Palliative Care Yields Cancer Wellbeing Support (Pal-Cycles): Evaluating a Transitional Palliative Care Intervention to Reduce Readmissions for Patients with Advanced Cancer and palliative care needs — An International Stepped-Wedge Randomized Clinical Trial Protocol

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Study protocol

Keywords: advanced cancer, transitional care, clinical trial, palliative care

Posted Date: February 3rd, 2026

DOI: https://doi.org/10.21203/rs.3.rs-8094492/v1

Additional Declarations: No competing interests reported.

Abstract

Background

Palliative care in combination with or after oncological treatment has been found to increase the quality of life and quality of care for patients with advanced cancer. This often means change in goals of care, sometimes along with a change of healthcare provider or place of care. These types of changes are frequently referred to as care transitions. Ensuring continuity of care during these types of transitions is crucial, yet previous research has shown that essential information is not always effectively communicated. Sometimes, this leads to avoidable hospital readmissions, which may cause distress and decreases the quality of life for patients in the last phase of life. This study aims to evaluate the effectiveness of a transitional palliative care intervention in reducing hospital readmissions.

Methods

This study will employ a stepped wedge cluster randomized controlled trial (RCT) design conducted across 14 settings in seven European countries. (Germany, Hungary, the Netherlands, Poland, Portugal, Romania and the United Kingdom). Over a 25 months recruitment-period, 1,050 patients with advanced cancer and if possible, a relative will be enrolled. Patients will be followed for 90 days after inclusion. The primary outcome is the number of hospital readmissions, with secondary outcomes being quality of life and quality of care. Once data collection is complete, a multilevel regression analysis will compare outcomes between the control and intervention groups within each setting, accounting for the hierarchical structure of the data.

Discussion

The study results will determine the effectiveness of the Pal-Cycles intervention in decreasing the number of readmissions to hospital, and increasing the quality of life and the quality of care for patients with advanced cancer.

Trial Registration number: ClinicalTrials.gov ID: NCT06259136, 2025-07-28, Study Details | NCT06259136 | Palliative Care Yields Cancer Wellbeing Support | ClinicalTrials.gov

1. Background

Palliative care has been found to increase the quality of life as well as the perceived quality of care for patients with advanced cancer (1, 2). The World Health Organization (WHO) has defined this type of care as an approach that improves the quality of life of patients and their families facing the problems 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 (3).

In European countries, for most patients, advanced cancer treatment is led by an oncologist possibly combined with palliative care practitioners, and is delivered under the supervision of the hospital services. As patients' palliative care needs increase, however, the proportion of care delivered by palliative care services correspondingly rises. This frequently means not only a change in goals of care, but also in care provider and place of care, as patients tend to prefer to receive palliative care at home delivered by primary or community care providers (4). These types of changes are defined in the literature as a care transition (5).

In order for these transitions to be executed well, the required information needs to be communicated in a timely, understandable, and transparent way(5, 6). Ideally, results of proactive care planning conversations are summarized and communicated via a hospital discharge letter to the General Practitioner (GP) and/or community care. However, studies conducted in the Netherlands and the United Kingdom have shown that often information deemed important by the GPs is missing from the letters from oncologists(7, 8). Consequently, treatment plans may not be clear from the onset when a patient is discharged to home care which can lead to unplanned readmissions to the hospital in the last six months of life, or may have a detrimental effect on quality of care. This can have a negative impact on patients and their carers and may create unnecessary expenditure for the healthcare systems (9, 10).

Nevertheless, the extent and nature of these care transitions vary across countries, reflecting the differences in availability and level of development of palliative care services (11). For example eastern European countries are often still in the process of establishing and expanding their palliative care services whereas palliative care services in western European countries are increasingly integrated into the healthcare system (12, 13). Furthermore there are also differences in the role of the GP across countries(7, 8), or the way homecare is organized(9). As well as how palliative care is organized in relation to general cancer care (14, 15)

In order to improve the communication between hospital and community care providers, interventions that focused on transitional care have been developed from the 1990's onwards (16). Since then several interventions have been developed mostly for frail older people (17–20), as well as for cancer patients (21, 22). Most of these interventions are designed for one specific setting only, but there is an increasing need for solutions and interventions that improve patient transition in the last months of life across healthcare organisations (23, 24).

For this reason, during the European research project Palliative Care Yields Cancer Wellbeing Support (Pal-Cycles), an intervention has been developed to enhance communication between hospital, patients and community care providers that can be implemented in different European countries.

2. Methods

The Pal-Cycles clinical trial protocol is presented following the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2025 guideline (25).

2.1 Objectives

The primary objective of the study is to evaluate the effectiveness of an intervention for transitional palliative cancer care (Pal-Cycles) in seven European countries (Germany, Hungary, the Netherlands, Poland, Portugal, Romania and the United Kingdom) and its consequent effects on the number of readmissions into hospital.

From this primary objective a hypothesis and two sub-objectives have been derived.

Firstly, the hypothesis is that patients in the intervention group, exposed to the Pal-Cycles intervention, will have fewer readmissions into hospital than patients in the control group.

Secondly, the two sub-objectives are as follows:

- To evaluate the effects of the Pal-Cycles intervention on the quality of life of patients and their family members in seven European countries.
- To evaluate the effect of the Pal-Cycles intervention on the planning and organisation of care transitions.

2.2 Trial design

In order to achieve these objectives, a stepped wedge cluster RCT will be conducted. In this design, clusters, defined here as groups of hospital departments, receive the intervention at different time points in a randomized order. Data are collected from all clusters throughout the study period.(26).

The design for the Pal-Cycles trial is described in Table 1 Stepped Wedge Cluster Randomized trial. The complete trial will last 28 months with the recruitment period for the trial lasting 25 months. The trial starts with an initial period of 5 months where all clusters are in the control group after which clusters are randomized into the intervention group at certain timepoints. For this purpose, the recruitment period has been divided in to five periods of five months (steps). In order to allow for data gathering in the last months of recruitment, a 90 day follow-up period is provided.

