Aus der Klinik für Pädiatrische Onkologie und Hämatologie

der Medizinischen Fakultät

der Universität des Saarlandes, Homburg/Saar

Pediatric Oncology in Transition: Implementing an ePRO-Based Digital Health Platform – The Multicenter Feasibility Study MyPal4Kids

Dissertation zur Erlangung des Grades eines Doktors
der Theoretischen Medizin der Medizinischen Fakultät

der UNIVERSITÄT DES SAARLANDES

2025

vorgelegt von: Marcel Meyerheim

geb. am: 07.04.1990 in Ludwigsburg

Tag der Promotion: 10. August 2026

Dekan: Univ.-Prof. Dr. med. dent. Matthias Hannig

Berichterstatter: Prof. Dr. Norbert Graf

Prof. Dr. Olga Kalinina

Table of Content

Abstract

As part of the MyPal project, a digital health platform with mobile applications was developed to promote the active involvement of patients and communication in pediatric oncology and palliative care by combining Electronic Patient-Reported Outcomes (ePROs) with age-appropriate gamification. To adequately capture children's perspectives, MyPal adopted a patient-centered approach as a complement to standard care. The platform targeted children and adolescents aged 6–17 years and their caregivers, aiming to facilitate timely symptom reporting and interaction with Healthcare Professionals (HCPs).

MyPal4Kids was conducted as a multicenter observational feasibility study from December 2020 to September 2022 at three clinical sites in Germany and the Czech Republic. A total of 83 pediatric patients with at least one parent each, and 10 HCPs participated. Using a mixed-methods approach, primary outcomes assessed platform acceptability, usability, and actual use, measured by rates of recruitment, attrition, adherence, and user feedback through focus groups. Secondary outcomes evaluated the feasibility of ePRO data collection and the platform's impact on clinical workflows and communication.

The recruitment rate was 38%, with an 18% attrition rate. Overall, usability received positive ratings, though platform use decreased over time. Older children found the game less appealing. Adherence varied by age group and depended on the extent of HCP feedback on reported symptoms. Improvements in communication were reported inconsistently, but some participants appreciated increased motivation to report symptoms and perceived support from the clinical team. In settings with limited in-person contact, the platform helped bridge communication gaps, although some HCPs reported higher workload.

These findings indicate that ePRO-based digital platforms hold promising potential to support pediatric oncology care, particularly when effectively integrated into clinical routines. Their success depends on context-sensitive implementation and clear definition of clinical responsibilities. Key challenges remain sustaining long-term motivation and ensuring timely feedback from HCPs. Future research should focus on even more adaptive, age-tailored designs and seamless integration into clinical workflows to enable sustainable and scalable implementation.

Deutsche Zusammenfassung

Im Rahmen des MyPal-Projektes wurde eine digitale Gesundheitsplattform mit mobilen Anwendungen entwickelt, um die aktive Mitwirkung von Patient*innen sowie die Kommunikation in der pädiatrischen Onkologie und Palliativversorgung zu fördern. Hierbei wurden Electronic Patient-Reported Outcomes (ePROs) mit altersgerechten spielerischen Elementen (Gamification) kombiniert. Um die Perspektiven von Kindern adäquat einzubeziehen, verfolgte MyPal einen patienten-zentrierten Ansatz ergänzend zur etablierten Behandlung. Die Plattform richtete sich an Kinder und Jugendliche im Alter von 6 bis 17 Jahren sowie deren Eltern und sollte die zeitnahe Meldung von Symptomen und den Austausch mit Gesundheitsfachkräften (Healthcare Professionals, HCPs) erleichtern.

MyPal4Kids wurde als multizentrische, beobachtende Machbarkeitsstudie von Dezember 2020 bis September 2022 an drei klinischen Standorten in Deutschland und der Tschechischen Republik durchgeführt. Insgesamt nahmen 83 pädiatrische Patient*innen, jeweils mindestens ein Elternteil pro Kind und 10 HCPs teil. Mithilfe eines Mixed-Methods-Ansatzes wurden als primäre Endpunkte Akzeptanz, Benutzer-freundlichkeit und Nutzungsverhalten der Plattform anhand von Rekrutierungs-, Abbruch- und Adhärenzraten sowie Nutzerfeedback durch Fokusgruppen bewertet. Sekundäre Endpunkte umfassten die Machbarkeit der ePRO-Datenerhebung sowie Auswirkungen auf klinische Arbeitsabläufe und Kommunikation.

Die Rekrutierungsrate betrug 38%, die Abbruchrate 18%. Die Plattform erhielt insgesamt positive Bewertungen hinsichtlich der Benutzerfreundlichkeit, wenngleich die Nutzung im Verlauf abnahm. Insbesondere ältere Kinder fanden das Spiel weniger ansprechend. Die Adhärenz variierte nach Altersgruppen und Ausmaß des HCP-Feedbacks zu Meldungen. Verbesserungen der Kommunikation wurden uneinheitlich berichtet, jedoch schätzten einige Teilnehmende eine gesteigerte Motivation zur Symptommeldung und wahrgenommene Unterstützung durch das Team. In Situationen mit eingeschränktem Kontakt half die Plattform, Kommunikationslücken zu überbrücken, während einige HCPs eine höhere Arbeitsbelastung berichteten.

Die Ergebnisse zeigen, dass ePRO-basierte digitale Plattformen ein vielversprechendes Potenzial zur Unterstützung der pädiatrischen Onkologie besitzen, insbesondere bei effektiver Integration in klinische Routinen. Ihr Erfolg hängt von kontextspezifischer Implementierung und klaren klinischen Verantwortlichkeiten ab. Zentrale Herausforderungen bleiben langfristige Motivation und zeitnahes Feedback durch HCPs. Zukünftige Forschung sollte weiter adaptierte, altersspezifische Ansätze und nahtlose Integration in klinische Abläufe prüfen, um eine nachhaltige und skalierbare Implementierung zu ermöglichen.

Preface

This dissertation is based on the manuscript entitled *"Feasibility of Implementing an ePRO-based Digital Health Platform in Pediatric Oncology and Palliative Care: Insights from the MyPal4Kids Multicenter Observational Study",* for which I am the first and corresponding author, responsible for conceptualization, data analysis, interpretation, and manuscript writing. The manuscript, submitted to *JMIR Cancer* on August 1, 2025, presents results from the *MyPal4Kids* feasibility study conducted within the framework of the EU-funded MyPal project (Horizon 2020, Grant Agreement: 825872), which evaluated a digital health platform integrating Electronic Patient-Reported Outcomes (ePROs) and gamification in pediatric oncology and palliative care.

Within the MyPal project, I served as lead coordinator of Work Package 6 (“Clinical Studies Implementation, Evaluation and Impact Assessment”) under the supervision of Prof. Dr. Norbert Graf. My responsibilities included study design, outcome selection, protocol development, ethics submissions, coordination with clinical and technical partners, platform testing, moderation of focus groups, and analyses.

This dissertation expands upon the submitted manuscript by providing:

- a more detailed presentation of baseline and optional participant characteristics to contextualize the study cohort.
- additional statistical analyses, including a two-factor Aligned Rank Transform Analysis of Variance (ART-ANOVA) on family-centered outcomes such as parents' satisfaction with cancer care, impact on family, and Health-Related Quality of Life (HRQoL).
- an in-depth qualitative analysis of focus group data with pediatric patients and their parents, including thematic descriptions and representative quotations.
- a broadened qualitative exploration of focus group findings with project-internal and external Healthcare Professionals with representative quotations, adding perspective on implementation challenges and facilitators.
- An expanded introduction and discussion situating the study within a broader context.

The core data and findings are identical to those of the submitted manuscript: no additional studies or data sets were included. I confirm that this dissertation is my own original work and that all contributions from collaborators have been appropriately acknowledged.

1 Introduction

1.1 Background

The illness trajectory of children and adolescents with cancer places substantial physical, emotional, and psychological strain on patients, their families, and peers [164, 204, 205]. In addition to navigating the complexities of treatment, many families face persistent fear of relapse or death during follow-up. Thus, burdens often extend beyond treatment, with lingering cognitive, educational, and social sequelae that affect reintegration into school and peer networks. These multidimensional challenges underscore the importance of comprehensive support, including palliative care, which is increasingly acknowledged as fundamental aspect of healthcare from the time of diagnosis, rather than being confined to the terminal phase [132]. Consistent with World Health Organization guidance, pediatric palliative care should be integrated early and alongside disease-directed therapies aimed at preventing and alleviating suffering across physical, psychosocial, and spiritual domains [13, 149, 199]. A recent global mapping of children's palliative care confirms progress in service availability but also highlights persisting inequities worldwide, underlining the urgency of scalable supportive innovations [40].

Against this backdrop, a paradigm shift has taken place in oncology and palliative cancer care, emphasizing patient-centered approaches and the incorporation of Patient-Reported Outcomes (PROs). PROs are information self-reported by patients concerning their health condition or Health-Related Quality of Life (HRQoL), typically captured via standardized questionnaires known as Patient-Reported Outcome Measures (PROMs) [191]. In their electronic form (ePROs/ePROMs), these tools have become increasingly relevant [74]. For consistency, this dissertation predominantly uses the term ePROs. In pediatric contexts, this shift has been increasingly acknowledged and explored [35, 62, 66, 68, 75, 96, 105, 108, 115, 138, 144, 196]. In parallel, digital health solutions, often referred to as Electronic Health (eHealth) interventions, are emerging. eHealth encompasses health services and information delivered via digital technologies, including mobile applications (mHealth), with ePROs representing a key component for symptom monitoring and communication. ePROs enable young patients to express a broad range of symptoms, needs, and concerns in real time, independent of clinical settings, thus allowing for a more nuanced understanding of their experience [27, 152]. Beyond facilitating expression, these tools aim to strengthen the perceived self-efficacy and HRQoL of patients and their families [21, 152].

Similar advances have been documented in adult oncology: routine ePRO monitoring has been linked to fewer emergency visits and hospitalizations and, in randomized trials, to

improved overall survival [11, 12, 36, 92]. More recently, implementation experiences have underlined clinicians' and patients' high acceptability of such tools, leading to actionable recommendations for integration of ePRO-based systems into routine care [114]. In line with this, the ESMO Clinical Practice Guideline (2022) outlines standards for ePRO selection, frequency of assessment, and necessary feedback mechanisms in adult cancer care to ensure their clinical utility and sustainability [100]. The PROTEUS-Trials Consortium provides methodological recommendations for optimizing ePRO capture in clinical trials, emphasizing patient interpretability and minimizing patient burden [165]. Similarly, Stover et al.'s (2021) framework for implementing ePRO instruments in routine practice synthesizes evidence on challenges such as workflow integration, technology readiness, and stakeholder engagement [175]. These guidelines, however, have been derived largely from adult oncology populations, and emphasize the need for validated, age-appropriate instruments with demonstrated measurement properties Complementary methodological frameworks have been developed to guide the systematic evaluation of such instruments across disease areas, offering practical criteria for assessing their developmental rigor and suitability for specific research or clinical purpose [49].

In response, pediatric oncology research has increasingly sought to adapt and extend these approaches [62, 153], with recent expert recommendations highlighting the importance of ensuring validity, reliability, and feasibility in ePRO development and use tailored to young cancer patients [2, 140]. Complementary to these methodological advances, the International Childhood Cancer Core Outcome Project has defined a harmonized set of core outcomes for pediatric cancer patients, providing a structured approach for data collection and visualization to support clinical care and research [79]. Related initiatives such as PediQUEST and the strengthened PediQUEST-Response model suggest feasibility and signal benefits for symptom management and HRQoL, though robust effectiveness data in routine practice are still emerging [139]. Recent reviews specific to pediatric oncology emphasize that, while validated, age-appropriate ePROs are increasingly available, their systematic use in both research and routine care remains limited [1, 57, 143, 151, 157]. Expert recommendations further underscore the importance of rigorous development and implementation strategies for pediatric ePRO-based systems to ensure usability, relevance, and integration into clinical workflows [69, 105, 206]. Together, these findings confirm that the evidence gap identified at the time of the *MyPal4Kids* study (2020–2022) remains highly relevant today.

Moreover, ePROs offer potential to improve communication between patients, caregivers, and Healthcare Professionals (HCPs) by supplementing time-limited clinical encounters with continuous and structured data [100, 203]. However, despite their demonstrated utility in clinical trials within pediatric oncology and palliative care [66, 68], the integration of ePROs

into everyday clinical routines remains limited [34, 68, 96]. A 2024 implementation review further highlights barriers such as workflow integration, clinician workload, and technology readiness, indicating that translating feasibility into sustainable practice continues to be a major challenge [1]. In addition, previous research emphasized the importance of minimizing assessment frequency and questionnaire length to optimize response rates, particularly among younger pediatric patients [193]. To address these barriers, gamification [37, 60, 146], including serious games [111], has been proposed as a strategy to enhance engagement among younger users, particularly in digital health [103, 112, 131, 155]. Evidence from serious games such as *Re-Mission* indicates that game mechanics can enhance motivation and adherence among adolescents and young adults with cancer, suggesting potential transferability to pediatric contexts [83]. However, despite high acceptability, the specific contribution of gamification to sustained engagement and long-term clinical benefit of pediatric ePRO-based platforms remains underexplored and robust evidence is still scarce [48, 78, 86, 96, 98, 119, 174, 177], in particular data on ePRO use in pediatric oncology routine care [97].

This study contributes to addressing that gap by evaluating how an ePRO-based digital health platform performs in real-world pediatric oncology and palliative care contexts. Thus, it also situates its findings within a research landscape where more recent studies reaffirm the urgency but also the incompleteness of current evidence.

1.2 The MyPal Project

The MyPal project (Horizon 2020, Grant Agreement: 825872, www.mypal-project.eu) was initiated to address the above challenges through the development and evaluation of ePRO-based digital health platforms for patients with cancer. The project included two clinical studies: *MyPal Adults* [156], targeting adult patients, and *MyPal4Kids* [110], focusing on pediatric patients. Both studies aimed to explore how integrating ePROs into clinical workflows can improve symptom management, communication, and patient engagement.

The study *MyPal4Kids* focused on children and adolescents aged 6–17 years and their families, aiming to assess the feasibility, acceptability, and perceived impact of an ePRO-based platform incorporating gamification, implemented across three clinical sites in Germany and the Czech Republic. An interdisciplinary consortium, comprising experts in pediatric oncology, palliative care, psychology, information technology, and software development, guided the process from platform design to clinical implementation and evaluation. Age-appropriate content, caregiver involvement, and data security were central design considerations.

Project-related publications can be grouped into three categories. First, cross-cutting outputs addressed overarching aspects of the MyPal project, including a systematic review on

challenges and opportunities in palliative cancer care [80], status and recommendation of technological and data-driven innovations [91], design and evaluation aspects [17, 94, 128], and stakeholder-driven policy recommendations [127]. Second, pediatric-focused outputs have specifically addressed ethical aspects of *MyPal4Kids* [51], serious game design [64], administrative and technical challenges [109], and psycho-oncological considerations linking emotion regulation and ePROs in pediatric oncology [113]. Third, publications dedicated to *MyPal Adults* have focused on participatory design [81], platform architecture [93], study randomization [16], usability and HRQoL outcomes [15, 18, 25].

1.3 Aims and Objectives of the Study

The *MyPal4Kids* clinical feasibility study was conducted to evaluate the integration of an ePRO-based digital health platform incorporating gamification into pediatric oncology and palliative care. The overarching aim is to explore whether such a platform can support more personalized, participatory, and sustainable care for children and adolescents with cancer.

The evaluation draws on both quantitative metrics (e.g., platform usage, adherence) and qualitative insights from focus groups, reflecting a mixed-methods approach to assessing usability, user engagement, communication dynamics, and practical implementation challenges from the perspectives of children, parents, and HCPs. This mixed-methods design supports triangulation between behavioral use data and stakeholder perspectives. These objectives build upon the predefined objectives of the *MyPal4Kids* study protocol [110], while framing them from a broader implementation and user-centered perspective.

- To assess the platform's acceptability and usability from the perspectives of children and adolescents with cancer, their parents, and HCPs.
- To explore the extent and nature of user engagement with the platform, including potential age-related differences.
- To investigate the perceived impact of the platform on communication, symptom reporting, and clinical workflows.
- To identify facilitators and barriers to the integration of such digital tools into routine pediatric oncology and palliative care settings.

These objectives provide the foundation for evaluating the potential contribution of ePRO-based digital health platforms to the future of supportive cancer care in pediatric populations. They also frame the findings within an implementation perspective, linking feasibility with practical considerations for sustained use.

2 Materials and Methods

Within the scope of the MyPal project, the multicenter observational feasibility study *MyPal4Kids* was conducted to evaluate the implementation of an ePRO-based digital health platform in pediatric oncology and palliative care [110]. The study was conducted over 21 months (December 2020–September 2022) at three clinical sites: Saarland University (USAAR) and Medical School Hannover (MHH) in Germany, and University Hospital Brno (FNBRNO) in the Czech Republic. Recruitment closed on March 22, 2022, with the last patient's first visit. Study monitoring and patient safety oversight were maintained throughout the study period by local principal investigators.

The study was designed as a clinical feasibility study, with key features consistent with methodological guidance on feasibility studies [124, 198]. Its focus was to assess the practical feasibility of implementing an ePRO-based platform, including recruitment and retention processes, adherence to study procedures, the suitability of the technical and administrative infrastructure, preliminary evaluation of user engagement and outcomes, and the identification of potential challenges to inform future implementation. This approach emphasizes evaluating whether the implementation of the platform can be successfully carried out in a real-world clinical context, rather than testing definitive clinical efficacy. Figure 1 presents an overview of the study's progression and timeline.

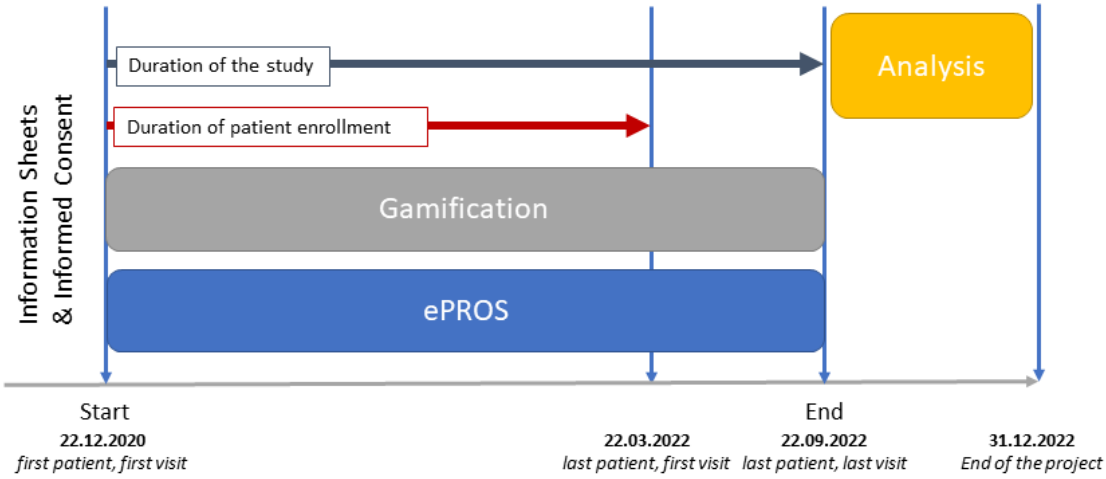


Figure 1 Study flow and overall timeline of the *MyPal4Kids* study. ePROs = Electronic Patient-Reported Outcomes.

2.1 Setting and Participants

Participants were recruited by trained clinical staff at each site. Eligible children and adolescents aged 6–17 years diagnosed with leukemia or solid tumors, who were receiving treatment or had been treated within the previous twelve months at one of the participating

centers, were invited to participate. Alongside at least one parent or legal guardian (hereafter referred to as 'parents' throughout this dissertation), eligible participants received detailed oral and written information about the study during a dedicated enrollment visit. Written informed consent was obtained from both patients and their parents prior to inclusion. Study personnel created user accounts for the platform and supported participants in installing the applications via QR codes and completing baseline assessments. Additional assistance was provided as needed. Given the observational nature of the study, no randomization or control groups were employed. Eligibility criteria for study participation are presented in Table 1, while detailed recruitment procedures are described in the protocol [110].

To comprehensively assess feasibility, a mixed-methods approach was employed, combining quantitative metrics such as platform engagement, adherence, and preliminary outcome measures with qualitative insights from follow-up focus groups. This design allows triangulation between behavioral data and stakeholder perspectives, ensuring that both practical implementation and user experience are thoroughly captured.

Table 1 Inclusion and exclusion criteria for the *MyPal4Kids* study (adapted from [110]).

Inclusion criteria for children	• 6–17 years of age • Diagnosed with pediatric leukemia or solid cancer within the past 12 months • Receiving anti-cancer treatment at one of the participating clinical sites • Age-appropriate speaking, reading, and comprehension skills in German or Czech • Signed informed consent from parents, and assent form from children aged 14 years and older • Access to an internet connection and a mobile device (e.g., smartphone or tablet)
Inclusion criteria for parents	• Parent(s) of a child eligible for the study, according to the inclusion and exclusion criteria • Ability to speak, read and understand German or Czech • Signed informed consent from parent(s) • Access to an internet connection and mobile device (e.g., smartphone or tablet)
Exclusion criteria for children/parents	• Individuals which are deemed unable to participate in the study based on the clinical judgment of the site's chief investigator or another authorized member of the research team. This judgment must be documented for each child not being enrolled.

2.2 The MyPal Digital Health Platform

In addition to standard care provided at the participating clinical sites, study participants were offered access to the MyPal Digital Health Platform during their six-month participation. The platform [64] was developed within the MyPal project by the technical consortium members and consists of three core components tailored to pediatric oncology care: a mobile application for patients (*MyPal-Child App*), a companion app for parents (*MyPal-Carer App*), and a browser-based interface for treating HCPs (*HCP-Interface*), i.e., physicians, nurses, psychologists or social workers. A brief overview of each component is provided in Table 2.

Table 2 Description of the three components of the MyPal Digital Health Platform evaluated in *MyPal4Kids*.

Component	Users	Functionality
MyPal-Child App	Pediatric patients	Serious game with integrated ePRO symptom self-reporting and diary; read-aloud option for young users
MyPal-Carer App	Parents/carers	Proxy symptom reporting and access to relevant web resources
HCP-Interface	HCPs	Browser-based real-time review of symptom reports and shared diary entries; documentation of treatment protocols and reactions

Note. ePRO = Electronic Patient-Reported Outcome; HCPs = Healthcare Professionals.

The *MyPal-Child App* is a mobile serious game designed specifically for children and adolescents with cancer. Integrated into the underwater-themed serious game *AquaScouts* [64] (see Figure 2), the app allows young patients to self-report symptoms and write diary entries. Symptom-related questions appear both within and outside the game interface, up to three times per day, guided by a prioritization algorithm based on previous symptom input. Diary entries could be optionally shared with the clinical team via the *MyPal-Child App* [64].

The *MyPal-Carer App* enables parents to proxy-report their child's symptoms and provides access to curated, reliable online resources relevant to pediatric cancer care. Both the *MyPal-Child* and *MyPal-Carer App* could be installed on patients' or parents' own mobile devices and were also used to complete the study-related ePROs, which served as outcome measures (see Figure 2).

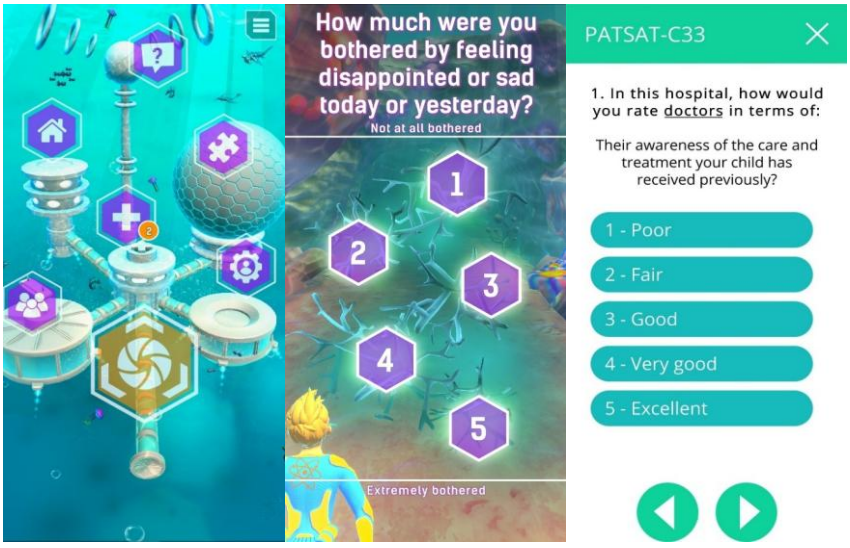


Figure 2 Screenshots of the MyPal platform (adapted from [64, 110]). Left: main menu of the *MyPal-Child App* with access to game start, ePROs, diary entries, and high scores; Middle: in-game symptom item from SSPedi; Right: parent-reported item on satisfaction with care in the *MyPal-Carer App*. ePROs = Electronic Patient Reported-Outcomes; SSPedi = Symptom Screening in Pediatrics Tool; PATSAT = Satisfaction with Cancer Care core questionnaire.

The *HCP-Interface* is a secure, password-protected browser-based application accessible via smartphone, tablet, or desktop. It allows real-time review of patient-reported symptoms (see

Figure 3) and, if shared by patients, diary entries using interactive visualizations. HCPs could also document treatment protocols, additional symptoms, and follow-up actions.

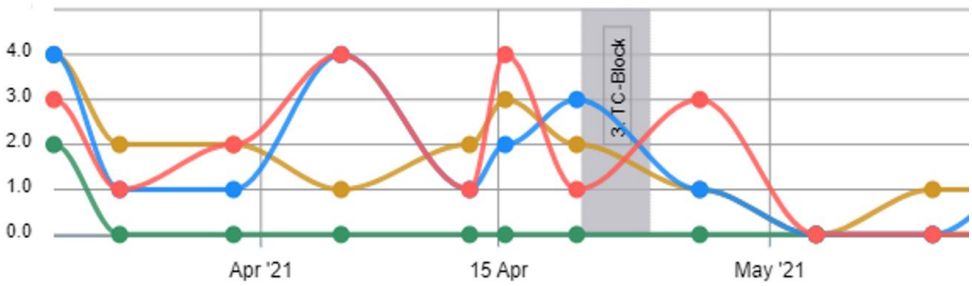


Figure 3 Symptom trajectories for a single patient as visualized in the *HCP-Interface*. Each dot represents a reporting time point. Symptoms are graded on a 0–4 scale (0 = not at all bothered, 4 = extremely bothered). Colors indicate symptoms: nausea/vomiting (red), change of appetite (blue), constipation (green), and diarrhea (orange). A treatment protocol entered by an HCP is shown as a grey bar. HCPs = Healthcare Professionals

All applications were available in German and Czech language, and a read-aloud function was implemented for the youngest eligible patients [64]. The platform was designed not only to support care but also to serve as feasibility evaluation tool, allowing the study to monitor user engagement, adherence, and interactions in a real-world context. By integrating the platform into standard care without imposing mandatory clinical responses, the study could assess the practical implementation, usability, and acceptability of the platform across multiple stakeholder groups. This approach also enabled the capture of authentic usage behaviors and the assessment of integration challenges in routine clinical workflows, a central element of the feasibility investigation.

2.3 Outcomes Measures

Participants were offered the *MyPal4Kids* platform with its components for a period of six months following enrollment. The primary and secondary study endpoints associated outcome measures (quantitative and qualitative), and their scheduled time points are presented in Table 3. Figure 4 illustrates the individual patient participation timeline, including the timing of regular ePRO assessments and optional platform interactions.

Table 3 The study endpoints and outcome measures in *MyPal4Kids*, adapted from the study protocol [110].

Primary Endpoints	**Outcome Measures and *ePROs***	**Assessment Time Points**
Acceptability of and engagement with the MyPal Platform	Recruitment rate, participation rate, attrition rate and adherence to the different components of the MyPal platform	M1-M6, continuously
	System usability (validated System Usability Scale [129]; adapted child version, see Supplement S1)	Once after M6

	Focus groups (children and parents)	Once after M6
Secondary Endpoints		
Demonstrating the **feasibility of ePRO-based measures**	Children's symptom burden (digital adaptation of the validated *Mini-SSPedi* and *SSPedi* [42, 179, 180, 202])	M1-M6, optional at any time
	Children's HRQoL (validated *PedsQL™ 3.0 Cancer Module* [145, 186])	Baseline and M1-M6, monthly
	Parents' satisfaction with cancer care (validated *EORTC PATSAT-C33* [22, 23] adapted to assess parents' satisfaction with children's cancer care)	Baseline and M1-M6, monthly
	Impact of pediatric illness on the family (validated *Impact on Family Scale* [IOFS] [171, 172])	Baseline and M1-M6, monthly
	Parents' HRQoL (*EuroQol EQ-5D-3L* [134])	Baseline and M1-M6, monthly
	Focus groups (children and parents)	Once after M6
Impact on HCPs of ePROs integration in care	Web-based follow-up questionnaire (see Supplement S2)	Once after M6
	Focus groups (project-internal and external HCPs involved in the study)	Once after M6

Note. ePROs = Electronic Patient-Related Outcomes; SSPedi = Symptom Screening in Pediatrics Tool; HRQoL = Health-Related Quality of Life; PedsQL™= Pediatric Quality of Life Inventory™; EORTC PATSAT = European Organisation for Research and Treatment of Cancer – Satisfaction with Cancer Care core questionnaire; IOFS = Impact on Family Scale; EQ-5D-3L = EuroQol Group five-dimension, three-level questionnaire; M[X] = month X of study participation; HCPs = Healthcare Professionals.

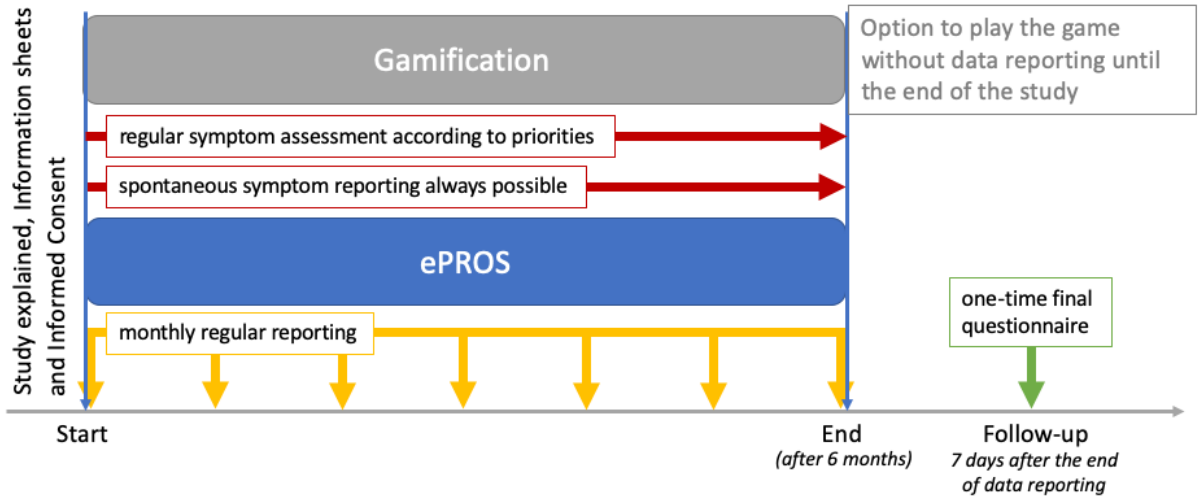


Figure 4 Individual patient participation timeline within the *MyPal4Kids* study [110]. ePROs = Electronic Patient-Reported Outcomes.

