have been used outside palliative care to identify recruiting staff's perceptions of the barriers and facilitators to trial recruitment and potential recruitment strategies (Isaksson et al., 2019; Kaur et al., 2012). The aims of this study were concerned with understanding the personal experiences and behaviours of health care professionals during the trial recruitment process. It also aimed to understand the meanings and motivations behind these personal experiences and behaviours in their social context.

Social context relates to factors such as the recruitment setting or relationships between professional groups. A research design that incorporated qualitative strategies seemed the most appropriate approach to *'elicit and identify the hidden challenges'* that make up clinical activity such as recruitment (Donovan et al., 2014) (p.1) and address the research question. Authors have argued that using qualitative research, both standalone and embedded within a trial, can contribute to a better understanding of trial recruitment issues (Hennessy et al., 2018; O'Cathain, 2018). There is no coherent definition of qualitative research, it can have a range of meanings and acts as an umbrella term for a number of different approaches (Aspers & Corte, 2019). Qualitative research focuses on how people understand and give meaning to their social world (Ritchie & Lewis, 2003). Aspers and Corte (2019) argue that qualitative research;

'..tends to focus on meanings and motivations that underlie cultural symbols, personal experiences, phenomena and detailed understanding of processes in the social world' (p.146)

Qualitative approaches are also iterative and provide the flexibility to explore new areas of enquiry that may emerge during a research study (Aspers & Corte, 2019; Bryman, 2012). Different qualitative approaches could have been used in this study to explore trial recruitment issues. For example, grounded theory could have been used to develop a theory to explain how clinicians undertake the process of recruitment as illustrated in a study exploring nurses views of wound care research (Lamb et al., 2016). An interpretative phenomenological approach could have been used to explain how recruiting staff experience working on a palliative care trial, as illustrated in a recent study exploring paramedics views of an emergency care trial (Charlton et al., 2019). An ethnographic design could have been used to observe recruitment interactions within their clinical settings to understand how health care professionals and palliative care patients discuss and deliberate about trial participation (Garrett et al., 2020). In this study, the decision was taken to use a qualitative case study approach. This approach has been used by a number of nurse researchers in the palliative care setting (Brogan et al., 2019). It has also been used to explore and understand recruitment processes in non-palliative care randomised controlled trials (Campbell et al., 2007; Rooshenas et al., 2019). The decision to use a case study approach was especially influenced by a National Institute for Health Research Health Technology Assessment funded study. This study aimed to identify factors associated with good and poor recruitment to multicentre trials. Within this study, they used a case study approach to understand, through the opinions of study coordinating and recruiting staff in four diverse exemplar trials, trial recruitment challenges and facilitators (Campbell et al., 2007).

Choice of research design is influenced by the epistemological and ontological 'tendencies' or orientations of the researcher (Bryman, 2012) and researchers should explicitly state

their philosophical approach (Brogan et al., 2019; Carolan et al., 2016). Epistemology relates to the nature of knowledge and how knowledge is acquired while ontology refers to the researchers view of the nature of the social world and what we can know about it (Ritchie & Lewis, 2003).

3.3.2 Epistemological and ontological issues in qualitative research

As discussed previously, qualitative research, both standalone and embedded within a trial, has been used to understand trial recruitment issues. Some argue that it is not possible to combine qualitative and quantitative approaches within a trial because they fall within different paradigms (O'Cathain, 2018; Walshe, 2018). Choosing a standalone qualitative research design, as in this study, to explore recruitment issues in randomised controlled trials would also on appear on the surface to be epistemologically and ontologically incompatible.

Trials are seen to fall within a positivist paradigm and those that believe in a positivist experimental approach accept that there is an orderly relationship between the cause, which is the intervention being trialled, and the effect, which is the study outcome (Maxwell & Mittapalli, 2010). There has been increasing recognition that context and social relationships can influence how causal pathways work in practice (O'Cathain, 2018; Papparini et al., 2020). This has led some researchers to embrace the use of qualitative research to help them understand how context and complexity can influence trial processes and interventions (O'Cathain, 2018; Wells et al., 2012) including in palliative care (Lim et al., 2017). Post positivists believe qualitative and quantitative research are compatible, but see qualitative research as playing a supportive role to quantitative research (Creswell & Poth, 2016;

O'Cathain, 2018). Post positivism focuses on theory testing, making comparisons across groups, validity, objectivity, limiting bias, and causal explanations so adopting a scientific approach to qualitative research (Creswell & Poth, 2016).

Critical realists also believe that qualitative and quantitative research are compatible with some authors even arguing that critical realist trials are possible (Porter et al., 2017). Critical realism fits with my own ontological and epistemological 'tendencies' as a researcher. The case study research design has been associated with the critical realist philosophical framework (Easton, 2010; Elger, 2010). There are different approaches to critical realism but all have a number of common characteristics (Maxwell & Mittapalli, 2010). Critical realism combines a realist ontology with a constructivist epistemology (Maxwell & Mittapalli, 2010). Critical realists, like positivists and post positivists, believe there is a real world that exists independently of our beliefs, perceptions, theories, constructions and understanding (Maxwell & Mittapalli, 2010; Ritchie & Lewis, 2003). Critical realists believe that even though there is an external reality, it cannot be easily accessed in the social world. They accept that reality is socially constructed (Maxwell & Mittapalli, 2010) which means that entry to the social world is always '*mediated and subjective*' (Bryman, 2012)(p.616). The social world is accessible to researchers via participant's interpretations of the social world, which maybe further interpreted by the researcher. Different views will yield different types of understanding and this adds richness to our understanding of the various ways in which external reality is experienced by individuals within the social world (Ritchie & Lewis, 2003). Therefore, while critical realism rejects the idea of "multiple realities", it accepts that there are valid perspectives on the world (Maxwell, 2009; Maxwell & Mittapalli, 2010). This contrasts with relativists and social constructivists who believe there are multiple realities

that are created as a result of *'our lived experience and interactions with others'* (Creswell & Poth, 2016) (p.35).

Bhaskar (2008), a prominent critical realist, believes there are three levels or domains of reality: the 'empirical', the 'actual' and the 'real'. Critical realism aims to explain causality by understanding the causal mechanisms and processes by which an event or situation occurs (e.g. recruitment to a palliative care trial). The empirical level is what can be observed or experienced (e.g. a screening log showing eligible patients are not being approached). The 'actual' level refers to what is known but cannot always be seen (e.g. evidence suggests clinician gatekeeping is a barrier to recruitment). Underpinning the 'actual' level are overlapping 'generative mechanisms' or social structures that are real but not directly accessible to observation (e.g. professional hierarchies, organisational culture, gender) (Bhaskar, 2008; Walsh & Evans, 2014). These 'generative mechanisms' contribute to the understanding of the 'actual' but are not definitive or fully explanatory (Walsh & Evans, 2014). Individuals or social groups (e.g. research nurses) may have different responses to similar situations (e.g. approaching a palliative care patient about a trial). These differences may be due to personal or cultural characteristics (e.g. previous clinical experience, family history) that are causally relevant to the outcome (e.g. recruitment to a palliative care trial) (Maxwell & Mittapalli, 2010). Individuals have the power to decide how to act depending on their interpretation of the situation (Porter et al., 2017). Awareness of these social structures and individual influences can explain why things are happening at the empirical level (Walsh & Evans, 2014). Generative mechanisms are only apparent through their 'empirical' effect so the use of hypotheses or theoretical propositions can be constructed to explore their effects (Bryman, 2012). The use of theoretical propositions in case study research is compared to hypothesis testing in experimental research and is explored in

further detail in section 3.4.1. Critical realists believe their approach to investigating causation is just as legitimate as a quantitative approach and can often be complementary (Maxwell & Mittapalli, 2010).

3.4 Case study

Case studies cross many disciplines and have been used to cover diverse topics and issues (Creswell & Poth, 2016; Harrison et al., 2017). They have been used, for example, in health care (Crowe et al., 2011; Paddock et al., 2019; Walshe et al., 2008), education (Merriam, 1998), management (Takahashi & Araujo, 2019) and marketing (Easton, 2010). Case study is a research design or approach rather than a research method (Rosenberg & Yates, 2007) and must not be confused with case reports that are found in medical journals (Alpi & Evans, 2019). It offers methodological flexibility as qualitative, quantitative or mixed methods may be used (Bryman, 2012; Rosenberg & Yates, 2007). The choice of method should reflect the issue being studied (Flyvbjerg, 2006) and can include interviews, surveys, documentation, observation and archival data such as patient clinical records (Yin, 2018).

Case study is viewed as an appropriate study design to answer how and why research questions as posed in this study (Yin, 2018). As discussed previously, trial recruitment is a contemporary, interactional activity and process that occurs in clinical practice settings. Recruitment is a complex process that is potentially lengthy and is not a one off event (Donovan et al., 2014). Multiple complex issues may influence the palliative care trial recruitment process and recruitment activity may occur in different clinical contexts as highlighted earlier. Case study aims to address complex contemporary phenomena, like

recruitment, within their real life clinical context (Crowe et al., 2011; Yin, 2018). Flyvbjerg (2006) believes that one of the strengths of the case study approach is that it can 'close in' on real-life events as they unfold in practice. It is useful when context is central to the study (Walshe et al., 2004) and when it is difficult to separate the case from the context in which it happens (Boblin et al., 2013). Assessing the context in which a trial takes place will lead to a greater understanding of the complexity of factors that are involved in the trial recruitment process (Campbell et al., 2007). The need to address complexity and context has led other researchers to use case study to explore trial related issues (Grant et al., 2020; Hagen et al., 2019; Wells et al., 2012), including recruitment processes (Campbell et al., 2007; Rooshenas et al., 2019), as discussed previously. It has also been seen as a useful approach in under researched areas, as in this study (Walshe et al., 2004).

3.4.1 Epistemological and ontological issues in case study research

Case study research offers paradigmatic flexibility as well as methodological flexibility (Grant et al., 2020; Rosenberg & Yates, 2007; Thomas, 2011). Yin (2018) and Stake (1995), two of the seminal case study protagonists, have different epistemological and ontological assumptions underpinning their approaches. Stake's approach to case study sits within a social constructivist paradigm and adopts a more flexible inductive approach to theory (Boblin et al., 2013; Harrison et al., 2017), seeing the conduct of case study research as more of an art (Creswell & Poth, 2016; Stake, 1995). This contrasts with Yin's approach that mirrors the structured and systematic approach found in experimental research. He argues that the natural and social sciences should and are able to use the same kind of approaches

to collecting data and explaining phenomenon (Bryman, 2012). Authors have suggested that Yin is a post positivist (Boblin et al., 2013; Creswell & Poth, 2016; Harrison et al., 2017; Hyett et al., 2014), even though he does not discuss his epistemological and ontological 'tendencies' apart from suggesting his approach sits generally within realism (Yin, 2018).

Yin's approach to case study appears to have critical realist traits, for example, he recommends the use of theoretical propositions or logic models to guide data collection and analysis to explore the deeper reasons for what can be observed (Pawson & Tilley, 1997; Walsh & Evans, 2014; Yin, 2018). The development of theoretical propositions involves the researcher predicting a theory about what may be learned from examining the case (Yin, 2018)(p.24). Theoretical propositions can be linked to the literature, theory and/or generalisations based on the study findings with some also basing them on personal or professional experience (Baxter & Jack, 2008). Each theoretical proposition is examined for each case and not for all the cases together as in hypothesis testing research. If cases confirm emergent relationships this enhances confidence in the validity of the relationship while those that disconfirm provide the opportunity to refine and extend the theory (Eisenhardt, 1989). Yin (2018) recommends that the theoretical propositions are reviewed during the study and refined or rejected as appropriate. Yin's approach to case study was chosen in this study as his assumptions about the nature of reality and knowledge, and how knowledge is acquired fit with my own critical realist 'tendencies' as a researcher (Bryman, 2012).

3.4.2 Types of case study

Yin (2018) outlines how case studies can be single or multiple. A single case may be chosen as it represents a unique phenomenon or a specific issue or problem while multiple cases can be selected to illustrate a particular issue across the cases. Yin (2018) recommends that if possible, researchers should undertake a multiple rather than a single case study. Case studies can also be explanatory, exploratory or descriptive depending on the research question and the phenomenon or event being studied (Yin, 2018). An explanatory case study may be suitable when the researcher aims to evaluate an initiative in a naturalistic setting by explaining how the initiative works as well as identifying its outcomes (Crowe et al., 2011; Yin, 2018). As with the experimental research designs in table 10, this approach was not appropriate in this study as there was no recruitment intervention to implement or evaluate.

An exploratory case study can be used as a pilot study to ascertain the questions to be asked or the data to be collected in a future research study which may not be another case study (Wells et al., 2012; Yin, 2018). A descriptive case study was chosen as this study aimed to describe how health care professionals recruit patients and their family carers to palliative care randomised controlled trials and explain why they use certain strategies during the recruitment process (Yin, 2012, 2018). A case study can also be prospective or retrospective. A prospective case study has a longitudinal design where the theoretical propositions are developed and tested against an ongoing social process (Bitektine, 2008) such as the implementation of a trial information video for potential study participants. There was some requirement in this study to identify the phenomena and its interconnections over time

(Bryman, 2012). A retrospective case study design was chosen to capture the order and sequence in which the palliative care trial recruitment process occurred. Within a single or multiple case design, there can also be single or multiple units of analysis. In a case study, the unit of analysis is 'the case' but there can be lesser units of analysis within the main case. Yin (2018) terms single unit of analysis cases as 'holistic' designs and multiple units of analysis as 'embedded' designs. The definition of the unit of analysis needs to be made a priori especially in multiple case studies so cross case comparisons can be made (Takahashi & Araujo, 2019; Yin, 2018).

The case study design chosen in this study was a retrospective, descriptive, qualitative multiple case study with embedded units of analysis. The reasons why a multiple case study design with embedded units of analysis was chosen is discussed in the next chapter. How the case was defined in this study along with the working research methods and the rationale for their use is also explored in detail in the following chapter.

3.5 Conclusion

Recruitment issues in palliative care trials could be studied using a wide variety of research designs and strategies. A non-experimental approach was identified as the most suitable to address the aims of this study, as there was not a need to express causality between variables. A qualitative approach was chosen, specifically a qualitative case study approach, as it enables the researcher to answer how and why questions and explore a complex phenomenon, like recruitment, in their real-life clinical context. Yin's case study approach was chosen as its ontological and epistemological underpinnings best reflect those of the

researcher and the topic of the research. How the research design was operationalised in practice is explored in the next chapter.

Chapter four: Working research methods

4.1 Introduction

The case study design chosen for this study was a retrospective, descriptive, qualitative multiple case study with embedded units of analysis (Yin, 2018). In this chapter, how this case study research design was operationalised in practice is outlined. How the case was defined along with the working research methods and the rationale for their use is explored in detail below.

4.2 The research question and study aims

The research question the case study design needed to address was:

How do health care professionals recruit patients and their family carers to palliative care randomised controlled trials and why do they use certain strategies during the recruitment process?

The aims of the study were to:

- *To identify how health care professionals involved in the recruitment process undertake the recruitment of patients and family carers to palliative care randomised controlled trials.*
- *To explore why health care professionals involved in the recruitment process choose to implement particular recruitment strategies, and the factors that influence their choices, when recruiting to palliative care randomised controlled trials.*

4.3 Study population

4.3.1 Defining and bounding the case

Case studies involve the in-depth exploration of a specific bounded system or case and how it relates to the environment (Flyvbjerg, 2006) or context (Stake, 1995; Yin, 2018). This bounded system or 'case' is the main focus of the research (Yin, 2018) and is '*a specific, a complex, functioning thing*' (Stake, 1995) (p.2). A case can be, for example, a community, an organisation, a person, an event or a specific project (Stake, 1995; Yin, 2018). A case may be bounded by factors such as place, timeframe, relevant social group or organisation (Creswell & Poth, 2016; Crowe et al., 2011). The act of defining the case allows the researcher to make decisions about what makes up the case and what makes up the context to the case (Flyvbjerg, 2006). This allows the researcher to set priorities for data collection and analysis and allows for comparison of findings (Yin, 2018). This is similar to experimental research where the study population is clearly defined before data collection begins. In practice, defining your case can be challenging as it needs to '*be a real world phenomenon that has some concrete manifestation*' rather than being an abstract concept such as recruitment (Yin, 2018)(p.31). Yin's (2018) advice to discuss the choice of case with colleagues, such as supervisors, was followed. The findings of the literature review in chapter two allowed for decisions to be made about the boundaries of the case. The greatest number of barriers and facilitators to palliative care trial recruitment identified within the literature could be mapped within the 'Working with Partners' category. This finding highlighted the key role that health care professionals play in the recruitment process and why they have been chosen as the focus of the case.

The case in this study, *'the real-life set of events from which data will be drawn'*, was a palliative care randomised controlled trial (Yin, 2004) (p. xiv). There are examples in the literature where research studies (Hickman et al., 2012) and more specifically randomised controlled trials had been chosen as the case to explore study related issues (Wells et al., 2012) including recruitment (Campbell et al., 2007). As discussed above, decisions need to be made about defining the boundaries of the case to distinguish between the phenomenon of interest and the context (Yin, 2018). Reflecting the study's research question and theoretical propositions, the case in this study focuses specifically on those health care professionals directly or indirectly involved in recruitment within a palliative care randomised controlled trial. Palliative patients and carers, for example, fall outside the boundaries of the case and form part of the context of the case. The case was bounded by place as only UK based trials were to be included. The case was also bounded by time as trials needed to be either ongoing, recently closed (within 12 months) or set up during the data collection period. This was so health care professionals could recall their experiences of recruiting to a trial.

As outlined in chapter one, defining a palliative trial can be challenging as there is no one clear definition of a palliative care trial population, intervention or study outcome and researchers need to decide on the definition they are going to use. Yin (2018) explains how the case needs to be defined clearly so that it can be operationalised in practice and he recommends using the literature as a guide. The definition below reflects how a palliative care trial is defined in the literature as illustrated in the literature review in chapter two.

In summary, the case definition was (see table 12 for further details):

- A palliative care randomised controlled trial aimed at adult patients with incurable cancer and/or advanced, progressive non-malignant disease and their family carers and either
- A palliative care randomised controlled trial where the primary endpoint is symptom control and/or quality of life.
- or
- A palliative care randomised controlled trial that tests an intervention that is clearly a palliative care intervention and the study primary endpoint is survival.

4.4 Theoretical Propositions

As discussed in the previous chapter, Yin (2018) borrows the use of theoretical propositions from experimental research. He recommends that pre-defined theoretical propositions are developed to guide data collection and analysis in all types of case study. He believes that focused research questions and theoretical propositions mean the case study is more likely to be manageable. Yin (2018) also argues that the use of theoretical propositions can strengthen a case study design by facilitating the process of analytical rather than statistical generalisation which is discussed later in this chapter.

In this study, the initial theoretical propositions were influenced by the '6 Ps' of the 'Social Marketing Mix Framework', the findings of the literature review outlined in chapter two and the wider trial recruitment literature (see table 11). Yin (2018) provides little practical guidance on how to generate theoretical propositions and how they work alongside an a

priori theoretical framework during the data collection and analysis process, as in this study. This lack of practical guidance influenced my decision to develop only a small number of theoretical propositions. Why these particular theoretical propositions were chosen and prioritised are presented in table 11. The theoretical propositions were revised and amended as the study progressed to reflect the study findings (Yin, 2018). The final theoretical propositions are outlined in chapter seven.

Table 11: The initial theoretical propositions and why they were chosen

Theoretical Proposition	'6 P'	Why chosen	Example literature based on
Study design influences how recruiting staff undertake the process of recruitment and the strategies they use.	Product: defining the product	Patient, carer and health care professional concerns about 'the product' are raised in the general and palliative care trial literature. The number of references within 'Product: defining the product' in the literature review in chapter two (see table 9)	Palliative care: Noble et al (2015), Bausewein et al (2010), Westcombe et el (2003), Buss et al (2008) General: Norris et al 2019
The involvement of specific research staff in the recruitment process impacts on how well the trial meets its recruitment target.	Working with Partners: partner referrals and recruitment	Strategy discussed most frequently in the literature review in chapter two.	Abernethy et al (2010), Ammari et al (2015), Bakitas et al, (2006), Cook et al (2002)
How recruiting staff undertake the recruitment of patients or carers is influenced by their professional role.	Working with Partners: partner referrals and recruitment	To reflect the choice of recruiting staff as an embedded unit of analysis in this study. The influence of professional role on recruitment practices has been identified in the general trial literature.	Donovan et al (2014)
Where recruitment activity takes place may influence the recruitment process.	Place	To reflect the choice of clinical recruitment centres as an embedded unit of analysis in this study and the findings of the literature review in chapter two (see table 9)	Storey (2004), Zambroski et al (2014), Fischer et al (2015), Sampson et al (2011)

4.5 Sampling

4.5.1 Sampling of the cases

Yin (2018) argues that cases should be chosen that are most likely to address the research question and the aims of the study. A set of criteria for cases to qualify for inclusion into the study were developed and are outlined in table 12.

Table 12: Inclusion criteria for the cases

- Palliative care randomised controlled trials aimed at adult patients with incurable cancer and/or advanced, progressive non-malignant disease and their family carers will be included.

and either

- Palliative care randomised controlled trials where the primary endpoint is symptom control and/or quality of life will be included.

or

- Palliative care randomised controlled trials that test an intervention that is clearly a palliative care intervention and the study primary endpoint is survival will be included.
- UK trials registered on relevant trial registers and databases. These databases were the National Institute for Health Research Portfolio database (renamed as UK Clinical Trials Gateway during the study), the International Standard Randomised Controlled Trial Number (ISCRTN) registry, Cancer Research UK and Clinical Trials.gov.

- Trials that are either ongoing, recently closed (within 12 months) or set up during the data collection period.
- Trials that have been open for at least four to six months to ensure enough time for a recruitment plan to have been trialled, assessed and changes implemented if required.
- For trials that are closed, this will need to have happened within the previous twelve months to ensure participants are able to recall their experiences of recruiting to the trials.

Cases are purposively selected based on their characteristics so should be carefully screened (Stake, 1995; Yin, 2018). These characteristics may include, for example, the recruitment setting, the type of intervention, the number of recruitment centres and whether they have research nurse support. An excel spreadsheet was created and populated to facilitate and document the case identification process. Potential cases were consecutively screened and identified from the publicly accessible trial databases listed in table 12.

Methodological and practical issues influenced how cases were identified and chosen in this study. The multiple case study approach is seen as a series of experiments with each case serving to confirm or disconfirm the hypothesis or theoretical propositions (Eisenhardt, 1989). Yin (2018) argues that in multiple case studies, cases should be purposively selected in terms of replication logic rather than sampling logic. This is similar to the approach used in hypothesis testing research (Eisenhardt, 1989). Cases can be chosen to represent literal replication or theoretical replication. When using literal replication, selected cases are predicted to follow similar processes and therefore share the same results. This study used theoretical replication which involves selecting cases that are predicted to have different findings because of contrasting characteristics. Given the diverse nature of palliative care trials, this approach was viewed as the most suitable option for selecting cases in this study.

In practice, only the main contrasting trial characteristics may be known during the screening process. Theoretical replication was also chosen because the findings from the study are seen as more robust if the cases corroborate each other. This is because the same experiences have been found in divergent cases (Yin, 2018).

Cases were chosen that had a variety of study designs and were recruiting participants from different clinical settings. The eligible trials available at the time of screening and those approached are presented in appendix 9. Case selection was guided by the studies theoretical propositions, the findings of the literature review in chapter two and the wider trial literature. The chosen cases contrasting characteristics identified during the screening process are outlined in table 13. Exemplar references from the literature are included, where available, to support the choices made. The contrasting characteristics of the cases uncovered during data collection and analysis are described in further detail in chapter five and in appendix 14. Case selection was also influenced by practical issues such as the number of eligible trials available in the UK at the time of sampling. A small number of trials could not be included as myself and my supervisors were involved in the trials. Trial databases were not always up to date so multiple databases needed to be used to screen for eligibility. Case selection and recruitment occurred in series rather than parallel

Table 13: The chosen cases main contrasting characteristics identified during the screening process with examples from the literature.

	Study intervention (Product)	Trial population (Identifying participants)	Recruitment setting (Place)	Chief Investigator (Partner referrals and recruitment)*
Case 1	Challenges of using a placebo Non pharmaceutical symptom control intervention versus placebo (Buss & Arnold, 2004; Hardy et al., 1998)	Advanced cancer	Challenges of recruiting from a hospice setting (Storey, 2004; Zambroski et al., 2014) Single centre trial	Lead clinician (Bakitas et al., 2006; Higginson et al., 2008)
Case 2	Challenges of maintaining clinical equipoise Parallel trial of a complex intervention versus standard care (Goodwin et al., 2000; Jones et al., 2013; Westcombe et al., 2003)	Advanced cancer	Challenges of recruiting from a hospital outpatient setting (Hanson et al., 2014; Latimer et al., 1998) Large multi-centre trial	Clinician
Case 3	Challenges of promoting a palliative care trial Cluster trial of a complex intervention versus usual care (Fowell et al., 2006; Jones et al., 2011)	Advanced cancer and non-cancer (end-of-life care)	Challenges of recruiting from a hospital inpatient setting (Fischer et al., 2015; Sampson et al., 2011) Feasibility multi-centre trial	Academic

* Accurate details about the type of professionals involved in the recruitment process (Donovan et al., 2014) and whether the trial had dedicated recruiting staff (Cook et al., 2002; Jordhøy et al., 1999) was not available during the screening process.

4.5.2 Sampling of individual participants within the cases

The aim was to sample a diverse mixture of professionals from each of the cases, with different roles in the recruitment process, from both the study coordinating centre and clinical recruitment centres (see table 14 for individual participant inclusion criteria)

Table 14: Inclusion criteria for the individual participants

Staff involved in the recruitment of patients or carers in the selected 'cases' from the study coordinating centre and clinical recruitment centres will be included such as the Chief Investigator, Trial Manager, Clinical Research Associate, Principal Investigator, Research Nurse or other clinicians.
18 years of age or over
Be able to read and communicate in English

Snowball sampling was used to select participants from the eligible population within each case (Mason, 2018). Snowball sampling can be useful in case study research as it allows for flexibility when the researcher does not know, as in this study, who they need to approach at the start of their research (Yin, 2018). The Chief Investigator of each case was initially asked to identify eligible staff within the study coordinating centre and clinical recruitment centres. These staff members were then approached and asked to propose other individuals who had experience relevant to the study (Bryman, 2012). Recruitment of participants ceased within the case when the pool of potentially eligible participants who were willing to participate in the study was exhausted.

4.5.2 Sampling procedure for trial documentary data

A preliminary assessment of what documents were available online in the public domain were made for each 'case' such as a published protocol (Mason, 2018; Yin, 2018). Snowball sampling was then used to select documents from the pool of potentially relevant trial documents within the case that were not accessible online. Those participants who had agreed to take part in the study were asked to identify documents that they felt may be relevant to the research questions.

4.6 Recruitment

4.6.1 Recruitment of the Chief Investigator and study coordinating centre staff

The Chief Investigators of the selected cases were approached by email to see if they were interested in taking part in the study. All of the Chief Investigators approached had contact details that were available online in the public domain. The research ethics committee approved email and supporting documentation, including the approval letter, were sent to the Chief Investigators. A reminder email was sent after 2-3 weeks if there was no response. The Chief Investigators of the selected three cases agreed to participate in the study. They were then asked to facilitate access to their study coordinating centre staff and the clinical recruitment centres involved in their trial. The Chief Investigator forwarded the study information to eligible study coordinating centre staff and/or passed on their contact details

with permission. Those contacted were asked to reply by email or telephone if they were interested in taking part in the study.

4.6.2 Recruitment of Principal Investigators and clinicians within the clinical recruitment centres

The Chief Investigator forwarded the study information to the Principal Investigators in the clinical recruitment centres. This process was facilitated by the trial coordinator /administrator in cases two and three. A couple of Principal Investigators were also contacted directly about the study in case two as their details were available in the public domain. If the Principal Investigators agreed to be contacted, they were sent an email with the study information. If the Principal Investigator agreed to support the study, the necessary organisational approval was obtained. The Principal Investigators were asked if they would be willing to take part in an interview and facilitate access to the relevant personnel involved in the recruitment process within their clinical area. In practice, the Chief Investigator also forwarded the study information to research nurses in the clinical recruitment centres and some of these got in contact directly to say they were interested in taking part in the study. All potential participants, including those identified as a result of snowballing sampling, received the study information and were asked to reply by email or telephone if they were interested in taking part in the study.

4.7 Methods of data collection

One of the key principles of case study research is the use of multiple sources of evidence to corroborate study findings and to gain an understanding of the complex issues, systems and perspectives that make up a process such as recruitment. This study used two complementary sources of evidence to address the research question (Yin, 2018). These were semi-structured interviews carried out over the telephone and trial related documentary evidence. Multiple perspectives of the recruitment process were also derived from the various accounts given by study coordinating centre and recruiting staff involved in the chosen cases who were interviewed in this study (Ritchie & Lewis, 2003). Data were collected from each case consecutively.

4.7.1 Semi structured Interviews

In case study, interview data is one of the most important sources of evidence as they can help address how and why questions (Yin, 2018). Interviewing captures participant's experiences, motivations (Silverman, 2013) and perspectives of social phenomenon such as the recruitment process (Yin, 2018). The process of interviewing also fits with the critical realist ontological and epistemological stance taken in this study as the social world is only accessible via participant's interpretations of the social world, which maybe further interpreted by the interviewer (Ritchie & Lewis, 2003). The aim of interviewing a diverse group of professionals involved in the recruitment process was to yield different types of

understanding. This process adds richness to our understanding of the various ways in which external reality is experienced by individuals within the social world (Ritchie & Lewis, 2003).

The interviews in this study were semi structured and took the form of a guided conversation (Yin, 2018). Semi structured interviews were used as the study had a clear focus of interest and to ensure that comparisons could be made across the cases (Bryman, 2012). McIntosh and Morse (2015) argue that it is the replicability and flexibility of semi-structured interviews that means pertinent and rich data are obtained. An interview topic guide was developed at the start of the study that reflected the research question and the literature review in chapter two (McIntosh & Morse, 2015). The topics covered included; recruitment procedures, exploration of phraseology used to discuss the trial with participants, how well the trial has recruited, factors that have helped or hindered recruitment, recruitment strategies and lessons learnt (see appendix 8).

The topic guide contained a number of open questions to generate discussion and was flexible enough to reflect individual trial characteristics and the professional role of the interviewee (Creswell & Poth, 2016; McIntosh & Morse, 2015). The topic guide was also iterative to respond to participant's responses and to allow the pursuit of new areas of inquiry during the study (Bryman, 2012). Two mock interviews took place with researcher colleagues to practice the interview and to ensure the topic guide was fit for purpose (McIntosh & Morse, 2015). Brief notes were made during the interview (Oltmann, 2016) and more detailed notes after each interview (Bryman, 2012).

4.7.2 Telephone interviews

The interviews were carried out over the telephone as this was seen as the best approach for this particular study for a number of reasons which are discussed below. Qualitative telephone interviews have been seen as a less attractive option to face-to-face interviews because of concerns about the depth and quality of the data collected (Novick, 2008; Oltmann, 2016). Creating a comfortable environment and building rapport are seen as important when carrying out interviews (Bryman, 2012). This can be more problematic in telephone interviews as the researcher is unable to use visual gestures to build rapport (Novick, 2008). Rapport was built prior to the interview by email and time was spent at the start of the interview discussing the study. Straightforward questions about the participant's recruitment experience were used at the start of the interview to build rapport (McIntosh & Morse, 2015). Non-threatening open 'how' questions were also used to try and understand participant behaviours and actions rather than asking participants directly why they acted in a certain way (Yin, 2018).