This design was chosen for the reason that logistically it is found more feasible to implement the intervention in small groups of clusters over time instead of in all the clusters at once. Furthermore, from an ethical point of view, the fact that all clusters receive the intervention eventually is thought to reduce concerns regarding denying benefits to the control group, especially, when there is already some evidence that the intervention is effective (27).

Table 1
Stepped Wedge Cluster Randomized trial

	5 Months	5 months	5 months	5 months	5 months	90 days (Recruitment stops)
Cluster 1–4	Control	Intervention*	Intervention	Intervention	Intervention	Follow-up
Cluster 5–8	Control	Control	Intervention*	Intervention	Intervention	Follow-up
Cluster 9–11	Control	Control	Control	Intervention*	Intervention	Follow-up
Cluster 12–14	Control	Control	Control	Control	Intervention*	Follow-up

Table 1 Stepped Wedge Cluster Randomized trial represents a stepped-wedge cluster randomized trial design, in which different clusters transition from the control phase to the intervention phase over time. Each row corresponds to a set of clusters, and each column represents a 5-month period. "Control" indicates that the cluster remains in the control phase, while "Intervention" denotes when the intervention is implemented. Cells marked with “Intervention*” indicate that a cluster receives the training for the intervention and starts with the implementation of the intervention. After the final intervention phase, a 90-day follow-up period begins, during which recruitment stops. Clusters progress sequentially through the intervention, ensuring staggered implementation across groups.

2.3 Participants & Setting

The study will be conducted in seven European countries (Germany, Hungary, the Netherlands, Poland, Portugal, Romania and the United Kingdom). In each country, patients with advanced cancer are recruited from two hospital departments either both located in the same hospital or in two separate hospitals. In Table 2 below a list of all participating countries and settings is given.

Table 2
List of participating countries and settings

Countries	Partner institution	Name of settings participating
Germany	University Hospital Bonn	Department of dermatology, University Hospital Bonn, Bonn
		Department of urology, University Hospital Bonn, Bonn
Hungary	University of Pécs	University of Pécs Clinical Centre, Pécs
		National Institute of Oncology, Budapest
The Netherlands	Radboud University Medical Centre	Radboud University Medical Centre, Nijmegen
		Rijnstate Hospital, Arnhem
Poland	University of Zielona Gora	University Hospital Karola Marcinkowskiego, Zielona Gora
		Holy Cross Cancer Centre, Kielce
Portugal	Catholic University of Portugal	Portuguese Institute of Oncology, Lisbon
		Hospital Professor Doutor Fernando Fonseca, Amadorra
Romania	Hospice Casa Sperantei	Brasov Emergency County Clinical Hospital, Brasov
		Medlife Brasovisi Hospital, Brasov
United Kingdom	Lancaster University	Blackpool Victoria Hospital, Blackpool
		Royal Blackburn Hospital, Blackburn

In Table 2 List of Participating Countries and Settings, an overview of the countries and settings participating in the study is given. The first column lists the countries involved in the study. The second column lists the partners which are part of the consortium. The third column lists which centres in the country are participating in the study.

2.4 Inclusion Criteria

- Patients aged 18 years or above
- Patients diagnosed with advanced cancer
- Patients that are expected to develop or already may have palliative care needs
- Patients who are in transition from oncological care (hospital) to community care

2.5 Exclusion Criterium

- People with cancer unable or unwilling to provide consent to participate in the study

2.6 The Intervention

2.6.1 Background and finetuning of the intervention

For the purpose of improving the transition of patients from oncology to community care, we finetuned the Pal-Cycles intervention model. This model was the result of a study conducted in the Netherlands on the subject of integrated palliative care on a regional level. The intervention evaluated in this study combined a training for homecare nurses, structured collaboration between patients, families, primary care and specialist teams and the use of a palliative care protocol(34–36). The steps integrated in the palliative care protocol have since been summarized in to the following five cornerstones:

1. Prior to hospital discharge, identification of a patient with palliative and supportive care needs in collaboration with the oncologist,
2. Compassionate communication towards the patient and their family;
3. Collaborative effort to establish a multidimensional treatment and care plan and follow-up in the home care setting;
4. Periodic discussion and evaluation of the treatment and care plan with patients and relatives, led by the GP, oncologist or palliative care team, depending on patient place of stay, care needs, and local possibilities;
5. Identification of the terminal phase (if there) based on the periodic evaluations, with appropriate intensification of treatment and end-of life conversations including consultation with patient and families about ethically and legally sensitive issues like withdrawal of treatment, preferred place of death, rituals in the last phase of life, etc., depending on local possibilities and norms.

For the purpose of adapting the five cornerstones, consultation meetings were held in all seven countries with healthcare professionals involved in the care for oncology patients such as oncologists, nurses, GPs and in 5 countries with patients and family carers.

2.6 2 The Training

As previously discussed there are substantial differences in the level of development and organization of palliative care across the seven countries. Therefore, as part of the project, a training program for the healthcare professionals was designed to ensure similar levels of knowledge on the topics needed to execute the intervention across all settings.

The training will be delivered, before the start of the intervention by a local trainer. These trainers are selected by the research teams and have received a comprehensive instruction in delivering the program, based on a train the trainer approach before the start of the trial.

The structure of the blended training programme will consist of five modules, each containing one or multiple teaching units, for a total of twelve. Again accounting for the different levels of training in

palliative care, two of the teaching units were made compulsory while the rest remains optional.

In Table 3 below an overview of the five modules, teaching units and whether or not they are compulsory can be found.

Table 3
Overview of blended training programme

Module	Teaching Unit	Compulsory/ Optional
Identification of patients with palliative care needs	Assessing prognosis for advanced cancer patients	Optional
	Identifying patients with palliative care needs	Compulsory
Holistic Assessment	Assessing needs in the physical dimension of suffering	Optional
	Assessment of psycho-social and spiritual needs	Optional
Compassionate communication	Compassionate communication with patients and families	Optional
	Sharing bad news with focus on prognostic communication	Optional
	Discussing goals of care	Compulsory
	Family meetings	Optional
	Inter-sectorial communication	Optional
Pain management	Pain assessment	Optional
	Pain management	Optional
Identification and management of dying phase	Identification and management of dying phase	Optional

Table 3 Overview of blended training programme gives an outline of the blended training programme. In the first column the modules are listed. In the second column the teaching units are given. In the third column it is described whether the settings can chose to provide their healthcare professionals with this unit. If the description ‘optional’ is given the countries can choose to include teaching unit in their training programme. If the description ‘compulsory’ is given the countries are required to include this teaching unit in their training programme.