For evaluating primary endpoints, platform engagement was quantified by recruitment rate (number of enrolled participants in relation to all eligible patients at the three clinical study sites), participation rate (proportion of participants who completed ≥ 70% of monthly ePROs), and attrition rate (proportion of participants not completing the six-month study period due to

withdrawal or death). Optional usage metrics across different platform components were monitored to assess adherence, stratified by user group (patients, parents, HCPs). In addition, system usability and acceptability were evaluated using a validated usability scale and subsequent focus groups.

The assessment of secondary endpoints focused on patient symptom burden and HRQoL, parental satisfaction with care, psychosocial impact on families, and HCP perception. These were operationalized using validated ePRO instruments administered via the *MyPal-Child App* and *MyPal-Carer App*. Instruments were selected based on scientific validity, availability in electronic format, and alignment with the study's pediatric care context. Table 4 summarizes the key characteristics of the implemented ePROs, including domains, rating formats, and scoring procedures. All instruments were administered as specified above in Table 3.

Table 4 ePROs used in the *MyPal4Kids* study, including domains, rating scales and scoring methods.

ePRO	Domains / Constructs	Rating	Scoring
SSPedi (incl. Mini-SSPedi)	Burden of 15 symptoms (e.g., sadness, headache, nausea)	5-point Likert per symptom (0 = not at all, 4 = extremely bothered)	No composite score: single items interpreted individually or descriptively summarized; response options were implemented as 0–4 for data capture, displayed as 1–5 in the app.
PedsQL™ 3.0 Cancer Module	8 HRQoL-related dimensions (e.g., pain, anxiety, cognition, communication)	5-point Likert per item (0 = never, 4 = almost always)	Items recoded and transformed to a 0–100 scale; scores averaged per dimension and overall; higher scores = better HRQoL.
EORTC PATSAT-C33 *(adapted for parents)*	7 multi-item scales + 5 single items (e.g., coordination, family involvement)	5-point Likert per item (1 = poor, 5 = excellent)	Multi-item scales and single items transformed to 0–100; higher scores = greater satisfaction.
Impact on Family Scale	4 factors (e.g., financial burden, personal strain)	4-point Likert per item (1 = strongly agree, 4 = strongly disagree)	3 subscales reverse-coded; total and factor scores summed; higher scores = greater family burden.
EuroQol EQ-5D-3L	5 dimensions (e.g., mobility, anxiety) + VAS	3-level scale per dimension and VAS (0–100)	Dimensions coded as 5-digit health profile; VAS reflects perceived health; higher scores = better HRQoL.

Note. ePROs = Electronic Patient-Related Outcomes; SSPedi = Symptom Screening in Pediatrics Tool; HRQoL = Health-Related Quality of Life; PedsQL™= Pediatric Quality of Life Inventory™; EORTC PATSAT = European Organisation for Research and Treatment of Cancer – Satisfaction with Cancer Care core questionnaire; EQ-5D-3L = EuroQol Group five-dimension, three-level questionnaire; VAS = Visual Analogue Scale; HCPs = Healthcare Professionals.

If known, reasons for missed assessments were documented by study staff using multiple-choice and free-text entries.

Adherence was defined separately for each user group: for patients, it included symptom reports, diary entries, and in-game (diver) personalization; for parents, proxy-reports on child symptoms; and for HCPs, treatment plans, reaction protocols, and proxy-reports on child

symptoms. All scoring procedures, including handling of missing data, followed the respective instrument guidelines.

Considering the secondary endpoints and ePRO-based measures, Mini-SSPedi and SSPedi are two age-specific versions (for patients aged 4–7 and 8–18 years, respectively) enabling pediatric patients to assess their perceived daily symptom burden, focusing on the impact and bother of symptoms rather than their mere prevalence. They are hereafter referred to collectively as SSPedi. The PedsQL™ 3.0 Cancer Module comprises three age-specific versions (for ages 5–7, 8–12, and 13–18 years) that map children's monthly HRQoL across eight dimensions, e.g., treatment anxiety, worry, and others.

2.4 Follow-up Focus Groups

Follow-up focus groups were conducted at all three clinical sites to obtain qualitative feedback on the MyPal platform. Participants included: a) children and young cancer patients together with their parents, and b) HCPs. The discussions aimed to explore users' experiences, challenges, barriers, facilitators, preferences, and recommendations to complement the quantitative study data.

Semi-structured interview guides were developed based on the mHealth App Usability Questionnaire [207] by the interdisciplinary consortium to be used for discussions. The guides contained prioritized, open-ended, unambiguous, and neutral questions to minimize bias (see Supplement S3 and S4). Children and their parents were invited to participate in the focus groups after completing their six-month study period. Due to scheduling constraints at FNBRNO, individual interviews were conducted, each involving one child and one parent.

Regarding HCPs, two subgroups were interviewed separately to avoid bias: Project-internal HCPs who had provided feedback during platform development, and project-external HCPs who were involved only during the study.

Written informed consent was obtained from all participants before interviews, which took place either in person or online, in the local language. Sessions lasted 45–60 minutes and were moderated by trained local researchers. Audio recordings were transcribed verbatim, translated into English, and pseudonymized for analysis.

2.5 Data and Statistical Analysis

Statistical analyses were conducted using R (Version 4.3.2) [133] and IBM® SPSS® Statistics (Version 28.0.1.1; IBM®, Armonk, New York, USA). Descriptive statistics summarize recruitment progress and baseline characteristics of the study cohort. Depending on variable type and distribution, results are presented as absolute or relative frequencies, means (*M*)

with standard deviations (*SD*), or medians (*Mdn*) with interquartile ranges (IQR). Graphical visualizations include violin plots, in which the width of the violin reflects the frequency of reported values for each measure, with white dots representing the median values, thick black bars indicating IQR and thin black bars indicating the 1.5 × IQR for each measure.

Parametric or nonparametric tests were applied as appropriate, with statistical significance set at a two-sided $p < 0.05$. Percentages are reported as whole numbers without decimal places for sample sizes under 100 participants to avoid implying unwarranted precision and to improve clarity of data presentation.

Data imputation followed the guidelines as specified by the authors of each ePRO. For symptom reports, the highest monthly symptom burden per patient was considered. Additionally, missing values were replaced using the last observation carried forward (LOCF) method was used for up to two missing responses per measure. If baseline data were missing, the first available subsequent measurement was carried forward and used as baseline. The initial target sample size was 100 participants [110]. Due to the smaller actual sample size and missing data, repeated measures over seven time points (baseline, M1 to M6) were aggregated into four intervals (baseline, M1-2, M3-4, M5-6). Therefore, equivalence of adjacent months had been assessed using nonparametric two one-sided tests (TOST) applied to Agresti's generalized odds ratio (GenOR) estimates, with conventional equivalence bounds [3, 192]. To corroborate TOST results, paired Wilcoxon signed-rank tests were also performed, which yielded comparable p-values. Effect sizes were expressed as GenOR, representing the probability that a randomly selected observation from one group exceeds that from another [3].

For longitudinal analyses, the Aligned Rank Transform (ART) method [195], implemented via the ARTool package [84], enabled nonparametric two-factor repeated measures analysis of variance (ART-ANOVA). Dependent variables were outcome measures assessed over time, by subgroup, and for interaction effects. Grouping variables included (a) birth sex (female/male), (b) age group (6–9 years, 10–13 years, 14–17 years), (c) diagnosis (leukemia/solid tumor), and (d) Karnofsky Performance Status (KPS) (below/above cohort median) as a prognostic indicator [82, 130]. These analyses were conducted on imputed complete datasets following the ePRO authors' recommendations.

Effect sizes were calculated as Partial Eta Squared ($\eta_p^{2)}$) and interpreted as small ($\eta_p^2 \geq 0.01$), medium ($\eta_p^2 \geq 0.06$), and large ($\eta_p^2 \geq 0.16$) [28]. Post-hoc pairwise comparisons between time points used Wilcoxon signed-rank tests, while group comparisons employed Mann-Whitney U tests. For significant interactions, rank-transformed differences between groups at each time

point were compared using Mann-Whitney U tests. Holm-Bonferroni correction was applied to adjust *p*-values for multiple testing.

Spearman's rank correlation coefficient (r_s) assessed monotonic associations between patients' self-reports and parents' proxy-reports of symptom burden per month, without imputation. Effect sizes were interpreted as weak ($|r_s| \geq 0.1$), moderate ($|r_s| \geq 0.3$), or strong ($|r_s| \geq 0.5$) [28].

Qualitative data from follow-up focus groups were analyzed with MAXQDA 2022 software (VERBI Software GmbH, Berlin, Germany). Both deductive (based on research questions) and inductive (data-driven) thematic analyses were applied following established methodologies [50]. Two independent researchers from participating clinical sites developed a consensus coding system. Statements were cross-coded where applicable (e.g., positive, neutral, negative) and paraphrased after joint review to ensure reliability and validity. All quotes were paraphrased to remove filler words, eliminate redundancies, and simplify phrasing while preserving the original meaning. Language was adjusted to ensure clarity, readability, and consistency across quotes.

2.6 Patient and Public Involvement

The adoption of a participatory design approach [77] was central to the development of the MyPal platform. It included literature research [80], pre-study focus groups [94], and discussions with young cancer patients, their parents, and HCPs. This collaborative process aimed to identify needs and preferences, validate tools, and assess usability.

The platform was developed in iterative feedback loops involving the interdisciplinary MyPal project team, allowing for continuous optimization. A two-week pilot phase was conducted prior to study initiation to evaluate the platform's feasibility and usability under real-world conditions [64].

Given the involvement of pediatric patients and their families as a particularly vulnerable population, special attention was paid to age-appropriate communication and digital literacy. The storage of sensitive data required comprehensive considerations on ethical aspects [51], and data protection regulations, particularly with respect to compliance with the General Data Protection Regulation (GDPR), were an integral part of the development process. These considerations informed the structure and content of participant-facing materials such as respective versions of information sheets and consent forms [110].

2.7 Ethical Considerations

The *MyPal4Kids* study protocol underwent review by the responsible ethics committees of all participating clinical sites, none of which raised objections to its conduct. A positive opinion was issued by the Ärztekammer des Saarlandes (reference: Ha 23/20, March 16, 2020) and subsequently acknowledged by the ethics committees of Medical School Hannover (reference: 9095_BO_K_2020, February 12, 2020) and University of Brno (reference: 01-1 20 220/EK, May 11, 2020).

All study procedures were conducted in accordance with the principles of the Declaration of Helsinki and complied with applicable national and European data protection regulations, including the GDPR. Written informed consent was obtained from the parents of all participants, and assent was obtained from the participants themselves, prior to study participation. Participants were free to withdraw from the study at any time without any negative consequences.

3 Results

3.1 Recruitment

Study recruitment lasted from December 2020 until March 2022, covering a total of 15 months, including a six-month extension due to the COVID-19 pandemic. Details on patient screening, eligibility, exclusions, and enrollment are illustrated in the flow diagram (see Figure 5).

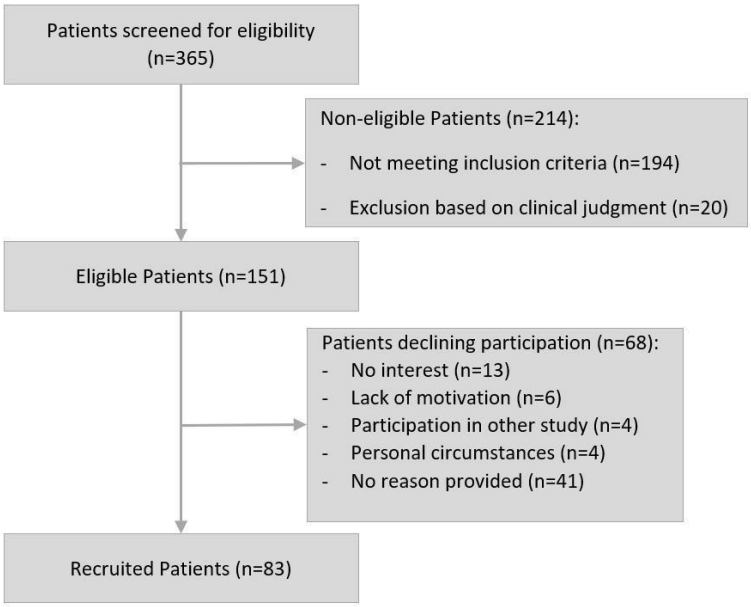


Figure 5 Flow diagram of patient screening, eligibility, and final recruitment across all three clinical sites in the *MyPal4Kids* study.

A total of 83 patients were enrolled, corresponding to 83% of the originally targeted sample size of 100 patients. Most participants were recruited during the initial three months of the recruitment phase (see Figure 6).

3.2 Baseline Characteristics of the Study Population

Baseline characteristics were documented during the creation of patients' user accounts on the platform. An overview of mandatory sociodemographic and clinical characteristics is provided in Table 5. In addition, optional baseline information was documented for 63 patients (76%), including further sociodemographic details (see Table 6).

Almost half of the recruited patients were between 14 and 17 years old. Birth sex distribution was nearly balanced, as was the proportion of patients receiving treatment. Nearly half of the cohort was diagnosed with a solid tumor. Most patients were newly diagnosed.

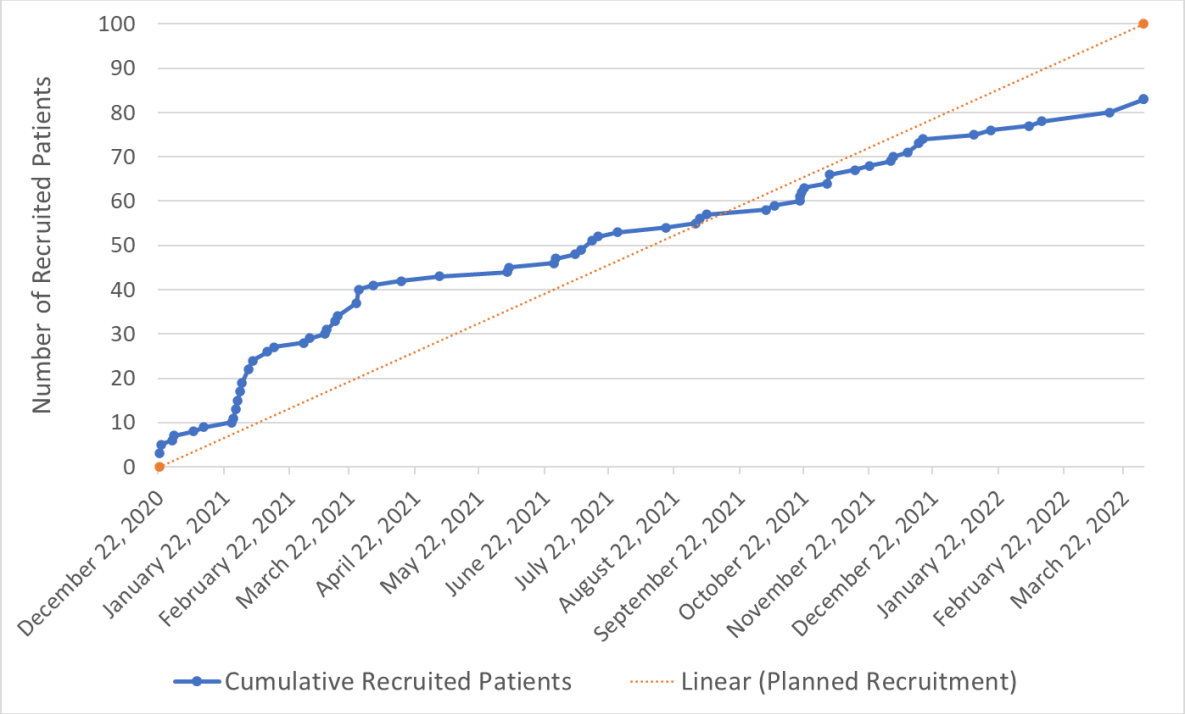


Figure 6 Cumulative recruitment progress across all three clinical sites, from the first patient enrollment (December 22, 2020) to last patient enrollment (March 31, 2022).

Among the 11 participants (13%) with reported handicap (Table 6), the following specifications were provided: prosthesis after total clavicle resection, tumor-related walking disability, short stature, left peripheral facial paralysis, prosthesis following distal femoral resection, paraplegia/triplegia, visual impairment of the left eye, right limb amputation, obesity per magna, and palsy of the right hand.

Table 5 Mandatory patient information collected at baseline.

Baseline Characteristics	**Study Cohort (*N* = 83)**	
	n	**%**
Birth sex		
Male	46	55
Female	37	45
Age group		
6-9 years	18	22
10-13 years	25	30
14-17 years	40	48
Diagnosis		
Brain tumor	14	17
Leukemia	29	35
Solid tumor	40	48
Stage		
New diagnosis	70	84
Relapse	13	16
On treatment		
Yes	45	54
No	38	46

Table 6 Optional patient information collected at baseline.

Baseline Characteristics	Study Cohort (*N* = 83)	
	n	**%**
Siblings		
Yes	34	42
No	12	15
N/A	36	43
Handicap		
Yes	11	13
No	45	54
N/A	27	33
Expected outcome		
Excellent	5	6
Good	29	35
Poor	8	10
Dismal	2	2
N/A	39	47
Risk (leukemia)		
High risk	6	21
Medium	2	7
Standard	5	17
N/A	16	55
Stage (solid and brain tumors)		
Stage I	3	6
Stage II	1	2
Stage III	4	7
Stage IV	6	11
Stage V	0	0
N/A	40	74
Metastatic cancer (solid tumors)		
Yes	13	33
No	21	53
N/A	6	15
Treatment		
Chemotherapy		
Yes	46	56
No	36	43
N/A	1	1
Immunotherapy		
Yes	8	10
No	75	90
N/A	0	0
Radiotherapy		
Yes	8	10
No	74	89
N/A	1	1
Surgery		
Yes	11	13
No	72	87
N/A	0	0
Targeted therapy		
Yes	4	5
No	79	95
N/A	0	0
Only palliative care		
Yes	2	2
No	80	97
N/A	1	1

Karnofsky Performance Status		
Documented	55	45
Mdn = 80 IQR = [80–90] Min = 50 Max = 100		
N/A	28	55

Note. N/A = no answer provided; *Mdn* = median; IQR = interquartile range; Min = minimum; Max = maximum.

3.3 Acceptability and Engagement With the MyPal Platform

3.3.1 Attrition, Participation, and Adherence

The study experienced an attrition rate of 18% (15 out of 83 participants), with most withdrawals on request (73%, *n* = 11) occurring within the first month (M1) of participation. followed by 2 patients in M2 and 1 patient each in M3 and M4. The dropouts included 8 males and 7 females, with diagnoses distributed as follows: 8 solid tumors, 6 leukemia, and 1 brain tumor. Age distribution among dropouts was 10 patients aged 14–17, 4 aged 10–13, and 1 aged 6–9 years. Fourteen of these participants were newly diagnosed, and 1 had relapsed. Nine patients were undergoing treatment at withdrawal, 6 were off treatment. Although withdrawal reasons were not mandatory, HCPs documented causes in 7 cases (multiple reasons possible), predominantly patient reluctance (*n* = 6) and disease progression (*n* = 4). No deaths occurred during active study participation.

According to protocol definitions prior to data imputation, 15 participants (16%) completed at least 70% of the monthly ePROs, while 19 (23%) completed at least 50%, and 22 (27%) at least 40%. Baseline completion of all four monthly ePROs was achieved by 46 participants (55%). HCPs documented reasons (multiple choice) for missed assessments in 32 cases (39%), most commonly citing patient reluctance (17), disease progression (15), intercurrent illness (2), and parental control settings preventing app installation (2).

Sixty-two patients (75%) assessed the burden of all 15 SSPedi symptoms at least once during their six-month participation. Assessment frequency declined over time. Diary entries were created by 42 patients (51%), also showing a decreasing trend (see Figure 7). Customization of the in-app game avatar was completed by 64 patients (77%).

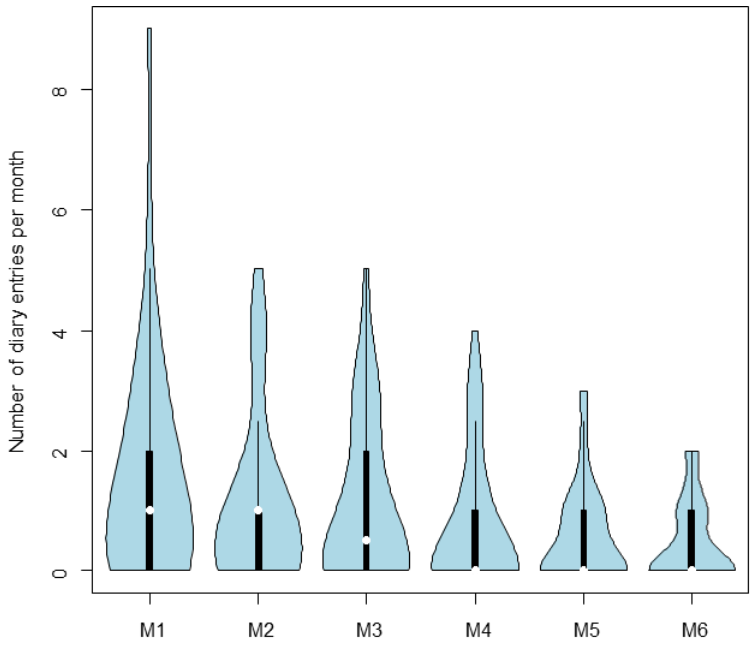


Figure 7 Violin plot depicting monthly frequencies of diary entries created by patients with at least one diary entry (*n* = 42, 51%).

Fifty-three parents (64%) provided proxy symptom reports covering all 15 SSPedi symptoms at least once via the MyPal-Carer App. HCPs created a total of 98 treatment plans for 29 patients (35%), with the number of plans per patient ranging from 1 to 8. Symptom documentation via the *HCP-Interface* was infrequent, occurring a total of 15 times across 13 patients (16%), while HCP reactions to reported symptoms were documented a total of 24 times across 15 patients (18%).

3.3.2 Usability of the MyPal Platform

Sixty out of 83 patients and parents (72%) completed the respective version of the System Usability Scale. Of the responding patients, 18 (30%) were under 10 years old, while 42 (70%) belonged to the older age group (≥ 10 years). Among the younger children, a clear majority indicated that they liked the game and found it easy to play (see Table 7). Slightly more than half enjoyed answering the questions within the game. In contrast, responses from the older patients were more varied: 55% liked the game and 93% found it easy to play. A significant association of small effect was found between age and liking the game, $\chi^2(1, n = 60) = 4.43$, $p = .035$, $\varphi = -0.27$, with younger children showing more favorable responses. Two additional questions, posed only to the older group, were positively rated by at least 57% of this group.

Free-text feedback was provided by 34 of 60 patients (57%). Positive comments highlighted avatar customization, point and artifact collection, colorful graphics and animations, confiding in their diary and easy control and management within the game. Criticism centered on the game's simplicity, repetitiveness, lack of increasing difficulty, and absence of win or loss

conditions. Some participants felt that the wording of some unspecified questions was ambiguous or disliked being reminded of their health condition through the questions. Suggestions included more avatar customization options, additional in-game achievements, and more questions.

Table 7 Answers to the adapted SUS evaluating the usability of the *MyPal-Child App* were received from 60 of 83 patients.

Adapted SUS for Children < 10 Years (*n* = 18)	**Yes**		**No**		**Indecisive**	
	n	**%**	***n***	**%**	***n***	**%**
Did you like the game?	15	83	3	17	0	0
Was the game easy to play?	15	83	2	11	1	6
Did you like to answer questions in the game?	10	56	8	44	0	0
Adapted SUS for Children ≥ 10 Years (*n* = 42)						
Did you like the game?	23	55	19	45	0	0
Was the game easy to play?	39	93	2	5	1	2
Did you like to answer questions in the game?	21	50	21	50	0	0
Were the questions asked to you relevant at the time?	25	60	15	36	2	5
Was the frequency of the reminders to answer questions appropriate?	24	57	18	43	0	0

Note. SUS = System Usability Scale.

Parents' SUS scores evaluating the usability of the *MyPal-Carer App* (*n* = 60) ranged from 42.5 to 97.5 (*M* = 76.8, *SD* = 15.9; *Mdn* = 82.5, IQR [63.1–90]) with an average SUS score, corresponding to a usability rating between good and excellent [129].

3.4 Feasibility of ePRO-Based Measures

3.4.1 Children's Symptom Burden (SSPedi)

Patient and Proxy-Reported Symptom Burden

During the six-month observation period, 42 out of 83 patients (51%) reported at least one high priority symptom (i.e., highest burden rating 4 = e*xtremely bothered*; see Figure 8A). Per month, less than 50% reported a high priority symptom. The most frequently reported symptoms with this rating were tiredness (*n* = 29), pain other than headache (*n* = 26), mouth sores (*n* = 23), and changes in appetite (*n* = 23). Proxy reports with the highest burden were submitted by 34 out of 83 parents (41%) (see Figure 8B). Among these, the most frequently reported symptoms were feeling disappointed or sad (*n* = 24), perceived changes in appearance (*n* = 23), and changes in appetite (*n* = 23). Thus, while there was some overlap between child and parent reports of symptoms with high priority, they only partially intersected.

Spearman's correlations were calculated across all 15 symptoms and 7 time points (baseline and M1 to M6) to explore alignment between parent and child reports on symptom burden. Significant correlations were revealed for 8 symptoms up to 3 at time points each (see Table 8). No significant correlations were found for the remaining 7 symptoms (problems with thinking or remembering, mouth sores, headache, feeling either more or less hungry than

usual, changes in taste, constipation, and diarrhea). The strength of significant correlations ranged from $r_s(24) = 0.39$ to $r_s(24) = 1.0$, indicating moderate to strong associations. However, these were not consistently observed across all symptoms or time points.

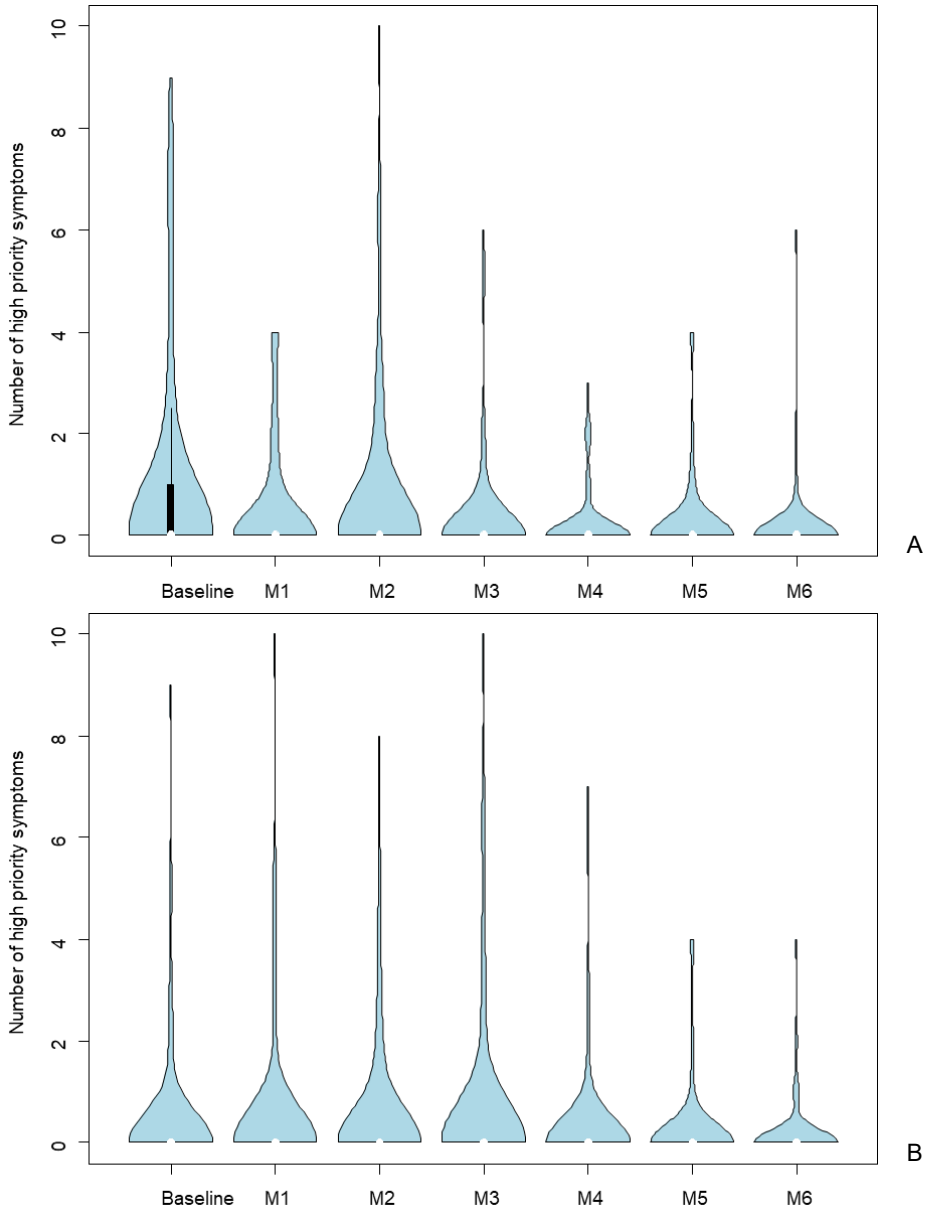


Figure 8 Frequency distribution of monthly symptom reports using SSPedi with high priority (= highest burden, rating = 4) during study participation. (A) Self-reports by children. (B) Proxy-reports by parents for their children. SSPedi = Symptom Screening in Pediatrics Tool.

Table 8 Spearman's correlation coefficients between children's and parents' reported symptom burden using SSPedi across time points.

Symptom	**Time Point**	***df***	**Correlation Coefficient (r_s)**
Feeling disappointed or sad	Baseline	24	0.18
	M1	22	0.09
	M2	22	0.16

	M3	13	0.21
	M4	13	0.14
	M5	12	**0.62** *
	M6	6	0.51
Feeling scared or worried	Baseline	25	0.22
	M1	21	**0.48** *
	M2	22	**0.46** *
	M3	12	-0.16
	M4	13	0.11
	M5	13	0.45
	M6	6	0.59
Feeling cranky or angry	Baseline	24	**0.39** *
	M1	22	**0.58** **
	M2	21	**0.54** **
	M3	11	0.19
	M4	14	0.16
	M5	12	0.46
	M6	5	0.73
Changes in how body or face look	Baseline	22	0.14
	M1	21	0.39
	M2	22	0.10
	M3	12	0.28
	M4	14	-0.11
	M5	12	**0.57** *
	M6	5	**0.87** *
Feeling tired	Baseline	21	0.22
	M1	21	**0.67** ***
	M2	22	**0.49** *
	M3	11	0.52
	M4	14	0.30
	M5	12	0.20
	M6	4	0.67
Feeling pain	Baseline	19	0.18
	M1	20	**0.47** *
	M2	21	0.26
	M3	12	0.38
	M4	13	0.36
	M5	11	0.42
	M6	4	**1.00** ***
Tingly or numb hands or feet	Baseline	19	0.20
	M1	20	**0.62** **
	M2	21	**0.54** **
	M3	11	0.32
	M4	13	0.31
	M5	11	0.22
	M6	4	0.50
Vomiting or nausea	Baseline	18	0.30
	M1	20	0.39
	M2	20	0.28
	M3	11	0.40
	M4	14	-0.30
	M5	11	**0.71** **
	M6	4	0.72

Note. SSPedi = Symptom Screening in Pediatrics Tool; *df* = n - 2 (degrees of freedom); M[X] = month X of study participation; * $p < .05$; ** $p < .01$; *** $p < .001$.

