Managing uncertain recovery for patients nearing the end of life in hospital; a mixed-method, feasibility cluster randomised controlled trial of the AMBER care bundle

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Abstract

Background The AMBER (Assessment; Management; Best practice; Engagement; Recovery uncertain) care bundle is a complex intervention used in UK hospitals to support patients with uncertain recovery. However, it has yet to be evaluated in a randomised controlled trial (RCT) to identify potential benefits or harms. Aim To investigate the feasibility of a cluster RCT of the AMBER care bundle. Methods Mixed-method, feasibility cluster RCT. Prospective, quantitative data collected from patients (or proxies lacking capacity) to (i) examine recruitment, retention and follow-up rates; (ii) test trial data collection tools and determine their optimum timing; (iii) test methods to identify use of financial resources; (iv) explore the acceptability of study procedures for health professionals and patients. Descriptive statistical analyses and thematic analysis using the Framework approach. Results 894 patients were screened, of whom, 220 were eligible and 19 (8.6%) declined to participate. Recruitment to the control arm was challenging; of the 728 patients screened, 647 (88.9%) were excluded. 65 (81.3% of the recruitment target) patients were recruited. Many were elderly (≥80 years 46.2%, n=30, mean-77.8 years SD=12.3 years). Over half (53.8%) had a non-cancer diagnosis, with a mean of 2.3 co-morbidities. 24.6% patients (n=16) died during their hospital stay and 35.4%, (n=23) within 100 days of discharge. In both trial arms, baseline IPOS subscale scores identified 'moderate' patient anxiety (mean 13.3 (SD 4.8) control, 13.3 (SD 5.1) intervention), and howRwe identified a 'good' care experience (mean 13.1 (SD 2.5) control, 11.5 (SD 2.1) intervention). Collection of quantitative service use/quality of life data was feasible. No patient participants regarded study involvement negatively. Focus groups with health professionals identified concerns regarding (i) subjectivity of the intervention eligibility criteria; (ii) the need to prognosticate to identify potential patients; (iii) consent procedures and questionnaire length. Conclusions A full trial of the AMBER care bundle is technically feasible but impractical due to inherent issues with recruitment arising from the intervention eligibility criteria. Since this complex intervention continues to be used in clinical care and advocated in policy, alternative research approaches must be considered and tested.

Background

Clinical uncertainty in hospital settings

Clinical uncertainty has been defined as the inability to determine the meaning and significance of illness-related events (1). It occurs in situations where health professionals are unable to accurately predict outcomes due to insufficient information. Evidence suggests that in the last 30 days of life, a combination of deteriorating health and clinical uncertainty are highly distressing for patients in hospital, and their families (2, 3). This is amplified when discussions about their situation, preferences for care and location of death are absent; the majority (67-80%) of people want to be informed about poor prognosis (4). Research, however, has identified that discussions about prognosis rarely occur (5). This increases the likelihood of hospital deaths and also leads to poor care satisfaction, mistrust, and loss of confidence among health professionals (6-9) and may lead to complaints (10). Clinical uncertainty also impacts on clinicians' confidence and their practice. Health professionals frequently struggle with uncertainty, which

can result in overtreatment or over-investigation (11), lack of communication with patients about their future (12, 13), and increased care costs (14).

The potential for better care and the AMBER care bundle

In recent years, complex interventions (15, 16), aimed at improving the care of patients who may be approaching the end of life, have become more common (17) (18). In 2010, the AMBER care bundle was developed to improve care in the acute hospital setting for patients who are: deteriorating, clinically unstable with limited reversibility, and at risk of dying in the next one to two months (19). This was subsequently amended to be at risk of dying during a patient's episode of hospital care, despite treatment. The AMBER care bundle's algorithmic intervention is designed to encourage health professionals to work with patients and families to develop and document a clear medical plan, including consideration of anticipated outcomes, cardiopulmonary resuscitation and escalation status, while acknowledging the uncertainty. This plan is revisited daily and encourages regular communication with the patient and family regarding treatment plans, place of care and any other concerns. The bundle was designed to work alongside active medical care when uncertainty about the outcome remains.

A recent non-randomised comparative study of the AMBER care bundle with standard care, conducted in the United Kingdom (UK), identified mixed findings. In comparison to similar patients in the control group, the use of the AMBER care bundle was associated with shorter lengths of hospital stay, increased frequency of discussions about prognosis between health professionals and patients, and higher awareness of prognosis by patients. Clarity of information, however, was rated lower than those in the control group (20). Qualitative research among health professionals has identified that the AMBER care bundle was often used as a tool to label or categorise patients, and indirectly served a symbolic purpose in affecting behaviours of individuals and teams. Participants described the importance of the training associated with the intervention but reported that adequate exposure to the intervention, and the learning, varied (21).

Clinical equipoise therefore still exists in relation to the AMBER care bundle. A robust comparative evaluation of the intervention compared to standard care is therefore needed. The UK Medical Research Council (MRC) guidance on the development and evaluation of complex interventions (22), and the Methods of Researching End-of-life Care (MORECare) statement (16) both recommend a feasibility study before a full evaluation. Feasibility studies, now more common in palliative and end of life care (23), enable researchers to identify problems that might undermine the acceptability and delivery of the intervention or the conduct of a fully-powered trial (24) (25). Researchers are then potentially able to remedy problems with the intervention or trial design or conduct, by returning to the development phase, rather than proceeding to a full trial. This has important implications for the efficient use of resources, ensuring they are not directed to studies that produce a null result due to unfeasible study design (26). Moreover, it is also unethical.

In this paper, we report on the feasibility of conducting a pragmatic, multi-centre, cluster randomised controlled trial of a hospital-based, complex intervention (the AMBER care bundle) to better serve patients

whose situations are clinically uncertain and where there is a risk that they will die during their hospital admission, versus standard care. Four feasibility objectives were specified:

1. To examine recruitment, retention and follow-up rates;

2. To test trial data collection tools and determine their optimum timing for a larger trial;

3. To test methods for identifying the use of financial resources;

4. To explore the acceptability of study procedures for patients and health professionals.

Methods

Design

This study was registered with the International Standard Randomised Controlled Trials (ISRCTN: 36040085). Favourable ethical opinions were obtained from the National Research Ethics Committee (REC) - Camden and King's Cross (REC Reference no: 16/LO/2010), and the Health Research Authority (HRA). NHS research governance approvals were obtained from each participating study hospital.

We conducted a parallel, cluster randomised control trial (RCT) with a 1:1 allocation ratio, employing convergent mixed-methods, with quantitative and qualitative data given equal importance. Data were collected sequentially and analysed concurrently. Our rationale for the cluster RCT design was the implementation and delivery of the intervention being at an organisational level, in this case, the hospital ward, and not the patient. Cluster RCTs are used to avoid potential `contamination' between treatment groups (27, 28). This study comprised the trial, examination of patients' clinical records and focus groups with health professionals.

Study setting

The study took place across purposefully selected general medical wards located in four clusters, in this case, district general hospital (DGHs) in England. DGHs represent major secondary care facilities that typically provide an array of diagnostic and therapeutic services to local populations. There are over 142 DGHs in the UK (29). The four DGHs selected serve diverse populations including those that comprise ethnic diversity and material deprivation. The hospitals have different strengths and weaknesses in terms of their Care Quality Commission (CQC) (30) ratings.

Participant recruitment and implementation of the AMBER care bundle were limited to one or two general medical wards at each hospital site. Selection of study wards at each site was informed by 'heat maps' that provided contextual information at a ward level on the number of deaths during, and up to 100 days after admission. Additional data comprised the number of patients who died with an individualised approach to the last days of life care, and the number of hospital readmissions prior to a patient's death. Wards with the highest number of deaths per year were considered to be suitable for the study.