Telephone interviews may help participants feel more comfortable and more open to discussing their views and experiences of a particular issue because of the virtual nature of communication (Trier-Bieniek, 2012). This applies to both nurses (Mealer & Jones, 2014) and doctors (Crowe et al., 2017). Visual cues such as body language or facial expression cannot be used to help interpret participant responses during telephone interviews (Novick, 2008; Oltmann, 2016). Unscripted probes were used to explore participant views and experiences more deeply (McIntosh & Morse, 2015), as well as the use of pauses and silence to allow participants time to consider their responses (Mason, 2018). Semi structured

qualitative telephone interviews led to rich and descriptive accounts of participant's experiences of recruiting patients and carers to palliative care randomised controlled trials. Participants spoke openly about their experiences and the challenges they faced recruiting vulnerable patients and carers to trials.

On a practical level, face-to-face interviews were not an option in this study as the data collection sites were not local to Lancaster University and no funding was available for data collection (Novick, 2008; Oltmann, 2016). Carrying out the interviews via the internet was an option but the research ethics committee had concerns about the security of communication software such as Skype and clinicians usually have limited access to these type of systems. It is likely this option would have now been more acceptable to research ethics committees and clinicians, as these methods of communication are now the norm because of the restrictions imposed by the COVID 19 pandemic.

Telephone interviews allowed for geographically dispersed participants to be included in the study at minimal cost (Novick, 2008; Oltmann, 2016). There were occasions when the interviews were interrupted, cancelled and rearranged at short notice and took place in the interviewees own time. Telephone interviews allowed for greater flexibility and responsiveness as eligible participants were usually time poor (Oltmann, 2016). Participants were asked how much time they had available at the start of the interview and asked whether they had time to continue during the conversation (Signorelli et al., 2018). The importance of researchers being flexible to maximise recruitment and data collection opportunities in clinical settings has been recognised (Barclay et al., 2019; Broyles et al., 2011; Coyne et al., 2016; Signorelli et al., 2018). Data collection would have been more challenging in this study without the use of telephone interviewing.

4.7.3 Collection of trial documents

Documents related to trial recruitment were collated as they revealed how the recruitment process and the strategies supporting it were formally expressed and communicated (Mason, 2018). Participants who agreed to take part in the study were asked to identify and provide documentation that they felt would be relevant to the research question. Case related documentation available in the public domain was also accessed from the internet. Reviewing trial documentation also lead to the identification of new areas of inquiry to pursue in the interviews (Yin, 2018). Documentation was largely provided by the study coordinating centre to ensure the research ethics committee proof of ownership requirement was met. In practice, carrying out the interviews face to face may have made documentary evidence collection easier as staff needed to feel comfortable and be fully bought into the idea of sharing documentation. As a result, the documents collected in this study were largely the 'official' trial documents rather than documentation created by recruiting staff in the clinical recruitment centres to support the recruitment process.

4.8 Reflexivity

Yin (2018) believes that in case study research the aim must be to minimise personal biases as much as possible. Reflexivity is an ongoing process that involves the researcher reflecting on how their choice of method as well as their values, biases, decisions and presence in the research situation may have influenced the knowledge of the social world they have generated (Bryman, 2012). Being sensitive to the researcher's *'cultural, political and social*

context' is also important (Bryman, 2012)(p. 393). Researcher biases and assumptions can influence the research topic and method chosen as well as how the data is collected, analysed, interpreted and presented (Borbasi et al., 2005; Bryman, 2012).

The importance of critical reflection and self-awareness during the study design, data collection and analysis process was recognised especially as my own 'personal biography' involved working as a palliative care research nurse in a hospice setting (Mauthner & Doucet, 2003). This experience strongly influenced the topic and focus of my research as I had some insight into the challenges faced when recruiting patients and carers to trials in palliative care. In addition, my 'personal biography' also included experience as a specialist nurse in a hospital and community setting which involved managing the complex physical and psychosocial needs of palliative care patients and their carers and working closely with members of the multi-disciplinary team. During my research, I was no longer involved in direct patient care but was working as a research associate on a number of palliative care trials.

Nurses can bring nursing specific qualities, skills and knowledge to the research process which can create methodological, practical and ethical challenges (Borbasi et al., 2005). For example, nurses can find it less challenging to communicate and 'fit in' with clinicians but this can raise issues of how involved they should become with research participants to build rapport (Borbasi et al., 2005). A researcher needs to be aware of and reflect on the relationship that exists between themselves and the interviewee (Creswell & Poth, 2016). Regular supervision meetings provided the opportunity to discuss some of the foreseen as well as some of the unforeseen challenges that could potentially occur during the research process. The decision was made at the start of the study not to disclose my professional

background to participants but inform them if they asked and agree to answer questions at the end of the interview. The stance taken in this study reflected the view that being truly objective is not possible and that researchers should be mindful of subjectivity throughout the research process to try and limit its effect (Bourke, 2014). This aligns with Yin's view that researcher bias must be avoided but recognising this may not be fully possible.

During the interviews, it was important to be alert to the fact that professional role can influence how you interact with other clinicians and may prevent you from asking certain questions or clarifying responses. Being over familiar with the clinical setting and the focus of the research can also mean important issues are disregarded (Borbasi et al., 2005). Supervisor feedback on the initial interview transcripts was also used to facilitate the process of reflexivity. Detailed reflexive notes were made after each interview to reflect on such issues and to consider areas to explore in future interviews. Reflexive notes were used to document the choices and decisions that were made during the data analysis and interpretation process. The use of charting during within and cross-case analysis also provided an audit trail of how the findings were reached (Ritchie & Lewis, 2003). Sharing, discussing and reflecting on the analysis during supervision meetings enhanced the process of reflexivity which proved invaluable especially when 'in the thick' of the analysis process (Mauthner & Doucet, 2003).

4.9 Ethical considerations

4.9.1 Research ethics and governance approval

As this study did not involve patients or carers, NHS research ethics committee approval was not required. Research ethics committee approval was obtained from the Lancaster University Faculty of Health and Medicine Research Ethics Committee (Reference number: FHMREC15042, 22nd February 2016). The ethics committee wanted reassurance that any contact details not in the public domain were only passed on to the researcher if the person had given their permission for this to occur. They also wanted reassurance that permission had been obtained from necessary parties to access and use trial documentation that was not available in the public domain. This study did involve NHS staff so organisational approval was obtained for all research sites via the Health Research Authority. Organisational approval was also obtained from the one hospice site taking part in the study. No data collection took place until all the necessary approvals were in place.

4.9.2 Consent

The research ethics committee permitted the use of verbal consent in this study as it was assessed as a low risk study (Preston et al., 2020). Verbal consent has been used in previous qualitative telephone interview studies with nurses (Mealer & Jones, 2014) and interviews with trial staff about their experiences of recruiting to a trial (Hanson et al., 2014). Those who gave permission to be contacted about the study were sent the participation

information sheet and consent form via email (Signorelli et al., 2018). If the participant expressed an interest in taking part in the study either by email and/or telephone, an appointment was made to carry out the telephone interview. Prior to commencing the interview, the study was discussed with participants and any questions or queries were answered. If the participant wished to take part in the interview, verbal consent was recorded on the digital recorder prior to any data collection taking place. Process consent was also followed in this study with participation renegotiated as appropriate during the interview. The requirement for participants to complete and return a consent form to take part in the study would have acted as a barrier to recruitment.

4.9.3 Risks, benefits and burdens

There were no direct benefits for those taking part in the study but it appeared that some participants valued the opportunity to talk about their experiences of recruiting to a palliative care trial. This assumption is based on their willingness to take part in the study and spend time away from their busy clinical workloads talking about their experiences. On the surface, the topic of this study did not appear sensitive but there were occasions when some participants expressed how recruiting to a palliative care trial could be emotionally challenging. No participants became distressed during the interviews but this response had not been expected when planning the study. This may have been because of my own clinical background where interacting with palliative care patients and their carers is the norm. In the participant information sheet, it was explained that if something was disclosed during the interview that made the researcher concerned the participant or someone else was at

risk of harm confidentiality would be broken. This did not occur during the study and there was no requirement to break confidentiality. There were concerns that staff may feel obliged to take part in the study if their manager, clinical lead or organisation were supporting the study but the number of participants who declined to take part suggests this was not a significant issue.

4.9.4 Confidentiality

Whether and how to maintain anonymity in case study research can be an issue as a description of the case may lead to the case and individual participants being identified (Yin, 2018). Given the small number of palliative care trials in the UK, it was recognised that participants and the trial may be identified because of information that is available about the trial in the public domain. This was highlighted in the participation information and consent form. The decision was taken to anonymise the case, clinical recruitment centres and individual participants and this assurance was included in the participant information and consent form. I was concerned that Chief Investigators may be reluctant to take part in this study if the trial was not anonymised. I was also concerned that study coordinating centre and recruiting staff would be reluctant to take part if they knew they could be potentially identifiable. I was also mindful that participant responses may not have been as open and honest if they knew the trial was not going to be anonymised.

A number of strategies were used to anonymise the cases, the participants and the trial documentation. How best to optimise and ensure anonymisation was discussed at length with my PhD supervisors. In order to maintain anonymity, detailed information about the

characteristics of the cases is not provided in the study findings. Each trial was allocated a number identifier; case one, case two and case three. Characteristics of the individual clinical recruitment centres are also not provided in the results as this could potentially lead to the clinical recruitment centres and their participants being identified. Individual clinical recruitment centres were allocated a number identifier to facilitate analysis but this was removed in the presentation of findings. Individual participant characteristics, apart from their professional role, are also not included in the findings to disguise their identity. Participants are identified by their professional role, the order of interview and the case number such as Specialist nurse one, case two. Identifying information was removed from trial documentation during analysis. Documentation is identified by the name of the document and the case number such as protocol, case three. A small number of trial characteristics were deliberately modified to maintain anonymity. These changes do not impact on the interpretation of the study findings.

During the study, all data (both paper and electronic) were treated as confidential and stored securely. Electronic data was stored on a secure University password protected computer and paper data in a locked cabinet. Transcripts were anonymised before uploading to NVivo, by removing identifying characteristics such as the participant's name, the name of the trial and the name of the clinical recruitment centre. A Lancaster University approved transcriber was used who signed a confidentiality agreement.

4.10 Data analysis

Data analysis was iterative in this study as this allowed for refinement of interview questions, review and updating of theoretical propositions and the opportunity to pursue new areas of inquiry (Evers & van Staa, 2010). It also helped shape the selection of cases including the number of cases needed and their characteristics (Paterson, 2010).

Yin (2018) recommends a number of strategies when analysing case study data. In this study within case analysis, embedded units of analysis, cross-case analysis and pattern matching were used (Yin, 2018). Framework analysis was the analytical approach used to facilitate this process (Gale et al., 2013; Ritchie & Lewis, 2003).

4.10.1 Within case analysis

Yin (2018) recommends that within case analysis occurs before cross-case analysis but provides little guidance for the researcher on how to operationalise this process in practice. The purpose of carrying out within case analysis is to identify each case's individual characteristics and patterns before identifying general patterns that occur across all of the cases (Paterson, 2010). For each case, the perspectives of the individual participants were examined independently and then across the participants for a within-case comparison. A standalone description of each of the cases was written up before the following case was analysed (Yin, 2018).

4.10.2 Framework analysis

Framework analysis, a form of thematic analysis, was chosen as it provides a systematic but flexible approach to data analysis and facilitates pattern matching (Ritchie & Lewis, 2003; Smith & Firth, 2011; Ward et al., 2013). The aims of qualitative thematic analysis approaches are to identify similarities, differences and relationships in the data so that descriptive and/or explanatory conclusions can be drawn (Gale et al., 2013). Framework analysis provides the researcher with the structure and process to compare and contrast the data within and across cases. It is also suited to the thematic analysis of semi-structured interview transcripts and documentary evidence as collected in this study (Ritchie & Lewis, 2003). Framework analysis is not aligned with a particular theoretical, epistemological or ontological approach and allows for inductive or deductive thematic analysis or both as in this study (Gale et al., 2013; Parkinson et al., 2016; Ritchie & Lewis, 2003).

Framework analysis is made up of a number of stages and processes that Ritchie and Lewis (2003), the developers of the method, term the 'analytic hierarchy'. This process is not linear but continuous and iterative and the researcher is required to move up and down the steps in the 'analytic hierarchy' throughout the analysis process (Ritchie & Lewis, 2003). The first stages involve managing the data where the raw data is reviewed, labelled, sorted and synthesised. Following on from this the researcher develops descriptive accounts by identifying key dimensions/elements, refining categories and developing classifications. Thirdly, the researcher develops explanations about why the data took the forms that are found and presented (Ritchie & Lewis, 2003).

4.10.3 Managing the data

The purpose of the initial data management activities are to identify initial categories, concepts and ideas. NVivo 11 was used to support the data management processes (Bazeley & Jackson, 2013). All of the interviews were digitally audio recorded and transcribed verbatim. All of the transcripts were checked against the original audio recording for accuracy. The first two transcripts were transcribed by the researcher to facilitate familiarisation with the data while a professional transcriber was used for the further transcripts. The term framework analysis comes from the conceptual framework which forms the central part of the method. The conceptual framework is used to classify and organise data according to the main classifications, subdivided by related categories. In this study, part of the framework existed before analysis and the rest was developed during the analysis process. The pre-existing framework comprised a number of classifications that reflected the '6 Ps' of the 'Social Marketing Mix Framework'. How and why additional overarching classifications were inductively developed during the analysis process and added to the pre-existing conceptual framework is discussed in more detail below.

The initial transcripts, trial documents and reflective notes were read and re read to identify recurring categories. Memos were used throughout the analysis process to capture thoughts and observations about the data (Yin, 2018). The categories identified were a mixture of predetermined 'a priori' index categories identified from the systematic review in chapter two, 'in vivo' index categories that reflected the language and the terms used by the participants and index categories that captured the essence of what was being discussed. The index categories were grouped into clusters around similar and interrelated ideas or

concepts and arranged within the appropriate classifications, reflecting the '6 Ps' of the 'Social Marketing Mix Framework', in a tree diagram structure (Gale et al., 2013). The conceptual framework was then applied systematically to the subsequent transcripts and documentary evidence. Ritchie and Lewis (2003) use the term indexing rather than coding to describe the activity of labelling the raw data and index categories rather than codes. The conceptual framework was reviewed, refined and discussed with my supervisors throughout the data analysis process to optimise methodological rigor (Morse, 2015).

The next stage was to summarise or synthesise the original data into charts through an activity called charting. The framework matrix function in NVivo 11 was used to produce the charts. The software produces a spreadsheet of the categories contained within the conceptual framework and places the indexed data within each cell. Each respondent is allocated a row while each category is displayed in a separate column (Miles & Huberman, 1994; Yin, 2018). Both interview and documentary data were synthesised within each cell and care was taken to ensure the summarised data reflected the original terms, thoughts and views of participants (Ritchie & Lewis, 2003) (see appendix 11 for an example). In this study, charts were created for each of the cases to facilitate within case analysis, analysis of the embedded units within the cases and cross-case analysis.

4.10.4 Developing descriptive and explanatory accounts of the data

Ritchie and Lewis (2003) recommend that the charted data be interrogated further to identify and map key elements/dimensions of a particular phenomenon or category. This process leads to a refinement of the framework's categories and sub categories and how

they are organised within the conceptual framework. The template suggested by Ritchie and Lewis was used to facilitate this process (see appendix 12 for an example). The charted data was scrutinised again within case and then it was compared across all three cases. This process led to further refinement of the categories/sub categories and how they were organised within the classifications (see appendix 13 for the final analytical framework). The original transcripts and documentation as well as the summarised data were revisited throughout data analysis process to check context and assumptions as well as aid interpretation.

The next stage involves searching for and developing explanations for how and why particular phenomenon or patterns occur in the data. Reasons can be related to situational or contextual factors and/or dispositional factors such as the individual's behaviour, intentions or motivations. In this study, explicit reasons were sometimes given by participants in their interview responses and/or they were contained within trial documentation. A number of strategies were used to develop explanations such as examining why an issue was mentioned by some participants and not others, why there was repeated coexistence of two sets of phenomena and why apparently unconnected categories were interweaved.

4.10.6 Embedded units of analysis within the cases

This case study was designed with two embedded units of analysis; recruiting staff and clinical recruitment centres. Clinical recruitment centres and recruiting staff were chosen as embedded units of analysis within the selected cases as these were the focus of recruitment

activity. This decision reflected the assumption that the context in which recruitment activity takes place may make a difference to the recruitment process and professional role would influence how staff undertake the process of recruitment and the strategies they use (Yin, 2018). The perspectives of different professional groups were examined and compared. For example, the differences and similarities between research nurses within a clinical recruitment centre were firstly explored. This was followed by an examination of the similarities and differences between research nurses across the clinical recruitment centres within the case. Moving and comparing the rows in the charts and writing up the cases facilitated this process. Clinical recruitment centres as a whole within the case were also compared with each other.

4.10.7 Cross-case analysis

Following within case analysis, a comparison of perspectives was conducted across all of the cases. Cross-case analysis also involved comparing the cases with each other as standalone entities (Chmiliar, 2010). The purpose of cross-case analysis is to identify commonalities and differences across the included cases. This process involves engaging with the data, detecting patterns within the data and allowing similarities and differences between the cases to be identified (Gale et al., 2013). The conceptual framework, reflecting 'the 6P's', was used to identify what categories were shared and what categories were unique to each case (Paterson, 2010). The findings generated from this process are then used to develop more general explanations of how and why a pattern or phenomenon may occur (Chmiliar, 2010). During within and cross-case analysis, the perspectives of outliers who did not fit with the

patterns that were emerging in the data were not ignored (Ritchie & Lewis, 2003). The data was interrogated further to try and identify and understand the reasons for why differences were occurring.

Three additional linked overarching classifications derived interpretatively from the data were added to the pre-existing conceptual framework during the cross case analysis process (see figure 2). This was because the findings indicated that there were deeper underlying contextual reasons for the participant's responses and behaviours that could not be fully explained by 'the 6 Ps' of the 'Social Marketing Mix Framework'. These classifications were; 'emotional labour', 'paternalism' and 'professional hierarchies and power relationships between clinicians'. This interpretative cross case analysis forms the basis of chapter six while chapter five, a more descriptive cross case analysis, relates the study findings to the '6 Ps' of the 'Social Marketing Mix Framework'.

4.10.8 Pattern matching

Pattern matching is a data analysis strategy recommended in the theoretical literature (Hak & Dul, 2010). Yin (2018) views it as the most desirable approach when carrying out case study research, even in descriptive case studies, as long as the expected pattern is specified prior to data collection. In pattern matching, the researcher compares a findings based pattern with a predicted pattern based on the studies theoretical propositions (Yin, 2018). Pattern matching logic is drawn from hypothesis testing but it does not use statistical testing methods (Almutairi et al., 2014). The analyst decides whether the patterns match so confirming the theoretical propositions or that they do not match so disconfirming the

theoretical propositions (Hak & Dul, 2010). The purpose of pattern matching is not just about confirming or disconfirming the theoretical propositions but explaining why the patterns are matched or not (Almutairi et al., 2014). Yin has been accused of being vague when explaining his analytical techniques (Evers & van Staa, 2010) and it can be challenging to implement the pattern matching technique in practice (Almutairi et al., 2014). Yin (2018) does suggest that the pattern matching process can focus on more major matches or mismatches rather than subtle patterns. In this study, for each of the individual cases and then across the three cases empirically based patterns were compared to the studies theoretical propositions (Evers & van Staa, 2010; Paterson, 2010 ; Yin, 2018). As discussed previously, the theoretical propositions were influenced by and reflected the '6 Ps' of the 'Social Marketing Framework'. One of the challenges for researchers when using a predefined conceptual framework is not to force fit the study findings into this framework (Bitektine, 2008; Crowe et al., 2011). The theoretical propositions were modified during the study to reflect the study's findings, including the newly developed interpretative classifications discussed above, and the updated propositions are outlined in chapter seven (Yin, 2018).

4.10.9 Number of cases included in this case study

Three diverse cases were included and analysed in this study for methodological and practical reasons. Yin explains how the case is not a sample of one and generalisation occurs through a process called 'analytic generalisation' rather than statistical generalisation as in experimental studies. This is when previously developed theory, the theoretical propositions

rather than grand theory, are used as a template with which to compare the study findings (Yin, 2012, 2018). Using a multiple rather than a single case study approach is seen to improve the potential for theory building, as comparisons can be made across all the cases (Bryman, 2012; Yin, 2018). Like in experimental research, the more cases included in the research the greater confidence or certainty there is in the study's findings (Yin, 2012). Resource issues also influenced the number of cases included in this study which Yin (2018) acknowledges can also be an influencing factor.

4.11 Addressing the issue of rigour in case study research

There are no mutually agreed standards for assessing the quality of qualitative research or the strategies researchers should follow to demonstrate methodological rigour (Ritchie & Lewis, 2003) and this also applies to case study research (Bryman, 2012; Riege, 2003). In empirical social research, terms such as validity, reliability and generalisability are used to address the issue of rigour (Morse, 2015). Some have argued that a set of criteria unique to qualitative research needs to be developed as qualitative and quantitative research sit within different paradigms (Lincoln & Guba, 1985). Others believe fixed criteria should be let go completely or are not appropriate as concepts such as validity are socially constructed so diverse context dependent perspectives of validity should be promoted (Sparkes, 2001).

Researchers need some way of demonstrating that they have paid attention to the methodological rigour of their study. Creswell and Poth (2016) argue that researchers should use the approach they are comfortable with and reference their terms and strategies. This study adopts the replication perspective (Sparkes, 2001), the idea that terms

and concepts used in quantitative research are compatible with qualitative research (Morse, 2015). This approach recognises, however, that different strategies may be used to achieve and demonstrate methodological rigour (Morse et al., 2002; Sparkes, 2001). The replication perspective has been chosen for a number of reasons. Firstly, this viewpoint fits with Yin's approach as he argues that the tests of construct validity, external validity and reliability are relevant to descriptive case studies though he does argue that the concept of internal validity only applies to explanatory case studies as this relates to causal relationships (Yin, 2018). Secondly, authors argue that this approach fits within the critical realist view of how rigour can be produced and assessed (Porter, 2007; Riege, 2003). Thirdly, these standardised criteria provide a shared language so those reading the study findings are able to assess whether the results are sufficiently accurate to implement into clinical practice (Porter, 2007).

Creswell and Poth (2016) suggest the use of multiple validation strategies but do not recommend which ones should be used. Morse (2015) believes that the *'indiscriminate use of strategies with any type of qualitative research'* is harmful to methodological rigor (p. 1219). Table 15 shows the tactics suggested by Yin that have been employed in this study. His recommendation to share the findings of the case study report with participants to enhance accuracy and increase construct validity was not followed. Authors have questioned the value of this strategy, referred to as respondent or member checking in the literature, as the data has been synthesised, abstracted and interpreted by the researcher so the individual participant may not agree or recognise their story (Morse, 2015; Morse et al., 2002).

Table 15: Case study tactics for four design tests (adapted from Yin, 2018)

Test	Definition	Case study tactics
Construct validity	Identifying the correct operational measure for the concepts being studied (Yin, 2018).	<ul style="list-style-type: none"> • Multiple sources of evidence were used to build construct measures that defined and distinguished them from other constructs. Multiple sources of evidence were used to generate, refine and substantiate study categories and theoretical propositions by interviewing professionals with different roles in the recruitment process as well as collecting and analysing trial documentation (Eisenhardt, 1989). • A chain of evidence was maintained to track how the data was categorised, charted and interpreted to promote greater transparency (Eisenhardt, 1989). NVivo 11 was used to support the process as well version controlling documentation.
External validity	External validity is concerned with whether the study findings can be generalised beyond the context of the study (Yin, 2018).	<ul style="list-style-type: none"> • By using replication logic in multiple case studies. In this study, theoretical replication was used. The idea that if the same experiences have been found in divergent cases the study findings are more robust and generalisable (Yin, 2018).
Reliability	Being able to demonstrate that if the same research methods were used the findings would be same. The aim is to minimise the errors and biases in a study (Yin, 2018).	<ul style="list-style-type: none"> • A case study protocol was developed that contained detailed information about how the case was defined, recruitment processes, data collection and analysis procedures. • A case study database was developed. This comprised; an excel spreadsheet to track interview invitations and responses; NVivo files to store anonymised raw data, excel and word charts containing summarised data, anonymised transcripts of the interviews. • The use of reflexivity as discussed above.

4.12 Conclusion

The case study design used in this study was a retrospective, descriptive, qualitative multiple case study with embedded units of analysis. The case was a palliative care randomised controlled trial with a specific focus on those health care professionals directly or indirectly involved in recruitment within the trial. Theoretical propositions were used to guide data collection and analysis. Data collection involved the use of semi-structured telephone interviews with study coordinating centre and recruiting staff and trial documentation. Framework analysis was used to facilitate within and across case analysis. The findings of the cross-case analysis are presented in the following two chapters.

Chapter five: Cross-case analysis findings in relation to the ‘6 Ps’ of the ‘Social Marketing Mix Framework.’

5.1 Introduction

The findings from this cross-case analysis are presented in this chapter and the following chapter. Data from each of the three cases is dispersed throughout the study findings (Yin, 2018). The cross-case analysis findings have been presented at the European Association for Palliative Care World Research Congress (see page 13 for further details).

An ‘abbreviated vignette’ of each of the three cases is presented initially to provide contextual information for the cross-case analysis (Yin, 2018). A more detailed within case analysis is presented in appendix 14. The summaries highlight the differences in clinical setting and study design between the three cases. The cases were purposively selected because of these differences to reflect the concept of theoretical replication as discussed in the previous chapter (Yin, 2018).

In this chapter, the cross-case analysis findings are explored in relation to the ‘6 Ps’ of the ‘Social Marketing Mix Framework’, as this was the a priori framework used in this study. The findings are presented within the overarching classifications that reflect the ‘6 Ps’ but they have been reordered to reflect the study findings. The categories identified during the analysis process are discussed within the relevant classification. The analysis is presented in eight sections: working with partners (partner referrals and recruitment); identifying participants; product (including product definition and competition); price (including type and minimisation); place; promoting the study; working with partners (barriers to

partnering) and finally working with partners (partner education). As discussed in chapter four, given the small number of palliative care trials that are carried out in the UK, detailed information about the trial and participant characteristics cannot be provided to maintain anonymity. Key case and participant characteristics and a list of trial documentation collected and analysed is presented in table 16 and in more detail in appendix 14.

5.2 Case and participant characteristics and trial documentation collected and analysed

Data collection occurred between March 2017 and June 2018 and 19 participants took part in a telephone interview (see table 16). The mean interview length was 39 minutes (range 25–60 minutes).

Table 16: Case and participant characteristics and trial documentation collected and analysed

	Case one	Case two	Case three
Recruitment setting	Hospice inpatients	Hospital outpatients	Hospital inpatients
Trial population	Advanced cancer patients	Advanced cancer patients and their carers	Advanced cancer and non-cancer patients (or proxy if required)
Trial design	Non-pharmaceutical placebo trial	Parallel trial of a complex non-pharmaceutical intervention	Feasibility cluster trial of a complex non-pharmaceutical intervention
Recruitment target	The recruitment rate was described as slow and at the time of data collection, approximately 83 % of the recruitment target had been met. This had taken a number of years to achieve and took longer than anticipated.	Achieved over 30 months rather than the anticipated 24 months.	Only 2 of the 4 sites reached their recruitment target with recruitment taking longer than the anticipated three months. One of the sites (intervention) took six months to reach its recruitment target while the other (control) took four and a half months.
Number of interviews	3 interviews	9 interviews	7 interviews
Type of participants	Palliative medicine consultant=1 Research nurse=2	Hospital consultant=2 Specialist nurse=2 Research nurse=5	Senior academic=2 Researcher=1 Palliative medicine consultant=1 Research nurse=3
Type of documentation collected and analysed	Study protocol, patient information sheet, patient consent form, GP letter, UK Clinical Trials Gateway website, results paper.	Study protocol, patient information sheet, patient consent form, carer Information sheet, carer consent form, carer GP letter, patient study	Study protocol, patient information sheet (intervention and control), patient consent form, carer Information sheet (intervention and control), carer consent

		<p>recruitment poster, trial recruitment figures for each hospital site, monthly recruitment figures for site four, an invitation to participate in the trial for clinical recruitment centres, 'Frequently asked questions' document for health care professionals, published protocol, published results papers, UK Clinical Trials Gateway website.</p>	<p>form, consultee information sheet (control and intervention), consultee approval form for continued participation if capacity is lost, recruitment letter to bereaved relative, trial recruitment figures for each site, clinical scenarios and materials to support recruitment for health care professionals, published study conference posters, published results papers, UK Clinical Trials Gateway website</p>
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5.2.1 Case one 'vignette'

Case one largely took place in a single voluntary organisation. The other organisation involved in the trial had only recruited a small number of patients and trial staff were unable to be interviewed because of staff shortages. All of the recruiting staff involved in the trial at the primary voluntary organisation agreed to take part in a telephone interview. All of the participants who were interviewed were experienced in recruiting to palliative care studies including trials.

In summary in case one, medical staff, usually the Chief Investigator, would initially approach the patient about the trial in the inpatient unit:

'I think largely it's for me to identify people on our ward rounds or when we go and see them. This is a study that is looking at hospice inpatients and then I'll flag them up, I'll mention the study to the patient and then flag them up to the research nurse to go and have a further chat with them.' (Chief Investigator, case one)

The research nurses would then discuss the study with the patient, provide written information and if the patient wished to enter the trial, they would then obtain written informed consent.

5.2.2 Case two 'vignette'

Case two was a large multi-centre trial and it was initially predicted that up to 10 hospital sites would be required to achieve the recruitment target. The trial actually required double that amount of sites to reach its target.

In this case study, five clinical recruitment centres out of the 18 that were approached via the study coordinating centre agreed to take part. Nine out of the 15 recruiting staff approached to take part agreed to participate in the interview. The main reason, when given, for staff declining to take part in the study was lack of time. The majority of the clinical recruitment centres that agreed to take part had met their recruitment targets. In these centres, the Principal Investigators were doctors apart from one site where the role was carried out by a specialist nurse. All of the interviewees were experienced in recruiting to oncology trials but case two was the first specific or 'overtly' (Specialist nurse two, case two) palliative care trial they had recruited to.

In summary in case two, the lead medical clinician and/or specialist nurse would initially approach the patient and carer about the trial in the outpatient department. Depending on the clinical recruitment centre, the research nurse, specialist nurse or doctor would then follow the patient up and obtain written informed consent from those participants who wished to take part in the trial.

5.2.3 Case three 'vignette'

In case three, all of the study coordinating centre staff agreed to take part in a telephone interview and four out of the 11 recruiting staff approached agreed to participate in the study. All of the staff interviewed were from two of the clinical recruitment centres that had not reached their recruitment targets. One of these centres had been delayed opening due to staffing issues but once opened reached nearly half of its target within three months.

Four of the interviewees had prior experience of working on palliative care studies but only two had worked on a palliative care randomised controlled trial previously.

In summary in case three, usually the trial would be initially introduced to the patient by the lead medical clinician. In the intervention arm, a specialist nurse was employed to coordinate the implementation of the intervention and they would sometimes introduce the trial to the patient. The research nurses would then approach the patient to discuss the study further and obtain written informed consent from those who wished to take part in the trial. If the patient lacked capacity, a consultee would be approached to provide proxy assent:

'...so you know if she'd been in (specialist nurse) she would say to me when I got on the ward right this patient's done, fully discussed, documented, they're aware of the study, you just need to go in and talk to them.' (Research nurse one, case three)

Some research nurses declined to work on the trial and the reasons why are explored in the next chapter.

The cross-case analysis is now presented as it relates to the '6 Ps' of the 'Social Marketing Mix Framework'; working with partners (partner referrals and recruitment); identifying participants; product (including product definition and competition); price (including type and minimisation); place; promoting the study; working with partners (barriers to partnering) and finally working with partners (partner education).

5.3 Working with partners: partner referrals and recruitment

Partners are organisations that are involved with a social change effort or serve as conduits to target audiences within the 'Social Marketing Mix framework' (Nichols et al., 2004).

Across the three cases, there were two analytical categories that were related to the theoretical classification of 'Working with partners: partner referrals and recruitment'.