Subgroup and Longitudinal Differences in Symptom Burden

Table 9 summarizes the results of the ART-ANOVA analyses, examining the effects of the factors time, group (birth sex, age, diagnosis, KPS), and their interactions on symptom burden reported via SSPedi. Three symptoms (i.e., feeling disappointed or sad, feeling scared or

worried, and feeling cranky or angry) and subgroups per symptom without significant findings were omitted for clarity. For subgroup analysis based on KPS, participants were categorized into those scoring above or below the median (*Mdn* = 80).

Table 9 Symptom burden reported using SSPedi with significant results derived from the ART-ANOVA analyses.

Symptom	Group	Subsamples (*n*)	Imp (*n*)	Time Effect		Group Effect		Interaction (Time × Group)	
				p	η_p^2	*p*	η_p^2	*p*	η_p^2
Feeling tired	Birth sex	Female = 16 Male = 12	13	.131	0.069	**.031**	**0.167** ***	.742	0.016
More/less hungry than usual (changes in appetite)	Birth sex	Female = 16 Male = 11	12	.733	0.017	**.021**	**0.194** ***	.739	0.019
Mouth sores	Diagnosis	Leukemia = 9 Solid tumor = 18	12	**.043**	**0.102** **	**.023**	**0.190** ***	.864	0.010
Hurt/pain (excluding headache)	Birth sex	Female = 16 Male = 11	12	**.043**	**0.102** **	.438	0.024	.474	0.033
Headache	KPS	KPS ≥ 80 = 11 KPS < 80 = 13	10	**.004**	**0.183** ***	.854	0.002	.100	0.090
Tingly/ numb hands/feet	Diagnosis	Leukemia = 9 Solid tumor = 18	12	**.012**	**0.136** **	.363	0.033	.311	0.046
Changes in how body/face look	Birth sex	Female = 17 Male = 12	13	**.024**	**0.109** **	.293	0.041	.408	0.035
	Age	6-9 years = 11 10-13 years = 8 14-17 years =10	13	**.010**	**0.134** **	.854	0.012	.994	0.009
	Diagnosis	Leukemia = 9 Solid tumor = 20	13	**.003**	**0.160** ***	.503	0.017	.320	0.042
	KPS	KPS ≥ 80 = 11 KPS < 80 = 13	9	**.016**	**0.144** ***	.810	0.003	.411	0.042
Changes in taste	Birth sex	Female = 16 Male = 11	12	**< .001**	**0.248** ***	.335	0.037	.691	0.019
	Age	6-9 years = 10 10-13 years = 8 14-17 years = 9	12	**.001**	**0.198** ***	.873	0.011	.830	0.038
	Diagnosis	Leukemia = 9 Solid tumor = 18	12	**< .001**	**0.284** ***	.555	0.014	**.019**	**0.123** **
	KPS	KPS ≥ 80 = 11 KPS < 80 = 13	10	**.001**	**0.223** ***	.543	0.017	.696	0.021
Vomiting/ nausea	Birth sex	Female = 16 Male = 11	12	**.009**	**0.142** ***	.471	0.021	.181	0.063

	Age	6-9 years = 10 10-13 years = 8 14-17 years = 9	12	**.003**	**0.175** ***	.775	0.021	.043	**0.161** ***
	Diagnosis	Leukemia = 9 Solid tumor = 18	12	**.005**	**0.157** ***	.905	0.001	.810	0.013
Problems with thinking/ remembering things	Birth sex	Female = 17 Male = 12	13	.571	0.024	**.001**	**0.321** ***	.561	0.025
	KPS	KPS ≥ 80 = 11 KPS < 80 = 13	9	.953	0.005	.149	0.092	**.034**	**0.123** **
Diarrhea	Birth sex	Female = 16 Male = 11	12	.084	0.084	.165	0.076	**.034**	**0.108** **
	Age	6-9 years = 10 10-13 years = 8 14-17 years = 9	12	.173	0.066	.296	0.096	**.022**	**0.181** ***
	Diagnosis	Leukemia = 9 Solid tumor = 18	12	**.002**	**0.181** ***	.271	0.048	**.009**	**0.143** ***
Constipation	Birth sex	Female = 17 Male = 12	12	.142	0.070	.297	0.043	**.031**	**0.111** **

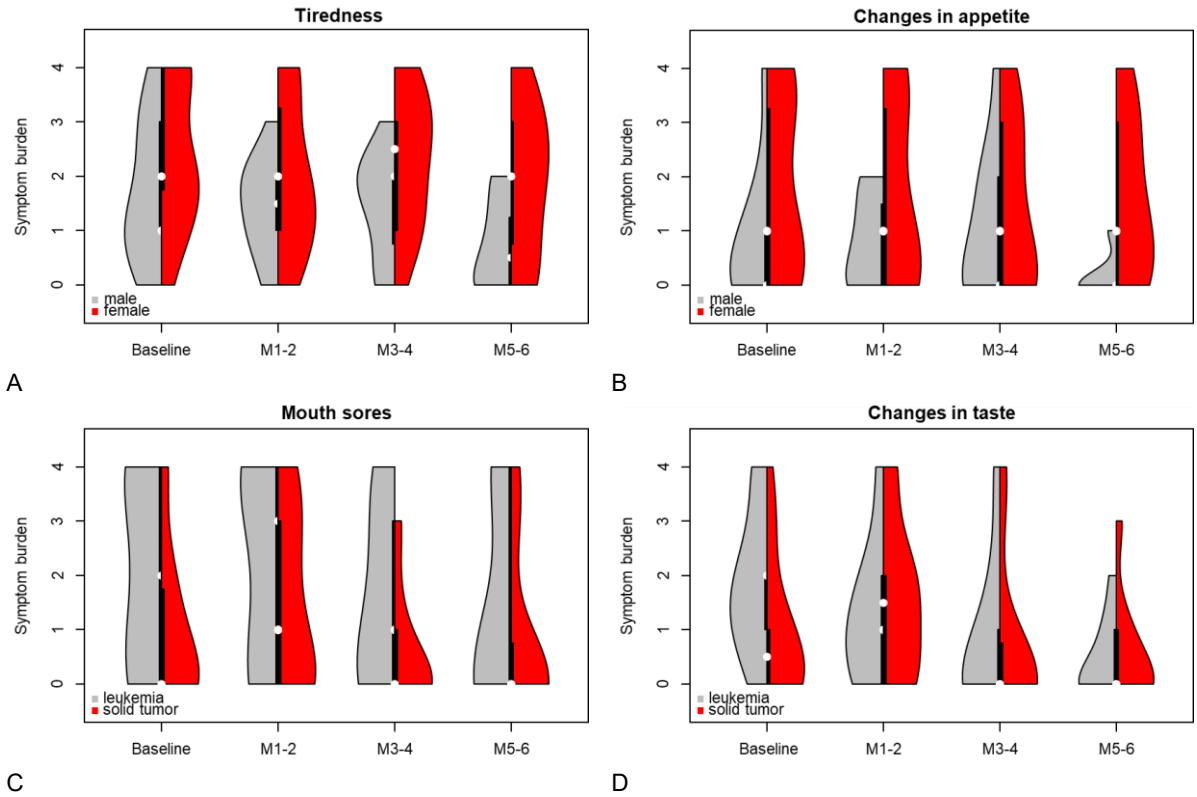
Note. SSPedi = Symptom Screening in Pediatrics Tool; ART-ANOVA = Aligned Rank Transform Analysis of Variance; Imp = imputed values; KPS = Karnofsky Performance Status; * small effect size η_p^2; ** medium effect size η_p^2; *** large effect size η_p^2.

We first present findings related to the most frequently reported symptoms with the highest burden by patients as identified in the descriptive analyses, before moving on to additional significant findings. A significant main effect of birth sex indicated that female patients reported higher burden from tiredness (see Figure 9A) and changes in appetite (see Figure 9B) than males, independent of time. A significant main effect of diagnosis showed that patients with leukemia experienced greater burden from mouth sores than those with solid tumors (see Figure 9C). The significant main effect of time was not supported by post-hoc comparisons, which did not reveal significant differences between time points for mouth sores or hurt/pain (excluding headache).

For headache, a significant main effect of time was found regardless of group, with post-hoc comparisons showing a decrease in symptom burden from M1-2 to M5-6, $p = .003$, $\eta_p^2 = 0.171$. Although a main effect of time was initially observed for tingly/numb extremities, post-hoc comparisons did not reveal significant differences across time points. Significant main effects for time were also found regarding both changes in appearance and changes in taste across groups: post-hoc tests indicated significant differences with a decrease in experienced burden from M1-2 to M5-6 regarding both symptoms, while the medium effect varied slightly across considered subsamples (changes in appearance – birth sex: $p = .034$, $\eta_p^2 = 0.091$; age: $p = .024$, $\eta_p^2 = 0.101$; diagnosis: $p = .044$, $\eta_p^2 = 0.082$; KPS: $p = .022$, $\eta_p^2 = 0.121$) (changes in

taste – birth sex: p = .003, η_p^2 = 0.151; age: p = .012, η_p^2 = 0.124; diagnosis: p = .007, η_p^2 = 0.118; KPS: p = .017, η_p^2 = 0.128).

Figure 9 Violin plots depicting the distribution of maximum burden (ranging from 0 = not at all bothered to 4 = extremely bothered) for four SSPedi symptoms, reported by two respective subgroups across four timepoints from baseline until the final two months of study participation (M5-6). SSPedi = Symptom Screening in Pediatrics Tool.

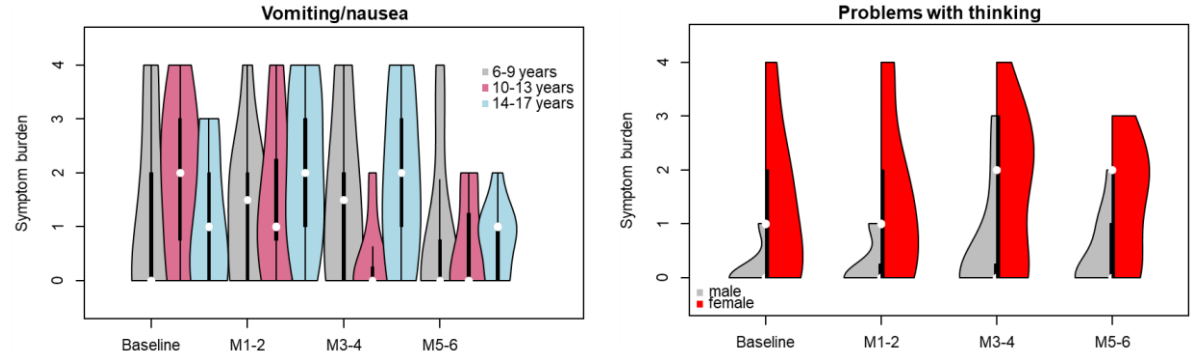


A significant interaction effect between time and diagnosis was observed for changes in taste, with burden increasing in solid tumor patients but decreasing in leukemia patients from baseline to M1-2, p = .022, η_p^2 = 0.108 (see Figure 9D).

For vomiting/nausea, a significant main effect of time was found across groups: post-hoc tests revealed a significant difference with a decreasing burden from M1-2 to M5-6, while the effect varied slightly across considered subgroup samples (birth sex: p = .012, η_p^2 = 0.120, age: p = .002, η_p^2 = 0.164, diagnosis: p = .011, η_p^2 = 0.122). An interaction effect between time and age group indicated symptom burden to be decreasing in the 10–13-year-olds but increasing in the 14–17-year-old group from baseline to M3-4, p = .023, η_p^2 = 0.135 (see Figure 10A).

For problems with thinking, female patients reported higher burden than males regardless of time (see Figure 10B). An interaction effect between time and KPS suggested diverging trends by performance status, which was not supported by post-hoc comparisons.

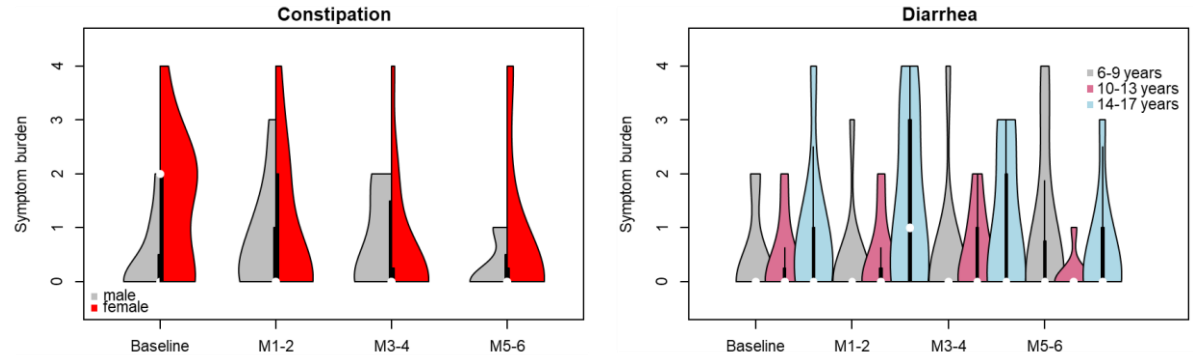
Figure 10 Violin plots depicting the distribution of maximum burden (ranging from 0 = not at all bothered to 4 = extremely bothered) for two SSPedi symptoms, reported by two respective subgroups across four timepoints from baseline until the final two months of study participation (M5-6). SSPedi = Symptom Screening in Pediatrics Tool.



A B

For constipation, an interaction between time and birth sex and post-hoc tests indicated burden decreasing in females but increasing in males from baseline to M3-4, p = .033, η_p^2 = 0.098 (see Figure 11A). For diarrhea, an interaction effect and post-hoc test indicated that burden increased in the 6–9-year-olds but decreased in 14–17-year-olds from M1-2 to M5-6, p = .016, η_p^2 = 0.069 (see Figure 11B). Additionally, this burden decreased in leukemia patients but remained low in solid tumor patients from baseline to M5-6, p = .026, η_p^2 = 0.099. Considering birth sex, an interaction effect was not supported by post-hoc which did not reveal significant differences.

Figure 11 Violin plots depicting the distribution of maximum burden (ranging from 0 = not at all bothered to 4 = extremely bothered) for two SSPedi symptoms, reported by two respective subgroups across four timepoints from baseline until the final two months of study participation (M5-6). SSPedi = Symptom Screening in Pediatrics Tool.



A B

3.4.2 Children's HRQoL (PedsQL™)

Table 10 summarizes the results of the ART-ANOVA analyses regarding children's HRQoL. Three problem scales (cognitive problems, perceived physical appearance, communication) and subgroups without significant findings were omitted from the table for clarity. Higher scale scores indicate better outcomes and fewer problems.

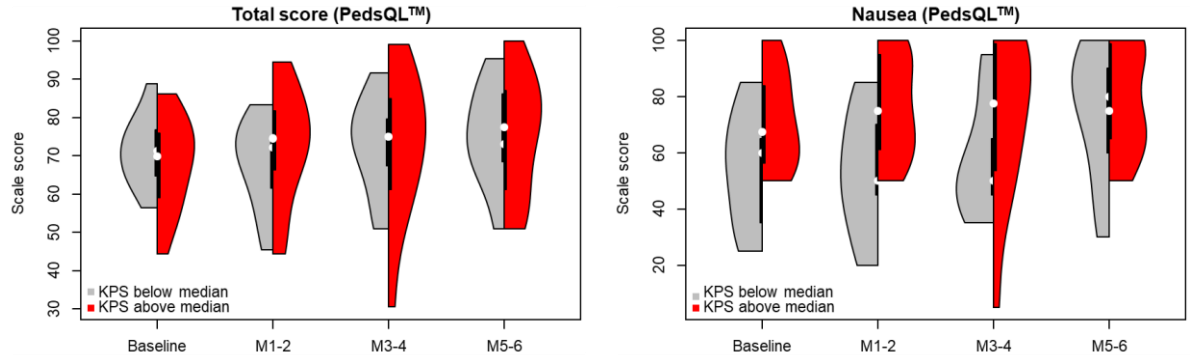
A significant main effect of time was found for the children's total score, independent of a group: post-hoc tests revealed a significant difference between baseline and M5-6, the total score increased from baseline to M5-6, p = .023, η_p^2 = 0.126 (see Figure 12A). Similarly, a significant main effect of time was observed for the nausea scale, with scores increasing from baseline to M5-6, p = .016, η_p^2 = 0.129 (see Figure 12B). In contrast, although a significant main effect of time emerged for the worry scale, post-hoc comparisons did not support significant differences between time points.

Table 10 PedsQL™ dimensional scores with significant results derived from the ART-ANOVA analyses.

Dimension	Group	Subsamples (*n*)	Imp (*n*)	Time Effect		Group Effect		Interaction (Time × Group)	
				p	η_p^2	*p*	η_p^2	*p*	η_p^2
Total Score	Diagnosis	Leukemia = 6 Solid tumor = 18	5	**.028**	**0.128** **	.242	0.062	.291	0.055
	KPS	KPS ≥ 80 = 14 KPS < 80 = 9	5	**.021**	**0.143** ***	.823	0.002	.357	0.050
Nausea	Birth sex	Female = 16 Male = 8	5	**.037**	**0.120** **	.524	0.019	.996	0.001
	Age	6-9 years = 9 10-13 years = 5 14-17 years = 10	5	**.048**	**0.117** **	.203	0.141	.237	0.116
	Diagnosis	Leukemia = 6 Solid tumor = 18	5	**.037**	**0.119** **	.344	0.041	.180	0.071
	KPS	KPS ≥ 80 = 14 KPS < 80 = 9	5	**.042**	**0.121** **	**.041**	**0.184** ***	.175	0.075
Treatment anxiety	Birth sex	Female = 16 Male = 8	5	.155	0.076	.084	0.130	**.036**	**0.120** **
	KPS	KPS ≥ 80 = 14 KPS < 80 = 9	5	.189	0.072	**.040**	**0.186** ***	.072	0.104
Procedural anxiety	Diagnosis	Leukemia = 6 Solid tumor = 18	5	.124	0.083	**.040**	**0.178** ***	.653	0.024
	Age	6-9 years = 9 10-13 years = 5 14-17 years = 10	5	.067	0.107	**.026**	**0.294** ***	.440	0.086
	KPS	KPS ≥ 80 = 14 KPS < 80 = 9	5	**.018**	**0.147** ***	.130	0.106	.100	0.094
Worry	Birth sex	Female = 16 Male = 8	5	**.025**	**0.131** **	.774	0.004	.738	0.019
Pain/Hurt	Diagnosis	Leukemia = 6 Solid tumor = 18	5	.747	0.018	.146	0.094	**.029**	**0.127** **

Note. PedsQL™ = Pediatric Quality of Life Inventory™; ART-ANOVA = Aligned Rank Transform Analysis of Variance; Imp = imputed values; KPS = Karnofsky Performance Status; * small effect size η_p^2; ** medium effect size η_p^2; *** large effect size η_p^2.

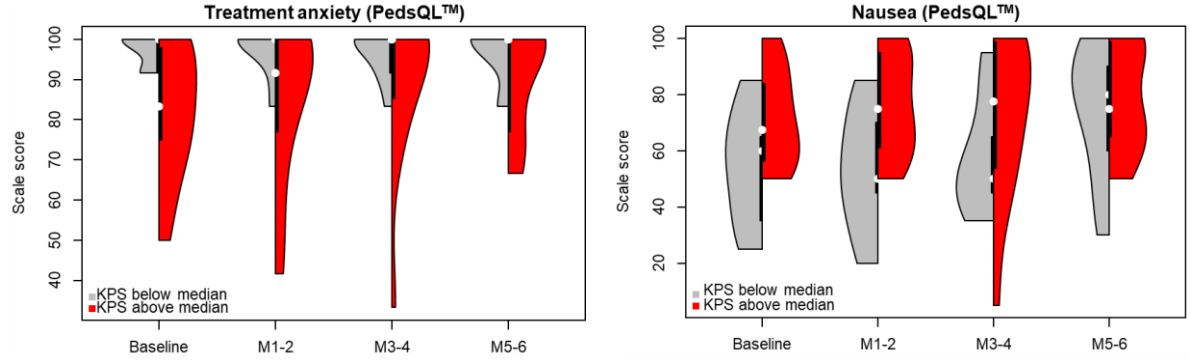
Figure 12 Violin plots depicting the distribution of two PedsQL™ dimensional scores, reported by two respective subgroups across four timepoints from baseline until the final two months of study participation (M5-6). PedsQL™ = Pediatric Quality of Life Inventory™; KPS = Karnofsky Performance Status.



A B

Regarding group difference, a significant main effect of KPS was found for treatment anxiety, with a higher burden in patients with KPS scores above the median compared to those below the median (see Figure 13A), independent of time. Conversely, problems with nausea were more prevalent in patients with KPS below the median than in those above (see Figure 13B). Significant interaction effects between time and group were identified for both treatment anxiety and pain/hurt, but post-hoc comparisons did not support these effects.

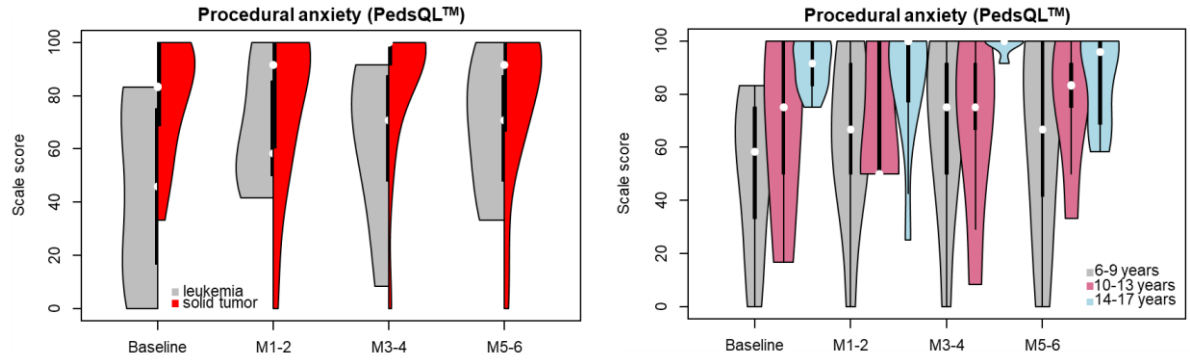
Figure 13 Violin plots depicting the distribution of two PedsQL™ dimensional scores, reported by two respective subgroups across four timepoints from baseline until the final two months of study participation (M5-6). PedsQL™ = Pediatric Quality of Life Inventory™; KPS = Karnofsky Performance Status.



A B

A significant main effect of diagnosis emerged for procedural anxiety, with higher burden reported by patients with leukemia than those with solid tumors, independent of time (see Figure 14A). Likewise, a significant main effect of age group was found (see Figure 14B): 6–9-year-olds reported higher levels of procedural anxiety than 14–17-year-olds, $p = .009$, $\eta_p^2 = 0.285$.

Figure 14 Violin plots depicting the distribution of two PedsQL™ dimensional scores, reported by two respective subgroups across four timepoints from baseline until the final two months of study participation (M5-6). PedsQL™ = Pediatric Quality of Life Inventory™;´.



A B

3.4.3 Parents' Satisfaction With Cancer Care (PATSAT)

The results of the ART-ANOVA analyses regarding parents' satisfaction with cancer care are summarized in Table 11. Four scales (technical skills, affective behavior, coordination, interaction with HCPs), three single items (family involvement, access/parking, environment), and subgroups without significant findings were omitted from the table for clarity. Higher scale scores indicate greater satisfaction.

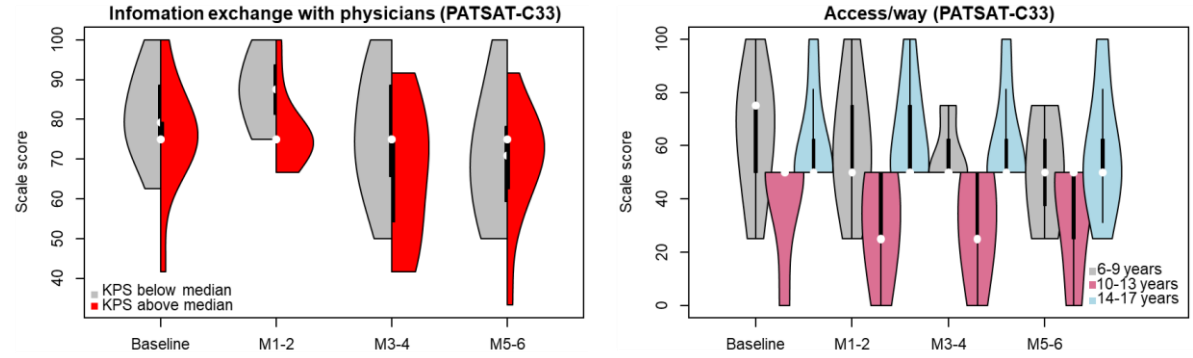
Table 11 PATSAT scales with significant results derived from the ART-ANOVA analyses.

Scale	**Group**	**Subsamples (*n*)**	**Imp (*n*)**	**Time Effect**		**Group Effect**		**Interaction (Time × Group)**	
				p	η_p^2	***p***	η_p^2	***p***	η_p^2
Overall care	Birth sex	Female = 12 Male = 7	6	.192	0.088	.542	.022	**.044**	**0.145** ***
Information exchange (with physicians)	Birth sex	Female = 12 Male = 7	6	**.018**	**0.178** ***	.481	0.030	.575	0.038
	Age	6-9 years = 7 10-13 years = 5 14-17 years = 7	6	**.042**	**0.155** **	.964	0.005	.613	0.086
	Diagnosis	Leukemia = 6 Solid tumor = 18	5	**.039**	**0.150** ***	.715	0.008	.438	0.051
	KPS	KPS ≥ 80 = 14 KPS < 80 = 9	5	**.012**	**0.190** ***	.146	0.120	.526	0.042
Information exchange (with nurses)	Age	6-9 years = 7 10-13 years = 5 14-17 years = 7	7	.081	0.130	.375	0.115	**.024**	**0.253** ***
Access/way	Age	6-9 years = 7 10-13 years = 5 14-17 years = 7	5	.131	.110	**.046**	**0.141** ***	.566	.116

Note. PATSAT = Satisfaction with Cancer Care core questionnaire; ART-ANOVA = Aligned Rank Transform Analysis of Variance; KPS = Karnofsky Performance Status; * small effect size η_p^2; ** medium effect size η_p^2; *** large effect size η_p^2.

A significant interaction effect between time and birth sex was found for the overall care score, which was not supported by post-hoc comparisons. A significant main effect of time emerged for satisfaction with information exchange with physicians, independent of group: post-hoc tests revealed a significant difference between M1-2 and M5-6, the score decreased from baseline to M5-6, p = .021, η_p^2 = 0.155 (see Figure 15A). Similarly, a significant interaction effect between time and age group was identified regarding information exchange with nurses: post-hoc tests shows a significant difference between M1-2 and M5-6, with satisfaction decreasing among parents of children aged 10–13 years while increasing among parents of patients aged 14–17 years, p = .006, η_p^2 = 0.238. Additionally, a significant main effect of age group was found regarding the ease with which parents found their way to the hospital's departments (access/way), independent of time: post-hoc tests indicated significant differences between all three age groups, with the highest satisfaction reported by parents of the youngest patients (6–9 years) and the lowest satisfaction in parents of children aged 10–13 years (see Figure 15B).

Figure 15 Violin plots depicting the distribution of two PATSAT scale scores, reported by two respective subgroups across four timepoints from baseline until the final two months of study participation (M5-6). PATSAT = Satisfaction with Cancer Care core questionnaire.



A B

3.4.4 Impact on Family Scale (IOFS)

Table 12 presents the results of the ART-ANOVA analyses concerning the perceived impact of the disease on the family as rated by parents. One factor (mastery) and subgroups without significant findings were omitted for clarity. Higher scale scores indicate greater perceived negative impact.

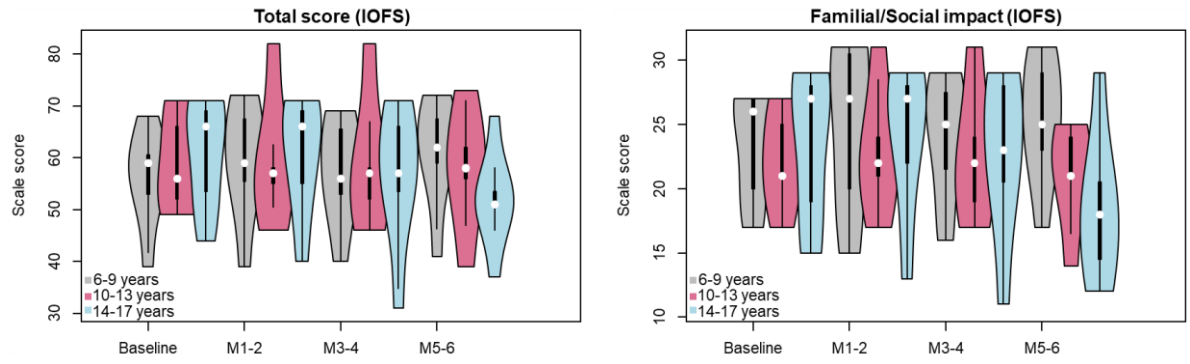
Table 12 IOFS factors with significant results derived from the ART-ANOVA analyses.

Factor	Group	Subsamples (*n*)	Imp (*n*)	Time Effect		Group Effect		Interaction (Time × Group)	
				p	η_p^2	***p***	η_p^2	***p***	η_p^2
Total score	Age	6-9 years = 7 10-13 years = 5 14-17 years = 7	5	.217	0.088	.974	0.003	**< .001**	**0.388** ***
Financial burden	Age	6-9 years = 7 10-13 years = 5 14-17 years = 7	5	.094	0.124	.592	0.063	**.039**	**0.233** ***
Familial/Social impact	Age	6-9 years = 7 10-13 years = 5 14-17 years = 7	5	**.029**	**0.170** ***	.603	0.061	**.022**	**0.256** ***
Personal strain	Age	6-9 years = 7 10-13 years = 5 14-17 years = 7	5	.682	0.030	.690	0.045	**.019**	**0.262** ***

Note. IOFS = Impact on Family Scale; ART-ANOVA = Aligned Rank Transform Analysis of Variance; KPS = Karnofsky Performance Status; * small effect size; ** medium effect size; *** large effect size.

Significant interaction effects between time and age group were found for the total score as well as three of the four factors. According to post-hoc comparisons, the total score differed significantly between baseline and M5-6 for parents of adolescents (14–17 years) compared to both the middle-aged group (10–13 years), p = .025, η_p^2 = 0.188, and the youngest group (6–9 years), p < .001, η_p^2 = 0.339 (see Figure 16A). Specifically, the perceived impact worsened in parents of the oldest age group while improving for the two younger age groups. For the familial/social factor, the impact differed significantly between baseline and M5-6 between parents of the oldest and youngest age groups, p = .013, η_p^2 = 0.213. While the perceived impact decreased in both age groups, it was initially higher in parents of adolescents and lower in parents of younger children, with the pattern reversing by M5-6 (see Figure 16B).

Figure 16 Violin plots depicting the distribution of two IOFS factors, reported by two respective subgroups across four timepoints from baseline until the final two months of study participation (M5-6). IOFS = Impact on Family Scale.



A B

3.4.5 Parents' HRQoL (EQ-5D-3L)

No significant effects were found for parents' HRQoL, neither over time nor between subgroups. Similarly, the trajectories of parental HRQoL did not differ significantly between the subgroups ($p \geq 0.05$).