Randomisation and masking

Hospitals were randomly assigned by computer to intervention (previously outlined) or control arms at the level of the cluster via an independent clinical trials unit by randomly sequencing the order of randomisation and then randomising the sites in this order into fixed blocks of two. Research nurses collecting the data from patient participants were not masked for the group allocation. Quantitative analyses were performed, masked for the group allocation.

Patient participants and the recruitment process

Research nurses identified patients (or their proxies) on the intervention and control wards daily who fulfilled the eligibility criteria aligned with those of the AMBER care bundle i.e. patients:

· who were deteriorating;

· whose situations were clinically uncertain, with limited reversibility;

· at risk of dying during their current episode of care, despite treatment;

· able to provide written informed consent or where a personal consultee could be identified and approached to give an opinion on whether the patient would have wished to participate in the study.

Research nurses scanned the hospital ward 'whiteboards' to identify potential patient participants who were then discussed with the clinicians to confirm their suitability for the study. All participants were considered to have mental capacity unless established otherwise, and all practicable steps were taken to enable individuals to decide for themselves if they wished to participate. Potential participants' level of capacity was discussed with referring clinicians to identify those with possible impaired capacity and to anticipate the likely consent procedure. Capacity was established on initial meeting, using the MCA four-step process (31):

(i) the individual is able to understand the information about the study;

(ii) retain the information (even for a short time);

(iii) use or weigh up that information; and

(iv) communicate his or her decision (by any means).

Recruitment to focus groups with staff members

Health professionals from study wards and the research nurses were invited via posters to participate in one of the four focus groups representing the study wards. Of those who expressed interest, we attempted to recruit a range of health professionals with different levels of experience. Written informed consent was obtained from health professionals prior to the focus groups taking place. Consent was

obtained at the end of the focus groups from any health professionals who joined late but wished to participate.

Data collection

Patient (or proxy) questionnaires and outcome measures

After obtaining informed consent or, for adults lacking capacity, permission from a proxy (third–party), research nurses conducted baseline face-to-face interviews with patient participants, or their proxies, on the study wards. A questionnaire captured patient participant demographic and clinical information, health performance status using the Australian Karnofksy Performance Scale (AKPS) (32), and the following components:

Patient/family anxiety and communication (time points - baseline, 3-5 days, 10-15 days)

The first of two candidate primary outcome measures was the 'patient/family anxiety and communication subscale' of the Integrated Palliative care Outcome Scale (IPOS) (33, 34). The selection of this patient-centred outcome was based on the intended benefits of the AMBER care bundle and the findings from a comparative observational study where psychosocial issues were identified as central concern to patients and their families (20). The 'patient/family anxiety and communication subscale' includes items on being in receipt of information, addressing practical matters, sharing feelings with family, being at peace, patients' levels of anxiety and depression and family distress/ability to share feelings.

Patient experience (time points - baseline, 3-5 days, 10-15 days)

The second candidate primary outcome measure was 'howRwe' (35); a patient-reported experience measure that examines changes in patients' reported experiences of care. The measure, used among patients who possessed mental capacity, is succinct, comprising just four items relating to the delivery and organisation of care. The 'howRwe' has been used successfully across in-patients, outpatients, general practice, care homes and domiciliary care (36) (37).

Health-related quality of life (time points - baseline, 3-5 days, 10-15 days) and health resource utilisation (time points - baseline, 10-15 days)

The EQ-5D-5L (38) was used to measure health-related quality of life. It measures five health-related quality of life dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression, using two descriptive systems and a visual analogue scale (VAS). Each dimension has five levels, ranging from having 'no problems' to 'being unable to perform'. The VAS records the respondent's self-rated health on a vertical scale, where the endpoints are labelled 'best imaginable health state' and 'worst imaginable health state'. This information can be used as a quantitative measure of health outcome as judged by individual respondents.

Data on health resource utilisation were collected using the Client Service Receipt Inventory (CSRI) (39) (40). The CSRI measures the use of health, social, and informal care in the three months prior to hospital admission, and then during the inpatient stay for up to 10-15 days (time point three).

Views on being involved in the study (time points - baseline, 3-5 days, 10-15 day)

Patient participants with mental capacity were asked to provide their views on being involved in the study on a scale from 1 (positive) to 3 (negative), and whether they would recommend involvement in the study to other patients (41). Free-text comments were also invited.

Quantitative data analysis

Analysis followed the Consolidated Standards of Reporting Trials (CONSORT) guidelines and was conducted in collaboration with the Clinical Trials Unit; two statisticians (GW, RW), the Chief Investigator (JK) and the health economist (DY) were blind to the randomisation outcome. Data were entered into pre-designed Epidata databases (42). Ten per cent of the data were double entered and cross-checks were conducted. No discordance was detected for the candidate primary outcome measures (100% match for IPOS subscale and howRwe) and very high accuracy for the rest of the questionnaires.

Since this was a feasibility study, a formal power calculation was not appropriate. Based on the information about number of deaths and prior studies, we aimed to recruit 40 patients per study arm to provide us with sufficient data to test data collection forms or questionnaires, examine the appropriateness of candidate primary outcome measures, determine their optimum data collection timing for a larger trial and explore the acceptability of study procedures to patient participants. Any investigations of changes in study parameters were exploratory only.

Descriptive statistics on demographic and study variables were completed in the form of means, medians, ranges, standard deviations (SDs), and percentages (categorical variables). No tests of significance were conducted. However, 95% confidence intervals (CIs), rounded up to one decimal point, were provided to indicate the precision of the estimates from the feasibility trial. Analysis of the IPOS focused only on those participating patients with complete data for all IPOS patient/family anxiety and communication subscale items.

Economic evaluation is an emergent area in palliative care and ambiguity still surrounds best practice (39). Procedures to inform the economic evaluation in the full cluster RCT protocol were reported, focusing on resource implications from health and social care, and societal perspectives. We aimed to make preliminary cost-effectiveness calculations (e.g. combining CSRI data on costs and EQ-5D score).

Responses to the five items in EQ-5D-5L were used to generate the index score for each patient. Theoretically, the index score ranges from 0 (death) to 1 (full health): some EQ-5D-5L profiles are evaluated as below zero, implying that the individual considers their current quality of life as worse than death.

Qualitative data

Focus groups

A topic guide was developed to explore health professionals' views on the conduct of the feasibility cluster RCT. The four focus groups were led by senior researchers (JK, CE). Both have experience in palliative care research and qualitative research. Field notes were taken by EY and HJ to provide a contextual understanding of any non-verbal communication expressed during the focus groups. All focus groups were audio-recorded and lasted between 49-65 minutes.

Qualitative data analysis

The qualitative data analysis was informed by the Framework approach, to inductively code and organise the data, and identify emerging themes from the focus groups (43). To address issues of rigour and trustworthiness in the analysis, we (JK, EY and HJ) independently examined focus group transcripts, met to develop a thematic framework, and then independently coded the transcripts. Where coding differed, these issues were reconsidered by JK, EY and HJ in detail until a consensus was achieved (44). To avoid making unwarranted claims about patterns and regularities in the data, care was taken to examine what appeared to be more unusual or non-confirmatory views and considered what the data told us about their causes (44). Excerpts from the focus group transcripts are presented to illustrate themes and represent a range of views rather than being reliant on selected individuals. All quotes from health professionals have been anonymised to preserve confidentiality.

