The European MyPal study:

Developing digital health for adults and children with cancer

Edited by

Sheila Payne, Yakubu Salifu,
Dunja Begovic, and Anthony Greenwood

MyPal

Foreword

At an international conference in Montreal in 1976 called "Principle and practice in palliative care," attended by pioneers in the field like Dame Cicely Saunders, Elisabeth Kübler Ross, and Balfour Mount, the approach to palliative care was described as depending "less on the technologic impedimenta of intensive care units than on personal, skilled care by staff of all disciplines" . The paper summarising this conference first identified the "high-person, low technology" paradigm as a central aspect of palliative care. This was an important step forward in person-centred care, because at that time in medicine, developments in technology fostered the attitude of doing what was technically feasible and not always considering what was reasonable in terms of the patient's disease trajectory and their physical, psychological, social, and spiritual needs. Over the past 50 years, those of us working in hospice and palliative care have identified with this paradigm. At the same time, technology and digitisation have evolved tremendously. Automation, the World Wide Web, the Internet of Things, communication devices, sensors, and wearables - to name a few - have significantly changed the way we live, the way we communicate, and the way we gather and use information. This is true for daily life, but also for healthcare in general.

In our field, too, we have started to think about how we can take advantage of digitisation and new technologies to best support patients and their families in palliative care. An important step in this disruptive evolution is the MyPal project, which is featured in this ebook. EAPC is proud to have been involved in this EU-funded project bringing together many interdisciplinary and international experts. MyPal can be an important step into the future to overcome our old paradigm of "high person-low technology", through a person-centred approach supported by appropriate technologies. I am sure that our pioneers would have enjoyed reading this book!

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Christoph Ostgathe
President European Association for Palliative Care, Belgium

Executive Summary

Sheila Payne, Dunja Begovic and Yakubu Salifu
International Observatory on End of Life Care, Lancaster University, United Kingdom

This ebook is designed to provide an accessible summary of the MyPal project for clinicians, researchers and the public.

The **aims of the MyPal project** were to foster palliative care for patients with cancer by leveraging electronic Patient Reported Outcome (ePRO) systems through their adaptation to the personal needs of patients with cancer and their caregivers. The MyPal intervention seeks to empower patients with cancer and their caregivers in capturing and reporting their symptoms more accurately, and communicating them in a seamless and effective way to their healthcare providers.

Three **sources of information** were drawn upon to inform the ebook:

1. The background literature on ePRO interventions for cancer palliative care (1).
2. The design and implementation of the digital MyPal system for adults and their healthcare providers and the serious game app for children.
3. The design, implementation, and baseline data from the randomised control trial to test the MyPal system with adults with haematological malignancies (2); and the MyPal Child non-randomised observational feasibility cohort study (3).

The **structure of the ebook** is as follows:

The Introductory chapter provides the rationale for the MyPal project. This is followed by Chapter 1 which presents a summary of the literature on digital and ehealth interventions in cancer palliative care, with special attention to the use of ePROs. Chapter 2 carefully considers the ethical approach taken in designing and implementing the MyPal system. In addition, it highlights the implications that digital interventions may have in relation to security, privacy and acceptability for older patients with cancer, children with cancer and their parents. The following two chapters provide an overview of the technical aspects of developing the MyPal Adult system (Chapter 3) and the MyPal Child gamification apps for children in different ages groups and their parents (Chapter 4). These complex interventions were implemented in two empirical studies: a randomised control trial for adults with blood cancers (Chapter 5), and in a non-experimental observational feasibility study with children with solid tumours and blood cancers (Chapter 6). Delays to recruitment and completion of these studies means that only baseline data are reported here, although full details of the studies findings will be published later. The concluding chapter (Chapter 7) offers an initial synthesis of the MyPal programme of work.

Key messages

- The MyPal project builds upon the existing evidence and literature on the use of ePROs to facilitate communication between patients and clinicians in cancer and palliative care contexts.
- The use of ePROs shows potential for contributing to patient-centred healthcare, including palliative care, as it can enhance the collection of various types of data directly from patients.
- The MyPal system for adults with blood cancer tested a complex intervention that included ePROs, wearable activity sensors, personalised motivational messages, medication reminders and access to cancer specific information.
- The MyPal Child study investigated the feasibility of a serious game to elicit ePROs adapted to different age groups.
- When testing digital health innovations, researchers and healthcare professionals should adopt an ethical approach and culture at all stages of the study design, implementation and conduct. Compliance with the relevant legal frameworks regarding data and privacy protection must be ensured.
- The introduction of digital health innovations is likely to encounter various organisational, administrative and logistical challenges.
- It is suggested that all end-users are involved before and during the development and testing phase of digital health innovations, to ensure high degrees of acceptability, usability and utility.

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A tribute to an exceptional individual – Vasilis Koutkias

Christina Karamanidou, Pantelis Natsiavas, Kostas Stamatopoulos
Institute of Applied Biosciences, Centre for Research and Technology Hellas, Greece

Vassilis Koutkias

MyPal was the brain child of the late lamented Vassilis Koutkias, who sadly passed away on December 14, 2019 at the age of 44, after a 3-year struggle with cancer.

Vassilis was the scientific coordinator of the project and he actively participated in it until the very end, despite the hindrances arising from, amongst others, the lack of adequate palliative care in Greece, the very focus of MyPal. As an intelligent and empathetic person with a scientific backgound in Biomedical Informatics and first-hand experience of a chronic, debilitating and life-threatening disease which eventually consumed him, Vassilis developed the idea to integrate eHealth in real-world healthcare settings for advancing palliative care in cancer. In a nutshell, this is what MyPal is about.

Vassilis was born on May 20, 1975, in Lamia, Greece. In 1993, he entered the Department of Electrical and Computer Engineering of the Aristotle University of Thessaloniki (AUTH) in Greece. In 2001, he received his PhD degree in Biomedical Informatics from AUTH which cemented his total commitment to research in this scientific field.

Vassilis had close links with France. In 2007, he first met Professor Régis Beuscart, Head of the CERIM Laboratory (Center of Studies and Research in Medical Informatics) in Lille, France, in the context of the European Project PSIP that focused on the automatic identification and prevention of Adverse Drug Events (ADEs) and adverse reactions to medications. A few years later, Vassilis started collaborating with Marie-Christine Jaulent, Head of the LIMICS (Laboratory of Medical Informatics and Knowledge Engineering for eHealth) in Paris, France, again on the topic of pharmacovigilance with a major emphasis in reinforcing signal detection through Knowledge Engineering approaches. For this work, he was awarded a Marie Curie individual fellowship conducted at the LIMICS and spent two very fruitful and happy

years in the lab that formed the basis for several joint initiatives until the very end of his life.

After his departure from France, Vassilis returned to Greece in 2016 and he was elected as a Junior Researcher at the Institute of Applied Biosciences of the Centre for Research & Technology Hellas (INAB | CERTH) in Thessaloniki. Thanks to his enthusiasm, commitment and personal ethos, he established the eHealth Lab at INAB | CERTH which soon attracted early career scientists for postgraduate research. Among his colleagues in Thessaloniki, Vassilis was widely respected as a colleague of great talent and integrity and an inspiring supervisor. Indeed, he became known as a great mentor constantly providing his students and team members with opportunities for personal development in a work environment conductive to research and individual fulfilment.

During his tragically short life, Vassilis epitomised scientific productivity at the very highest level. As a PhD student and postgraduate researcher he was involved in various European projects between 1999 and 2016. Then, between 2016 and his passing way in 2019, he was the Principal Investigator of several additional European projects, a track record attesting to his remarkable intellectual agility, his extraordinary ability to work in various consortia and on various topics in Biomedical Informatics. As the result of this sustained research activity, he was the editor of four books, and author of more than 100 original papers including about 70 papers published in peer-reviewed journals, peer-reviewed papers in books and book series, and peer-reviewed papers published in international conference proceedings.

Vassilis had a charisma in motivating those around him to work together around a theme. He shared his vision of MyPal first within the Institute and then in the wide network of the MyPal partners in a clear and concise way and invested precious personal time on the design and the deployment of the MyPal clinical study protocols, the relevant technical developments and the coordination of the project. His tireless effort, great style and patience set a high bar for the entire MyPal consortium.

We are sure that most of us who were associated with him have fond memories of Vassilis and are inspired by his intelligence, tenacity and integrity. He will be dearly missed by his many friends, former students and postdocs and collaborators throughout the world, including the MyPal community. He is survived by his wife Antigoni Malousi and two daughters, Zetta and Stella.

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Introduction: Background to the MyPal project and rationale for the use of ePROs in digital health

Pantelis Natsiavas and Christina Karamanidou
Institute of Applied Biosciences, Centre for Research and Technology Hellas, Greece

Summary

This chapter presents the rationale for the MyPal project and its aims, and outlines the project's approach and methodology.

The MyPal project is novel as it links the 'point of care' with the 'point of life', by empowering patients and caregivers to accurately record patients' symptoms and communicate them to healthcare providers. In this way, important changes in patients' quality of life (QoL), physical and psychological states, can be identified, enabling the personalisation of palliative care delivery. As an eHealth project, MyPal uses technology to collect patient-reported outcomes (PROs) and integrate them into general palliative care services within healthcare settings, to enhance the quality of care delivered to patients with cancer. MyPal aims to develop and test personalised palliative care interventions in two different patient groups, namely: 1) adults diagnosed with blood cancers, and 2) children with solid tumours or blood cancers. MyPal targets different age groups and cancer types, through carefully designed clinical studies conducted in diverse healthcare settings across Europe.

Keywords: palliative care, symptom reporting, personalised healthcare, patients with cancer needs, electronic patient-reported outcomes, children

Introduction

The MyPal project consisted of designing and testing a patient-centred palliative care intervention for patients with cancer (adults and children). Since the needs of patients with cancer are complex and diverse, such an intervention should be based on a thorough understanding of patients' varying needs across their disease trajectories. [1-2] Such comprehensive and adaptive palliative interventions are currently lacking, partly because they require interdisciplinary expertise and the consideration of many clinical and psychosocial aspects. Multiple factors are considered crucial to the successful management of patients with cancer towards the end of life. These include: the patient's age, overall physical condition, life expectancy, personal preferences and health literacy, the treatment aim, the medication plan and the impact on QoL.

Such palliative care interventions seem even more difficult in the context of healthcare systems, where the majority of patients worldwide do not have access to integrated palliative care. Integrated palliative care brings together administrative, organisational, clinical and service aspects in order to realise the continuity of care. [3] Lack of access to integrated palliative care often means that patients are not able to receive care in their preferred place, but are transferred between sites. Thus, continuity of care between all actors involved in the care network is not established. [4] Efforts need to be directed towards planning palliative care services that are integrated into the healthcare and social care system, linking the 'point of life' with the 'point of care' in an effective way, thus achieving an improved health status and QoL. Integrating palliative care within the overall frame of management of patients with life-threatening diseases is supported by a growing amount of evidence, [5-6] demonstrating the effectiveness of palliative care delivery on the improvement of patients' QoL.

The MyPal project aims to support a paradigm shift in palliative care delivery for patients with cancer by adapting care to the personal needs of patients and their caregiver(s). Specifically, MyPal aspires to empower patients with cancer and their caregivers to capture and record symptoms accurately and communicate them in an effective way to the respective healthcare professionals. This process focuses on the prompt identification of important changes in the patient's physical and psychological state, as well as their QoL, in order to personalise palliative care delivery.

Within the context of MyPal, patients' active participation was facilitated through the use of Patient-Reported Outcome (PRO) systems. PROs allow a shift from passive patient reporting to active patient engagement. The MyPal platform, therefore, helps to bridge the gap between patient reporting and the timely, personalised actions performed by healthcare providers to address their varying needs.

The rationale for the use of electronic PROs (ePROs) in palliative care

To foster palliative care for patients with cancer, MyPal uses technology to support their care, and to allow them, their family caregivers and healthcare professionals (HCPs), to interact and share information through a mobile health app.

Research findings suggest that clinicians might underestimate the prevalence and severity of symptoms that patients with cancer face in everyday life. [7-10] PROs can be more sensitive and reliable, and can often provide better quality data than clinician-reported data. [11] This is because PROs are "measurements based on reports that come directly from the patient about the status of the patient's health condition without amendment or interpretation of the patient's responses by a physician or anyone else". [12] A growing number of efforts to integrate PROs into routine clinical care processes have also triggered the development of relevant commercial information technology (IT) platform endeavours, [13-14] as these patient-generated health data offer a more comprehensive account of the patients' experience outside the healthcare environment. Indeed, the use of PROs has been associated with improvements in clinical outcomes. [15-16] PROs have become a prominent topic in healthcare innovation, highlighting the role of patient experience as a key measure of healthcare quality. [17]

A growing body of literature supports the feasibility of the electronic collection of PROs, and their integration into standard healthcare settings to enhance the quality of care delivered to patients with cancer. [18-20] The incorporation of ePRO assessments into standard healthcare settings is just one component of the growing body of attempts to collect various types of data directly from patients. Specifically, patient data can be collected via biosensors, home-based digital devices such as scales and blood-pressure monitors, and actigraphy measures of physical activity. Conversely, data received directly from patients can come from standardised questionnaires, nutritional diaries, or proxy reports of the patient's well-being from caregivers. Patient-generated health data can include health history, symptoms, treatment history, lifestyle choices, and other information — created, recorded, gathered, or inferred by or from patients or their proxies to help address a health issue/concern. These data do not replace those gathered by physicians directly or indirectly using medical tests, but rather provide information about variables different from those that can be measured via any physical examination, laboratory test, or imaging modality.

Nevertheless, ePROs have not been yet widely adopted, due to difficulties in integrating them into clinical workflows and electronic medical record systems. [21-22] For the use of ePROs to become routine practice, especially for palliative care, a patient-centred approach is required, adaptable to each patient's needs; however, trained professionals, appropriate policies and eHealth solutions also need to be in place. In addition, ePROs have to be studied further with regard to their application in different cultural contexts and disease types, as well as the varying digital literacy of potential users.

Finally, the perspectives of all stakeholders with regard to the feasibility and acceptability of using ePROs in daily clinical practice ought to be explored. The drivers and barriers for adoption and engagement, as well as perceived benefits and concerns, will inform both future research and practice efforts to integrate ePROs into routine cancer care. MyPal has designed an intervention considering the social and clinical drivers for PRO system adoption, based on clinical practice and the everyday routine of patients with cancer. Furthermore, MyPal has tried to identify and overcome the limitations of current ePRO systems, by employing methods to engage the user in the design of the ePRO digital health system. Patients were encouraged to report their needs and state their preferences; user experience was assessed and validated; and suggestions were gathered via extensive focus groups, think-aloud sessions and other qualitative methods. All of the above led to decisions which have supported the design of the MyPal system. [23]

Specifically, the MyPal project is a non-pharmacological intervention which focuses particularly on ePRO systems, by adapting them to the personal needs of the cancer patient. For adult patients, MyPal developed a mobile application for patient reporting coupled with unobtrusive sensing through smartphones. For children and teenagers, MyPal employed a gamification approach for patient reporting through smartphones and portable devices. Both interventions aimed to enhance patients' QoL, facilitate better patient outcomes, and support effective communication between patients and healthcare providers.