3.4.6 Focus Groups With Children and Parents

A total of ten parent-child pairs who had completed their six-month participation in the study consented to take part in focus groups, including three pairs from USAAR, four from MHH, and three from FNBRNO. All three age groups defined in the study were represented: two participants were aged 6–9 years, two were aged 10–13 years, and six were aged 14–17 years.

The focus groups provided valuable insights into participants' perceptions of the MyPal Apps. Figure 17 displays the coding system developed through thematic analysis, linking key categories to participants' statements. Key code categories were partially further organized into subcategories reflecting specific aspects of participants' experiences. For example, 'Consequences of App Usage' included 'Benefits' and 'Consequences', 'User Experience' was nested under 'Influences on Motivation', 'Multidisciplinary Approach' fell under 'Recommendations', and both 'Family Communication' and 'HCP-Patient Communication' were grouped within 'Communication'.

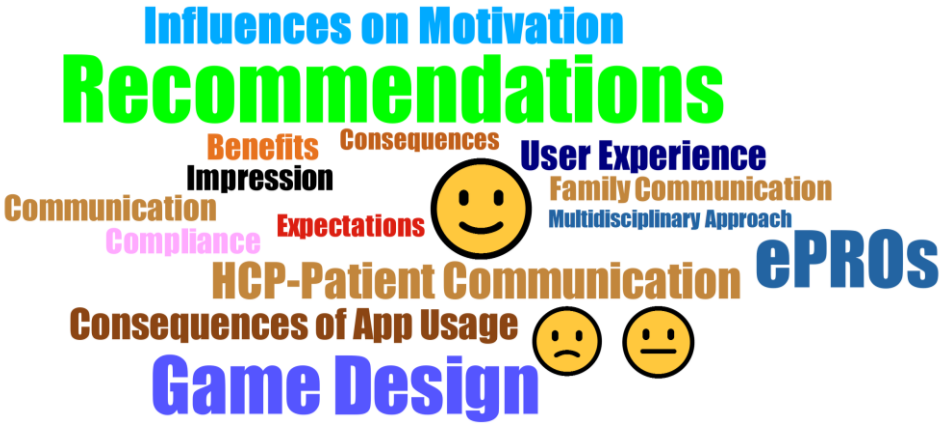


Figure 17 Cloud map from focus groups with children and parents across all three study sites. Font size and emoji size reflect the frequency of coded statements, with emojis additionally indicating sentiment (positive, neutral, negative). ePROs = Electronic Patient-Reported Outcomes; HCPs = Healthcare Professionals.

An overview of the main thematic categories with brief summaries is provided in Supplement S5, while the following section presents a detailed analysis supported by illustrative paraphrased quotes.

Game Design

Children generally appreciated the customizable elements of the *MyPal-Child App*, such as the ability to personalize their avatar's appearance, including suit, skin color and hairstyle. They also enjoyed the appealing colorful underwater theme. However, several aspects of the game were met with criticism. Many participants criticized the lack of challenge and perceived repetitiveness of the game, making it more appealing for younger than for older children. Several children expressed disappointment that the game lacked consequences, such as the possibility of failure or progression through new levels, which reduced long-term engagement:

> *It wasn't going anywhere. It was repetitive. There were no new levels. No need to be afraid of losing, nothing could happen to you, you couldn't even die.*
> *(Patient 1, FNBRNO)*

Expectations were often centered around the gameplay rather than ePROs, with patients anticipating a more dynamic experience, with increasing difficulty adapting to their progress, including more interactive features such as in-app purchases or challenges.

ePROs

Parents largely viewed the symptom-reporting function positively, noting that it could help HCPs monitor their child's condition over time. While some patients found the ePRO questions easy to understand and answer, others felt they were repetitive or not relevant when they were symptom-free. Several patients admitted to answering questions without much attention, especially when they were feeling well:

> *When I was hospitalized and had to process a lot, it was helpful for me and I used it often, because these questions fit at the time. It helped me process it all, both in the hospital and at home. (Patient 1, USAAR)*

Parents appreciated the flexibility of being able to complete questions outside the game as an option. However, they raised concerns about children underreporting symptoms, often out of optimism or avoiding focusing on illness:

> *My child would rate his health better than it really was. He indicated that some symptoms weren't that bad, although they were perhaps worse than he would have admitted. (Parent 2, USAAR)*

> *My child was answering optimistically even though he was having strong symptoms. Not at all matching my observations. I let him answer according to his perception. If in my opinion he was not doing well, I would report it as such separately. (Parent 3, MHH)*

Despite these concerns, many parents valued that the apps prompted both themselves and their children to pay closer attention to symptoms that might otherwise have gone unnoticed:

The app and the questions made me more sensitive and made me pay more attention to things that I wouldn't have thought of otherwise or that could easily be overlooked. (Parent 4, MHH)

It was quite good for my child to think about such things, to really listen to oneself and not always answer „everything is fine". (Parent 2, MHH)

However, a minority felt that questions were not appropriate for younger children at times, who struggled to relate to or understand them:

The questions were unfitting at times, and my child couldn't really make sense out of it. Small children don't bother about such questions. (Parent 1, FNBRNO)

Benefits and Consequences of App Usage

The apps were perceived as particularly helpful at the beginning of treatment, when participants were more motivated to engage and had more time to use it. At this stage, many found it beneficial for reflecting on symptoms, documenting concerns, and expressing emotions at any time, especially during periods when direct communication with HCPs was limited:

You need to find the time to concentrate and be truthful. If I received a notification while we are going through a difficult time, I used the opportunity to write things down. It helped, especially at the beginning of the treatment. (MHH, Parent 3)

Several parents and patients described the apps as offering a valuable opportunity for self-reflection. Documenting everyday concerns and symptoms was seen as helpful for not forgetting important details that might otherwise be overlooked during aftercare or medical appointments:

I liked to be sensitized to some issues and things that happen in everyday life that don't get forgotten because they got noted down. (Parent 2, MHH)

This reflective process was also described as intuitive and unfiltered, allowing some users to express themselves more naturally than they might during direct conversations with HCPs:

You're on a different level when you're playing and answering, and I think that's good that you don't have to really concentrate and think too profoundly when you are answering. The answers come naturally, from your interior. The answers come from within and not from thinking about what I wanted to say or how I wanted to express it to the doctor. That's gone. (Parent 3, MHH)

Another important benefit mentioned was the emotional reassurance the apps provided, with some participants highlighting a sense of being listened to and not feeling alone:

I always had the feeling that I was being listened to. I always had someone to talk to. We never felt like we were on our own. Maybe the app contributed to that feeling. (Parent 3, MHH)

The *MyPal-Child App* also offered patients an alternative way to express their feelings and reflect on their well-being without the pressure of direct conversation with HCPs. Additionally, it provided a form of distraction:

> *The app gives children the opportunity to distract themselves and to deal with questions on how they feel without having the typical conversation with the doctor, to express themselves in another context. (Parent 3, MHH)*

However, not all participants experienced substantial effects. Some reported that the *MyPal-Child App* had little impact when their condition was stable. In these cases, the app's influence was described as subtle but still positive in raising awareness of emotional states:

> *The app didn't have a significant effect on me. Just when my mood was off, it made me become aware of it, I would say. (Patient 1, MHH)*

Others highlighted that simply being asked questions through the *MyPal-Carer App* helped them become more attentive to their child's well-being, even if the perceived impact remained minimal:

> *I would say that the effect is interdependent. That alone the fact that I'm asked those questions makes me become more sensitive about my child's well-being. The effect of the app is not uncomforting, it's minimal and rather positive. (Parent 4, MHH)*

Compliance

Participants described varying degrees of regularity in app usage, with enjoyment and entertainment value playing an important role. Many reported forgetting to use the apps unless it was engaging or integrated into their daily routine. The context of usage, such as waiting times or spare moments, also influenced frequency:

> *I tried to use the app at least once weekly. However, when I noticed mood changes or deteriorations in my child, I used it more frequently. (Parent 1, MHH)*

> *I tried playing once a week or during my medical appointments. (Patient 2, FNBRNO)*

> *I used the app whenever I had some spare time on the bus, train or in the car. (Patient 3, USAAR)*

Some participants used the *MyPal-Child App* during hospital stays but less at home, where daily distractions were more likely to take priority. Several highlighted the convenience of briefly completing ePROs between other activities:

> *My child used it mostly on the ward during waiting times when there was nothing to do. At home there was always something else to do. (Parent 2, USAAR)*

> *With the app I could stay right there on the tablet and briefly answer questionnaires and then continue playing. (Patient 2, MHH)*

Feedback from HCPs was identified as a key factor for sustained engagement. Many participants felt demotivated when their reports were not acknowledged:

> *It was a pity that the doctors didn't react to my reports. If they did, you would have even more reason to use the app. (Patient 1, MHH)*

> *I would have used the app more regularly if there had been consequences with the follow-up medical appointments. Otherwise, it was only for self-reflection, but the reach of the app is broader. (Parent 2, MHH)*

If participants received follow-up from the HCPs involved in the study, it motivated ongoing use:

> *I knew the MyPal team was expecting my involvement. They regularly checked-up on us and that also worked as a reminder that I had to use the app. I would have perhaps forgotten otherwise. (Parent 3, MHH)*

> *It was more like a to-do I had on my list, until I got a call from a MyPal Team member because I had reported a symptom conspicuously often. That is when I realized there is a feedback loop. [...]. I understood the purpose of the app and this purpose became tangible when I got the call. (Parent 4, MHH)*

Influences on Motivation

Beyond perceived benefits and HCP feedback, additional motivational factors emerged. Many participants were driven by the sense of contributing to research:

> *We were not just doing it for ourselves, but to benefit others through our participation in the study. (Parent 3, MHH)*

External reminders (from parents or HCPs) also influenced motivation, as did competing priorities such as school or personal needs, e.g., the need for digital breaks.

User Experience

User experiences varied. While some parents found the *MyPal-Child App* too complex, the flexibility of offline access and features like the read-aloud function were appreciated by patients:

> *Something positive was that you could also use the app without the internet, and I could play in the car or while on the train. (Patient 3, USAAR)*

> *I don't enjoy reading very much, so I liked the read-aloud function. (Patient 2, MHH)*

Communication

The apps' influence on communication with HCPs and within families was mixed. While for some it provided a valuable starting point for discussions, many participants reported that they had not perceived substantial changes in how they communicated.

It was considered particularly useful during follow-up care when direct contact with clinicals was less frequent. Having tools like the apps helped to maintain a sense of connection.

For some patients, the *MyPal-Child App* also created a less intimidating, more comfortable way to share feelings compared to direct, face-to-face conversations:

> *I like that you can just write something down or express your feelings without having to talk directly to someone, it's kind of anonymous. (Patient 3, USAAR)*
> *For a patient, the app is an easy way to talk about your problems, for me easier than doing it face-to-face. (Patient 2, MHH)*

> *The app is a safe place, where you can tell the truth. In the app I can give free rein to my feelings. (Patient 3, USAAR)*

Parents highlighted that the *MyPal-Child App* sometimes lowered barriers for their children. One parent observed:

> *It was better for my child to share things through the app. For me, it was the same. I would share through the app things I wouldn't share face-to-face. When something was worrying me at a specific moment, I got it out of my chest and moved on. (Parent 3, FNBRNO)*

Other parents noted that this effect might vary depending on the child's personality, with one remarking:

> *Unlike my child, an introverted child would feel more comfortable sharing things through the game. (Parent 1, FNBRNO)*

However, other participants expressed that they did not perceive a difference in communication, in particular if they were generally comfortable discussing their health directly.

Family Communication

The apps' impact on communication within families depended largely on pre-existing communication routines. For some families, the apps had little or no perceived effect on how they discussed health-related issues, as such conversations were already part of their communication culture:

> *I couldn't detect much of a difference with the app. We often talk about the state of health anyway; I couldn't say that the app has had an impact there. (Parent 1, USAAR)*

Others, however, reported that the apps allowed them to express emotions more freely or communicate in a less intensive way:

> *Our communication does not depend on the app. We communicate about the fears and griefs we are currently going through. However, I reported stronger feelings like aggression freely in the app. Privately we talked differently. (Parent 1, MHH)*

A patient similarly reflected that completing reports provided a way to communicate without overly burdening family members:

> *I think it's better this way than speaking to my mum about it for 2 hours. (Patient 3, MHH)*

The apps also fostered shared moments of interactions for some, as reflected by one parent:

> *My child would ask me sometimes how to proceed, if there were any doubts on how to answer. (Parent 2, USAAR)*

> *Sometimes I would sit down with my mum, and we did it together, we filled it out, because I knew more than she did, I knew best what was hurting me. (Patient 2, FNBRNO)*

Nonetheless, participants emphasized that broader changes in family communication were often tied more to the experience of the diagnosis than to the apps themselves:

> *As a consequence of the diagnosis, we now talk differently about health, with or without an app. I can´t be certain that this difference was only due to the app. (Parent 4, MHH)*

HCP-Patient Communication

The degree to which the information provided via the apps was incorporated into clinical encounters varied considerably. While some reports were reviewed and discussed during consultations, others were not, leading to divergent experiences among participants.

Several participants expressed disappointment when their reports were not acknowledged or addressed during appointments:

> *The doctors did ask me if I had used the app, but my reports were not discussed. (Patient 4, MHH)*

> *The lack of reactions from HCPs was disappointing. (Patient 1, MHH)*

> *It was a pity that the doctors didn't react to my reports. If they did, you would have all the more reason to use the app. (Patient 1, MHH)*

For others, the absence of discussion was not perceived as problematic, as they felt that either personal visits already covered the necessary aspects of care, or they were not expecting to be asked specifically as reaction to reports:

> *The fact that you need to attend the hospital frequently is enough, you don't need to share things via app. It’s all covered by personal visits. (Patient 2, FNBRNO)*

> *I would have answered if someone had asked. But it didn't necessarily have to be that way. (Patient 3, USAAR)*

Some participants observed redundancies between the in-app questions and in-person consultations, but felt these duplications were reasonable for further clarification:

> *In the doctor's consultation, the questions they make are in part redundant to the questions you get in the app. But it makes sense to talk about them again in person during appointments. (Patient 4, MHH)*

Impression

Overall, the concept of the platform was well-received, though its game design and clinical integration were viewed as needing improvement:

> *So, the concept and the idea were great, it's just the way it was carried out. (Parent 1, FNBRNO)*

> *For MyPal to work, you definitely have to try to get the whole clinical staff on board. A real exchange will only be possible if everyone is involved. (Parent 2, MHH)*

Recommendations

Participants suggested extending the setting beyond oncology, enhancing cross-disciplinary information flow, and increasing the apps' interactivity and customization:

> *It would be great if the information that we entered into the app would also flow into other specialty departments and not just oncology. Maybe markers could be added to help identify when to start certain therapies or when to refer to another specialty. (Parent 4, MHH)*

> *It would be better to involve the entire staff of the clinic, the doctors and the psychosocial service. If this is not possible, there should be a MyPal team on site that is informed about everything, like in this case. (Parent 3, MHH)*

The participants offered several recommendations to enhance the game design, emphasizing the need for more game level variety expending the underwater theme, more interaction options, customizable and personalization features, game characters, and purchasable gimmicks:

> *It would be cool if you could do something with the artifacts you collect, like building a house. (Patient 1, FNBRNO)*

More differentiated versions for different age groups and opportunities for social connection (e.g., a multiplayer game mode) were also highlighted:

> *By sharing the game with other children who have the same illness, it builds a sort of community. (Parent 3, MHH)*

> *A function to enable communication with other parents and patients would be helpful. We are all going through the same and you should be able to talk to others who are in a comparable situation. (Parent 1, MHH)*

One frequently mentioned suggestion concerned the ability to visualize the trajectory of self-reports over time, enabling patients to monitor changes in their health status or emotional well-being more independently on their own. A functionality which was limited to HCPs in the study.

Another central recommendation was the implementation of a feedback mechanism that would provide patients with a response after submitting reports, particularly in cases where notable symptoms or concerns are reported. Such a feature was perceived as potentially reinforcing the sense that their input is being acknowledged, thereby fostering more consistent and candid engagement with the apps.

3.5 Impact on HCPs Due to the Integration of ePROs in Care

3.5.1 Follow-up Questionnaire

A total of 10 HCPs actively involved in the study at the clinical sites completed the follow-up questionnaire regarding their experience with the MyPal platform. Of these, five were project-internal and five were external HCPs. Responses to the twelve Likert-scale items are presented in Figure 18. No significant differences in responses were found between internal and external HCPs. Overall, responses indicated good general usability, while the platform was perceived as adding to the workload rather than reducing it.

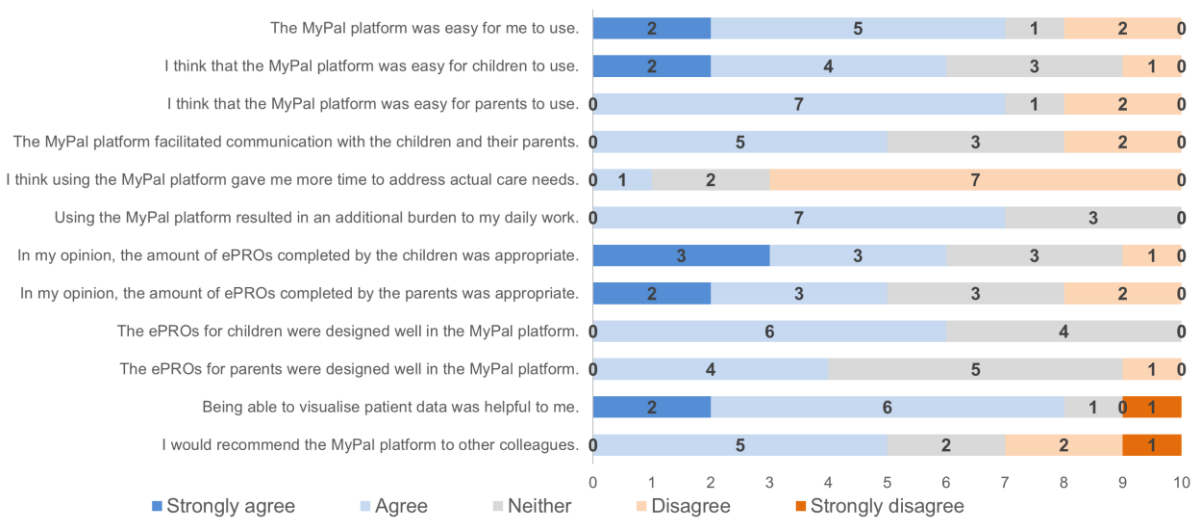


Figure 18 Distribution of the absolute frequencies of the HCPs' responses to the items of the web-based follow-up questionnaire (*n* = 10). ePROS = Electronic Patient-Reported Outcomes; HCPs = Healthcare Professionals.

The free-text comment section at the end of the questionnaire was completed by half of the HCPs. Several of them emphasized the value of online communication, particularly during situations where in-person contact was limited, such as during the COVID-19 pandemic. However, personal contact with patients and their relatives was still considered essential and favored, also to detect subtle changes in patient condition that go unreported if children

disengaged from using the *MyPal-Child App*. Further suggestions addressed both structural and functional aspects of the platform's components. HCPs recommended a more seamless integration into existing clinical infrastructures, for example through shared login systems, to reduce barriers to adoption. Additional proposals included enhancements to data visualization, such as more intuitive layout, clearer color coding for symptom severity, and a more engaging extension of the game elements to sustain children's motivation over time.

3.5.2 Focus Groups With HCPs

A total of nine HCPs who had been involved in the study participated in focus groups conducted at the three clinical sites as conclusion of the study. This included four physicians (two from MHH, one from FNBRNO, one from USAAR), one nurse (MHH) and one psychologist (MHH) among the project-internal HCPs, as well as one physician (MHH), one psychologist (MHH) and one physician (FNBRNO) among the project-external HCPs. Figure 19 and Figure 20 present the resulting coding system and frequencies of the code categories.

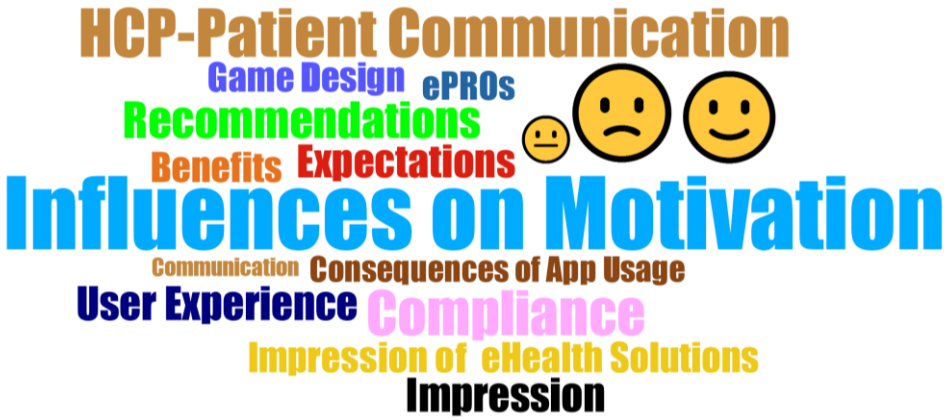


Figure 19 Cloud map from focus groups with project-internal HCPs across all three study sites. Font size and emoji size reflect the frequency of coded statements, with emojis additionally indicating sentiment (positive, neutral, negative). ePROs = Electronic Patient-Reported Outcomes; HCPs = Healthcare Professionals.

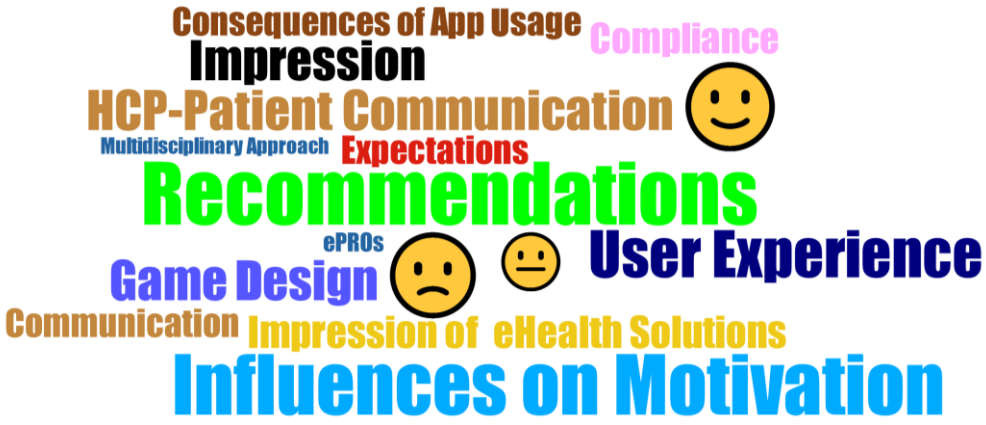


Figure 20 Cloud map from focus groups with project-external HCPs across all three study sites. Font size and emoji size reflect the frequency of coded statements, with emojis additionally indicating sentiment (positive, neutral, negative). ePROs = Electronic Patient-Reported Outcomes; HCPs = Healthcare Professionals.

The coding system largely corresponded to the one developed from focus groups with children and their parents. However, fewer statements by HCPs were assigned to the code categories ‘Game design’ and ‘ePROs’, while ‘Influences on motivation’, ‘HCP-Patent Communication’ and ‘Compliance’ were more frequently addressed. In terms of content, project-external HCPs provided fewer negative statements compared to the internal counterparts. They focused more on sharing user experiences and making recommendations for improvement. An overview of the main thematic categories with brief summaries is provided in Supplement S5, while the following section presents a detailed analysis supported by illustrative paraphrased quotes.

Project-Internal HCPs

Game Design

Similar to feedback from children and parents, HCPs observed that the game design failed to sustain engagement. While patients were initially motivated, many quickly lost interest, particularly if they were accustomed to more competitive or fast-paced games:

> *They enjoy games that are competitive. They didn't find the purpose of this game; it was not catchy enough. (Physician, USAAR)*

Expectations

HCPs described approaching the platform with both curiosity and skepticism prior to study initiation. They found the concept of gamified ePROs appealing but doubted whether the platform could maintain long-term engagement or integrate smoothly into their already demanding workflows:

> *It would be interesting to see if the children would use and benefit from ePROs. Would it help them deal with the disease? What are the benefits for the HCPs? Would the parents be supportive? (Physician, USAAR)*

> *I had questions rather than expectations: how will it work? What are patients going to report to us? How are families going to deal with this? Is there skepticism? Can we establish this here in the clinic? Will it be accepted? (Physician, MHH)*

HCPs recalled speculating about whether differences in reporting behavior would be observed depending on care phase (acute vs. follow-up) or patients’ general media use and consumption habits.

ePROs

HCPs noted that some patients avoided using the *MyPal-Child App* because they felt the regular questions served as a constant reminder of their illness, especially when they were at home:

> *We had some patients that told us they didn't use the app because it reminded them of their disease. They didn't want to have anything to do with the hospital as long as they were at home. (Physician, MHH)*

Consequences of App Usage

The perceived consequences of using the apps varied. Many HCPs felt that symptom reports were only reviewed when participants explicitly drew attention to them. For some, the time invested in logging in and reviewing reports seemed disproportionate to the benefit, though this depended on the volume of reports and the clinic's communication culture:

> *It didn't have an impact on the communication of the team. It was just an addition to the things we do directly. (Physician, MHH)*

Benefits

Despite challenges, HCPs identified distinct benefits. The platform offered an additional communication channel, which could be particularly valuable for shy or anxious patients, particularly teenagers who preferred to express concerns in writing:

> *Teenagers would write down things that they might not have brought up in front of their doctor. It offered them an easier path to let things out. [...]. They use it to avoid interactions, uncomfortable or intimate situations, especially if they are prone to shyness or anxiety. (Psychologist, MHH)*

It was also considered valuable in follow-up care, where direct contact was less frequent:

> *Being in follow-up care gives you more certainty. You have less acute problems, the burden drops, you have more freedom. And in the background, you have this opportunity to make reports and communicate, to stay in contact. (Psychologist, MHH)*

HCPs also highlighted instances where the platform fostered trust and improved clinical interactions:

> *When I reported something that a patient had notified through the app, the outpatient*
>
> *clinic was actually very grateful for it. All my reports were well received. [....]. I remember a patient, a teenager, who reported something he didn't want to report face-to-face. He thanked me afterwards. The feedback that I got was always positive. (Nurse, MHH)*

At the same time, frequent in-person visits in acute treatment phases reduced the need for using the *MyPal-Child App* for reports:

If I am already being treated acutely and I am there every other day, I don't need to overreport my status. (Psychologist, MHH)

Others emphasized that, from a patient perspective, the platform fostered agency and active involvement:

From the patient's point of view, it is different because you're involved in your diagnostic and treatment process, you have a completely different ability to act, your agency is completely different. It is a communication channel. It empowers. (Psychologist, MHH)

Compliance

HCPs generally found ten to fifteen minutes sufficient to check for new reports via the *HCP-Interface*. However, both the frequency of reports and the frequency with which HCPs reviewed the *HCP-Interface* varied considerably. HCPs observed that some families used the apps regularly, while others hardly engaged, and the relevance of the reported information also varied between users.

Influences on Motivation

According to the HCPs, most patients and parents initially appeared motivated and willing to try the apps. The apps made a positive first impression, and their purpose was perceived as clear. One key motivator for their use, as reported by the HCPs, was the willingness to contribute to research by participating in the study and engaging with the apps:

Using the diary function was motivating. They used it either to share something with us or to write something from the depths of their souls. (Psychologist, MHH)

However, the game component was seen as insufficiently engaging to sustain motivation over time, and the lack of feedback on submitted reports discouraged continued use. Several HCPs observed that patients and parents questioned whether the effort was worthwhile when their reports appeared to go unnoticed:

The return on investment is rather low. They are already overloaded, then they are supposed to do a lot and then they do not get much in return. It becomes a cost-benefit issue. Should I keep investing energy? It became a minor priority. (Psychologist, MHH)

Some HCPs noted that reminders and regular contact helped maintain awareness of the apps, though there was concern that frequent prompting might bias usage. Others emphasized that intrinsic motivation was preferable:

App usage depended on many factors, e.g., we reminded them regularly, we showed presence to let them know that the app has a purpose. That if you make a report, it's going to get somewhere, to someone, to the HCPs. (Psychologist, MHH)

I could have reminded the patients to use the app, but I think it would bias the results. They should use it on a voluntary basis. The motivation should be different. (Physician, USAAR)

Concerns were expressed that patients in poor health also were less inclined to use the *MyPal-Child App*:

At some moments, when we need most of the information from them, they are often so tired that they don't feel like playing the game. (Physician, FNBRNO)

The timing of study inclusion also played a role:

We had families who didn't agree to participate in the study, not because they didn't like the idea, but for other reasons: the resources were not available, or they were overwhelmed. There is too much strain and uncertainty shortly after the diagnosis. (Psychologist, MHH)

Gender and care phase differences were speculated:

Boys tend to play and gamble more. And girls, especially teenagers, are more prone to share emotion and social information. Communicating or being socially compliant because they are participating in a study. In that respect there could be a gender effect (Psychologist, MHH)

I noted differences between patients in follow-up vs acute care. Follow-up patients tended to be more diligent. Perhaps they were doing a lot better or had more free time. However, most of them were girls. Is it an effect of health-status or of gender? (Physician, MHH)

Some HCPs expressed frustration that the *HCP-Interface* was not integrated with existing clinical systems, which discouraged use.

When you have something new, it is still inefficient, it comes with a risk, so people tend to use the tools they already are familiar with, because they are more reliable to use. (Psychologist, MHH)

Some HCPs seemed to rely on the study team members to monitor and communicate relevant information, reducing their own need to log in:

They knew that the MyPal team would read the patient notifications and would report if something was off. They knew that really life-threatening things wouldn't be shared through the app. (Physician, MHH)

Staffing shortages, particularly during the pandemic, further reduced willingness to engage with the platform:

Because of the pandemic, there were staff shortages. For example, the nurses were worried that with MyPal they would be assuming an extra responsibility that would cost them time. So, they didn't want to get involved. At first the nurses were in favor, then it became a time management issue. They are working overtime and have to cover the

shifts of sick colleagues. The project was already running, and they thought, if I already missed the start, why should I begin now? (Nurse, MHH)

User Experience

HCPs considered the apps to be well-designed for patients and parents but noted that the *HCP-Interface* intended for their own use required improvements in intuitiveness and technical stability.

