Lancaster University at the heart of research about palliative care in Europe

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The International Observatory on End of Life Care at Lancaster University conducts research to improve palliative and end of life care for patients and family carers as well as providing educational opportunities to study for a PhD in Palliative Care. Palliative and end of life care is mainly focused on the last year of life, but can offer support to people at any stage of their illness. Where palliative care was traditionally thought of just for people with cancer, it is increasingly seen as relevant and recommended for everyone. Palliative care encompasses a holistic approach including physical, spiritual, psychological and social support. Most health care professionals provide palliative care but sometimes specialist palliative care is required for people with complex needs.

The UK is the world leader in providing palliative care with much of specialist palliative care provided by hospices. Researchers at the International Observatory on End of Life Care come from a range of backgrounds including nursing, medicine, social work and work closely with clinical colleagues across Morecambe Bay. We run a part-time PhD in Palliative Care, which includes students from all over the world and the UK, conducting their research in their own country. We also work with European partners in large-scale research projects. In recent years, this has included a study to evaluate prescribing of opioids, best practice in developing integrated palliative care services, a study to develop palliative care in nursing homes and a large trial of advance care planning. This year we commenced two new studies funded through the Horizon 2020 European Funding stream, Palliative Sedation and MyPal, which are described below.

PALLIATIVE SEDATION https://palliativesedation.eu/

WHAT IS THE PALLIATIVE SEDATION PROJECT ABOUT?

As patients approach the end of life, they often experience a range of distressing symptoms and concerns such as pain, delirium and breathlessness. Whilst most symptoms and concerns are amenable to pharmacological and/or non-pharmacological interventions, there may be a few that are too difficult to treat or treatment options fail. These are called *refractory symptoms* because treatment: 1) does not work, 2) the effects take too long to happen, or 3) the side-effects are not acceptable to the patient. Refractory symptoms are not restricted to physical symptoms, and therefore a multidimensional approach is needed to fully assess and manage the patient's condition. For example, existential suffering may be particularly difficult to assess and manage. In these cases, an alternative option is to sedate the patient using medication to reduce consciousness and therefore decrease awareness of the distress. The use of palliative sedation may vary in its duration (intermittent or continuous until death) and depth of consciousness (light or deep).

There is known to be considerable diversity in how palliative sedation is used in Europe. Estimates suggest that it is used in 10-18% of all deaths in Europe. While there are national and international clinical guidelines for palliative sedation (such as the European Association for Palliative Care Framework,[1] the quality and content of guidelines vary because the terminology and concepts lack consensus, and they are infrequently used.[2-4] The practice of palliative sedation raises important and controversial issues because it has been suggested that it may result in life-shortening effects and potentially result in 'slow' euthanasia, although the empirical evidence does not support this contention. The practice therefore raises many moral and ethical dilemmas for clinicians, and is poorly understood by patients and families. In addition, witnessing the 'intolerable' suffering of others is distressing, both for family members and the clinical team. However, there is a lack of clarity in the assessment and management of refractory symptoms, the influence of different cultural, religious and social norms, and how health professionals, patients and families understand these processes and options.

In this new project, we are seeking to examine the concept and practice of proportional palliative sedation for refractory symptoms throughout Europe, where sedation is regarded on a continuum from light to deep, and where medication is titrated to that required for symptom relief to ensure maximum patient comfort and quality of dying.

HOW WILL THE PROJECT INVESTIGATE PALLIATIVE SEDATION?

This project will use a number of research methods to investigate the assessment of refractory symptoms and the use of palliative sedation.

- *Literature reviews* – we start by examining the extensive published evidence to determine both its quality and its usefulness in defining terminology.
- *International country level survey* – we will investigate the level of integration of clinical recommendations into current clinical practice in Europe and obtain an overview of national practices.
- *Observational study of clinical practice* in five countries (The Netherlands, Italy, Germany, Belgium and Spain) to examine local practices and identify how patient comfort is assessed during sedation.
- *Multiple case studies* will provide in-depth information on 10 patient cases per clinical site.
- *Moral case deliberations* – we will use vignettes describing palliative sedation to elicit discussions about end of life decision making with groups of clinicians in 16 clinical centres in eight countries (The Netherlands, Italy, Germany, Belgium, Hungary, Romania, England and Spain).
- *Cost consequence analysis* will be used to inform policy recommendations.

WHO WILL IT BE INVOLVED IN THESE STUDIES?

The Palliative Sedation project is led by Professor Jeroen Hasselaar from Radmoud University Medical Centre, Nijmegen, The Netherlands, along with eight other internationally renowned universities and clinical centres. In addition, the project is supported by the European Cancer Patients Alliance and the European Association for Palliative Care (EAPC) to ensure that patient and professional perspectives are addressed. The International Observatory on End of Life Care at Lancaster University will lead on the online education programme.

WHAT ARE THE LIKELY BENEFITS?

This project is likely to provide detailed and extensive evidence about how refractory symptoms are managed and how palliative sedation is used to increase patient comfort in the final days of life. We will start to understand more about clinical decision making near the end of life from the moral case deliberations, and identify differences and similarities across Europe, and the factors that influence them.