2.6.3 The Execution of the Intervention in the Settings

The patient, after giving informed consent, will be asked to complete the Edmonton Symptoms Assessment System Revised (ESAS-r). This is a short questionnaire that can provide more information the symptoms and the severity of those symptoms experienced by patients with cancer (37). The results from the questionnaire will then be reviewed by the medical team, who can use the information provided by the ESAS-r to inform the Goals of Care Conversations(s). For instance if a patient really struggles with multiple symptoms, this could be a way to start the discussion regarding the quality of life.

After the questionnaire has been completed a Goals of Care Conversation will be conducted. Within this study, a Goals of Care Conversations refers to a discussion or a series of discussions, between an oncology related healthcare professionals possibly assisted by other relevant specialists (such as those from palliative care), with patients and where appropriate their relatives, with the aim of developing a shared treatment and care plan.

In these conversations topics such as: the patients wishes and values regarding the end of life, the disease progression and prognosis, as well as the content of the future treatment and care plan are discussed.

The results of these conversation(s) will be summarized in the Summary of Goals of Care form, which will be available as a paper or electronic based form. As study sites differ in how far digital health data exchange is implemented.

Here what has been discussed regarding the patients understanding of their illness as well as the primary recommendations and decisions regarding the treatment and care plan can be recorded.

- Here what has been discussed regarding the patients understanding of their illness as well as the primary recommendations and decisions regarding the treatment and care can be recorded If using a paper summary form, this will be a physical copy of the form, one copy of which will be stored in the patient’s notes, one will be offered to the patient and one will be sent to the patient’s GP.
- If using an electronic summary form, this will be saved in the patient's medical records, a copy will be printed and offered to the patient or other forms of electronic document sharing used. The GP will also be sent a copy of the Summary of Goals of Care form either via post or other forms of electronic document sharing.

During participation in the intervention, patients are allowed to continue their normal treatment and are not prohibited from any type of care.

2.6.4 Care as Usual

Care as usual is the normal discharge process, including the way of having goals of care conversations (if any) and the way treatment and care plans are or are not, communicated to the patient and other involved healthcare professionals by a letter or digitally. There are currently considerable differences between countries but also between settings in what care as usual means and how the transfer of

patients to the community takes place (38). This has been noticed during the design of the project and of the intervention.

2.7 Outcome measures

2.7.1 Primary outcome

An overview the different outcome measures used in this study is described in Table 2 Outcomes. The primary outcome measure will be the difference between the hospital readmission rate for the control group and the intervention group.

The rationale for choosing readmission as the primary outcome is when patients are discharged from hospital, essential elements of the treatment and care plan may not have been sufficiently communicated to or clarified with the community care setting leading to readmissions (39). With this in mind, the number of readmissions has been used in previous studies as primary outcome measure regarding transitional care, such as the study on the Transitional Care model (22). One of its advantages is that it is a feasible and often well-documented outcome measure which can be retrieved across multiple sites in multiple countries.

In the case of the Pal-Cycles study, readmissions will be registered by the researchers in collaboration with the clinical team. The data about the readmissions collected by the researchers will concern: whether the readmissions was planned or unplanned, in which department(s) the patient were admitted during their time in hospital, the length of the stay in each department and where the patient was discharged to once they left the hospital.

2.7.2 Secondary outcomes

The data for the secondary outcomes will be collected by using questionnaires on the quality of life and the quality of care.

2.7.2.1 Quality of Life

Firstly, the quality of life will be measured from the perspective of the patient through the use of two questionnaires. One of these being the European Organization for Research and Treatment for Cancer Quality of Life Questionnaire (EORTC-QLQ-C30), this questionnaire has specifically been developed to assess cancer patient's quality of life. The EORTC QLQ-C30 comprises of thirty questions assessing their ability to function from a physical, emotional, cognitive and functional point of view. Additionally, the questionnaire pays attention to symptom severity and overall quality of life. For 28 of the questions the response can be given via a four-point Likert scale giving the options: not at all, a little, quite a bit and very much. The last two questions can be responded to via a visual analogue scale from 1 to7 (poor to excellent) (40, 41).

Additionally, the Functional Assessment of Cancer Therapy - General (FACT-G) will be asked, which was specifically developed to measure the patient's with cancer health-related quality of life. This questionnaire for current and former cancer patients, is made up of 27 questions regarding quality of life by assessing wellbeing in four domains: physical, emotional, cognitive and functional. All questions can be responded to by filling in a 5 point Likert scale; not at all, a little bit, somewhat, quite a bit and very much (42).

Even though these questionnaires overlap in some aspects, the questionnaires cover different elements of quality of life (43). FACT-G for instance assesses the social domain in more depth than the EORTC QLQ C30 (44, 45). This was deemed important because a transition in care setting involves also social aspects, like availability of care at home and support by family caregivers. Both questionnaires will be completed by the patient at the time of inclusion, after 30 days and 90 days. The questionnaires have both been translated and validated in all partner languages(40–42, 46, 47).

2.7.2.2 Quality of care

The quality of care will be measured from both the point of view of the patient and their relative. The patient will receive two questionnaires regarding the quality care. The first one will be focused on the goals of care conversation and the empathy perceived during this consultation. This will be measured using the Consultation and Relational Empathy (CARE) Measure questionnaire at 14 days post baseline. The patients can respond to the questionnaire by using a five-point Likert scale consisting of the following options: poor, fair, good, very good, excellent(48, 49) .