Communication

Many HCPs felt that communication within their teams and with families remained largely unchanged by the platform, particularly when communication was already effective:

> *The communication between HCP remained the same. When communication between all team members and with patients and their parents is already working optimally, then such apps become secondary. If communication is not working optimally, such apps could be helpful for children and their parents. I think this also has an influence on the motivation to use it. If the clinic offers good communication, then this is less important. (Physician, USAAR)*

HCP-Patient Communication

Some HCPs reported that the platform offered value by helping to structure visits and serving as a conversational anchor, particularly when reports where actively reviewed:

> *The app gave us material for conversation. We could ask about their symptoms and their context. It allowed us to develop better communication with patients and parents. They knew we were reading their notifications; we were keeping up. (Physician, MHH)*

> *We had something tangible. We would visit them with our tablet, we could see their reports, show them their progress. We had a basis for communication. It made things easier, a conversational anchor. (Psychologist, MHH)*

However, leveraging this potential required regular reports and consistent feedback on submitted reports. Several HCPs reflected that greater willingness among staff to engage with the platform could have increased its utility. One physician assumed that, because the clinical HCP teams understood the platform as part of a research study and not intended for emergency situations, some perceived its use as optional or less relevant. At times, some clinical staff members preferred to rely on established communication procedures rather than adopt the platform:

> *Normally the patients have to report via phone call. In particular cases, if the patient reported something through the app, some of the staff at the clinic would tell them to report things by phone, not through the app. In our case, it was counterproductive. (Physician, MHH)*

Impression of eHealth Solutions

HCPs generally perceived eHealth solutions, like the MyPal platform, as valuable when used as a supplement rather than a replacement for existing care processes:

> *It makes sense if it is supplementary and not substitutive. If it's complementary, it has its place and its context. (Psychologist, MHH)*

HCPs acknowledged the growing role of such digital health solutions, driven by policy initiatives, research and funding priorities. At the same time, they stressed the importance of quality assurance and careful implementation to avoid disrupting personal interactions or already efficient routines:

> *eHealth is making an impact, as a fact. In politics, they talk about money to fund apps, as they are perhaps more profitable. It is also a big research topic. The question is how to assure their quality. The market is large. (Psychologist, MHH)*

> *It should become a tool for certain situations. We can't get around eHealth, we live in a digital world. But the quality with which it has to be done is yet to be defined. (Physician, MHH)*

Despite these acknowledgments, some HCPs remained skeptical regarding the actual impact of such tools on patient care. They noted that communication habits, such as phone calls, would persist regardless of such a platform, and expressed concerns about potentially negative effects if tools failed to ensure meaningful interaction:

> *I am not sure that health care can really be improved with eHealth solutions. Parents and children will continue to make phone calls, regardless of such apps. (Physician, USAAR)*

> *It definitely has an impact, but in which direction? One would desire that the impact is favorable. But we have seen that if I communicate and nothing comes back, it can have the opposite effects. It depends on the conditions. (Psychologist, MHH)*

Another point of discussion concerned the blurring of professional and private boundaries. For example, one nurse highlighted the reluctance to use personal devices for work-related purposes:

> *Why should I install this app on my private mobile? I keep work and private life apart from each other. (Nurse, MHH).*

While HCPs recognized that eHealth solutions could enhance communication and support patient self-management, many reiterated that these benefits could not replace the direct examination and personal bond between HCPs, patients, and their families. Some also noted the increasing prevalence of prescribed medical apps, which can offer patients more autonomy, but only when appropriately integrated into care.

Recommendations

HCPs suggested improving the *HCP-Interface* by adding a triage function to prioritize urgent notifications, daily overviews, and the ability to track which reports have been reviewed and by whom, to streamline workflow and ensure timely follow-up.

They also recommended enhancing such platforms by incorporating passive data collection (e.g., via wearables or sensors) to reduce the need for manual self-reporting:

> *Sensors, pedometers, pulsometers, and such could give us information that you don't usually get from the patient directly [through self-reports]. These could motivate the HCP team to act. (Psychologist, MHH)*

> *Could you get information through other methods where the patient does not have to actively report something: (e.g., pain = heart rate increases)? The patient plays and we get information indirectly, e.g., counting steps to determine physical activity. (Physician, USAAR)*

Beyond improving reporting, HCPs highlighted that the integration of such data streams could also serve research by enabling more advanced predictive modeling. For example, this could facilitate early interventions before symptoms escalate:

> *For research purposes it is important to create prediction models out of direct data, but also data out of social networks, step counts, pulse, wearables, is needed to make big data prediction models. E.g., if you could forecast pain, you could act up front (Psychologist, MHH)*

Project-External HCPs

Game Design

External HCPs shared similar views to internal HCPs regarding game design. They reported that the *MyPal-Child App's* game component did not sustain patients' engagement over time, as it lacked the complexity and stimulation typical of commercial games, which limited its appeal. HCPs acknowledged the competitive nature of the gaming market, emphasizing the challenge of holding children's attention when they are accustomed to highly developed video games:

> *The market these days is full of good video games and as such it's tricky. (Physician, FNBRNO)*

Expectations

HCPs described their expectations toward the platform as being shaped by curiosity and optimism. They highlighted the app's potential to offer constructive and purposeful activities, positioning it as a meaningful alternative to passive media consumption. They did not assume risks of overuse, as children uninterested in the app would likely not engage with it:

That it would be something where they don't mindlessly consume a game or video but do something meaningful with it. Children who don't know what to do with it probably wouldn't have used it anyway. So, we wouldn't have driven anyone into media consumption with it. (Psychologist, MHH)

Consequences of App Usage

Most HCPs noted that the apps had little impact on their daily routines, with occasional benefits for specific patient cases. While some found the symptom-tracking feature helpful, particularly when families used the apps to recall events more precisely, the platform was not used by all clinical staff members it had been offered:

There was also a phase when I had a few patients for whom this was helpful because they sometimes entered something that I was looking after, especially in the outpatient clinic. [...]. Otherwise, it hasn't changed anything for my psychological work area, our social workers haven't actually used this app, so it doesn't seem to have any significance for their work either. And the nursery teacher didn't use it either. (Psychologist, MHH)

One family once said that there were some symptoms, but they couldn't remember exactly. Then they took out the app and looked up for themselves when it actually happened. They were then able to sort it out a bit for themselves. (Physician, MHH)

No, it didn't have any impact on daily practice. (Physician, FNBRNO)

Compliance

Integration into the routine and perceived utility of the platform emerged as crucial factors influencing HCP engagement. A lack of self-reports by patients or proxy-reports by parents led to inactivity among HCPs, while infrequent logins increased perceived workload due to the need to repeatedly recall login credentials and navigation steps:

I've often had patients ask me specifically about a symptom and say: 'I've entered that too.' Then I looked it up. Otherwise, to be honest, the inhibition threshold was quite high, I simply didn't do that in everyday life, especially not in this routine of seeing acute outpatient children (Psychologist, MHH)

There was no data to check, as the kids didn't play it. Therefore, I must admit I wasn't that active. (Physician, FNBRNO)

It would probably have been less time-consuming if you had been in there more often. Because then you would have had more automatisms. It was time-consuming that way, if you're not in for a while you have to think about how to get there, what my password was, what my username was again. That was time-consuming. Yes. (Physician, MHH)

Influences on Motivation

HCPs discussed potential contextual influences on usage habits and motivation to use the platform, including the patient health status, availability of alternative activities, parental engagement, and the age of the users:

> *I imagine that the better the patients feel and the more active they can be, the fewer people use the app because they are sitting or lying around less and the more time patients spend in bed or resting, the more time they spend using their tablets and mobile phones. (Physician, MHH)*

> *Some children actually use tablets and mobile phones a lot in hospital and parents are happy that they are no longer so present at home. Maybe that's also because, nicely, other activities are available again and the mobile phone is no longer so attractive and no longer so present for some children. (Psychologist, MHH)*

> *I have the feeling that parents who were particularly interested in keeping a close eye on their children and also keeping a close eye on what is happening during the time they are at home so that they can make the best possible use of it for the therapy, so that their children can also be looked after in the best possible way. That was an incentive for them to simply write down what they might otherwise have brought with them on a piece of paper. (Psychologist, MHH)*

> *The older the users were, the more I had the feeling that it was less about playing and more about sharing information. (Physician, MHH)*

User Experience

Most HCPs did not perceive usability as a major issue, though some admitted that they had not explored all the features of the *HCP-Interface*. Those who engaged more with it found specific updates, such as quick checks of progression of thematically related symptoms clusters, useful:

> *That I could look very quickly if something was conspicuous in the psychological area, are there any physical symptoms which occur together? [...]. I actually found that a very practical update. (Psychologist, MHH)*

HCPs also reiterated that long-term patient engagement remained a challenge, despite initial enthusiasm.

Communication

HCPs noted that children, as digital natives, might find apps a more comfortable medium for expressing their emotions:

> *I believe that exactly this kind of children, who are hooked on the apps, grow up on them, and it can be a more pleasant way for them to share their feelings.*
> *(Physician, FNBRNO)*

HCP-Patient Communication

While HCPs did not observe notable changes in parent-child communication, they highlighted that the platform could enhance in-person interactions by providing a discussion basis during consultations, especially when symptom fluctuations occurred between visits:

> *There is added value if information is accessible in an easy way. I think I would actively ask certain questions in certain directions much more often if the patient directed me in this direction by describing their symptoms. Reports through the app could be used to guide the patient a little more towards certain issues that are perhaps being overlooked. (Physician, MHH)*

> *If I meet them once and they tell me they're fine and then I meet them again in a few weeks and they're fine and that means everything is always okay. But if I saw an entry in the app that things were different for a while, then I could talk to them again and remind them: 'Look, you entered something there, what was going on?'. Then we would be even more likely to get in touch again about an unpleasant topic.*
> *(Psychologist, MHH)*

Nevertheless, some underscored that digital reporting should not replace nuanced in-person conversations, as subtle meanings often become clear only during face-to-face discussions:

> *An interaction is something else when I can personally correct something, meaning that something develops, or when I can personally ask again how things were meant. When you answer, you have to decide, for example on a categorization or something. And it only becomes clear in the conversation what is really meant by it. That is something that perhaps cannot be grasped in this way [i.e., the platform].*
> *(Psychologist, MHH)*

Impression of eHealth Solutions

HCPs expressed a generally positive outlook on the growing role of eHealth and digitalization in clinical practice and medical care, acknowledging its potential to streamline care processes, reduce emergency service strain, and facilitate access to care, e.g., remote consultations for vulnerable patients, such as those with immunosuppression:

> *I think that nowadays, digitalization makes sense and we're heading there in all areas of activity. I personally see a big boom in these things in medicine in general. (Physician, MHH)*

> *I see that e-medicine and e-counselling are really in nowadays, which I think is very useful to reduce the burden of emergency offices. You can discuss some things online instead of coming to the hospital in person with less severe issues. Overall, yes, it's a way, in my opinion. (Physician, FNBRNO)*

> *In general, I do believe that many of the e-approaches improve medical care in terms of content, but also in terms of organization. There are certainly apps that remind you of appointments, for example, or that allow you to simply scan and send findings and know where to send them. (Physician, MHH)*

However, they stressed again that digital health solutions must remain complementary to established care practices to avoid excluding families who face language barriers or lack the digital skills and infrastructure to engage effectively:

> *It must be complementary, not substitutive. I couldn't imagine it any other way. Because with how many families do we need an interpreter to communicate with our hands and feet? They wouldn't be able to use it at all. They would no longer have access. (Psychologist, MHH)*

Additionally, it was pointed out that poor digital infrastructure and bureaucratic barriers posed substantial challenges to the widespread implementation of eHealth solutions. Their success hinges on user-friendliness and seamless integration into existing healthcare frameworks for which permit requirements need to be met. Both patients and HCPs need easy access to these tools for them to be effective.

Practical challenges and barriers, including improvable digital infrastructure, administrative and data protection requirements, and a lack of integration into clinical routines, were seen as major hurdles to the broader adoption of eHealth solutions:

> *You have to go through a lot of places again to really be able to use it and we would have to function much more digitally overall to really be able to use these e-health applications such that every patient is able to install an app on their mobile phone. I think that's a really big issue. Even if we could, the MHH would first have to say that it really is a program that is allowed to run. So, there are also administrative and data protection hurdles. They're insanely high. (Physician, MHH)*

> *Both sides must have good access to it. I believe that the problematic side is less the patient side than the healthcare provider side. (Physician, MHH)*

> *As with some other things, it would have to become established. And that means it has to be uncomplicated. As uncomplicated as possible. (Psychologist, MHH)*

> *The flow of information in such large teams is quite difficult...well, I also experience this with other things, and it has to be repeated regularly, if it is not part of everyday life for the respective professional groups, it is not automatically considered during introduction. (Psychologist, MHH)*

Recommendations

HCPs emphasized that investments in human resources and infrastructure should precede the large-scale implementation of eHealth solutions. To enhance the game's engagement, they suggested incorporating more personalization options and dynamic features, such more diverse game modes or virtual companions, to encourage sustained use:

> *Or these types of games where you build your own town every day. You just have to visit the app every day, because you collect money from the houses you've built. If you*

don't collect it, you lose it. So, something of this kind, which makes you open the app at least once a day, even if it was for 5 minutes. (Physician, FNBRNO)

Tamagotchi seems like a great idea, also because it can become sort of a buddy to you for the treatment. The questions on a health state, which, on the current app, were emerging anonymously from somewhere deep down, would be asked by your Tamagotchi. And you get a digital during the treatment. All we want from the app could be delivered by this virtual avatar, which you can also create, customize, etc. (Physician, FNBRNO)

For the *HCP-Interface*, suggestions focused on improving usability and integration into existing workflows. Recommendations included highlighting new data since the last login, enabling installation on business mobile phones, embedding the *HCP-Interface* within clinical systems (e.g., as a quick-access button), and implementing a triage system (e.g., traffic light coding) to help prioritize urgent notifications.

4 Discussion

4.1 Principal Findings

The *MyPal4Kids* study evaluated the feasibility and acceptability of an ePRO-based digital health platform incorporating gamification in pediatric oncology and palliative care. The findings indicate that active participation of children and their families in symptom reporting is achievable, particularly when bidirectional communication and timely feedback from HCPs are ensured. Patient engagement was strongly shaped by the perceived utility of the platform, closely tied to the frequency and quality of HCP feedback and the game's ability to sustain motivation. Although usability was not identified as a significant barrier for patients and parents, it played a greater role for HCPs, many of whom viewed the platform as increasing their workload instead of facilitating their tasks.

The core hypothesis that gamification would enhance the attractiveness of self-reporting for young patients was only partially supported. While initial interest and uptake were high, long-term engagement declined over the study period. Participants and usage data alike suggested that the gamified elements, while initially motivating, lacked sufficient variation or progression to maintain users' interest over time. Engagement with the MyPal platform appeared to follow a cyclical dynamic: reduced reporting by patients led to fewer platform reviews by HCPs, resulting in less direct feedback, which further discouraged patient participation. This reciprocal disengagement highlights the importance of sustained feedback loops and perceived clinical relevance for maintaining motivation over time.

4.2 Recruitment and Enrollment Characteristics

Recruitment was shaped by both contextual and procedural factors. Initial enrollment was facilitated by a broader pool of eligible patients, comprising both newly diagnosed children and those diagnosed within the previous twelve months. This procedural constraint coincided with the onset of COVID-19, which disrupted clinical routines and contributed to a marked decline in recruitment rates. Reduced face-to-face appointments and restrictions on parental presence during clinical visits complicated informed consent and onboarding. Despite these obstacles, 83 patients were successfully enrolled (recruitment rate: 55%), which fell short of the original target of 100 patients but was acceptable under the circumstances.

Intrinsic factors also played a role. Informal communication among families might have influenced willingness to participate, with both encouragement and discouragement reported by HCPs involved in the study. Emotional distress shortly after diagnosis often reduces willingness to participate in research, a phenomenon documented in qualitative and

methodological studies of pediatric oncology recruitment and discussed in systematic reviews of informed consent in pediatric oncology [117, 162, 170]. This underscores the importance of sensitive timing and tailored approaches to recruitment.

The cohort's demographic composition deviated from the broader pediatric oncology population: adolescents aged 14–17 were overrepresented, whereas children under four, the group with the highest incidence of pediatric cancers [173], were excluded due to literacy barriers. As most participants (84%) were newly diagnosed, generalizability to patients with chronic or relapsed disease trajectories is limited.

Optional data fields (20% missing) showed inconsistencies in clinical descriptors (e.g., more patients listed as having metastatic disease than stage IV), likely reflecting incomplete or heterogeneous data rather than true discordance. Optional free text items also varied in detail and terminology, e.g., the description of handicaps, limiting standardization for analysis.

4.3 Acceptability and Engagement With the MyPal Platform

The acceptability and engagement of the MyPal platform were shaped by multiple interacting factors, encompassing design aspects, patient-HCP interactions, and gamification as an embedded motivational feature. This aligns with the Technology Acceptance Model, which suggests that the likelihood of adopting a technology is primarily influenced by users' perceptions of its ease of use and practical value [135]. Overall, sustained engagement proved challenging, as reflected by the declining proportion of symptom reports and monthly ePROs completed across the study period.

Several preventive measures were incorporated into the study design to mitigate missing data, a well-documented issue in patient-reported data collection [106]. These included a seven-day completion window for monthly ePROs, retrospective completion of the baseline assessment during the first month of study participation, and offline functionality to accommodate inconsistent connectivity. In line with instrument-specific guidelines, established recommendations for handling missing items were also applied during data analysis, as described in Section 2.5. Despite these strategies, compliance only improved modestly. Gamification alone was insufficient to offset the overall decline in participation.

As described in Section 4.1, patient engagement was closely tied to the feedback received from HCPs. Comparable feedback-engagement cycles, characterized by declining reporting and reduced feedback, have been observed in previous digital health research [4, 7, 8, 10, 53, 76, 101]. This effect may be especially pronounced in pediatric oncology, as the emotional burden on children and their families combines with HCPs' competing demands, together influencing communication [14, 163]. Several contextual likely contributed to this engagement

dynamic: Many assessed symptoms recorded through the platform reflected expected chemotherapy side effects [29, 38], about which patients and parents had received prior information. Consequently, limited feedback may have reflected clinical perception that many reports did not require additional discussion, or a broader lack of prioritization of symptom management within institutional workflows [45, 176]. However, clinically relevant symptoms, such as tingling or numbness in the extremities, can inform treatment adaptations [61, 104].

While this study did not systematically analyze demographic or socioeconomic predictors of adherence, previous research using SSPedi found significant variability in usage patterns across such factors, including age, income, and ethnicity [44]. These findings suggest that engagement with symptom reporting tools may be influenced by broader contextual and individual factors, which could partly explain heterogeneous participation patterns observed in this study.

Prior research has shown that ePRO data improve outcomes only when coupled with structured response mechanisms [10, 19, 137]. Dupuis et al. (2024) further demonstrated that linking pediatric symptom screening with predefined care pathways improved symptom control compared with usual care, although such interventions were implemented surprisingly infrequently. According to the authors, sustainable impact requires institutional prioritization, systematic implementation and ongoing monitoring is needed to ensure that reported symptoms consistently trigger appropriate clinical follow-up [45, 183]. These findings underscore that digital health solutions alone cannot ensure engagement, their perceived value depends on a functioning feedback loop between patients, parents, and clinicians. Strengthening this loop through automated notifications, structured review schedules, and visible feedback may help sustain motivation and reinforce the platform's clinical relevance.

Besides feedback, other motivational features embedded in the platform, such as gamification, were intended to sustain engagement. While usability itself did not emerge as a barrier, the gamified component of the platform was insufficient to sustain motivation over time, particularly among older children. The risk of waning engagement had been recognized during development, and engagement strategies of gamification, such as a reward system and competitive high score lists were integrated. However, while such mechanisms often show strong short-term engagement, it tends to still decline over time, especially in studies with smaller user bases [155], suggesting that social or competitive gamification features may require a sufficiently active community to maintain effectiveness [126]. The game was deliberately designed for brief daily use, age- and gender-neutral, and avoiding risk of overuse. In practice, underutilization rather than overuse became a challenge, suggesting that these development constraints for broad applicability and safety may have limited its overall appeal.

The game levels and activities were perceived as repetitive over time and provided limited novelty to sustain engagement.

4.4 Feasibility of ePRO-Based Measures

The use of ePRO-based assessments for monitoring symptom burden and related outcomes in pediatric oncology proved feasible overall, with some limitations. The platform captured symptom trajectories throughout the six-month study period in which around half of the participants reported at least one symptom with highest burden. Clinicians could review individual symptom patterns, highlighting the platform's potential for patient-centered care. However, the feasibility of such measures depends strongly on sustained patient engagement (as previously discussed in Section 4.3). Reporting frequency declined over time, consistent with trends observed in other pediatric ePRO studies [41, 107, 147]. Such a decline may reflect both actual symptom improvement, individual patient conditions [97] and the practical challenges of maintaining regular platform use over time, which remains a limiting factor for wider implementation.

One of the most consistent results across child self-reports was a general decrease in symptom burden over time for several physical symptoms such as headache, changes in taste, appearance, and nausea/vomiting, as captured with SSPedi. This improvement may partially reflect typical treatment trajectories, where acute side effects often decrease after the most intensive treatment phases, as well as children's adaptation to treatment regimens and supportive care measures [43, 63, 67, 201]. However, as suggested in prior SSPedi research, repeated administration itself may also influence symptom perception, either through habituation or by encouraging reflection that reduces symptom distress over time. In this view, the act of regular self-reporting could contribute to symptom relief [45].

In parallel, children's HRQoL, as assessed by the PedsQL™ total score, improved from baseline to study completion. These improvements appear to mirror the observed symptom burden reductions, highlighting how symptom management and adaptation over time contribute to overall well-being. Simultaneously, declining reporting frequency complicates interpretation of symptom and HRQoL trajectories, as observed improvements may partly reflect genuine clinical changes but also reduced data capture, with families more likely to report when burden was high and less likely when it was low. In addition, the broader COVID-19 context may have influenced both reporting behaviors and self-reported experiences, further limiting interpretability. Systematic reviews and empirical studies have documented pandemic-associated declines or changes in HRQoL and disruptions to ePRO research in general and pediatric populations [65, 120, 122, 182].

Beyond engagement, the interpretation of ePRO-based measures is also shaped by differences in self-reports by patients and proxy-reports by parents, which aligns with evidence in literature [26, 88, 99, 136, 181]. Correlation analyses showed measurable inconsistencies, suggesting that children and their parents may perceive or recall symptoms differently. Such differences highlight the importance of routinely comparing self- and proxy-reports in clinical assessments, as each perspective can provide unique and complementary insights. At the same time, several high correlation coefficients in our study did not reach statistical significance, which might be attributable to the relatively small sample sizes rather than an absence of true associations.

Analyses of main and interaction effects further demonstrated the utility of ePRO-based measures data in detecting meaningful subgroup (demographic and clinical characteristics) and temporal differences. The findings of this study revealed several notable patterns in symptom burden, HRQoL, satisfaction with care, and the perceived impact of illness on the family. Female patients reported a higher burden for symptoms such as tiredness, appetite changes, and cognitive problems in agreement with literature [201]. Such gender-specific differences in symptom burden and HRQoL have also been reported in other studies [54, 87]. Children with leukemia experienced higher burden by mouth sores and procedural anxiety than those with solid tumors, a finding consistent with the aggressive nature of hematologic treatment regimens and their association with invasive procedures and mucositis [142]. Age-related patterns were also evident. Younger children reported higher procedural anxiety, consistent with observation in pediatric oncology populations [26, 194]. In contrast, adolescents tend to report threats to life, such as the seriousness of diagnosis or ineffectiveness of treatment, more frequently than younger children [194]. The interaction of time with age and diagnosis highlighted the platform's ability to capture nuanced symptom evolution.

Parental outcomes showed similar complexity: In our study, parental satisfaction varied with the child's age and time since diagnosis, suggesting that demographic and temporal factors may influence parents' perceptions of care. In contrast, Stanek et al. (2015) found that after controlling for symptom burden, the parent-oncologist alliance was the only factor significantly explaining satisfaction with care, whereas demographic variables had no effect in their study, highlighting the crucial role of the therapeutic relationship [169]. Similarly, involvement of family doctors has been associated with higher emotional support scores among cancer patients, underscoring the importance of coordinated, relationship-based care [190]. More broadly, research indicates that factors such as clear communication, emotional support, involvement in care decisions, and access to information consistently contribute to parental satisfaction in pediatric oncology [160].

4.5 Focus Groups with Children and Parents

To complement quantitative insights, qualitative data from focus groups with children and parents provided a deeper understanding of engagement dynamics and perceived usability. In summary, the apps were valued by many for fostering reflection, providing a safe space for emotional expression, offering practical documentation of symptoms and concerns, and creating a subtle but meaningful sense of support. Several participants described that the process of completing symptom questionnaires encouraged them to think more consciously about how they and/or their family members felt, recognize changes over time, and prepare more effectively for clinical discussions. This reflective process was perceived as a benefit in itself, even when the platform did not directly influence clinical care, which aligns with findings in the literature [98]. However, several factors limited its long-term impact. As previously discussed in Section 4.3, gamification did not prevent the decline in ePRO completion over time. Focus group participants described similar experiences, noting that the novelty of the game component faded quickly and that its motivational impact was limited, especially among older children. These observations are consistent with studies on broader mHealth and digital game-based interventions, which also reported declining engagement after initial uptake [118, 148, 189]. Participants further highlighted that engagement depended not only on gamification but also on timely feedback from HCPs, reinforcing the theme, first identified in Section 4.3, that interactive feedback is a key determinant of sustained participation.

The sessions echoed earlier discussed quantitative findings from this study regarding discrepancies between child and parent symptom reports, with some parents perceiving that their children rated certain symptoms as less severe than they themselves would have estimated.

Children and parents emphasized a preference for visually appealing, short, and age-appropriate tools with brief recall periods, generally ranging from several days up to a week, supporting the notion that digital health applications such as MyPal should complement instead of replacing face-to-face interactions [32]. These insights underscore the importance of differentiated developmentally sensitive design to ensure sustained participation and perceived relevance [31, 184].

4.6 Impact on HCPs

While the previous findings illuminate patient and caregiver experiences, understanding the platform’s impact on clinical staff is equally essential [95]. The generally positive quantitative feedback from HCPs regarding the MyPal platform, highlighting its usability, child-appropriate design, and helpful visualization of patient data, supports the technical feasibility and user-

centered development of such a platform. However, results from the follow-up survey also revealed that many HCPs perceived the platform as increasing, rather than reducing, their daily workload. Nearly half were reluctant to fully endorse its wider adoption, reflecting concerns not only about technical usability but also about workflow integration and communication efficiency. This highlights a critical tension in care: digital health solutions, while promising for patient management, risk adding administrative burdens if not embedded seamlessly into clinical workflows [10, 20, 39, 85, 101, 150, 200]. Limited interoperability across both existing commercial clinical systems and ePRO-based platforms can hinder seamless integration into routine workflows [6, 157]. One potential solution would be to have dedicated staff for data review and the propagation of such digital health solutions [34]. As emphasized in the literature, *"adequate resources should be allocated to this responsibility, rather than adding it on top of other duties"* [100], especially in light of staff cuts and workload redistribution in healthcare settings. Without such structural support, even well-designed platforms risk reduced clinical utility and user fatigue. The HCPs' feedback reflected the dual necessity of meeting both clinical and user experience needs. Engagement strategies must consider not only patient motivation but also provider efficiency and satisfaction, reinforcing the platform's dual role in supporting individualized care and facilitating research.

4.7 Focus Groups with HCPs

The focus group discussions with internal and external HCPs highlighted tensions between the technological potential of the MyPal platform and its practical feasibility in routine care. Consistent with Section 4.1 and 4.3, both HCP groups highlighted the challenge of sustaining long-term engagement among pediatric patients. Importantly, these qualitative insights provided context for interpreting the quantitative ratings, clarifying the reasons behind HCPs' assessments and the factors influencing their overall evaluation of the platform. HCPs' reflections mirrored those of patients and parents. They observed that while gamification initially stimulated interest, its effect diminished over time. Participants highlighted the need for continuous content renewal and personalization to maintain engagement, emphasizing that motivational design must be supported by visible clinical responsiveness to remain meaningful.

Divergent perspectives between project-internal and external HCPs highlight the complexities of digital health implementation. Internal HCPs, who were involved in the development, took a more critical stance, shaped by knowledge of the platform's intended features and potential. External HCPs adopted a pragmatic view, emphasizing usability and workflow integration barriers. Both groups emphasized that digital health solutions should augment, not take the place of, direct clinical care, consistent with the perspectives of children and parents described

in Section 4.5, highlighting the importance of face-to-face interactions. These qualitative insights further contextualize the quantitative findings reported in Section 4.6 regarding perceived workload and integration challenges. Sustainable implementation requires a balance of engaging, developmentally tailored interfaces with intuitive data representation [166] and practical clinician-oriented solutions that respect workflow constraints.

HCPs emphasized that the impact of digital health solutions like the MyPal platform also depends on the effectiveness of clinical communication, both within the ward and with patients and families. In settings where communication workflows are already suboptimal, such tools may help prevent loss of critical information during brief clinical encounters. Evidence suggests that the timing of symptom reporting is crucial for effective care [30]. For example, during periods with few in-person appointments, the MyPal platform enabled patients and parents to report symptoms remotely, potentially improving follow-up care, especially for outpatients. These qualitative insights illustrate the mechanisms underlying the feedback loops described in Section 4.1 and highlight how perceived clinical relevance can affect engagement.

4.8 Platform Utility for Clinical Care and Research

The quantitative and qualitative findings of this study indicate that ePRO-based systems like the MyPal platform offer dual functionality by supporting both individualized clinical care and pediatric oncology research. Achieving this potential depends on sustained user engagement, integration into clinical routines with adequate resource allocation, and continuous user-centered refinement. Tracking individual symptom burden and other outcomes over time can help to bridge gaps between infrequent clinical visits, a feature particularly valuable for outpatient care [30, 158, 188].

Larger datasets could strengthen the research utility of such platforms, for example by enabling comparisons of different treatment regimens regarding side effects or recovery profiles. While such analyses exceeded the scope of this feasibility study, they illustrate the potential to inform treatment optimization and evidence-based supportive care strategies.

4.9 Contextual Factors Influencing Implementation

Successful implementation of digital health solutions like MyPal is strongly influenced by contextual factors beyond technical design, notably the quality of communication within clinical teams and between HCPs and patients. In teams with strained communication, the platform may help bridging information gaps during brief clinical encounters, supporting both engagement and follow-up care. Conversely, in teams with effective communication, the platform’s added value could be perceived as more limited. This underscores that the

effectiveness of digital health solutions is contingent on the communicative culture into which they are introduced, complementing the feedback and engagement dynamics described in Sections 4.1 and 4.7.

Technical infrastructure and institutional support are also critical. Unstable Wi-Fi connections on hospital wards posed a practical barrier, and although an offline mode was available, connectivity remains often essential for seamless operation. Data protection requirements often mandate internal hospital servers, increasing technical complexity and implementation effort, a challenge already identified during the study's preparatory phase [109]. This highlights that even well-designed digital health solutions require a supportive technical environment to function optimally.

Legal and ethical frameworks further shape usage and perception. The platform was not intended as an emergency alert system, clearly communicated during informed consent. While this avoided unrealistic expectations regarding real-time feedback, it may also have constrained perceived clinical relevance for some users.

4.10 Strengths and Limitations

This feasibility study benefited from several methodological and conceptual strengths. The MyPal project was a collaborative effort involving pediatric oncologists, palliative care experts, software engineers, and researchers. Its interdisciplinary and multicenter design enabled testing the MyPal platform across diverse clinical settings, including inpatient and outpatient care, accounting for local differences in care delivery and readiness for digital health solutions. Active involvement of patients, parents, and HCPs through mixed methods provided a comprehensive understanding of platform usability, engagement dynamics, and perceived value. This approach aligns with methodological recommendations emphasizing the importance of combining qualitative and quantitative methods to achieve a comprehensive assessment of eHealth usability [102], thereby allowing for a holistic evaluation across user groups and enhancing interpretability.

Ethical safeguards supported the inclusion of pediatric cancer patients as a vulnerable population, including proxy reporting and parental presence during focus groups. Deployment was facilitated by on-site preparations, including tailored training materials, standard operating procedures, and technical infrastructure support from project partners, ensuring smooth implementation. The study contributes to the evidence base on integrating ePROs into gamified mobile applications in pediatric oncology and palliative care, offering insights into both conceptual promise and practical challenges.