A key challenge for the MyPal project was the fact that this intervention was conducted in the context of the COVID-19 pandemic, which affected recruitment into the clinical studies. However, the COVID-19 pandemic has also highlighted the potential of using health technologies to decentralise and support healthcare ubiquitously. This book summarises the project's rationale and describes the methodological and ethical approach of the studies and technical features of the apps developed, as well as presenting some baseline findings.

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Chapter 1: Summary of the literature

Christina Karamanidou, Pantelis Natsiavas
Institute of Applied Biosciences, Centre for Research and Technology Hellas, Greece

Summary

Patient-reported outcomes (PROs), and especially electronic PROs (ePROs), are expected to play an important role in the development of future eHealth paradigms. These include palliative care for patients with cancer, which has been identified as a key target for such applications. This chapter presents a summary of a published systematic and mapping literature review conducted during the MyPal project. [1] Technical developments extending the focus of ePRO platforms beyond palliative care for patients with cancer are also discussed.

The main findings of the review can be summarised as follows: (1) ePRO systems are typically used as part of research studies, rather than as a tool which could support everyday healthcare; (2) literature has not (yet) fully adopted the updated definitions of palliative care, [2,3] i.e. a wide domain of services including, but notably not restricted to, end-of-life care; (3) there is a lack of use of electronic devices (e.g. smart activity trackers) for palliative care support; and (4) the benefits of ePRO technologies are maximised when focusing on a specific cancer target. In technical terms, there are already (sometimes even commercially) available platforms which could be used in clinical research. However, their integration in terms of usability and unobtrusiveness, as part of clinical research or everyday clinical practice is not yet fully realised. To this end, it is critically important to conduct more research into understanding the psychological factors which affect the adoption of eHealth tools and into improving the overall user experience and the overlap between the use of software and the decision-making process.

Keywords: Electronic patient-reported outcomes, eHealth, palliative care, mHealth, digital health, literature review, children

Introduction

Technical developments enable the use of eHealth tools such as mobile apps and clinical decision support systems as part of everyday clinical practice. Although many issues such as how these systems can be clinically validated ensuring their efficiency and ultimately patient safety are still open, the introduction of these tools has already initiated a new vision of more decentralised healthcare. This decentralisation process has two key aspects: (a) spatial decentralisation and (b) decision-making process decentralisation. Spatial decentralisation refers to the adoption of tools and methods which can support the patient even when they are not hospitalised or visiting a doctor, moving the healthcare processes further away from the clinical environment and closer to the patient's living space. Decision-making process decentralisation refers to the active participation of the patient and their family in the treatment decision-making process (in terms of lifestyle preferences and personal beliefs), moving towards a more patient-centred healthcare paradigm instead of leaving all the decisions to healthcare professionals.

The vision of the MyPal project is that PROs, and more specifically ePROs, are expected to play a prominent role in this new emerging paradigm of healthcare and clinical research, which moves from a hospital-based, doctor-centric approach towards a decentralised and patient-oriented, participatory co-decision-making model.

Thus, identifying patterns of already applied research and identifying gaps for potential future developments could be crucial to support this emerging healthcare paradigm. To this end, in this chapter, we have tried to address the following three questions:

1. What are the current ePRO-based approaches for cancer palliative care?
2. What are ePROs' contribution/value in the domain of cancer palliative care?
3. What are the potential gaps, challenges, and opportunities for further research?

The studies presented and discussed in this chapter were identified as part of a systematic and mapping literature review. [1] This review identified relevant papers which were thoroughly reviewed by the MyPal project team and mapped against a set of evaluation criteria, including which type of patients the study was focusing on and what kind of devices were used. Beyond that, a few more papers and technical developments are also discussed, extending the focus to ePRO platforms which do not necessarily focus on palliative care.

Analysis

In total, 24 studies were included in the review. [4,5,14–23,6,24–27,7–13] Most of the reviewed studies present study protocols (n = 9), while acceptability/feasibility/pilot studies (n = 7) and technical solutions (n = 7) are also quite common.

The vast majority of the research papers that were identified as relevant focused on interventions aimed at adults, with only one intervention targeting children [17] and only two designed for adolescents. [10,21] The lack of focus on children/adolescents indicates a clear gap in the literature and also a potential research opportunity.

It should be highlighted that many studies did not focus on a specific cancer type but rather aim at cancers in general (n = 10). All the identified studies aim to address palliative care for patients with solid tumours, with 10 of them also targeting blood cancers. Most of the included studies (n = 14) focused on specific cancer types with some interventions focusing on more than one cancer type (i.e., prostate cancer (n = 3), lung cancer (n = 2), gastro-intestinal cancer (n = 1), head and neck cancer (n = 1), pancreatic cancer (n = 1), and sarcoma (n = 1), gynaecological cancers, including breast cancer (n = 6)).

To this end, four main themes regarding the reviewed articles/systems/tools have been identified:

- Increasing PRO frequency, ultimately aiming to provide more insights for healthcare professionals [4,5,24,27,28,7,9,13,14,16,18,20,22]
- Promoting patients' self-management of symptoms [5,10–12,14,15,17,19,23]
- Facilitating personalised medicine services [8,20]
- Supporting healthcare professionals in terms of both behaviour and skills [6]

Users' perspective

In terms of evaluating the technical developments from an end-user perspective, both widely adopted frameworks (e.g. the System Usability Scale), [25] and customised approaches have been used. [5,18,20] Interviews have also been undertaken to identify potential barriers, facilitators, and improvement hints. [8] The elaborated eHealth solutions have been largely positively evaluated, in terms of overall satisfaction, usability and user acceptance. However, in some cases, end-users raised serious concerns. [21,27] As a whole, it is clear that end-user interaction with the respective software/platform could be significantly improved, [9,12,13,16,19,24,27] along with improvements regarding symptom management. [19,21,22,27]

It should be noted that this need for better user experience is very common and not

only related to the domain of ePROs or palliative care. One study of patients with lung cancer estimated that 98% of people only use a mobile health (mHealth) application for a short time before quitting. [27] Thus, it should be highlighted that while technical developments might enable the use of mHealth for various health-related use cases, there is still a lot of room for improvement in terms of designing mobile apps which could have significant impact for everyday patient care.

Discussion

As a whole, the reviewed studies argue that there is potential for ePROs to provide a significant impact for end-users. More specifically, the published evidence indicates not only that patients with cancer are generally in favour of ePRO-based interventions, but also that ePRO interventions could contribute to improved health outcomes, such as: an improvement in physical activity; [7] a reduction in anxiety and drowsiness; [27] lower levels of fatigue, nausea, insomnia, [22] and pain intensity; [21] as well as a significant improvement in emotional and social functioning. [21]

A recent meta-review presented by Finucane et al. concluded that digital health interventions in palliative care could positively affect patients, especially regarding education, information sharing, decision-making, communication, and costs (both for patients and providers). [29] Furthermore, it is also clearly identified that palliative care (at least as it is outlined by the reviewed articles) tends to be associated with advanced cancer stages and end-of-life care, which suggests that digital health research does not adequately embrace the updated definition and wider-scope of palliative care.

Furthermore, it should be highlighted that a common pattern emerges with regards to the structure of digital health interventions for cancer palliative care, outlined by the following workflow: (1) ePRO data on specific disease-related symptoms or QoL information are collected; (2) self-care advice is provided via the respective eHealth system and/or the patient is encouraged to monitor their own health status and make informed decisions about their care in collaboration with the healthcare team; (3) the collected ePRO data are presented to the healthcare professional(s), in real time if possible; and (4) the healthcare professional(s) review the data and update the treatment accordingly. This information workflow should be considered

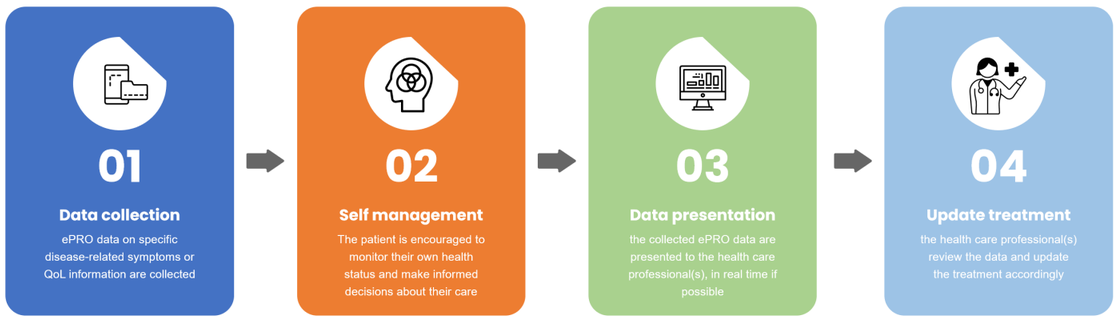

Figure 1.1: ePRO systems' main rationale

and actively revisited to ultimately improve the overall user experience (ease of use, unobtrusiveness), and increase the value for the patient.

Notably, some advanced technical developments have not yet actively been adopted in this context. For example, the use of Artificial Intelligence or the use of wearable devices (smart watches, smart wristbands) is not emphasised. Despite the fact that smart devices (watches, wristbands, glasses, activity trackers, virtual reality headsets) are widely adopted for other purposes, they still seem to be relatively unexplored in the context of palliative care.

It should be noted that there are already available software platforms supporting the ePRO paradigm (e.g. the FDA MyStudies app is a prominent open-source example, [30] but there are also commercially available services [31][32]), which are adaptable for specific studies in terms of specific questionnaires used, setup of protocol specific reminders. However, these platforms are not used in the context of palliative care. This finding might indicate a "re-inventing the wheel" pattern, leading to lower quality in terms of software, thus hindering end-user acceptance.

To conclude, given the vision of P4 Medicine (predictive, preventative, personalised, participatory), [33] the ePRO paradigm can be considered crucial. The literature review summarised in this chapter reveals that scientific research on the exploitation of ePROs for developing digital cancer palliative care interventions is active; however, significant gaps remain. The literature demonstrates a number of success stories, while also highlighting significant room for further research to facilitate the information flow between patients and healthcare experts, in order to eventually close the information loop.

Key messages

- ePROs provide a promising opportunity for patient-centred healthcare (including palliative care) as they can enhance the collection of various types of data directly from or about patients, such as via biosensors, home-based digital devices, scales and blood-pressure monitors, physical activity measures, nutritional diaries, or descriptive reports of patient well-being from caregivers.
- Research in this domain is active and has demonstrated promising results. Better clinical outcomes can be achieved if patients with cancer are empowered to report the psychological and physical symptoms connected with their cancer and its treatment in real-time.
- Currently, Artificial Intelligence and wearables are not frequently used in palliative care contexts, and this can be identified as a potential area for future clinical research.
- Beyond technical developments, information workflow and user experience (e.g. in terms of usability) should be actively emphasised in terms of end-user acceptance, especially regarding mHealth apps.

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Chapter 2: The ethical approach of the MyPal digital health intervention

Tina Garani-Papadatos
Laboratory for Health Technology Assessment, Department of Public Health Policy, School of Public Health, University of West Attica, Greece

Dunja Begović
International Observatory on End of Life Care, Division of Health Research, Faculty of Health and Medicine, Lancaster University, United Kingdom

Summary

This chapter shows how the MyPal project aimed to address the ethical challenges arising at the intersection of palliative care and digital technology. In particular, it looks at the use of improved electronic patient-reported outcomes (ePROs) systems to identify the personal needs of patients with cancer and their caregivers. Fostering the electronic collection of PROs provided by patients themselves (or a proxy), in contrast to clinically reported data, has wide-ranging ethical ramifications stemming from the interaction of patients with technology. Thus, special attention must be given to ethical commitments, such as safeguarding the dignity and autonomy of participants, continuous oversight of the research process for compliance with relevant ethical and legal aspects, proper procedures for recruitment and for obtaining informed consent, and ethical management of data. In the MyPal project, we have taken the approach of early identification and management of potential ethical issues. This chapter describes the ethical approach taken - the rationale for it and the steps within it – as well as situating it within the existing literature on ethics at the intersection of digital health and palliative care.

Keywords: palliative care, ePROs, digital health, technology, ethics, cancer care

Introduction

This chapter aims to address the ethical issues arising in the implementation of the MyPal project, which introduced a digital health-based, personalised intervention for patients with cancer palliative care needs, utilising electronic patient-reported outcomes (ePROs). The ePRO approach is based on the use of tools and apps for the self-reporting and tracking of health outcomes, without amendment or interpretation of the patient's response by a healthcare professional (HCP) or anyone else. An important aim of digital medicine is empowering patients with cancer (and their family members) towards a better understanding and reporting of their symptoms and improved communication with healthcare providers.

Although digital technologies raise a number of ethical challenges, the development of ethical guidelines in parallel with a growing ethical awareness seems to justify optimism about a new and respectful digital medicine. [1] Empowering patients while ensuring ethical issues are recognised and addressed has been a main objective of the MyPal project. We attempted to meet this aim by developing and implementing the intervention in a safe, secure and responsible environment, preventing possible harms and safeguarding the dignity and integrity of participating individuals as well as generating robust and reliable scientific evidence.

Three key features of the MyPal project played a fundamental role in understanding the associated ethical issues. Firstly, the MyPal context was shaped by the fact that the relationship under investigation was a dual one, between humans and each other, and between humans and technology. Thus, various parameters, or even barriers, had to be considered, such as the disposition of patients towards the use of mobile health apps and their level of digital literacy. [2-3] Secondly, the discrepancy between the promises of digital health technologies and the actual outcomes and benefits of their implementation were carefully considered in order to achieve a trustworthy clinical and research environment. Existing evidence points to the rejection or abandonment of mobile health (mHealth) apps that look untrustworthy to the users. [4] Finally, the MyPal ethical approach was shaped by the understanding that cancer studies may take place in a context of suffering, vulnerability and pain, where there is an even

greater need to approach patients with due respect for their dignity, wellbeing and privacy. These key aspects were kept in mind when determining the project's overall ethical approach described in the rest of this chapter.

Integrating ethics early on

The application of digital technologies and ePROs in early palliative care creates new roles and responsibilities, both for patients and for HCPs. [5] It also requires a specific ethical framework to cover all the stages of experimentation and implementation - the final aim being to harness the technology for the benefit of the patients, tailored to their specific and evolving needs. Figure 1 shows the main steps in a user-centred approach to research which integrates ethical issues from the outset.