Results

Recruitment, retention and follow-up rates

Between June 2017 and March 2018, a total of 894 patients (130 in the intervention and 764 in the control arms) were screened for eligibility. 29 patients were recruited to the intervention arm and 36 to the control arms. Figure 1 depicts the CONSORT flow diagram of participant recruitment from screening to three data collection time points, and thenceforth to analysis. Recruitment rate by cluster varied.

Table 1 presents the number of patients screened and successfully recruited at each of the study sites. Only 1.9% (n=8) and 8.9% (n=28) of those screened in the control arm (Site 1 and Site 2) were eventually recruited. The screening log for control site 1 provided detailed information on the characteristics of eligible and ineligible patients, and those who consented or refused. The log reported that while 55 (15.1%) patients screened met the first eligibility criterion (*deteriorating, clinically uncertain, with limited reversibility*), they did not meet the second criterion (*at risk of dying during their current episode of care)*. Other sites provided only a limited range of information concerning potential recruits and control Site 2 did not routinely keep a recruitment log. Recruitment rates were higher at the intervention sites where 25.0% (n=20) and 18.0% (n=9) of those screened were recruited, respectively.

Clinicians and research nurses at the control sites reported challenges in the identification of potential patients who fulfilled the eligibility criteria, particularly regarding the *'risk of dying during their current episode of care'* criterion. Unlike health professionals at the intervention sites, they were not trained and guided in identifying these patients, as providing this education and support may have resulted in potential contamination of patient care. Since one of our study objectives was to critically examine how the study operated under field conditions, we reviewed patient recruitment alongside the eligibility criteria over a four-month period to assess its feasibility. As a result, a pragmatic decision was made with the Trial Steering Group to remove the 'risk of dying' criterion, focusing instead on just the first AMBER care bundle eligibility criterion i.e. '*patients who are deteriorating and patients whose situations are clinically uncertain, with limited reversibility'*. A substantial protocol amendment was obtained from the NHS REC, in addition to local research governance permissions. We planned to monitor the effect of this change on recruitment, but control Site 1 did not have the capacity to implement the revised recruitment strategy by the time approvals had been obtained: control Site 2 recruited eight more participants after this change.

(Insert table 1 about here)

Sample characteristics

Table 2 presents the demographic characteristics for participants by trial arm. Participants in both trial arms were predominantly White British and widowed, and most were either 'living comfortably' or 'coping with their present level of income'. Control Site 2, located in an urban setting, had a more ethnically diverse sample profile compared to other sites. There were differences between the trial arms (table 2). In the control arm, most patients were men aged between 65-79 years with a cancer diagnosis, while in the intervention arm the majority were women aged 80 years or older with a non-cancer diagnosis. The older age and non-cancer diagnoses of the patients in the intervention arm are likely due to the inclusion of two care of the elderly wards located at intervention Site 1.

(Insert table 2 about here)

Reasons for hospital admission

Reasons for patient participants' admission to hospital included shortness of breath, falls and confusion (Table 3): 62 out of 65 participants (95.4%) had an unplanned admission to hospital through the emergency department. A range of different illnesses were present [average of 2.3 comorbidities (range 1-4)], the most common being those associated with circulatory disorders

(Insert table 3 about here)

Descriptive analyses of candidate primary outcome measures

Table 4 presents the levels of missing data and exploratory analysis of patient primary outcomes for the IPOS subscale and the howRwe at each of the time points (mean and SD). The mean IPOS subscale score at baseline was 13.3 (SD 4.8) in the control arm and 13.3 (SD 5.1) in the intervention arm i.e. within

the moderate range. This remained fairly consistent across time points (13.3 at 3-5 day time point (change of 0 from baseline) and 10.3 at 10-15 days (change of -3.0 from baseline) in the control arm; 14.6 at 3-5 day time point (change of +1.3 from baseline) and 13.9 at 10-15 day time point (change of +0.6 from baseline) in the intervention arm). Although the howRwe scores changed across time points it is not possible to comment on whether this is clinically significant because of the small sample size and the high rate of attrition between time points.

(insert table 4 about here)

Economic evaluation process

The descriptive statistics of service use showed that utilisation was within plausible ranges, for example, length of stay in the hospital did not exceed three months (Table 5). Patients interviewed at 10 – 15 days, reported the use of investigations/tests and the informal care provided, but no health service use due to hospitalisation was reported between baseline and follow-up. Deriving EQ-5D index score was feasible for those who answered the questions on five dimensions.

It was feasible to collect the data on health and social care service use, informal care provision and quality of life at baseline and at 10-15 days. Missing values in the data were not problematic (less than 9.0%). We made the decision not to calculate preliminary cost-effectiveness because attrition at 10-15 days reduced the number of paired samples available to twelve.

(insert table 5 about here)

Patient participant views on being involved in the study

Patient participants considered their involvement in the study positively: only one participant in the control arm did not want to complete the study questionnaire (no reason was stated). Some stated they were happy to participate due to the positive interaction with the research nurses, for example: '*the research coordinator is very polite and explained everything about the study* (Con2-014). Others were motivated by a sense of altruism, believing involvement would help others and improve services: '*If you can help others, then it's worth doing'. (*Int2-007). A number of participants also encouraged other patients to take part in the study, reiterating that their involvement would *'help others'*.

Focus groups with health professionals

In total, we conducted four focus groups with health professionals; one at each of the four study sites. Their views focused on the following issues: (i) the eligibility criteria for the AMBER care bundle and its implications for patient eligibility in the study; (ii) considerations of study settings and processes, and; (iii) the impact of the feasibility study on research nurses. Details of the participants in the four focus groups at each of the study sites are presented in table 6. Themes and illustrative quotes are presented in table 7.

(Insert table 6 about here)

(i) Eligibility criteria and issues with prognostication

Participants were concerned about the study's eligibility criteria, which were informed by the intervention's eligibility conditions. At times, the discussion focused on what was understood to be 'clinical uncertainty'. This included confusion about the 'middle-ground' between patients who were being 'actively treated' and those at 'the end-of-life'. There was evidence of disagreement between professional groups about which patients were potential cases. We observed a sentiment of a perceived disparity of power between doctors and nurses concerning how decisions were made on which patients could be approached. At control Site 1, the research nurse and ward sister explained their difficulty with recruitment because the concept of clinical uncertainty was not fully understood by doctors as being a legitimate entity. Medical staff raised serious concern that they perceived prognostication was required to confirm a patient as at 'risk of dying' during the admission to meet eligibility criteria. The concept of 'at risk' was problematic to implement as an objective criterion, with perceptions of subjectivity surrounding 'risk' and variation in interpretation of 'risk' within and across the clusters.

There was also discussion about when an 'episode of care' ended: while this was objectively on a patient's discharge, there was a strong sentiment that the recommendations of care should be maintained from hospital to home/care home. This was not within the scope of the study to investigate.

Although we did not ask about study contamination at the control sites' focus groups, a small number of participants stated that merely thinking about clinical uncertainty, albeit in the absence of an intervention to guide them, had influenced their clinical practice. Participants mentioned that the study provided them with a platform to broach difficult topics, such as clinical uncertainty and advance care planning with patients and their families.

(ii) Consideration of study settings and processes

Views were shared about site-level factors external to the study protocol and how this had a bearing on the success of how the study operated. The system of 'consultant oversight' for the ward was a critical factor to consider when setting up the study. At one of the control sites, by the time a consultant had become familiar with the study and its requirements, they were changed by a new consultant who needed to be introduced to the study.