Another questionnaire measuring quality of care is the Caregiver Network Analysis questionnaire. This instrument has previously been developed and used during another European Research Project Patient-centred palliative care pathways in advanced cancer and chronic disease (INSUPC) (5)). The Caregiver Network Analysis consists of 12 questions about which healthcare providers the patient has contact with as well as how the patient perceives their level of cooperation and quality of care. The answer options vary from dichotomous answer categories and open-ended answers to 5-point Likert scales which have either a range from 0 (excellent) to 4 (poor), or from 0 (completely agree) to 4 (completely disagree) In this study it is used as a way to assess which care providers are involved 30 days after inclusion.

The relative will also be asked about the quality of care by using the FAMCARE(50, 51). This questionnaire consists of 20 questions to which can be responded to by a five-point Likert scale ranging from very dissatisfied, dissatisfied, neither dissatisfied or satisfied, satisfied and very satisfied. The questionnaire will be asked 14 days post baseline.

The three questionnaires regarding the quality of care mentioned above, have not all been validated and translated into all seven languages needed. Firstly, the CARE Measure has been translated and validated in three of the seven languages needed during the trial (48, 49, 52). Secondly, the FAMCARE has only been translated into English (53). Third, the Caregiver Network Analysis has been used in a previous

European project in which the Hungary, the Netherlands and the United Kingdom participated. Therefore, it has been assumed that a translation of the questionnaire is available in these countries (5).

Consequently, the CARE measure, the Caregiver Network Analysis and the FAMCARE will need to be translated in to the other languages as well. For the purpose of those translation a back and forward translation protocol has been developed.

The forward translation from English to the national language and was made independently by a native speaker of the national language. This translation was made by someone with knowledge of health and palliative care terminology. Afterwards a back translation was executed by a second bilingual translator who has not seen the original text. Finally, the translators compared the original and the back translated versions of the questionnaire to prepare the final draft in in the national language.

2.7.2.3 Additional data

The following data will be taken from the medical record: place and date of death, presence of Advance decisions to refuse treatment (ADRTs) and Advance care plans (ACPs) as referred to in the hospital medical records, referrals to palliative care services. This will be measured at the end of 90 days.

Table 4
Timeline of Data Collection

Questionnaires	Person who gives data	T0 Base line	T1 14 days	T2 30 days	T3 90 Days	At the end of inclusion period	Time required
Demographic questionnaire	Patient	X					5 minutes
EORTC QLQ-C30	Patient	X		X	X		11 minutes (40)
FACT-G	Patient	X		X	X		10 minutes(42)
CARE Measure	Patient		X				10 minutes (54)
Caregiver network analysis	Patient			X			15 minutes
FAMCARE	Relative		X				Short (55)
Readmissions	Medical record					X	N.A
Evidence of advanced care planning	Medical record					X	N.A.
Palliative care services referral	Medical record					X	N.A

Table 4 Timeline of Data Collection represents the data collected during the trial. Each row describes the data for each questionnaire. In the first column the person who is supposed to complete the questionnaire or data collection is given with patient, family member or researcher. The second column until the sixth column represent a time point at which data is collected. The last column the estimated amount of time a patient requires to complete the questionnaire is given.

2.8 Sample Size Calculation

The sample size was calculated based on the assumption that the patients receiving the Pal-Cycles intervention would have a lower number of readmissions than the patients in the control group, as was previously shown in other studies regarding transitional care programmes(56–58). Based on these studies, a power calculation showed that with 15 patients per cluster per period and a study design with 4 sequences of 5 periods and 14 clusters in total, will result in at least 80% power to detect a decline in hospital readmission rates from 55% to 38% (alpha = 0.05, two-sided). Implying a need to include 75 patients per hospital, 150 patients per country, resulting in a total of 1,050 patients included in the study. There is a risk that not all included patients will be a complete case with full follow up data.

2.9 Recruitment procedure

2.9.1 Patient

For most sites the initial screening with the inclusion criteria is done by a member of the clinical staff either during an admission at the hospital or a visit to the outpatient clinic.

For the purpose of operationalizing thethird inclusion criteria: “patients that are expected to develop or already may have palliative care needs,” part of the screening will be the use ofthe surprise question. This consists of the member of the clinical staff asking themselves reflectively whether or not they would be surprised if the patient were to die within the next six months. If the answer is ‘no’ the patient they fulfil the third inclusion criteria. Originally, the surprise question was developed with a 12 month timeframe in mind(28). However, for the purposes of this study this was changed to six months as most readmissions (our primary outcome measure) occur in the last few months of life (29, 30). Meta-analyses have shown that changing the timeframe does not have any significant effect on its effectiveness(31, 32). Thereby, the surprise question not only ensures that patients are at an appropriate stage for palliative care but also that all patients are at a similar point in the care trajectory.

If the patient then also fulfils the other inclusion criteria, the study is briefly explained to them and they are asked if they would be willing to participate. If the patient expresses interest, they will receive an information letter and an informed consent form. They are given the opportunity to read the information letter and to ask any questions they might have. If the patient decides to participate they complete the informed consent form and return it to the responsible person in the setting. Patient can withdraw at any time if they want. Participation is on a voluntary basis.

2.9.2 Relative of the patient

Patients will be asked to identify a relative who might be willing to be involved in the trial. On the informed consent form of the patient, it is asked if a relative would be willing to participate. If this is the case the relative is asked to complete the informed consent form included in the information package. However, having a relative who wants to participate in the trial will not be an inclusion criterium for the study. For the reason that this could form an extra barrier to participation for a patient group that has already proven difficult to engage in research(59).

2.10 Randomization

All sites will start the trial in the control arm. The sites will be randomized in a balanced process during a computer randomization in which it will be ensured that one setting from each country will be in one of the second and third steps, while the other will be in the last two steps as shown in Fig. 1. The randomization is executed by a statistician from Radboudumc.

The randomization was not blinded, as the researchers responsible for the coordination of the study on the sites, needed to know the date of randomization as soon as possible. In order to allow for the planning of the training and the implementation of the intervention.

2.11 Statistical analysis

The primary outcome, readmission rate/frequency, will be compared between the intervention and control patients. This will be done using a logistic mixed method approach with a random effect for cluster and fixed effects for setting or country and time at each step. The time effect is included to allow for secular trends. A fixed effect interaction term between settings and time will be added to allow for varying secular trends between countries. Gender will be added as a covariate in the analysis together with age.