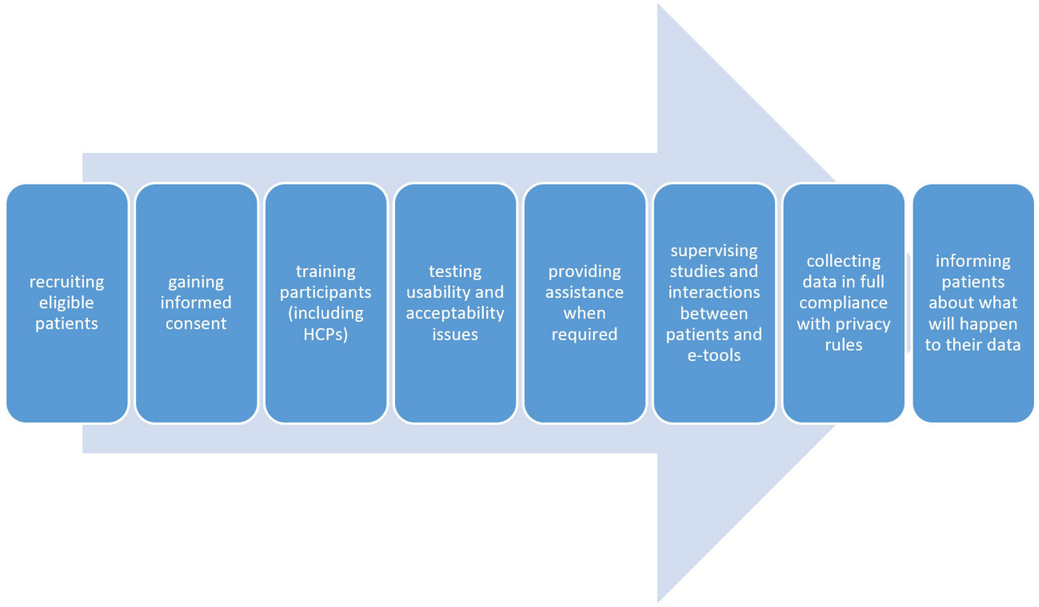

Figure 2.1: The main steps of the MyPal ethical framework

Although the first of these steps (determining the eligibility of patients to enter studies of digital health applications) may seem to be a purely methodological issue, it involves a number of ethical considerations. Patients' competence to consent must be evaluated; some patients with a shorter life expectancy are excluded as longitudinal follow-up was deemed implausible; and potential participants who have shown interest have to be briefed appropriately. This approach of recognising and addressing ethical issues from the very beginning of the study was also applied in the subsequent steps of recruitment.

Consent and communication

A key principle of ethical conduct in health care and research is ensuring that patients/study participants are given appropriate information and that this is done in an accessible and sensitive way. [6] Information which traditionally has to be provided to the patient includes the aim, duration and place of the study, the role of the participant, the possible risks and benefits to them, and their right to withdraw from the study at any time and without giving a reason.

Fostering palliative care for patients with cancer by promoting ePROs requires the collection of personal information in order to observe trends in the ePROs of each patient and tailor health and medical care to individual needs. Such information includes data from the activity tracker on sleep quality and physical activity, data collected on personal symptoms including emotional ones, as well as data on personal feelings of the participants, e.g. motivation, expectations, emotional distress or self-efficacy. The ePROs also provide further insights on treatment response, disease evolution, quality of life, disease burden and behavioural aspects of participants. The ePRO-based interventions entail more frequent data provision by the patients compared to conventional reporting, resulting in a significantly larger amount of collected data. Patient-generated data in the case of ePROs, while not replacing clinical data, usually provide information about different variables from those that can be measured in conventional clinical ways, such as feelings, opinions, and observational data. [7] Therefore, respecting the privacy of participants needs to be addressed as both a legal and an ethical issue under headings such as accountability and responsibility.

The fundamental ethico-legal rule that patients/study participants must willingly give their informed consent for treatment/study participation remains equally valid in the context of digital health. [8-9]. Explicit information must be provided about the tools and applications to be used, in particular regarding what the use of these technologies entails for the patients in terms of benefits, data protection and potential adverse events. Prospective participants must be given the opportunity to ask questions and receive comprehensible answers before deciding whether to take part in the study. The importance of this procedure is reflected in the legal framework which requires that copies and records of informed consent must be kept on file, in compliance with the relevant articles of the General Data Protection Regulation (GDPR) and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Guideline 2016, [10-11] so that the participant's agreement to the collection and processing of their personal data can be established unambiguously.

In the same vein, and to ensure consent is freely given, specific and informed, the manner in which information is presented to potential participants is also of major importance. Care must be taken to address all issues in a manner that is emotionally appropriate for persons suffering from a serious disease, but also in a language understandable to all population categories. With regard to children, an advanced layer of protection must be applied in obtaining assent from paediatric patients themselves and consent from their legal guardians. Although children are not legally permitted to decide for themselves, it is important that sufficient and understandable information be provided to them Additionally, the information provided to children must be age-adjusted, given that there is variation in children's awareness of their disease in relation to the question of open disclosure of their diagnosis and prognosis, but also variation in their cognitive abilities and stages of development. [12-13]

Issues of relational autonomy are also evident in this context. A relational approach to personal autonomy takes the interdependence of human beings as a starting point rather than an obstacle to be overcome, and acknowledges the centrality of social relations to the construction of our selves. [14] The concept of relational autonomy is especially relevant in cancer and palliative care given the relational perspective in health care practices in these situations, [15] and the pronounced vulnerability of many patients with palliative care and cancer care needs. [16] Therefore, respecting the autonomy of participants in this context may involve considering not only their individual perspectives but also the impact of other factors in their lives, such as the wishes of their family members.

Studies have shown that serious ethical issues in the treatment of patients with cancer mainly concern the conflicting perspectives of patients, carers and health professionals, as well as the challenges of maintaining a successful collaboration between all involved parties. For example, in a study by Breslin et al, [17] disagreements between patient/family and HCPs (concerning for example the significance attributed to a symptom) ranked top in a list of ethical challenges in health care. One of the added values of ePROs is the potential to address this particular disadvantage of traditional clinical practice, by allowing the patient's unmediated assessment to be central.

Specific considerations during study design

The usability and acceptability (user acceptance) of a digital intervention constitute a major challenge which is not only methodological but ethical as well, [18] given that these interventions aim to benefit the patient and promote patient autonomy. In MyPal, a user engagement strategy was deployed involving focus groups to identify and collect input on user needs, establish close interaction with potential end-users (patients and healthcare providers) and contribute to empowering patients and enhancing their autonomy. The focus groups consisted of adult patients with a diagnosis of either Chronic Lymphocytic Leukaemia (CLL) or Myelodysplastic Syndromes (MDS); HCPs working at participating clinical sites; and children linked to paediatric oncology services. These groups proved particularly useful in addressing technical drawbacks and in providing patients' insights. Through the use of case vignettes, the participants addressed issues such as user needs, engagement and personalisation. They also gave feedback on various applications.

The different age groups engaged in the MyPal studies had distinctive features that affected the potential challenges of their interaction with the intervention. Some older people, such as those involved in the MyPal-Adult study, may struggle with digital technology in general, so interventions aimed at them have to be designed to be very user-friendly and not introduce any additional burdens. [19]

Children and young people are characterised by a significantly broader exposure to digital technologies, [20-21] which may increase their willingness to participate in this type of study. Nevertheless, a distinct concern arises in their case, namely the implications of cancer and its treatment on cognitive abilities such as comprehension, problem-solving, emotional ability, self-esteem, relational ability and communication skills. Overall negative implications must be mitigated, and different levels of physical functioning and customisation of functionalities must be considered in order to better handle the case of deteriorating health or cognitive status of paediatric patients. Motivational messaging, for example, encourages adolescent patients to seek additional information if they come across difficult and confusing terminology, access specific links providing information about their illness, or prepare a list of questions in cases where patients find it hard to remember what they would like to discuss during consultations.

Overall, the study and intervention design processes have important ethical dimensions, and in MyPal we took the approach of identifying the potential challenges for users early on through direct consultation on patients' preferences and needs.

Key messages

The following recommendations for healthcare professionals and research staff may be of use in the design and implementation of digital health technologies:

- Familiarise yourself with relevant literature which will help you identify the main ethical issues relating to your intervention.
- Adopt an ethical approach and culture early on during the study design stage.
- Ensure compliance with the relevant legal framework regarding data and privacy protection, especially among patients with cancer where there are other sensitive data to be collected.
- Think of what may constitute benefit and harm for your patients with regard to their rights, privacy and dignity.

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Chapter 3: The MyPal-Adult system: Design and development of technical aspects

Fatima Schera
Fraunhofer Institute for Biomedical Engineering, Sulzbach, Germany

Lefteris Koumakis
Foundation for Research and Technology Hellas, Greece

Summary

Health informatics is a vital part of healthcare reform, linking healthcare and information technology for better health management. Nowadays, more patient-oriented systems supporting the active participation of patients in decision-making are available. The MyPal-Adult system aims to support patients requiring a palliative care approach with a digital healthcare platform focusing on the patient's needs regardless of the place of care (e.g. inpatient, at home, in hospice care). The platform consists of numerous tools and services seamlessly integrated into a digital health ecosystem. It provides two sub-systems: the MyPal-Adult app for patients and the MyPal-HCP web application for healthcare professionals (HCPs).

The MyPal-Adult mobile app allows patients with blood cancers to provide reports on QoL, side effects of cancer therapy, and medication adherence to their treating HCPs. Patients can also provide reports on factors related to their engagement, enabling risk factors for non-adherence to treatment to be identified. Additionally, they can record and send their symptoms ad hoc, view data collected from an activity tracker, search validated medical information and enter their medications to provide reminders.

The MyPal-HCP web application provides tools to the HCPs to support timely symptom management of patients and facilitate patient-clinician communication. Such tools include a notification panel for patients' events, an aggregated dashboard for all the patients, individual dashboards, a discussion tool, a cost case report form and a management tool for the MyPal search engine.

The MyPal system was evaluated in two clinical studies in order to assess its potential impact on QoL and service delivery.

Keywords: health informatics, digital intervention, mHealth, eHealth, ePROs, behavioural informatics

Introduction

Health informatics is a vital discipline linking healthcare and information technology with the aim of better health management. Initially, health informatics focused on providing digital information to HCPs in the hospital setting. Nowadays systems are more patient-oriented, supporting patients' active participation in health decision-making. [1] In order to comprehend a complex software system such as the MyPal digital health intervention, we have to understand what each of its components actually does, how they work together, and how they interact with the world around them—in other words, its software architecture. The 'architecture' of a software system is a metaphor, analogous to the architecture of a building. It functions as a blueprint for the system and the developing project, laying out the tasks necessary to be executed by the software design teams.

The MyPal system aims to support patients with blood cancers. The MyPal system supports adults with blood cancers and children with solid tumours and blood cancers, with two mobile applications. This chapter focuses on the MyPal-Adult system, while Chapter 4 focuses on the MyPal-Child app.

Methodology

The MyPal software architecture was designed based on user scenarios and uses cases that the platform has to support, while relying on participatory design principles [2]. More specifically, the main participatory method employed was that of focus groups, i.e., focused discussions among groups of end-user representatives (both patients and HCPs). The end-users participating in the focus groups were adult patients with blood

cancers who were not eligible for the trial; and haematologists, clinical psychologists, nurses and family caregivers who did not participate in the clinical trial. The main advantage of focus groups is obtaining direct data from end-users, which can provide better insights into the needs of patients and thus give an opportunity to devise more efficient follow-up strategies. The technical artifacts for data capturing were selected considering current technological advances in mobile health (mHealth), and patients were engaged in the entire design and development process.

The implementation followed a rigorous and iterative process, offering prototypes of the tools in the first year of the project and ensuring close and constructive collaboration among all stakeholders (technology providers, patients and healthcare providers). Before conducting the clinical studies, a pilot-testing phase was initiated, aiming to assure that the tools employed in the clinical studies met the specific requirements of patients with blood cancers. Based on the feedback obtained, the technical solution was refined, and necessary preparations and training for conducting the clinical studies took place.

Components of the MyPal system

The MyPal-Adult system is divided into the MyPal-Adult mobile app and the MyPal-HCP web application. The MyPal-Adult mobile app allowed patients to provide reports on quality of life, side effects of cancer therapy, and medication adherence to their treating HCPs. Additionally, patients could provide reports on factors related to patient engagement in symptom reporting, risk factors for non-adherence to treatment, record and send their symptoms ad hoc, view the data collected from an activity tracker, search validated medical content and enter their medications to provide reminders. The main functionalities of the MyPal-Adult mobile app are:

- **Data collection and submission** to the MyPal server based on validated PROs, including:
  - » the Study Support Survey for patient engagement (e.g. motivation, expectations).the Treatment Support Survey related to risk factors for treatment non-adherence. Patients being treated for chronic lymphocytic leukaemia (CLL) or myelodysplastic syndrome (MDS) answer ePROs and the results can guide the HCP to conduct a tailored patient discussion during the next appointment using the HCP web application.
  - » questionnaires about symptoms (Edmonton Symptom Assessment System), pain (Brief Pain Inventory) and emotional state (Emotion Thermometers).

- **Notifications**
  - » The app notifies patients when they are due to complete the questionnaires with mobile reminders.
  - » Motivational messages are shown to the patients at specific intervals depending on their answers to the ePROs.

Patients are able to:

- Record and spontaneously report on their **symptoms** (including text and images).
- View **physical activity and sleep quality** data based on the activity tracker that they wear.
- Enter their **medications** into the app and set reminders.

- Access the **search engine** where they can search for medical information (text, audio and videos files) approved by their HCPs.

The app was available in five languages: Greek, Italian, Swedish, Czech and English. Indicative screenshots of the MyPal-Adult mobile app are shown in Figure 3.1.

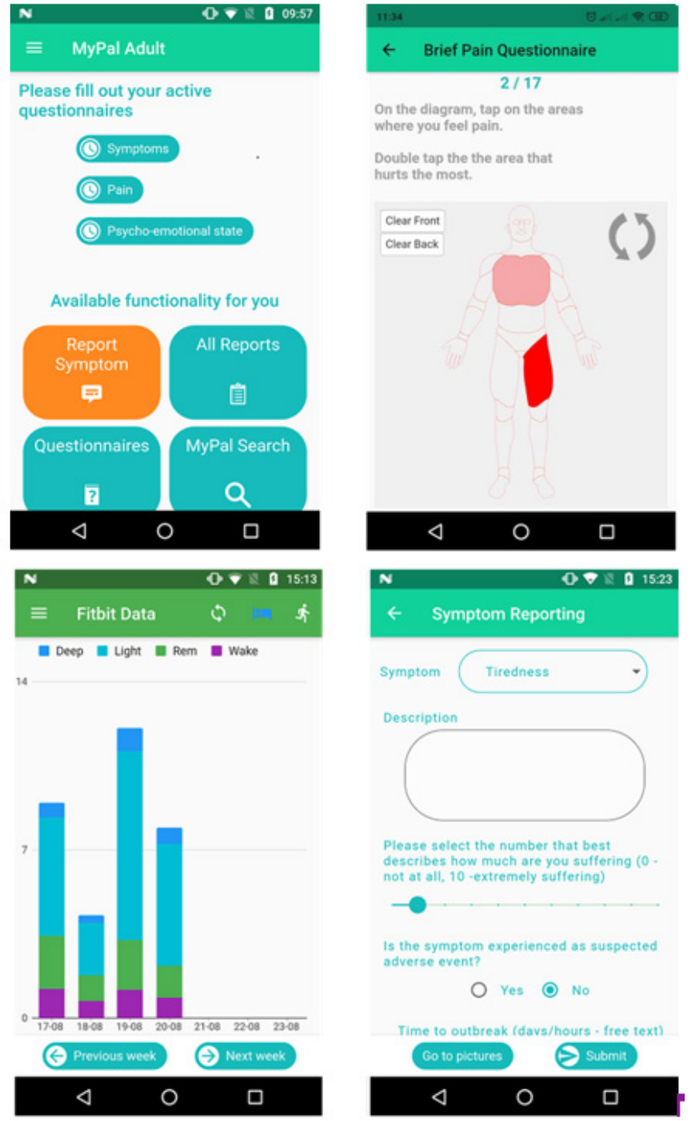

Figure 3.1: The MyPal-Adult app: main menu (top left), a visual questionnaire about pain (top right), activity data (bottom left) and the symptom reporting form (bottom right)

The MyPal-HCP web application complements the MyPal-Adult app, providing tools to the HCP for timely symptom management of patients and reinforcement of patient-clinician communication. Such tools include a notification panel for patients' events, an aggregated dashboard for all the patients, individual dashboards for each patient, a discussion tool, a cost case report form and a management tool for the MyPal search engine. The MyPal-HCP web application can retrieve and visualise patient data about individual scores on each scale and the combination of scores in different

biomedical and psychosocial variables. The main modules of the MyPal-HCP web application are:

- **The notifications**, where the HCP can have an overview of the completed or missed ePROs by the patients.
- **The aggregated dashboard** that provides an overview of the data (demographics, treatment and scores of the completed PROs) of all the patients using descriptive statistics and advanced interactive graphs. Interactive graphs provide the functionality to the HCP to create subgroups of patients by choosing any of the available attributes and identify patterns in the data.
- **The individual patient's dashboard** that represents graphically the complete data of a patient throughout the lifespan of the treatment. It allows HCPs to easily identify changes in one or more factors, such as QoL, emotional status, activity, sleep quality, symptoms etc., at specific time periods. All the graphs are interactive, so the healthcare professional can focus on a specific time period, group data, and hide or show final scores of the supported ePROs factors. Moreover, the HCP can provide data for the patient related to treatment plans, future appointments and clinical notes.
- **The discussion tool** interprets and prioritises patient responses to a non-adherence risk screener that assesses key patient risk factors related to non-adherence (known as the Treatment Support Survey as presented through the MyPal-Adult app). This helps optimise patient adherence to CLL or MDS medication and deliver personalised interventions and advice on topics of the highest relevance at that time.
- **The search engine management** is the tool that feeds content to the search engine for patients and is available to the patient through the MyPal-Adult app, enabling them to search for high quality information about their disease and support to improve their quality of life. The search engine provides health-related content to patients from a validated set of relevant documents.
- **The cost case report form (CRF)** is a questionnaire for economic evaluation that the HCP administers to the patient during their visit. It is based on the comparative measurements (and change over time) of health-related QoL, as well as costs for the intervention vs. non-intervention cohorts.