Explaining the study to patients and families, with the study documentation, was challenging for some as they assumed that the primary focus was dying. This was not the case, but these comments further highlight the degree of specificity needed when training staff in study processes and interpreting the intervention's eligibility conditions which governed the study's eligibility criteria.

Health professionals also reported the consent/consultee assent process as challenging, highlighting the extensive length the participant information sheets, and the manner in which consent was sought (as required by the research ethics committee). They suggested modifications to streamline this process.

(iii) **The impact of the feasibility study on research nurses**

The emotive and complex nature of the study was discussed. At one site there had been a hope for a larger team of research nurses, given the need to screen patients daily: only a few research nurses felt adequately skilled to attend ward handover meetings to identify potential patients and then lead potentially distressing encounters with patients, many of whom were very unwell. Other research nurses felt that the unique focus of the study provided them with a privileged position and opportunity to develop deeper relationships with the patient participants.

(insert table 7 about here)

Discussion

This account of the design and execution of this feasibility cluster RCT of the AMBER care bundle provides evidence of the important methodological issues that arise in studies of interventions for patients nearing the end of life. Whilst a full trial of the AMBER care bundle is technically possible, it would not be realistic using the methods employed. This feasibility cluster RCT study was difficult to perform for a myriad of logistical and methodological reasons: however, it provides vital evidence to inform future research evaluating complex interventions for patients nearing the end of life in hospital settings.

The study has several important strengths. It was a clinical trial of a complex, hospital-based intervention, recruiting 65 patient participants, many whom were elderly, frail with multiple morbidities, achieving 81.3% of our recruitment target, over an extended recruitment period. Moreover, it collected data from these individuals at multiple time points. The knowledge gained from this study contributes to progressing how research can be conducted with patients near the end of life (45) (46). Patient participants viewed involvement in the study positively and many were grateful for the opportunity to share their views and experiences. This challenges commonly held misconceptions that research among this patient population is unnecessarily intrusive (47). Additionally, we purposefully selected four hospitals, with different specialties, serving different parts of the country, which enhances the generalisability of our findings.

Study eligibility criteria and recruitment

Referring clinicians and research nurses need the eligibility criteria for a clinical trial to be clear and unambiguous. In the present study the criteria created a number of sampling challenges outlined below.

First, the AMBER care bundle eligibility conditions operated as the eligibility criteria for the feasibility trial. Beyond a patient being identified as *'deteriorating, clinically unstable with limited reversibility'*, patients were also required *'to be at risk of dying during their current episode of care, despite treatment'*. The combined evidence from the screening logs and the views from health professionals in the focus groups highlighted that the prognostic element of the criteria was a major obstacle to identifying and recruiting

potential patient participants. Whilst this finding was germane to both trial arms, it was more pronounced in the control arm due to lack of training and confidence in identifying potential patients. Prognostic models vary in levels of sophistication, ranging from clinical intuition to more intricate multivariate statistical models that combine multiple factors to yield an assessment (48). If *'risk of dying'* is to be retained as an eligibility criterion, there is a strong risk of two sampling biases due to the unknown (or inconsistent) manner in which health professionals currently interpret this: firstly, the unpredictable and often unreliable identification of potential participants within and across study sites, and secondly their exclusion. The findings from the health professional focus groups and analysis of the recruitment logs suggest both biases were present. Although models to enhance the identification of dying patients using prognostic models are improving for patients with cancer (49) (50) (51), there is far less consensus on methods to assess patients with non-malignant conditions, which are more common in studies of this nature (52, 53). If similar complex interventions are to be evaluated, the subjectivity in prognostication must be avoided or greater emphasis should be placed on objective clinical indicators, for example, poor performance status scores, the presence and severity of cognitive impairment, weight loss, and dysphagia.

Second, equipped with the participant information sheets, clinicians were required to introduce the study to potential patient participants and its relevance to them in relation to their clinical situation. Some clinicians, especially at the control sites, reported they lacked the confidence and skills to talk openly with patients about their circumstances. This challenge was exacerbated by research nurses' reports that while convinced that some patients identified were ideal for the study, their views were challenged by clinical colleagues who disagreed on their suitability, stating they were unclear that they were 'at risk of dying' during the admission. This inadvertent 'gate-keeping' represented an important barrier to recruitment. In the clinical care of people approaching the end of life, patients value their autonomy in decision-making. This also applies to research participation, where the opportunity to help others, and to be heard, must be respected (54). Preventing this, whether intentionally or unintentionally, may violate the ethical principle of fairness (55). Future studies should test methods that train health professionals in conducting difficult conversations about introducing studies of this nature to potential patient participants, whilst being mindful that this training does not contaminate the study by corresponding too closely to the intervention to be tested.

Third, it was challenging to ensure homogeneity in how patients were identified at and across sites. Frequent staff turnover (notable at one site) may lead to inconsistencies (and potentially bias) in the way potential patients are identified and recruited. It proved challenging for research site's Principle Investigators and researchers to identify whether criteria were systematically applied, and to track reasons for non-participation. Such tracking is invaluable, alerting researchers to the need to amend recruitment approaches before the study progresses too far and a vital pool of potentially eligible patients are inadvertently excluded. Related to this, accurate reporting of the number and characteristics of patient participants successfully recruited, and data on non-participants, greatly assist in the identification of possible sample bias that may compromise a study's validity (56) (57). We adopted the CONSORT and Transparent Reporting of Evaluations framework (58) aiming to clearly and transparently report the study

sample selection in relation to the study's eligibility criteria, the characteristics of participants and non-participants and refusals. However, only one study site provided a detailed screening log that adequately met this requirement. Without this information, not only does it become more challenging to identify and correct instances of misinterpretation of study eligibility criteria and manage potential gate-keeping, it also prevents the wider research community from understanding potential threats to the internal validity of studies examining similar issues. Researchers need to be transparent about the resources required for the screening process during the planning stage of the study and require study sites to record this information. Whilst there is currently no agreed standard for the ethical capture of non-identifiable information within screening logs exists (59), training research staff, or delegated individuals, at each of study sites to collect minimum patient-based data may improve matters.

Study involvement procedures

A number of important findings are evident from the process of seeking informed consent from patient participants. The participation information sheets and consent sheets were developed in concert with our patient and public involvement members and subsequently approved to the satisfaction of the research ethics committee and the UK Health Research Authority. However, we discovered they were not always suited to their intended audience; those who were older, often frail and very unwell. The research nurses highlighted that the documentation was lengthy, too detailed, and complex, a result of the need to include information and contingencies for those patient participants who might lose capacity during the study. The effect of this was a number of potential patient participants were discouraged from engaging in the study. Whilst research has focused on the ethical requirements of dementia-related research, where important lessons can be learned (60), little guidance currently exists for developing study documentation for end-of-life care studies that are adequately detailed to satisfy potential participants and research ethics committees alike (61). Future studies working in this area of health care should be permitted to evaluate the extent to which a briefer participant information sheet conveys adequate information about the study, any potential benefits and risks to potential participants, and the influence of this in relation to study uptake. This could be compared to the current 'standard' typically required by the Health Research Authority.

The process of providing, and indeed the need for (62), informed consent also requires consideration. According to the Department of Health, informed consent can be written or oral (63). It has been suggested that written consent is neither sufficient nor necessary for a valid consent to be present (64). Based on the above, we propose future studies, that aim to recruit similar patient populations, incorporate a more pragmatic process of obtaining consent where the patient participant agrees to what is proposed by the researcher, and he or she notes this. This approach should be similarly compared to approaches currently required to examine their relative acceptability. Although we should strive to obtain informed consent from patients, the Council of International Organizations of Medical Science International Ethical Guidelines for Biomedical Research Involving Human Subjects, a widely recognised commentary on the Declaration of Helsinki, suggests that for studies involving minimal risk and where the need to obtain informed consent would make the research impracticable, ethical review committees, in some instances,

may waive the need to obtain it (65). In a modified study, that makes use of different sources of patient centred-data, it reasonable to test research ethics committee's willingness to relinquish the requirement for informed consent when study participation represents only minimal risk and when it is not always feasible to obtain it.