It is envisaged that the earlier questionnaires of secondary outcome measures will have a higher likelihood of being completed than the later questionnaires as a patient's condition deteriorates. It is expected that a sensitivity analysis will be conducted.

2.12 Ethics

The study protocol prepared in the Netherlands, has been reviewed and approved by ethics review boards at all participating centers. In the Netherlands, the ethics committee decided that the study does not fall in the under the scope Medical Scientific Research Act. As a result, the committee waived the requirement for further ethical review. Hence, a data monitoring committee was not obliged.

Given the low-risk nature of the study, there is no obligation to report potential harms. Participants will continue to receive standard care following the trial, and if needed patients can contact an independent physician during the follow-up of the trial.

2.13 Data management

A data management plan has been made and has been approved by Radboudumc and the European Commission. Clinical trial agreements have been developed, including data transfer considerations.

The data will be collected by researchers in the respective countries and will be transferred to the Netherlands by using the Electronic Data Capture platform called Castor Electronic Data Capture (Castoredc), in which online electronic case report forms have been programmed. Each partner (except the coordinator) will only have access to data from their own site and participants. With the use of Castor data quality assurance processes are covered. Input in Castor is controlled by using ranges and multiple-choice options. The final dataset will be locked and audited by an audit trail.

During the analysis, to accommodate for collaboration between the different researchers, the Digital Research Environment (DRE) owned by RadboudUMC will be used. This is a cloud-based research environment which is globally available and adhering to General Data Protection Regulation standards. By using this environment other centres can access their data while it is still safely secured and not physically transferred between settings. Similarly, DRE has an audit trail and it limits access to those authorized by the coordinator.

After the dataset has been completed and Radboudumc has checked the quality, the data will be stored for 15 years. Moreover, the data will be made available for reuse by submitting the non-sensitive data to DANS EASY.

2.14 Monitoring

The intervention in this study focuses on improving the communication between the oncologist, patient and GP during the transition towards palliative care. Therefore the expected risks of harm to the participants is considered negligible. Moreover, the cultural differences and differences in regulation will be taken into account when asked for informed consent. Therefore the need for monitoring in this study can be argued to be minimal.

This has been translated into practice by having an on-site initiation visit for Radboudumc, whereas the other 13 centres remote initiation visits will be organized by Radboudumc. During the study, Radboudumc will have two interim visits on site, one after three or four patients have been included in the study, the other after eight to ten patients have completed the entire procedure. For the other centres one remote monitoring visit will be convened. An onsite close out visit will be organized for Radboudumc and a remote close out visit will be organized for all participating centres.

2.15 Public disclosure and publication policy

Dissemination of our findings will be presented at relevant conferences, meetings and through peer-reviewed journals, and is expected at the end of 2027. More information about all dissemination activities can be found at the project website (https://palliativeprojects.eu/palcycles/).

3. Discussion

The stepped wedge randomized controlled trial embedded in the Pal-Cycles project aims to evaluate the effectiveness of the Pal-Cycles intervention.

One of the challenges of the study is that with the intervention needing to fit in so many different settings, tailor made adjustments as per the setting are needed. This will need to be carefully balanced with the robustness of the intervention. Another limitation is that the intervention is designed to be implemented in hospital-based settings, which may limit its “fitness” to homecare settings, also taking into account that the community setting widely differs across countries, including the availability of palliative care within these settings.

However, the study also has several strengths. It is recommended by the MOREcare guidance that due to the short life expectancy of palliative care patients, data needs to be collected over a short period of time, to prevent attrition. Consequently one of the strengths of this study is that the effect measures are recorded within 90 days of discharge, providing an increased chance that the data will be complete (60).

Furthermore, the stepped wedge design allows all settings to implement the intervention, consequently all settings can also be evaluated with control data taken from their own sites(27, 61). This has an advantage that cultural differences can be taken into account during the analysis.

This study will evaluate the effectiveness of a transitional care programme (Pal-Cycles intervention) in seven European countries as a way to decrease the number of hospital readmissions and increase quality of life and the quality of care of patients with advanced cancer. One of the primary characteristics the Pal-Cycles intervention aimed to have during its development was that it should be implementable in multiple cultures and their subsequent healthcare settings. This will be tested and evaluated during the current study in a wide range of European settings using the same outcome measures, making them comparable to each other. A qualitative process analysis will be executed simultaneous with the trial.

Abbreviations

GP
General Practitioner
WHO
World Health Organization
RCT
Randomized Controlled Trial
SPIRIT Guideline
Standard Protocol Items: Recommendations for Interventional Trials Guideline
EORTC QLQ-C30
European Organization for Research and Treatment for Cancer Quality of Life Questionnaire
FACT-g
Functional Assessment of Cancer Therapy
CARE measure
Consultational and Relational Empathy
ESAS
Edmonton Symptom Assessment Scale
INSUPC
Patient-centered palliative care pathways in advanced cancer and chronic disease
WMO
Scientific Medical Research Law
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Declarations

Ethics approval and consent to participate

The settings participating in the study in collaboration with University Hospital Bonn are both situated at the University Hospital Bonn. (The Department of dermatology and the Department of urology) Therefore both centres gained ethical approval by the Research Ethics Committee (REC) of the medical faculty Rheinische Friedrich-Wilhelm’s University in Bonn (ref.nr. 2024-59-BO).

For the centres collaborating with the University of Pécs (the University of Pécs Clinical Centre in Pécs and the National Institute of Oncology in Budapest), both centres received ethical approval by the REC of the University of Pécs Clinical Centre (ref.nr. BM/8844-1/2024, April 2024).

For the centres cooperating with the Radboud University Medical Centre: both centres, (Radboud University Medical Centre and Rijnstate Hospital), received a waiver for ethical approval from the REC of the Radboud University Medical Centre in Nijmegen (ref.nr.2023-16796, January 2024).