These categories were 'recruiting clinical recruitment centres' and 'identifying patients and carers'.

5.3.1 Recruiting clinical recruitment centres

In cases two and three, the Chief Investigators discussed how they identified clinical recruitment centres for their trials. In case two, some of the clinical recruitment centres were identified via the National Institute for Health Research (NIHR) Clinical Research Network. The Clinical Research Network provides financial and other practical support to help clinical recruitment centres recruit to high quality research studies in England (National Institute for Health Research, 2019a). How much network funding and support the clinical recruitment centres receive is determined by the number of participants they recruit and the study design. As discussed previously, randomised controlled trials receive the greatest funding and support from the Clinical Research Network (National Institute for Health Research, 2019c). The Chief Investigator in case two described how the trial was attractive to clinical recruitment centres as it was a randomised controlled trial and it involved recruiting both the patient and their carer. The centres would therefore potentially receive

more funding and support as a result of their involvement in the trial as both the patient and carer would be counted as participants and the study design was a randomised controlled trial. This information was reflected in the trial documentation that invited eligible clinical recruitment centres to participate:

'This study is on the NIHR portfolio and as such will generate benefits of associated NIHR network support and activity based funding. This study also involves recruiting the patient's primary caregiver as a separate participant giving centres the opportunity to generate double the number of accruals for this RCT. In addition there will be a per patient tariff of £200 at randomisation and £50 on completion of all study paperwork amounting to a total of £250.' (Invitation to participate in [name of case] palliative care trial document)

In cases two and three, those clinicians who were interested in the topic of the research would approach the study coordinating centre to express an interest in taking part in the trial. The Chief Investigator in case two felt that an expression of interest from clinicians was not enough to guarantee suitable centres were recruited. Organisations also needed to demonstrate that they had a good reputation as a clinical recruitment centre. This required centres with a successful recruitment record, research infrastructure and experience of recruiting to similar trials. This viewpoint was supported by one of the research nurses in case one:

'...I think we've, over these few years, we've been able to establish ourselves within, sort of, the UK as a good site to recruit. And, so we've always recruited for studies that we've been participating in. And, I think, on the whole, I believe we've met our targets. But, again, because we're only a small unit, our target might be four

patients. But, that we've, you know, still managed to achieve that.' (Research nurse two, case one)

In cases two and three, it was a requirement not only to have staff available with the necessary skills and expertise to recruit to the trial but also have access to staff who were able to deliver the intervention. This avoided the study coordinating centre having to invest a large amount of additional resources to set the recruitment centre up. In case two, the study coordinating centre used a formal screening log to assess clinical recruitment centre eligibility:

'The other thing then was to vet every centre as we did.., to make sure that they passed the test and that they've got a recruitment record and that we didn't have to invest a great deal of resource to set them up in order to do the trial, 'cos there's no point having somebody with interest but no access to research method..' (Chief Investigator, case two)

5.3.2 Identifying patients and carers

All of the study coordinating centres used screening logs to monitor recruitment activity within the clinical recruitment centres. Across the three cases, identifying potential participants was a role carried out by a variety of health care professionals that included research nurses, specialist nurses, doctors and inpatient nurses. In all three cases, routine multi-disciplinary team meetings were used to screen for potentially eligible participants:

'After discussion of your case with a number of cancer specialists we have identified that you may be suitable to take part in this study.' (Patient information sheet, case two)

In cases one and two, recruiting staff used the meetings as a forum to screen patients for a number of studies. All of the clinical recruitment centres had access to research nurse support during the trials and research nurses attended multi-disciplinary team meetings to identify potential participants:

'...they have a short ward handover meeting with the consultant and the occupational therapist, physios etc. and we were attending that and trying to pick patients out of there who would be eligible for the study.' (Research nurse two, case three)

In case two, research nurses were not always able to attend the multi-disciplinary meeting because of a lack of time. Systems were in place to ensure they still received referrals for potential participants from the meeting. The research nurses received these referrals via email or through discussions with medical or specialist nurse colleagues who had attended the meeting. Across all three cases, informal discussions between clinicians were also used as opportunities to screen for potentially eligible participants:

'Well I work very very closely with the oncologist and the research team and we always sort of like did a recce of the patients coming forward and before we even met the patients we would try and work out whether they were suitable for (name of case).' (Specialist nurse one, case two)

There were other screening activities that occurred outside the formal multi-disciplinary team meetings. In case two, outpatient clinic referral lists were screened by research nurses and the study coordinating centre also ran a dedicated nurse led telephone line to answer eligibility queries from clinical recruitment centres. Following on from this initial screening process, the research nurses described how they would review the patient's medical notes to confirm the potential participant met all of the inclusion criteria and did not meet any of the exclusion criteria. In case one, confirming eligibility also required checking with the patient that they were still symptomatic. Checking the patient was eligible for the trial was viewed by the research nurses as an important part of their role:

'...well we should have the time to scrutinise you know the inclusion, exclusion and look through the notes properly 'cos there might be something and that's what I like, you know doing things properly. I think it's 'cos I'm a control freak.' (Research nurse four, case two)

Across the three cases, there were additional contextual factors that influenced how clinical recruitment centres were recruited and how patients and carers were identified that are explored in the next chapter.

5.4 Identifying participants: defining the target audience

The category, 'type of eligibility criteria', influenced how the target audience was defined in each case. As the three cases were palliative care trials, they included patients with advanced disease. Predicting a patient's prognosis was also a requirement when determining eligibility. In cases one and three, the eligibility criteria required the clinician to

estimate the patient's prognosis while in case two the eligibility criteria contained a performance status scale to aid prognostication.

The use of subjective criteria to predict a patient's prognosis proved particularly problematic in case three. Medical staff were required to predict the patient's risk of dying during the hospital admission. This proved especially challenging in the control arm as supporting and training medical staff to apply the trial's subjective criteria could potentially lead to contamination. In this example, treatment contamination refers to a situation where clinicians in the control arm may learn about the intervention and adopt it into their clinical practice. This may lead to a type II error which leads to the rejection of an effective intervention because the observed effect size was neither statistically or clinically significant (Torgerson, 2001).

'Without this level of education and support there is wide variability on the interpretation of this criterion with tendency for prognostication rather than consideration of risk. However, providing this level of education and support would result in contamination in the control sites.' (Protocol, case three)

The inclusion criteria that required medical staff to predict that the patient was at risk of dying was removed from the control arm during the trial for pragmatic reasons, as one of the aims of the trial was to assess the feasibility of recruitment. Recruitment improved in one control site while the other control site was unable to continue in the study for practical reasons. In case one, to try and avoid contamination, patients were excluded from the study if they were sharing a room with someone already in the trial, as this could influence the results of the study:

'If there was someone else in the room that was part of the study, we can't put someone else into the study because you know they might compare (name of intervention) or talk about them or see each others and it would, it could possibly influence the study.' (Research nurse one, case one)

In case two, the Chief Investigator described how they had designed the study to ensure the eligibility criteria were *'as inclusive as possible'* which one of the nurses felt made identifying patients for the trial *'quite easy'* (Specialist nurse two, case two). Why clinicians find identifying eligible participants challenging in a palliative care trial is not fully explained by the 'Social Marketing Mix Framework' and is discussed further in the following chapter.

5.5 Product: The product's competition

The amount of competition for the participant's time and energy is an important factor to consider when applying the 'Social Marketing Mix Framework' (Nichols et al., 2004). There were two main categories that were relevant to the classification of 'Product: the product's competition' and they relate to the issue of 'competing treatment trials' and 'competing treatments'. In case two, competition from treatment trials was a notable barrier to recruitment. Organisations that were specialist centres could have multiple trials available with similar eligibility criteria. Recruiting staff prioritised discussing and recruiting patients to treatment trials over the trial in case two. They would also consider prioritising the trial that was struggling to meet the agreed recruitment target or was going to close to recruitment first. This was because clinical recruitment centres receive funding to meet individual trial recruitment targets as discussed above:

'...so whenever we sign up to a trial we are asked to say how many patients we should be able to get into that trial in over a certain period of time, and so we have and we get sort of paid as a Trust and a research department for meeting those targets that we set. And so we sort of are constantly aware I guess that we have a certain number of patients to get into each trial, so I don't think as a team that is at all at the forefront of any decisions that are made but potentially for trials that aren't recruiting so well, and if someone was eligible for a few different trials that were not for the same thing, and equally could benefit that patient then I personally think sometimes we might lean towards the one that was maybe not recruiting so well you know to help with numbers.' (Research nurse five, case two)

In case two, competition from chemotherapy treatment was also an issue because of the study population. One of the exclusion criteria outlined in the protocol was having started chemotherapy treatment prior to consent. This could *'make it tricky'* (Research nurse five, case two) for research nurses to recruit the patient before treatment was commenced. Patients were sometimes keen to start treatment and did not want to consider taking part in a palliative care trial at that time:

'...some would say there's just so much going on now I can't even think about this and I just want to get onto treatment and so declined...' (Specialist nurse one, case two)

Competing treatments were also an issue in case one as the protocol outlined how patients were ineligible for the trial if they or a close relative had used the intervention before. This was felt to exclude *'quite a few people'* (Research nurse one, case one) because the intervention was routinely available.

5.6 Product: Defining the product

Within the 'Social Marketing Mix Framework', the product is the intervention (Nichols et al., 2004). The categories that were applicable to the classification of 'Product: Defining the product' were; 'level of patient and carer interest in the trial' and 'maintaining clinical equipoise'. Across the three cases, recruiting staff described why they thought patients and carers were or were not interested in the 'product'. In case one, the Chief Investigator felt patients were interested in the trial because it was not a drug trial and described how some patients liked to avoid drugs. They had carried out a pilot study prior to the main trial to assess its acceptability to patients. Patients were permitted to continue on their symptom control drugs, access extra medication if needed and access the intervention after the trial if they had found it helpful:

'You can continue normal medication and if you need extra (name of symptom) medication you can have it.' (Patient information sheet, case one)

In case two, recruiting staff reported variable levels of interest among patients and carers. Research nurses spoke about patients being interested in the trial as it included both patients and carers and ensured regular research nurse support, even in the control arm. The Chief Investigator commented on how nearly every carer agreed to participate in the trial along with the patient participant. This high carer response rate is supported by the recruitment data published in the trial's findings paper. Research nurses described how some patients and carers were not interested in the trial as they felt they did not need what the intervention was offering them or because it was not a treatment trial. Some patients

did not want to commit to the extra hospital visits that were required while others were not interested in taking part in any trials:

'Some patients they will say to you, do you know what, no offence but I don't want to be coming into hospital regularly, I just want to go and live my life and I'm feeling good at the moment and no thank you, I don't want to participate and that's absolutely fine, whereas others do want that extra support I guess and knowing that they have the research team available to them helps I think.' (Research nurse one, case two)

Recruiting staff reported that patients were not always in clinical equipoise and could have preconceived ideas about which arm of the trial they wanted to be allocated to. This could influence their level of interest in the trial. Recruiting staff also struggled with equipoise and managing patient expectations but the 'Social Marketing Mix Framework' does not explain this, as 'Product' does not apply to clinicians.

5.7 Price: 'Type of costs' and Price: 'Minimising the costs'

The concept of 'Price' is the cost to the potential participant of taking part in the trial and applies to the patient or carer (Nichols et al., 2004). Across all three cases, there were a number of categories that were related to the classifications of 'Price: Type of Costs' and 'Price: 'Minimising the costs''. As the cases were palliative care trials, the type of costs were related to the 'patient's condition' and the associated 'costs for carers'. The importance of 'minimising patient burden' and understanding the 'participant's motivations for taking part in the research' was also recognised.

In cases one and three, recruiting staff felt that the patient's unstable and fluctuating physical condition was a 'cost' for patients and influenced their ability to engage in the recruitment process. Patients were often fatigued and had variable levels of symptom burden which could be influenced by their diagnosis. Research nurses would read and go through the participation information sheets and consent forms with patients to try and minimise recruitment costs and burden:

'...I had a couple of oncology patients on our ward with lung CA [cancer], and you know they were very different, they were very different compared to most COPD [Chronic Obstructive Pulmonary Disease] secondary respiratory failure patients that I was seeing. You know they did, I mean she died unexpectedly but again I had to go and see her a couple of times because she was on cpap [continuous positive airway pressure] as well to try and go through the information leaflet, but you know she was up, she was walking around, she was able to hold a conversation, compared to my normal respiratory patients which can't actually do that because they are so short of breath. You know she came in because she had side effects from a second round of chemo. She came up to us because she had lung CA [cancer]. So a very different patient, very different level of sickness.' (Research nurse one, case three)

Recruiting staff felt that minimising study burden for patients was important to increase trial acceptability. In all three cases, patient and public involvement representatives had been involved in the development of the participant information sheets. Across the three cases, the lengths of the patient information sheets varied from 997 to 2545 words. They were all presented in A4 documents with a font size ranging from 11 to 16. Readability statistics indicated Flesch-Kincaid Grade Level scores and Flesch Reading Ease scores ranging from

7.7/68.4 to 9.8/59.7 respectively. Higher Flesch-Kincaid Grade Level scores and lower Flesch Reading Ease scores indicate poorer readability. The recommended reading level for participation information sheets is Flesch-Kincaid Grade Level 6, which equates to a reading age of 11–12 years (Ennis & Wykes, 2016), so the information sheets across the three cases were written at a level higher than the recommended reading age.

In case three, research nurses were concerned about the length of the participant information sheets and consent forms. One of the research nurses suggested the use of implied consent as a potential strategy to reduce patient and carer burden as the study only involved collecting questionnaire data and information from the patient's medical records. Implied consent refers to a situation where an informed participant signals by their behaviour that they agree to take part in the study. In this study, patients were able to provide explicit consent either in writing or verbally (if witnessed) (British Medical Association, 2018). Concerns about the costs of the consent process were fed back to the study coordinating centre by the research nurses and the Chief Investigator acknowledged that given the low risk nature of the intervention a simpler consent process may have been more suitable in this trial.

The patient's unstable and fluctuating condition could also influence the carer's role in the trial and therefore the costs of participating for the carer. If the patient lacked capacity, the carer would be approached to see if they were willing to act as a personal consultee and provide proxy assent on the patient's behalf. A personal consultee is a person who is involved in caring for the participant who lacks capacity, not professionally or for payment. Their role is to advise the researcher on what the participant's wishes and feelings would be if they were able to consent for themselves, and on whether they should take part in the

study (Department for Constitutional Affairs, 2007). Research nurses and study coordinating centre staff reported that the costs of taking on the role of consultee could be too burdensome for some carers. Carers could be too busy to engage in the recruitment process because of competing demands on their time:

'...a relative would be like we're quite busy with some other paperwork and we don't know what's going on, we need to get some you know equipment in place before discharge, so it's most of the time they people do not have a problem about the topic of research, but it's mostly about not having time or not having the energy to complete the questionnaires or even go through the consent process really.'

(Researcher, case three)

All recruiting staff in case three felt the costs of data collection for patients was also an issue. Research nurses helped patients to complete questionnaires to try and minimise study burden. One of the Principal Investigators felt questionnaire burden *'did put some people off'* (Doctor, case three) and was a reason for patients declining to take part in the study. Research nurses reflected on whether less burdensome approaches to data collection may have been more suitable in this study population:

'...I mean some of these people died like three or four days later or you're asking them to read this or go through this document with you and I'm not saying treat people like idiots even though they're dying, I'm not saying that at all, but what I'm saying is you know maybe they want to spend the time in other ways with the family instead of going through these documents, I don't know, maybe like you're doing with me, maybe a chat at the bedside, a recorded interview, would that have been better?' (Research nurse three, case three)

In case one, a pilot study led the study coordinating centre to reduce the number of times patients were asked about their symptoms in the trial to minimise the costs of taking part. Recruiting staff felt the study was attractive to patients because it was a short study that only required a small amount of their time:

'...it's about a 10-minute questionnaire that tries to lighten the burden of participating in studies, because, again, with palliative patients, it, fatigue is a major issue. So, it's quite a good study to recruit to, just because it is a small amount of time that you are taking.' (Research nurse two, case one)

In all three cases, recruiting staff also felt that costs related to the patient's psychological and emotional well-being impacted on their ability to engage in the recruitment process. Patients were perceived as not always being *'in the right frame of mind'* (Chief Investigator, case one) to consider taking part in research. This could be due to a number of factors such as just being diagnosed with a terminal illness, living with uncertainty or requiring hospice care. The eligibility criteria outlined in case two's protocol allowed patients to be recruited up to six weeks after diagnosis so acknowledging the costs of approaching patients around the time of diagnosis of advanced disease. Given the sensitive timing, recruiting staff wanted to minimise study burden for patients by introducing them to the study at an *'appropriate'* (Research nurse five, case two) time.

Across the three cases, recruiting staff discussed why they felt some patients and carers agreed to participate in the trials despite facing many challenges and costs. Understandably, the chance they may actually get some benefit from taking part in the trial was a reason given by some patients. Some patients felt that it gave them a purpose as they had something to do while they were sitting in an inpatient unit. Recruiting staff felt patients

and carers took part for altruistic reasons as they believed their participation could help others in the future despite facing many personal costs. Altruism was discussed as part of the informed consent procedure by the research nurses and is included in all of the three cases participant information sheets:

'...because it was something that didn't necessarily make any difference to their relative's care, that's quite difficult to mention to someone, but then some of them were really good because as soon as you said oh it'll improve care eventually then some of them (carers) got on board with that.' (Research Nurse two, case three)

Across the three cases, there were costs for clinicians associated with recruiting patients and carers to palliative care trials that the 'Social Marketing Mix Framework' does not explain, as 'Price' applies to the patient and carer.

5.8 Place

The concept of place relates to the location where the participant will receive information about, or engage in, the intervention (Nichols et al., 2004). Across the three cases, there were a number of categories that were relevant to the classification of 'Place'. These were 'travel to the clinical recruitment centre', 'pool of participants' and 'understanding the patient's care pathway'. In case two, nurses felt that some patients were discouraged from taking part in the trial because they needed to travel to the clinical recruitment centre. The patient and carer information sheets explained how travel costs would be covered by the study. Some patients were still reluctant to take part because of the distance they needed to travel and the difficulties of parking in the hospital:

'...just thinking about having to come and park and do extra follow up appointments is a massive thing in our hospital, that's a huge thing that patients say when they talk about trials, how am I going to come in and park? How am I going to get in there?'
(Research nurse three, case two)

The 'Place' where recruitment was taking place influenced the pool of potentially eligible participants. In case one, the pace of recruitment was described as slow because they were largely recruiting from a single centre organisation. The study coordinating centre needed to recruit extra recruitment centres in case two to increase the pool of potentially eligible participants. The need to recruit extra clinical recruitment centres to meet the trial's recruitment target had been anticipated by the study coordinating centre in the protocol:

'It is anticipated that expansion to further centres will be required to achieve adequate recruitment rates and target accrual.' (Protocol, case two)

Eligibility rates could fluctuate within individual clinical recruitment centres with some months being busier than others. The importance of understanding the patient's care pathway when estimating clinical recruitment centres eligibility rates was highlighted in cases two and three. Study coordinating centres needed to understand at what points on the care pathway patients may be receptive to receiving information about the trial. The Chief Investigator in case two explained how specialist hospitals as organisations may have high numbers of eligible patients but this may not always be the most appropriate 'place' to approach the patient about a palliative care trial:

'so even though they said we see lots of (name of diagnosis), actually they only saw them for the diagnostic bit, when it came to the care, he was transferred to another

local hospital....So what we did was open a centre where they were sending the patients out to, so recognising the patient pathway....' (Chief investigator, case two)

In case two, the pool of potentially eligible participants was also reduced in one of the specialist hospitals because the trial intervention did not cover all of the hospital's catchment area. Patients could also have been recruited to a trial before being seen in a specialist hospital. In case three, non-specialist hospital sites were the 'places' where recruitment took place and they needed to be kept open for longer than anticipated because the number of eligible patients was less than predicted:

'...and then we had a problem that you know when we first spoke to the site they as always oh we've got lots of people who meet eligibility, you know we can recruit within two months, so we scheduled recruitment to be over three months and it took longer than that. So that was then also required renegotiation with the sites that they would keep recruitment open...' (Chief Investigator two, case three)

5.9 Working with partners: barriers to partnering

There were three categories related to the classification of 'Working with partners: barriers to partnering'; 'health care professional gatekeeping', 'lack of clinician engagement in research' and 'resource issues'. In all three cases, both medical and nursing staff acted as gatekeepers. Research nurses accepted the opinion of other clinicians that it was not appropriate to approach certain eligible patients about the trial. In case one, the research nurses sometimes decided not to accept their opinion and would bypass certain members of staff and approach the patient. Their decision was based on how much they trusted the

opinion of the individual staff member that it was not appropriate to approach the patient. The research nurses would sometimes seek a second opinion from the lead medical clinician who was also the Chief Investigator for the trial:

'...quite senior medical staff some that just think we shouldn't be doing research, that it's not ethical that patients don't want to be bothered, they have too much going on and you know I'm always happy to hear their opinions but I often get a second opinion with other because there are certain members of staff that I know don't want to and I have tried, you know I have really tried to engage and I have done little sessions on research and why we do it and you know the importance of progress and so on. Umm but yes that's I say that's quite high up on what I find most challenging about my job really.' (Research nurse one, case one)

Lack of clinician engagement in the trial made addressing health care professional gatekeeping challenging. This was particularly an issue for the research nurses who were recruiting in the inpatient setting. Clinician rotation and turnover in the inpatient setting made medical staff engagement particularly challenging for the research nurses:

'...a phenomenally high turnover of medical doctors if they're on rotation, so it would mean the research nurses would talk about the study, it would all be fine, and then those individuals would rotate onto another ward, and then they'd have to begin again in explaining the study, so that made it very difficult to get the medical team's involvement and support for the study.' (Chief Investigator two, case three)

Clinicians were often too busy to engage in the recruitment process and some had a limited knowledge of research, including randomised controlled trials, and did not see research as part of their role or part of routine care. In case three, the research nurses in the control

arm were limited in how much education they could provide to clinicians about the trial because of the risk of contamination. Identifying and utilising the support of staff who were the most engaged in research was viewed as a useful strategy for managing health care professional gatekeeping:

'I think that you learn to fight your battles. I think that you know who you can approach, and who is less open to research, within staff.' (Research nurse two, case one)

The contextual reasons for why health care professionals acted as gatekeepers across the three cases and why there was a lack of clinician engagement in research was not fully explained by the 'Social Marketing Mix Framework.'

Across all of the three cases, resource issues acted as a barrier to partnering. The time that Principal Investigators could spend working on the trial was influenced by the demands of their clinical workload and could be exacerbated by staff shortages or only working part time. In case two, staffing shortages and heavy workloads among those providing the intervention could also be detrimental to recruitment. Clinicians who were providing the intervention sometimes requested that recruitment to the trial be limited so they could cope with the additional demand that the trial was creating. Across the three cases, eligible patients were missed because the research nurses were unavailable. Research nurses were allocated to work on a number of studies by their organisations and these could also be resource intensive studies:

'I did miss some of the visits,..I completely missed a couple of patients...., I had another study at the time and I had about 25 patients in that and that study was so.... intense, it nearly broke me to be honest...' (Research nurse four, case two)

In one of the clinical recruitment centres in case three, the research nurses worked as a generic research team to try and manage this issue. A nurse would act as the lead for the study while other research nurses would assist when necessary. This would ensure trial recruitment could continue if the lead nurse was unavailable. This approach was not possible in case one as the research nurse worked part time and often on her own:

'...she (research nurse) is not here all the time, I'm not here all time so you do miss the odd patient...' (Chief Investigator, case one)

Working within a voluntary hospice organisation was seen to make recruitment more challenging because of the limited research infrastructure. In contrast to the other cases, research nurse time was directly funded by money generated from commercial studies. A volunteer was also used to provide administrative support to the research nurse. The ability to network with, engage and recruit other hospices to take part in research was also limited by the lack of funding.

5.9 Promoting the study

Promoting the study involves identifying the acceptable avenues that reach the target trial population (Nichols et al., 2004). Across the three cases, there were a number of categories that were relevant when promoting the study to participants. These were; 'increase trial visibility', 'flexibility and respectful persistence', 'building trust and rapport' and 'key and careful messaging'. In case two, the Chief Investigator described the strategies they used to increase the visibility of the trial among clinicians and potential participants. The study had a trial website with a patient and health care professional section to ensure they had visibility

on the internet. They were less successful with the use of social media as the trial was recruiting an older population *'that is not very internet savvy'* (Chief Investigator, case two). The study had its own acronym and merchandise to help promote the trial brand. The study coordinating centre worked with national organisations to publicise the trial which the Chief Investigator felt increased awareness among patients and carers as well as potential clinical recruitment centres.

The value of organisations promoting research as part of its *'core business'* (Chief Investigator, case one) and seeing it as a way of improving care was highlighted in both cases one and two. Being asked to consider taking part in research could be viewed as unusual by patients which organisational buy in could help address:

'...there's quite a lot done here that promotes research at the Trust and a few patients have commented on oh yeah I saw that about you know the research that was done here, and I think that kind of helps us when approaching patients, is that they're already aware that there's a good chance they might be approached about research and that sort of helps that they kind of know there's a good chance everyone is being asked about something and it's sort of a bit more normal rather than them feeling like they're being asked to be a guinea-pig or anything like that...'
(Research nurse five, case two)

In all three cases, it was important for recruiting staff to be flexible and demonstrate respectful persistence when promoting the trial to patients and carers. Research nurses often had to take account of the patient's physical condition, clinical care, family visiting times and their psychological and emotional well-being when promoting the trial. All of these factors required a flexible but respectfully persistent approach:

'And, you're very flexible, because, again, with palliative patients, you may plan to go and see somebody at a certain time, and they're ill, or they're on the toilet, or their family's come, so you really do need that, sort of, flexibility'. (Research nurse two, case one)

When promoting the trial, recruiting staffs' roles and responsibilities were determined by professional role. In cases one and three, the initial approach was usually made by the doctor in charge of the patient's care. In case two, the specialist nurse took on this role, with or without the doctor. They would seek permission from the patient for the research nurses to approach them about the study. Research nurses would not go and speak to the patient about the trial before seeking medical permission:

'...I would never go and umm I would never go and see that patient, what I would do is then I would then flag the potential patient up to the medical staff and then what would normally happen is they would say you know we're doing a study, it's looking at (name of intervention) would you be happy to speak to our RN'. (Research nurse one, case one)

The research nurses would discuss the study with the patient and if they were interested, give them a copy of the participant information sheet. They would arrange face-to-face follow up to answer any further questions and obtain written consent if the patient confirmed that they wished to take part in the trial. In case two, the nurses would sometimes telephone the patient prior to the consent visit to confirm they were interested in taking part in the trial:

'...I thank them for speaking with me initially and then I'll say you know that I know you've got a lot to take in today, so I don't want to bamboozle you with so much

information, and invite them to take the information home and we'll agree a time and a date for me to ring back. And that is certainly no less than 24 hours but it's generally 24 to 48 hours. I also say to the patients as well you know if you've got any questions about anything at all you know do use me as I say as a resource. And then I will call them at that set time and date that was agreed and I'll say what are your thoughts, do you have any questions, and once they've confirmed that they would like to take part, then we will make another appointment for them to physically come in and see me.' (Research nurse two, case two)

Across the three cases, nurses felt building trust and rapport with potential participants was important when promoting the trial. Engaging carers in the recruitment process was seen as a useful way of building trust and rapport. Carers had the option of taking part in the trial in case two and also in case three if the patient lacked capacity. In case one, they were not potential participants but the research nurses still felt it was important to engage with carers because of the patient's vulnerability. In all three cases, joint patient-carer discussions or advising patients to discuss taking part with their families were suggested strategies to engage carers. In cases one and three, it was suggested it was important to speak to carers out of courtesy or politeness with one nurse reflecting on how if her parents had been approached about a trial, she would like to see information about the study. Identifying the key people to engage with was seen as important. Research nurses believed carer engagement was a way of reassuring patients and carers that it was voluntary to take part in the trial and no coercion had taken place. Unsurprisingly, having had previous clinical contact with patients and carers was seen to make engaging carers and building trust and rapport more straightforward:

'Well I think the patients that I recruited I already knew, and so it was easy for me to go to them 'cos I'd been involved in some prostate studies and the patients that I recruited were those patients that had become end of life, so my approach was very much you know we already had a relationship.' (Research nurse three, case three)

In all three cases, there was a need for recruiting staff to pay attention to key and careful messaging when introducing and explaining the trial to participants. Recruiting staff supported their verbal explanation of the study with a participant information sheet. Research nurses sometimes used additional written prompts to remind them of what needed to be covered in their discussions with patients.

The need to use key and careful messaging when explaining randomisation as part of the informed consent process was a requirement in cases one and two but not in case three as it was a cluster trial. As discussed previously, in a cluster trial, randomisation occurs at the cluster level rather than the individual level so the informed consent process is tailored to the study arm to which the cluster has been allocated (McRae et al., 2011). Nurses felt randomisation was a difficult concept for patients to understand in all trials and not just those in palliative care. They felt there was a need to *'spend quite a lot of time'* (Research nurse one, case one) explaining it to patients. Some nurses used percentages to explain randomisation, some used tossing of a coin as an example, while some explained it was decided by a computer. Recruiting staff also explained that they had no control over the intervention allocation when discussing randomisation with patients:

'It's quite a hard concept for some people to get their head round I think, and so we try and do it as simply as possible, you know we kind of say we have no control over we'd obviously explain that the study has two arms and one of them is the standard

care for the (name of study) trial and the other would involve the (name of intervention)..... And for this trial you obviously need to have something that's always the same to compare it against what you're changing, so that they can find out whether it is better or not better or the same, to see if practice they can suggest that practice should change and we have no control over saying whether or not you'll receive the standard care or whether or not you would receive the extra (name of intervention).' (Research nurse one, case two)

There was a need to keep checking understanding as patients could often struggle to retain the information that had been given to them about randomisation.

In cases two and three, there was a requirement for recruiting staff to discuss palliative and end-of-life care with patients and carers as part of the informed consent process. This was because of the type of intervention being tested, the wording contained within the participant information and the organisational setting where recruitment was taking place.

In case two, recruiting staff explained how patients could often associate palliative care with end-of-life care when they were promoting the trial. The patient information sheet attempts to address this viewpoint by explaining it can be provided '*at any time during the illness*'.

The decision was made by the study coordinating centre to remove the words palliative care from the study title and shift the focus to symptom control as '*we thought that was a better sell, to try and get older patients in*' (Chief Investigator, case two).

Recruiting staff would explain palliative care in terms of symptom control and extra support to demystify the terms and to increase patient and carer acceptance of the trial. They would also sometimes stress that the trial would not interfere with any of their current treatments:

'Well we did say that it was after we discussed other clinical studies I must admit, but we would say that we have also got a trial which is up and running now which you are able to think about and enter into if you like, and this was looking at your quality of life and how we could help you with any symptoms as soon as possible, to try and keep you as well as possible for as long as possible, and that you know if there were any symptoms that hopefully we could pick them up and deal with them as soon as we possibly could and for the carer that they would get the support as well.'

(Specialist nurse one, case two)

Recruiting staff could find promoting a palliative trial to patients and carers challenging and the reasons why are not fully illuminated by the 'Social Marketing Mix Framework'.

5.10 Working with partners: partner education

The categories that are relevant to the classification of 'working with partners: partner education' are 'engaging recruiting staff', 'engaging clinicians' and 'preparation for sensitive conversations'. The research nurse's previous clinical experience influenced how much preparation and training they needed to work on a palliative care trial. All of the research nurses were experienced research nurses but they came from a variety of nursing backgrounds. In all three cases, there were research nurses that had gained their experience of caring for palliative care patients while working in oncology and/or on oncology trials:

'I probably worked with all sorts of different patients with cancer since I qualified and I've been in respiratory for a long time but I also went and did quite a lot of haematology and oncology for a few years, and worked with quite a lot younger

people who were also palliative and things so I think it's never easy, but I think maybe a bit of experience as well over the years definitely helps.' (Research nurse five, case two)

Study coordinating centres felt that it was important to ensure regular contact was maintained with recruiting staff in the clinical recruitment centres to promote trial engagement and partnering:

'One good thing we've learnt is a centre will soon have a short term memory and loose interest in the trial if you're not constantly for want of a better terms in their face.' (Chief Investigator, case two)

In case two, they promptly closed down a couple of clinical recruitment centres during the trial because they did not recruit any participants. They used videoconferencing for the site initiation process so they could open clinical recruitment centres around the UK with minimal cost. Study coordinating centres used various partner education strategies during the trial to facilitate trial engagement with recruiting staff which included; a weekly study newsletter (case two), site visits (case three), regular teleconferences (case two and three) and incentives for clinicians (iPad and per patient recruitment tariffs).