Recruitment challenges, already outlined in Section 4.2, were amplified by COVID-19-related disruptions and the emotional strain of a recent cancer diagnosis, which likely reduced participation willingness. The resulting sample showed an overrepresentation of adolescents and the exclusion of younger children due to literacy constraints, limiting generalizability. Moreover, selection bias cannot be ruled out, as families with higher digital literacy or stronger engagement with clinical care may have favored participation [70]. The six-month study duration constrained assessment of long-term engagement.

Optional data fields reduced granularity and limited analysis depth. However, this did not affect the present evaluation, as these fields were not required for the primary analyses. Measures such as flexible assessment windows and offline functionality only partially mitigated these engagement challenges. Treatment documentation by HCPs was not mandatory and no systematic recording of therapy regimens was implemented. Consequently, a detailed analysis of symptom-treatment relationships was not feasible, which limits interpretability of symptom trajectories and outcomes. Although the platform successfully tracked symptom burden and HRQoL over time and revealed subgroup patterns, declining participation further reduced the robustness of longitudinal analyses, highlighting the need for improved strategies to sustain engagement and ensure standardized data collection. Detailed analyses, such as correlations between symptom reports and treatment regimens or physical activity data, were not performed, as the primary objective of this feasibility study was to assess platform acceptability and implementation. Since treatment regimens were not systematically recorded, no comparisons by treatment scheme were conducted, further emphasizing the study's focus on feasibility rather than treatment-specific effects.. Planned pre-/post-implementation comparisons could not be conducted due to pandemic disruptions. Broader contextual factors, including the COVID-19 pandemic, may have influenced self-reported outcomes, as discussed in Section 4.4.

The sample size was sufficient to identify trends consistent with existing literature, but limited size and variable data completeness constrained subgroup and longitudinal analyses even after imputation and adherence to guidelines for missing data. For the same reasons, certain clinically relevant groups, such as patients with brain tumors, who are more prone to neurological symptoms [185], could not be analyzed separately.

Dual reporting by children and parents was optional and inconsistently applied, constraining analyses of proxy validity. Parents of children with cancer often experience elevated levels of psychological distress [73], which may interfere with symptom monitoring and reporting. Parental presence during focus groups with children, though ethically justified, may have introduced a bias related to social desirability. The PedsQL™ 3.0 Cancer Module does not capture social support and psychological interventions as domains, which have been identified

as key predictors of HRQoL in pediatric cancer patients [125], while another key factor, procedural anxiety, is considered [154]. Limited perceived clinical relevance may have stemmed from the restricted set of outcomes visible to HCPs during the study, as certain measures, such as satisfaction with care, were collected for evaluative rather than clinical purposes. Broader access to selected outcome measures could potentially strengthen the feedback loop between families and HCPs.

Technical barriers, such as unstable Wi-Fi and data protection requirements for internal servers, complicated implementation despite an available offline functionality for the apps. The cautious gamification design, motivated by ethical concerns over addictive or violent content, may have limited appeal, particularly for older children. Despite initial enthusiasm, gamification alone was insufficient to sustain long-term engagement.

While this feasibility study identified important trends, it did not assess cost-benefit aspects or long-term impacts on care quality, which remain relevant topics for future research.

4.11 Implications for Future Research and Clinical Practice

Seamless integration into existing clinical processes and decision-making routines is essential for sustainability: this includes ensuring interoperability with Electronic Health Record (EHR) systems, establishing automated data flows, and providing clear guidelines for the use of ePRO-based platforms in pediatric populations [52, 69]. The importance of embedding digital interventions into routine care is supported by a recent review [71]. Implementation frameworks highlight that even feasible and well-designed technologies may fail to be adopted or sustained without alignment to clinical workflows and organizational context [55, 56, 175, 197]. As discussed in Section 4.10, restricted visibility of certain patient-reported data may have limited perceived clinical relevance. Building on these findings, future implementations should also consider selectively granting HCPs access to additional outcome measures to enhance the feedback loop between patients and providers.

A major strength of the MyPal platform lies in its modular and flexible architecture, enabling integration of diverse ePRO measures and gamification strategies, and allowing adaptation to different clinical contexts, institutional workflows, and patient subgroups. Future development should leverage this modularity to create more age-appropriate and culturally sensitive designs. Equally important is iterative refinement based on continuous user feedback along all phases of development [155]. Exploring emerging technologies, such as adaptive algorithms or wearable integration, could further enhance scalability and adaptability over time [184]. In this context, assessing children's conditions through automatically generated measures (e.g., from wearables or passive sensing) versus self-reports represents an important area for future investigation [90, 178]. This includes multimodal approaches, such

as combining symptom monitoring with exercise coaching [116]. Differences between proxy- and self-reports have been consistently demonstrated in the literature and were also evident in the present study, as discussed earlier. Evidence from prior studies shows that, when using age-appropriate instruments, children as young as five can provide valid and reliable self-reports of their HRQoL [187], underscoring the importance of systematically capturing their perspectives rather than relying on parental reports. Expanding the diversity and complexity of gamification elements, while balancing ethical concerns [168] including addiction or inappropriate content, may help maintain children's motivation and engagement over time. This includes the personalization of game features, items and adaptive feedback mechanisms according to developmental stages and individual user characteristics [70, 89, 97, 98]. It may also involve social interaction elements [119] as well as archetypes of gamification [159]. Ultimately, digital interventions in pediatric oncology need to integrate these motivational strategies into designs that also account for functional requirements, emotional and cognitive needs of children and families, as well as usability, data security, and trust [33] to ensure sustainable use.

Longer-term studies with larger and more representative samples would allow for assessing the durability of engagement and the potential clinical benefits of platforms like MyPal, particularly in light of evidence that gamified interventions often exhibit an initial novelty effect followed by a familiarization phase [148]. Such studies would enable more nuanced analyses of behavioral changes over time and their relationship to treatment regimens, symptoms, and psychosocial outcomes. Future studies should build on this feasibility work by linking ePRO data with treatment regimens or physical activity measures to better understand treatment-specific symptom patterns and inform individualized supportive care. Standardizing data collection (e.g., mandatory baseline characteristics, structured treatment documentation) will be critical to facilitate these analyses and increase comparability between studies [46]. Furthermore, randomized controlled trials (RCTs) should be conducted to examine the platform's impact on patient-reported outcomes, care quality, and clinical endpoints. However, given the iterative and context-dependent nature of digital health interventions, traditional RCT frameworks may need to be complemented by more flexible and adaptive evaluation designs [58], also regarding validation [59]. Additionally, establishing benchmark datasets, such as the recent PedsQL™ cancer module evaluation in a large Dutch national cohort of pediatric cancer patients, could help to contextualize and compare HRQoL outcomes across populations [72]. Economic evaluations, such as cost-effectiveness and cost-benefit analyses, will also be necessary to support large-scale implementation.

The platform was not intended as an emergency alert system, a limitation that was clearly communicated during the consent process. Due to legal concerns regarding accountability for

unmonitored or alarming reports, clinicians' use of the platform remained non-obligatory, reflecting a broader challenge in digital health: balancing the added value of continuous data collection with realistic expectations about clinical responsibility and system responsiveness. As highlighted by Bull et al. (2022), the successful implementation of patient-reported outcome and experience measures requires clearly defined accountability structures, alignment with institutional priorities, and integration into existing health system processes to ensure sustainability [24]. Novel methods, such as Data-Enabled Design, present promising solutions by drawing on data generated by users to progressively adjust systems in response to real-world application. While this approach supports flexible, context-aware solutions, its exploratory and iterative character may conflict with the strict, standardized protocols required for assessing safety and efficacy in clinical trial settings [123]. Future pediatric digital health solutions could benefit from such adaptive methodologies to align continuous data collection with feasible clinical workflows and responsiveness expectations. These approaches should also account for contextual factors and resource constraints, as technologies often face challenges in scale-up and sustainability if user, organizational, and system-level considerations are not addressed [56].

Beyond these operational considerations, the broader conceptual landscape of pediatric digital health solutions warrants reflection. While the field is rapidly evolving, tools either focus on narrow aspects of care or try to offer a comprehensive approach. This raises a fundamental question for future developments: should we pursue integrated platforms that combine multiple care functions (one-size-fits-all), such as symptom monitoring, psychosocial support, and communication facilitation, or rely on separate, specialized applications? Both strategies entail significant trade-offs. Holistic platforms promise convenience and continuity but risk becoming overly complex, insufficiently differentiating and difficult to maintain [47, 155]. Multiple specialized tools may create fragmentation, increase cognitive burden for families, complicate clinical workflows, and make the digital health landscape increasingly difficult to navigate [27]. These challenges are further amplified by concerns about whether ePRO-based measures, validated for research, are appropriate for other uses such as clinical decision-making [27]. The lack of explicit guidelines for pediatric ePRO implementation adds another layer of complexity. This hampers standardization of practices and comparability across settings [34]. Future research must address not only which patient populations benefit most from continuous ePRO-based monitoring, but also which design paradigm, i.e., comprehensive versus modular, offers the greatest clinical and practical value. Adaptive strategies that balance coverage and usability while minimizing burden will be critical for optimizing outcomes and resource allocation [5]. Overly numerous or nonessential questions can cause participants to lose engagement and view the collection of PROs as burdensome

rather than advantageous [5, 161]. Inappropriate recall periods can further increase respondent burden [121]. The use of multiple ePROs similarly increases time demands and patient burden [141]. Tailored approaches, for example computer-adaptive testing utilizing item response theory, have been proposed to minimize irrelevant items for individual respondents [167]. Beyond instrument design, structured assessment of perceived response burden may help refine ePRO implementation. Atkinson et al. created the Response Burden Questionnaire, a six-item instrument designed to assess how patients perceive a questionnaire's relevance, comfort, length, repetitiveness, and the extent to which it represents their health experiences [9]. Although originally validated in adult populations, such instruments could inform future pediatric-specific adaptations and evaluation of ePRO usability. Eventually, regulatory frameworks and professional guidelines must evolve to support safe and evidence-based integration of these digital health solutions. Taken together, these insights suggest pathways to optimize ePRO-based digital health platforms for pediatric oncology and palliative care.

4.12 Conclusions

MyPal4Kids represents one of the first efforts to evaluate a gamified, ePRO-based digital health platform for pediatric oncology and palliative care in real-world clinical settings. Beyond technical feasibility, this study examined how young patients, caregivers, and HCPs engaged with the platform and what factors influenced its usability and perceived value.

A core aim of the MyPal platform was to promote patient-centered care by fostering active engagement and improving communication between patients, families, and clinicians. The study demonstrates that digital health solutions can support these goals, but only under specific conditions. Successful implementation and sustained engagement depend on three interrelated factors: developmentally sensitive design, mechanisms that validate and act upon reported data, and integration into clinical workflows with active clinician engagement. Timely feedback, perceived relevance, and motivational features further reinforce engagement, while personalized, age-appropriate design are essential for long-term adherence. Participant feedback also highlighted challenges such as heterogeneous engagement among patients and families and varying clinician time commitments, underscoring the need for adaptable, resource-sensitive integration strategies.

Future iterations should leverage continuous user feedback, diversify engagement strategies, and ensure timely feedback from HCPs. Emerging technologies, such as wearable integration and adaptive algorithms, should be considered thoughtfully while maintaining scalability across care contexts. Comprehensiveness must be balanced with high usability to ensure accessibility and sustainability.

Larger, long-term studies, including randomized controlled trials, are necessary to determine clinical effectiveness, cost-efficiency, and optimal use cases. Ultimately, ePRO-based platforms like the one tested in the *MyPal4Kids* study can advance personalized, empathetic care if they remain user-centered, clinically integrated, and adaptable to needs of all users.

References

1. Aanes SG, Wiig S, Nieder C, Haukland EC (2024) Implementing digital patient-reported outcomes in routine cancer care: barriers and facilitators. ESMO Real World Data and Digital Oncology 6:100088. doi: 10.1016/j.esmorw.2024.100088
2. Adams M, Taylor RM (2025) Developing patient reported outcome measures for children with cancer: A current perspective. EJC Paediatr Oncol 6:100312. doi: 10.1016/j.ejcped.2025.100312
3. Agresti A (1980) Generalized Odds Ratios for Ordinal Data. Biometrics 36:59–67. doi: 10.2307/2530495
4. Aiyegbusi OL, Kyte D, Cockwell P, Marshall T, Dutton M, Walmsley-Allen N, Slade A, McMullan C, Calvert M (2019) Patient and Clinician Perspectives on Electronic Patient-Reported Outcome Measures in the Management of Advanced CKD: A Qualitative Study. Am J Kidney Dis 74:167–178. doi: 10.1053/j.ajkd.2019.02.011
5. Aiyegbusi OL, Roydhouse J, Rivera SC, Kamudoni P, Schache P, Wilson R, Stephens R, Calvert M (2022) Key considerations to reduce or address respondent burden in patient-reported outcome (PRO) data collection. Nat Commun 13:6026. doi: 10.1038/s41467-022-33826-4
6. Alarilla A, Sebire NJ, Keith J, Cortina-Borja M, Wray J, Davies G (2025) A scoping review of the electronic collection and capture of patient reported outcome measures for children and young people in the hospital setting. PLOS Digit Health 4:e0000704. doi: 10.1371/journal.pdig.0000704
7. Alpert JM, Dyer KE, Lafata JE (2017) Patient-centered communication in digital medical encounters. Patient Educ Couns 100:1852–1858. doi: 10.1016/j.pec.2017.04.019
8. Anderson NE, McMullan C, Calvert M, Dutton M, Cockwell P, Aiyegbusi OL, Kyte D (2021) Using patient-reported outcome measures during the management of patients with end-stage kidney disease requiring treatment with haemodialysis (PROM-HD): a qualitative study. BMJ Open 11:e052629. doi: 10.1136/bmjopen-2021-052629

9. Atkinson TM, Schwartz CE, Goldstein L, Garcia I, Storfer DF, Li Y, Zhang J, Bochner BH, Rapkin BD (2019) Perceptions of Response Burden Associated with Completion of Patient-Reported Outcome Assessments in Oncology. Value Health 22:225–230. doi: 10.1016/j.jval.2018.07.875

10. Basch E, Barbera L, Kerrigan CL, Velikova G (2018) Implementation of Patient-Reported Outcomes in Routine Medical Care. Am Soc Clin Oncol Educ Book 38:122–134. doi: 10.1200/EDBK_200383

11. Basch E, Deal AM, Dueck AC, Scher HI, Kris MG, Hudis C, Schrag D (2017) Overall Survival Results of a Trial Assessing Patient-Reported Outcomes for Symptom Monitoring During Routine Cancer Treatment. JAMA 318:197–198. doi: 10.1001/jama.2017.7156

12. Basch E, Deal AM, Kris MG, Scher HI, Hudis CA, Sabbatini P, Rogak L, Bennett A V., Dueck AC, Atkinson TM, Chou JF, Dulko D, Sit L, Barz A, Novotny P, Fruscione M, Sloan JA, Schrag D (2016) Symptom Monitoring With Patient-Reported Outcomes During Routine Cancer Treatment: A Randomized Controlled Trial. Journal of Clinical Oncology 34:557–565. doi: 10.1200/JCO.2015.63.0830

13. Benini F, Papadatou D, Bernadá M, Craig F, De Zen L, Downing J, Drake R, Friedrichsdorf S, Garros D, Giacomelli L, Lacerda A, Lazzarin P, Marceglia S, Marston J, Muckaden MA, Papa S, Parravicini E, Pellegatta F, Wolfe J (2022) International Standards for Pediatric Palliative Care: From IMPaCCT to GO-PPaCS. J Pain Symptom Manage 63:e529–e543. doi: 10.1016/j.jpainsymman.2021.12.031

14. Blazin L, Cecchini C, Habashy C, Kaye E, Baker J (2018) Communicating Effectively in Pediatric Cancer Care: Translating Evidence into Practice. Children (Basel) 5:40. doi: 10.3390/children5030040

15. Bonotis P, Angelidis P, Natsiavas P (2025) Usability and User Experience Testing of a Co-Designed Electronic Patient-Reported Outcomes App (“MyPal for Adults”) for Palliative Cancer Care: Mixed Methods Study. JMIR Hum Factors 12:e57342. doi: 10.2196/57342

16. Bonotis P, Chytas A, Zacharioudakis G, Karamanidou C, Koumakis L, Stamatopoulos K, Natsiavas P (2021) Randomization of Clinical Trial Participants via an Integrated Web Service. In: Mantas J, Stoicu-Tivadar L, Chronaki C, Hasman A, Weber P, Gallos P, Crişan-Vida M, Zoulias E, Chirila O (eds) Public Health and Informatics: Proceedings of MIE 2021 (Stud Health Technol Inform). IOS Press, Amsterdam, pp 1124–1125

17. Bonotis P, Meyerheim M, Kakalou C, Scarfo L, Natsiavas P, Karamanidou C (2025) Enhancing Healthcare Professionals' Adherence to the MyPal Project Digital Health Intervention Protocol Through Quick Reference Guides. In: Andrikopoulou E, Gallos P, Arvanitis T, Austin R, Benis A, Cornert R, Panagiotis C, Dejaco A, Dusseljee-Peute L, Mohasseb A, Natsiavas P, Nakkas H, Scott P (eds) Intelligent Health Systems – From Technology to Data and Knowledge: Proceedings of MIE 2025 (Stud Health Technol Inform). IOS Press, Amsterdam, pp 283–287

18. Bonotis P, Natsiavas P (2023) Physician-Reported Experience and Usability of the MyPal Platform: A Palliative Care Digital Health Intervention. In: Hägglund M, Blusi M, Bonacina S, Nilsson L, Cort Madsen I, Pelayo S, Moen A, Benis A, Lindsköld L, Gallos P (eds) Caring is Sharing – Exploiting the Value in Data for Health and Innovation: Proceedings of MIE 2023 (Stud Health Technol Inform). IOS Press, Amsterdam, pp 686–687

19. Boyce MB, Browne JP (2013) Does providing feedback on patient-reported outcomes to healthcare professionals result in better outcomes for patients? A systematic review. Qual Life Res 22:2265–2278. doi: 10.1007/s11136-013-0390-0

20. Boyce MB, Browne JP, Greenhalgh J (2014) The experiences of professionals with using information from patient-reported outcome measures to improve the quality of healthcare: a systematic review of qualitative research. BMJ Qual Saf 23:508–518. doi: 10.1136/bmjqs-2013-002524

21. Bravo L, Killela MK, Reyes BL, Santos KMB, Torres V, Huang C-C, Jacob E (2020) Self-Management, Self-Efficacy, and Health-Related Quality of Life in Children With Chronic Illness and Medical Complexity. J Pediatr Health Care 34:304–314. doi: 10.1016/j.pedhc.2019.11.009

22. Brédart A, Anota A, Young T, Tomaszewski KA, Arraras JI, Moura De Albuquerque Melo H, Schmidt H, Friend E, Bergenmar M, Costantini A, Vassiliou V, Hureaux J, Marchal F, Tomaszewska IM, Chie W-C, Ramage J, Beaudeau A, Conroy T, Bleiker E, Kulis D, Bonnetain F, Aaronson NK (2018) Phase III study of the European Organisation for Research and Treatment of Cancer satisfaction with cancer care core questionnaire (EORTC PATSAT-C33) and specific complementary outpatient module (EORTC OUT-PATSAT7). Eur J Cancer 27:e12786. doi: 10.1111/ecc.12786

23. Brédart A, Beaudeau A, Young T, Moura De Alberquerque Melo H, Arraras JI, Friend L, Schmidt H, Tomaszewski KA, Bergenmar M, Anota A, Costantini A, Marchal F, Tomaszewska IM, Vassiliou V, Chie W, Hureaux J, Conroy T, Ramage J, Bonnetain F, Kulis D, Aaronson NK (2017) The European organization for research and treatment of

cancer — satisfaction with cancer care questionnaire: revision and extended application development. Psychosoc Oncol 26:400–404. doi: 10.1002/pon.4127

24. Bull C, Teede H, Watson D, Callander EJ (2022) Selecting and Implementing Patient-Reported Outcome and Experience Measures to Assess Health System Performance. JAMA Health Forum 3:e220326. doi: 10.1001/jamahealthforum.2022.0326

25. Chatzikonstantinou T, Vasilopoulou M, Kyrou D, Karakatsoulis G, Argyropaidas P, Besikli-Dimou S, Bonotis P, Chatzimina M, Didi J, Dimosthenous C, Garani-Papadatos T, Hoffman S, Kakalou C, Kazantzaki E, Kiefer S, Koumakis L, Ling J, Maramis C, Meyerheim M, Payne C, Papangelou C, Payne S, Pontikoglou C, Reston R, Ryblom H, Sander A, Schera F, Smedby KE, Zacharioudakis G, Chatzidimitriou A, Doubek M, Stavroyianni N, Ghia P, Papadaki HA, Rosenquist R, Graf N, Natsiavas P, Stamatopoulos K, Karamanidou C, Scarfò L (2025) Assessing an eHealth Intervention on Quality of Life in Patients With Chronic Lymphocytic Leukemia and Myelodysplastic Syndromes: The MyPal Randomized Controlled Trial. JCO Oncol Pract OP2500087. doi: 10.1200/OP-25-00087

26. Cheng L, Liu F, Feng S, Wang Y, Gu Y, Kang Q (2019) Symptom Experience of Children With Cancer Younger Than Eight Years of Age: An Integrative Review. J Pain Symptom Manage 58:157–166. doi: 10.1016/j.jpainsymman.2019.03.021

27. Churruca K, Pomare C, Ellis LA, Long JC, Henderson SB, Murphy LED, Leahy CJ, Braithwaite J (2021) Patient-reported outcome measures (PROMs): A review of generic and condition-specific measures and a discussion of trends and issues. Health Expect 24:1015–1024. doi: 10.1111/hex.13254

28. Cohen J (2013) Statistical Power Analysis for the Behavioral Sciences, 2nd ed. Routledge, Hillsdale, NJ

29. Collins JJ, Byrnes ME, Dunkel IJ, Lapin J, Nadel T, Thaler HT, Polyak T, Rapkin B, Portenoy RK (2000) The Measurement of Symptoms in Children with Cancer. J Pain Symptom Manage 19:363–377. doi: 10.1016/S0885-3924(00)00127-5

30. Coolbrandt A, Van den Heede K, Vanhove E, De Bom A, Milisen K, Wildiers H (2011) Immediate versus delayed self-reporting of symptoms and side effects during chemotherapy: Does timing matter? Eur J Oncol Nurs 15:130–136. doi: 10.1016/j.ejon.2010.06.010

31. Coombes L, Bristowe K, Ellis-Smith C, Aworinde J, Fraser LK, Downing J, Bluebond-Langner M, Chambers L, Murtagh FEM, Harding R (2021) Enhancing validity, reliability and participation in self-reported health outcome measurement for children and young

people: a systematic review of recall period, response scale format, and administration modality. Qual Life Res 30:1803–1832. doi: 10.1007/s11136-021-02814-4

32. Coombes L, Harðardóttir D, Braybrook D, Roach A, Scott H, Bristowe K, Ellis-Smith C, Downing J, Bluebond-Langner M, Fraser LK, Murtagh FEM, Harding R (2023) Design and Administration of Patient-Centred Outcome Measures: The Perspectives of Children and Young People with Life-Limiting or Life-Threatening Conditions and Their Family Members. Patient 16:473–483. doi: 10.1007/s40271-023-00627-w

33. Coons SJ, Eremenco S, Lundy JJ, O'Donohoe P, O'Gorman H, Malizia W (2015) Capturing Patient-Reported Outcome (PRO) Data Electronically: The Past, Present, and Promise of ePRO Measurement in Clinical Trials. J Patient Rep Outcomes 8:301–309. doi: 10.1007/s40271-014-0090-z

34. Cracchiolo JR, Arafat W, Atreja A, Bruckner L, Emamekhoo H, Heinrichs T, Raldow AC, Smerage J, Stetson P, Sugalski J, Tevaarwerk AJ (2023) Getting ready for real-world use of electronic patient-reported outcomes (ePROs) for patients with cancer: A National Comprehensive Cancer Network ePRO Workgroup paper. Cancer 129:2441–2449. doi: 10.1002/cncr.34844

35. Crane S, Ganci A, Robb SL, Gibbs KD, Nosich R, Miller AD (2025) Development of an electronic system for self/proxy symptom tracking alongside children with cancer and their caregivers: a co-design exemplar. Support Care Cancer 33:810. doi: 10.1007/s00520-025-09865-0

36. Denis F, Basch E, Septans A-L, Bennouna J, Urban T, Dueck AC, Letellier C (2019) Two-Year Survival Comparing Web-Based Symptom Monitoring vs Routine Surveillance Following Treatment for Lung Cancer. JAMA 321:306–307. doi: 10.1001/jama.2018.18085

37. Deterding S, Dixon D, Khaled R, Nacke L (2011) From game design elements to gamefulness: defining "gamification." In: Proceedings of the 15th International Academic MindTrek Conference: Envisioning Future Media Environments. ACM, New York, NY, USA, pp 9–15

38. Dobrozsi S, Yan K, Hoffmann R, Panepinto J (2017) Patient-reported health status during pediatric cancer treatment. Pediatr Blood Cancer 64:e26295. doi: 10.1002/pbc.26295

39. Doig M, Cunningham A, Bedford V, Le H, O'Connor M, Bezak E, Parange N, Hutchinson A, Gorayski P, Short M (2025) Healthcare Professional Perspectives on

Digital Health-Related Quality-of-Life Assessment in Paediatric Radiation Therapy: A Qualitative Study. J Med Radiat Sci. doi: 10.1002/jmrs.880

40. Downing J, Chambers L, Daniels A, Ling J, Hamzah E, Luyirika E, Okhuysen-Cawley R, Doherty M, Baker JN (2025) Mapping of Children's Palliative Care Development Globally in 2023. Children (Basel) 12:440. doi: 10.3390/children12040440

41. Dreher J, Meryk A, Giesinger JM, Schneeberger-Carta V, Riedl D, Haid A, Kropshofer G, Hetzer B, Rumpold G, Holzner B, Crazzolara R, Lehmann J (2025) Adherence to daily electronic symptom screening in pediatric cancer: associations with time, location and pain. Qual Life Res 34:2363–2375. doi: 10.1007/s11136-025-04002-0

42. Dupuis LL, Johnston DL, Baggott C, Hyslop S, Tomlinson D, Gibson P, Orsey A, Dix D, Price V, Vanan M, Portwine C, Kuczynski S, Spiegler B, Tomlinson GA, Sung L (2018) Validation of the Symptom Screening in Pediatrics Tool in Children Receiving Cancer Treatments. J Natl Cancer Inst 110:661–668. doi: 10.1093/jnci/djx250

43. Dupuis LL, Lu X, Mitchell H, Sung L, Devidas M, Mattano LA, Carroll WL, Winick N, Hunger SP, Maloney KW, Kadan-Lottick NS (2016) Anxiety, pain, and nausea during the treatment of standard-risk childhood acute lymphoblastic leukemia: A prospective, longitudinal study from the Children's Oncology Group. Cancer 122:1116–1125. doi: 10.1002/cncr.29876

44. Dupuis LL, Vettese E, Aftandilian C, Agarwal V, Baggott C, Bradfield SM, Crellin-Parsons N, Freyer DR, Kelly KM, King AA, Kyono W, Nagasubramanian R, Orgel E, Roth ME, Sherani F, Yu L, Grimes AC, Beauchemin MP, Klesges LM, Tomlinson GA, Sung L (2025) Factors Associated With Self-Report Symptom Screening Adherence in Pediatric Cancer Patients. Cancer Med 14:e71053. doi: 10.1002/cam4.71053

45. Dupuis LL, Vettese E, Grimes AC, Beauchemin MP, Klesges LM, Baggott C, Demedis J, Aftandilian C, Freyer DR, Crellin-Parsons N, Orgel E, Dickens D, Kelly KM, Kyono W, Walsh A, Sherani F, Cannone D, Orsey AD, King AA, Yu L, Woods-Swafford W, Bradfield SM, Roth ME, Esbenshade AJ, Caywood EH, Agarwal V, Nagasubramanian R, Tomlinson GA, Sung L (2024) Symptom Screening Linked to Care Pathways for Pediatric Patients With Cancer. JAMA 332:1981–1991. doi: 10.1001/jama.2024.19585

46. Escriva Boulley G, Leroy T, Bernetière C, Paquienseguy F, Desfriches-Doria O, Préau M (2018) Digital health interventions to help living with cancer: A systematic review of participants' engagement and psychosocial effects. Psychooncology 27:2677–2686. doi: 10.1002/pon.4867

47. Fleming T, Merry S, Stasiak K, Hopkins S, Patolo T, Ruru S, Latu M, Shepherd M, Christie G, Goodyear-Smith F (2019) The Importance of User Segmentation for Designing Digital Therapy for Adolescent Mental Health: Findings From Scoping Processes. JMIR Ment Health 6:e12656. doi: 10.2196/12656

48. Fortier MA, Chung WW, Martinez A, Gago-Masague S, Sender L (2016) Pain buddy: A novel use of m-health in the management of children's cancer pain. Comput Biol Med 76:202–214. doi: 10.1016/j.compbiomed.2016.07.012

49. Francis DO, McPheeters ML, Noud M, Penson DF, Feurer ID (2016) Checklist to operationalize measurement characteristics of patient-reported outcome measures. Sys Rev 5:129. doi: 10.1186/s13643-016-0307-4

50. Gale NK, Heath G, Cameron E, Rashid S, Redwood S (2013) Using the framework method for the analysis of qualitative data in multi-disciplinary health research. BMC Med Res Methodol 13:117. doi: 10.1186/1471-2288-13-117

51. Garani-Papadatos T, Natsiavas P, Meyerheim M, Hoffmann S, Karamanidou C, Payne SA (2022) Ethical Principles in Digital Palliative Care for Children: The MyPal Project and Experiences Made in Designing a Trustworthy Approach. Front Digit Health 4:730430. doi: 10.3389/fdgth.2022.730430

52. Gensheimer SG, Wu AW, Snyder CF (2018) Oh, the Places We'll Go: Patient-Reported Outcomes and Electronic Health Records. Patient 11:591–598. doi: 10.1007/s40271-018-0321-9

53. Girgis A, Durcinoska I, Arnold A, Delaney GP (2019) Interpreting and Acting on the PRO Scores From the Patient-reported Outcomes for Personalized Treatment and Care (PROMPT-Care) eHealth System. Med Care 57:S85–S91. doi: 10.1097/MLR.0000000000001094

54. Van Gorp M, Irestorm E, Twisk JWR, Dors N, Mavinkurve-Groothuis A, Meeteren AYNS van, de Bont J, van den Bergh EMM, van der Meer W van de P, Beek LR, Aarsen FK, Streefkerk N, van Litsenburg RRL, Grootenhuis MA (2023) The course of health-related quality of life after the diagnosis of childhood cancer: a national cohort study. BMC Cancer 23:855. doi: 10.1186/s12885-023-11379-z

55. Greenhalgh T, Maylor H, Shaw S, Wherton J, Papoutsi C, Betton V, Nelissen N, Gremyr A, Rushforth A, Koshkouei M, Taylor J (2020) The NASSS-CAT Tools for Understanding, Guiding, Monitoring, and Researching Technology Implementation Projects in Health and Social Care: Protocol for an Evaluation Study in Real-World Settings. JMIR Res Protoc 9:e16861. doi: 10.2196/16861

56. Greenhalgh T, Wherton J, Papoutsi C, Lynch J, Hughes G, A'Court C, Hinder S, Fahy N, Procter R, Shaw S (2017) Beyond Adoption: A New Framework for Theorizing and Evaluating Nonadoption, Abandonment, and Challenges to the Scale-Up, Spread, and Sustainability of Health and Care Technologies. J Med Internet Res 19:e367. doi: 10.2196/jmir.8775