Indicative screenshots of the aggregated dashboard and the individual's dashboard of MyPal HCP web application are shown in Figure 3.2 on the next page.

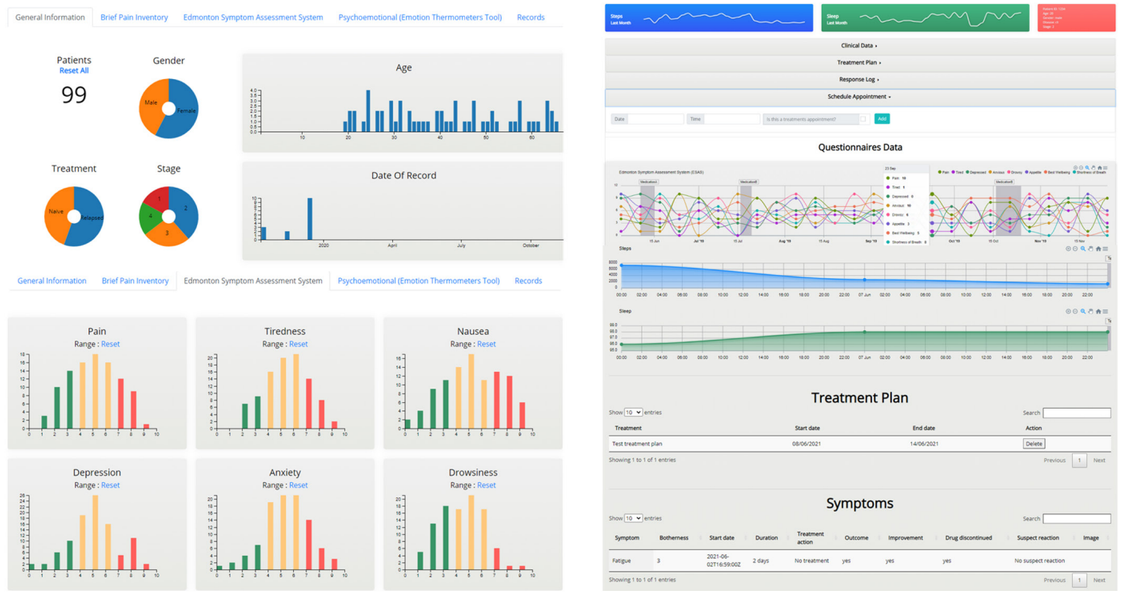

Figure 3.2: The aggregated dashboard (left part) and the individual's dashboard (right part) of MyPal HCP web application

A graphical representation of the MyPal-Adult system architecture, its main components and their interactions, is shown in Figure 3.3.

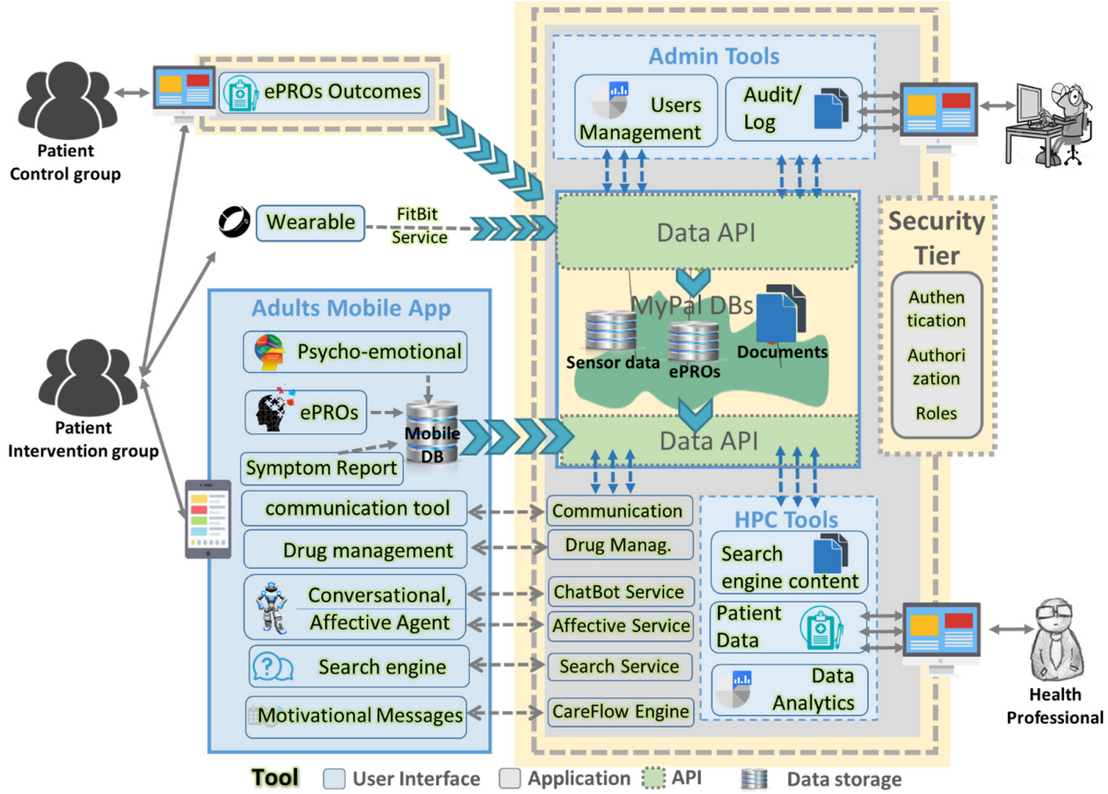

Figure 3.3: The MyPal software architecture

Technical information about the MyPal-Adult app and the MyPal-HCP web application is described in more detail in Koumakis et al. [3]

Conclusions

Digital health solutions including mHealth, wearable devices, telemedicine and health information technology are evolving rapidly. [4] Nevertheless, most of the available solutions do not take into account the actual needs of the users (patients and HCPs), a key component for a successful digital health system. [5] MyPal designed a novel palliative care digital system guided by patients, carers and HCPs. The platform relies mainly on validated ePROs and aims to improve the QoL of patients with blood cancers through encouraging better self-management of the disease symptoms and facilitating timely assessment of the reported symptoms by the treating HCPs.

Key messages

- Digital health systems provide opportunities for communication between all the involved people (patients, physicians, healthcare teams, informal caregivers).
- Mobile apps can collect health related data for a patient without the need for a clinic visit.
- Reporting health related symptoms when they appear using text and multimedia can provide more accurate information to HCPs.
- Simple, visual one-page displays of patient data may be helpful for HCPs.

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Chapter 4: The MyPal-Child serious game app for children with cancer: Design and development

Robert Schraut, Malin Sweers, Stefan Hoffman, Wiebke Scholz, Thomas Kröll

Serious Games Solutions, Promotion Software GmbH, Tübingen, Germany

Summary

The MyPal-Child study included the development of the serious game AquaScouts. This game app was created with the aim of reducing the psychological burden and 'reporting fatigue' for children and adolescents undergoing cancer treatment. This chapter will present the way the design goals of this game were formulated and the intentions behind the central design decisions. It explains how the goals were realised and what challenges we faced during the process, as well as the measures taken to overcome those challenges. It concludes with a discussion about what can be learned from the development of the AquaScouts serious game and what health care professionals can take away from this.

Keywords: childhood cancer, serious games, eHealth, mHealth, patient-reported outcomes, palliative care

Introduction

As part of the MyPal-Child study, the serious game AquaScouts was developed to collect input from children and adolescents with cancer between the ages of 6 and 17 years. The main goal of the game app was to reduce the psychological burden and 'reporting fatigue' that children may feel while undergoing treatment, in particular when reporting their symptoms.

The MyPal-Child gamification process includes many features that make use of the motivational aspect of games to encourage health status reporting, while also avoiding potential negative effects (e.g. game addiction). This chapter is partly based on an article published in the Frontiers in Digital Health journal, [1] which discusses these issues in more detail.

Design Goals

In order to formulate the design goals for the AquaScouts serious game, usage scenarios were created, which is to say that each step the user took when interacting with the game was documented. Focus groups with children with cancer were then used to elaborate on these usage scenarios. In this process, we built on the project partners' expertise in providing and researching palliative care for children, along with their experience from the development of previous serious games.

Through this process the following main goals, among others, were determined: 1) for the game to keep players motivated, so that information on their health could be collected over a long time period (high long-term motivation); 2) for the game to attract the player to voluntarily return and play multiple times (high retention); 3) for players to make consistent and frequent reports of their symptoms, in order to gain a thorough understanding of their condition and needs (high sample rate); 4) for the game not to have a 'game-over', so that players cannot lose.

In the following sections, we will explain how we sought to achieve these goals in the game design and what challenges we faced in this process. We hope to offer helpful insights on how apps should be designed to allow patient reporting in the palliative care context, especially when it comes to children and adolescents with cancer.

The Design of the App

An important aspect to keep in mind is that AquaScouts is a serious game and not simply a game for entertainment. Dörner et al. define the term 'serious game' as a "digital game created with the intention to entertain and to achieve at least one additional goal (e.g., learning or health)". [2] In this case, the purpose is to make use of the entertainment aspects of the game in order to gain more precise information about the symptoms that the young cancer patients are experiencing.

The original idea for the app was to create a compelling theme that engages the player right from the beginning. In AquaScouts, players take on the role of scientific explorers investigating an alien underwater world. In a type of runner game, the player's avatar, a diver, searches through tunnels to collect artefacts such as fragments of alien machinery or pieces of dinosaur fossils while encountering a non-indigenous parasite threatening the ecosystem. The runner game was chosen as it is a non-violent game that reaches a broad audience and can be played in short increments (runs).

From a graphical perspective, a very colourful and bright art style was chosen to create a cheerful atmosphere that would appeal to all ages and genders. The art style was specifically meant to fit our target group of children and adolescents. We ultimately opted for a detailed and colourful 3D art style (Figure 4.1) to bring the underwater world to life (Figure 4.2).

Figure 4.1: 2D concept drawing of the player's avatar for the 3D diver model. Players can choose a female or male diver character and customise their appearance.

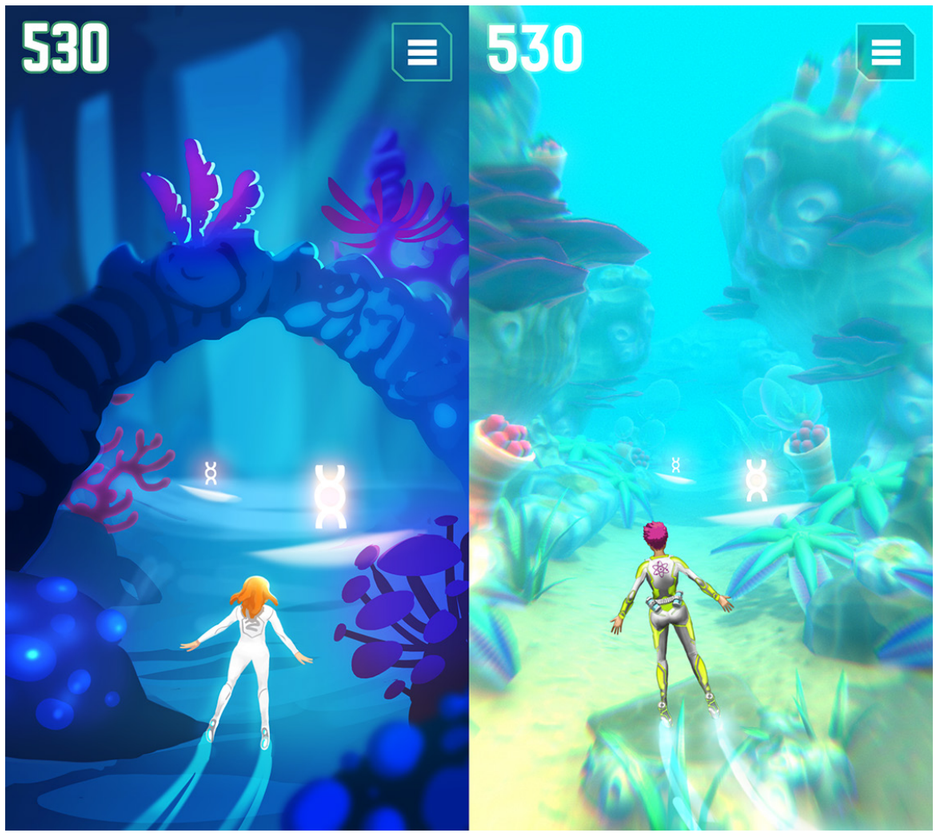

Figure 4.2: Visual style development of the underwater world

Gameplay

In the game itself, players get three new challenges (runs) per day, each one designed to last around three minutes. This is in line with our design goals, as the game itself does not require much cognitive effort and should be played as often as possible to achieve a high sample rate, but only a few minutes at a time so negative effects like game addiction can be prevented. Xu et al. state that playtime is a key force in developing high levels of addiction. [3]

During a single run, players try to collect as many points as possible in order to cure the parasitic infestation. For each challenge they complete, players get a special reward in the form of an artefact fragment. Once all the fragments of an artefact are collected, the player receives the artefact. This aspect of the game appeals to the human collecting instinct and works in favour of the long-term motivation design goal (Figure 4.3 on the next page).