Contamination of the control group

When designing this feasibility study, we deliberately made use of a cluster design to minimise the potential of study contamination (27, 28) (66) associated with the movement of health professionals acquainted with the AMBER care bundle from other wards, to control wards, and this then influencing their care. This represented an improvement in the design from our previous comparative evaluation of the AMBER care bundle (20). We were also mindful not to select study sites where similar interventions were in place. This is because changes to the 'standard' or 'usual care' during the course of a clinical trial could impair the validity of the study. Although Control Site 1 did experience relatively frequent turnover of medical staff, to the best of our knowledge no health professionals were familiar with the AMBER care bundle from having worked elsewhere. However, at Control Site 2, we become aware of a change in clinical practice associated with subtleties in maturation, or 'naturally occurring changes' (67) in health professionals' clinical practice resulting from them becoming more familiar with the concept of 'clinical uncertainty'. Due to the small number of participating patients in both arms of the study, it was not possible to accurately quantify the effect of this change, which was not accompanied with any formal intervention training in patient and family care.

Data collection and completeness of candidate primary outcome measures

We examined whether relevant clinical outcomes can be measured using instruments that could be easily completed by unwell patients whose recovery is clinically uncertain (68). All participants (n=65) who provided consent or proxy assent successfully completed baseline measures. Overall, levels of missing data for self-reported outcomes and those provided by proxies were very low for both candidate primary outcome measures. However, the howRwe is a patient-completed experience measure, which could not be used for those who lacked adequate mental capacity. This severely restricted the number of participants who were able to complete this measure. Nevertheless, the findings indicate that data collection was generally possible. We also now believe health utilisation at follow-up could be replaced by exploring patients' medical records, assuming all patients stay on wards. Costs associated with care service use would then be obtained using unit costs for each service item and opportunity costs (e.g. minimum wage).

Acceptability of the study to patient participants

We have demonstrated that patient participants were generally very positive about being involved in this feasibility study. This continued for all those who remained in the trial until 10-15 days. Within this study, we have refuted legitimate concerns about engaging with what could be perceived as 'vulnerable' patient populations at the end of life (69-71). This study, therefore, demonstrates that when ethical and

pragmatic decisions are made in relation to study design, combined with highly sensitized research nurses and researchers, the voice of patients can be heard.

Study limitations

There are a number of study limitations associated with this feasibility study beyond those already discussed. First, guided by the AMBER care bundle development team, we used 'heat maps' to identify wards with the highest number of annual patient deaths. Consequently, we did not identify wards with similar specialties across trial arms. This resulted in a case-mix of patients that were quite different. The effect of this was most pronounced with the inclusion of care of the elderly wards that skewed the age balance across the trial arms. The mean age of the participants in the intervention arm was higher compared to the control arm. Future studies should aim not to base the selection of study wards solely on the number of deaths per ward, and consider other important factors, for example, ward specialty, the potential for active engagement of ward staff, and the presence of Principal Investigators on the ward.

Second, we had aimed to recruit 80 participants throughout the trial. Instead, we recruited 65 participants. This limited our ability to identify statistically significant differences in the candidate primary outcome measures, hence limiting the assessment of the preliminary effectiveness of the intervention. Additionally, the relatively small number of clusters included in the study meant that we were not able to calculate the intra-cluster correlation coefficient required for a future trial. Feasibility studies adopting this trial design should consider extending the number of clusters.

Third, the main reason for the loss to follow-up was due to discharge from the study ward, a finding evident in both arms of the study. As our data collection was restricted to the time frame patients were located on the study wards, we were not able to continue data collection. Future similar studies should consider designing a study that either aims to recruit patients at an earlier point in their hospital admission or permits follow-up after discharge. A potentially more appropriate commencement point for recruitment within the hospitals could be acute medical units (referred to as AMUs). Instances of clinical uncertainty and decisions regarding patients' further treatment and care within the hospitals often take place in the AMUs. This would extend the potential of collecting data for a larger number of patient participants at the third time point (10-15 days) who would otherwise have been discharged at this point.

RECOMMENDATIONS AND CONCLUSIONS

In recent years the number of feasibility trials conducted in palliative care has increased and become an important requirement for funding bodies as well as being of high value to researchers in justifying study designs (to both funders and ethics committees). However, noticeably absent from many feasibility studies reported are those that conform to the recommendation that clear feasibility objectives are in situ a priori to inform whether the study protocol is ultimately feasible (23) (72). This feasibility study conformed to this recommendation and concluded that, whilst the study was indeed technically possible, based on the challenges reported and the number of design modifications required, it would be impractical to use the tested protocol to guide a full trial of the AMBER care bundle. This study has

therefore accomplished an important positive feasibility trial objective (26) - the de-risking of funding of a full clinical trial estimated to be £1.2 million that would be unlikely to meet the necessary patient recruitment/retention rates necessary to identify a clinically meaningful outcome. Meanwhile, the AMBER care bundle continues to be used extensively in many hospitals and endorsed in policy (73).

We suggest that future studies attempting to conduct research among this patient population, and importantly the complex interventions designed to benefit them, should consider the following four recommendations:

1. Effective timely participant recruitment is essential; it has a significant impact on findings. Health professionals and research nurses involved in studies of this nature therefore require specific training to providing them with the skills and to feel confident identifying and then recruiting potential patient participants. Some may feel hesitant and on occasion upset given the focus of the study. Training should therefore be accompanied by regular debriefing to openly discuss instances of study-invoked distress.

2. Palliative populations are heterogeneous with a range of disease trajectories (74). Study populations should therefore reflect the real world and be feasible to study. This may therefore require broad (75) rather than overly-specific eligibility criteria.

3. Make use of population-based, retrospective hospital-based data to examine and compare patients supported by an intervention with controls, adjusted for propensity matching. Similar approaches have been successfully employed to examine the quality of care received by cancer patients (76). Areas of care would have to be specified for patients who died during their hospital stay or within 100 days of discharge, and importantly for those who survived – a central feature of the design of the AMBER care bundle. Domains of interest might include informing family members when death was imminent, the use of validated tools to assess common symptoms (e.g. pain), prescribing drugs for anxiety, the use of bereavement support, where available, length of hospital stay, preferred and actual place of death, number of hospital readmissions, and admissions to emergency departments.

4. In clinical trials, intervention success largely rests on the achievement of statistical significance between the intervention and control group using quantitative measures. As outlined above, there are innumerable complications in exclusively using quantitative measures for evaluating clinically meaningful change, leading to faulty conclusions about intervention efficacy. Qualitative data can contribute fundamentally to appreciating the effectiveness of clinical interventions, providing information about the perceived value of the intervention as seen through the eyes of participants (77) (78). Without methods that address the within-group differences that attenuate effect sizes, researchers may inaccurately conclude that interventions are ineffective. The addition of qualitative assessments for evaluating outcomes in RCTs is likely to improve the ability to more fully assess intervention efficacy based on changes that are perceived to be meaningful to patients and their families.

5. Feasibility studies that examine methods to research complex interventions focused on clinical uncertainty and at the end of life are vital for improving the design of future trials, giving them a greater

chance of being completed successfully, on time and with the required sample size (66) (79) (80).