Research nurses felt it was crucial to personally engage with clinicians in the clinical recruitment centres and to maintain their engagement throughout the trial. Personal contact was seen as important to facilitate the recruitment process and to attempt to address gatekeeping. Research nurses used a variety of formal and informal partner education strategies to engage with clinicians. The strategies used included; research presentations (case one), attendance at staff meetings (case one), email communication

(cases one and two), attendance at multi-disciplinary team meetings (all three cases) and one to one contact with clinicians (all three cases).

Across the three cases, having a 'research champion' within the clinical recruitment centre was seen as important to promote the trial and to engage with other clinicians. This role was largely carried out by the lead medical clinician in the clinical recruitment centres:

'The PI for (name of case) is also a senior physician within that MDT as well, and he's very very proactive...it does depend on you know the proactivity of the people involved.' (Research nurse two, case two)

In case three, the 'research champion' role was not always carried out by the lead medical clinician. Specialist palliative care professionals who had a consulting role within the clinical recruitment centre also took on the role. As discussed in chapter one, specialist palliative care doctors and nurses work in the hospital and community setting and their role is to provide advice and support to the patient's usual care team (Bausewein & Higginson, 2012). Both study coordinating centre staff and recruiting staff felt this had a detrimental impact on trial recruitment, as the 'research champion' was often unavailable to engage with other clinicians and undertake partner education:

'...we had two sites where the PIs were absolutely on board with it, this is important, we're committed to doing this, we're going to do it, and they were both sort of positioned within a functioning clinical team, so that was one control and one intervention. And they were basically able to sort of lead their team, we're doing this study, this is important, and then got everybody on board and committed and worked with the research nurses...' (Chief Investigator two, case three)

Across the three cases, there were a number of contextual issues that influenced the process of partner education that are not explained by the 'Social Marketing Mix Framework'. These included why the professional role of the 'research champion' was important and why research nurses adopted certain strategies to prepare themselves to have sensitive conversations with patients and carers.

5.11 Conclusion

The 'abbreviated vignettes' at the beginning of this chapter and the within case analysis in appendix 14 highlighted the differences between the three cases in their clinical setting and study design. Despite the three cases having different characteristics, similar issues were identified in all of the trials in the cross-case analysis. As discussed in chapter four, theoretical replication was used in this study because if findings from divergent cases corroborate each other, they are seen as more robust. The '6 Ps' of the 'Social Marketing Mix Framework' provided a useful and practical guide to inform data collection and analysis in this study, both within case and across the three cases. They highlighted important issues that need consideration when planning and implementing a recruitment strategy in the context of a palliative care trial. It was however, as commented on in the previous chapter, challenging not to avoid force fitting the study findings into this theoretical framework. This required many discussions with my supervisors and hours of reflection to address this limitation of using an a priori theoretical framework. The findings indicated that there were underlying contextual reasons for the clinician's recruitment behaviours that could not be fully explained by the framework. In the next chapter, study findings are discussed and

presented within three overarching but linked classifications; 'emotional labour', 'paternalism' and 'professional hierarchies and power relationships between clinicians'. These additional classifications provide a more in-depth understanding of the '6 Ps' within the context of palliative care trial recruitment.

Chapter six: Cross-case analysis findings in relation to ‘emotional labour’, ‘paternalism’ and ‘professional hierarchies and power relationships between clinicians’.

6.1 Introduction

In the previous chapter, the ‘6 Ps’ of the ‘Social Marketing Mix Framework’ were used to present findings from the cross-case analysis. The cross-case analysis suggested that the ‘6 Ps’ only partially explained health care professional’s recruitment behaviours and wider contextual issues needed to be incorporated into the framework. In this second findings chapter, three overarching but linked classifications, derived interpretatively from the data, are used to explain the cross-case analysis findings. They highlight important issues that need consideration when planning and implementing a recruitment strategy in the context of a palliative care trial.

Firstly, the impact of the ‘emotional labour’ of recruiting patients and carers to palliative care trials on clinician’s recruitment practices is described. The categories explored within this classification are; ‘costs for research nurses’, ‘choosing the best time to approach patients’, ‘explaining palliative care’, ‘preparation for sensitive conversations’ and ‘managing patient expectations’. Secondly, how ‘paternalism’ influences the recruitment process is discussed and the categories explored are; ‘health care professional gatekeeping’ and ‘carer gatekeeping’. Finally, how ‘professional hierarchies and power relationships between clinicians’ can effect recruitment processes is then outlined and the categories,

'recruiting clinical recruitment centres', 'confirming eligibility' and 'research champion' are discussed within this classification.

6.2 The 'emotional labour' of recruiting patients and carers to palliative care randomised controlled trials.

The term 'emotional labour' was first introduced by Hochschild (Hochschild, 2012) and involves the management and regulation of feelings in the workplace. It is broadly defined as *'the induction or suppression of feeling in order to sustain an outward appearance that produces in others a sense of being cared for in a convivial safe place'* (Smith, 2012) (p. 11). Recruiting staff in all three cases had to manage the 'emotional labour' of approaching patients and carers at a difficult time in the patient's illness trajectory. In case one, this was during hospice admission, in case two, at the time of diagnosis of advanced disease and in case three, when the patient was at risk of dying. The need for recruiting staff to respond rapidly to recruit eligible patients and carers during what appeared to be a short window of opportunity was evident in all three cases. This time pressure could be due to the risk of patients deteriorating as in cases one and three or commencement of treatment for their underlying disease as in case two:

'I think because these patients have got a lot going on, they're poorly people, they deteriorate before you have a chance to recruit them or something changes which means they no longer fit the eligibility criteria. (Chief Investigator, case one)

6.2.1 Costs for research nurses

The 'Social Marketing Mix Framework' does not acknowledge the 'Price' or 'emotional labour' of recruitment for research nurses and the types of costs they may experience when recruiting to a palliative care trial. Balancing the need to respond rapidly while taking account of the patient's unstable and fluctuating condition was an issue for the research nurses in cases one and three. Recruiting patients to a palliative care trial could be time consuming for the research nurses as multiple visits were often required because of the patient's condition. Recruitment visits could be lengthy because of the level of support patients required to go through the participation sheets and consent forms:

'...you know they've said, you know I can't actually, I've not felt up to reading it or you know I can't read the information, you know so I have sort of read it to them and then gone through it with them so things just take a bit longer and you need oodles of sort of patience and also not giving up really. Cause it would be very easy to sort of say oh no you know, they were sick, that happened, you know I am not going to do that but just to go back but always making sure, are you happy to talk about it, is it a good time for you you know, I am happy to go away and come back tomorrow.'

(Research nurse one, case one)

The 'emotional labour' of recruiting palliative care patients and carers could be exacerbated by wider resource issues such as having to work on other trials at the same time, staff shortages or working part time. Lengthy and complex consent processes proved particularly challenging for the research nurses in case three as they were required to recruit patients who lacked capacity as well as those that were at risk of losing capacity. They were required

to assess capacity using the processes outlined in the Mental Capacity Act (Department for Constitutional Affairs, 2007). The act provides a legal framework, in England and Wales, for acting and making decisions on behalf of those who are 16 and over who lack the mental capacity to make particular decisions for themselves (Department for Constitutional Affairs, 2007). The research nurses were required to seek assent from a personal or nominated consultee if the patient lacked capacity. The definitions of a personal and nominated consultee were contained within the study protocol:

'A personal consultee comprises next of kin, immediate carer or attorney with Lasting Power of Attorney.....The nominated consultee will have a professional relationship with the potential participant, but cannot be connected to study e.g. a geriatrician, social worker.' (protocol, case three)

If the patient had capacity, advance consent procedures needed to be followed. As discussed in chapter one, advance consent involves asking patients if they were to lose capacity in the future whether they would wish to continue in the trial. If so they are asked to nominate a consultee who the researchers can approach to ask their opinion on the patients continued participation in the study (Agar et al., 2013; Department for Constitutional Affairs, 2007). Operationalising this aspect of the protocol proved challenging and problematic for some of the research nurses. Research nurses could lack confidence and skill when assessing capacity and they could also be unclear about who was permitted to act as a consultee. For example, the documented next of kin may not have been the carer who visited the patient in the hospital so the research nurse could be unsure about who was permitted to act as a consultee. Lack of experience and training contributed to this

recruitment barrier with the Chief Investigator reflecting on how they should have prepared the research nurses better to enact this aspect of the protocol:

'So I sort of felt that we should have prepared the research nurses better, they were prepared in terms of site initiation visit and but it sort of came to light then that they had never used an advance consent before, never used a consultee before, and that they were learning. So then we sat and went through all of that, I felt that I could have managed that better in anticipating the need for training on that.' (Chief Investigator two, case three)

Obtaining consultee assent could also be challenging for the research nurses and involved 'emotional labour'. Potential consultees could often be too busy to engage in the recruitment process. Research nurses had to visit the inpatient unit multiple times to speak to carers and some consultees felt they needed to discuss it with other family members before making a decision. Allowing carers the time they needed to make a decision about whether they would be willing to act as consultee with balancing the pressure to recruit patients within a short window of opportunity could lead the research nurses to face a difficult dilemma and experience increased emotional burden:

'...but I can't say to somebody I know you want to discuss it with your brother but your mum's only eligible right now and she could change tomorrow, do you know what I mean, I can't say that to them. I just have to go that's fine, they can discuss it with whoever they want, you know they can take as long as they want, and the trouble is that they were taking such a long time that they were then passing away or coming off (name of intervention) or whatever.' (Research nurse one, case three)

The costs of recruiting to a palliative care trial, such as managing the patient's unstable and fluctuating condition, complex consent procedures and the impact of wider resource issues, contributed to the 'emotional labour' of recruitment for research nurses.

6.2.2 Choosing the best time to approach patients

Across all three cases, recruiting staff described how they made judgements about when to introduce the trial to patients. Their judgements were not only based on their concerns about the patient's physical condition or practical considerations such as visiting times but were also related to their concerns about the patient's psychological and emotional wellbeing. Recruiting staff appeared mindful of the major challenges patients and carers were facing at the time of recruitment. Staff were concerned that patients were 'overwhelmed' (Research nurse one, case two) with information as they were being approached around the time of diagnosis of advanced disease or at the end of their lives. In case two, the Chief Investigator expressed that there was never an ideal time for the clinician to approach a patient about taking part in a palliative care trial because of the patient's situation. He felt there was a need for those involved in the recruitment process to overcome their fears and approach patients about research:

'...at the end of it you can't be too sensitive about it, you've got to approach them it's just finding out which is the least worse time out of all of that.' (Chief Investigator, case two)

Nurses described the strategies they used to support patients during the trial recruitment process. In all three cases, they felt allowing patients some time to process or digest what

was happening to them before introducing the study was important to increase their acceptance of the trial. They also used this approach in trials outside palliative care:

'I think it's an issue with all trials, that you have to pick the right time to pitch it to the patient otherwise they're just going to say a straight no because I think sometimes at the time of diagnosis they get so much information that to try and add another element in, and I manage to get a feel somehow for whether that consultation was the right time or whether it needed to wait a week or two 'til I saw them again to raise it, otherwise I found that they were less effective.' (Specialist nurse two, case two)

This specialist nurse felt comfortable re-introducing the study to patients if she felt she had got the initial timing wrong.

Allowing time for patients to process or digest what was happening to them before introducing the trial also appeared to be beneficial for recruiting staff. Across all three cases, this appeared to be particularly the case for the research nurses:

'People's understanding of hospices, tends to be that it is a place you go to to die. So, when people are referred to the in-patient unit, and they're admitted, there is that, sort of, automatic barrier comes up, so, oh my God, is this it? So, it's, from my perspective, really helpful not to see somebody within the first 48 hours. Because, they need to gain a confidence in what we are doing, as an organisation, that the place is, you know, a good place to be, and they need to, sort of, feel safe and secure.' (Research nurse two, case one)

Choosing when is the best time to approach a patient about a palliative care trial contributed to the 'emotional labour' of recruitment for recruiting staff, particularly the research nurses, because of the patient's challenging situation.

When initially introducing the study to patients, research nurses would vary the amount of information they gave about the trial to manage the 'emotional labour' of 'promoting' a palliative care trial. Research nurses felt it was important to adopt an individualised approach and make a judgement on a case-by-case basis. They adapted the level of information they gave about the trial depending on the patient's response, the patient's level of understanding and their own level of comfort:

'...I think it differs very much from patient to patient in terms of how much information I think you give them as well, depending on how they sort of take in the initial bit of information. Sometimes you have patients who as soon as there's any mention of anything like cancer it's like you see them shut down immediately, so we don't necessarily give them too much information, so we try and kind of make it so it's most appropriate for that patient sat in front of us.' (Research nurse five, case two)

Recruiting staff reported that patients responded to being approached about a palliative care trial in a variety of ways. Some patients were very accepting and viewed it positively while others were less open to the idea of participating in a palliative care study. Recruiting staff discussed how some patients were not ready to acknowledge or talk about the palliative nature of their illness. In case three, a research nurse described how a minority of patients became distressed when the trial was introduced. She felt this was because they

were in denial about the seriousness of their condition and she sought reassurance from the medical staff that the patient had been informed:

'...and then I had a couple of patients who actually got really angry in that leave my room, I don't want to talk to you, I'm going to get better, how dare you start talking about such, you know, that I'm not going to get better, that's negative thoughts, I don't need that, go away, you know sort of real mixed kind of responses, sort of total denial so the patient had been told, so I would then go running to the doctors and go are you sure you discussed it with the patient 'cos they don't seem to either know about it or they're saying that it's not the case, they're getting mixed messages,...'
(Research nurse one, case three)

The 'emotional labour' of introducing the study to patients appeared less demanding for those nurses who had had previous clinical contact with the patients. They may have met the patient previously because of having a dual clinical role and/or previous contact during the diagnosis process or recruited patients to a previous oncology trial. Striking up an instant rapport and knowing what the patient understood about their condition were seen as the advantages of having previous clinical contact with the patient:

'the patients I approach they were known to me and I think the haematology patients were known to the haematology team so I think that was easier knowing your patients and knowing that they already knew and understood that they were on an end of life pathway.' *(Research nurse three, case three)*

As discussed in the previous chapter, nurses believed engaging carers in the recruitment process was important when promoting the trial to help build trust and rapport and increase patient and carer acceptance of the trial. Involving carers in the recruitment

process and stressing the voluntary nature of taking part also appeared to help nurses cope with their anxieties about approaching vulnerable participants:

'...a lot of patients are quite vulnerable so I think engaging with the family and talking to them and explaining what we're doing and why we're doing it that's really helpful...' (Research nurse one, case one)

Varying the amount of information given, involving carers and stressing the voluntary nature of taking part were strategies used by nurses to manage the 'emotional labour' of recruitment to a palliative care trial. Previous clinical contact with the patient also helped minimise the emotional burden of recruitment for nursing staff.

6.2.3 Explaining palliative care

In cases two and three, recruiting staff could find explaining palliative care as part of the recruitment process challenging. One of the medical staff in case two felt it was difficult discussing palliative care without acknowledging its association with end-of-life care.

Research nurses were required to broach issues that they would not routinely have to discuss in their day-to-day practice. The need to work outside their usual role caused some of the research nurses to feel worried and anxious:

'...I actually think I made a mountain out of a molehill 'cos actually I think the patients were quite fine about it, I think it was a lot of it was our worry about how they would feel, because we'd kind of never it was quite new to us. Most of our trials are very much like this is a therapy that might make you feel better, you know we're

going to do this drainage or something, so this was just completely new so but actually I think the patients were quite responsive to it and understood that you know it wasn't that we were saying they were dying, we very much talked about it was all about symptom relief...'(Research nurse three, case two)

In case two, the protocol and carer information sheet required recruiting staff to broach the topic of a bereavement questionnaire with patients and carers at the time of consent. Some research nurses felt very uncomfortable introducing this aspect of the study around the time of diagnosis even though patients had a diagnosis of advanced disease:

'The loss of the person you are caring for is always a difficult time for you as their carer. We would therefore like to see if the (name of intervention) helps the main caregiver cope. With your agreement, this would involve completing a final questionnaire over the telephone 24 weeks after bereavement.' (Carer information sheet, case two)

Research nurses were apprehensive about how participants may react to this part of the study. There were concerns that it may lead to patients and carers asking them further questions about their prognosis or care that they felt they did not have the skills to answer. One of the research nurses stressed the importance of highlighting this sensitive aspect of the trial contained within the participant information sheet to potential participants, to limit the potential for distress:

'...I had that discussion she burst into tears, so it wasn't ideal, and she said to me afterwards she was like I'm really pleased that you highlighted that from the information because I wouldn't have wanted to have been at home and burst into tears having read this, but she said that's really upsetting and she sort of said I can

see why you want to do it and it makes sense.....And then there is one of the other sort of couples, the patient's wife was very much like you know yeah this makes sense that you want to see how I was doing afterwards as well, and actually they were very sort of practical and you know they weren't so you know quite so shocked I don't think by it. So yeah I think it depended where people were in terms of accepting or you know struggling with things.' (Research nurse five, case two)

In case three, the protocol and study information did not require recruiting staff to discuss the bereavement questionnaire with participants in advance as carers were invited to continue in the study post bereavement. This approach did not always appear to reduce research nurse discomfort, as one of nurses spoke about telephoning the carers to check they were happy to receive the questionnaire even though this procedure was not contained within the protocol. Both case two and three's protocols, contained detailed justification for their chosen approach. In case two, the study team had taken advice from two palliative care clinician researchers who had experience of carrying out bereavement research. One of the researchers had used the same recruitment approach in a previous study. In case three, the protocol cited research and guidance that demonstrated the importance of including bereaved carers in research and the acceptability of postal recruitment methods. They had sought advice from clinicians and experts in ethics, end-of-life care and bereavement research:

'A postal approach to recruitment respects participants' privacy and gives them ample freedom to consider taking part in the study. In case they agree, it offers opportunity for participants to revisit consent after completing the questionnaire, by deciding whether or not to return it. Carers will be contacted NO EARLIER than THREE

months following bereavement to minimise any distress and potential harm.'

(Protocol, case three)

The 'emotional labour' of explaining palliative care as part of the recruitment process was not raised as an issue in case one. This may have been due to the type of intervention or the hospice recruitment setting, where the palliative nature of the patient's condition is openly acknowledged.

6.2.4 Preparation for a sensitive conversation

In all three cases, those research nurses who had previous experience of talking to palliative care patients and their carers appeared to find having sensitive conversations less emotionally demanding than those without similar experience. Research nurse discomfort and inexperience manifested itself in nurses declining to work on case three. Clinical recruitment centres had to use a core team of research nurses who felt comfortable working on the study:

'And the nature of the patients, some of our team didn't like approaching them because they weren't used to that type of patient, that was a problem as well.'

(Research nurse two, case three)

Despite previous palliative care experience, concerns around how to broach conversations around death with patients and carers was still raised by some research nurses in cases two and three. The assumption that research nurses, by virtue of their role, would have the

necessary skills to approach and discuss such sensitive issues with palliative care patients and their carers was evident in case three:

'The research nurse who is highly trained to talk about sensitive issues will present to talk with you.' If required, she or he will refer you to a colleague who can help you more.' (Patient information sheet, case three)

In cases two and three, research nurses adopted their own strategies to help prepare for and cope with having sensitive discussions with patients and carers. They discussed how best to approach these types of conversations within their own research nurse team as well as sometimes seeking advice from the palliative care team:

'...most of our patients are palliative, so we do have conversations like that with them, realistically just when we're sat chatting to them it comes up obviously, but again we have had a chat as a team and I chatted to the palliative care team about how it was best for us to talk to patients about it. (Research nurse three, case two)'

Clinical shadowing was used as a strategy in case three for a research nurse who had no previous palliative care experience. Research nurses across the three cases sought wider support from their Principal Investigators and other members of the research team when available. The opportunity for 'more exposure' (Research nurse three, case three) to palliative care studies was seen as a way of increasing confidence when approaching patients. Working within a voluntary organisation as a research nurse, where research resources are limited, could make coping with the emotional burden of working in palliative care research more challenging:

'...working on your own can be quite difficult and I've always been part of a research team so you know in my last job, we had various different disease sites for cancer, so some would cover lung some would cover GI or whatever so you would have your and you would do lots of research based on your disease site but you've always got those colleagues that are working in exactly the same way as you that you can run things by or umm you know I'm very, I'm quite isolated really in my job and at times it can really upsetting and stressful and challenging and I don't always feel that I really have anyone to share that with.' (Research nurse one, case one)

Research nurses adopted a number of strategies to manage the 'emotional labour' of working on a palliative care trial. Previous palliative care experience helped reduce burden but working in the voluntary sector was associated with additional emotional costs.

6.2.5 Managing patient expectations

In cases one and two, nurses explained how they managed patient expectations by maintaining clinical equipoise. The majority of recruiting staff reported how patients can sometimes be disappointed when they are allocated to the control arm in randomised controlled trials and this was especially so in treatment trials or drug symptom control trials. Some recruiting staff felt patient disappointment was less of an issue in cases one and two because of the nature of the intervention, and in case two, patients would still have access to support even in the control arm. Despite the reduced '*emotional risk*' (Chief Investigator, case two), some recruiting staff in case two still felt patients sometimes had preconceived ideas about which arm they wanted to be allocated to:

'...sometimes you get patients saying oh but I want that extra care and it's trying to explain to them we can't guarantee that you will get that, but the only option to receive that is through the trial and it's not something we offer unless you're in need of it clinically and currently.' (Research nurse one, case two)

Nurses spoke about maintaining equipoise by not over promoting the treatment arm and by explaining to patients that it is unknown whether the intervention is better or as good as standard care. They would sometimes stress to patients that the information they were going to provide in the control arm was of equal benefit. This was to cope with the 'emotional labour' of managing patient expectations in a randomised controlled trial:

'... you've just got to tell them, but the information that they're going to give us, as a consequence of this, of doing a standardised arm, is equally of benefit, because it gives us a balance. And, so, again, trying to let them know how much of a difference their participation will make to us, although, it may not make a lot of difference to them, with, in regards to symptom management.' (Research nurse two, case one).

In order to deal with the 'emotional labour' of operationalising random allocation, nurses could have preconceived views about the potential benefits or lack of benefits of the intervention. They appeared not always to believe in equipoise even though they spoke about trying to maintain it to manage patient expectations:

'I think it's to take that line of equipoise..... that you know this isn't black and white really, we didn't know that one arm would be different from the other arm and that's the whole reason for the trial, but letting them see that they wouldn't be disadvantaged because they would still have the contact...' (Specialist nurse one, case two)

Most of the research nurses in case two, spoke about how some patients were interested in the study as it provided regular research nurse support even in the control arm. The idea that patients would get some direct benefit from being involved in the trial appeared important for the research nurses. The nurses seemed to find their support role satisfying and appeared to move beyond their recruitment role to become part of the intervention team:

'...they felt that they had an extra set of eyes on them.....regardless of whether they got the (name of intervention) arm or not, they knew that they had a research nurse who was essentially keeping an eye on them, and I would have, obviously 'cos they have regular visits with me and telephone calls with me, and they also utilise me as a resource as well.' (Research nurse two, case two)

One of the research nurses, however, expressed how carrying out this support role could become more emotionally demanding as the patient's disease progressed and their condition deteriorated. Operationalising randomisation procedures, including managing patient expectations, involves 'emotional labour' for recruiting staff with staff not always believing in clinical equipoise even though they speak about trying to maintain it.

6.2.6 Summary of emotional labour

In summary, in all three cases recruiting staff had to manage the 'emotional labour' of approaching palliative care patients and carers at difficult time in the patient's illness trajectory with only a short window of opportunity for recruitment. The patient's unstable and fluctuating condition, alongside managing patient expectations and wider resource

issues, contributed to the 'emotional labour' of recruitment particularly for research nurses. They used various strategies to manage the 'emotional labour' of recruitment with previous clinical contact and palliative care experience helping to reduce recruitment burden.

6.3 The influence of 'paternalism' on recruitment to randomised controlled trials in palliative care.

The term paternalism refers to; *'the intentional overriding of one person's preferences or actions by another person, where the person who overrides justifies this action by appeal to the goal of benefitting or of preventing or mitigating harm to the person whose preferences or actions are overridden'* (Beauchamp & Childress, 2013) (p.215). In all three cases, there was evidence that paternalism could override patient autonomy in the trial recruitment process with health care professionals, including recruiting staff, demonstrating paternalistic gatekeeping behaviours. This was despite some of the recruiting staff verbally acknowledging the importance of involving palliative care patients in research. Carers could also demonstrate paternalistic behaviours because of their perception of the 'Price' or 'cost' to the patient of taking part in the trial.

6.3 1 Health care professional gatekeeping

As discussed in the previous chapter, health care professional gatekeeping was a barrier to recruitment in all three cases. Paternalistic gatekeeping practices manifested themselves in a variety of ways. In all three cases, health care professionals acted in a paternalistic way by

applying their own unofficial eligibility criteria during the screening process. In case three, one of the Chief Investigators expressed that the reasons why clinicians included or did not include patients in the trial could be hidden. The paternalistic criteria applied by health care professionals included: staff deciding patients did not want to be bothered or had too much going on to take part in the trial (case one), the patient's suitability for a treatment trial, the perception that the patient was struggling with their diagnosis or even a patient's personality (case two):

'...and when we look into it they might meet all the eligibility criteria, and none of the exclusion criteria but there's another issue that would mean actually recruitment wouldn't be great for this particular patient.....It could be their how can I put it, their personality, could we you know would they be able to comply with the requirements of the study.' (Research nurse two, case two)

In case two, some recruiting staff acted in a paternalistic way by making a conscious decision to withhold information from patients about all the trials they were eligible for. They believed they were acting in the patient's best interest by protecting them from having to read multiple patient information sheets and having to make difficult choices about their current plan of care:

'...we had to edit what we presented to people, if there were three different things, if you present a randomised controlled trial of two different drugs against radiotherapy or no radiotherapy, against (name of case), when they could only do one of them, was just unfair. So we very much, there were a number of people with (name of diagnosis) we did not mention this to.' (Doctor, case two)

Treatment trials were seen as having the potential to *'actually benefit (the patient) clinically'* (Research nurse three, case two) so were prioritised by the health care team. Assumptions were made that patients would not want to consider a palliative care trial when they had been offered chemotherapy or radiotherapy treatment for their underlying disease. This was not always the case as the specialist nurses explained how they discussed the palliative care trial with patients alongside the treatment trials that were available:

'...so I do raise them all and we talk about referral to other centres for second opinions and things like that, so I keep it as open as I can.' (Specialist nurse two, case two)

One of the specialist nurses did acknowledge, however, that treatment trials were discussed first with patients so illustrating the priority given to treatment trials in health care. Across all three cases, health care professional paternalism was evident with a variety of gatekeeping strategies and behaviours used by clinicians during the recruitment process.

6.3.2 Carer gatekeeping

The carer's perception of the 'Price' or 'cost' of the patient participating in the trial also led them to demonstrate paternalistic gatekeeping behaviours. The extent to which research nurses felt carer gatekeeping impacted on recruitment appeared to vary among the three cases. Research nurses spoke about approaching patients and carers together. Carers preventing access to patients did not appear to be an issue in cases one and two but families could sometimes express their concerns about unnecessary burden when the research nurses were providing information about the study. In case three, the patients

unstable condition meant the research nurses sometimes needed to introduce themselves to the carer before or at the same time as speaking to the patient. Families could sometimes be aware of the patient's clinical condition but not the patient themselves. One of the research nurses was fearful of approaching patients with the family present in the room, as she was worried about how they would react, including concerns they may make a complaint. Families could become annoyed and it could be a dilemma for research nurses balancing the right to approach a patient with capacity to discuss taking part in research with managing the carer's distress:

'I literally couldn't even tell them who I was and what I was doing or finish the sentence before they were like now's not the time, how dare you? Well it's just we do have to ask at such a difficult time because of the timing of the research, I appreciate it's difficult but the timing is necessary. But it's not appropriate, they just weren't listening.' (Research nurse one, case three)

Carers, like health care professionals, could also demonstrate paternalistic gatekeeping behaviours during the recruitment process and this was particularly an issue in case three where the patients were at risk of dying.

6.4 The influence of 'professional hierarchies and power relationships between clinicians' on recruitment practices.

Professional hierarchies and power relationships between clinicians influenced recruitment practices in a number of ways. These hierarchies and relationships influenced the

recruitment of clinical recruitment centres, trial participants and the research champion within the clinical recruitment centres.

6.4.1 Recruiting clinical recruitment centres

In case two, the Chief Investigator, a senior doctor, used his professional medical contacts to identify and recruit potential clinical recruitment centres for the trial:

'...then you had centres that were just part of a national network of you know investigators knowing each other and doing each other's trials for them, so that was important.' (Chief Investigator, case two)

In case one, the Chief Investigator was also a senior doctor who was proactive and networked with medical colleagues to promote his organisation as a potential clinical recruitment centre. In contrast in case three, the Chief Investigator, who was an academic, spoke about needing to build up relationships with clinicians. Access needed to be negotiated into potential clinical recruitment centres and this could take a long time:

'...in between hearing about whether my expression of interest had been shortlisted, I started making contacts with the different studies because I knew that bit would take some time, so several months and visiting the different sites and building relationships and trust with them in terms of telling them that this was a really important salient area of health services research and telling them that we were the right crew of people who could do the work on time and safely. So it was really just a question of convincing them and just negotiating with them and building levels of rapport which I think were really really critical. It's not just a question of parachuting

into a site, there's so much ground work that needs to take place beforehand.' (Chief Investigator one, case three)

Chief Investigators who were also senior doctors used their professional medical contacts to identify and recruit clinical recruitment centres. The Chief Investigator from an academic background needed to negotiate access into the clinical recruitment centres by building up relationships with clinicians.

6.4.2 Confirming eligibility

Across the three cases, recruitment roles and responsibilities were determined by professional role. Medical staff who had overall clinical responsibility within the trial as well as overall clinical responsibility outside the trial had the greatest influence over whether patients were or were not recruited to the trial.

All health care professionals involved in the patient's care were permitted to identify potentially eligible participants. In cases one and three, this included staff who were not directly involved in the recruitment process such as inpatient nurses or doctors. In these two cases, research nurses disagreed over how helpful inpatient nurses were at giving them *'the heads up'* (Research nurse three, case three) that a patient may be eligible. The research nurse below felt inpatient nurses were not engaged enough in the trial to identify potential participants:

'...I don't think they really got it, if I'm honest, I mean I think a couple of them did eventually and sort of got to know what we were looking for, but they certainly never really referred patients onto us...' (Research nurse two, case three)

Confirmation of trial eligibility was always the responsibility of the lead medical clinician for the patient as they held overall ownership of the patient's care within the clinical recruitment centres. Medical confirmation that the patient was a palliative or end-of-life care patient was required. Trial recruitment procedures outlined in the study protocols and discussed by study coordinating and recruiting staff, reflected this need to seek permission from the lead medical clinician before approaching an eligible patient about a trial:

'So in several of the sites, the PI was there and was very easy to access and could answer questions about the study and was there as the source of information that the research nurses and other clinicians could call on and would be there to help them in negotiating what patients to include or not to include in relation to whether somebody could go up and introduce the study to them or not.' (Chief Investigator one, case three)

Research nurses used formal multi-disciplinary team meetings within their organisations to identify eligible patients and to seek medical confirmation of eligibility. Multi-disciplinary meetings could be used as a forum for medical staff to decide who the nursing staff could and could not approach about a palliative care trial. This appeared to be the case even for senior nurses whose role was to provide specialist care to patients:

'So if they were somebody that was likely to be fit enough for a chemotherapy trial, then we would get them to see the medical oncologist and the nurse specialist would not talk to them about (name of trial). If they were suitable for the radiotherapy trial,

the same applied with the radiotherapy, if we felt that they were not really suitable for either then we would then get the nurse specialist to discuss with them and then the nurse specialist would then try and see them at the time they got their diagnosis from the (name of speciality) consultant and give them the information at that point.'