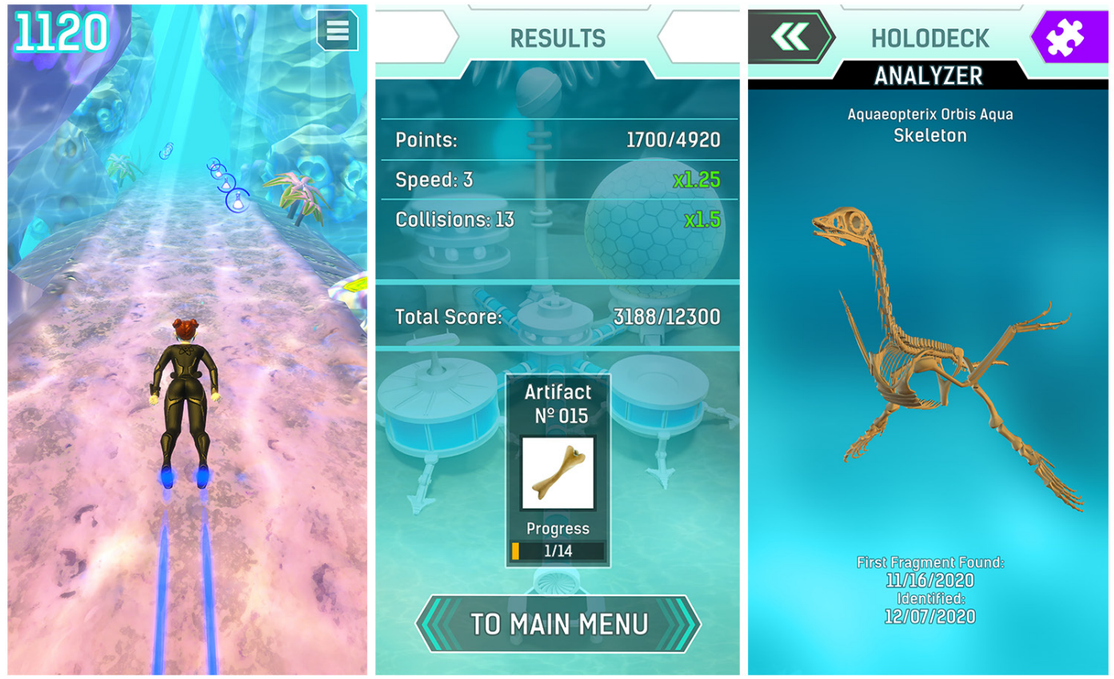

Figure 4.3. Left: Example of gameplay. Pink, blue and green 'blibs' can be collected for points. Obstacles need to be avoided. Centre: Result screen with reward. Right: Exemplary finished artefact

Another design requirement from our partners in palliative care was that it should not be possible to lose the game. As the game was designed for children and adolescents with cancer, the possibility of death in the game was considered insensitive. A 'game-over' was therefore ruled out as an option from the start. Challenges can be repeated to score a better result, but no additional special reward is given.

During a run, the player is asked up to five questions regarding their symptoms. The 15 different in-game questions are based on the Symptom Screening in Paediatrics (SSPedi) Tool, [4] and Mini-SSPEDI questionnaire. [5] The questions enquire about the severity of specific symptoms (on a scale of 1-5, from 1: The symptom is not present to 5: The symptom is extremely strong; see Figure 4.4). Some question examples are: "How much were you bothered by headaches today or yesterday?" "How much were you bothered by changes in how your body or face looked today or yesterday?" "How much were you bothered by pain (other than headache) today or yesterday?" A wide range of symptoms is covered, but the questions are still easy to understand.

The algorithm was designed to give a higher priority to those topics where previous answers indicated a higher probability that a symptom is currently present. At the same time, it was ensured that all symptoms were queried sufficiently frequently during regular use.

To avoid questions being answered without any reflection a 'long tap' (three seconds) is required to answer a question. Players may be tempted to simply tap any answer to quickly continue playing without properly reading the question. This time window is enough for a young patient to recognise the question being asked and, if the symptom is relevant, to abort a tap away attempt and to actually answer honestly.

The questions can also be answered in a separate section of the app in the form of a classic digital questionnaire at any time. This enables patients to play the game

uninterrupted (Figure 4.4).

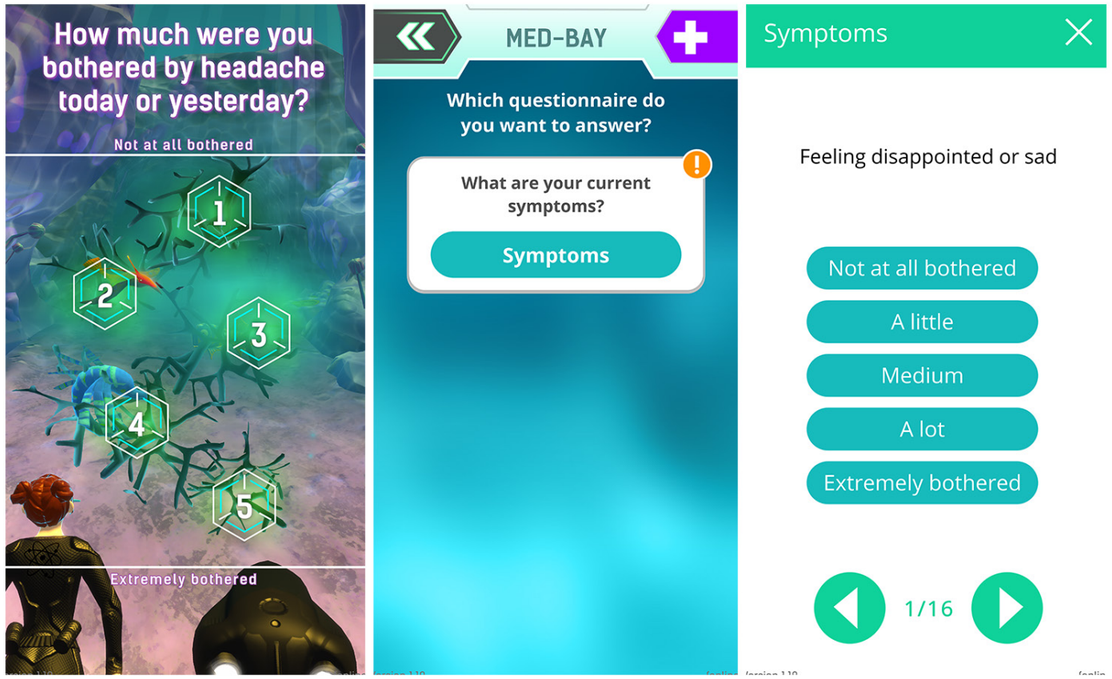

Figure 4.4: Left: In-game question. Centre: Med-Bay with one questionnaire. More questionnaires can be shown here if available. Right: Exemplary symptom questionnaire.

In addition to the game app for children, a separate questions-only app was developed for family carers. All questionnaire input from both apps is stored in a local database through a server at the clinical site, allowing clinicians to access all the data there (Figure 4.5).

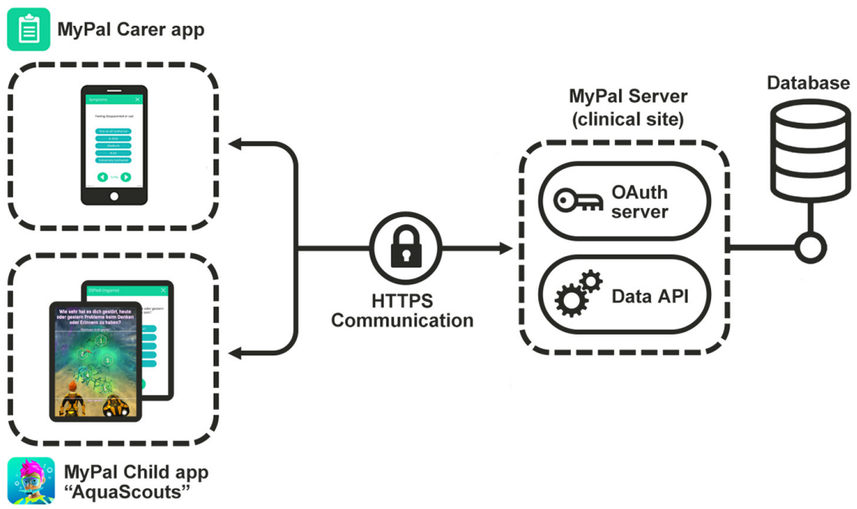

Figure 4.5: Overview of the technical infrastructure.

Discussion

Overall, most of the design goals were successfully realised; however, there were some requested game modifications from the partners that impacted on end users experience. While the artefact collecting and high scores contribute to high long-term motivation, the lack of variety in game runs and lack of competitiveness due to there being no 'game-over' hindered the success of these mechanisms. Although there were three new game courses generated each day, the basic playing system was always the same simplistic runner game. While the decision not to have a 'game-over' feature may be an important point from a moral perspective, this somewhat hampered the effectiveness of the game, as it became very low-stakes and thus less appealing to the players.

The same challenges arose regarding the goals of high retention and high sample rate. The long-term stimulus of play was not pronounced enough to encourage long-term regular reporting by the players. To combat this, we designed a retention enhancement package which included a daily login bonus and new items players could use in the game. This package was used in the last six months of the clinical study. At the time of writing, feedback on this new feature from the clinical partners was positive, but its impact has yet to be assessed.

Conclusion

The MyPal-Child *AquaScouts* serious game was created to encourage children and adolescents with cancer to regularly report on their symptoms, so that HCPs could use those reports to improve the care of their patients. For this purpose, it was imperative to design a fun game that would engage children and adolescents alike over a long timeframe. While this was achieved in part, several challenges in designing this game were faced, which we then addressed with a retention enhancement package. Many of the challenges stemmed from a general fear of causing game addiction, as the line between engaging and addicting can be hard to navigate (e.g. playtime had to be limited while also trying to get the players to return to the game regularly). For further research, it would be interesting to see the effect of the additions to the game.

Key messages

- A serious game might be a good alternative to classic ePRO systems, especially for children and adolescents with cancer.
- The game app can reduce the burden on children and adolescents with cancer by making symptom reporting simpler and more fun.
- The data gathered from the app can be used by clinicians to improve the care of their patients.
- While it is important to make sure the game serves the purpose of collecting patient data, the entertainment aspects must also be considered. The game should still be fun and motivate the players, otherwise, it affects retention negatively.

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Chapter 5: The MyPal-Adult study: Design and preliminary outcomes

Lydia Scarfò and Paolo Ghia

Università Vita Salute and IRCCS Ospedale San Raffaele, Milan, Italy

Summary

The MyPal-Adult study aimed to evaluate the effectiveness and cost-effectiveness of use of the MyPal system for delivering ePROs as a novel, patient-centred, palliative care intervention for patients with blood cancers (chronic lymphocytic leukaemia (CLL) or myelodysplastic syndrome (MDS)).

We designed a randomised controlled clinical trial, in which it was planned that 300 patients with CLL or MDS from Greece, Italy, Czech Republic and Sweden, would be randomly allocated to receive early palliative care using the MyPal system (n=150) versus standard care (n=150). Patients randomised to the intervention arm were given access to the MyPal Digital Health system, using purposely-designed software available on smartphones and/or tablets. The platform entails physical and psycho-emotional symptom reporting via regular questionnaire completion, spontaneous self-reporting, motivational messages, medication management, and a personalised search engine that retrieves health information (as described in Chapter 3). Data on daily step count and sleep quality were automatically collected via wearable devices (Fitbit). The MyPal Digital Health system was regularly used for 6 months, over the duration of the trial.

The primary endpoint was improved quality of life (QoL) compared to standard care as evidenced by statistically significant higher scores in the EORTC QLQ-C30 General Questionnaire and the EuroQol EQ-5D. Relevant secondary endpoints include improvement in physical and emotional functioning, increase in satisfaction with care, and prolonged overall survival.

One hundred sixty-eight patients were enrolled into the study, with a median age of 60.5 years (range 29-90). 63% patients were male, 37% female, 80% were diagnosed with CLL, and 20% with MDS. Sixty-nine percent were previously treated, while 31% were receiving their first-line treatment after initial diagnosis. Twenty-five percent had received chemoimmunotherapy, 62% targeted agents, and 13% were off treatment during the study. Sixty-eight patients were randomised to the intervention arm, 100 to the standard arm. No statistically significant differences were present at enrolment between the intervention and standard arms.

Challenges for the study included the elderly population enrolled (median age of diagnosis of about 70 years), for which the use of eHealth systems might be less straight-forward, and the COVID-19 pandemic which delayed study initiation and required ad hoc adaptations for data collection.

Keywords: Patient-centred care, eHealth, ePROs, palliative care, digital health platform, chronic lymphocytic leukaemia, myelodysplastic syndrome, randomised controlled trial, cancer

Introduction

CLL and MDS are two of the most frequent haematological malignancies in the Western world, both usually occurring in older individuals (median age at diagnosis of around 70 years). [1,2] Although being classified as "chronic" conditions, their biology and clinical course are heterogeneous, ranging from stable or slowly progressive to extremely aggressive. With the recent introduction of novel targeted agents, the treatment landscape for CLL and MDS has radically changed resulting in improved outcomes, including increased overall survival. [3] Despite this, both CLL and MDS remain essentially incurable, and current therapies aim at controlling the disease long-term. Therefore, it is crucial to understand the impact of CLL and MDS and their treatment on QoL in regards to disease-related symptoms, therapy-related toxicities, and the emotional, socio-economic, and functional effects of living with an incurable illness. [4]

Patients with CLL have poorer QoL compared to the general population, being significantly bothered by physical symptoms (81% reporting fatigue and 56% sleep disturbances) at treatment initiation. [5] Similarly, patients with MDS may suffer from a wide variety of symptoms, including fatigue, anxiety, and insomnia, amongst others, which result in impaired QoL. [6,7] This evidence supports a key role for early palliative care, including management of physical symptoms and psychosocial distress, with concurrent cancer-specific care throughout the disease course.

Study design

We designed a multi-national randomised controlled trial, enrolling patients with CLL or MDS at 5 clinical sites (specialised haematology clinics and wards) in Greece, Italy, the Czech Republic and Sweden. The main aim of the MyPal-Adult study was to evaluate the effectiveness and cost-effectiveness of use of the MyPal ePRO system as a novel, patient-centred, palliative care intervention for patients with blood cancers (CLL or MDS).

The primary objective was to determine whether the MyPal-Adult intervention could lead to improved QoL compared to standard care, as evidenced by statistically significant higher scores in the EORTC QLQ-C30 General Questionnaire, [8] and the EuroQol EQ-5D. [9]

Secondary objectives included patient improvement in physical and emotional functioning, [10] increase in satisfaction with care, [11] increase in overall survival; cost-effectiveness; reduction in symptom burden, [12] pain score, [13] and emotional distress; [14] and an increase in patient engagement with care by satisfactory adherence to reporting.

Eligibility criteria included adult (≥18 years) patients with CLL or MDS diagnosis, scheduled to receive any line of treatment for CLL/SLL or MDS or who had been previously exposed to any treatment for CLL/SLL or MDS, able to understand and communicate in the respective language of the study site, users of an Internet connected device (smartphone/tablet).