57. Greenzang KA, Montgomery KE, DuVall A, Roth ME, Krailo M, Nuño MM, Renfro L, DelRocco N, Doski J, Kelly K, Castellino SM, McNeer J, O'Brien MM, Reed D, Janeway K, Hinds PS, Zupanec S, Parsons SK (2025) Incorporation of patient-reported outcomes in pediatric cancer clinical trials: design, implementation, and dissemination. J Natl Cancer Inst 117:1764–1773. doi: 10.1093/jnci/djaf083

58. Guo C, Ashrafian H, Ghafur S, Fontana G, Gardner C, Prime M (2020) Challenges for the evaluation of digital health solutions—A call for innovative evidence generation approaches. npj Digit Med 3:110. doi: 10.1038/s41746-020-00314-2

59. Hawkins M, Elsworth GR, Osborne RH (2018) Application of validity theory and methodology to patient-reported outcome measures (PROMs): building an argument for validity. Qual Life Res 27:1695–1710. doi: 10.1007/s11136-018-1815-6

60. Helmefalk M (2019) An interdisciplinary perspective on gamification: Mechanics, psychological mediators and outcomes. Int J Serious Games 6:3–26. doi: 10.17083/ijsg.v6i1.262

61. Heneghan MB, Parsons SK, Keller FG, Renfro LA, Pei Q, Rodday AM, Wu Y, Punnett A, Belsky JA, Henderson TO, Kelly KM, Castellino SM (2025) Protocol-Stipulated Dose Modification to Manage Chemotherapy-Induced Peripheral Neuropathy in Children, Adolescents, and Young Adults With High-Risk Hodgkin Lymphoma. JCO Oncol Pract 21:526–534. doi: 10.1200/OP.24.00089

62. Hinds PS, Nuss SL, Ruccione KS, Withycombe JS, Jacobs S, DeLuca H, Faulkner C, Liu Y, Cheng YI, Gross HE, Wang J, DeWalt DA (2013) PROMIS pediatric measures in pediatric oncology: Valid and clinically feasible indicators of patient-reported outcomes. Pediatr Blood Cancer 60:402–408. doi: 10.1002/pbc.24233

63. Hockenberry MJ, Hooke MC, Rodgers C, Taylor O, Koerner KM, Mitby P, Moore I, Scheurer ME, Pan W (2017) Symptom Trajectories in Children Receiving Treatment for Leukemia: A Latent Class Growth Analysis With Multitrajectory Modeling. J Pain Symptom Manage 54:1–8. doi: 10.1016/j.jpainsymman.2017.03.002

64. Hoffmann S, Schraut R, Kröll T, Scholz W, Belova T, Erhardt J, Gollmer D, Mauck C, Zacharioudakis G, Meyerheim M, Bonotis P, Kakalou C, Chatzimina M, Karamanidou

C, Sander A, Didi J, Graf N, Natsiavas P (2021) AquaScouts: ePROs Implemented as a Serious Game for Children With Cancer to Support Palliative Care. Front Digit Health 3:1–10. doi: 10.3389/fdgth.2021.730948

65. Holch P, Turner G, Keetharuth AD, Gibbons E, Cocks K, Absolom KL (2023) The impact of COVID-19 on PRO development, collection and implementation: views of UK and Ireland professionals. J Patient Rep Outcomes 7:121. doi: 10.1186/s41687-023-00663-y

66. Holmen H, Winger A, Steindal SA, Riiser K, Castor C, Kvarme LG, Mariussen KL, Lee A (2023) Patient-reported outcome measures in children, adolescents, and young adults with palliative care needs—a scoping review. BMC Palliat Care 22:148. doi: 10.1186/s12904-023-01271-9

67. Hooke MC, Linder LA (2019) Symptoms in Children Receiving Treatment for Cancer—Part I: Fatigue, Sleep Disturbance, and Nausea/Vomiting. J Pediatr Oncol Nurs 36:244–261. doi: 10.1177/1043454219849576

68. Horan MR, Sim J, Krull KR, Baker JN, Huang I-C (2022) A Review of Patient-Reported Outcome Measures in Childhood Cancer. Children (Basel) 9:1497. doi: 10.3390/children9101497

69. Horan MR, Sim J, Krull KR, Ness KK, Yasui Y, Robison LL, Hudson MM, Baker JN, Huang I-C (2023) Ten Considerations for Integrating Patient-Reported Outcomes into Clinical Care for Childhood Cancer Survivors. Cancers (Basel) 15:1024. doi: 10.3390/cancers15041024

70. Huang X, Xiang X, Liu Y, Wang Z, Jiang Z, Huang L (2023) The Use of Gamification in the Self-Management of Patients With Chronic Diseases: Scoping Review. JMIR Serious Games 11:e39019. doi: 10.2196/39019

71. Hubel NJ, Vorbach SM, de Ligt KM, Rathgeber IS, Beyer K, Wintner LM, Faller B, Nemec J, Holzner B, Sztankay M, Lehmann J (2025) Sustainability and Time Trends in Electronic Patient-Reported Outcome Assessment in Routine Cancer Care: Systematic Scoping Review and Follow-Up Survey. J Med Internet Res 27:e69398. doi: 10.2196/69398

72. Irestorm E, Bakker A, Tissing WJE, Maurice-Stam H, Dors N, Mavinkurve-Groothuis A, Plasschaert SLA, van Bindsbergen KLA, Grootenhuis MA, van Litsenburg RRL (2025) Benchmarking the pediatric quality of life (PedsQL) cancer module in a large Dutch national cohort of childhood cancer patients. BMC Cancer 25:915. doi: 10.1186/s12885-025-14322-6

73. Isabel Tan XW, Mordiffi SZ, Lopez V, Leong K (2021) Psychological Distress in Parents of Children with Cancer: A Descriptive Correlational Study. Asia Pac J Oncol Nurs 8:94–102. doi: 10.4103/apjon.apjon_46_20

74. Jackman L, Kamran R (2025) Transforming Patient-Reported Outcome Measurement With Digital Health Technology. J Eval Clin Pract 31:e70107. doi: 10.1111/jep.70107

75. Janssens A, Thompson Coon J, Rogers M, Allen K, Green C, Jenkinson C, Tennant A, Logan S, Morris C (2015) A Systematic Review of Generic Multidimensional Patient-Reported Outcome Measures for Children, Part I: Descriptive Characteristics. Value Health 18:315–333. doi: 10.1016/j.jval.2014.12.006

76. Jensen LWH, Ghaffari A, Rahbek O, Dinesen B, Kold S (2024) The use of asynchronous digital two-way communication between patients and healthcare professionals after hospital discharge: A scoping review. Patient Educ Couns 128:108393. doi: 10.1016/j.pec.2024.108393

77. Jessen S, Mirkovic J, Ruland CM (2018) Creating Gameful Design in mHealth: A Participatory Co-Design Approach. JMIR Mhealth Uhealth 6:e11579. doi: 10.2196/11579

78. Jibb LA, Stevens BJ, Nathan PC, Seto E, Cafazzo JA, Johnston DL, Hum V, Stinson JN (2017) Implementation and preliminary effectiveness of a real-time pain management smartphone app for adolescents with cancer: A multicenter pilot clinical study. Pediatr Blood Cancer 64:e26554. doi: 10.1002/pbc.26554

79. Van Kalsbeek RJ, Grundeken LH, Mulder RL, Hudson MM, Ehrhardt MJ, den Hartogh JG, Riezebos RJ, van Tinteren H, Kollen WJW, Grootenhuis MA, Pieters R, Kremer LCM, van der Heiden-van der Loo M, Aarsen FK, Bouts MJRJ, Dierselhuis MP, Feijen EAM, Franke NE, Goemans BF, de Haas V, Hoving EW, Heitink-Polle KMJ, Kilsdonk E, Lindemans CA, Meijer L, Merks H, Meyer-Wentrup FAG, Mavinkurve-Groothuis AMC, Oomen DWGD, Partanen M, Plasschaert SLA, Schouten-Meeteren AYN, Teepen JC, van den Bos C, van den Heuvel-Eibrink MM, van Grotel M, van Litsenburg RRL, van Noesel MM, van Santen HM, Vincent MJ, Vormoor HJ, van Vuurden D, Wijnen MHWA, Zsiros J (2025) A structured approach for data collection and visualization of the International Childhood Cancer Core Outcomes. EJC Paediatr Oncol 5:100239. doi: 10.1016/j.ejcped.2025.100239

80. Karamanidou C, Natsiavas P, Koumakis L, Marias K, Schera F, Schäfer M, Payne S, Maramis C (2020) Electronic Patient-Reported Outcome–Based Interventions for

Palliative Cancer Care: A Systematic and Mapping Review. JCO Clin Cancer Inform 647–656. doi: 10.1200/CCI.20.00015

81. Karamanidou Christina, Maramis Christos, Stamatopoulos Kostas, Koutkias Vassilis (2020) Development of a ePRO-Based Palliative Care Intervention for Cancer Patients: A Participatory Design Approach. In: Pape-Haugaard L, Lovis C, Madsen I, Weber P, Hostrup Nielsen P, Scott P (eds) Digital Personalized Health and Medicine: Proceesdings of MIE 2020 (Stud Health Technol Inform). IOS Press, Amsterdam, pp 941–945

82. Karnofsky DA, Abelmann WH, Craver LF, Burchenal JH (1948) The use of the nitrogen mustards in the palliative treatment of carcinoma. With particular reference to bronchogenic carcinoma. Cancer 1:634–656. doi: 10.1002/1097-0142(194811)1:4<634::AID-CNCR2820010410>3.0.CO;2-L

83. Kato PM, Cole SW, Bradlyn AS, Pollock BH (2008) A Video Game Improves Behavioral Outcomes in Adolescents and Young Adults With Cancer: A Randomized Trial. Pediatrics 122:e305–e317. doi: 10.1542/peds.2007-3134

84. Kay M, Elkin LA, Higgins JJ, Wobbrock JO (2021) ARTool: Aligned Rank Transform for Nonparametric Factorial ANOVAs

85. Keuper J, van Tuyl LHD, de Geit E, Rijpkema C, Vis E, Batenburg R, Verheij R (2024) The impact of eHealth use on general practice workload in the pre-COVID-19 era: a systematic review. BMC Health Serv Res 24:1099. doi: 10.1186/s12913-024-11524-9

86. Kim S, Wilson P, Abraham O (2024) Investigating the Use of Serious Games for Cancer Control Among Children and Adolescents: Scoping Review. JMIR Serious Games 12:e58724. doi: 10.2196/58724

87. Klages KL, James RN, Kain ZN, Phipps S, Alberts NM, Fortier MA (2025) Biopsychosocial risk factors for pain in early phases of pediatric cancer treatment. Front Psychol 16:1507560. doi: 10.3389/fpsyg.2025.1507560

88. Klassen AF, Anthony SJ, Khan A, Sung L, Klaassen R (2011) Identifying determinants of quality of life of children with cancer and childhood cancer survivors: a systematic review. Support Care Cancer 19:1275–1287. doi: 10.1007/s00520-011-1193-x

89. Klock ACT, Gasparini I, Pimenta MS, Hamari J (2020) Tailored gamification: A review of literature. Int J Hum Comput Stud 144:102495. doi: 10.1016/j.ijhcs.2020.102495

90. Koenig C, Ammann RA, Brack E (2025) Non-invasive wearable devices in paediatric cancer care: Advancing personalized medicine, addressing challenges and shaping the future. EJC Paediatr Oncol 5:100220. doi: 10.1016/j.ejcped.2025.100220

91. Kondylakis H, Axenie C, (Kiran) Bastola D, Katehakis DG, Kouroubali A, Kurz D, Larburu N, Macía I, Maguire R, Maramis C, Marias K, Morrow P, Muro N, Núñez-Benjumea FJ, Rampun A, Rivera-Romero O, Scotney B, Signorelli G, Wang H, Tsiknakis M, Zwiggelaar R (2020) Status and Recommendations of Technological and Data-Driven Innovations in Cancer Care: Focus Group Study. J Med Internet Res 22:e22034. doi: 10.2196/22034

92. Kotronoulas G, Kearney N, Maguire R, Harrow A, Di Domenico D, Croy S, MacGillivray S (2014) What Is the Value of the Routine Use of Patient-Reported Outcome Measures Toward Improvement of Patient Outcomes, Processes of Care, and Health Service Outcomes in Cancer Care? A Systematic Review of Controlled Trials. J Clin Oncol 32:1480–1501. doi: 10.1200/JCO.2013.53.5948

93. Koumakis L, Schera F, Parker H, Bonotis P, Chatzimina M, Argyropaidas P, Zacharioudakis G, Schäfer M, Kakalou C, Karamanidou C, Didi J, Kazantzaki E, Scarfo L, Marias K, Natsiavas P (2021) Fostering Palliative Care Through Digital Intervention: A Platform for Adult Patients With Hematologic Malignancies. Front Digit Health 3:730722. doi: 10.3389/fdgth.2021.730722

94. Kyrou D, Bonotis P, Kakalou C, Vasilopoulou M, Scarfò L, Meyerheim M, Sander A, Arpáš T, Kazantzaki E, Maramis C, Karamanidou C (2025) Perceptions and Needs of Stakeholders Regarding MyPal Project's Electronic Patient-Reported Outcome App: Cross-Sectional Qualitative Focus Group Study. JMIR Cancer 11:e57388. doi: 10.2196/57388

95. Laitio A-M, Giunti G, Halonen R (2023) Perceived Barriers and Facilitators in Using Patient-Reported Outcome Systems for Cancer Care: Systematic Mapping Study. JMIR Cancer 9:e40875. doi: 10.2196/40875

96. Leahy AB, Feudtner C, Basch E (2018) Symptom Monitoring in Pediatric Oncology Using Patient-Reported Outcomes: Why, How, and Where Next. Patient 11:147–153. doi: 10.1007/s40271-017-0279-z

97. Leahy AB, Schwartz LA, Li Y, Reeve BB, Bekelman JE, Aplenc R, Basch EM (2021) Electronic symptom monitoring in pediatric patients hospitalized for chemotherapy. Cancer 127:2980–2989. doi: 10.1002/cncr.33617

98. Linder LA, Newman AR, Stegenga K, Chiu Y-S, Wawrzynski SE, Kramer H, Weir C, Narus S, Altizer R (2021) Feasibility and acceptability of a game-based symptom-reporting app for children with cancer: perspectives of children and parents. Support Cancer Care 29:301–310. doi: 10.1007/s00520-020-05495-w

99. Mack JW, McFatrich M, Withycombe JS, Maurer SH, Jacobs SS, Lin L, Lucas NR, Baker JN, Mann CM, Sung L, Tomlinson D, Hinds PS, Reeve BB (2020) Agreement Between Child Self-report and Caregiver-Proxy Report for Symptoms and Functioning of Children Undergoing Cancer Treatment. JAMA Pediatr 174:e202861. doi: 10.1001/jamapediatrics.2020.2861

100. Di Maio M, Basch E, Denis F, Fallowfield LJ, Ganz PA, Howell D, Kowalski C, Perrone F, Stover AM, Sundaresan P, Warrington L, Zhang L, Apostolidis K, Freeman-Daily J, Ripamonti CI, Santini D (2022) The role of patient-reported outcome measures in the continuum of cancer clinical care: ESMO Clinical Practice Guideline. Ann Oncol 33:878–892. doi: 10.1016/j.annonc.2022.04.007

101. Mair JL, Hashim J, Thai L, Tai ES, Ryan JC, Kowatsch T, Müller-Riemenschneider F, Edney SM (2025) Understanding and overcoming barriers to digital health adoption: a patient and public involvement study. Transl Behav Med 15:ibaf010. doi: 10.1093/tbm/ibaf010

102. Maramba I, Chatterjee A, Newman C (2019) Methods of usability testing in the development of eHealth applications: A scoping review. Int J Med Inform 126:95–104. doi: 10.1016/j.ijmedinf.2019.03.018

103. Martin A, Caon M, Adorni F, Andreoni G, Ascolese A, Atkinson S, Bul K, Carrion C, Castell C, Ciociola V, Condon L, Espallargues M, Hanley J, Jesuthasan N, Lafortuna CL, Lang A, Prinelli F, Puidomenech Puig E, Tabozzi SA, McKinstry B (2020) A Mobile Phone Intervention to Improve Obesity-Related Health Behaviors of Adolescents Across Europe: Iterative Co-Design and Feasibility Study. JMIR Mhealth Uhealth 8:e14118. doi: 10.2196/14118

104. Mattar M, Umutoni F, Hassan MA, Wamburu MW, Turner R, Patton JS, Chen X, Lei W (2024) Chemotherapy-Induced Peripheral Neuropathy: A Recent Update on Pathophysiology and Treatment. Life (Basel) 14:991. doi: 10.3390/life14080991

105. Matza LS, Patrick DL, Riley AW, Alexander JJ, Rajmil L, Pleil AM, Bullinger M (2013) Pediatric Patient-Reported Outcome Instruments for Research to Support Medical Product Labeling: Report of the ISPOR PRO Good Research Practices for the

Assessment of Children and Adolescents Task Force. Value Health 16:461–479. doi: 10.1016/j.jval.2013.04.004

106. Mercieca-Bebber R, Palmer MJ, Brundage M, Calvert M, Stockler MR, King MT (2016) Design, implementation and reporting strategies to reduce the instance and impact of missing patient-reported outcome (PRO) data: a systematic review. BMJ Open 6:e010938. doi: 10.1136/bmjopen-2015-010938

107. Meryk A, Kropshofer G, Hetzer B, Riedl D, Lehmann J, Rumpold G, Haid A, Schneeberger-Carta V, Holzner B, Crazzolara R (2022) Use of Daily Patient-Reported Outcome Measurements in Pediatric Cancer Care. JAMA Netw Open 5:e2223701. doi: 10.1001/jamanetworkopen.2022.23701

108. Merz A, Feifer D, Avery M, Tsuchiyose E, Eche I, Awofeso O, Wolfe J, Dussel V, Requena ML (2023) Patient-Reported Outcome Benefits for Children with Advanced Cancer and Parents: A Qualitative Study. J Pain Symptom Manage 66:e327–e334. doi: 10.1016/j.jpainsymman.2023.05.016

109. Meyerheim M, Burns-Gebhart A, Mirzaie K, Garani-Papadatos T, Braun Y, Graf N (2021) Challenges and Pitfalls for Implementing Digital Health Solutions in Clinical Studies in Europe. Front Digit Health 3:730680. doi: 10.3389/fdgth.2021.730680

110. Meyerheim M, Karamanidou C, Payne S, Garani-Papadatos T, Sander A, Downing J, Stamatopoulos K, Ling J, Payne C, Scarfò L, Lokaj P, Maramis C, Graf N (2021) MyPal-Child study protocol: an observational prospective clinical feasibility study of the MyPal ePRO-based early palliative care digital system in paediatric oncology patients. BMJ Open 11:e045226. doi: 10.1136/bmjopen-2020-045226

111. Michael DR, Chen SL (2005) Serious games: Games that educate, train, and inform. Muska & Lipman/Premier-Trade

112. Miller AS, Cafazzo JA, Seto E (2016) A game plan: Gamification design principles in mHealth applications for chronic disease management. Health Informatics J 22:184–193. doi: 10.1177/1460458214537511

113. Mirzaie K, Burns-Gebhart A, Meyerheim M, Sander A, Graf N (2022) Emotion Regulation Flexibility and Electronic Patient-Reported Outcomes: A Framework for Understanding Symptoms and Affect Dynamics in Pediatric Psycho-Oncology. Cancers (Basel) 14:3874. doi: 10.3390/cancers14163874

114. Mody GN, Bennett A V., Stover AM, Jonsson M, Teal R, Vu M, Carda-Auten J, Jansen J, Carr P, Dueck A, Henson S, Basch E (2025) Implementation of Symptom Monitoring With Electronic Patient-Reported Outcomes: Perspectives and Recommendations

From Community Oncology Practices (Alliance AFT-39). JCO Oncol Pract OP2400627. doi: 10.1200/OP-24-00627

115. Montgomery KE, Raybin JL, Ward J, Balian C, Gilger E, Murray P, Li Z (2020) Using Patient-Reported Outcomes to Measure Symptoms in Children With Advanced Cancer. Cancer Nurs 43:281–289. doi: 10.1097/NCC.0000000000000721

116. Moraitis AM, Iacob E, Wong B, Beck SL, Echeverria C, Donaldson G, Mooney K (2024) Pairing automated exercise coaching with patient-reported symptom monitoring: A way to nudge exercise uptake during cancer treatment? Support Care Cancer 32:258. doi: 10.1007/s00520-024-08450-1

117. Morgan TL, Clark OE, Whiteside S, Audino A, Yeager ND, Klosky JL, O'Brien SH, Quinn GP, Gerhardt CA, Nahata L (2019) Recruiting families and children newly diagnosed with cancer for behavioral research: Important considerations and successful strategies. Psychooncology 28:928–930. doi: 10.1002/pon.5012

118. Mustafa AS, Ali N, Dhillon JS, Alkawsi G, Baashar Y (2022) User Engagement and Abandonment of mHealth: A Cross-Sectional Survey. Healthcare (Basel) 10:221. doi: 10.3390/healthcare10020221

119. Navarro-Alamán J, Lacuesta R, Garcia-Magariño I, Gallardo J (2020) A methodology for the design and development of gamified mobile apps for monitoring cancer survivors. J Biomed Inform 106:103439. doi: 10.1016/j.jbi.2020.103439

120. Nobari H, Fashi M, Eskandari A, Villafaina S, Murillo-Garcia Á, Pérez-Gómez J (2021) Effect of COVID-19 on Health-Related Quality of Life in Adolescents and Children: A Systematic Review. Int J Environ Res Public Health 18:4563. doi: 10.3390/ijerph18094563

121. Norquist JM, Girman C, Fehnel S, DeMuro-Mercon C, Santanello N (2012) Choice of recall period for patient-reported outcome (PRO) measures: criteria for consideration. Qual Life Res 21:1013–1020. doi: 10.1007/s11136-011-0003-8

122. Nshimirimana DA, Kokonya D, Gitaka J, Wesonga B, Mativo JN, Rukanikigitero JMV (2023) Impact of COVID-19 on health-related quality of life in the general population: A systematic review and meta-analysis. PLOS Glob Public Health 3:e0002137. doi: 10.1371/journal.pgph.0002137

123. Ornelas HCM, Kleinsmann M, Kortuem G, van Deutekom AW (2025) Reconciling data-enabled design and clinical trials: conceptual phases for eHealth development. Proc Des Soc 5:2681–2690. doi: 10.1017/pds.2025.10282

124. Orsmond GI, Cohn ES (2015) The Distinctive Features of a Feasibility Study. OTJR (Thorofare N J) 35:169–177. doi: 10.1177/1539449215578649

125. Pan H-T, Wu L-M, Wen S-H (2017) Quality of Life and Its Predictors Among Children and Adolescents With Cancer. Cancer Nurs 40:343–351. doi: 10.1097/NCC.0000000000000433

126. Patel MS, Small DS, Harrison JD, Fortunato MP, Oon AL, Rareshide CAL, Reh G, Szwartz G, Guszcza J, Steier D, Kalra P, Hilbert V (2019) Effectiveness of Behaviorally Designed Gamification Interventions With Social Incentives for Increasing Physical Activity Among Overweight and Obese Adults Across the United States. JAMA Intern Med 179:1624–1632. doi: 10.1001/jamainternmed.2019.3505

127. Payne S, Begovic D, Salifu Y, Nelson A, Payne C, Downing J, Natsiavas P, Ling J (2024) Applying Digital Health in Cancer and Palliative Care in Europe: Policy Recommendations from an International Expert Workshop (MyPal Project). J Palliat Med 2:216–223. doi: 10.1089/jpm.2023.0309

128. Payne SA, Moore DC, Stamatopoulos K (2021) MyPal: Designing and Evaluating Digital Patient-Reported Outcome Systems for Cancer Palliative Care in Europe. J Palliat Med 24:962–964. doi: 10.1089/jpm.2021.0120

129. Peres SC, Pham T, Phillips R (2013) Validation of the System Usability Scale (SUS). Proc Hum Factors Ergon Soc Annu Meet 57:192–196. doi: 10.1177/1541931213571043

130. Péus D, Newcomb N, Hofer S (2013) Appraisal of the Karnofsky Performance Status and proposal of a simple algorithmic system for its evaluation. BMC Med Inform Decis Mak 13:72. doi: 10.1186/1472-6947-13-72

131. Pramana G, Parmanto B, Lomas J, Lindhiem O, Kendall PC, Silk J (2018) Using Mobile Health Gamification to Facilitate Cognitive Behavioral Therapy Skills Practice in Child Anxiety Treatment: Open Clinical Trial. JMIR Serious Games 6:e9. doi: 10.2196/games.8902

132. Pyke-Grimm KA, Fisher B, Haskamp A, Bell CJ, Newman AR (2021) Providing Palliative and Hospice Care to Children, Adolescents and Young Adults with Cancer. Semin Oncol Nurs 37:151166. doi: 10.1016/j.soncn.2021.151166

133. R Core Team (2022) R: A language and environment for statistical computing

134. Rabin R, Charro F de (2001) EQ-5D: a measure of health status from the EuroQol Group. Ann Med 33:337–343. doi: 10.3109/07853890109002087

135. Rahimi B, Nadri H, Lotfnezhad Afshar H, Timpka T (2018) A Systematic Review of the Technology Acceptance Model in Health Informatics. Appl Clin Inform 9:604–634. doi: 10.1055/s-0038-1668091

136. Rajmil L, López A, López-Aguilà S, Alonso J (2013) Parent–child agreement on health-related quality of life (HRQOL): a longitudinal study. Health Qual Life Outcomes 11:101. doi: 10.1186/1477-7525-11-101

137. Ramsey WA, Heidelberg RE, Gilbert AM, Heneghan MB, Badawy SM, Alberts NM (2020) eHealth and mHealth interventions in pediatric cancer: A systematic review of interventions across the cancer continuum. Psychooncology 29:17–37. doi: 10.1002/pon.5280

138. Reeve BB, Greenzang KA, Sung L (2023) Patient-Reported Outcomes in Pediatric Patients With Cancer. Am Soc Clin Oncol Educ Book e390272. doi: 10.1200/EDBK_390272

139. Requena ML, Avery M, Feraco AM, Uzal LG, Wolfe J, Dussel V (2022) Normalization of Symptoms in Advanced Child Cancer: The PediQUEST-Response Case Study. J Pain Symptom Manage 63:548–562. doi: 10.1016/j.jpainsymman.2021.12.009

140. Retzer A, Al-Jilaihawi S, Bailey S, Buenger V, Damery S, Darlington AS, Diezi M, Peipert JD, Roydhouse J, Reeve BB (2025) Assessing patient-reported outcomes (PROs) in paediatric oncology research: Which PRO would a pro pick, if a pro was picking PROs? EJC Paediatr Oncol 5:100232. doi: 10.1016/j.ejcped.2025.100232

141. Retzer A, Calvert M, Ahmed K, Keeley T, Armes J, Brown JM, Calman L, Gavin A, Glaser AW, Greenfield DM, Lanceley A, Taylor RM, Velikova G, Brundage M, Efficace F, Mercieca-Bebber R, King MT, Kyte D (2021) International perspectives on suboptimal patient-reported outcome trial design and reporting in cancer clinical trials: A qualitative study. Cancer Med 10:5475–5487. doi: 10.1002/cam4.4111

142. Ribeiro ILA, Silva SM, Limeira RRT, Bonan PRF, Valença AMG, Lima Neto EA de, Castro RD de (2020) Differences between the oral changes presented by patients with solid and hematologic tumors during the chemotherapeutic treatment. J Appl Oral Sci 28:e20190020. doi: 10.1590/1678-7757-2019-0020

143. Riedl D, Hubel N, Endres A, Vetrano C, Meryk A, Crazzolara R (2024) Enhancing pediatric oncology clinical trials through patient reported outcomes (PROs). EJC Paediatr Oncol 4:100199. doi: 10.1016/j.ejcped.2024.100199

144. Riedl D, Rothmund M, Darlington A-S, Sodergren S, Crazzolara R, de Rojas T (2021) Rare use of patient-reported outcomes in childhood cancer clinical trials – a systematic

review of clinical trial registries. Eur J Cancer 152:90–99. doi: 10.1016/j.ejca.2021.04.023

145. Robert RS, Paxton RJ, Palla SL, Yang G, Askins MA, Joy SE, Ater JL (2012) Feasibility, reliability, and validity of the pediatric quality of life inventory™ generic core scales, cancer module, and multidimensional fatigue scale in long-term adult survivors of pediatric cancer. Pediatr Blood Cancer 59:703–707. doi: 10.1002/pbc.24099

146. Robson K, Plangger K, Kietzmann JH, McCarthy I, Pitt L (2015) Is it all a game? Understanding the principles of gamification. Bus Horiz 58:411–420. doi: 10.1016/j.bushor.2015.03.006

147. Rodgers C, Wills-Bagnato P, Sloane R, Hockenberry M (2015) Health-Related Quality of Life among Children and Adolescents during Hematopoietic Stem Cell Transplant Recovery. J Pediatr Oncol Nurs 32:329–336. doi: 10.1177/1043454214563413

148. Rodrigues L, Pereira FD, Toda AM, Palomino PT, Pessoa M, Carvalho LSG, Fernandes D, Oliveira EHT, Cristea AI, Isotani S (2022) Gamification suffers from the novelty effect but benefits from the familiarization effect: Findings from a longitudinal study. Int J Educ Technol High Educ 19:13. doi: 10.1186/s41239-021-00314-6

149. Rosa WE, Connor S, Aggarwal G, Alsirafy S, Brennan J, Davies H, Downing J, Ferrell B, Harding R, Knaul FM, Luyirika EBK, Marroquín MM, Marston J, Radbruch L, Rajagopal MR, Sallnow L, Krakauer EL (2025) Relieve the suffering: palliative care for the next decade. Lancet 405:1802–1804. doi: 10.1016/S0140-6736(25)00678-6

150. Ross J, Stevenson F, Lau R, Murray E (2016) Factors that influence the implementation of e-health: a systematic review of systematic reviews (an update). Implement Sci 11:146. doi: 10.1186/s13012-016-0510-7

151. Rothmund M, Lehmann J, Moser W, de Rojas T, Sodergren SC, Darlington A-S, Riedl D (2022) Patient-reported outcomes are under-utilised in evaluating supportive therapies in paediatric oncology – A systematic review of clinical trial registries. Crit Rev Oncol Hematol 176:103755. doi: 10.1016/j.critrevonc.2022.103755

152. Rothmund M, Sodergren S, Rohde G, de Rojas T, Paratico G, Albini G, Mur J, Darlington A-S, Majorana A, Riedl D (2023) Updating our understanding of health-related quality of life issues in children with cancer: a systematic review of patient-reported outcome measures and qualitative studies. Qual Life Res 32:965–976. doi: 10.1007/s11136-022-03259-z

153. Rusconi D, Basile I, Rampichini F, Colombo S, Arba L, Pancheri ML, Consolo L, Lusignani M (2024) Electronic Patient Reported Outcomes Measures (e-PROMs) in

Pediatric Palliative Oncology Care: A Scoping Review. J Palliat Care 39:298–315. doi: 10.1177/08258597241274027

154. Saleh MS, Mohammed AM, Bassiouni D, Mostafa HH, Monir ZM (2023) Evaluation of health-related quality of life and its domains in pediatric patients with cancer. J Egypt Natl Canc Inst 35:9. doi: 10.1186/s43046-023-00168-1