(Doctor, case two)

Obtaining medical confirmation of eligibility via the multidisciplinary team meeting appeared to be more problematic in case three for a number of reasons. Some medical staff appeared reticent and fearful of making the decision that the patient may die under their hospital care and how it could be difficult for recruiting staff to *'get past people's inherent optimism'* (Doctor, case three). Dealing with medical staff reticence to admit that the patient may be at risk of dying could be difficult for recruiting staff especially when their own clinical view was the patient was eligible:

'...the patients that we thought were eligible, the medics didn't have the same view for a lot of them.....they don't go on the negative side very much, they're all very positive the medics, so it was a little bit against the grain, to say well this could all happen but so could this, so it was actually quite difficult to get them on board...'

(Research nurse two, case three)

Confirming the patient was eligible for the trial meant the medical staff had to have a difficult conversation with the patient and family about the patient's clinical condition. This could be challenging for medical staff as they may not have met the patient before admission and as a result may have had a limited understanding of what the patient understood about their illness:

'In the intervention sites, the ward staff received you know training, they had a clinical educator who worked with them for several months, so it's been much easier for them and they've got because they had the education they felt much more comfortable speaking with the patients and relatives after a while...' (Researcher, case three)

In order to feel more comfortable about approaching patients, research nurses wanted to make sure the medical staff had spoken to the patient about their unstable condition before they made their approach, once again reflecting the influence of hierarchy and power relationships amongst clinicians:

'...we made a conscious decision that we would not approach any patient without the consultants talking to them first. So that's why we had the agreement that the consultants would well obviously clinically they've got the say on whether the patients were eligible but for them to have the conversations first before the research team went in.' (Research nurse three, case three)

Conversations between medical staff and patients and families could be poorly documented which could make it difficult for research nurses to find out what had been discussed. In all three cases, research nurses checked the medical notes to confirm trial eligibility but obtaining written medical confirmation that a patient was eligible for the trial appeared particularly challenging for the research nurses in case three. They needed to find evidence that discussions had taken place with the patient and/or family regarding the patient's unstable condition. Seeking out confirmation of eligibility could be a time consuming process for research nurses as they often had to *'play detective'* (Research Nurse one, case

three), by finding out information in various ways. In one site, they devised a study criteria proforma to place on the patient's medical notes to try and address this recruitment barrier:

'And then if we thought we found a patient that was eligible, we would put that on the medical notes or give it to the consultant if they were on the ward and get them to just fill it in and just sign the bottom, and then we took that that the patient yes was eligible and we could approach them. And that worked a little bit better, but it improved it but not vastly. But we did try.' (Research nurse two, case three)

Research nurses appeared to need to see written confirmation from medical staff that it was safe for them to approach the patient about a palliative care trial. This was because of the sensitive nature of the information they needed to present and the risk patients and families may not have remembered what had been discussed or be in denial about what they had been told. Similar concerns were raised by a palliative medicine doctor:

'...we couldn't go to people who didn't know, weren't aware obviously that would come as a shock, perhaps they had been told but then forgotten, or that we were concerned that if they read that they you know they might not have realised, you really have to have an in-depth knowledge of how much the patient knew about their risk of dying during the admission, which isn't often, it's not somewhere you can find from the notes, and often something the doctors who are looking after them might not know about how much they've understood particularly. 'Cos ideally with this study you probably want to get people as soon as they arrive on the ward...' (Doctor, case three)

Despite medical staff having to confirm trial eligibility, research nurses also had the power to influence whether or not a potential participant was recruited to the trial. Research

nurses felt they were *'the patient's advocate'* (Research nurse three, case two) and their role was to act in the patient's best interest. They would sometimes disagree with a medical colleague's suggestion that a patient was eligible for a trial. Research nurses would also have the power to decide on when was the most appropriate time for them to introduce the trial to a potential participant:

'...one of the consultants used to come out and go oh you can go in now, I've just literally come out, I've just explained it to them, I've literally just come out the room and I'm like I'm not going to go in now when you've just told somebody that they might be getting better, they might not be getting better, I'm not going to go in there two seconds later. You know I would leave an appropriate amount of time, and also relatives would be crying, they'd be very upset and so I had to leave an adequate amount of time for that. (Research nurse one, case three)

Reflecting the influence of professional hierarchies and power relationships amongst clinicians, medical staff were required to confirm trial eligibility but research nurses ultimately had the power to decide whether or not a patient was recruited to the trial.

6.4.3 Research Champion

As discussed in chapter two, a research champion assists with access to potential participants and helps promote the study among patients and other health care professionals. The requirement for the lead medical clinician to confirm trial eligibility influenced who was the most appropriate professional to act as the 'research champion' for the trial. In case three, study coordinating centre and recruiting staff felt choosing a

Principal Investigator who was a lead clinician rather than a consulting physician or nurse was a more useful strategy. The Principal Investigator only being available in the clinical recruitment centre intermittently and not having overall responsibility for the patient's care meant the nurses still needed to seek medical confirmation of eligibility from the lead clinician. In practice, who took on the role of Principal Investigator was often a practical decision and based on their enthusiasm for the topic of the research:

'...I mean to some extent it was practical and also to some extent based on the enthusiasm of the people I approached,in one hospital, the palliative care physician that I originally approached said I don't think it's a good idea that I am the PI on this study because I would like it to be owned by the general medical consultant who looks after that ward, you know there's not a conflict of interest but if it's owned by that consultant, the intervention should we be a site might work better. You know they will understand the purpose of the intervention and they will be signed up to it and it will have a greater chance of working, whereas it seems that the palliative care team are coming in to make that study work, the enthusiasm for it may, well people might be less signed up and less enthusiastic.' (Chief Investigator one, case three)

In case two, the specialist nurses role in supporting the lead clinician to identify and approach eligible patients about the trial was formalised in the trial protocol. One of the specialist nurses took on the role of Principal Investigator in a successfully recruiting site. Following disclosure of the patient's diagnosis, medical staff would delegate the management of the patient and carer's emotional fallout to the specialist nurses. Specialist nurses would spend time alone with patients and carers away from the medical consulting room. They would provide support and information and they had the power and were

responsible for making the decision about whether and when to introduce the trial to patients:

'...the MDT team makes a decision, the news is broken to the patient, and then ordinarily there's like a small break out room where the patients can you know deal with...their emotions, and then the specialist nurses had a choice basically between either whether the patients were receptive at that stage to learn about the trial...'

(Chief Investigator, case two)

The specialist nurses appeared to accept and value this aspect of their professional role. They felt they were experts in the care of patients in their specialist field and viewed research as an important part of their nursing role. They accepted that medical staff could be busy and had limited time to recruit patients to trials:

'...nurses actually have quite a big role in recruiting into clinical trials, it's very often us that are left to fill in the details of trials, consultations with doctors can be quite difficult and a bit time pressured if you like, and what we certainly find is that often the nurses would take the patient, 'cos we've got more time to sit and talk about things and over all the years I have found that it you become quite involved in recruitment, or at least in giving information to people about the trials and treatments that are available to them, and answering questions to help them decide which is the right way for them to go.' (Specialist nurse two, case two)

One of the specialist nurses, being a Principal Investigator, was keen for the study to be a success. In cases two and three, the research nurses expressed that they valued the support of the specialist nurses during the recruitment process. They valued the time the specialist

nurses spent talking to patients and carers about their illness as it freed them up to focus on the more practical aspects of the recruitment process:

'...so they do a lot of the work..with the (name of diagnosis) patients.., so that takes a lot of the burden off me if that helps, so I'm just there for the nitty gritty, because they're there..to, I'm there to reassure them as well but that's a big part of their role as well.' (Research nurse four, case two)

Across the three cases, permission to approach potential participants about the palliative care trial was granted by the lead medical clinician in the clinical recruitment centres. This is why in case three, the lead medical clinician was best placed to take on the role of Principal Investigator rather than a consulting clinician. In case two, the Principal Investigator role was also carried out successfully by a specialist nurse. This reflects the role specialist nurses have within the medically led multi-disciplinary team. They are responsible for managing the patient and carer's emotional and information needs during and after a diagnosis of advanced disease.

How clinical recruitment centres are recruited, how trial eligibility is confirmed and who should take on the 'research champion' role in a palliative care trial is influenced by the professional hierarchies and power relationships that exist between clinicians. Figure 2 below illustrates the new palliative care trial recruitment framework proposed that reflects the study findings. An adapted 'Social Marketing Mix Framework' that incorporates the wider overarching contextual issues of 'emotional labour', 'professional hierarchies and power relationships between clinicians' and 'paternalism'.



Figure 2: New palliative care trial recruitment framework proposed

6.5 Conclusion

As in the previous chapter, similar issues were identified across the three cases despite the trials having different characteristics. In this chapter, the theory of 'emotional labour' was used to present the study findings along with the concepts of 'paternalism' and 'professional hierarchies and power relationships between clinicians'. These three concepts are interlinked and they provide a useful theoretical lens to help understand recruitment behaviours in the context of a palliative care trial (Collins & Stockton, 2018; Ritchie & Lewis, 2003). The 'emotional labour' of recruiting patients and carers to palliative care trials leads health care professionals to demonstrate paternalistic behaviours during the recruitment process. Professional hierarchies and power relationships between clinicians facilitate and support these paternalistic recruitment practices. They also influence how 'emotional labour' is experienced by different professional groups. The concept of paternalism can also influence how carers respond to the patient taking part in the trial. The overall findings of this study suggest that the '6 Ps' of the 'Social Marketing Mix Framework' provide a useful and practical guide to inform trial recruitment planning and implementation processes but the wider contextual issues of 'emotional labour', 'paternalism' and 'professional hierarchies and power relationships between clinicians' need to be incorporated into the framework. The study findings are now explored and discussed in the context of the wider palliative care and trial literature.

Chapter seven: Discussion

7.1 Introduction

In this chapter, how the study findings contribute to the knowledge base in palliative care are discussed. The revised theoretical propositions that reflect the study findings and the wider literature are then outlined. This is followed by the recommendations for clinical practice, policy and future research and the strengths and limitations of this case study.

7.2 How the study findings contribute to the knowledge base in palliative care.

The cross-case analysis suggests that the 'Social Marketing Mix Framework' concepts of; identifying participants; product (including product definition and competition); price (including type and minimisation); place; promoting the study; working with partners (including barriers to partnering, partner referrals and recruitment and partner education), are relevant in the context of palliative care trial recruitment. The findings also indicate, however, that wider contextual issues also need to be mapped and incorporated into the 'Social Marketing Mix Framework' to make it more relevant for the palliative care setting. In this cross-case analysis, health care professionals experienced 'emotional labour' when they were 'promoting' and recruiting to a palliative care trial which led to paternalistic recruitment practices. The study findings highlight how carers can feel the 'Price' of the patients or their own involvement in a palliative care trial which can also lead to paternalism. The 'professional hierarchies and power relationships' that existed between clinicians influenced how 'emotional labour' was experienced by medical and nursing staff in

this case study. Professional hierarchies and power relationships between clinicians also facilitated and supported paternalistic recruitment practices.

7.2.1 Key study findings discussed in this chapter

An overview of how the theory of 'emotional labour' influences the '6Ps' of the 'Social Marketing Mix Framework' in the context of palliative care trial recruitment is initially presented. The key study findings discussed in depth are; the 'emotional labour' of 'Promoting' a palliative care trial as a 'Product'; how 'emotional labour' and 'professional hierarchies and power relationships between clinicians' influence 'Identifying participants' and 'Working with Partners' (partner referrals and recruitment); how the 'emotional labour' of 'Promoting' a palliative care trial as a 'Product' can lead to paternalism and finally the role of 'Working with Partners (Partner education) to address 'emotional labour' and health care professional paternalism in the context of palliative care trial recruitment.

These key study findings are considered in relation to the existing literature on trial recruitment within palliative care (Ritchie & Lewis, 2003). Aspects of this study that reinforce what is already known about palliative care trial recruitment are discussed, as well as new areas of knowledge that have been identified. The trial recruitment literature outside palliative care is also used to explore the study findings, as the majority of what is currently known about palliative care trial recruitment is largely anecdotal, as highlighted in chapter two. There is a dearth of literature on communication issues in the context of palliative care trial recruitment so research that looks at communication issues in the wider palliative care literature has been consulted.

7.3 An overview of how the theory of ‘emotional labour’ influences the ‘6Ps’ of the ‘Social Marketing Mix Framework’ in the context of palliative care trial recruitment.

The findings of this study, like those of the literature review in chapter two, illustrated the importance of considering and minimising the ‘Price’ of taking part in the trial for patients and carers by ‘minimising the cost’ of consent and data collection processes. This study also found that there is an emotional ‘Price’ for health care professionals when recruiting to a palliative care randomised controlled trial that is not fully explained by the ‘Social Marketing Mix Framework’ or the palliative care trial literature. The theory of ‘emotional labour’ appears to provide a useful explanation for why clinicians adopt certain behaviours during the recruitment process. As discussed in chapter six, the term ‘emotional labour’ was first introduced by Hochschild (2012) but her work has been extended to focus on the work of health care professionals (Huynh et al., 2008; Kerasidou & Horn, 2016), particularly the caring role of nurses (Huynh et al., 2008; James, 1993; Smith, 2012; Theodosius, 2008). The ‘emotional labour’ of caring for dying patients and their families has been viewed as particularly demanding (James, 1993; Smith, 2012) with death and dying in hospital being seen as ‘the ultimate emotional labour’ (Smith, 2012) (p.132).

Palliative care is carried out in an emotion laden context (Ferrer et al., 2016) with clinicians often having to deal with appropriate but powerful emotions from palliative care patients and their carers such as denial, anger, frustration and loss. These contextual factors can also be an issue in trial recruitment, as illustrated in the study findings. In clinical practice, there is an expectation that nurses will manage the emotional fallout from difficult encounters (James, 1993). Nurses are seen to be able to manage and cope with extremes of feeling

(Smith, 2012) with them often being '*portrayed as the keepers and carers of emotional needs*' (Theodosius, 2008) (p.30-31). In many Western Countries, the idea of a technically skilled, rational doctor who remains detached from their own as well as their patient's emotions is favoured (Kerasidou & Horn, 2016) with medical staff learning how they are expected to behave from their peers and their medical training (Baker, 1996). Feeling rules, a key concept within 'emotional labour', refers to the power of social conventions to dictate emotion (Hochschild, 2012). Feeling rules can consciously or unconsciously influence what emotions we should express in a particular situation even if this is different to how we really feel. Feeling rules dictate that nurses are emotionally caring and there is a belief that nurses have more time than doctors to sit and talk with patients and carers to address their psychosocial needs (Chattoo & Atkin, 2009; Hibbert et al., 2003). Nurses are also seen to be able to educate and communicate with families on a more personal, individualised level (Anderson et al., 2019; Hibbert et al., 2003).

Carrying out 'emotional labour' can be a positive experience for nurses as they can experience a sense of personal and professional accomplishment. It can lead to an increased sense of connection between the nurse and the patient and greater job satisfaction (Huynh et al., 2008). These positive aspects of 'emotional labour' were seen in the study findings but some research nurses did not always feel comfortable recruiting patients and carers to a palliative care trial. Trial study coordinating centre staff assumed research nurses would have the necessary skills to carry out the 'emotional labour' of recruiting to a palliative care trial because of their professional role. The literature suggests, as in this case study, that 'emotional labour' is influenced by work experiences and is more likely to be performed by experienced nurses (Brown et al., 2019; Huynh et al., 2008). Carrying out 'emotional labour' can also be more challenging when working in a busy clinical environment (Smith, 2012) and

the importance of having adequate and sufficient organisational and staffing resources to mitigate recruitment burden has been highlighted in the general (Skea et al., 2017) and palliative care trial literature (Serfaty et al., 2019).

The 'emotional labour' of trial recruitment for clinicians is not new with a number of issues being previously cited in the general and palliative care trial literature. These include, as discussed in chapter two, struggling to maintain clinical equipoise (Donovan et al., 2014; Fletcher et al., 2012; Holm et al., 2017) and clinician's applying their own suitability rather than eligibility criteria (Brown et al., 2019; Donovan et al., 2014; Froggatt et al., 2020).

Clinicians can worry about overburdening and overwhelming participants with information at a difficult time (Brown et al., 2019; Valerie et al., 2011). Research nurses can worry about bothering patients and struggle with balancing their recruiting role with their perceived role as patient advocate (Boxall et al., 2016; Donovan et al., 2014; Larkin et al., 2019; Tomlin et al., 2014). Research nurse decisions can reflect their own views and prejudices and are seen to have a detrimental influence on trial recruitment (Tomlin et al., 2014). Research nurses can lack confidence when working on trials outside of their specialty (Valerie et al., 2011). Research nurses have to work around and build relationships with staff gatekeepers and they can feel isolated in their role (Hernon et al., 2020; Spilsbury et al., 2008). They manage 'emotional labour', as in this case study, by accessing support from their research nurse colleagues or by developing relationships with specialist nurses (Spilsbury et al., 2008).

Emotional challenges previously reported in the general trial literature were less burdensome issues for clinicians in this study. These include feeling under pressure to meet recruitment targets (Hernon et al., 2020; Lawton et al., 2015; Valerie et al., 2011) and managing patient disappointment and anger following treatment allocation (Lawton et al.,

2015). The reasons for these differences are discussed in the previous two chapters. In this case study, clinician's experienced an additional type of 'emotional labour' during the recruitment process that was related to 'Promoting' the palliative care trial to patients and carers.

7.4 The 'emotional labour' of 'Promoting' a palliative care trial as a 'Product' to patients and carers.

Promoting a trial by using predefined key and careful messaging is recommended under the 'Social Marketing Mix Framework'. Patients and carers often associate palliative care with death and dying (McIlpatrick et al., 2014; Sarradon-Eck et al., 2019), an issue also reported in this study. In the participant information sheets, there was evidence that consideration had been given by the study coordinating centres to how the concepts of palliative and end-of-life care were to be presented to patients and carers. The 'emotional labour' of introducing and explaining these terms to patients and carers for health care professionals had been given less consideration.

Outside research, clinicians can find having conversations around deterioration and end-of-life care challenging and stressful, so it is unsurprising this was also the case in a trial recruitment context. Doctors can feel ill prepared for end-of-life communication and they can be fearful of destroying a patient's hope (Buiting et al., 2011; Hancock et al., 2007). Concerns about the lack of adequate palliative and end-of-life care training for medical and nursing undergraduates continue to be raised (Martins Pereira et al., 2020; Wells et al., 2020). Clinicians often wait for patients or families to initiate end-of-life conversations

rather than actively broaching the topic themselves (Almack et al., 2012; Flierman et al., 2019), and they can struggle to introduce and explain the concept of palliative care (Sarradon-Eck et al., 2019). Patients assume that health care professionals will initiate end-of-life type conversations (Almack et al., 2012) because they may find it difficult to raise themselves (Momen et al., 2012). These contextual issues are problematic in the recruitment context as an 'active' rather than a 'passive' communication stance is required when introducing a palliative care trial (Pfeil et al., 2015). This is especially so when under pressure to recruit patients and carers within a 'short window of opportunity' and similar issues have been reported in emergency medicine (Brown et al., 2019) and stroke trials (Boxall et al., 2016).

The 'emotional labour' of trying to find out what the patient and carer had been told about their condition before approaching them about the trial could be challenging for recruiting staff. Similar experiences have been reported in the general palliative care literature with patient deterioration not always being communicated to the patient and family and when this does occur this can be poorly or inconsistently documented (Bloomer, Botti, et al., 2018). This issue was illustrated in a recent palliative care trial, where patients and carers were not always fully aware of the patient's condition or the palliative focus of their care (Holm et al., 2017).

Research and specialist nurses attempted to assess the patient's understanding of their condition and their readiness to engage in a palliative care trial conversation. When to initiate or continue these discussions, as in clinical practice, was often guided by the nurses intuition or clues from the patient (Almack et al., 2012). The need to practice compassionate 'conditional candour' (Abdul-Razzak et al., 2014) appeared important during the

recruitment process, which involves evaluating the patient's readiness, inviting them to take part in the conversation and then being attentive to contextual factors such as appropriate timing and sensitive language (Zwakman et al., 2020).

Tailoring information according to the individual patient and carer's level of understanding and readiness is viewed as paramount in end-of-life communication (Etkind et al., 2017; Hancock et al., 2007; Parker et al., 2007; Silverman et al., 2017). This can be challenging for recruiting staff who need to go through a standardised participant information sheet as part of the informed consent procedure. Having the opportunity to build up a rapport with patients and carers through previous clinical contact can reduce the 'emotional labour' of having difficult conversations (Almack et al., 2012). As discussed in chapter one, how trials can become part of routine care and best utilise current clinical care pathways was identified as the number one question in the PRioRiTy study (Healy et al., 2018). Integrating research into routine health care was also a recommendation identified in the MORECare palliative care research methods project (Gysels et al., 2013).

In the palliative care literature, there are differing reports of how open and willing patients are to discussing end-of-life care issues. Patients have been reported to be reticent and reluctant (Almack et al., 2012; Momen et al., 2012) while other studies have found the majority are willing to engage in end-of-life care conversations (Emanuel et al., 2004; Piers et al., 2013). Patients can be in denial about the seriousness of their illness or not feel ready or able at that particular time to discuss the topic openly (Abdul-Razzak et al., 2014; Almack et al., 2012; Zwakman et al., 2020) which can influence the 'emotional labour' of promoting a trial for clinicians.

Glaser and Strauss (1965), in their seminal study of dying in hospital, identified a number of awareness contexts that have implications for the process of trial recruitment in palliative care. 'Open awareness' is where doctors, nurses, patients and family members openly acknowledge that the patient's illness will lead to their death while 'closed awareness' is when family and clinicians are aware but not the patient (Glaser & Strauss, 1965; Small & Gott, 2012). They also described two intermediate stages; 'suspected awareness' and 'mutual pretence'. 'Suspected awareness' is when a patient suspects they are dying and they have attempted to get clinical staff and family to confirm this while 'mutual pretence' is when everyone knows the patient is dying but it is not openly acknowledged (Field & Copp, 1999; Glaser & Strauss, 1965). This suggests that recruiting patients to a palliative care trial in a non 'open awareness' context can be challenging for recruiting staff and can facilitate clinician and carer gatekeeping.

More recently, 'open awareness' has been seen to be a fluid rather than a fixed state (Field & Copp, 1999) with even patients who are receiving care in an 'open awareness context' such as a hospice fluctuating between denial and acceptance as a coping strategy (Copp & Field, 2002). The way in which patient and families emotionally cope with a terminal diagnosis is believed to define the 'awareness context' and is related to their wish to retain hope (Timmermans, 1994). Fluctuating levels of patient and carer awareness can make it challenging for recruiting staff to 'promote' a palliative care trial even in an 'open awareness' context. Respecting patient and carer 'awareness' preferences is important (Small & Gott, 2012), including during the trial recruitment process, but this must not be used by clinicians as a reason to avoid difficult conversations (Field & Copp, 1999). This includes a conversation that involves 'Promoting' a palliative care trial.

7.5 How ‘Identifying participants’ and ‘Working with Partners (partner referrals and recruitment) is influenced by the theory of ‘emotional labour’ and ‘professional hierarchies and power relationships between clinicians’.

In health care, there is a ‘division of emotional labour’ with senior doctors being viewed as being largely responsible for disclosing *‘life affecting information’* (James, 1993) (p.100). This ‘division of emotional labour’ is also present in the context of palliative care trial recruitment. In the general palliative care literature, doctors are seen to be responsible, by other professionals (Anderson et al., 2019; Bloomer, Botti, et al., 2018) and families (Anderson et al., 2019), for discussing prognosis and making treatment decisions. The importance of using medically led multi-disciplinary team meetings to identify eligible patients has also been reported in the general trial literature (Donovan et al., 2014; Strong et al., 2016). James (1993) argues that until the bad news is formally acknowledged by the senior doctor responsible for the patient’s care, the ‘emotional labour’ of other professionals, patients and carers is *‘carried out in secret or semi-secret’* (p.100). The ‘emotional labour’ of working in a ‘closed awareness’ context for nurses has been reported in the general palliative care literature (Testoni et al., 2020).

The definition and scope of the specialist nurse role can vary internationally (Begley et al., 2013) but they have been identified as core members of the multi-disciplinary team in the context of cancer and non-cancer care both in the UK (Cox et al., 2017; Wallace et al., 2019) and internationally (Fleure & Sara, 2020; Liljeroos & Strömberg, 2019). Specialist nurses can take on an advocacy role in the multi-disciplinary team by spending time with patients and carers and by taking the lead on communication issues (Wallace et al., 2019). They can support medical staff by breaking bad news and by discussing potential treatment options

with patients and carers (Fleure & Sara, 2020). There are reports, however, of medical staff dominating decision making within multi-disciplinary team meetings (Rowlands & Callen, 2013). There is the potential to harness the specialist nurse role within the multi-disciplinary team to facilitate recruitment to palliative care trials while acknowledging the impact of professional hierarchies and power relationships between clinicians on decision-making. Country specific factors related to the remit of the specialist nurse's role and the type of training they have received also need to be recognised.

Palliative care as a field of health care involves high stake decision making (Ferrer et al., 2016) and the 'emotional labour' of predicting a patient's prognosis has been identified as a reason for doctors avoiding prognosis and end-of-life care discussions (Flierman et al., 2019; Hancock et al., 2007). Glaser and Strauss (1965) identified four trajectories of dying in the hospital setting; certain death/known time; certain death/unknown time; uncertain death but a known time when uncertainty will be resolved; uncertain death and uncertain time when uncertainty will be resolved (Glaser & Strauss, 1965; Small & Gott, 2012). The first two refer to a situation where it has been recognised that there is '*nothing more to do*' for the patient and whether or not the time of death can be predicted (Glaser & Strauss, 1965) (p. 235). The third category refers to a patient receiving intensive or emergency care and the later when someone is seriously ill and the outcome is unclear. Glaser and Strauss (1965) describe how patients can vacillate between certainty and uncertainty or be seen to linger. Where a predictable dying trajectory is too difficult to identify, this results in the doctor's reluctance to communicate the terminal nature of the illness to the patient so perpetuating 'closed awareness' (Glaser & Strauss, 1965; Small & Gott, 2012). This interrelationship between predicting a patient's prognosis and talking to patient's about the palliative nature of their condition has implications for the trial recruitment process. Lack of certainty

regarding the patient's prognosis can lead to a reluctance to confirm trial eligibility and 'promote' the trial to patients and carers.

Medical staff can struggle to recognise when a patient is approaching the end of their life (Bloomer, Botti, et al., 2018; Butow et al., 2020; Johnson et al., 2020) and this can be the case even in specialist palliative care (Pontin & Jordan, 2011; White et al., 2020). Small and Gott (2012) argue that changes in the epidemiology of dying with people living longer with comorbidities and complex needs means it is challenging for clinicians to predict a patient's illness trajectory. Prognostic uncertainty can be an issue especially in the non-cancer population (Chattoo & Atkin, 2009; Flierman et al., 2019). Clinician prediction of survival remains the most commonly used approach to formulating a prognosis with doctors tending to overestimate survival (White et al., 2016). The role and value of prognostication tools to support clinical decision making in advanced disease including in clinical trials requires further research (Hui, 2015; Simmons et al., 2017). Nurses can be hesitant to disclose their observations of the patient's deteriorating condition to medical staff but doctors can value their opinions (Flierman et al., 2019; Johnson et al., 2020) and nurses may be better at predicting survival but further research is required (White et al., 2016; White et al., 2020).

Palliative care is often seen as a failure by clinicians and providing end-of-life care, particularly in the acute hospital setting, is challenging because of the priority given to interventions and treatments that aim to prolong life (Gardiner et al., 2011; Hibbert et al., 2003; Salins et al., 2020; Willard & Luker, 2006). There is also a public expectation that patients who go into hospital will get better (Gardiner et al., 2011). There can be tensions between the speciality of palliative care that promotes a more holistic and non-interventionist approach (Hibbert et al., 2003) and other medical specialities that focus on a

more acute model of care (Chattoo & Atkin, 2009; Small & Gott, 2012). Specialist palliative care provides advice and support to other medical specialities so professionals who work within palliative care, even medical staff, have to negotiate their input into a patient's care (Hibbert et al., 2003; Salins et al., 2020). Specialist palliative care being a consult service was identified as a barrier to recruitment in chapter two and the findings of this study help to explain why it is important to select a Principal Investigator or 'research champion' who has overall responsibility for the patient's care.

7.6 How the 'emotional labour' of 'Promoting' a palliative care trial as a 'Product' can lead to 'paternalism'.

Patients have the right to receive information and make independent judgements about their treatment and care (Beauchamp & Childress, 2013). Respect for patient autonomy is a key principle of palliative care (Radbruch & Payne, 2009) and was identified as a key recommendation from the MORECare research methods project;

'Respect is required for autonomous decisions of patients and carers regarding their participation in research to avoid limiting their participation through inappropriate gatekeeping and paternalistic attitudes' (Gysels et al., 2013) (p. 913).

Health care professional paternalism took a number of forms in this study, for example, in order to protect the patient, clinicians decided not to inform them of all the research studies they were eligible for. These type of decisions were generally not based on an assessment that involved the patient (Kars et al., 2016). Clinicians struggle with the dilemma and conflict of balancing the ethical principles of respect for autonomy with the demands of

beneficence, acting in the patient's best interest (Beauchamp & Childress, 2013). The act of withholding information from a patient, also called gatekeeping in the literature as previously discussed, prevents the patient from making an informed and voluntary choice about trial participation (Beauchamp & Childress, 2013). Beauchamp and Childress (2013) define this type of behaviour as 'hard paternalism' and believe it is not ethically justifiable in this context. Periera and Hernández-Marrero (2019) argue that this type of paternalistic behaviour is misguided and the focus should be on the protection of palliative care patients by scrutinising a study's ethical soundness rather than excluding them from research they are eligible for.

Studies have shown that palliative care patients and their carers can value the opportunity to participate in research (Bloomer, Hutchinson, et al., 2018; White & Hardy, 2010), including palliative care trials (Aoun et al., 2017; Lovell et al., 2020; Middlemiss et al., 2015). For example, a feasibility study that involved collecting urine samples from patients in the last weeks of life achieved a recruitment rate of 57% (Coyle et al., 2016). Aoun et al (2017) interviewed 316 carers of patients receiving home based palliative care about their experiences of trial participation. Carers in both the control and intervention group appreciated the opportunity to participate and benefited from their involvement in research. A limitation of these studies is that they do not capture the views of those patients and carers who decline to take part (Aoun et al., 2017; Lovell et al., 2020; Middlemiss et al., 2015) or they ask their views of taking part in hypothetical studies (Todd et al., 2009; White et al., 2008). In the general palliative care literature, there is some evidence that sensitive discussions around prognosis or end-of-life care are not associated with poorer psychological patient outcomes (Hancock et al., 2007; Wright et al., 2008) and that the

majority of terminally ill patients and their relatives do not find talking about death, dying and bereavement stressful (Emanuel et al., 2004).

Carers can also demonstrate paternalistic attitudes by sometimes overriding the patient's autonomy by acting as the patient's surrogate decision maker even when the patient has capacity. The 'emotional labour' for clinicians of balancing the patient's interests with the carer's interests have been noted in the general palliative care (Hancock et al., 2007) and the research literature (Gysels et al., 2013). Carers may not want the clinician to be truthful with the patient about their condition in order to maintain hope. The policy imperative to be open with patients about their prognosis so they can make autonomous decisions regarding their care does not always resonate with lay culture (Noble et al., 2015; Testoni et al., 2020). The 'emotional labour' of balancing the patient's interests with the carers emotional needs can be stressful and distressing for clinicians (Butow et al., 2020; Noble et al., 2015; Testoni et al., 2020).