Declarations

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Approval for this study was obtained from the National Research Ethics Committee (REC) - Camden and King's Cross (REC Reference no: 16/LO/2010), and the Health Research Authority (HRA). NHS research governance approvals were obtained from each participating study hospital. All participants (and for those who lacked mental capacity, their consultees) provided written informed consent after randomization and prior to completion of questionnaires and involvement in focus groups.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and analysed during the feasibility study are available from the corresponding author on reasonable request

COMPETING INTERESTS

None declared.

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AUTHORS' CONTRIBUTIONS

The following authors (JK, CE, FM, DY, GW, AP and SB) made substantial contributions to the conception and design of the study, wrote the protocol, won funding, oversaw the study, and contributed to all components. JK, EY, CE, LS, JD, MF and TP were responsible for the organisation and conduct of the study. EY, JK, CE and HJ were responsible for the acquisition of study data. JK, EY, HJ, RW and DY were responsible for the analysis and interpretation of study data. JK drafted this manuscript and all authors (CE, EY, HJ, FM, DY, GW, SB, LS, JD, MF and TP) critiqued the output for important intellectual content. All authors read and approved the final manuscript.

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Tables

Table 1: Summary of numbers screened, excluded and recruited, by site and study arm

	Study Sites				Total
	Control Site 1	**Control Site 2**	**Intervention Site 1**	**Intervention Site 2**	
Screened	449	315	80	50	894
Not eligible	365	282	22	5	674
N (%) of those screened who were eligible	84 (18.7)	33 (10.4)	58 (72.5)	45 (90)	220 (24.6)
Reasons for non-recruitment					
• lacked capacity & no caregiver	4	2	8	6	20
• too unwell	19	0	2	6	27
• died	0	0	7	5	12
• discharged/discharge planned	13	0	6	2	21
• declined	5	2	6	6	19
• clinical review/tasks	28	1	4	8	41
• no reason provided	7	0	5	3	15
N and % of those eligible who were recruited	**8 (9.5)**	**28 (84.8)**	**20 (34.4)**	**9 (20)**	65 (29.5)

Table 2: Baseline participant characteristics by trial arm, N (%)

		Whole sample, N=65	Control, N=36	Intervention, N=29
Gender	Male	33 (50.8)	22 (61.1)	11 (37.9)
	Female	32 (49.2)	14 (38.9)	18 (62.1)
Age	50-64	10 (15.4)	9 (25.0)	1 (3.5)
	65-79	25 (38.5)	18 (50.0)	7 (24.1)
	80+	30 (46.2)	9 (25.0)	21 (72.4)
	Mean (SD)	77.8 (12.3)	71.8 (10.8)	85.3 (9.7)
Disease group	Cancer	30 (46.2)	23 (63.9)	7 (24.1)
	Non-cancer	35 (53.8)	13 (36.1)	22 (75.9)
Patient had capacity	Yes	23 (35.4)	17 (47.2)	6 (20.7)
	No	42 (64.6)	19 (52.8)	23 (79.3)
Education	Did not go to school	3 (4.6)	3 (8.3)	0
	Secondary school (GCSE/O Level)	21 (32.3)	9 (25.0)	12 (41.3)
	Secondary school (A Level)	15 (23.1)	6 (16.7)	9 (31.0)
	Vocational qualification	4 (6.2)	2 (5.6)	2 (6.9)
	University	11 (16.9)	7 (19.4)	4 (13.8)
	Prefer not to say	7 (10.8)	6 (16.7)	1 (3.5)
	Missing	*4 (6.2)*	*3 (8.3)*	*1 (3.5)*
Marital status	Single	10 (15.4)	6 (16.7)	4 (13.8)
	Widowed	26 (40.0)	9 (25.0)	17 (58.6)
	Married/civil partnership/long-term relationship	27 (41.5)	19 (52.8)	8 (27.6)
	Divorced	1 (1.5)	1 (2.8)	0
	Missing	*1 (1.5)*	*1 (2.8)*	*0*
Ethnicity	White British	45 (69.2)	17 (47.2)	28 (96.6)
	Other white	2 (3.1)	1 (2.8)	1 (3.5)
	White and black African	1 (2.8)	1 (2.8)	0
	White and Asian	1 (2.8)	1 (2.8)	0
	Other mixed	1 (2.8)	1 (2.8)	0
	Indian	7 (10.8)	7 (19.4)	0
	Pakistani	1 (2.8)	1 (2.8)	0
	Other Asian	4 (6.2)	4 (11.1)	0
	Caribbean	1 (2.8)	1 (2.8)	0
	Other black	1 (2.8)	1 (2.8)	0
	Missing	*1 (2.8)*	*1 (2.8)*	*0*
Income	Living comfortably at present	26 (40.0)	14 (38.9)	12 (41.4)
	Coping on present income	21 (32.3)	12 (33.3)	9 (31.0)
	Difficult on present income	5 (7.7)	0	5 (17.2)
	Very difficult on present income	2 (3.1)	2 (5.6)	0
	Prefer not to say	2 (3.1)	0	2 (6.9)
	Don’t know	6 (9.2)	5 (13.9)	1 (3.5)
	Missing	*3 (4.6)*	*3 (8.3)*	*0*

Table 3: Morbidities by study sites, study arms, and total

					Study arm		
Study Site	Control Site 1 N=8	Intervention Site 1 N=20	Intervention Site 2 N=9	Control Site 2 N=28	Control N=36	Intervention N=29	Total N=65
Morbidities: Number of morbidities by International Classification of Diseases -10							
Neoplasms	7	2	1	17	24	3	27
Respiratory system	0	1	4	7	7	5	12
Mental disorders	1	11	1	3	4	12	16
Circulatory system	4	8	3	14	18	11	29
Musculoskeletal	0	4	2	4	4	6	10
Blood disorder/endocrine	4	2	1	11	15	3	18
Digestive system	3	2	0	3	6	2	8
Neurological	0	4	3	4	4	7	11
Other	0	1	2	1	1	3	4
Mean (SD) morbidities/pt	2.38 (0.74)	1.84 (0.96)	2.13 (1.13)	2.29 (1.05)	2.31 (0.98)	1.93 (1.00)	2.33 (1.09)
missing	0	1	1	0	0	2	2
1	1	9	3	7	8	12	20
2	3	5	2	11	14	7	21
3	4	4	2	5	9	6	15
4	0	1	1	5	5	2	7

Table 4: Descriptive analysis of participant self-reported outcomes for participants who had data at baseline and 3-5 days, by study arm

Primary outcome measures		Baseline, mean (SD)	3-5 days, mean (SD)	10-15 days, mean (SD)
IPOS subscale [4]	Control, N=12	13.3 (4.8)	13.3 (3.9)	10.3 (1.2) [1]
	Intervention, N=12	13.3 (5.1)	14.6 (4.1)	13.9 (5.3) [2]
howRwe [5]	Control, N=8	13.1 (2.5)	13.9 (2.5)	14 (2.0) [3]
	Intervention, N=2	11.5 (2.1)	12.0 (0)	11 (N/A)[4]

[1] N=3
[2] N=7
[3] N=3

[4]N=1

[4] **IPOS subscale** (and symptoms) - **higher score is worse** for patients. For the subscale, there are 7 items scored 0-4, possible score ranges from 0-28,

[5] **howRwe**, **higher score is better**. Four items scored from 1-4, possible score ranges 4-16.