Patients were excluded if already participating in another interventional study, in need of immediate referral for specialised palliative care, with a life expectancy <3 months, or having experienced transformation to aggressive lymphoma (Richter's transformation, CLL cohort only).

Patients were randomly assigned in a 1:1 fashion to receive early cancer palliative care using the MyPal Digital Health system (intervention group) versus standard care which could include general palliative care if needed (control group), stratified by cancer type (i.e. CLL/SLL vs MDS), using a computer-generated number sequence, based on the blocked randomisation approach. [15]

The intervention focused on the reporting of physical and psycho-emotional symptoms by the patient via the MyPal smartphone app installed on their personal smartphone or tablet. The reported symptoms were immediately delivered to the healthcare professionals (HCP) via the MyPal web app, which was the main interface of the HCP to the system (as described in Chapter 3). Finally, the smart wristband, Fitbit Ionic™, was employed for monitoring the physical activity and sleep quality of the patient.

Upon registration, patients randomised to the intervention arm had access to the MyPal system with a number of user-initiated and system-initiated functionalities for 6

months.

Due to recruitment issues and the prolonged recruitment period, study duration was shortened from the initial 12 months to 6 months in protocol amendment 1.

The fidelity of the intervention implementation was evaluated by collecting the information on the web interface (to be completed by the HCPs accessing the system), including review of reported symptoms and questionnaires by HCPs (audit trail) and action taken by HCPs, if any.

Data collected in both the intervention and standard arms of the study are reported in Table 1.

Table 5.1: The primary and secondary objectives in MyPal-Adult

Item	Intervention Arm	Standard Arm
Demographic (e.g. age, gender)	√	√
Clinical information, including disease and treatment-related features, frequency of appointments and events occurring during the observation time	√	√
Assessment questionnaires: • The EORTC QLQ-C30 • The EuroQol, EQ-5D – 3L • The Integrated Palliative Outcome Scale (IPOS • The Satisfaction with Cancer Care developed by The European Organisation for Research and Treatment of Cancer (EORTC) group.	√	√
Fitbit-derived (e.g. activity and sleep patterns)	√	-
Symptoms (through both spontaneous and scheduled reporting)	√	-
Intervention questionnaires: • The Edmonton Symptom Assessment System (ESAS) • The Brief Pain Inventory (BPI) • The Emotional Thermometers	√	-

The planned sample size for the study was 300 patients (150 randomised to the intervention arm, 150 to the standard arm), assuming acceptable values for the attrition rate (i.e., 20%) and the missing data (i.e., 30%). [16] Descriptive statistics were calculated for demographics (gender, age group, origin) and clinical characteristics (diagnosis, disease stage) recorded at baseline. The aim of the analysis was to evaluate the changes in outcome measures over time (1) in the intervention arm and (2) in the intervention arm in comparison with the standard arm, using one-way and two-way repeated measures analysis of variance (ANOVA) (or a non-parametric equivalent), respectively. Post-hoc analyses were applied as appropriate. Further subgroup analysis of the outcome measures is planned comparing baseline and month 6.

Results and outcome

Two hundred ninety-three patients were screened for the study at five participating sites in four countries (Figure 5.1).

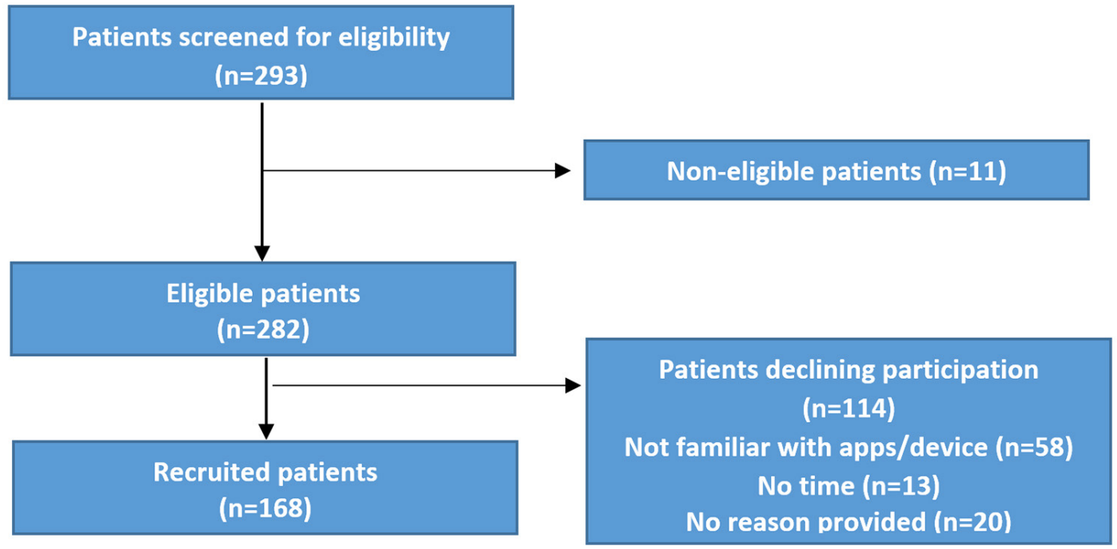

Figure 5.1: Flow diagram for the MyPal-Adult study

168 of the screened patients were enrolled into the study, while 125 were not eligible. Among these 125, the main non-eligibility reason was refusal to participate (46.4% "not familiar with the use of apps/device"; 10.4% "no time"; 16% "no reason provided"; 18.4% "other", while 8.8% were excluded because of concurrent participation in another clinical trial). Patient demographics of the non-eligible cohort was not significantly different from the recruited cohort, with a male prevalence (63.2% male vs 36.8% female), 71.2% with CLL, 28.8% with MDS.

In terms of age distribution, 24% of enrolled participants were below 60 years of age, 42.4% between 60 and 70, 28.8% between 70 and 80, almost 5% >80. The 168 recruited patients had a median age of 60.5 years (range 29-90), 63% were male, 37% female, 80% were diagnosed with CLL, 20% with MDS. Sixty-nine percent were previously treated, while 31% were receiving their first-line treatment. In line with the current treatment strategies, 25% had received or were treated at the time of enrolment with chemoimmunotherapy, 62% with targeted agents, and 13% were off treatment while participating in the study. Sixty-eight patients were randomised to the intervention arm, and 100 to the standard arm. No statistically significant differences were present at enrolment between the intervention and standard arm in terms of demographic characteristics.

Discussion

Digital health technologies offer the potential for rapid and spontaneous reporting of symptoms, facilitating remote monitoring and communication between patients and HCPs, and have been increasingly implemented in routine practice in all areas of healthcare, especially during the COVID-19 pandemic. However, concerns remain about their acceptability to patients, especially older people, and the degree to which they may alter patient-clinician relationships in palliative care contexts. [17]

Some of these concerns also hampered recruitment into the MyPal-Adult study. We enrolled patients diagnosed with CLL or MDS and decided to include into the study only patients undergoing treatment or who were previously treated, who would benefit the most from a palliative care approach. That notwithstanding, study recruitment faced many hurdles and we could not reach the enrolment goal of 300 patients even though the recruitment period was extended and the actual number of patients to whom the study has been proposed was in line with the original plan. The main reasons may be identified in 1) the unpredictable occurrence of the COVID-19 pandemic; 2) the older age of the patients, who were unfamiliar with the technology and did not have access to the devices needed for trial participation.

The COVID-19 pandemic greatly impacted the study recruitment and adherence and required some changes in the type of assessments, switching from in-hospital questionnaire completion to home-based questionnaire completion for the control group. At the beginning of the pandemic, patients were advised to avoid coming to the hospital, thus decreasing the chance of discussing the project and being enrolled into the trial. In the subsequent months, hospital visits were reduced and therefore some of the study assessments were missed, thus increasing the amount of missing data to be handled. On the other hand, patients being unfamiliar with the apps/devices was reported as main reason for refusal of study participation at participating clinical sites, and poor technological skills became particularly relevant in some countries where patients were not familiar with the use of mobile technology. This was particularly evident among the older patients affected with CLL or MDS, as shown by the fact that the median age of recruited patients was about 10 years younger than the median age of the general population with CLL or MDS (60.5 years versus 70 years).

Key messages

- Digital health tools may provide significant support in the setting of continuous and/or prolonged treatment facilitating remote monitoring and communication between patients and HCPs.
- Digital health innovations may face significant challenges for older people with blood cancers.
- eHealth tools should be carefully designed and consider the digital literacy of the patient population in order to ensure high usability and utility.
- Currently tested strategies have room for improvement and need to be refined based on the feedback received from end-users.

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Chapter 6: The MyPal-Child study: Design and preliminary outcomes

Marcel Meyerheim, Norbert Graf
Clinic of Paediatric Oncology and Haematology, Faculty of Medicine, Saarland University Hospital and Saarland University, Homburg, Germany

Anna Burns-Gebhart, Annette Sander
Clinic for Paediatric Oncology and Haematology, Hannover Medical School, Hannover, Germany

Summary

The aim of the MyPal-Child study was to assess the feasibility of using a digital health platform as a patient-centred approach in paediatric oncology and palliative care by adapting and advancing ePRO systems. The key motivation was to broaden the concept of care by integrating a digital feedback system, and thus improve symptom control and quality of life for children and adolescents with cancer and their parents.[1]

MyPal-Child study was designed as a clinical observational prospective feasibility study and conducted at three clinical sites: two in Germany and one in the Czech Republic. During the recruitment phase lasting 15 months, 83 children and adolescents with cancer (age range 6-17 years) were enrolled into the study with at least one of their parents. During the 6-month study period, participants were offered the digital health system developed within the MyPal project in addition to the standard care provided by the clinical sites involved. The platform includes two mobile applications, one designed for children and adolescents with cancer and one for their parents, enabling ePRO-based symptom self-reports and diary entries. Additionally, a web platform was offered to the treating health care professionals (HCPs) to monitor these reports. The study's endpoints focus on evaluating the acceptability of the digital health platform. Therefore, quantitative and qualitative data were collected during the 6-month study and as follow-up.

This chapter provides details of the study design, methodology, implementation and challenges, as well as preliminary results on recruitment and baseline characteristics of the participants. The final results will be part of future publications.

Keywords: Patient-centred care, eHealth, ePROs, paediatric oncology, palliative care, digital health platform, cancer, children, young people, adolescents, complex care, family-centred care, parents

Introduction

The aim of this chapter is to present the MyPal-Child study which was conducted at three clinical sites in two European countries from December 2020 until March 2022. Saarland University (Germany) was the leading clinical site, with the other two being Hannover Medical School (Germany) and the University Hospital Brno (Czech Republic).

A participatory design approach was adopted during the development of the digital health platform for MyPal-Child. This involved a series of pre-study focus groups and discussions with patients and parents as well as HCPs, in order to identify individual needs and preferences as well as to validate tools and assess user experience.

The electronic digital health platform developed for the MyPal-Child study comprises two mobile applications: the first one particularly designed for young cancer patients, the second one for their parents, which could be installed on their own mobile devices, i.e., smartphones or tablets (as described in Chapter 4). These apps enabled ePRO-based self-reports of symptoms and diary entries for children inside and outside of a game, as well as proxy symptom reports for parents. HCPs could monitor the patients' and parents' graphically visualised reports via a web-based application (see Figure 6.1). The storage of sensitive data required comprehensive considerations on data privacy and security, as set out in Chapter 2.

[1] *The term parent(s) includes legal guardian(s).*

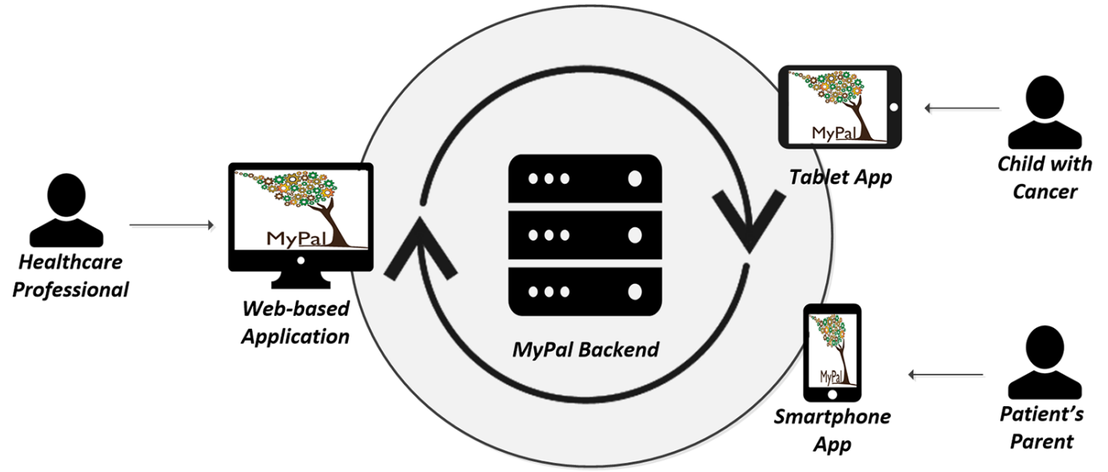

Figure 6.1: Software and Hardware components of MyPal-Child. Children and parents installed and used the developed mobile applications with their own mobile devices (smartphone/tablet). Healthcare professionals reviewed the reported data through the web-based application. [1]

Study Design and Protocol

The MyPal-Child study was designed as an observational prospective clinical feasibility study. Due to children and adolescents with cancer being a vulnerable group, it was jointly decided by the consortium at an early stage of the project that only an observational pilot study was ethically appropriate, in contrast to a randomised controlled trial (RCT) which had been chosen as the methodology for the MyPal-Adult study. As a feasibility study, MyPal-Child assessed the practicality of recruitment to the study, and the acceptability of the integration of a novel ePRO-based digital health platform and its viability in order to determine its likelihood of success. Therefore, legal, ethical, technical, operational and time feasibility factors are usually evaluated. [2]

Eligible participants for MyPal-Child were children and adolescents with cancer between the ages of 6 and 17 years, who had been diagnosed with a solid tumour or leukaemia and received anticancer treatment at one of the participating clinical sites within the previous 12 months. Consent from at least one of their parents to participate was also required. Further details on the inclusion and exclusion criteria can be found in the published study protocol. [1] The recruitment phase ended in March 2022, and the active study period finished at the end of September 2022 after an overall study running time of 21 months.