The project has some specific activities and outputs including:

- Revising and updating the *EAPC Framework on Palliative Sedation* (first published in 2009).[1]
- Preparing and delivering a *free online education programme* for clinicians and the public about what dying well means and how palliative sedation can be used to increase quality of dying.
- An *ebook* which will provide examples of how refractory symptoms are managed and palliative sedation used in different countries, and highlighting 'best practices'.
- A conference, scientific presentations and publications will target different audiences including health professionals, patients and family carers, researchers and policy makers.

MYPAL https://mypal-project.eu/ WHAT IS THE MYPAL PROJECT ABOUT?

MyPal (Fostering Palliative Care of Adults and Children with Cancer through Advanced Patient Reported Outcome Systems) is a European Commission funded Horizon 2020 project involving 16 organisations from 7 European countries. The project was awarded €3,999, 308. It started on 1 January 2019 and will last for 42 months. It is one of 10 projects funded under a call for "Novel patient-centred approaches for survivorship, palliation and/or end-of-life care."[5]

The aim of all the projects is to demonstrate the effectiveness of new or improved interventions to relieve symptoms and suffering caused either by life threatening non-communicable diseases or by the serious late and long-term side effects of disease treatments.

While a number of different interventions are currently in use to achieve these aims, they are often not sufficiently validated or adapted to the particular needs of patients affected with a specific chronic disease.[5] The aim of all the projects funded through this grant call is to begin to remedy this deficiency, and includes both pharmalogical and/or non-pharmalogical interventions.

Patients with cancer often experience a range of distressing symptoms and concerns. If these symptoms and concerns can be communicated to their healthcare providers in a timely and accurate way, so that they can be dealt with promptly, it is anticipated that this will improve their quality of life

The use of electronic Patient Reported Outcomes (ePRO) is at the heart of the MyPal intervention. Although Patient Reported Outcomes (PRO), reports coming directly from patients about how they experience their condition and its treatment, were principally developed for use in clinical trials to help assess the effectiveness of an intervention, recently there has been a growing interest in using PROs to monitor a patient's condition as part of routine clinical practice.[6] This move has been given added momentum by the possibilities opened up by digital health and the use of mobile applications.

MyPal aims to exploit these advances in digital and mobile technologies to develop and evaluate two new ePRO based interventions for cancer patients: one for adults with haematological malignancies and another for children with haematological malignancies and solid tumours.

HOW WILL THE MYPAL APPLICATIONS WORK?

MyPal-ADULT

The first intervention is a smartphone application for adult patients with either chronic lymphocytic leukemia (CLL) or myelodysplastic syndromes (MDS). The application will enable patients to regularly complete a short set of standardised ePRO questionnaires corresponding to their condition. There will also be a customised ePRO form for the patient to report any changes that occur in between times. The ePROS will be completed and submitted using the patient's smartphone or tablet. All the information will then be made available in real-time to the patient's healthcare professionals (HCP) through a customised, web-based application so their healthcare team can log in at any time.

MyPal-CHILD study

The second intervention is targeted at children with both solid and hematologic malignancies. Conceptually, it is very similar to the MyPal adult intervention. The main difference is that the children will use a specially designed video game, which they will play on a tablet or smartphone, to answer the questions. The purpose of the game is motivate the children to regularly use the application by making answering the questions about their condition entertaining and enjoyable.

Complementary information about the child's symptoms and any changes in their condition will also be provided by their parent or guardian through ePRO questionnaires integrated into a custom smartphone application designed for this purpose.

As with MyPal-ADULT, both the child's and parent/carer's reports will made available to the HCPs though the HCPs web-based application.

The core idea underlying both the adult and child interventions is that by enabling patients to more accurately record any changes in their symptoms and condition, and then communicate this to their HCPs in a timely and effective way, there is the possibility of enhancing the care the patient receives. This is what will be tested.

HOW WILL IT BE TESTED?

To assess the adult intervention, there will be an interventional, unblinded, 1:1 randomized controlled clinical trial (RCT) with an expected enrolment of 300 participants diagnosed with chronic lymphocytic leukaemia or myelodysplastic syndrome. The trial will take place at five clinical centres: Karolinska Institute, Sweden; University Vita-Salute San Raffaele, Italy; University Hospital of Crete, Greece; C.Papanicolaou Hospital, Thessaliniki, Greece, and University Hospital Brno, Czech Republic.

For the child intervention, there will be a non-interventional, observational study of 100 participating children and their parents. This will take place across three centres: Hannover Medical School, Germany; University Hospital Brno, Czech Republic; and Saarland University, Germany.

Both the MyPal-ADULT and the MyPal-CHILD studies are expected to start in May 2020 and data collection will continue for 21 months.

The International Observatory on End of Life Care (IOELC) at Lancaster University is responsible for the Dissemination and Exploitation of Results (PDER) to ensure that the activities and outcomes of the project are made as widely available as possible. Along with running the project's website and social media, and coordinating and promoting journal articles and conference papers, IOELC will also be producing an eBook and organising a special session at the European Association for Palliative Care (EAPC) Congress at the end of the project.

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GP v's Consultant Badminton Trophy