For the centres cooperating with the University of Zielona Gora, both centres gained separate ethical approval. Firstly, University Hospital Karola Marcinkowskiego in Zielona Gora received ethical approval by the REC of the University Hospital Karola Marcinkowskiego in Zielona Gora (ref.nr, RCM-CM-KBUZ.0015.22.2024, June 2024). Secondly, the Holy Cross Cancer Centres in Kielce received ethical approval from the REC of the Holy Cross Cancer Centres (ref.nr. 64.2024).

The centres cooperating with the Catholic University of Portugal: gained separate ethical approval. Firstly, the Portuguese Institute of Oncology has gained ethical approval by the REC of the Portuguese Institute of Oncology (ref.nr. UIC 1688). Secondly, Hospital Professor Doutor Fernando in Amadorra gained ethical approval by REC of the Hospital Professor Doutor Fernando in Amadorra (ref.nr 091/2025).

For the centres cooperating with Hospice Casa Sperantei: both institutions gained separate ethical approval. Firstly, Medlife Brasivisi Hospital gained ethical approval by the REC of the Medlife Brasovisi Hospital (ref.nr. 03/10.04.2024), April 2024). Secondly, the Brasov Emergency County Clinical Hospital gained ethical approval from the REC of the Brasov Emergency County Clinical Hospital (ref.nr. 45/25.04.2024, April 2024).

For the centres in cooperating with Lancaster University, both the Royal Blackburn Hospital and Blackpool Victoria Hospital, gained ethical approval by the Health Research Authority and Healthcare Research Wales (ref.nr. 24/NW/0142).

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that theyhave no competing interests.

Funding

The Pal-Cycles study is funded by the HorizonEurope EU funding, grant number: 101057243. The design of the study was peer-reviewed by the funding body prior to awarding the grant. This funding source will not have any role during the execution, analyses, interpretation of the data, or decision to submit results of the study. The contribution of Lancaster University to the Pal-Cycles project was funded by Horizon Europe Guarantee UKRI, grant number: 10038822

Author contributions

IK, JH, NP conceptualized and designed the study. PB, IK, JH wrote the protocol. HB, AC, BDF, PHM, FH, EK, WL, DM, SP, NP, SS and JH contributed to the protocol by participating in discussions and providing feedback on drafts of the protocol. PB build the electronic case report form in CASTOR for this study. Sites from Germany, Hungary, Portugal, Poland ,the Netherlands, Romania, UK recruit patients for the study. PB, IK, JH wrote the manuscript. All authors read, provided feedback and approved the final manuscript.

Acknowledgements

The Pal-Cycles coordinating institution, Radboudumc (Stichting Radboud Universitair Medisch Centrum), Netherlands, as well as the other partners: Radboudumc (Stichting Radboud Universitair Medisch Centrum), Netherlands: Jeroen Hasselaar, Pippa van den Brand; Lancaster University (ULANC), United Kingdom: Nancy Preston, Sheila Payne, Rachel Hooley; Universitätsklinikum Bonn (UKB), Germany: Lukas Radbruch, Birgit Jaspers, Holger Brunsch, Séverine Surges; University of Pécs (Pecsi Tudomanyegyetem, UP), Hungary: Veronika Lukacs, Balázs Fülöp, Ágnes Csikós, Universidade Católica Portuguesa (UCP), Portugal: Sandra Martins Pereira, Pablo Hernández Marrero; Hospice Casa Sperantei (HCS), Romania: Daniela Mosoiu, Flavia Hurducas, Doina Gaman, Camelia Ancuta; Universidad de Navarra (UNAV), Spain: Maria Arantzamendi, Eduardo Garralda Domezain, Carlos Centeno, Alazne Belar Beitia, Marina García, Tamara Radojicic; European Association for Palliative Care (EAPC): Cathy Payne, Carla Reigada; University of Zielona Góra (Uniwersytet Zielonogorski, CM UZ), Poland: Wojciech Leppert.

References

1. Courteau C, Chaput G, Musgrave L, Khadoury A. Patients with Advanced Cancer: When, Why, and How to Refer to Palliative Care Services. Curr Oncol. 2018;25(6):403–8.
2. Zimmermann C, Swami N, Krzyzanowska M, Hannon B, Leighl N, Oza A, et al. Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. Lancet. 2014;383(9930):1721–30.
3. WHO. National Cancer Control Programmes, Policies and managerial guidelines. 2002 May.

4. Nysæter TM, Olsson C, Sandsdalen T, Wilde-Larsson B, Hov R, Larsson M. Preferences for home care to enable home death among adult patients with cancer in late palliative phase – a grounded theory study. BMC Palliat Care. 2022;21(1):49.
5. den Herder-van, der Eerden M, Ebenau A, Payne S, Preston N, Radbruch L, Linge-Dahl L, et al. Integrated palliative care networks from the perspectives of patients: A cross-sectional explorative study in five European countries. Palliat Med. 2018;32(6):1103–13.
6. den Herder-van, der Eerden M, Hasselaar J, Payne S, Varey S, Schwabe S, Radbruch L, et al. How continuity of care is experienced within the context of integrated palliative care: A qualitative study with patients and family caregivers in five European countries. Palliat Med. 2017;31(10):946–55.
7. Engel M, van der Padt-Pruijsten A, Huijben AMT, Kuijper TM, Leys MBL, Talsma A, et al. Quality of hospital discharge letters for patients at the end of life: A retrospective medical record review. Eur J Cancer Care (Engl). 2022;31(1):e13524.
8. Weetman K, Spencer R, Dale J, Scott E, Schnurr S. What makes a successful or unsuccessful discharge letter? Hospital clinician and General Practitioner assessments of the quality of discharge letters. BMC Health Serv Res. 2021;21(1):349.
9. Hesselink G, Schoonhoven L, Barach P, Spijker A, Gademan P, Kalkman C, et al. Improving Patient Handovers From Hospital to Primary Care. Ann Intern Med. 2012;157(6):417–28.
10. Gibson S, McConigley R. Unplanned oncology admissions within 14 days of non-surgical discharge: a retrospective study. Support Care Cancer. 2016;24(1):311–7.
11. Garralda E, Tripodoro VA, Ling J, Brennan J, Montero Á, Bastos F, et al. EAPC Atlas of Palliative Care in the European region 2025. Pamplona: EUNSA; 2025.
12. Arias-Casais N, Garralda E, Rhee J. EAPC atlas of palliative care in Europe. Romania. 2019;122(6).
13. Garralda E, Tripodoro VA, Ling J, Brennan J, Montero Á, Bastos F et al. EAPC Atlas of Palliative Care in the European Region 2025. 2025.
14. Payne S, Harding A, Williams T, Ling J, Ostgathe C. Revised recommendations on standards and norms for palliative care in Europe from the European Association for Palliative Care (EAPC): A Delphi study. Palliat Med. 2022;36(4):680–97.
15. Hui D, Bruera E. Models of Palliative Care Delivery for Patients With Cancer. J Clin Oncol. 2020;38(9):852–65.
16. Naylor MD, Bowles KH, McCauley KM, Maccoy MC, Maislin G, Pauly MV, et al. High-value transitional care: translation of research into practice. J Eval Clin Pract. 2013;19(5):727–33.
17. Finlayson K, Chang AM, Courtney MD, Edwards HE, Parker AW, Hamilton K, et al. Transitional care interventions reduce unplanned hospital readmissions in high-risk older adults. BMC Health Serv Res. 2018;18(1):956.
18. Nielsen LM, Maribo T, Kirkegaard H, Petersen KS, Lisby M, Oestergaard LG. Effectiveness of the Elderly Activity Performance Intervention on elderly patients' discharge from a short-stay unit at the emergency department: a quasi-experimental trial. Clin Interv Aging. 2018;13:737–47.