Snowden and Young (2017) argue that judging all acts of health care professional gatekeeping during a trial as paternalism is an oversimplification of the phenomenon, an idea that fits with the findings of this case study. They analysed the gatekeeping literature related to nurses and data from two focus groups with hospice community nurses (n=9). The nurses were involved in recruitment to a trial of a holistic needs assessment intervention in community palliative care. The trial had to be stopped after two years because of poor recruitment. They found a continuum of gatekeeping among nurses from unconsciously forgetting about the study because of other distractions to more active conscious disengagement caused by discomfort and distress.

7.7 The role of 'Working with partners' (partner education) to manage 'emotional labour' and health care professional paternalism.

Training research site staff has been identified as the number one priority for evaluation when considering interventions to improve trial recruitment in the general trial literature (Bower et al., 2014). Training interventions have tended to be used in the context of cancer trials and have taken a workshop format covering generic and trial specific issues over one or two days with a mix of health care professionals (Townsend et al., 2015). There has been a call for more tailored support for clinicians involved in the recruitment process (Lawton et al., 2015).

Within the nursing literature, it is argued that 'emotional labour' needs to be taught so that nurses know how to deal with situations that occur in clinical practice and manage their feelings more effectively (Smith, 2012). Smith (2012) argues that it is wrong to assume that an individual will be able to cope with a difficult and upsetting situation by virtue of their role and seniority. Doctors should also accept their own emotional responses. These responses should not be a detractor from objective clinical reasoning but rather a source of true empathy and an important non-medical factor in the decision making process (Pfeil et al., 2015).

Hochschild (2012) describes how individuals in the workplace use 'surface acting' and 'deep acting' to ensure emotions are expressed according to social and cultural norms. The use of the term 'acting' has been seen as controversial in some of the nursing literature as it suggests nurses are displaying their emotions in an unauthentic way (Huynh et al., 2008).

When 'surface acting' we '*deceive others about how we are feeling without deceiving ourselves*' (Hochschild, 2012)(p.33). It involves changing our outer expression to make our

inner feelings correspond to how we appear (Smith, 2012). An example of this would be, presenting a 'professional face' to patients, while privately feeling uncomfortable about approaching them about a trial (Theodosius, 2008).

In contrast, when 'deep acting' the individual works on and learns to believe in the emotions they are expressing. They do this by using their imagination, such as transferring positive memories of talking to patient to a current situation, or by exhorting emotion, such as 'psyche' themselves up to do something they are not looking forward to (Hochschild, 2012; Theodosius, 2008). This learning process can eventually lead to the person being unaware that they have worked on and created the required emotional response such as feeling comfortable approaching the patient (Hochschild, 2012; Theodosius, 2008) . In Hochschild's (2012) study of flight attendants, more mature and experienced staff members were found to be better at 'deep acting'. This meant they were better able to distinguish between their private and work selves (Smith, 2012). This may explain why specialist nurses and research nurses who had experience of talking to palliative care patients and carers felt more comfortable recruiting to a palliative care trial in this case study.

The 'emotional labour' of caring for palliative care patients and carers can be overlooked and as Hochschild (2012) questions '*what is it that "peoples jobs" actually require of workers.*' (p.10) There is a risk that if emotions are not addressed they may accumulate (Brighton et al., 2019) and may lead to job related stress and burnout (Hochschild, 2012; Huynh et al., 2008). In a study of generalist palliative care professionals, a range of emotions were present during difficult conversations with patients and carers. Across disciplines and experience levels; anxiety, sadness, empathy, frustration and insecurity influenced care

delivery with anxiety and empathy being the most common emotions experienced (Luff et al., 2016; Martin et al., 2015).

Brighton et al (2019) identified two types of emotions experienced by non-medical generalist professionals during difficult patient and carer conversations that support the findings of this study. These were 'skill focused' emotions and 'situation focused' emotions. Skill focused emotions relate to a health care professionals lack of confidence in their ability. Situation focused emotions are the clinician's emotional response to the situation based on their assessment of the situation and what others may be feeling. The use of pro-active strategies such as palliative care skills training to address skill focused emotions and more reactive strategies such as reflective practice, to address situation based emotions were seen as potentially useful strategies to reduce avoidance in non-medical generalist professionals (Brighton et al., 2019).

Training is needed to help clinicians to translate communication guidelines into practice while considering their own emotional needs (Anderson et al., 2019). The literature on end-of-life communication can be contradictory and difficult to follow (Brighton & Bristowe, 2016). Studies have found that communication style is as important if not more important than the content of end-of-life care discussions for patients and carers (Parker et al., 2007). Patients and carers value many core non-specialist communication skills (Brighton & Bristowe, 2016) that include empathy, care, compassion, and honesty, balanced with sensitivity and hope, encourage questions and check understanding (Parker et al., 2007). There is some evidence from paediatric trials that even in the most difficult situations, parents can understand and accept the timing and reasons for a clinician approaching them about a trial as long as it is carried out in a considerate way (Valerie et al., 2011).

The type of strategies used by recruiting staff in this study to prepare for 'Promoting' a palliative care trial are reflected in the communication literature. In order to manage the 'emotional labour' of having a difficult conversation, generalist palliative care clinicians have reported using a variety of strategies. These include; self-care such as self-reflection, preparatory work such as rehearsing a conversation beforehand, using a team approach as a source of support and forum for processing challenging situations and using professional identity to enable separation of professional self from personal self (Luff et al., 2016). The way in which recruiting staff support each other when working on a palliative care trial suggests the presence of 'emotional intelligence'. There are disagreements over the term (Nightingale et al., 2018) but 'emotional intelligence' is generally seen as the ability to recognise and regulate emotion in oneself and others while 'emotional labour' involves emotional self-regulation (Huynh et al., 2008; Raghubir, 2018). Understanding and being aware of others emotions, as well as your own, and managing relationships are key attributes of 'emotional intelligence'. It is argued that those professionals who work in an emotionally intelligent way work more collaboratively, make better decisions and care for their patients more effectively (Raghubir, 2018). Strategies that develop and support emotionally intelligent practices such as self-reflection, are important in the context of trial recruitment, as in end-of-life-care (Bailey et al., 2011; Johnson et al., 2020) and health care generally (Nightingale et al., 2018), to help manage the 'emotional labour' of recruitment and address health care professional paternalism.

The requirement to assess and manage the patient's fluctuating mental capacity, follow advance consent procedures and involve proxies, as appropriate, in the recruitment process contributes to the 'emotional labour' of 'promoting' a palliative care trial. As discussed in chapter one, end-of-life care research is likely to involve patients who are at risk of losing

capacity or lack capacity (White et al., 2019) and this is something researchers need to anticipate (Gysels et al., 2013). This issue is not unique to palliative care research (Brown et al., 2019; Hamilton et al., 2017; Ries et al., 2020) and it has been estimated that 26 % of patients in general medical inpatients lack capacity (Sessums et al., 2011). Establishing capacity, particularly in those with mild cognitive impairment can be challenging (Agar et al., 2013; Jayes et al., 2019). Clinicians can lack confidence and awareness of how to assess capacity (Jayes et al., 2019). They can also have a lack of understanding of legal requirements such as who can act as a proxy decision maker (Shepherd, 2020b). Trials that involve patients who lack capacity are resource intensive. This is because of the skills and time required to conduct sensitive capacity assessments, identify and contact suitable proxies and seek their assent (Shepherd, 2020b). Carers may experience emotional and decisional burdens when acting as a proxy in the context of research and may need support to enact this role (Shepherd et al., 2019). Nominated consultees may also lack confidence and understanding of their role (Evans et al., 2020). In the context of stroke trials, those research nurses with more experience of caring for stroke patients felt more comfortable assessing capacity in patients with severe stroke symptoms (Boxall et al., 2016).

In this study, recruiting staff were used to explaining randomisation to patients as part of the informed consent procedure. This is a generic recruitment skill and all clinicians in this study were experienced in recruiting to trials. Specialist palliative care professionals may feel less confident and require training as highlighted in a recent palliative care trial (Holm et al., 2017). The general trial literature and the study findings suggest that even the most experienced recruiting staff can experience 'emotional labour' when operationalising randomisation procedures. The need for health care professional training and support to

enact randomisation procedures has been identified in the general trial literature (Donovan et al., 2014; Donovan et al., 2014; Rooshenas et al., 2016).

7.8 The final theoretical propositions for this study

The study's theoretical propositions have been iteratively developed to reflect the study findings and the wider literature discussed above. The final theoretical propositions are:

- The use of subjective criteria to predict a patient's prognosis as part of a palliative care trial's eligibility criteria acts as a barrier to recruitment.
- Involving recruiting staff who have previous experience of caring for palliative care patients and their carers will be a facilitator to recruitment.
- The provision of training for recruiting staff on how to introduce a palliative care trial to patients and carers will help address health care professional gatekeeping.
- The provision of ongoing support for those involved in recruiting to a palliative care trial will help address health care professional gatekeeping.
- Choosing a Principal Investigator who has overall responsibility for the patient's care influences how well the trial meets its recruitment target.

7.9 Recommendations for clinical practice and policy

The new palliative care trial recruitment framework proposed that reflects the study findings is an adapted 'Social Marketing Mix Framework' that incorporates the wider

overarching contextual issues of ‘emotional labour’, ‘professional hierarchies and power relationships between clinicians’ and ‘paternalism’ (see figure 2 in chapter six). The requirement to take account of trial specific and local circumstances when applying the updated framework still needs to be recognised.

It is recommended when choosing a ‘research champion’ to consider the influence of ‘professional hierarchies and power relationships between clinicians’ on the recruitment process. The study findings illuminate why the lead medical clinician may be the best person to take on the role of Principal Investigator to facilitate the recruitment process but they also suggest that specialist nurses can take on this role because of their position in the multi-disciplinary team. There has been a growing recognition that non-medical professionals should be encouraged and supported to take on key research roles including that of Principal Investigator (National Institute for Health Research, 2021). There is a need to expand palliative and end-of-life care research activity so the assumption that the lead medical clinician is best placed to take on the role of ‘research champion’ needs to be challenged. This should also be the case for the role of Chief Investigator as the study findings suggest that an investigator with a medical background can make engaging and recruiting research sites more straightforward and less time consuming. Palliative care promotes a multi-disciplinary approach to care and this needs to be reflected in the trial context. Who is the best person to take on the role of Principal Investigator and Chief Investigator in a palliative care trial is an area of practice that requires further research.

The findings of this study have highlighted that those health care professionals who are involved in recruiting patients and carers to a palliative care trial, should have access to 'partner education' to manage their emotional labour. It has been previously recognised that researchers and clinicians need training to address the practical and ethical challenges associated with conducting end-of-life care research (Gysels et al., 2013). This 'partner education' is in addition to the generic training that is recommended in the general trial literature that aims to address the challenges, for clinicians, of exploring patient preferences and discussing key trial concepts such as equipoise, randomisation and uncertainty (Fletcher et al., 2012; Townsend et al., 2015).

Study coordinating centres need to incorporate recruitment training into trial planning and set up processes to address emotional labour. Those running a trial should not assume health care professionals will have the necessary skills and confidence, by virtue of their professional role, to recruit to a palliative care trial. As discussed previously, the recruitment process is an interactional activity between a patient and a recruiter so focusing purely on how information is presented in a participant information sheet will not address this recruitment barrier. There is evidence from the general trial literature that even when the trial's target population informs the content, format and appearance of the participant information, this makes little or no difference to recruitment rates (Treweek et al., 2018). Outside palliative care, there is evidence that the communication style of the recruiter is a key factor influencing the patient's willingness to take part in the trial (Albrecht et al., 2008; Jenkins & Fallowfield, 2000). The need to provide training on how to discuss a palliative care trial to address emotional labour echoes one of the recent recommendations from the updated MORECare project;

'19. Clinicians should be supported and provided with training to ensure they are confident in their skills to discuss research studies with patients (and/or family members) during routine clinical contact.' (Evans et al., 2020)(p. 480)

Any training should reflect the characteristics of the trial and the health care professional's experience. The training may need to cover a number of issues which are outlined in table 17.

Table 17: Recommendations for palliative care trial training to address emotional labour

- How to explain palliative and end-of-life care to patients and carers and dispel the myths surrounding the terms (Reigada et al., 2020).
- The use of general verbal and non-verbal communication skills to assess the potential participant's understanding of their condition and willingness to engage in a trial conversation (Moore et al., 2018).
- How to manage the patient's fluctuating physical condition and the psychological needs of patients and carers (Oechsle, 2019; Wang et al., 2018).
- How to assess capacity and enact proxy and advance consent procedures (Evans et al., 2020; Gysels et al., 2013).
- Stressing the importance of approaching patients to maintain patient autonomy (Evans et al., 2020; Gysels et al., 2013).
- Ideally, there would be opportunities for clinicians to role-play potential clinical recruitment scenarios in a supportive environment (Luff et al., 2016; Townsend et al., 2015).

* The training needs to reflect the characteristics of the trial and the health care professional's experience.

There is currently little evidence of the positive impact of trial recruitment training on recruitment rates, patient understanding, satisfaction or levels of informed consent. A review of trial recruiter training programmes showed that training was well received by

clinicians, including role play, and some programmes were shown to increase recruiter confidence in communicating key trial concepts (Townsend et al., 2015). The challenge in palliative care trials is ensuring 'partner education' does not contaminate the study by corresponding too closely to the intervention being tested (Koffman et al., 2019). Involving patient and public involvement representatives in training programmes or directly in the recruitment process may help address gatekeeping (Froggatt et al., 2020) but evidence supporting the impact of such involvement in palliative care research is limited (Chambers et al., 2019). The importance of training for health care professionals responsible for recruiting adults who lack or are at risk of losing capacity has been identified but more research is needed to explore their experiences and support needs (Shepherd, 2020b). Outside of research, how professionals communicate decision options to patients and test their decision-making abilities is unclear (Jayes et al., 2019). In relation to prognostication in palliative care, there is currently no clear guidance on how clinicians can be taught to perform this aspect of their role better (White et al., 2016).

Clinical supervision models of support have been recommended for research nurses in the general trial literature to address the 'emotional labour' associated with their role (Boxall et al., 2016; Hernon et al., 2020). Smith (2012) argues that nurses need an arena where they can work on their feelings and emotions and learn from them but this requires organisational support. The opportunity to reflect on the impact, both positive and negative, of working on a palliative care trial should be available to clinicians throughout the trial as recruitment interactions may go smoothly or there may be difficulties. It maybe that the 'emotional labour' of recruiting to a palliative care trial is something that not all clinicians are able or want to undertake but this needs to be openly acknowledged. In their seminal study of dying in hospital, Glaser and Strauss (1965) identified that nurses who did not want

to talk about end-of-life care would hand the patient over to a nurse who was comfortable discussing such issues, a nurse they termed a 'death talker'. They described how a division of labour could develop among nurses to protect those who are unable to take on this role.

This study has illustrated the resource intensive nature of palliative care trial recruitment and the impact it can have on recruiting staff. As highlighted in chapter one, palliative care research is underfunded and more funding is required to ensure those who are recruiting to a palliative care trial have the necessary resources, training and support to carry out their role. As discussed in chapter five, accrual-based metrics are used in the UK to determine the level of recruiting staff support a trial may receive. This may unfairly discriminate against palliative care studies because of the time and resources required to recruit patients. Similar concerns have been raised in trials aimed at those with complex cognitive and communication needs (Shepherd, 2020b).

7.10 Recommendations for future research

Full scale trials that struggle or do not meet recruitment targets are costly and wasteful and the importance of reducing research waste in health care (Chalmers & Glasziou, 2009), including in palliative care (Sleeman & Murtagh, 2014), has been raised in the literature. Feasibility and pilot studies have a role in reducing research waste by identifying successful recruitment strategies and/or designing out any issues that may negatively impact on a trial's recruitment success (Blatch-Jones et al., 2018). They may also identify that a study is in fact not feasible (Morgan et al., 2018), as illustrated in a recent study of peer support to maintain psychological wellbeing in people with advanced cancer (Walshe et al., 2020). The

use of embedded randomised controlled trials within a study to test a recruitment strategy, such as changes to a patient information sheet (Cockayne et al., 2017), is also an approach that is being developed in the field of trial methodology (Rick et al., 2014) and has the potential to be used within palliative care research.

The role and value of qualitative research in addressing recruitment related issues and identifying key areas for 'partner education' has been identified in trials outside palliative care. The QuinteT Recruitment Intervention (qualitative research integrated into trials) has been used in a number of non-palliative care randomised controlled trials over the last two decades. The intervention is seen as particularly useful in trials that are predicted to be challenging and difficult to recruit to and its impact on recruitment rates has recently been evaluated (Rooshenas et al., 2019). The QuinteT Recruitment Intervention's purpose is to understand why a trial may be experiencing recruitment difficulties so that tailored support can be provided to recruiting staff. It is recommended that the intervention is integrated into the feasibility or main phase of a study or used when a trial is struggling to reach its recruitment target (Donovan et al., 2016; Rooshenas et al., 2019). Applying approaches used in the QuinteT intervention may lead to a greater understanding of the 'clear obstacles' and 'hidden challenges' that prevent a palliative care trial reaching its recruitment target (Donovan et al., 2014).

As used in this study, the intervention involves carrying out semi-structured interviews with study coordinating centre and recruiting staff and reviewing trial documentation. A more challenging aspect of the intervention for the palliative care setting, but not impossible (Noble et al., 2015), is inviting those patients who have declined to take part in the trial to take part in an interview. This may be challenging because of potential concerns raised by

health care professionals, carers and research ethics committees and the patient's unstable condition. Patients and carers can provide valuable insights into how the trial or 'product' has been 'promoted' to them and the reasons why they declined to take part (Houghton et al., 2020; Hughes-Morley et al., 2016; Stevens & Ahmedzai, 2004). A recent Cochrane review of potential participants' views and experiences of the trial recruitment process, including those who agreed to take part and those who declined, has called for more research exploring underrepresented groups including adults who lack capacity to consent (Houghton et al., 2020).

An important part of the process is the audio recording of the appointment where recruiting staff introduce and explain the trial to potential participants. This process would provide valuable insights into how a palliative care trial is 'promoted' to patients and carers during a recruitment consultation. This is in addition to how well randomisation procedures have been explained and clinical equipoise maintained. This process would allow an assessment of how well patients and health care professionals have grasped the key concepts to support informed consent. It would also lead to a better understanding of how willing and accepting patients and carers are to being approached about a palliative care trial. Tailored strategies can then be put in place to address recruitment challenges such as individual and group recruiter feedback, research nurse training, 'tips' and 'guidance' documentation, changes to participant information, review and discussion of screening logs and scrutiny of patient pathways (Rooshenas et al., 2019).

The fact multiple recruitment visits are often required in palliative care trials, recruitment activity does not always occur in the out-patient setting and the cost implications of carrying out this type of research means this approach may not always be possible but should be

considered, where appropriate, as a means of capturing the recruitment process in 'real time'. Patients, carers and health care professionals also need to feel comfortable being recorded. Recording and analysis of end-of-life conversations between patients and clinicians has taken place in the trial context, as illustrated in a trial of early palliative care, where patients consented to palliative care clinic visits being audio recorded (Lim et al., 2017) and in palliative care research generally (Parry et al., 2014).

7.11 Strengths of the study

To the author's knowledge, this is the first qualitative multiple case study focusing on recruitment issues in palliative care randomised controlled trials. As discussed in chapter two, the evidence underpinning how clinicians recruit palliative care patients and carers to palliative care randomised controlled trials is largely anecdotal. In-depth semi structured qualitative interviews with study coordinating centre and recruiting staff from three diverse UK trials, as well as trial documentation, produced new insights into the recruitment process in palliative care trials.

Outside the trial recruitment context, health care professionals struggle with the 'emotional labour' of prognostication and discussing palliative and end-of-life care with patients and carers. Professional hierarchies and power relationships between clinicians support paternalistic practices and influence how 'emotional labour' is experienced by health care professionals in clinical practice. The study findings contribute to the knowledge base in palliative care as they have identified how these wider contextual factors also influence the trial recruitment process. They help to explain why paternalism is a particularly challenging

issue in palliative care randomised controlled trials. The study findings have identified the importance of 'partner education' to help address the 'emotional labour' of palliative care trial recruitment in addition to generic randomised controlled trial training. The findings are relevant and applicable to palliative care research generally and not just randomised controlled trials. They build upon the findings of the literature review in chapter two and Kars et al's (2015) review of reasons for gatekeeping in palliative care research.

The study findings also help meet the priorities set by the Prioritising Recruitment in Randomised Trials study (Healy et al., 2018), specifically questions 5 and 7;

5 'What are the barriers and enablers for clinicians/healthcare professionals in helping conduct randomised trials?'

7 'What are the best approaches to ensure inclusion and participation of under-represented or vulnerable groups in randomised trials?'

One of the concerns raised about case study research is how the study findings can be generalised beyond a single or small number of cases. Unlike experimental research, generalisation occurs through analytical rather than statistical generalisation. As previously discussed, theoretical propositions were used to guide data collection and analysis in this study. The 'Social Marketing Mix Framework' and the findings of the literature review in chapter two informed the initial theoretical propositions. The theoretical propositions were updated during the study and at the end of the study to reflect the emerging findings and the wider theoretical, palliative care and trial recruitment literature. The concept of analytical generalisation means the findings can be used to understand trial recruitment processes beyond the three cases used in this study (Ritchie & Lewis, 2003; Yin, 2018).

Additionally, theory building was strengthened by using multiple diverse cases rather than a single case (Yin, 2018).

There is a limited choice of theories for researchers to draw upon to help them understand the trial recruitment process. Recently, the 'Social Marketing Mix framework' has also been used as an analytical framework to understand trial recruitment processes in a non-palliative care trial (Tompkins et al., 2019). The '6 Ps' of the 'Social Marketing Mix Framework' provided a useful and practical guide to inform data collection and analysis in this study, both within case and across the three cases. At a descriptive level, the theory highlighted important issues that need consideration when planning and implementing a recruitment strategy in the context of a palliative care trial so was a useful theory to use. Despite this, it was challenging to see beyond the theory to fully understand the contextual reasons for why similar patterns were being seen across the cases. Whether collecting, analysing and interpreting the data without the use of an a priori framework would have been more straightforward is difficult to say. The concepts of 'emotional labour', 'paternalism' and 'professional hierarchies and power relationships between clinicians' were required as an additional theoretical lens to fully interpret the findings in this study to reflect the palliative care context. This case study is the first study, to the author's knowledge, to adapt the 'Social Marketing Mix Framework' to reflect the wider contextual issues of 'emotional labour', 'paternalism' and 'professional hierarchies and power relationships between clinicians' found in palliative care.

7.12 Study limitations

In the systematic review in chapter two, the literature was searched until October 2016. This reflects the state of knowledge in this area at the time that the empirical data collection was planned, and the results of the synthesis of this literature review informed the design and conduct of the empirical study. Rather, then, than updating this and potentially causing confusion about what literature was available to inform the empirical study, studies published since this date were captured through citation tracking and other literature notifications and was incorporated into the discussion to contextualise the findings of the empirical study. This approach may have meant key papers exploring recruitment issues in palliative care randomised controlled trials may have been missed. These papers may have supported or challenged the findings of this study.

When choosing a research design, the researcher needs to be aware of its limitations. Case studies require multiple skills (Walshe et al., 2004) and can be very time consuming and resource intensive (Baxter & Jack, 2008; Creswell & Poth, 2016). They have been described as being '*simple in theory yet complex in nature*' (Harrison et al., 2017) (p.3) with data analysis being particularly challenging because of the need to bring together large amounts of data (Crowe et al., 2011). Managing the issue of anonymity can also be challenging in case study research as an in depth description of the case may lead to individual participants and organisations being identified. This was a particular issue in this study as there are only a small number of palliative care trials active in the UK at any one time. Details of how anonymity was managed and why this approach was taken in this study is discussed in detail in chapter four. The decision to anonymise the case, clinical recruitment centres and individual participants may have meant Chief Investigators, study coordinating centre and

recruiting staff were more willing to take part in this study and be more open and honest in their responses. A limitation of this approach is that the reader does not have access to a detailed description of the case when reviewing and interpreting the study findings.

Practical as well as methodological considerations influenced case selection in this study as well as resource issues. Yin (2018) recommends that the number of cases included in a study should be no more than 4 or 5 because of their complexity. A further case would have been selected in this study if additional resources had been available. This is because the findings suggested that recruiting to a pharmaceutical symptom control trial may raise particular issues for recruiting staff. Resource issues impacting on how many cases are included in a study is acknowledged in the case study literature (Creswell & Poth, 2016; Yin, 2018).

The aim was to sample and recruit clinical recruitment centres and recruiting staff with different characteristics such as those centres who had and had not recruited to target and staff with different roles and clinical backgrounds. In practice, clinical recruitment centres and recruiting staff were included in the study as they agreed to take part. Recruiting clinicians to take part in a qualitative research study, including research nurses (Elliott et al., 2018), can be a challenging and time consuming process (Barclay et al., 2019; Broyles et al., 2011; Signorelli et al., 2018). Those who were interested usually responded quickly to the invitation and the reasons for staff declining included not having the time or that the study was not on the National Institute for Health Research portfolio. Lack of time and workload demands have been previously reported as barriers to recruiting clinicians to participate in qualitative research (Barclay et al., 2019; Broyles et al., 2011; Signorelli et al., 2018). Using snowball sampling within the Health Research Authority approval system added additional complexity to the recruitment process. Having previous experience of the Health Research

Authority approval system and liaising with NHS Research and Development departments was useful in this study.

Those who were willing to discuss their views and experiences of trial recruitment self-selected themselves to take part in the study and those with no time declined to take part. Participant views may not be representative of other professionals who are involved in the palliative care trial recruitment process. Recall bias may also have been an issue as health care professionals needed to remember their experiences of recruiting patients and carers to a palliative care trial (Forero et al., 2018). Social desirability bias can also be an issue in qualitative research studies, the idea that participants present themselves, and their social context, in a way that is perceived to be socially acceptable such as denying the presence of health care professional gatekeeping. Gentle probing during the telephone interviews was used as a strategy in this study to help minimise social desirability bias (Bergen & Labonté, 2020). This study does not capture the patient and carer's perspective of being recruited to a palliative care trial. Their views and experiences may be different to those expressed by health care professionals, an issue found in the general trial literature (Valerie et al., 2011).

The inability to be on site to collect data due to resource issues meant collecting observational data and/or recording of recruitment consultations was not an option in this study. Observing and/or listening to how health care professionals recruit patients and carers to trials and comparing this to their interview responses would have strengthened the findings of this study. As discussed in chapter four, being on site may have made documentary evidence collection easier as staff needed to feel comfortable and be fully bought into the idea of sharing documentation. The ability to fully understand the organisational factors that influenced the recruitment process are also limited by the

primary source of data being semi structured interviews with health care professionals involved in the recruitment process.

This study took place in a UK context and it is important to acknowledge that palliative care provision and resources, both clinical and research, may differ internationally which may affect the trial recruitment process. In 2017, only 14% of the global population had access to palliative care that was integrated into main stream health care services and this access was concentrated in European countries that included the UK (Clark et al., 2020). The cultural context can also influence communication issues in palliative and end-of-life care, such as patient and carer preferences for prognosis disclosure and willingness to engage in end-of-care discussions (Moore et al., 2018; Shah et al., 2020; Shen et al., 2018; Zafar et al., 2016). Health care professionals can also be a culturally diverse group. Cultural issues have the potential, therefore, to influence the palliative care trial recruitment process. Research ethics and governance requirements may also differ between nations, such as the type of information that needs to be included in the participant information sheet or mode of consent, which will also affect the trial recruitment process (Gardiner et al., 2010; Preston et al., 2020).

The benefits of having palliative care clinical and research experience and supervisors with a similar background meant that study design, data collection, interpretation and data presentation decisions could be developed, discussed and reviewed by a research team with relevant experience 'in the field'. A limitation of this approach is that other specialist and generalist palliative care clinical and research professional's interpretations of recruitment issues in palliative care trials may not reflect those presented in this thesis.

As discussed in chapter one, relevant stakeholders for the research question were health care professionals with experience of palliative care trials. Additional stakeholders were not involved in this study as both myself and my supervisors are experienced palliative care clinicians and have relevant trial experience. The advantages of this were; the small pool of eligible health care professionals with relevant trial experience was not limited further, there were no study delays due to trying to engage busy health care professionals and there was no additional costs. Involving additional stakeholders in the study design process could have influenced; the choice of theoretical framework; the research question; the definition of the case and the development of recruitment materials and data collection procedures. Presenting and discussing study findings and recommendations with stakeholders may have facilitated and strengthened the outputs from this study. How best to disseminate the study findings could also have been discussed with stakeholders. Some would argue that it is unethical to carry out a study without formal stakeholder engagement. Ideally, this would have occurred, despite my own and my supervisor's relevant experience, but practical issues influenced the decision not to engage additional health care professional stakeholders. The study findings have subsequently been presented at conferences attended by national and international palliative care clinicians and researchers.

7.13 Key messages and dissemination

Table 18: Key study messages

- An adapted 'Social Marketing Mix Framework' that incorporates the wider overarching contextual issues of 'emotional labour', 'professional hierarchies and power relationships between clinicians' and 'paternalism' is a useful framework for planning and monitoring recruitment activity in a palliative care trial (see figure 2).
- Trial specific and local circumstances still need to be recognised when applying the updated framework.
- Study coordinating centres need to incorporate recruitment training and support when planning, setting up and running a palliative care trial to address emotional labour. They should not assume clinicians will have the necessary skills and confidence, by virtue of their professional role, to recruit to a palliative care trial.
- There is a need to expand palliative and end-of-life care research activity so the assumption that the lead medical clinician is best placed to take on the role of 'research champion' needs to be challenged.
- This should also be the case for the role of Chief Investigator as the study findings suggest that an investigator with a medical background can make engaging and recruiting research sites more straightforward and less time consuming. Palliative care promotes a multi-disciplinary approach to care and this needs to be reflected in the trial context.
- Further research is required to explore who is the best person to take on the role of Chief Investigator and Principal Investigator in a palliative care trial and the type of training required to address the 'emotional labour' of recruitment.

It is important that these key messages are disseminated to a wide audience both nationally and internationally. This audience includes; research nurses, palliative care researchers, trial methodologists, clinicians involved in the care of palliative care patients, health care organisations responsible for providing palliative care. Specifically in the UK, the National Institute for Health Research Clinical Research Network who as discussed previously provide funding and support for research carried out within the NHS. A number of strategies will be

used to disseminate the study findings. This will include; an overall findings paper, a paper focusing on the nursing aspects of the study findings, with both of these articles being submitted to a peer review journal. Other forms of communication will be used to disseminate the study findings into practice such as newsletters, blogs and twitter. As discussed previously, the literature review and study findings have already been presented at international conferences (see page 13 for details).

7.13: The Covid-19 Pandemic

This thesis was written during the COVID-19 pandemic where the importance of health care research, particularly the role of adequately powered randomised controlled trials to treat or vaccinate against COVID 19, was highlighted in the media (Wilkinson, 2020). The impact of the COVID-19 pandemic on palliative care research, including trials, is more difficult to assess. As discussed in chapter one, the pandemic and the associated social distancing requirements has led to more flexible approaches to consent being accepted by research ethics committees. This may continue post pandemic which may have the potential to reduce patient, carer and clinician burden. The impact of the economic fallout of COVID-19 on palliative care research is a concern. As discussed in chapter one, palliative care research is historically underfunded and has a limited infrastructure. Concerns have already been raised about the impact of the pandemic on future research funding and infrastructure outside the speciality of palliative care (Griffiths et al., 2020). This lack of funding could also have a detrimental impact on palliative care research, including randomised controlled

trials, over the next few years. This is a notable concern as the societal need for palliative care is predicted to increase substantially globally by 2060 (Sleeman et al., 2019).