Primary and Secondary Objectives

Table 1: The primary and secondary objectives in MyPal-Child. Adapted from [1]

Primary Objective	
Objective 1	To assess the feasibility of a comprehensive, patient-centred service for palliative care in children with cancer by adapting and advancing ePRO systems
Secondary Objectives	
Objective 2	To determine the usage and evaluation of the MyPal apps, including the gamified ePRO, by children with cancer
Objective 3	To demonstrate the appropriateness and acceptability of measures of symptom burden for children with cancer
Objective 4	To demonstrate the appropriateness and acceptability of measures of quality of life of children with cancer
Objective 5	To demonstrate the appropriateness and acceptability of measures of parents' burden
Objective 6	To demonstrate the appropriateness and acceptability of measures of parents' quality of life having children with cancer
Objective 7	To contribute to the evidence -base of the effectiveness of ePROs for palliative care for children with cancer
Objective 8	To determine the impact on health care professionals across Europe due to the integration of ePROs in palliative care

Endpoints and Outcome Measures

Table 2: The study endpoints and outcome measures in MyPal-Child. Adapted from [1]

Primary Endpoint	**Outcome Measures**	**Aligned with Objectives**
Acceptability of and engagement with the MyPal Platform	• Recording of Rates (Participation, Recruitment, Premature Discontinuation Rate and Adherence to the components of the platform) • Quantitative data (validated System Usability Scale [3] for parents and an adapted version for children) • Qualitative data (focus groups with children and parents)	1, 2
Secondary Endpoints	**Outcome Measures**	**Aligned with Objectives**
Demonstrating the feasibility of measuring	• Children's symptom burden (adaptation of the validated Mini-SSPedi [4] and SSPedi [5]) • Children's quality of life (validated PedsQLTM Cancer Module [6,7]) • Parents' satisfaction with cancer care (validated EORTC PATSAT C33 [8,9] adapted to assess parents' satisfaction with children's cancer care). • Impact of paediatric illness on the family (validated Impact on Family Scale [10]) • Parents' quality of life (validated EQ-5D-3L [11])	3, 7 4 2 5 6
Impact on health care professionals due to the integration of ePROs in palliative care	• Quantitative data (web-based questionnaire developed for HCPs) • Qualitative data (focus groups with project-internal and external HCPs involved in the study)	7, 8

Figure 6.2 depicts how patients were able to interact with the digital health platform during the study after having been enrolled into MyPal-Child study. During a 6-month period, patients could regularly report symptoms and their severity within the gamified MyPal-Child App after installing the apps on their own mobile devices, as explained in more detail in Chapter 4. Completion of symptom reports were also possible outside of the game through the app. The ePROs covering the patients' quality of life were completed at monthly intervals. Patients could continue playing the game without further data reporting after the 6-month period until the end of the overall study time at the end of September 2022. A follow-up questionnaire on usability was provided shortly after the end of study participation.

Parents could use the MyPal-Carer App to add proxy-reports on their children's symptoms and quality of life. Additionally, they were asked to complete monthly questionnaires on their own satisfaction with the child's cancer care, the impact of the illness on the family and their own quality of life. Parents were also presented with a follow-up questionnaire on usability shortly after the end of study participation.

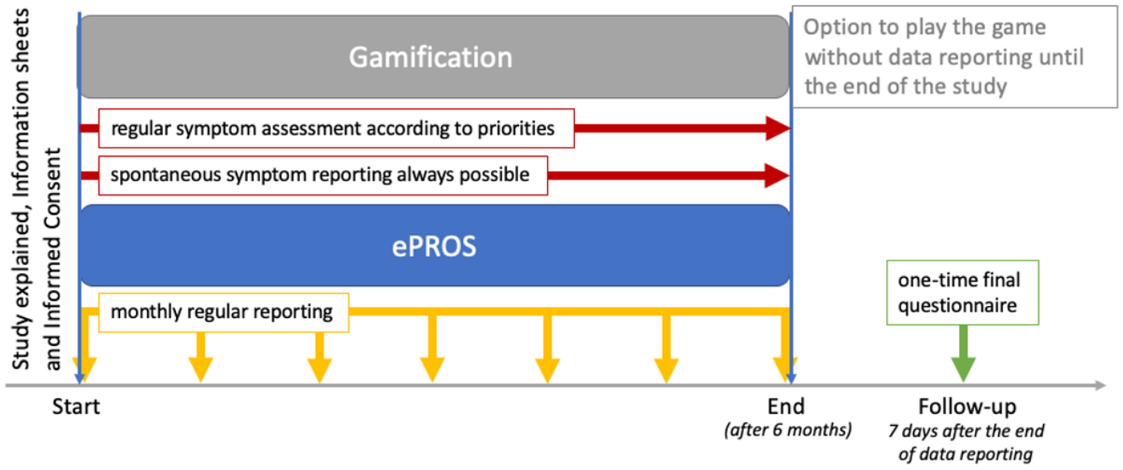

Figure 6.2: Schema for patient involvement in MyPal-Child. [1]

On-site preparations at the clinical sites included setting up the technical infrastructures and training the local study staff through carefully designed presentations, instruction guidelines and a standard operating procedure for recruitment provided by the project partners. Eligible children, adolescents and parents were informed about the study by the local study staff and provided with age-appropriate information sheets and informed consent forms. While being enrolled into the study, children, adolescents and parents were provided with leaflets to help with the first steps, i.e., installation of the apps and completion of the baseline questionnaires and assisted by the local study staff while doing so.

In order to gather qualitative data to evaluate participants' experiences of the study, eight focus groups were conducted at the three clinical sites near the end of the study with: a) children and parents who participated in the study, b) HCPs who had been involved in the development of the platform, and c) HCPs who had not been involved in the development of the platform but were engaged in the study.

Results and Outcomes

Description of Participant Selection and Recruitment

A total of 83 out of the planned 100 patients were recruited at all three clinical sites (18 at Saarland University, 39 at Medical School Hannover, and 26 at University Hospital Brno) during the 15-month recruitment period. Figure 6.3 depicts the overall cumulative recruitment at all three clinical sites. Initially, all eligible patients who had been diagnosed with cancer within the past 12 months were invited to participate, which is reflected in the faster rise of recruited patients at the beginning of the study. Subsequently, only newly diagnosed eligible patients could be recruited, which slowed down the recruitment.

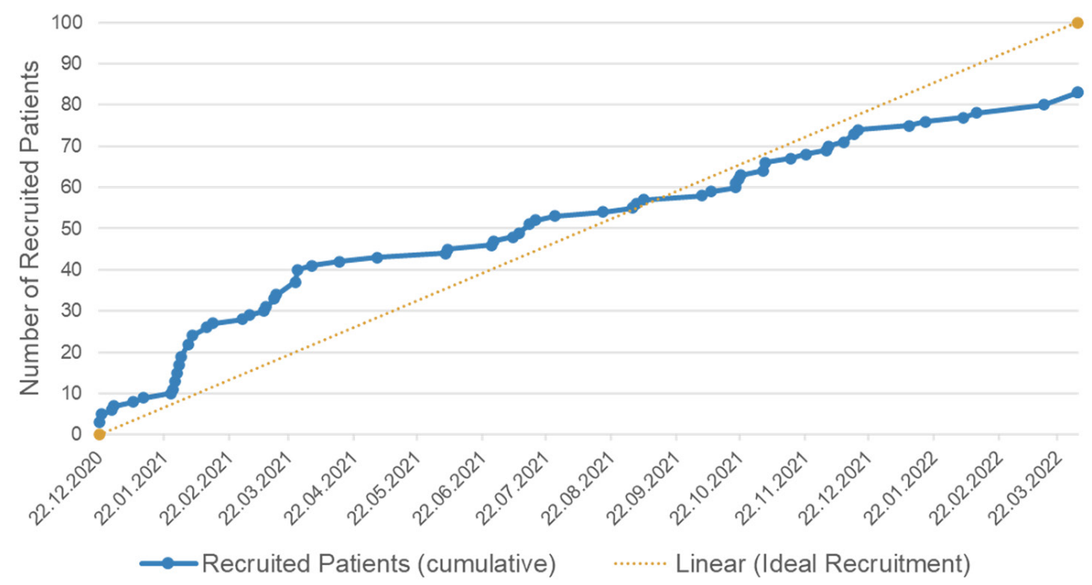

Figure 6.3: The overall recruitment progress at all three clinical sites involved in MyPal-Child with first patient, first visit on December 22, 2020 and last patient, first visit on March 3, 2022.

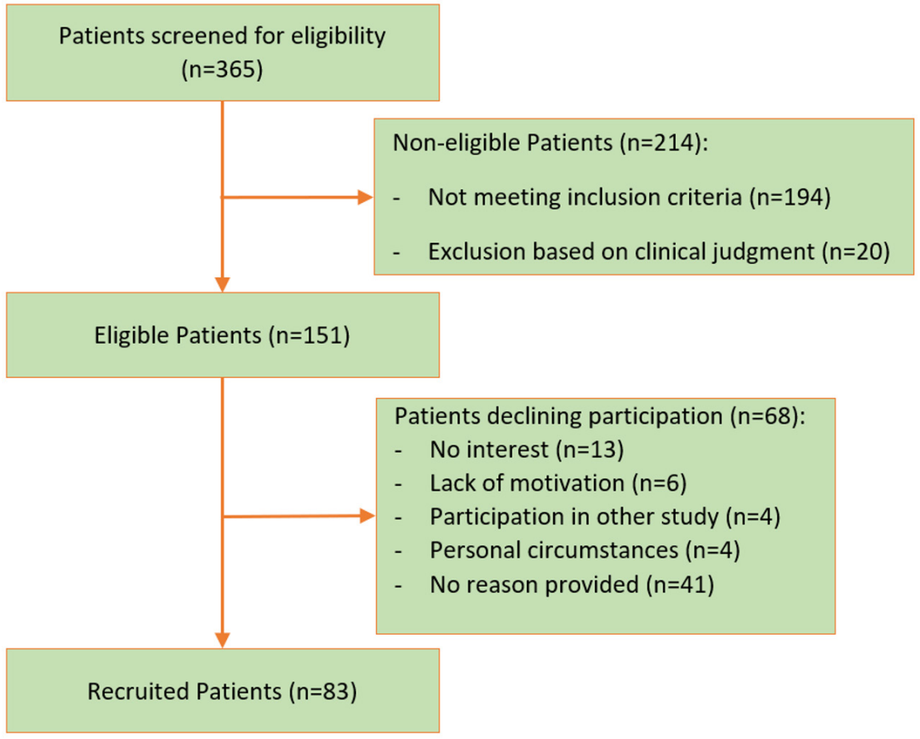

Figure 6.4: Flow diagram for the MyPal-Child study.

Figure 6.5 shows that 151 (41%) of the 365 screened patients at all three clinical sites were eligible for the study according to the inclusion and exclusion criteria. Of the remaining 214 non-eligible patients, 194 (90%) did not meet the inclusion criteria while 20 (10%) were excluded on the clinical judgment of the hospital-based principal investigators. Eighty-three (55%) of the 151 eligible patients were recruited into the study (55% ≙ primary endpoint recruitment rate), while 68 (45%) refused to participate providing reasons such as personal circumstances, lack of motivation, no interest or participation in other studies, among others.

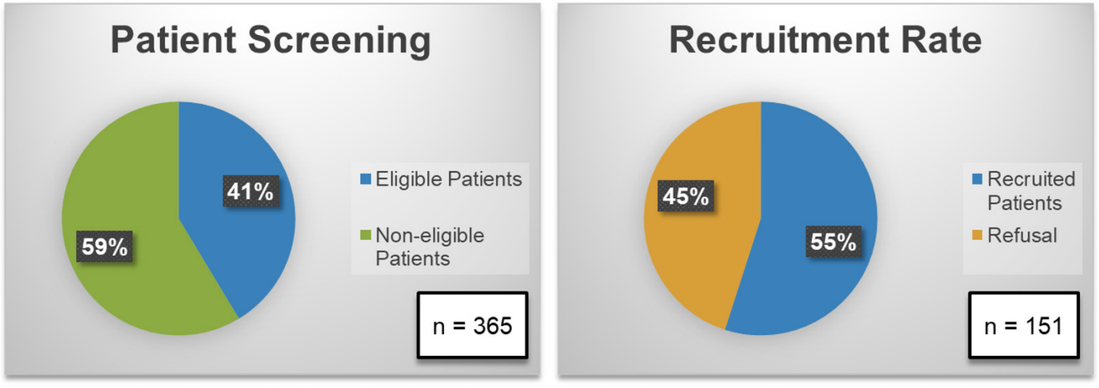

Figure 6.5: The rates of eligible patients (41% ≙ 151 patients) among all screened patients (n=365) as well as the rate of recruited patients (55% ≙ 83 patients) among the eligible patients (n=151) at all three clinical sites.

Study Population Characteristics

Figure 6.6 on the next page presents the characteristics of the study population of children and adolescents with cancer (n=83) in terms of age, gender, diagnosis and stage of diagnosis. The sample of older patients (14-17 years) was higher than expected, given the prevalence of childhood cancer being higher among younger patient groups, especially regarding leukaemia and renal tumours as one type of solid tumours. [13] At the same time, the patient group with the highest incidence for cancer (0-4 years) were not eligible for the study due to the low level of literacy. [13] Brain tumours were considered separately from solid tumours as resulting neurological effects and respective symptoms are more likely to be prevalent among this group. [14] Among the recruited patients (n=83), the number of children and adolescents newly diagnosed with cancer was substantially higher (84% ≙ 70 patients) than those whose disease had relapsed (16% ≙ 13 patients).

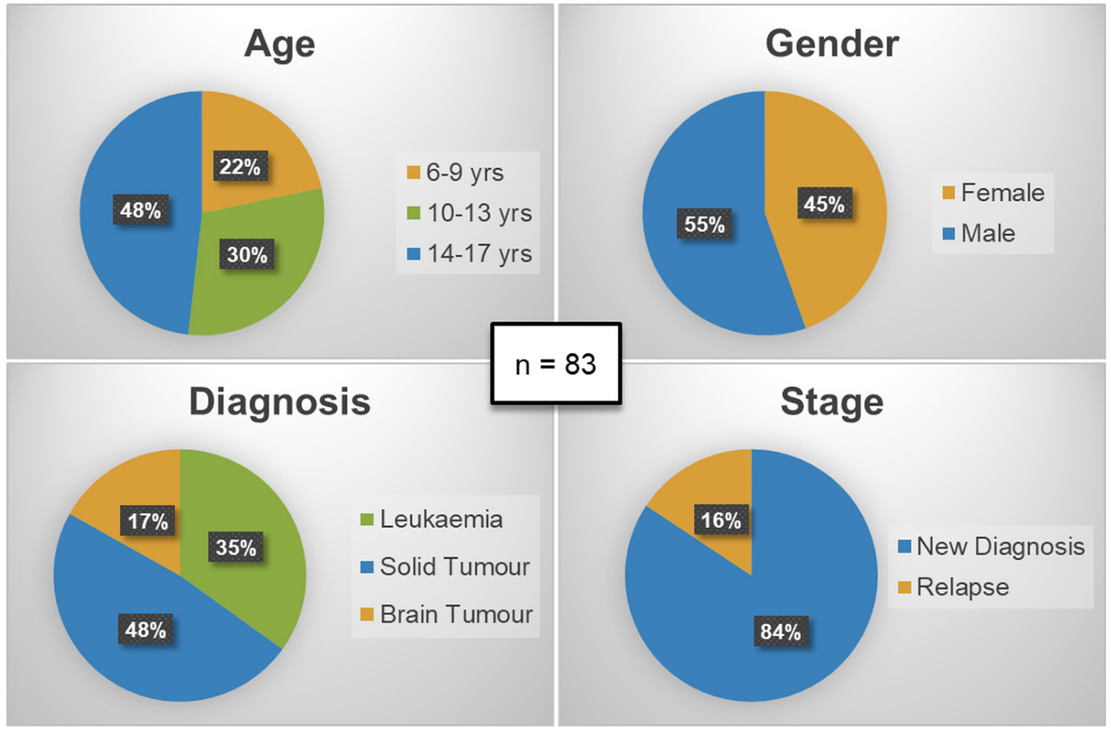

Figure 6.6: Study patients' characteristics in terms of age, gender, diagnosis and stage of diagnosis.