19. Sahota O, Pulikottil-Jacob R, Marshall F, Montgomery A, Tan W, Sach T, et al. The Community In-reach Rehabilitation and Care Transition (CIRACT) clinical and cost-effectiveness randomisation controlled trial in older people admitted to hospital as an acute medical emergency. Age Ageing. 2017;46(1):26–32.
20. Mora K, Dorrejo XM, Carreon KM, Butt S. Nurse practitioner-led transitional care interventions: An integrative review. J Am Association Nurse Practitioners. 2017;29(12):773–90.
21. Leung C, Andersen CR, Wilson K, Nortje N, George M, Flowers C, et al. The impact of a multidisciplinary goals-of-care program on unplanned readmission rates at a comprehensive cancer center. Support Care Cancer. 2023;32(1):66.
22. Shimada N, Ishiki H, Iwase S, Chiba T, Fujiwara N, Watanabe A, et al. Cancer Transitional Care for Terminally Ill Cancer Patients Can Reduce the Number of Emergency Admissions and Emergency Department Visits. Am J Hospice Palliat Medicine®. 2017;34(9):831–7.
23. Pivodic L, Pardon K, Miccinesi G, Alonso TV, Moreels S, Donker GA, et al. Hospitalisations at the end of life in four European countries: a population-based study via epidemiological surveillance networks. J Epidemiol Commun Health. 2016;70(5):430–6.
24. Overbeek A, Van den Block L, Korfage IJ, Penders YWH, van der Heide A, Rietjens JAC. Admissions to inpatient care facilities in the last year of life of community-dwelling older people in Europe. Eur J Pub Health. 2017;27(5):814–21.
25. Chan AW, Boutron I, Hopewell S, Moher D, Schulz KF, Collins GS, et al. SPIRIT 2025 statement: Updated guideline for protocols of randomised trials. PLoS Med. 2025;22(4):e1004589.
26. Copas AJ, Lewis JJ, Thompson JA, Davey C, Baio G, Hargreaves JR. Designing a stepped wedge trial: three main designs, carry-over effects and randomisation approaches. Trials. 2015;16(1):352.
27. Prost A, Binik A, Abubakar I, Roy A, De Allegri M, Mouchoux C, et al. Logistic, ethical, and political dimensions of stepped wedge trials: critical review and case studies. Trials. 2015;16(1):351.
28. White N, Kupeli N, Vickerstaff V, Stone P. How accurate is the 'Surprise Question' at identifying patients at the end of life? A systematic review and meta-analysis. BMC Med. 2017;15(139).
29. Mercadante S, Adile C, Ferrera P, Casuccio A. Characteristics of advanced cancer patients who were readmitted to an acute palliative/supportive care unit. Support Care Cancer. 2017;25(6):1947–52.
30. OECD. OECD Health Policy Studies. Time for Better Care at the End of Life. Paris: OECD Publishing; 2023.
31. Downar J, Goldman R, Pinto R, Englesakis M, Adhikari NK. The surprise question for predicting death in seriously ill patients: a systematic review and meta-analysis. CMAJ. 2017;189(13):E484–93.
32. White N, Kupeli N, Vickerstaff V, Stone P. How accurate is the ‘Surprise Question’ at identifying patients at the end of life? A systematic review and meta-analysis. BMC Med. 2017;15(1):139.
33. !!! INVALID CITATION !!! (31, 32).
34. Hooley RL, Payne S, Begovic D, Correa-Morales JE, Harding A, Hasselaar J, et al. Collaboration, coordination and communication as facilitators of transitions for patients with advanced cancer: a

scoping review linked to the Pal-Cycles project. BMC Palliat Care. 2024;23(1):204.