7.14 Conclusion

The findings of this qualitative multiple case study suggest that the 'Social Marketing Mix Framework' provides useful practical guidance for those planning and implementing a trial recruitment strategy in the palliative care setting. This study has highlighted that many of the health care professional related issues that influence the trial recruitment process can be hidden and reflect wider contextual issues. Paternalism is present in palliative care research but why it occurs is complex. Professional hierarchies and power relationships between clinicians support paternalistic practices and influence how 'emotional labour' is experienced. The 'emotional labour' of recruiting to a palliative care trial for health care professionals needs to be recognised in order to address paternalistic practices. It needs to be addressed and managed by those responsible for designing and running palliative care trials as well as those organisations that employ clinicians involved in the recruitment process. It also needs to be recognised by health care professionals themselves. The requirement to take account of trial specific and local circumstances when applying the updated framework needs to be recognised. The findings of this study may also be useful for researchers and clinicians involved in palliative care research outside the context of randomised controlled trials.

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<https://doi.org/10.1007/s00520-020-05799-x>

Appendix 1: Search strategy for the literature review in chapter two

	Search strategies
Medline via EBSCOhost	<ul style="list-style-type: none"> - 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	<ul style="list-style-type: none"> - 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: human, 01/01/1990 to 08/10/2016, clinical trial
CINHAL via EBSCOhost	<ul style="list-style-type: none"> - 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: human, 01/01/1990 to 08/10/2016, exclude Medline
Embase via Ovid	<ul style="list-style-type: none"> - palliat* or - hospice* or - terminal care or - exp palliative therapy/or - terminal care/and - randomi*ed controlled* or - randomized controlled trial/ - limits: human, 01/01/1990 to 08/10/2016, RCTs,

Appendix 2: A hierarchy of evidence tool, adapted for the purposes of this review (Eagar et al 2007).

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 (Participant's opinion): suggested as a possible barrier/facilitator/strategy by research participant

Appendix 3: Research ethics committee approval letter



Applicant: Lesley Dunleavy
Supervisor: Catherine Walshe/Nancy Preston
Department: Health Research
FHMREC Reference: FHMREC15042
22 February 2016

Dear Lesley

Re: Recruitment of patients or family carers to palliative care randomised controlled trials via health care professionals: a qualitative case study

Thank you for submitting your research ethics application for the above project for review by the Faculty of Health and Medicine Research Ethics Committee (FHMREC). The application was recommended for approval by FHMREC, and on behalf of the Chair of the University Research Ethics Committee (UREC), I can confirm that approval has been granted for this research project.

As principal investigator your responsibilities include:

- ensuring that (where applicable) all the necessary legal and regulatory requirements in order to conduct the research are met, and the necessary licenses and approvals have been obtained;
- reporting any ethics-related issues that occur during the course of the research or arising from the research to the Research Ethics Officer (e.g. unforeseen ethical issues, complaints about the conduct of the research, adverse reactions such as extreme distress);
- submitting details of proposed substantive amendments to the protocol to the Research Ethics Officer for approval.

Please contact the Diane Hopkins (01542 592838 fhmresearchsupport@lancaster.ac.uk) if you have any queries or require further information.

Yours sincerely,

A handwritten signature in black ink that reads "Diane Hopkins".

Dr Diane Hopkins
Research Development Officer
CC Ethics@Lancaster; Professor Roger Pickup (Chair, FHMREC)

Appendix 4: Invitation email/letter to the trial's Chief Investigator

Dear Dr/Professor,

I am currently undertaking a PhD in Health Research at Lancaster University and my area of interest is recruitment issues in palliative care RCTs. Recruitment is a real challenge in clinical practice with less than 50% of trials meeting their recruitment targets (Treweek et al 2013). I obtained your contact details from the..... database/website and I believe you are the Chief Investigator for the.....trial.

I am contacting you to see if you would be interested in supporting my PhD research. I wish to explore how those involved in the recruitment process carry out the recruitment of patients or family carers to palliative care RCTs and to look at why they implement certain recruitment strategies and the factors that influence their choices. Having a better understanding of this process has the potential to help address this complex but key issue in clinical practice.

I am using a qualitative case study approach and I would like to interview those staff members involved in recruitment both from the study coordinating centre and clinical recruitment centres as well as collect and analyse ,with the appropriate permissions, recruitment related trial documentation (not documentation containing identifiable patient/carer data).

This study has been reviewed by the Faculty of Health and Medicine Research Ethics Committee, and approved by the University Research Ethics Committee at Lancaster University (approval letter attached with REC approved supporting documentation).

What does taking part involve?

- I would need you to forward the relevant study information to those within your study coordinating centre who have knowledge of the recruitment process for your trial. I would need you to confirm whether any management approval was required before you approached them about the study.

I would need you to forward the relevant study information to the PIs at your clinical recruitment centres. If the PIs details are also in the public domain or you have their permission to pass their details on to me, I will also contact them directly, to see if their organisations are interested in taking part but would only do this once you have agreed to take part in the study.

- If the PIs agree to support the study they will be asked to forward the study information to the recruiting staff in their centre. The PIs will be asked what

management approval will be required by their organisation to carry out the study before staff are approached.

- The study information can be provided in electronic or paper format.

Thank you for taking the time to read this email/letter. Please do not hesitate to contact me if you have any queries or questions about the study. If I have not heard from you within 2 to 3 weeks I will presume you are happy for me to give you a call about the study to discuss further.

Kind Regards

Lesley Dunleavy

Lesley Dunleavy

International Observatory on End of Life Care

Faculty of Health and Medicine

Division of Health Research

Furness C67

Lancaster University

LA1 4YG

l.dunleavy@lancaster.ac.uk

01524 592183 (office)

Treweek, S., Lockhart, P., Pitkethly, M., Cook, J.A., Kjeldstrøm, M., Johansen, M., Taskila, T.K., Sullivan, F.M., Wilson, S., Jackson, C. and Jones, R., 2013. Methods to improve recruitment to randomised controlled trials: Cochrane systematic review and meta-analysis. *BMJ open*, 3(2).

Appendix 5: Example invitation letter/email to study participants

Email/letter to the staff involved in the recruitment of patients or carers in each clinical recruitment centre

Dear Dr, Sir or Madam,

I am currently undertaking a PhD in Health Research at Lancaster University and my area of interest is recruitment issues in palliative care RCTs. Recruitment is a real challenge in clinical practice with less than 50% of trials meeting their recruitment targets (Treweek et al 2013). The Chief Investigator for thetrial and your Principal Investigator have kindly agreed to support my research. I am contacting you to see if you would be interested in taking part in my study.

I wish to explore how those involved in the recruitment process carry out the recruitment of patients or carers to palliative care RCTs and to look at why they implement certain recruitment strategies and the factors that influence their choices. Having a greater understanding of this process has the potential to help address this complex but key issue in clinical practice.

I have attached a participant information sheet which explains more about what is involved in taking part in the study. If you are interested in taking part in the study or have any queries or questions please do not hesitate to contact me on the contact details below. Thank you for taking the time to read this letter/email.

Kind Regards,

Lesley Dunleavy

Lesley Dunleavy

International Observatory on End of Life Care

Faculty of Health and Medicine

Division of Health Research

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Lancaster University

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Treweek, S., Lockhart, P., Pitkethly, M., Cook, J.A., Kjeldstrøm, M., Johansen, M., Taskila, T.K., Sullivan, F.M., Wilson, S., Jackson, C. and Jones, R., 2013. Methods to improve recruitment to randomised controlled trials: Cochrane systematic review and meta-analysis. *BMJ open*, 3(2).

Appendix 6: Study Participant Information Sheet

Recruitment of patients or family carers to palliative care randomised controlled trials via health care professionals: A qualitative case study

My name is Lesley Dunleavy and I am conducting this research for my PhD in Health Research at Lancaster University.

What is the study about?

Randomised controlled trials (RCTs) are accepted as the 'gold standard' for evaluating the effectiveness of interventions in health care. Recruiting the required number of participants to RCTs remains a major challenge and this is especially so in palliative care. The purpose of this study is to explore how those involved in the recruitment process undertake the recruitment of patients and/or family carers to palliative care RCTs and to look at the strategies they use and why they make the choices they do. Having a greater understanding of this process has the potential to help address this complex but key issue in clinical practice.

Why have I been approached?

You have been approached because the study requires information from people who have experience of recruiting patients and/or family carers to palliative care RCTs. We understand you are or have been recently involved in a palliative care RCT. The Chief Investigator of the trial has agreed to support the study but you are under no obligation to take part. We are approaching people to be interviewed with different roles and experiences of the trial recruitment process from the study coordinating centre or from clinical recruitment centres.

Do I have to take part?

No. It is completely up to you to decide whether or not you want to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to confirm that you consent to take part in the study at the start of the recorded interview. If you do decide to take part, you are still free to withdraw without giving any reason. However, once your data has been anonymised and incorporated into themes it might not be possible for it to be withdrawn, though every attempt will be made to extract your data, up to the point of publication.

What will I be asked to do if I take part?

If you decide you would like to take part, you would be asked to:

- Confirm on the audio recording that you agree with the non-optional statements on the consent form prior to the start of the interview.

- Take part in a recorded telephone, WebEx/Skype or face to face interview with the researcher about your experiences of recruiting patients and/or family carers to a palliative care RCT. Participants who wish to use Skype should be aware that the internet cannot be guaranteed to be a completely secure means of communication. The interview will not involve discussion of individual patients and we must ensure that there is no disclosure of information about individual patients during the interview. The interview is expected to last around 30-60 minutes.

The part of the study that is optional:

- Confirm on the audio recording that you agree with the optional statement on the consent form.
- Provide the researcher with any non-patient identifiable documentation related to trial recruitment such as participant information sheets, posters, staff training presentations.

Will my data be identifiable?

The information you provide will be anonymised. The typed version of your interview will be made anonymous by removing any identifying information including your name, the trials name and the name of the site where recruitment is taking place or has taken place. Anonymised direct quotations from your interview may be used in the reports or publications from the study, so your name will not be attached to them. Trial documentation collected and analysed as part of this case study will also be anonymised prior to being reported or published.

However, given the small number of palliative care trials carried out in the UK, it is possible that you and the trial maybe identified because of information that is available about the trial in the public domain. We will take every step we can to anonymise the data and to use the data sensitively in this study.

How will my data be stored?

The data collected for this study will be stored securely and only the researcher and her supervisors will have access to this data. If a transcriber is used they will be asked to sign a Lancaster University confidentiality agreement and the audio files sent to the transcriber will be encrypted.

Audio recordings will be deleted once the project has been examined.

- Hard copies of written transcripts and study documentation will be kept in a locked cabinet.
- The files on the computer will be stored on a secure university password protected computer.

- At the end of the study, hard copies of written transcripts and study documentation will be kept securely in a locked cabinet for ten years. At the end of this period, they will be destroyed.
- All your personal data will be confidential and will be kept separately from your interview responses.

There are some limits to confidentiality: if what is said in the interview makes me think that you, or someone else, is at significant risk of harm, I will have to break confidentiality and speak to a member of staff about this. If possible, I will tell you if I have to do this.

What will happen to the results?

The results will be summarised and reported in a thesis and may be submitted for publication in an academic or professional journal and presented at national and international conferences. You will not be personally identified in any report or publication.

Are there any risks?

There are no risks anticipated with participating in this study. However, if you have any queries or concerns following participation you are encouraged to inform the researcher on the contact details listed below.

Are there any benefits to taking part?

Although you may find participating interesting, there are no direct benefits in taking part.

Who has reviewed the project?

This study has been reviewed by the Faculty of Health and Medicine Research Ethics Committee, and approved by the University Research Ethics Committee at Lancaster University.

Where can I obtain further information about the study if I need it?

If you have any questions about the study, please contact the main researcher:

Lesley Dunleavy

International Observatory on End of Life Care, Faculty of Health and Medicine, Division of Health Research, Furness C67, Lancaster University, LA1 4YG, 01524 592183 (office),
l.dunleavy@lancaster.ac.uk

Supervisors

Dr Catherine Walshe

International Observatory on End of Life Care, Division of Health Research, C52 Furness Building, Lancaster University, Lancaster, LA1 4YG, 01524 510124, c.walshe@lancaster.ac.uk

Dr Nancy Preston

International Observatory of End of Life Care, Faculty of Health and Medicine, Furness College, Lancaster University, LA1 4YG, 01524 592802, n.j.preston@lancaster.ac.uk

Complaints

If you wish to make a complaint or raise concerns about any aspect of this study and do not want to speak to the researcher, you can contact:

Professor Bruce Hollingsworth
Head of Division
Division of Health Research
Faculty of Health and Medicine
Lancaster University
Lancaster LA1 4YG
01524 594154
b.hollingsworth@lancaster.ac.uk

If you wish to speak to someone outside of the Division of Health Research, you may also contact:

Professor Roger Pickup
Associate Dean for Research
Faculty of Health and Medicine
(Division of Biomedical and Life Sciences)
Lancaster University
Lancaster LA1 4YD
01524 593746
r.pickup@lancaster.ac.uk

Thank you for taking the time to read this information sheet.

Appendix 7: Consent form

Recruitment of patients or family carers to palliative care randomised controlled trials: A qualitative case study

We are asking if you would like to take part in a research study that aims to explore how those involved in the recruitment process undertake the recruitment of patients and/or family carers to palliative care RCTs. Before you consent to participating in the study, we ask that you read the participant information sheet and confirm for the audio recording that you agree with each of the statements below. If you have any questions or queries before confirming your agreement to take part, please discuss the study with the main researcher, Lesley Dunleavy.

Date of consent: Please confirm for the audio recording

Name of participant: Please confirm for the audio recording

Name of researcher: Please confirm for the audio recording

1. I confirm that I have read the information sheet (version 2.1, dated 14/06/2017) and fully understand what is expected of me within this study
2. I confirm that I have had the opportunity to ask any questions and to have them answered.
3. I understand that my interview will be audio recorded and then made into an anonymised written transcript.
4. I understand that audio recordings will be kept until the research project has been examined.
5. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my legal rights being affected.
6. I understand that once my data have been anonymised and incorporated into themes it might not be possible for it to be withdrawn, though every attempt will be made to extract my data, up to the point of publication.
7. I understand that the information from my interview will be pooled with other participants' responses, anonymised and may be published.
8. I consent to information and quotations from my interview being used in reports, conferences and training events.
9. I understand that given the small number of palliative care trials carried out in the UK, it is possible that myself and the trial maybe identified because of information that is available about the trial in the public domain. I understand that every step will

be taken by the researcher to anonymise the data and to use the data sensitively in this study.

10. I understand that any information I give will remain strictly confidential and anonymous unless it is thought that there is a risk of harm to myself or others, in which case the researcher may need to share this information with her research supervisor.
11. I consent to Lancaster University keeping written transcriptions of the interview for 10 years after the study has finished.
12. I consent to take part in the above study.

The optional part of the study

13. I agree to provide non-patient identifiable documentation related to trial recruitment such as participant information sheets, posters, staff training presentations. I understand that any trial documentation collected and analysed as part of this case study will also be anonymised prior to being reported or published.

Appendix 8: Interview Topic Guide

This is a semi structured interview topic guide for those professionals/staff members involved in recruitment for the palliative care randomised controlled trials selected as 'cases' for this study. The interview topic guide will be iterative and flexible and the topics listed below may not necessarily be covered in order. It will be adapted as appropriate to reflect the individual characteristics of the trial and whether staff from the study coordinating centre is being interviewed or those from a clinical recruitment centre. The interview schedule may be modified and developed further as a result of the interview responses. How the topic guide relates to the '6 Ps' has been highlighted.

- The participant's professional and work experience related to research and palliative care.
- Roles and responsibilities, team composition (Working with partners: partner referrals and recruitment) and the characteristics of the setting/s where recruitment activity takes place (Place).
- Characteristics of the trial such as inclusion/exclusion criteria guided by the documentation obtained about the trial prior to the interview. (Product: defining the product/Identifying Participants: defining the target audience).
- Recruitment procedures for trial participants (How identified, approached and consented) (Working with partners: partners referrals and recruitment, Promoting the study, Price)
- Exploration of phraseology used to discuss the trial with participants (Promoting the study).
- How well the trial is recruiting or has recruited.
- What factors have helped or hindered recruitment to the trial. (Dependent on the responses of the participant)
- Recruitment strategies (Dependent on the responses of the participant)
- Lessons learnt about recruitment (Dependent on the responses of the participant)
- Any other issues (Dependent on the responses of the participant)

Appendix 9: Eligible trials available at time of screening with those approached highlighted (from 11/2016-10/2017)

	Trial design	Intervention	Setting	Trial Population	Multiple/ single centre	Chief Investigator	Funder
1	Wait list trial	Complex service intervention	Hospital	Non-cancer	Multiple	Academic/medical clinician	Public
2	Blinded placebo trial	Non pharmacological symptom control intervention	Hospice	Cancer	Single	Medical clinician	Charity
3	Feasibility trial	Digital application	Hospital	Non-cancer	Unknown	Academic/medical clinician	Charity
4	Parallel trial	Complex service intervention	Hospital	Cancer	Multiple	Medical clinician	Charity
5	Parallel trial	Psychological intervention	Hospital/ hospice	Cancer	Multiple	Academic/medical clinician	Public
6	Feasibility trial	Psychological intervention	Unknown	Cancer	Unknown	Academic/medical clinician	Public
7	Feasibility trial	Pain management (non-pharmacological)	Hospital outpatients /community	Cancer	Multiple	Academic/medical clinician	Public

8	Feasibility cluster trial	Artificial hydration	Hospital/hospice	Cancer	Multiple	Academic/medical clinician	Public
9	Phase 2 placebo trial	Analgesia	Hospital	Cancer	Single	Academic/medical clinician	Pharma/public
10	Parallel trial	Analgesia	Hospital/primary care	Cancer	Multiple	Academic/medical clinician	Pharma
11	Blinded parallel trial	Analgesia	Hospital/hospice	Cancer	Multiple	Academic/medical clinician	Pharma
12	Parallel trial	Psychoeducational intervention	Unknown	Cancer	Unknown	Academic	Public
13	Feasibility trial	Music therapy	Hospice	Cancer	Single	Academic	Charity
14	Feasibility trial	Long term drain	Hospital	Non cancer	Multiple	Unknown	Public
15	Feasibility trial	Educational symptom control intervention for carers	Primary care	Cancer and non-cancer	Multiple	Academic/medical clinician	Public
16	Feasibility trial	Advance care planning	Hospital	Non cancer	Multiple	Academic	Charity
17	Feasibility trial	Complex organisational intervention	Hospital	Cancer and non-cancer	Multiple	Academic	Public
18	Feasibility trial	Pharmacological symptom control intervention	Hospital	Cancer and non-cancer	Multiple	Academic/medical clinician	Charity

Appendix 10: Extract of interview from case one (early analysis in NVivo)

recruitment is challenging. Are there any other challenges that you think make palliative care research, you know to RCTs more difficult?

P Definitely, I mean the most I would say, the biggest challenge really is you know we're a specialist palliative care unit so the patients that come here, you know have got complex problems and the reason that they've been admitted is for us to try and help support them umm so they may you know be experiencing lots of pain or problems with their hearing or sight or you know so something that in my previous job was quite sort of straightforward, you know in terms of discussing the study,

you know going through the consent process, you know that could easily be done in you know 40 minutes to 45 minutes, obviously you would give them time to think and so on, now you know that can be a very lengthy process, you know I might start talking about a study and then something happens and I need to go away and then come back a little bit later on when it's a better time for them or you know I often you know they've said, you know I can't actually, I've not felt up to reading it or you know I can't read the information, you know so I have sort of read it to them and then gone through it with them so things just take a bit longer and you need oodles of sort of patience and also not giving up really. Cause it would be very easy to sort of say oh no you know, they were sick, that happened, you know I am not going to do that but just to go back but always making sure, are you happy to talk about it, is it a good time for you you know, I am happy to go away and come back tomorrow. I always sort of try and get other family members involved as well because I think that's really important and I certainly think from I know from the way I would feel if it were a family member. I think I would turn up and you know my parents said oh I am in a trial. Woh What have you signed up to? Sort of thing.

R Yes

P You know you think. You know, a lot of patients are quite vulnerable ummm so I think engaging with the family and talking to them and explaining what we're doing and why we're doing it that's really helpful umm and yes.

R I mean you've touched on there how you do engage with family, you know, how do you engage with family as you obviously think it's important?

P Yes, I mean, I just, I think, it's really, I mean it is a bit of double edged sword really as cause sometimes you get so many different opinions I mean I generally try and work out who the you know from the nursing staff, I go to handover in the morning so I hear you know who the next of kin is, and you know, you know, the husband you know he is in every day and he is there a lot of the

lengthy recruitment p

patient condition illness

feasibility and persist

Coding Density

lengthy recruitment process

level of medical staff engagement

seek second opinion

patients medication for talking part

patient condition illness

feasibility and persistence

stressing and anxiety nature of talking part

engaging with families

timing of approach

time, well you know he comes in every afternoon then I'll think oh right well perhaps I'll go and speak to them this afternoon if it's convenient but then sometimes I can go and they say actually no cause I am only going to here for an hour and I just want to spend that time with my wife and that's absolutely fine you know I'm always lead by the patient and by their loved ones and the other really really important thing is that I haven't said or explained is that one of the first things I say it's completely voluntary.

R yes of course

P participation is you know and if you decide it's not for you it won't affect your care in anyway, cause I think often the patients that we have can feel quite indebted if we've sorted things out but then on the other side of that we have patients that you know really enjoy being engaged with something and ask to be part of it and have said things like oh I felt like they gave up with me at the hospital, you know. I wasn't asked my opinion or my and then there are others that will say you know I think it is really important, I want to give something back, I want to help others umm you know that, those sort of feelings as well but when they do say that I always say well is it right for you as well you know, don't do that and compromise you know your own sort of wellbeing, so yes, I can't remember what the question was now sorry I have probably gone completely off track.

R no, you haven't at all, you were talking about how you engage family members and patients as well in the recruitment process.

P yes, I mean I try not to engage too many family members cause then it can just get really complicated but just sort of working at identifying the key people and having them involved. I think just sort out of politeness as well just I know if it was my mum or my dad that I would like to be ummm. I mean they would probably tell me that they did not want me involved but I would like to know about it, just at least read through the information and you know may have some questions umm. You know

R As you are probably aware, in the literature they do sometimes talk about you know carer gatekeeping, I mean is that something that you have some across you know with the (name of study)?

P ummm (pause) I suppose I have actually yes, I mean I kind of, I want to say no but truthfully I think I think there is a fair amount of gatekeeping and it is mainly with the medical staff.

R right ok

P quite senior medical staff umm some that just think we shouldn't be doing research, that it's not ethical that patients don't want to be bothered, they have too much going on and you know I'm always happy to hear their opinions but I often get a second opinion with other because there are certain members of staff that I know don't want to and I have tried, you know I have really tried to engage and I have done little sessions on research and why we do it and you know the importance of progress and so on. Umm but yes that's I say that's quite high up on what I find most challenging about my job really.

R right ok



Appendix 11: An example section of charting (original data summarised with short summary in bold) from case two for the classification ‘Working with partners: partner referrals and recruitment’.

Study participant/ documentation	Screening/ identification strategies	Multi-disciplinary team meeting	Screen clinical notes/clinic lists
Chief Investigator, case two		All potentially eligible patients discussed at MDT. They were lucky in that everybody with a diagnosis of (name of diagnosis) comes through a cancer multi-disciplinary team.	
Specialist nurse one, case two			Research nurses screened referral and patient lists. Research nurses looked at the referral and patients lists so they would all be aware of who was coming to clinic and who was suitable.
Specialist nurse two, case two			
Doctor, case two		All patients with (name of diagnosis) come through their (name of speciality) MDT so identified there and decision made regarding what trial to discuss. All of the patients with (name of diagnosis) come through their (name of speciality) MDT so they were identified there. Decision made at that point which way we thought they were going to go. If fit enough for chemotherapy/radiotherapy trial, they would see the oncologist. The nurse specialist would not talk to them about (name of trial). If not really suitable for treatment the nurse specialist would then try and see them at the time	

		they got their diagnosis from the (name of speciality) consultant and give them the information at that point.	
Research nurse one, case two		Patients would normally be identified at the MDT. Patients would normally be identified and discussed at the MDT. That is where they would get their initial diagnosis so they would be picked up then if we did not know about them previously.	Check clinic lists for eligible patients. Checks clinic lists for the (name of speciality) clinics.
Research nurse two, case two		Identify patients through the (name of speciality) MDT, PI a senior physician within the MDT, he is very proactive, process works well in practice. Identify patients through the (name of speciality) MDT. RN would forward all the details of the study comprehensively to everybody who attends the MDT and also have printed sheets of inclusion/exclusion available. PI for (name of trial) is a senior physician within that MDT and he is very very proactive. Feels process works well in practice.	
Research nurse three, case two		Cancer MDTs where they pick up a lot of their patients, thinks it is quite good, also have a regional MDT that runs at her site. RNs would attend the cancer MDT for the newly diagnosed patients. That is where they pick up a lot of their patients and get the results and she thinks it is quite good. Also have a regional MDT that runs at her site so all of the regional patients come through them, so feels they are quite lucky in that respect.	Screen from notes, clinic letters, pathology, scans. Recheck the details in the notes, screen all the clinics. Screen for eligible patients from the notes, clinic letters, pathology, scans and things. Even if already aware of patients, they recheck the details in the notes. Before clinic, RNs screen all the clinics and pick eligible patients up from there.
Research nurse four, case two			Screens notes, letters, pathology reports and clinic lists, doctors do not look at the nitty gritty of the inclusion criteria. She would read the notes, clinic letters/lists and pathology reports to identify patients and to make sure they actually fit the criteria. Expressed that doctors do not look at the

			nitty gritty of the inclusion criteria. Feels RNs should have the time to scrutinise the criteria and look through the notes properly. She likes doing things properly, thinks she is a control freak.
Research nurse five, case two		Made aware of patients through MDT, gets an email about the outcomes of the meeting, other team members attend. Made aware of patients diagnosis through the MDT meeting. Does not attend that meeting so much these days because of time, gets an email about the outcomes of that meeting. Other team members attend.	
Protocol, case two		Patients screened for eligibility in the MDT. All new patients discussed at the regional MDT will be screened during the meeting.	
Patient information sheet, case two		Patients screened for eligibility in the MDT. Discussion of your case with a number of different cancer specialists we have identified that you may be suitable to take part in this study.	

Appendix 12: An example section of descriptive mapping charting for the classification ‘Working with partners: Partner Education’ from case three.

Study participant/ information	Preparing for difficult conversations	Elements	Categories/sub-categories
<p>Chief Investigator one, case three</p>	<p>Easier in the intervention wards as facilitator who provided training on how to support patients and carers at the end-of-life. Much easier in the intervention wards, facilitator who worked with clinicians to help them understand what (inclusion criteria) was, not to be frightened of it, she provided training for them in supporting patients and their family members. Some RNs had not worked in end-of-life care, felt this was an issue in its own right.</p>	<p>Clinical educator</p> <p>Nursing background</p>	<p>Preparation for sensitive conversations (category)</p> <p>Training/formal training (sub-categories)</p> <p>Previous relevant clinical experience (sub-category)</p>
<p>Chief Investigator two, case three</p>	<p>Palliative care clinical shadowing for RNs RN with no palliative care clinical experience did some shadowing in clinical practice to increase her understanding of palliative care.</p> <p>Takes time and skill to assess and consent patients with cognitive impairment. RNs were unfamiliar with procedures in non-drug trials. Preparation and training needed. A lot of patients in one site were assessed as lacking capacity, when researchers met patients they felt they probably had capacity but were unwell. The consent process required a lot of facilitation and enablement. She felt it takes time and skill to explain a study to someone who might have a degree of cognitive impairment. She felt RNs were more familiar with</p>	<p>Clinical shadowing</p> <p>Assessing capacity</p>	<p>Preparation for sensitive conversation (category)</p> <p>Training/formal training (sub-categories)</p> <p>Training/formal training (sub-categories)</p>

	lack of capacity regulation in drug trials but they had never used an advance consent or consultee before and they were learning. Felt that should have prepared the RNs better and anticipated the need for training.	Advance consent/involving consultees	Training/formal training (sub-categories)
Researcher, case three	Clinical educator made staff feel more comfortable talking to patients and carers. Staff in the intervention arm felt much more comfortable speaking with the patients and relatives after a while as they had a clinical educator who worked with them for several months.	Clinical educator	Preparation for sensitive conversation (category) Training/formal training (sub categories)
Research nurse one, case three	No experience of patient denial, new situations. Accessed support from colleagues, RN colleagues did not want to work on study as felt uncomfortable and no palliative care experience. Never dealt with patients in denial before, a real shock for her, really interesting situations that had never come across before and did not know what to do. Accessed valuable support from the ward team, lead palliative care nurse and the Principal Investigator. Other research nurses in the team did not want to be involved in the study due to lack of experience and feeling uncomfortable. Details of clinical background removed to anonymise.	Nursing background Support/reflective practice Using a 'core team'	Preparation for sensitive conversation (category) Previous relevant clinical experience/previous experience of talking to palliative care patients and carers (sub-categories) Discussions with colleagues/research team discussions/discussions with the palliative care team (sub-categories)
Research nurse two, case three	Some RNs lacked experience and felt uncomfortable approaching palliative care patients, used a core team of nurses, needs to be considered. Some of her team did not like approaching eligible patients as they were not used to this type of patient. They managed this as a team by only involving core people who were comfortable and this did improve the situation a little. Felt important to think about who approaching patients to make sure comfortable and have got that expertise. She felt it got easier for her after	Nursing background using a 'core team'	Preparation for sensitive conversation (category) Previous relevant clinical experience/previous experience of talking to palliative care patients and carers (sub-categories) Discussions with colleagues/research team discussions (sub-categories)

	recruiting a couple of patients as you get used to what you were going to say. Details of clinical background removed to anonymise.		
Research nurse three, case three	More experience of palliative care studies would give you more confidence. Previous clinical contact helps. Did not think she was adequately prepared to approach patients about this study, having more 'exposure' to end-of-life care studies would give you a little bit more confidence. Patients she approached were already known to her, easier as you knew what they understood about their condition. Details of clinical background removed to anonymise.	Learning from other palliative care studies Previous clinical contact Nursing background	Preparation for sensitive conversation (category) Training/informal training (sub-categories) Previous relevant clinical experience/previous experience of talking to palliative care patients and carers (sub-categories)
Doctor case three	RNs fearful of having conversations, surprised at patient response, supported them through the process. New area of practice for RNs, those with palliative care experience supported those with less experience. Thought the RNs were fearful, they thought it was going to be worse than it actually was, patients were much more open about having those sorts of conversations, were quite surprised at how much the patients felt the benefits. He nurtured them through that process of understanding what it is like in palliative care and it is not as scary as it seems. Experienced team of RNs, some found it was a new area, more used to intervention trials. Patient conversations more challenging as talking about new issues, some had more experience of those sorts of conversations because of nurse training, providing support to the nurses who were a bit less experienced in that area.	Discuss with research team/palliative care team Nursing background Discuss with research team	Preparation for sensitive conversation (category) Discussions with colleagues/research team discussions/discussions with the palliative care team (sub-categories) Previous relevant clinical experience/previous experience of talking to palliative care patients and carers (sub-categories) Discussions with colleagues/research team discussions (sub-categories)

Protocol	Have to use the Mental Capacity Act's 4 step criteria to assess capacity.	Assessing capacity	Preparation for sensitive conversation (category) Training/formal training (sub-categories)
Participant information sheets (control and intervention)	Research nurse is highly trained to talk about sensitive issues but can refer to a colleague if required.	Nursing background	Preparation for sensitive conversation (category) Previous relevant clinical experience/previous experience of talking to palliative care patients and carers (sub-categories)