Table 5: Health and social care utilisation and informal care provision for the past three months at baseline interview

	Control					Intervention				
	N	User		Utilisation		N	User		Utilisation	
		n	%	mean	s.d.		n	%	mean	s.d.
Overnight stay										
Intensive care unit	36	6	17.0	4.2	5.4	29	0	0.0	n/a	n/a
Inpatient ward	36	22	61.0	10.8	10.2	29	15	52.0	22.3	25.9
Hospice	36	3	8.0	60.0	n/a	29	0	0.0	n/a	n/a
Nursing home	36	2	6.0	3.0	n/a	29	1	3.0	76.0	n/a
Residential home	36	2	6.0	69.5	13.4	29	4	14.0	55.0	29.8
A&E	36	15	42.0	1.9	1.1	29	12	41.0	1.8	1.7
Emergency ambulance	36	15	42.0	1.9	1.3	29	13	45.0	1.5	0.7
Outpatient										
Palliative care	36	4	11.0	2.0	0.8	29	1	3.0	1.0	n/a
Radiotherapy	36	7	19.0	2.0	1.2	29	0	0.0	n/a	n/a
Oncology clinic	36	13	36.0	2.5	1.5	29	1	3.0	2.0	n/a
Other appointment	36	12	33.0	2.5	1.4	29	6	21.0	2.0	1.3
Hospital transport ambulance	36	2	6.0	12.5	16.3	29	4	14.0	7.3	5.6
.....GP face to face	36	28	78.0	2.7	1.6	29	25	86.0	3.4	2.6
.....GP on the phone	36	24	67.0	2.9	1.2	29	17	59.0	2.6	2.5
Nurse										
Marie Curie	36	4	11.0	1.3	0.5	29	1	3.0	2.0	n/a
McMillan or palliative care	36	9	25.0	3.4	2.3	29	1	3.0	1.0	n/a
Other	36	4	11.0	1.5	0.7	29	3	10.0	1.0	0.0
Palliative care or ‘hospice at home’ team	36	7	19.0	3.0	2.6	29	0	0.0	n/a	n/a
Physiotherapist	36	8	22.0	2.4	0.9	29	7	24.0	2.5	1.9
Occupational therapist	36	6	17.0	2.0	1.1	29	6	21.0	2.4	1.5
Psychiatrist	36	0	0.0	n/a	n/a	29	0	0.0	n/a	n/a
Psychologist or counsellor	36	3	8.0	1.7	1.2	29	0	0.0	n/a	n/a
Spiritual care person	36	0	0.0	n/a	n/a	29	3	10.0	6.3	3.8
Social worker	36	5	14.0	3.5	4.4	29	0	0.0	n/a	n/a
Paid formal carer	36	4	11.0	90.0	0.0	29	13	45.0	20.7	24.0
Dietician	36	9	25.0	1.8	0.7	29	4	14.0	3.0	2.6
Voluntary service	36	1	3.0	0.0	n/a	29	0	0.0	n/a	n/a
Other professionals	36	4	11.0	1.0	0.0	29	2	7.0	35.5	48.8
Investigation/diagnostic tests										
Blood test	36	35	97.0	13.8	8.7	29	18	62.0	5.6	6.5
X-ray	36	28	78.0	3.3	3.8	29	13	45.0	2.7	1.1

Echocardiogram	36	9	25.0	1.5	0.5	29	5	17.0	1.0	0.0
Electrocardiogram	36	20	56.0	1.9	1.0	29	10	34.0	1.2	0.4
Ultrasound	36	17	47.0	1.5	0.8	29	3	10.0	1.5	0.7
CT/CAT scan	36	27	75.0	1.8	1.0	29	7	24.0	1.2	0.4
Magnetic Resonance Image	36	13	36.0	1.6	0.9	29	1	3.0	2.0	n/a
Other	36	17	47.0	4.3	6.0	29	7	24.0	1.2	0.4
Informal care (hours)										
Personal care	36	20	56.0	30.9	44.8	29	15	52.0	16.3	29.6
Help with medical procedures	36	18	50.0	8.4	5.6	29	12	41.0	5.5	9.2
Help inside the home	36	24	67.0	6.6	4.3	29	17	59.0	6.5	4.2
Help outside the home	36	25	69.0	8.3	6.9	29	17	59.0	2.3	1.4
Time spent ‘on-call’	36	13	36.0	26.5	51.7	29	11	38.0	48.2	68.6
Other	36	4	11.0	4.7	2.5	29	4	14.0	7.3	9.5
EQ-5D index score	33			0.00	0.33	28			-0.08	0.14

Table 6: Characteristics of health professionals attending focus groups by study site

Arm	Intervention		Control	
Site	**Site 1** *(N=11)*	**Site 2** *(N=15)*	**Site 1** *(N=9)*	**Site 2** *(N=11)*
Specialties in involved	Geriatrics	Respiratory	Haematology Diabetes	Rheumatology Endocrinology
Professionals involved (Gender)	Consultant Geriatrician-Ward X (F) Consultant Geriatrician-Ward Y (M) Ward Clerk-Ward Y (F) Ward sister-Ward Y (F) Ward manager (F) Ward manager assistant (F) Physician Associate-Ward X (F) Matron-Ward X (M) Nurse assistant (M) Research nurse (F) Research nurse (F)	Junior Ward Sister (F) Staff nurse (F) Registrar (F) Senior house office (F) F1 (F) Senior house office (F) Junior doctor (M) Matron (F) Palliative Care CNS (F) Research nurse (F) Ward manager (F) Junior doctor (M) Senior house office (F) Registrar (M) F1 (M)	Locum Senior House Officer (M) Band 5 Occupational Therapist (F) Ward sister (F) Research nurse (F) Research practitioner (F) Matron of research (F) Staff nurse (F) Palliative care consultant (M) Senior House Officer (F)	Consultant Rheumatologist (M) Consultant Endocrinologist (F) Physiotherapy Technician (F) Research Coordinator (F) Rheumatology senior house officer (F) GP senior house officer (F) F1 (M) Registrar Rheumatologist (M) F1 (F)
Duration	50 minutes	49 minutes	60 minutes	65 minutes

Table 7: Themes and illustrative quotes from focus groups with health professionals

Issues	Illustrative quotes
Concerns relating to study eligibility criteria	
Subtleties in relation to the study eligibility criteria	*It's quite subjective, but that's probably good. If you put strict criteria, you might miss some. Like we were saying, it's almost like a feeling isn't it, that's someone is uncertain. It's not this metric thing. You know, otherwise like this is a marker of uncertainty. I quite like the fact that the criteria are... just that, uncertain.* Int1013-M-CONS *My reflection is I think it's just a bad expression (the eligibility criteria). It's the question of defining what the 'episode of care' is. It's really what's it came down to, wasn't it? Initially, I was told that the episode of care finishes as the patient leaves the backdoor, which really isn't true, is it? That's the whole point of whoever is following their care to the community, as far as a patient is concerned. I'm hoping their perception of episode of care isn't the 'back door is closed, you're in the ambulance going home and that's it'.* Con2020-M-CONS
Professional discordance and the eligibility criteria	*I think that's been particularly difficult in this study. I think that is why we struggled to recruit. Because what we perceived to be a patient wasn't certain (i.e. uncertain), and this was not the view of the medical team. I think it's either "We are actively treating." or "End of life" [approving hhhmms in the background from the other research nurses]. You know there's no 'in-between'.* Con1021-F-RN *The medics would say "No, they're not." (to patients identified as fulfilling study eligibility criteria). But just listening to the handovers, it was like you'd identify everybody on the ward.* Con1018-F-WS *It came to a point where we (the research nurses) had explained it (the study) and explained it again. I think it got to a point where they (the clinicians) just said: "No, no, they're not eligible."* Con1021-F-RN
Issues with prognostication of dying	*My worry is 'the risk of death' can be differently interpreted. So, I think being a bit more concrete about 'risk of death' would be good.* Con2020-M-CONS *Well, sometimes it's hard predicting whether they'll die during this admission or when they're going home.... They might not die in this admission, but they are at the end of life in the next few months.* Int2019-F-SHO
Contamination of usual care	*I've learned a lot from being involved in the ImproveCare study. I think it made it much more comfortable for me to go for these discussions. I think when I was earlier, pretty early in my training days, it was very difficult, when we got asked all these different questions, probably I didn't have answers for and they kept asking why can't we do this, why can't we do that and I didn't understand but then when you get a better understanding of it, if you're comfortable in touching these subjects* Con2019-M-REG
Study setting and study processes	
Consultant oversight of study ward	*The consultant changes every week and there's there are five or six of them, aren't there? So, they're there every fifth week and you know, you happen to tell them every week about the study, remind them that the study is going on.* Con1023-M-CONS