35. Hasselaar J, Duenk R, Jansen Schuiling M, van der Sande R, Vissers K. Implementing a Transmural Palliative Care Protocol in a Homecare Region: A Mixed Methods Study Including Costs and Effects. Palliat Med. 2022;36(1suppl):39–40.
36. ZonMW. Een continuüm van vertrouwen en deskundigheid: Ontwikkeling en evaluatie van een regionaal protocol voor 24/7 beschikbaarheid van gespecialiseerde palliatieve zorg in de thuissituatie ZonMW Projecten2021 [Available from: https://projecten.zonmw.nl/nl/project/een-continuum-van-vertrouwen-en-deskundigheid-ontwikkeling-en-evaluatie-van-een-regionaal
37. Monteiro Dda R, Almeida Mde A, Kruse MH. [Translation and cross-cultural adaptation of the Edmonton Symptom Assessment System for use in Palliative Care]. Rev Gaucha Enferm. 2013;34(2):163–71.
38. Woitha K, Garralda E, Martin-Moreno JM, Clark D, Centeno C. Ranking of Palliative Care Development in the Countries of the European Union. J Pain Symptom Manag. 2016;52(3):370–7.
39. Coleman EA, Boult C. Improving the Quality of Transitional Care for Persons with Complex Care Needs. J Am Geriatr Soc. 2003;51(4):556–7.
40. Koller M, Kussman J, Lorenz W, Jenkins M, Voss M, Arens E, et al. Symptom reporting in cancer patients: The role of negative affect and experienced social stigma. Cancer. 1996;77(5):983–95.
41. Jocham HR, Dassen T, Widdershoven G, Halfens R. Reliability and validity of the EORTC QLQ-C30 in palliatieve care cancer patients. Cent Eur J Med. 2008;4(3):348–57.
42. FACIT. FACT-G: Functional Assessment of Cancer Therapy. facitorg2021.
43. Kemmler G, Holzner B, Kopp M, Dünser M, Margreiter R, Greil R, et al. Comparison of Two Quality-of-Life Instruments for Cancer Patients: The Functional Assessment of Cancer Therapy-General and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30. J Clin Oncol. 1999;17(9):2932.
44. Holzner B, Bode RK, Hahn EA, Cella D, Kopp M, Sperner-Unterweger B, et al. Equating EORTC QLQ-C30 and FACT-G scores and its use in oncological research. Eur J Cancer. 2006;42(18):3169–77.
45. Luckett T, King MT, Butow PN, Oguchi M, Rankin N, Price MA, et al. Choosing between the EORTC QLQ-C30 and FACT-G for measuring health-related quality of life in cancer clinical research: issues, evidence and recommendations. Ann Oncol. 2011;22(10):2179–90.
46. EORTC Quality of Life. EORTC Core 2023 [Available from: https://qol.eortc.org/core/
47. Cella DF, Tulsky DS, Gray G, Sarafian B, Linn E, Bonomi A, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. J Clin Oncol. 1993;11(3):570–9.
48. Mercer SW, Maxwell M, Heaney D, Watt GC. The consultation and relational empathy (CARE) measure: development and preliminary validation and reliability of an empathy-based consultation process measure. Fam Pract. 2004;21(6):699–705.
49. Witz M, Boecker M, Forkmann T, Neumann M. Evaluation of the Consultation and Relational Empathy (CARE) measure by means of Rasch-analysis at the example of cancer patients. Patient Educ

Couns. 2011;82(3):298–306.
50. Kristjanson LJ. Validity and reliability testing of the FAMCARE Scale: measuring family satisfaction with advanced cancer care. Soc Sci Med. 1993;36(5):693–701.
51. Lo C, Burman D, Hales S, Swami N, Rodin G, Zimmermann C. The FAMCARE-Patient scale: Measuring satisfaction with care of outpatients with advanced cancer. Eur J Cancer. 2009;45(18):3182–8.
52. van Dijk I, Scholten Meilink Lenferink N, Lucassen PL, Mercer SW, van Weel C, Olde Hartman TC, et al. Reliability and validity of the Dutch version of the Consultation and Relational Empathy Measure in primary care. Fam Pract. 2017;34(1):119–24.
53. Ringdal GI, Jordhøy MS, Kaasa S. Measuring quality of palliative care: Psychometric properties of the FAMCARE Scale. Qual Life Res. 2003;12(2):167–76.
54. Décary S, Toupin-April K, Légaré F, Barton JL. Five Golden Rings to Measure Patient-Centered Care in Rheumatology. Arthritis Care Res (Hoboken). 2020;72(Suppl 10):686–702.
55. Osse BHP, Vernooij-Dassen MJFJ, de Vree BPW, Schadé E, Grol RPTM. Assessment of the need for palliative care as perceived by individual cancer patients and their families. Cancer. 2000;88(4):900–11.
56. Naylor M, Brooten D, Jones R, Lavizzo-Mourey R, Mezey M, Pauly M. Comprehensive discharge planning for the hospitalized elderly. A randomized clinical trial. Ann Intern Med. 1994;120(12):999–1006.
57. Scott M, Shaver N, Lapenskie J, Isenberg SR, Saunders S, Hsu AT, et al. Does inpatient palliative care consultation impact outcomes following hospital discharge? A narrative systematic review. Palliat Med. 2020;34(1):5–15.
58. Barkley JE, McCall A, Maslow AL, Skudlarska BA, Chen X. Timing of Palliative Care Consultation and the Impact on Thirty-Day Readmissions and Inpatient Mortality. J Palliat Med. 2019;22:393–9.
59. Brickey J, Flannery M, Cuthel A, Cho J, Grudzen CR, Blaum C, et al. Barriers to recruitment into emergency department-initiated palliative care: a sub-study of a multi-site, randomized controlled trial. BMC Palliat Care. 2022;21(1):22.
60. Oriani A, Dunleavy L, Sharples P, Perez Algorta G, Preston NJ. Are the MORECare guidelines on reporting of attrition in palliative care research populations appropriate? A systematic review and meta-analysis of randomised controlled trials. BMC Palliat Care. 2020;19(1):6.
61. Durovni B, Saraceni V, Moulton LH, Pacheco AG, Cavalcante SC, King BS, et al. Effect of improved tuberculosis screening and isoniazid preventive therapy on incidence of tuberculosis and death in patients with HIV in clinics in Rio de Janeiro, Brazil: a stepped wedge, cluster-randomised trial. Lancet Infect Dis. 2013;13(10):852–8.
62. Appendix I.

Figures

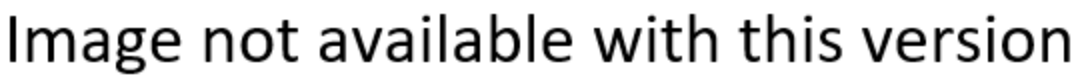

Figure 1

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Supplementary Files

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- AppendixI.docx