Appendix 13: Final analytical framework

Classification	Category	Sub-category	Sub-category	Elements
Working with partners: Partner referrals and recruitment	Recruiting clinical recruitment centres	Identifying clinical recruitment centres	National Institute for Health Research (NIHR) Clinical Research Network	funding/support
			Expression of interest	clinical area of interest
			Clinical professional networking	negotiating access, building relationships with clinicians
		Screening clinical recruitment centres	Reputation as a good clinical recruitment centre	clinical recruitment centre screening log, previous similar trial experience, previous recruitment record
			Clinical recruitment centre able to deliver the intervention	
	Identifying patients and carers	Who identifies potential participants		doctors, principal investigators, research nurses, specialist nurses, inpatient nurses
		Initial screening	Multi-disciplinary team meetings	screening by memory, screen for multiple studies, research nurse has a 'presence' in handover, team 'recce'/discussions, email referrals
			Screening tools	telephone reminder for principal investigator, screening crib list for research nurse, nurse led telephone line, screening logs, patient lists
			Clinicians apply own eligibility criteria	personality, patients do not want to be bothered, patients have too much going on, patient advocate
		Confirming eligibility	Active questioning	symptom assessment
			Checking patient medical notes	condition discussed with patient, screening pro-forma

Classification	Category	Sub-category	Sub-category	Elements
Identifying participants: defining the target audience	Type of eligibility criteria	Broad versus narrow eligibility criteria		
		Predicting prognosis		objective measure, subjective criteria, performance status scale, clinical judgement, risk of contamination in the control arm
Product: Defining the product	Level of patient and carer interest in the trial	Patient/carer interested		not a drug trial, pilot study, regular research nurse contact and support even in control arm, popular study/also includes carer, access to intervention after the trial, continue on current medication, access to extra medication
		Patient/carer not interested		no treatment, extra hospital visits, not interested in any trial, intervention not needed, not ready to talk about palliative care, time commitment
	Maintaining clinical equipoise	Managing patient expectations		implementing the blinding process, do not know if better or as good as standard care, maintaining a balance between the two arms, not over promoting the intervention arm, patients disappointed when allocated to the control, information they provide of equal benefit, not disadvantaged by being in the control arm, patients have preconceived ideas about which arm they want to be in
		Maintaining equipoise among clinical staff		maintaining clinical staff blinding, clinical staff have preconceived ideas about treatment benefits
Product: The Product's competition	Competing treatment trials			competing trial discussions, order of priority for studies, edit what present, present all studies eligible for, incentives
	Competing treatments			intervention routinely available, competing treatment discussions/decisions

Classification	Category	Sub-category	Sub-category	Elements	
Price: Type of costs	Patient condition	Psychological/emotional issues		not in right frame of mind, overwhelmed with information, dealing with uncertainty, level of acceptance of diagnosis	
		Unstable/fluctuating condition		deterioration, fatigue/tiredness, too poorly, complex symptoms, symptom burden, frail disease group, cognitive impairment	
	Participants motivations for taking part in the research	Altruism		give something back to help others	
		Purpose		do something valuable, gives them purpose	
		Potential benefit for themselves		benefit to themselves, nothing else working, nothing to lose, participate in something together, somebody interested in them	
	Costs for carers	Carer gatekeeping		not an issue, family raise concerns, 'heavy' gatekeeping, family annoyed	
		Proxy consent		time commitment	
	Costs for research nurses			limited support, working in isolation, time pressured, emotionally wearing, time consuming	
	Price: Minimising costs	Minimising patient burden	Reduce data collection burden		pilot study, study length, short questionnaires, questionnaires too long
			Consent process		research nurse support required to go through participant information sheet, simpler consent process, vary amount of information given
Choosing the best time to approach patients				visiting time, not at time of admission, short window between diagnosis and randomisation, before treatment, time of diagnosis, post diagnosis follow up appointment, re-approach, assessed on a patient by patient basis, not at time of discussions around uncertainty	

Classification	Category	Sub-category	Sub-category	Elements
	Minimising research nurse burden	Good support network		principal investigator support, specialist nurse support, clinical supervision, reflective practice, administrative support, ward team support
Place	Pool of potential participants	Recruiting from a single centre		low incidence of symptom burden, size of recruitment centre (hospice inpatients)
		Recruiting from multiple centres		high incidence of disease burden, fluctuating rates of eligible patients, 'patients are like buses'
	Understanding the patient's care pathway	Recruiting from a specialist hospital		diagnostic centre, recruitment centre catchment area (hospice catchment area), competing recruitment centres
		Recruiting from a non-specialist centre		hospital inpatients overestimating eligibility rates
	Travel to the clinical recruitment centre	Distance to travel		travel to specialist centre, travel costs covered
		Limited parking		
Working with Partners: Barriers to partnering	Resource issues	Availability of staff to support the research	Clinician rotation-turnover	medical staff rotation
			Research nurse availability	small part-time research team
			Principal Investigator availability	small part-time research team, propping up clinical services
			Staff not available to provide the intervention	Staffing issues
	Limited research infrastructure	Limited research funding	funding from commercial studies, no funding for networking activities, volunteer administration support	

Classification	Category	Sub-category	Sub-category	Elements	
			Research governance issues	research naïve clinical units, research governance support, indemnity cover, non-NHS sites	
	Health care professional gatekeeping	Gatekeepers	Medical staff	not ethical to be doing research with this population, overprotectiveness, reluctance to diagnose dying	
			Nursing staff	overprotectiveness	
			Research nurses	adapt the protocol, overt/covert	
		Research nurses strategies for managing gatekeeping	Accept clinical staff's opinion	not always appropriate to approach, accept certain clinical staff's opinion	
			Bypass clinical staff	bypass medical staff, bypass nursing staff, all patients should be offered research, seek second opinion	
	Lack of clinician engagement in research	Lack of medical staff engagement		limited knowledge of randomised controlled trials/research, research not seen as important, some more engaged than others, staff too busy	
		Lack of nursing staff engagement		staff too busy some more engaged than others	
	Promoting the study	Increase trial visibility	Organisational promotion of research		centre of excellence, want to improve care, research is core business
			Visibility on the internet		social media, trial website
Trial branding				acronym, merchandise	
Working with national organisations				newsletter, attend study days	

Classification	Category	Sub-category	Sub-category	Elements
	Key and careful messaging	Explaining palliative care	Symptom control	looking at quality of life, amended study title to focus on symptom control, fewer symptoms, not just end of life care, not interfere with treatments
			Extra support	extra support for patients, extra support for families, something slightly different
			Talking about death	associate with end of life, bereaved carer questionnaire, hospice care, ask questions about prognosis, advance care planning, loss of a loved one
		Explaining randomisation		clinical team unaware of allocation, clinical staff no control over allocation, patient no control over allocation, tossing a coin, use percentages, decided by computer, difficult to understand, patients struggle to retain the information, the need to check understanding
		Written participant information	Using the participant information sheet	Written prompts, too long, too complicated/wordy
			Preparing participant information	Patient and public involvement input
	Building trust and rapport	Engaging family carers		Joint patient/carer discussions, joint decision, carer participant, carer non participant, courtesy to involve
		Previous clinical contact		dual clinical roles, explain differences in roles to patients
		Stress voluntary nature of taking part		being honest about what is involved, not affect care if decline, can withdraw at any time, no coercion, process consent

Classification	Category	Sub-category	Sub-category	Elements
	Flexibility and respectful persistence	Initial approach	First approach by doctor	principal investigator approaches first, lead clinician approaches first, doctor seeks patient permission for research nurse to approach
			First approach by specialist nurse	specialist nurse seeks patient permission for research nurse to approach
			First approach by specialist nurse and doctor	
		Follow up contact	Face to face follow up	medical permission for research nurse to approach patients, research nurse/doctor/specialist nurse/principal investigator follow up/multiple follow up visits/proxy consent
			Telephone follow up	research nurse/specialist nurse telephone follow up
Working with partners: Partner education	Preparation for sensitive conversations	Previous relevant clinical experience	Previous experience of discussing randomised controlled trials with patients and carers	nursing background
			Previous experience of talking to palliative care patients and carers	nursing background
		Discussions with colleagues	Research team discussions	using a 'core team'
			Discussions with the palliative care team	Pre-existing clinical relationship
		Training	Formal training	clinical educator, clinical shadowing, assessing capacity, advance consent/involving consultees
			Informal training	knowing the study inside out, learning from other palliative care studies

Classification	Category	Sub-category	Sub-category	Elements
	Engaging clinicians in clinical recruitment sites	Research champion	Dedicated specialist nurse	nurse principal investigator
			Support of lead clinician	medical principal investigator, consult service, principal investigator on site, selection of principal investigator pragmatic choice
		Personal repeated contact with clinicians	Formal strategies	presentations, attend staff meetings, email communication, dissemination of research findings, attend handover/multi-disciplinary team meeting
			Informal strategies	one to one contact, being approachable, networking, provide research advice and support, being accessible, out of hours support
	Engaging recruiting staff in clinical recruitment centres	Regular study coordinating centre contact with clinical recruitment centres	Site initiation process	provide study materials, opening sites remotely
			Ongoing trial management support and advice	site visits, email communication, trial teleconference newsletters, incentives (recruitment tariff, Ipad), close down quickly if do not recruit

Appendix 14: Within case analysis

In this appendices, a summary of the within case analysis findings for the three cases is presented in relation to the '6 Ps' of the 'Social Marketing Mix Framework', as this was the a priori framework used in this study. An 'abbreviated vignette' of each of the three cases is presented in chapter five to provide contextual information for the detailed cross-case analysis in chapters five and six. The summaries below highlight the differences in clinical setting and study design between the three cases. The cases were purposively selected because of these differences to reflect the concept of theoretical replication as discussed previously (Yin, 2018).

As discussed in chapter five, data collection for the three selected cases was carried out sequentially and occurred between March 2017 and June 2018. Nineteen participants took part in a telephone interview and the mean interview length was 39 minutes (range 25–60 minutes). The data collection details for each of the individual cases is included in the vignettes below.

Case one

Case one largely took place in a single voluntary organisation. Another specialist palliative care unit also recruited a small number of participants to this study but they were unable to take part in an interview due to staffing shortages. All of the recruiting staff involved in the trial at the primary voluntary organisation agreed to take part in a telephone interview. The main research nurse for this study worked part time and often on her own. The Chief

Investigator also worked in another organisation so was not always available to recruit to the trial. As the study was taking place in a charitable organisation and outside the National Health Service, a volunteer was used for research administrative support. The organisation funded research nurse time by working on studies that had financial incentives including commercial studies. One of the research nurses also had a clinical role within the organisation.

Case one ‘vignette’

Characteristics of the case	
Trial design	A double blind non-pharmaceutical placebo controlled trial
Intervention	Non-pharmaceutical intervention
Control	Non-pharmaceutical placebo
Participants	Patients with advanced cancer
Primary Outcome	Symptom control
Study duration	≤ one week
Single or multi centre	Largely single centre
Setting	Hospice inpatients
Recruitment target	The recruitment rate was described as slow and at the time of data collection, approximately 83 % of the recruitment target had been met. This had taken a number of years to achieve and took longer than anticipated.
Recruitment achieved	≤ 60 patients recruited over a 7.5 year period
Recruitment procedures	In summary in case one, medical staff, usually the Chief Investigator, would initially approach the patient about the trial in the inpatient unit: <i>‘I think largely it’s for me to identify people on our ward rounds or when we go and see them. This is a study that is looking at hospice inpatients and then I’ll flag them up, I’ll mention the study to the patient and then flag them up to the</i>

	<p><i>research nurse to go and have a further chat with them.'</i> (Chief Investigator, case one)</p> <p>The research nurses would then discuss the study with the patient, provide written information and if the patient wished to enter the trial, they would then obtain written informed consent.</p>
Participant characteristics, data collected and analysed	
Period of data collection	03/2017-05/2017
Number of interviews	3 interviews
Mean interview length	38 minutes (range 25-55)
Type of participant	Principal Investigator/Palliative Medicine consultant (also the Chief Investigator for the trial)=1 Research nurse=2
Prior experience in palliative care trial recruitment	All of the participants were experienced in recruiting to palliative care studies including trials.
Type of documentation collected and analysed	Study protocol, patient information sheet, patient consent form, GP letter, UK Clinical Trials Gateway website, results paper.

Summary of the within case analysis for case one

Identifying participants: defining the target audience
<ul style="list-style-type: none"> • An estimation of the patient's prognosis was required when determining eligibility. • Patients could not take part in the study if they were sharing a room with somebody already in the trial to avoid contamination.
Product: Defining the product
<ul style="list-style-type: none"> • A pilot study assessed the trial's acceptability to patients. • Patients could continue on their symptom control medication and access extra as needed. They could access the intervention after the trial if they found it helpful. • Managing patient disappointment when allocated to the control arm was less of an issue in this trial as it was not a pharmaceutical symptom control trial.

Product: The product's competition
<ul style="list-style-type: none"> • Patients were ineligible if they or a close relative had used the intervention before. The intervention was routinely available so this excluded quite a few participants
Price: 'Type of Costs' and Price: 'Minimising the costs'
<ul style="list-style-type: none"> • Symptom burden and fatigue had an impact on the patient's ability to engage in the recruitment process. • To minimise study burden, research nurses would read and go through the participation information sheet and consent form with patients. • Recruiting staff felt that the trial was attractive to patients, as it only required a small amount of their time. • Carer gatekeeping did not appear to be an issue in this trial. • Research nurses allowed patients time to process or digest what was happening to them before introducing the trial (generally not within 48 hours of admission). • Working within the hospice as a research nurse could feel isolating and not like working as part of a hospital team.
Place
<ul style="list-style-type: none"> • The recruitment rate was described as slow as they were largely recruiting from a single centre voluntary organisation with a small number of beds.
Promoting the study
<ul style="list-style-type: none"> • The hospice promoted research as part of its '<i>core business</i>' (<i>Chief Investigator, case one</i>). • The research nurses used a flexible and respectfully persistent approach when recruiting patients because of their physical, psychological and emotional well-being and the need to work around clinical care and family visiting times. • Research nurses would seek medical permission before approaching patients about the trial. • Research nurses felt it was important to engage carers in the recruitment process to build trust and rapport because of the patient's vulnerability. • There was a need for key and careful messaging when explaining the concept of randomisation as it was a difficult concept for patients to understand.
Working with partners: barriers to partnering
<ul style="list-style-type: none"> • Health care professional gatekeeping was an issue but research nurses did not always accept the clinician's view that the patient was not eligible. This was dependent on how much they trusted the opinion of the staff member. They would sometimes seek a second opinion from the lead medical clinician who was the Chief Investigator. • A useful strategy for managing gatekeeping was identifying and using the support of staff who were the most engaged in research. • Clinician rotation and turnover in the hospice made medical staff engagement particularly challenging for the research nurses.

Working with partners: partner education

- The 'research champion' was the lead medical clinician in the hospice.
- Research nurses used a number of strategies to engage with clinicians including one to one contact, email communication, research presentations and attending staff and multi-disciplinary team meetings.

Working with partners: partner referrals and recruitment

- Research nurses attended the inpatient unit 'handover' to screen for potential participants.
- Confirmation of trial eligibility required checking with the patient that they were still symptomatic.
- The Chief Investigator was proactive and networked with medical colleagues to promote his organisation as a potential clinical recruitment centre.

In summary, case one was a double blind non pharmaceutical placebo controlled trial for symptom control, largely recruiting patients with advanced cancer from inpatients within a single voluntary organisation. The recruitment rate was described as slow with ≤ 60 patients recruited over a 7.5 year period. The Chief Investigator was a doctor and all of the interviewees were experienced in recruiting to palliative care studies, including trials. Clinician prognostication was required when 'identifying participants'. Managing patient disappointment when they were randomised to the control arm was less of an issue in this trial as the 'product' was not a pharmaceutical symptom control intervention. Research nurses supported symptomatic and fatigued patients through the recruitment process to 'minimise the costs' of taking part. They would seek medical permission to 'promote' the trial to patients and used key and careful messaging when explaining randomisation. Health care professional gatekeeping and clinician rotation and turnover was a 'barrier to partnering'. Research nurses used a number of 'partner education' strategies to engage clinicians in the recruitment process and the lead medical clinician was the 'research champion' within the organisation. The inpatient unit 'handover' was used to screen for

eligible 'partner referrals' and the Chief Investigator used their medical contacts to promote his organisation as a research site.

Case two

In this case study, five clinical recruitment centres out of the 18 that were approached via the study coordinating centre agreed to take part and this included three specialist tertiary centres. All but one of the clinical recruitment centres that agreed to take part, a specialist tertiary hospital, had met their recruitment targets. Two of the sites that agreed to participate had recruited the highest number of participants in the trial. These sites were the study coordinating centre and a specialist tertiary hospital. Nine out of the 15 recruiting staff approached across the five cases agreed to participate in an interview. The main reason, when given, for staff declining to take part in the study was lack of time.

Case two 'vignette'

Characteristics of the case	
Trial design	Two arm parallel trial, no blinding
Intervention	Complex service intervention
Control	Usual care
Participants	Patients (and their family carers) newly diagnosed with advanced cancer (within six weeks of diagnosis and not on chemotherapy at time of enrolment)
Primary Outcome	Quality of life
Study duration	24 weeks

Single or multi centre	Multi centre
Setting	Secondary or specialist tertiary hospital outpatient departments
Recruitment target	≤ 200 patients in 2 years over 10 sites
Recruitment achieved	≤ 200 patients in 30 months over 20 sites
Recruitment procedures	In summary in case two, the lead medical clinician and/or specialist nurse would initially approach the patient and carer about the trial in the outpatient department. Depending on the clinical recruitment centre, the research nurse, specialist nurse or doctor would then follow the patient up and obtain written informed consent from those participants who wished to take part in the trial.
Participant characteristics and data collected and analysed	
Period of data collection	10/2017-12/2017.
Number of interviews	9 interviews
Mean interview length	36 minutes (range 25-52)
Type of participant	Principal Investigator/Hospital consultant (also the Chief Investigator for the trial)=1 Principal Investigator/Hospital consultant=1 Principal Investigator/Specialist nurse=1 Specialist nurse=1 Research nurse=5
Prior experience in palliative care trial recruitment	The Chief Investigator, also the Principal Investigator in the study coordinating centre, was an experienced hospital consultant and clinical researcher in (name of speciality) medicine. They were a generalist palliative care professional rather than a specialist palliative care professional. In the other participating centres, the Principal Investigators were hospital consultants apart from one site, a specialist tertiary centre, where the role was carried out by a cancer specialist nurse. This was not the first time the specialist nurse had taken on the role of Principal Investigator in a (name of speciality) trial. All of the interviewees were experienced in recruiting to trials but case two was the first specific or 'overtly' (Specialist nurse two, case two) palliative care trial they had recruited to. All of the clinical recruitment centres had research nurse support and in one of the sites, the research nurses had both clinical and research roles. The research nurses that were interviewed came from a variety of nursing

	backgrounds but currently worked on oncology studies. Both of the cancer specialist nurses that took part in this study had worked in this role for a number of years.
Type of documentation collected and analysed	Study protocol, patient information sheet, patient consent form, carer Information sheet, carer consent form, carer GP letter, patient study recruitment poster, trial recruitment figures for each hospital site, monthly recruitment figures for site four, an invitation to participate in the trial for clinical recruitment centres, 'Frequently asked questions' document for health care professionals, published protocol, published results papers, UK Clinical Trials Gateway website.

Summary of the within case analysis for case two

Identifying participants: defining the target audience
<ul style="list-style-type: none"> • The inclusion criteria included a performance status scale to aid prognostication. • The eligibility criteria were broad which facilitated recruitment to the trial.
Product: Defining the product
<ul style="list-style-type: none"> • Research nurses felt patients were interested in the trial as it involved both patients and carers, and ensured regular research nurse support, even in the control arm. • Research nurses described how some patients and carers were not interested in the trial. This could be because; it was not a treatment trial; they felt they did not need the intervention; they did not want to commit to the extra hospital visits or they were not interested in taking part in any trials. • Patients and health care professionals were not always in clinical equipoise. • Managing patient disappointment when they were allocated to the control arm was less of an issue for recruiting staff in this trial as it was not a treatment trial. Patients could still access support in the control arm.
Product: The product's competition
<ul style="list-style-type: none"> • Competing treatment trials recruiting from the same patient population was a key barrier to recruitment especially in the specialist centres. Treatment trials were prioritised by health care professionals.

<ul style="list-style-type: none"> • There was only a short window of opportunity for recruiting staff to enrol patients into the trial (within six weeks of diagnosis and before was chemotherapy commenced).
Price: ‘Type of Costs’ and Price: ‘Minimising the costs’
<ul style="list-style-type: none"> • Recruiting staff were concerned about the patient’s psychological and emotional well-being as they had just been diagnosed with advanced cancer. • Nurses felt it was important to adopt an individualised approach when introducing the trial to patients and carers. • Research nurses felt carer gatekeeping was not a notable issue in this trial.
Place
<ul style="list-style-type: none"> • Having to travel to the hospital sites and the difficulties of parking deterred some patients from taking part in the trial. • There was a need for the study coordinating centre to understand the patient’s care pathway to identify when patients may be receptive to receiving information about the trial.
Promoting the study
<ul style="list-style-type: none"> • The study coordinating centre had a presence on the internet and used trial branding to promote the trial. • There was a need for key and careful messaging when explaining the concept of randomisation as it was a difficult concept for patients to understand. • Patients and carers could often associate palliative care with end-of-life care. Explaining palliative care could be challenging for recruiting staff and they explained it in terms of symptom control and extra support. • There was a requirement to discuss a bereavement questionnaire at the time of consent which could make research nurses feel uncomfortable. • Previous clinical contact with the patient made promoting the trial less demanding for research nurses.
Working with partners: barriers to partnering
<ul style="list-style-type: none"> • Research nurses and medical staff acted as gatekeepers in this trial. • Some eligible patients were missed as research nurses were unavailable as they were working on other studies.
Working with partners: partner education
<ul style="list-style-type: none"> • The study coordinating centre kept in regular contact with clinical recruitment centres to promote engagement. • Research nurses gained their experience of caring for palliative care patients while working in oncology and/or on oncology trials. • Research nurses prepared themselves for sensitive discussions by discussing as a team and sometimes seeking advice from the palliative care team. • Specialist nurses acted as research champions in this trial. They played a key role in the recruitment process and the research nurses valued their input.

Working with partners: partner referrals and recruitment

- The cancer multi-disciplinary team meeting was a key strategy for identifying eligible patients in this trial.
- Clinical recruitment centres were recruited via the National Institute for Health Research Clinical Research Network and the professional medical contacts of the Chief Investigator.
- Organisations needed to demonstrate their reputation as a good clinical recruitment centre to be involved in the trial.
- In this trial, organisations also needed access to staff who were able to deliver the intervention.

In summary, case two was a multi-centre parallel trial of a complex service intervention for patients (and their family carers) newly diagnosed with advanced cancer. The trial recruited from secondary or specialist tertiary centre outpatients and ≤ 200 patients were recruited in 30 months over 20 sites. The Chief Investigator was a doctor and the Principal Investigators were doctors apart from one site where the role was carried out by a specialist nurse. All of those interviewed were experienced in recruiting to trials but this was the first palliative care trial they had recruited to. The trial's eligibility criteria were broad which facilitated 'identifying participants' but patients and health care professionals were not always in clinical equipoise. The 'products competition' were treatment trials recruiting from the same patient population. Patients were newly diagnosed with advanced cancer so recruiting staff were concerned about their emotional well-being, and so they adopted an individualised approach when introducing the trial to 'minimise costs'. Travel to and limited parking at the 'place' of recruitment deterred some patients from taking part in the trial. Explaining palliative care could be challenging for recruiting staff but having had previous clinical contact with the patient made 'promoting' the trial less demanding. Research nurses working on other studies was a 'barrier to partnering' in this trial. Specialist nurses acted as

‘research champions’ in case two and research nurses used their colleagues and the palliative care team to prepare for sensitive discussions with patients and carers. Cancer multi-disciplinary team meetings were used to identify potential participants and clinical recruitment centres were recruited via the National Institute for Health Research and the professional medical contacts of the Chief Investigator.

Case three

In case three, all of the study coordinating centre staff agreed to take part in a telephone interview and four out of the 11 recruiting staff approached agreed to participate in the study. The main reason, when given, for staff declining to take part in the study was lack of time. All of the staff interviewed were from two of the clinical recruitment centres that had not reached their recruitment targets. One of these centres had been delayed opening due to staffing issues but once opened reached nearly half of its target within three months.

Case three ‘vignette’

Characteristics of the trial	
Trial design	Feasibility, parallel cluster trial
Intervention	Complex organisational level intervention
Control	Usual care
Participants	Advanced cancer and non-cancer patients at the end of life (or proxy if required)
Primary Outcome	Symptom control and quality of life
Study duration	2 weeks
Single or multi centre	Multi centre

Setting	Hospital inpatients (general medical wards)
Recruitment target	40-45 patients in each arm over three months.
Recruitment achieved	Only half of the sites reached their recruitment target with recruitment taking longer than the anticipated three months. One of the sites (intervention) took six months to reach its recruitment target while the other (control) took four and a half months.
Recruitment procedures	<p>In summary in case three, usually the trial would be initially introduced to the patient by the lead medical clinician. In the intervention arm, a specialist nurse was employed to coordinate the implementation of the intervention and they would sometimes introduce the trial to the patient. The research nurses would then approach the patient to discuss the study further and obtain written informed consent from those who wished to take part in the trial. If the patient lacked capacity, a consultee would be approached to provide proxy assent:</p> <p><i>'...so you know if she'd been in (specialist nurse) she would say to me when I got on the ward right this patient's done, fully discussed, documented, they're aware of the study, you just need to go in and talk to them.'</i> (Research nurse one, case three)</p> <p>Some research nurses declined to work on the trial and the reasons why are explored in chapter six.</p>
Participant characteristics and data collected and analysed	
Period of data collection	03/18-06/18
Number of interviews	7 interviews
Mean interview length	43 minutes (range 32-60)
Type of participant	<p>Chief Investigator/senior academic (non-medical professionals)=2 Researcher based in the study coordinating centre=1 Principal Investigator (control arm)/Palliative medicine consultant=1 Research nurse (intervention arm)=1 Research nurse (control arm)=2</p>
Prior experience in palliative care trial recruitment	The Chief Investigators were experienced palliative care researchers but one of them had not worked on a trial before. The Principal Investigator that was interviewed had been involved in palliative care randomised controlled trials previously but this was their first cluster trial. All of the nurses were experienced research nurses and had

	experience of recruiting to trials. Two of the nurses had worked on palliative care studies previously but not randomised controlled trials.
Type of documentation collected and analysed	Study protocol, patient information sheet (intervention and control), patient consent form, carer Information sheet (intervention and control), carer consent form, consultee information sheet (control and intervention), consultee approval form for continued participation if capacity is lost, recruitment letter to bereaved relative, trial recruitment figures for each site, clinical scenarios and materials to support recruitment for health care professionals, published study conference posters, published results papers, UK Clinical Trials Gateway website

Summary of the within case analysis for case three

Identifying participants: defining the target audience
<ul style="list-style-type: none"> • Medical staff were required to estimate the patient's risk of dying during the hospital admission. This eligibility criteria could be challenging to implement especially in the control arm. • There was a risk of contamination if medical staff were supported and trained in how to apply this eligibility criteria. The risk of dying criteria was removed from the control arm during the trial for pragmatic reasons.
Product: Defining the product
<ul style="list-style-type: none"> • Randomisation occurred at the organisational level rather than the individual level as it was a cluster trial. The intervention was aimed at the organisation rather than directly at the patient or carer but they were asked to complete questionnaires.
Product: The product's competition
<ul style="list-style-type: none"> • There were no trials competing for the same patient population within the hospital inpatient units at the time of recruitment.
Price: 'Type of Costs' and Price: 'Minimising the costs'
<ul style="list-style-type: none"> • The patient's unstable and fluctuating condition influenced their ability to engage in the recruitment process. • Research nurses were concerned about the length of the study information. They read and went through the documentation with patients to try and minimise study burden. • Recruiting staff were also concerned about the burden of data collection for patients.

<ul style="list-style-type: none"> • The costs of taking on the role of consultee could be too burdensome for some carers. • Research nurses were not always clear about who was able to act as a consultee and could lack confidence and skill when assessing capacity. • Carer gatekeeping was an issue in this case. Research nurses were worried in some instances that families may make a complaint.
Place
<ul style="list-style-type: none"> • The clinical recruitment centres were non-specialist hospitals and they had less eligible patients than predicted. Sites needed to be kept open to recruitment longer than anticipated.
Promoting the study
<ul style="list-style-type: none"> • There was no need for recruiting staff to explain randomisation as part of the informed consent procedure as it was a cluster trial. • The research nurses used a flexible and respectfully persistent approach when recruiting patients because of their physical, psychological and emotional well-being and the need to work around clinical care and family visiting times. • A minority of patients became distressed when they were introduced to the trial. • Carers were invited to complete a questionnaire post bereavement rather than at the time of consent. This could still make research nurses feel uncomfortable.
Working with partners: barriers to partnering
<ul style="list-style-type: none"> • It was challenging for research nurses to engage medical staff in the inpatient setting because of clinician rotation and turnover. • In one of the sites, research nurses worked as a generic research team to ensure recruitment could continue if the nurse was unavailable. A nurse would act as the lead for the study while other research nurses would assist when necessary.
Working with partners: partner education
<ul style="list-style-type: none"> • Specialist palliative care professionals who had a consulting role within the clinical recruitment centre also took on the role of 'research champion' but they were often unavailable and did not have overall responsibility for the patient's care. • Research nurses who had previous experience of talking to palliative care patients and their carers and/or previous clinical contact appeared to find having sensitive conversations less emotionally demanding than those without similar experience. • Clinical recruitment centres had to use a core team of research nurses who felt comfortable working on the study.
Working with partners: partner referrals and recruitment
<ul style="list-style-type: none"> • The Chief Investigator, a non-medical academic, needed to build up relationships with clinicians in clinical recruitment centres to negotiate access and this could take a long time. • To be eligible to take part in the trial, organisations needed access to staff who were able to deliver the intervention.

- Research nurses used routine multi-disciplinary team meetings on the inpatient units to screen for potentially eligible participants.
- The lead medical clinician was responsible for confirming trial eligibility but some medical staff appeared reticent and fearful of making the decision that the patient may die under their care. This decision required them to have a difficult conversation with the patient.

In summary, case three was a multi-centre feasibility cluster trial of a complex organisational level intervention for patients (or proxy if required) with advanced cancer or non-cancer at the end of life. The trial recruited from non-specialist hospital inpatients and only half of the four sites reached their recruitment target. The Chief Investigators were non-medical senior academics and experienced palliative care researchers. All of the research nurses who took part in the interview had general trial recruitment experience. Medical staff were required to predict the patient's risk of dying when 'identifying participants' which was challenging to operationalise especially in the control arm. Research nurses were concerned about the 'costs' of consent procedures for patients because of their condition. Carer gatekeeping was an issue in this trial and research nurses could be concerned that families may make a complaint. When 'promoting' the trial research nurses used a flexible and respectfully persistent approach because of the patient's condition. A minority of patients became distressed when they were introduced to the trial. Clinician rotation and turnover in the inpatient setting was a 'barrier to recruitment' in this trial. Those research nurses with previous palliative care experience and/or who had previous clinical contact with the patient found having sensitive conversations less emotionally demanding. Some research nurses declined to work on the trial. Confirmation of trial eligibility was the responsibility of the lead medical clinician but they could be reticent and fearful of making the decision that the patient may die under their care because it required

them to have a difficult conversation with the patient. Negotiating access into clinical recruitment centres required the Chief Investigator, a non-medical academic, to build up relationships with clinicians which could take a long time.

To conclude, a summary of the within case analysis findings for the three cases is presented in relation to the '6 Ps' of the 'Social Marketing Mix Framework', as this was the a priori framework used in this study. The summaries highlight the differences in clinical setting and study design between the three cases. An 'abbreviated vignette' of each of the three cases is also presented in chapter five. This is to provide contextual information for the detailed cross-case analysis that is outlined in chapters five and six.