As previously stated, the MyPal system had been designed as an add-on to the usual care provided at the three clinical centres in the context of an observational study, and thus no data from HCPs were collected. Nevertheless, the reports made by patients and parents were regularly checked by the treating HCPs using the web-based platform, which might have triggered follow-up actions as depicted in Figure 6.7.

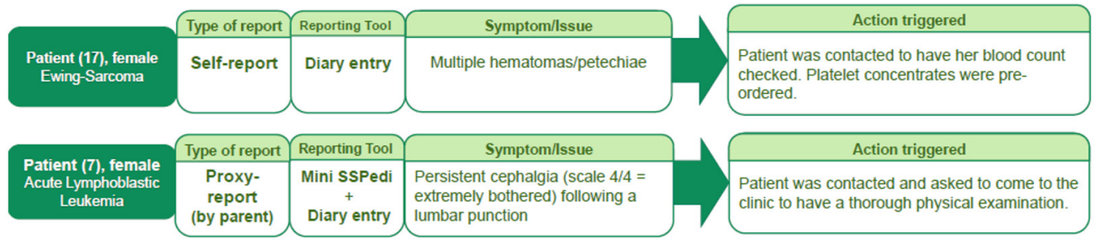

Figure 6.7: Two examples of symptoms/issues reported by patients or their parents via the mobile applications. The reports were reviewed by treating HCPs who took actions in response to the observations made. Derived from [15,16]

Challenges to the Implementation of the Study

The challenges faced during the pre-study on-site preparation phase for the clinical study at the clinical sites, including the setting up of the technical infrastructure as well as administrative and logistic issues, were outlined in an article published in September 2021. This policy brief provides actionable recommendations on how to circumvent the challenges encountered during the implementation of digital health innovations in clinical studies. [12]

The COVID-19 pandemic starting in January 2020 also affected the pre-study preparations as well as the recruitment phase, leading to a 7-month delay in study initiation at the end of December 2020. Nevertheless, since the use of the digital health platform during the study enabled patients and their parents to report symptoms to HCPs at times when personal appointments were less likely to be scheduled, communication with HCPs could be facilitated and appeared to be useful, especially for outpatients. According to the preliminary results, the study indicates evidence for the feasibility of recruitment.

Conclusion

This chapter has provided an insight into the design and methodology of the MyPal-Child non- experimental observational feasibility study and presented preliminary results regarding screening and recruitment, as well as an overview of the study population characteristics, and how the MyPal-Child apps worked.

Detailed results and outcomes of the complete statistical analysis will cover the evaluation of the quantitative and qualitative data regarding the defined study endpoints (see Table 2) and be presented in forthcoming publications. This includes detecting significant changes of outcome measures along the study period using repeated measures analysis of variance and post-hoc analysis. Moreover, subgroup analyses of the outcome measures will be performed regarding the grouping variables: age, gender, clinical centre, country of residence, cancer type and stage, using one-, two- and three-way analysis of variance.

Key messages

- The introduction of digital health innovations, within or outside the scope of a clinical study, involves various challenges regarding organisational, administrative and logistical issues, which must be approached carefully. [12]
- All end-users of eHealth must be strongly involved before and during the development as well as testing phase of digital health innovations, through iterative feedback loops to ensure high degrees of usability and utility. Focus group discussions, both before and after the implementation of digital health solutions, can be used to complement the evaluation of the proposed system and may be helpful in identifying potential bottlenecks or issues that could be minimised in further interventions.
- According to observations made during the recruitment phase, the idea of testing a gamified mobile application for active patient engagement without pharmaceutical intervention was in general a highly appealing incentive to participate in the study for the majority of young cancer patients, as well as their parents.
- The timing of inviting newly diagnosed children and adolescents and their families to participate in a study like this must be chosen very carefully, since they are strongly emotionally impacted by the diagnosis of cancer.
- To ensure long term motivation among children and adolescents with cancer, different age groups must be addressed in a differentiated and age-appropriate manner and a clear benefit of the app's usage must be evident to all user groups involved.
- The MyPal system enabled real-time electronic capture of symptom reports generated by patients or proxies. As a result, the integration of such ePROs into clinical practice could become useful in supporting clinical decision-making in individual cases and could prove to be a valuable tool for procedural and therapeutic follow-up in children and adolescents with cancer (Fig. 8). In the future, such tools could lead to improvements in the quality of routine care in paediatric oncology. The full findings of this research will be available in a separate publication.

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Chapter 7: Patient reported outcomes and their role in palliative care for patients with cancer: Conclusions from the MyPal project

Christina Karamanidou, Pantelis Natsiavas, Kostas Stamatopoulos
Institute of Applied Biosciences, Centre for Research and Technology Hellas, Greece

Summary

Several landmark randomised controlled trials (RCTs) of palliative-care interventions in patients with advanced-stage cancer have used endpoints based on patient reported outcomes (PROs) to assess clinical benefit. [1-4] PROs are a prominent topic in healthcare innovation, highlighting the role of the patient experience as a key measure of healthcare quality. [5] A PRO is defined as "a measurement based on a report that comes directly from the patient about the status of a patient's health condition without amendment or interpretation of the patient's response by a physician or anyone else." [6] The recording of PROs enables direct measurement of the experiences of patients with chronic conditions, including cancer; thus, PROs are a critical element of person-centred, high-quality care for patients with cancer. [7]

An evolving body of literature supports the feasibility of electronic collection of PROs, yielding reliable data that are sometimes of better quality than clinician-reported data. The incorporation of electronic PRO (ePRO) assessments into standard healthcare settings appears to improve the quality of care delivered to patients with cancer. [8] PROs can also be used to assess outcomes for caregivers, demonstrating the beneficial effects of early administration of palliative care for other members of the family unit.

A growing number of efforts to integrate PROs into routine clinical care processes are currently in place. This paradigm shift is changing the landscape of using PROs in oncology, recognising the central role of PROs as a tool to enhance the patient's voice in cancer care, including palliative care. Nevertheless, wide adoption of ePROs in a clinical context has not yet been achieved due to a number of scientific, technical and societal challenges. [9]

Summary of the MyPal project

The MyPal project was designed specifically to develop novel ePRO-based digital interventions for patients with cancer palliative care needs and subsequently to evaluate these interventions via two clinical studies, namely an RCT to test the MyPal intervention in adult patients with blood cancers, and a feasibility observational prospective study of children with solid tumours and haematological cancers and their parents. The MyPal-Adult study (described in Chapter 5) was a multi-centred RCT which facilitated the collection of physical and emotional symptoms from patients with CLL or MDS via the use of a digital health platform. The MyPal-Child study (described in Chapter 6) was an observational feasibility study utilising a serious game, AquaScouts (described in Chapter 4) to reduce the psychological burden of reporting symptoms in paediatric cancer patients between the ages of 6 and 17 years.

MyPal adopted a patient-centred approach harnessing technology for the benefit of patients, tailored to their specific and evolving needs, while also considering the fundamentally different profiles of patients and caregivers of different age groups, as well as differences in digital and health literacy. In what follows, we present some of the main lessons learned from the project and insights that can inform future research and practice in this area.

Lessons learned from the MyPal project

Among the main preliminary findings of the MyPal project is that, although perceptions differ across Europe, the value of palliative care in oncology is increasingly acknowledged by HCPs who are eager, at least in principle, to endorse PRO-based delivery of palliative care. As pointed out in Chapter 1, ePROs could provide an opportunity for leveraging patient-centred palliative care: firstly, by empowering patients to report psychological and physical symptoms in real time and, secondly, by providing HCPs with the data needed to improve the care of their patients.

Indeed, eHealth and palliative care can be complementary and mutually reinforcing, however major challenges still must be addressed in order to achieve the seamless communication required between the two fields. As discussed in Chapter 1, the design of smart eHealth solutions should go beyond focusing on technical characteristics by actively addressing the dimension of user experience. As described in Chapter 2, a user engagement strategy was deployed in MyPal from the beginning in order to collect input on user needs and establish connections with end-users.

The implementation of the MyPal interventions uncovered many challenges, extending from limited technical support at the clinical sites to varying time available from HCPs to incorporate MyPal within the context of their everyday duties. Other significant factors that emerged concerned the health literacy and digital literacy of patients and caregivers, which varied widely. In the particular case of the MyPal-Adult study, lower levels of digital literacy in this older patient group were clearly demonstrated by the fact that nearly half of screened patients (46.6%) who were not enrolled in the study listed 'not familiar with the use of apps/device' as their reason for declining to participate (Chapter 5).

MyPal highlighted a well-recognised challenge in conducting clinical research in palliative care, which manifested in the low recruitment and high attrition rate in both the MyPal-Adult and the MyPal-Child studies. This indicates the need for further multi-disciplinary research (biomedicine, humanities, ICT) towards the development of acceptable paradigms than can engage both HCPs and patients/caregivers.

Conclusions

Despite the challenges arising during its implementation, the MyPal system has the potential to provide a substantial improvement in the management of patients with palliative care needs in the context of cancer. Indeed, MyPal offered a promising model for maximising access to care through the implementation of an ePRO-based intervention with none or minimal discrimination pertaining to age or physical distance from the point of care. Capitalising on the experience gained throughout the implementation of the project, the MyPal consortium plans to refine its IT-based intervention towards generating valuable information with no increase in workload, potentially freeing up time to deliver more efficient and equitable patient-centred care in cancer and beyond.

Based on the lessons learned throughout the MyPal project, the adoption of eHealth solutions in routine clinical care appears to still be challenging. Despite ongoing political initiatives at a European level (e.g. the European Health Data Space regulation) and novel certification and reimbursement schemes focusing on eHealth apps, a shift in attitude is clearly warranted. Multidimensional activities that could assist in this include relevant research, education to train HCPs, novel technical

validation schemes to ensure quality of the relevant applications, vigilance in post-market settings and commitment at the level of national policies.

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Contributors to the ebook are:

Begović Dunja (Executive Summary and Chapter 2) is a Research Associate at the International Observatory on End of Life Care, Lancaster University, UK.

Burns-Gebhart Anna (Chapter 6) is a Research Associate at the Hannover Medical School, Germany.

Garani-Papadatos Tina (Chapter 2) is Professor of Public Health Bioethics at the School of Public Health, University of West Attica, Greece.

Ghia Paolo (Chapter 5) is Full Professor in Medical Oncology at Vita-Salute San Raffaele University, Italy.

Graf Norbert (Chapter 6) is a Paediatric Oncologist and Professor of Paediatrics at Saarland University, Germany.

Hoffmann Stefan (Chapter 4) is Head of Studio at Serious Games Solutions/ Promotion Software GmbH, Germany.

Karamanidou Christina (Introduction, Chapters 1 and 7) is a Post-Doctoral Researcher at the Centre for Research and Technology Hellas, Greece.

Koumakis Lefteris (Chapter 3) is a Researcher at the Foundation for Research and Technology Hellas, Greece.

Kröll Thomas (Chapter 4) is a Technical Developer at Serious Games Solutions/ Promotion Software GmbH, Germany.

Meyerheim Marcel (Chapter 6) is a Research Assistant at Saarland University, Germany.

Natsiavas Pantelis (Introduction, Chapters 1 and 7) is a Researcher at the Centre for Research and Technology Hellas, Greece.

Ostgathe Christoph (Foreword) is the President of the European Association for Palliative Care.

Payne Sheila (Executive Summary) is Emeritus Professor in Palliative Care at the International Observatory on End of Life Care, Lancaster University, UK.

Salifu Yakubu (Executive Summary) is a Lecturer in Palliative Care at the International Observatory on End of Life Care, Lancaster University, UK.

Sander Annette (Chapter 6) is a Paediatric Oncologist at the Hannover Medical School, Germany.

Scarfò Lydia (Chapter 5) is an Assistant Professor and Physician-Scientist at Vita-Salute San Raffaele University, Italy.

Schera Fatima (Chapter 3) is a Software Developer at Fraunhofer Institute for Biomedical Engineering, Germany.

Scholz Wiebke (Chapter 4) is a 2D Artist/UX Specialist at Serious Games Solutions/ Promotion Software GmbH, Germany.

Schraut Robert (Chapter 4) is a Game Designer and a former employee of Serious Games Solutions/ Promotion Software GmbH, Germany.

Stamatopoulos Kostas (Chapter 7) is Director of the Institute of Applied Biosciences at the Centre for Research and Technology Hellas, Greece.

Sweers Malin (Chapter 4) is a Project Assistant at Serious Games Solutions/ Promotion Software GmbH, Germany.

Production of ebook

The ebook was edited by **Sheila Payne**, **Yakubu Salifu** and **Dunja Begović** (ULANC). The design, layout and production were undertaken by **Anthony Greenwood** (ULANC). Proof reading was undertaken by **Fiona Tankard**. Critical review was provided by **Cathy Payne** (EAPC) and **Julia Downing** (ICPCN).

Appendix 1:
Glossary of abbreviations

CLL (chronic lymphocytic leukaemia) is a type of cancer affecting white blood cells. It is the most common type of leukaemia, usually diagnosed in people over 60 years of age.

EU (European Union) is a political and economic alliance comprising 27 countries with an internal single market and various common policies and laws. Through its programmes for scientific development, the EU funds numerous research projects including MyPal.

GDPR (General Data Protection Regulation) is the European Union's legislation on collecting and processing personal data. It regulates data protection and data privacy in the European Union and European Economic Area.

HCP (health care professional) is a term covering a variety of individuals working in health care settings, such as doctors, nurses, pharmacists, dentists and others. It usually implies the possession of a professional qualification or license required in the particular health care context.

eHealth (electronic health) refers to the use of information and communication technologies to support health care provision. This can include, for example, electronically inputting and accessing health records and other medical data, or the possibility of remote communication with health care professionals.

mHealth (mobile health) is the use of mobile and wireless technologies, such as mobile phones and tablets, to improve health outcomes, health care services, and health research.

MDS (myelodysplastic syndrome) is a rare type of blood cancer, most commonly presenting in people over the age of 70 years.

PRO (patient-reported outcome) is a health outcome reported directly by a patient, for example, by answering a questionnaire or survey on symptoms, quality of life and other outcomes.

ePROs (electronic patient-reported outcomes) are PROs that are collected electronically, for instance through a computer or mobile phone application.

RCT (randomised controlled trial) is a type of experimental study assessing the effects of an intervention, where study participants are randomly assigned to an intervention or control group.

QoL (quality of life) is a concept referring to a person's ability to be healthy and comfortable and enjoy normal life activities. It is a multi-dimensional concept incorporating both subjective and objective measures of well-being and it includes physical, social, psychological and spiritual aspects.

WHO (World Health Organization) is a specialised agency of the United Nations focusing on the promotion of international public health. Its work includes advocacy, technical assistance, and research and reporting on a variety of health topics.

Appendix 2: MyPal project - list of publications

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MyPal: Contributing Organisations

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Fraunhofer IBMT
MUNI | CEITEC
FORTH INSTITUTE OF COMPUTER SCIENCE COMPUTATIONAL BIOMEDICINE LABORATORY
Lancaster University
Karolinska Institutet
www.pagni.gr Πα.Γ.Ν.Η.
MHH Hannover Medical School
UNIVERSITÄT DES SAARLANDES
icpcn international children's palliative care network
FAKULTNÍ NEMOCNICE BRNO
SERIOUS GAMES SOLUTIONS The Gamification Experts A DIVISION OF PROMOTION SOFTWARE GMBH
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