Misinterpreting clinicians' explanations of study	*The daughter of the patient told me I was "Dr Death" and "the Grim Ripper"! They were very upset about it and I think it was largely because they didn't understand...* Con2020-M-CONS
Process of seeking consent	*You give the 4-sided A4 booklet PIS (participant information sheet) to an 80 year-old. It knackers them out. They say read it to me. I get halfway through and they're falling asleep because they are so, so, sick.* Int2003-F-RN *The consent process also needs to be changed. There is nothing to say, you have to get a 'written consent' and I think you need to be pushing these boundaries with the ethics committees. This is why research in this specialty is not being done. You would've had dozens more questionnaires completed, dozens. Why can't when I go in to a see a patient ask: "Mr. Smith would you mind answering some questions about your condition and how we've been treating you?" "Yes, no problem." "Okay." "Mr Smith you do understand that you don't have to do this?" "Yes" "You do understand that you can stop at any time." "Yes." So, I can tick those and start asking questions. You would've had an 80% completion rate!* Int2003-F-RN
Challenges of recruiting patients who lacked mental capacity	*The actual recruitment process was sometimes quite difficult because of what you said, the families not being here. Most of the patients we approached, we had to contact the relatives because the patients were too unwell. So being able to liaise with the families was difficult. We can't be waiting for the families here, so we were called back about relatives that were here and popping back and asking the ward staff to tell us when they're here. So the practicalities were difficult.* Int1033-F-RN
Views on being involved in the feasibility study	
Mixed views on involvement in study recruitment	*It was just two members of staff who came up every day, looking. A lot of the other staff felt so uncomfortable working in this area is if we're honest. The two who did do it in the end found all the end-of-life stuff really tiring, even though wasn't a strictly and 'end-of-life' care study. The fact is that we got a paediatric nurse and a stroke nurse, and they felt a bit out of their depth.* Con1020-F-RP *For the patients, I don't think there was negative impact. ...However, I don't think the staff on the ward were keen.* Con1021-F-RN *I was really, really impressed about how on-board everybody was and everybody knew what AMBER was. On the whole, generally 90% of the time people were very supportive of our presence and what we needed to do.* Int1033-F-RN
Greater insight into patients' experiences	*(The study) gave us a unique relationship with the relatives. So, in a strange way, you're in a unique position that they talk to you about things that sometimes they feel that they can't take forward with certain ward staff. So, we are able to encourage them into having those conversations making sure that those communications were taking place with ward staff if they, the family has signed society, or certain query. So, whether because we were seen as external or whether we would able to form a relationship over questionnaires being done different points, I just don't know.* Int1033-F-RN

Figures

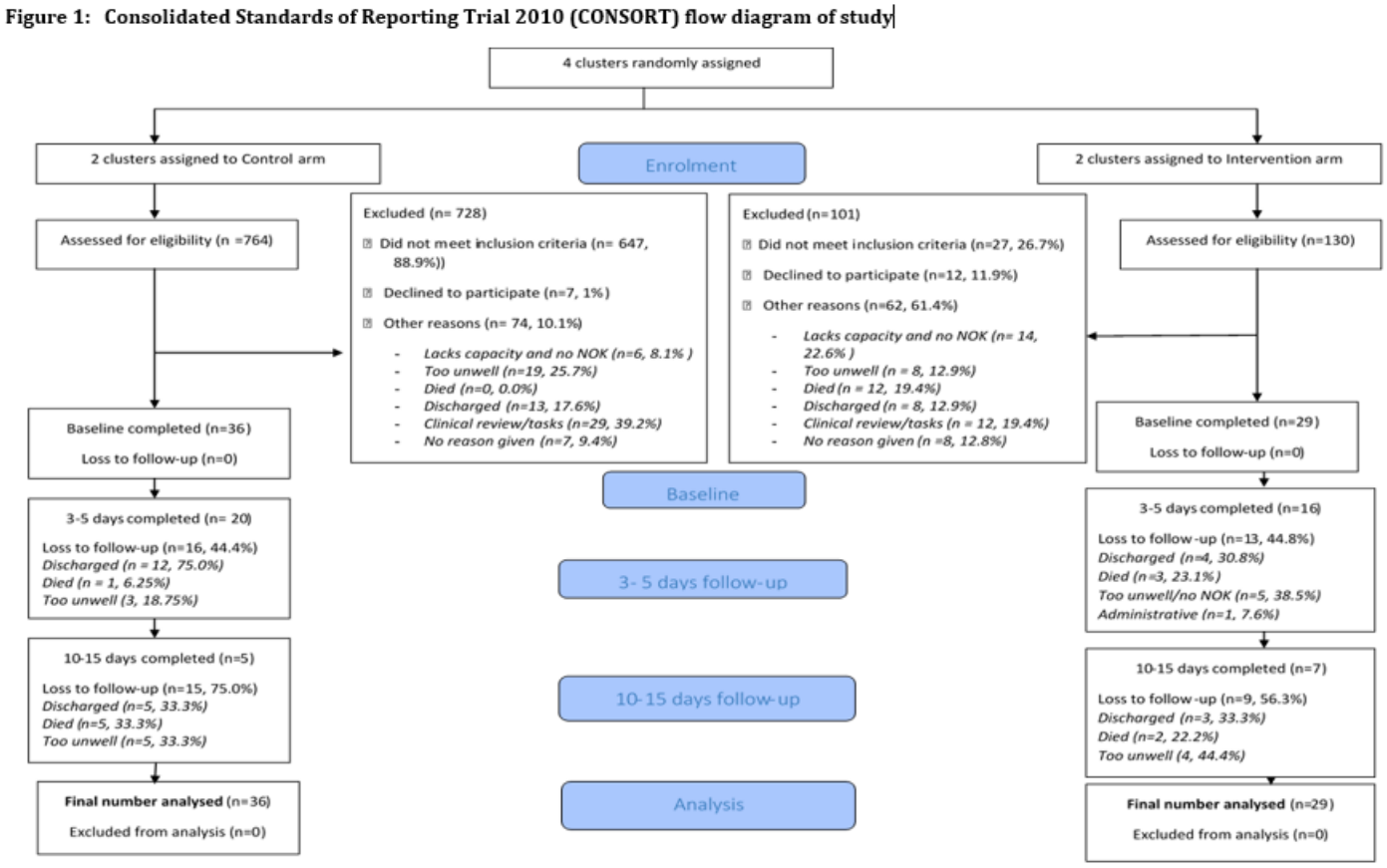

Figure 1

Consolidated Standards of Reporting Trial 2010 (CONSORT) flow diagram of study

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