155. Sardi L, Idri A, Fernández-Alemán JL (2017) A systematic review of gamification in e-Health. J Biomed Inform 71:31–48. doi: 10.1016/j.jbi.2017.05.011

156. Scarfò L, Karamanidou C, Doubek M, Garani-Papadatos T, Didi J, Pontikoglou C, Ling J, Payne C, Papadaki HA, Rosenquist R, Stavroyianni N, Payne S, Ghia P, Natsiavas P, Maramis C, Stamatopoulos K (2021) MyPal ADULT study protocol: a randomised clinical trial of the MyPal ePRO-based early palliative care system in adult patients with haematological malignancies. BMJ Open 11:e050256. doi: 10.1136/bmjopen-2021-050256

157. Schepers SA, Haverman L, Zadeh S, Grootenhuis MA, Wiener L (2016) Healthcare Professionals' Preferences and Perceived Barriers for Routine Assessment of Patient-Reported Outcomes in Pediatric Oncology Practice: Moving Toward International Processes of Change. Pediatr Blood Cancer 63:2181–2188. doi: 10.1002/pbc.26135

158. Schepers SA, Sint Nicolaas SM, Haverman L, Wensing M, Schouten van Meeteren AYN, Veening MA, Caron HN, Hoogerbrugge PM, Kaspers GJL, Verhaak CM, Grootenhuis MA (2017) Real-world implementation of electronic patient-reported outcomes in outpatient pediatric cancer care. Psychooncology 26:951–959. doi: 10.1002/pon.4242

159. Schmidt-Kraepelin M, Toussaint PA, Thiebes S, Hamari J, Sunyaev A (2020) Archetypes of Gamification: Analysis of mHealth Apps. JMIR Mhealth Uhealth 8:e19280. doi: 10.2196/19280

160. Van Schoors M, De Paepe AL, Lemiere J, Morez A, Norga K, Lambrecht K, Goubert L, Verhofstadt LL (2019) Family Adjustment When Facing Pediatric Cancer: The Role of Parental Psychological Flexibility, Dyadic Coping, and Network Support. Front Psychol 10:2740. doi: 10.3389/fpsyg.2019.02740

161. Schwartz CE, Stark RB, Balasuberamaniam P, Shrikumar M, Wasim A, Finkelstein JA (2020) Responsiveness of standard spine outcome tools: do they measure up? J Neurosurg Spine 33:106–113. doi: 10.3171/2019.12.SPINE191367

162. Shilling V, Young B (2009) How do parents experience being asked to enter a child in a randomised controlled trial? BMC Med Ethics 10:1. doi: 10.1186/1472-6939-10-1

163. Sisk BA, Friedrich AB, DuBois J, Mack JW (2020) Emotional Communication in Advanced Pediatric Cancer Conversations. J Pain Symptom Manage 59:808-817.e2. doi: 10.1016/j.jpainsymman.2019.11.005

164. Smrke A, Leung B, Srikanthan A, McDonald M, Bates A, Ho C (2020) Distinct Features of Psychosocial Distress of Adolescents and Young Adults with Cancer Compared to Adults at Diagnosis: Patient-Reported Domains of Concern. J Adolesc Young Adult Oncol 9:540–545. doi: 10.1089/jayao.2019.0157

165. Snyder C, Crossnohere N, King M, Reeve BB, Bottomley A, Calvert M, Thorner E, Wu AW, Brundage M (2022) The PROTEUS-Trials Consortium: Optimizing the use of patient-reported outcomes in clinical trials. Clin Trials 19:277–284. doi: 10.1177/17407745221077691

166. Snyder C, Smith K, Holzner B, Rivera YM, Bantug E, Brundage M (2019) Making a picture worth a thousand numbers: recommendations for graphically displaying patient-reported outcomes data. Qual Life Res 28:345–356. doi: 10.1007/s11136-018-2020-3

167. Snyder CF, Jensen RE, Geller G, Carducci MA, Wu AW (2010) Relevant content for a patient-reported outcomes questionnaire for use in oncology clinical practice: Putting doctors and patients on the same page. Qual Life Res 19:1045–1055. doi: 10.1007/s11136-010-9655-z

168. Spahl W, Motta V, Woodcock K, Rubeis G (2024) Gamified Digital Mental Health Interventions for Young People: Scoping Review of Ethical Aspects During Development and Implementation. JMIR Serious Games 12:e64488. doi: 10.2196/64488

169. Stanek CJ, Hill KN, Roche CI, Olsavsky AL, Himelhoch AC, Kenney AE, Humphrey L, Olshefski R, Nahata L, Gerhardt CA (2025) Healthcare Satisfaction Among Parents of Children With Advanced Cancer: Impact of Parent-Oncologist Therapeutic Alliance. Am J Hosp Palliat Care 10499091251339476. doi: 10.1177/10499091251339475

170. Stehl ML, Kazak AE, Alderfer MA, Rodriguez A, Hwang W-T, Pai ALH, Boeving A, Reilly A (2009) Conducting a Randomized Clinical Trial of an Psychological Intervention for Parents/Caregivers of Children with Cancer Shortly after Diagnosis. J Pediatr Psychol 34:803–816. doi: 10.1093/jpepsy/jsn130

171. Stein R, Jessop D (2003) The Impact on Family Scale Revisited: Further Psychometric Data. J Dev Behav Pediatr 24:9–16. doi: 10.1097/00004703-200302000-00004

172. Stein REK, Riessman CK (1980) The Development of an Impact-on-Family Scale: Preliminary Findings. Med Care 18:465–472. doi: 10.1097/00005650-198004000-00010

173. Steliarova-Foucher E, Colombet M, Ries LAG, Moreno F, Dolya A, Bray F, Hesseling P, Shin HY, Stiller CA, Bouzbid S, Hamdi-Cherif M, Hablas A, Chirpaz E, Buziba N, Chesumbai G, Manraj S, Reynders D, Wabinga H, Chokunonga E, Moreno F, Lima C, Asturian Laporte C, de Oliveira J, de Aquino JP, Gallagher SV, Uribe C, Bravo L, Yepez Chamorro M, Torres Alvarado G, Galán Alvarez Y, Martinez Reyes F, Castillo Calvas J, Mendoza Alava M, Cueva Ayala P, Hanchard B, Fajardo-Gutiérrez A, Zavala Zegarra D, Barrios E, Nikiforuk C, Woods R, Turner D, MacIntyre M, Corriveau A, Navaneelan T, Bertrand C, Stuart-Panko H, Wilson R, Kosary C, Shen X, Brockhouse J, Yee G, Mitchell T, Snipes K, West D, Rao C, Bolick S, Rycroft R, Mueller L, Zheng Y, Dosch K, Brown H, Vargas A, Levin G, Bayakly R, Johnson C, Shen T, Ruppert L, Lynch C, Lai S, Tucker T, Wu X, Schwenn M, Stern K, Gershman S, Copeland G, Bushhouse S, Rogers D, Jackson Thompson J, Lemons D, Frederick S, Harris J, Riddle B, Stroup A, Wiggins C, Schymura M, Giljahn L, Sheikh A, Schubert S, Aldinger W, Fulton J, Whiteside M, Nogueira L, Sweeney C, Johnson A, Martin J, Farley S, Harrelson D, Malicki R, Espinoza J, Hernandez B, Abulfateh N, Wang N, Ngan R, Lingegowda K, Swaminathan R, Koyande S, Silverman B, Ozasa K, Kanemura S, Soda M, Miyashiro I, Shibata A, Nimri O, Won Y, Kim C, Hong N, Nam H, Kweon S, Kim W, Huh J, Jung K, Yoo C, Elbasmy A, Laudico A, Lumague M, AlMutlag H, Buasom R, Srisukho S, Tanabodee J, Wiangnon S, Pongnikorn D, Sriplung H, Dirican O, Eser S, Le Hoang M, Hackl M, Zborovskaya A, Dimitrova N, Valerianova Z, Sekerija M, Pavlou P, Dušek M, Mägi M, Clavel J, Lacour B, Guizard A, Bouvier V, Troussard X, Woronoff A, Tretarre B, Colonna M, Molinié F, Bara S, Velten M, Marrer E, Ganry O, Grosclaude P, Kaatsch P, Zeissig S, Holleczek B, Katalinic A, Jakab Z, Birgisson H, Walsh P, Mangone L, Merletti F, Magoni M, Mangone L, Ferretti S, Serraino D, Spagnoli G, Fusco M, Michiara M, Tumino R, Falcini F, Sensi F, Tisano F, Piffer S, Stracci F, Tagliabue G, Smailyte G, Agius D, Visser O, Ursin G, Didkowska J, Trojanowski M, Wojciechowska U, Forjaz de Lacerda G, Silva M, Laranja Pontes J, da Costa Miranda A, Kaiserova E, Primic Žakelj M, Peris-Bonet R, Vicente Raneda M, Almar Marqués E, Quirós Garcia J, Ramos Monserrat M, Errezola Saizar M, Alemán Herrera A, Díaz García J, Marcos-Gragera R, Sanchez-Perez M, Ardanaz Aicua E, Galceran J, Klint A, Kuehni C, Bouchardy C, Levi F, Bordoni A, Konzelmann I, Rohrmann S, Stiller C, Gavin A, Brewster D, Phung H, Rushton S, Guthridge S, Aitken J, D'Onise K, Venn A, Farrugian H, Threlfall T, Laumond S, Yen Kai Sun L, Hendrix J, Ballantine K, Colombet M, Dolya A, Masuyer E,

Steliarova-Foucher E (2017) International incidence of childhood cancer, 2001–10: a population-based registry study. Lancet Oncol 18:719–731. doi: 10.1016/S1470-2045(17)30186-9

174. Stinson JN, Jibb LA, Nguyen C, Nathan PC, Maloney AM, Dupuis LL, Gerstle JT, Hopyan S, Alman BA, Strahlendorf C, Portwine C, Johnston DL (2015) Construct validity and reliability of a real-time multidimensional smartphone app to assess pain in children and adolescents with cancer. Pain 156:2607–2615. doi: 10.1097/j.pain.0000000000000385

175. Stover AM, Haverman L, van Oers HA, Greenhalgh J, Potter CM, Ahmed S, Greenhalgh J, Gibbons E, Haverman L, Manalili K, Potter C, Roberts N, Santana M, Stover AM, van Oers H (2021) Using an implementation science approach to implement and evaluate patient-reported outcome measures (PROM) initiatives in routine care settings. Qual Life Res 30:3015–3033. doi: 10.1007/s11136-020-02564-9

176. Sugalski AJ, Lo T, Beauchemin M, Grimes AC, Robinson PD, Walsh AM, Santesso N, Dang H, Fisher BT, Wrightson AR, Yu LC, Sung L, Dupuis LL (2021) Facilitators and barriers to clinical practice guideline-consistent supportive care at pediatric oncology institutions: a Children's Oncology Group study. Implement Sci Commun 2:106. doi: 10.1186/s43058-021-00200-2

177. Tark R, Metelitsa M, Akkermann K, Saks K, Mikkel S, Haljas K (2019) Usability, Acceptability, Feasibility, and Effectiveness of a Gamified Mobile Health Intervention (Triumf) for Pediatric Patients: Qualitative Study. JMIR Serious Games 7:e13776. doi: 10.2196/13776

178. Taylor MR, Scott SR, Steineck A, Rosenberg AR (2021) Objectifying the Subjective: The Use of Heart Rate Variability as a Psychosocial Symptom Biomarker in Hospice and Palliative Care Research. J Pain Symptom Manage 62:e315–e321. doi: 10.1016/j.jpainsymman.2021.04.015

179. Tomlinson D, Dupuis LL, Johnston DL, Kuczynski S, Patel S, Schechter T, Vettese E, Mairs M, Tomlinson GA, Sung L (2022) Reliability and validity of proxy-SSPedi and mini-SSPedi in pediatric patients 2-7 years receiving cancer treatments. BMC Cancer 22:730. doi: 10.1186/s12885-022-09814-8

180. Tomlinson D, Hyslop S, Stein E, Spiegler B, Vettese E, Kuczynski S, Schechter T, Dupuis LL, Sung L (2019) Development of mini-SSPedi for children 4–7 years of age receiving cancer treatments. BMC Cancer 19:32. doi: 10.1186/s12885-018-5210-z

181. Tomlinson D, Plenert E, Dadzie G, Loves R, Cook S, Schechter T, Dupuis LL, Sung L (2021) Reasons for disagreement between proxy-report and self-report rating of symptoms in children receiving cancer therapies. Support Care Cancer 29:4165–4170. doi: 10.1007/s00520-020-05930-y

182. Tran A, Hou SHJ, Forbes C, Cho S, Forster VJ, Stokoe M, Wakefield CE, Wiener L, Heathcote LC, Michel G, Patterson P, Reynolds K, Schulte FSM (2023) The Impact of the Early COVID-19 Global Pandemic on Children Undergoing Active Cancer Treatment and Their Parents. Curr Oncol 30:2441–2456. doi: 10.3390/curroncol30020186

183. Trotti A, Colevas AD, Setser A, Basch E (2007) Patient-Reported Outcomes and the Evolution of Adverse Event Reporting in Oncology. J Clin Oncol 25:5121–5127. doi: 10.1200/JCO.2007.12.4784

184. Tzimourta KD (2025) Human-Centered Design and Development in Digital Health: Approaches, Challenges, and Emerging Trends. Cureus 17:e85897. doi: 10.7759/cureus.85897

185. Udaka YT, Packer RJ (2018) Pediatric Brain Tumors. Neurol Clin 36:533–556. doi: 10.1016/j.ncl.2018.04.009

186. Varni JW, Burwinkle TM, Katz ER, Meeske K, Dickinson P (2002) The PedsQL™ in pediatric cancer. Cancer 94:2090–2106. doi: 10.1002/cncr.10428

187. Varni JW, Limbers CA, Burwinkle TM (2007) How young can children reliably and validly self-report their health-related quality of life?: An analysis of 8,591 children across age subgroups with the PedsQL™ 4.0 Generic Core Scales. Health Qual Life Outcomes 5:1. doi: 10.1186/1477-7525-5-1

188. Velikova G, Keding A, Harley C, Cocks K, Booth L, Smith AB, Wright P, Selby PJ, Brown JM (2010) Patients report improvements in continuity of care when quality of life assessments are used routinely in oncology practice: Secondary outcomes of a randomised controlled trial. Eur J Cancer 46:2381–2388. doi: 10.1016/j.ejca.2010.04.030

189. Wang M, Xu J, Zhou X, Li X, Zheng Y (2025) Effectiveness of Gamification Interventions to Improve Physical Activity and Sedentary Behavior in Children and Adolescents: Systematic Review and Meta-Analysis. JMIR Serious Games 13:e68151. doi: 10.2196/68151

190. Watson L, Link C, Qi S, DeIure A (2023) Quantifying the Impact of Family Doctors on the Care Experiences of Patients with Cancer: Exploring Evidence from the 2021

Ambulatory Oncology Patient Satisfaction Survey in Alberta, Canada. Curr Oncol 30:641–652. doi: 10.3390/curroncol30010049

191. Weldring T, Smith SMS (2013) Patient-Reported Outcomes (PROs) and Patient-Reported Outcome Measures (PROMs). Health Serv Insights 6:61–68. doi: 10.4137/HSI.S11093

192. Wellek S (2010) Testing Statistical Hypotheses of Equivalence and Noninferiority, 2nd ed. Chapman and Hall/CRC, New York

193. Whitlow PG, Caparas M, Cullen P, Trask C, Schulte F, Embry L, Nagarajan R, Johnston DL, Sung L (2015) Strategies to improve success of pediatric cancer cooperative group quality of life studies: a report from the Children's Oncology Group. Qual Life Res 24:1297–1301. doi: 10.1007/s11136-014-0855-9

194. Winter MA, Greenlee J, Al Ghriwati N, Garr KN, Sahler OJZ, O'Connor TG (2021) Children's appraisals of threat in pediatric cancer. SSM - Mental Health 1:100037. doi: 10.1016/j.ssmmh.2021.100037

195. Wobbrock JO, Findlater L, Gergle D, Higgins JJ (2011) The aligned rank transform for nonparametric factorial analyses using only anova procedures. In: Proc SIGCHI Conf Hum Factor Comput Syst. ACM, New York, NY, USA, pp 143–146

196. Wolfe J, Orellana L, Ullrich C, Cook EF, Kang TI, Rosenberg A, Geyer R, Feudtner C, Dussel V (2015) Symptoms and Distress in Children With Advanced Cancer: Prospective Patient-Reported Outcomes From the PediQUEST Study. J Clin Oncol 33:1928–1935. doi: 10.1200/JCO.2014.59.1222

197. Wolff AC, Absolom K, Ahmed S, Bartlett SJ, Santana MJ, Stover AM, Austin EJ (2025) Enhancing provider adoption of patient-reported outcome measures (PROMs) through implementation science: insights from two international workshops. J Patient Rep Outcomes 9:77. doi: 10.1186/s41687-025-00911-3

198. World Health Organization (WHO) (2016) Monitoring and evaluating digital health interventions: a practical guide to conducting research and assessment. Geneva

199. World Health Organization (WHO) (2018) Integrating palliative care and symptom relief into paediatrics: a WHO guide for health care planners, implementers and manager. Geneva

200. Wosny M, Strasser LM, Hastings J (2023) Experience of Health Care Professionals Using Digital Tools in the Hospital: Qualitative Systematic Review. JMIR Hum Factors 10:e50357. doi: 10.2196/50357

201. Yan AP, Dupuis LL, Aftandilian C, Agarwal V, Baggott C, Beauchemin MP, Bradfield SM, Cannone D, Caywood EH, Crellin-Parsons N, Demedis J, Dickens D, Esbenshade AJ, Freyer DR, Grimes AC, Kelly KM, King AA, Klesges LM, Kyono W, Nagasubramanian R, Orgel E, Orsey AD, Roth ME, Sherani F, Vettese E, Walsh A, Woods-Swafford W, Yu LC, Tomlinson GA, Sung L (2025) Factors Associated With Symptom Burden Among Pediatric Patients With Cancer. JCO Oncol Pract OP2500244. doi: 10.1200/OP-25-00244

202. Yan AP, Tomlinson D, Dupuis LL, Sung L (2025) SSPedi and SPARK: Promise for the future of electronic patient reported outcomes in pediatric oncology. EJC Paediatr Oncol 5:100238. doi: 10.1016/j.ejcped.2025.100238

203. Yang LY, Manhas DS, Howard AF, Olson RA (2018) Patient-reported outcome use in oncology: a systematic review of the impact on patient-clinician communication. Support Care Cancer 26:41–60. doi: 10.1007/s00520-017-3865-7

204. Zebrack BJ, Butler M (2012) Context for Understanding Psychosocial Outcomes and Behavior Among Adolescents and Young Adults With Cancer. J Natl Compr Cancer Netw 10:1151–1156. doi: 10.6004/jnccn.2012.0118

205. Zebrack BJ, Corbett V, Embry L, Aguilar C, Meeske KA, Hayes-Lattin B, Block R, Zeman DT, Cole S (2014) Psychological distress and unsatisfied need for psychosocial support in adolescent and young adult cancer patients during the first year following diagnosis. Psychooncology 23:1267–1275. doi: 10.1002/pon.3533

206. Zettl A, Gsell H, Maślak K, Karjalainen A, Leiss U, Kienesberger A, Schneider C (2025) HOW ARE YOU FEELING TODAY? – Gaps and opportunities in capturing patient reported outcomes (PROs) in Pediatric Cancer Care. EJC Paediatr Oncol 6:100306. doi: 10.1016/j.ejcped.2025.100306

207. Zhou L, Bao J, Setiawan IMA, Saptono A, Parmanto B (2019) The mHealth App Usability Questionnaire (MAUQ): Development and Validation Study. JMIR Mhealth Uhealth 7:e11500. doi: 10.2196/11500

List of Abbreviations

App	Mobile Application
ART-ANOVA	Aligned Rank Transform Analysis of Variance
eHealth	Electronic Health
EHR	Electronic Health Record
EORTC PATSAT	European Organisation for Research and Treatment of Cancer – Satisfaction with cancer care core questionnaire
ePRO(s)	Electronic Patient-Reported Outcome(s)
ESMO	European Society for Medical Oncology
EQ-5D-3L	EuroQol Group five-dimension, three-level questionnaire
FNBRNO	University Hospital Brno
GDPR	General Data Protection Regulation
GenOR	Generalized odds ratio
HCP(s)	Healthcare Professional(s)
HRQoL	Health-Related Quality of Life
IOFS	Impact on Family Scale
Imp	Imputed values
KPS	Karnofsky Performance Status
LOCF	Last Observation Carried Forward
mHealth	Mobile Health
MHH	Medical School Hannover
M[X]	Month X of study participation (e.g., M1 = first month)
N/A	No answer provided
PedsQL™	Pediatric Quality of Life Inventory™
PRO(s)	Patient-Reported Outcome(s)
PROM(s)	Patient-Reported Outcome Measure(s)
RCT	Randomized controlled trial
SSPedi	Symptom Screening in Pediatrics Tool

SUS	System Usability Scale
TOST	Two one-sided tests
USAAR	Saarland University
VAS	Visual Analogue Scale

List of Figures

List of Tables

Supplement

Supplement 1 System Usability Scale Adapted for Children

Version for Children < 10 years

Dear AquaScout!

Thank you for taking part in the MyPal4Kids study!

Please answer the following questions about the app:

1. Did you like the game? Yes | No

2. Was the game easy to play? Yes | No

3. Did you enjoy answering questions in the game? Yes | No

Please write a few words about what you liked or disliked about the app and the game:

Free text answer

Version for Children ≥ 10 years

Dear AquaScout!

Thank you for taking part in the MyPal4Kids study!

Please answer the following questions about the app:

1. Did you like the game? Yes | No

2. Was the game easy to play? Yes | No

3. Did you enjoy answering questions in the game? Yes | No

4. Were the questions that were asked appropriate at the time? Yes | No

5. Was the frequency of reminders to answer questions appropriate? Yes | No

Please write a few words about what you liked or disliked about the app and the game:

Free text answer

Supplement 2 Web-Based Questionnaire for HCPs

The Impact on Healthcare Professionals Due to the Integration of ePROs in Palliative Care

We are interested in understanding your experiences of using the MyPal platform. Below are a number of statements about the MyPal platform. Please indicate to what extent you agree or disagree with the following statements:

1) Were you already involved in the MyPal project before the study period?
    - Yes
    - No

2) The MyPal platform was easy for me to use.
    - Strongly agree
    - Agree
    - Neither agree nor disagree
    - Disagree
    - Strongly disagree

3) I think that the MyPal platform was easy for children to use.
    - Strongly agree
    - Agree
    - Neither agree nor disagree
    - Disagree
    - Strongly disagree

4) I think that the MyPal platform was easy for parents to use.
    - Strongly agree
    - Agree
    - Neither agree nor disagree
    - Disagree
    - Strongly disagree

5) The MyPal platform facilitated communication with the children and their parents.
    - Strongly disagree
    - Disagree
    - Neither agree nor disagree
    - Agree
    - Strongly agree

6) I think using the MyPal platform gave me more time to address actual care needs.
    - Strongly agree
    - Agree
    - Neither agree nor disagree
    - Disagree
    - Strongly disagree

7) Using the MyPal platform resulted in an additional burden on my daily work.
    - Strongly agree
    - Agree
    - Neither agree nor disagree
    - Disagree
    - Strongly disagree

8) In my opinion, the amount of ePROs completed by the children was appropriate.
    - Strongly agree
    - Agree
    - Neither agree nor disagree
    - Disagree
    - Strongly disagree

9) In my opinion, the amount of ePROs completed by the parents was appropriate.
    - Strongly agree
    - Agree
    - Neither agree nor disagree
    - Disagree
    - Strongly disagree

10) The ePROs for children were designed well on the MyPal platform.
    - Strongly agree
    - Agree
    - Neither agree nor disagree
    - Disagree
    - Strongly disagree

11) The ePROs for parents were designed well in the MyPal platform.
    - Strongly agree
    - Agree
    - Neither agree nor disagree
    - Disagree
    - Strongly disagree

12) Being able to visualize patient data was helpful to me
    - Strongly agree
    - Agree
    - Neither agree nor disagree
    - Disagree
    - Strongly disagree

13) I would recommend the MyPal platform to other colleagues
    - Strongly agree
    - Agree
    - Neither agree nor disagree
    - Disagree
    - Strongly disagree

14) Would you like to continue using the MyPal platform?
    - Yes
    - No

15) Please provide further comments / suggestions / remarks about the MyPal platform and its features in the following box: Free text answer

Supplement 3 Questions for Follow-Up Focus Groups with Patients and Parents

1. If you had to explain to a friend in a few sentences your impression of the apps, what would you say? **[children = c and parents = p]**
    a. What did you like most and what least about the apps? **[c and p]**

2. How did you find the questions and answer options that popped up during the game? **[only c]**
    a. Would you change any of them? If yes, what would you change? **[only c]**
    b. What did you find helpful? **[only c]**

3. Talking about one's state of health and mood often is not easy, sometimes even uncomfortable: How did you feel about frequently reporting about your mood and state of health? **[only c]**
    a. How much did the app help you with it? **[only c]**
    b. How would you describe the impact the app had for you, dealing with your condition and mood? **[only c]**
    c. Now that the study is over, can you identify any benefits or drawbacks for you or your child, of the app's use?" **[only p]**
    d. Have you noticed any differences in the way your child communicates about his/her health? Would you say it improved or got worse? **[only p]**

4. What should have been done so that you used the apps more often? **[c and p]**
    a. In your opinion, what extras should the apps have? **[c and p]**
    b. What would you leave out or change? **[c and p]**

5. How much have the doctors and nurses responded to what you have shared through the app? **[only c]**
    a. What did you think of the frequency and the content when your physician referred to it? **[only c]**
    b. How did you wish it to be? **[only c]**

6. Imagine you are an inventor, and you have the chance to invent your own app that helps you, other children and their relatives with the illness, what will your app look like? What would your app be able to do? **[c and p]**

7. When we first introduced you to the app, you certainly had some thoughts or feelings towards it: What did you expect from the apps? **[c and p]**
    a. Have your expectations been met and why (not)? **[c and p]**
    b. What do you feel the apps are lacking, according to your preferences? **[c and p]**
    c. How time consuming was it for you to use the apps? **[c and p]**

8. Sometimes we do not feel like playing or answering questions: But when you did use the app, what made you use the app? What motivated you? **[only c]**
    a. What were the reasons why you did NOT use the app regularly? **[only c]**

9. You really helped us during the time of the project. Now the project is almost over. Could you imagine continuing to use the apps? **[only c]**

Supplement 4 Questions for Follow-Up Focus Group with HCPs

1. When we first introduced you to the MyPal platform and the apps, what were your thoughts or feelings towards it: What did you expect from it?

2. After using the MyPal platform and the apps, please tell us about the following:
    a. What would you leave out or change?
    b. What is missing that you think should be included?

3. What is your impression of how the children and parents perceived and used the apps?
    a. Based on your experience, what encouraged people to use the apps regularly?
    b. Based on your experience, what discouraged people from using the apps regularly?
    c. Have you observed differences between certain groups of patients? If yes, can you think of possible explanations?

4. What impact did the apps have on how the children and their parents communicated with your team, e.g., were there changes in the way they reported their symptoms?

5. How frequently have you checked the answers of the patients?
    a. What impact did the apps have on your own communication with the children and their parents?
    b. What impact did the apps have on communication within your team?

6. In your opinion, how do such eHealth solutions influence care? How else can these make a valuable contribution?

Supplement 5 Summaries of all Focus Groups Conducted

Table S5.1 Key findings from the focus groups with children and their parents.

Code Category	Summary
Game Design	Children frequently mentioned enjoying the customization features and underwater theme. Comments on gameplay included perceptions of repetitiveness and limited challenge.
ePROs	Parents appreciated symptom reporting but noted some children underreported, often due to fatigue. Both parents and children found the questions understandable, but some described the questions as repetitive or less relevant during symptom-free periods.
Consequences of App Usage	The app felt most beneficial at the treatment's onset. However, engagement decreased over time. It was useful for self-reflection and documenting symptoms, particularly when direct communication with HCPs was limited.
Communication	The app was not commonly perceived as improving communication but was reported as enabling some children to express feelings outside face-to-face interactions. However, infrequent feedback from HCPs as response to symptom reports led to frustration.
Recommendations	Participants suggested expanding gameplay variety, customization options, tailoring the app for different age groups, and adding multiplayer modes and peer support as social interaction features as well as HCP feedback to enhance engagement.

Note. ePROs = Electronic Patient-Reported Outcomes; HCPs = Healthcare Professionals.

Table S5.2 Key findings from the focus groups with project-internal HCPs.

Code Category	Summary
Game Design	HCPs observed that older children were less engaged, mentioning limited variety and a perceived lack of competitiveness in the game.
Expectations	Initial expectations ranged from mixed curiosity to skepticism regarding the platform's ability to sustain engagement and seamlessly integrate into clinical workflows.
Consequences of App Usage	HCPs noted that some patients seemed to avoid the app as it reminded them of their illness, leading to disengagement, especially at home.

Communication	The app served as an additional communication channel, particularly for teenagers who preferred expressing themselves digitally. However, its impact on team communication seemed to highly depend on the strength of existing communication between HCPs, patients, and families. In cases of weaker communication, digital tools were seen as helpful for capturing and preserving important information.
Influences on Motivation	Initial curiosity waned due to limited feedback. HCPs reported more consistent use among girls and follow-up patients compared to boys or those in acute care.
Recommendations	HCPs recommended incorporating automated data collection (e.g., wearables) and enhancing the HCP interface for better notification management. However, they also highlighted the need to address data protection and institutional barriers in general before effective implementation is possible.

Note. HCPs = Healthcare Professionals.

Table S5.2 Key findings from the focus groups with project-internal HCPs.

Code Category	Summary
Game Design	External HCPs found the game's long–term engagement insufficient, citing competition with highly stimulating commercial games as a major hurdle.
Expectations	Initially, HCPs were optimistic about the app providing a constructive, meaningful alternative to passive media consumption for children.
Consequences of App Usage	HCPs described limited changes in daily workflows, although some noted occasional use for symptom tracking. Families sometimes used it to recall symptoms during appointments, but it did not seem to substantially alter HCP working routines.
Communication	The app aided communication for children more comfortable with digital tools, though HCPs emphasized that digital reporting ought to supplement rather than substitute for face-to-face interactions.
Influences on Motivation	HCPs observed reduced engagement over time, particularly as patients' health improved. Parents of younger children were more engaged in symptom tracking, while older children primarily used the diary function for information sharing. Participants described engagement as influenced by usage habits, perceived utility, and occasional technical challenges (e.g., login issues).
Impression of eHealth Solutions	HCPs were generally optimistic about the growing role of eHealth but stressed that such digital health solutions must complement traditional care. Challenges included administrative barriers and insufficient digital infrastructure.
Recommendations	External HCPs suggested additional personalized game features to increase long–term engagement and enhancing the app interface for HCPs, including a priority system to highlight urgent issues.

Note. HCPs = Healthcare Professionals; eHealth = Electronic Health.

Acknowledgments

I would like to express my sincere gratitude to all those who have supported and accompanied me on my journey toward completing this doctoral thesis.

I am deeply grateful to my doctoral supervisor, Prof. Dr. med. Norbert Graf, for giving me the opportunity to pursue this dissertation, for his dedicated mentorship, and for his continuous guidance throughout my development as a researcher. His valuable insights, encouragement, and trust have been instrumental in shaping both this work and my scientific growth.

My heartfelt thanks also go to all members of the MyPal project consortium, including the participating clinical sites, for the excellent collaboration and for creating the foundation that made this dissertation possible. I am especially grateful to Lenka Radová, PhD, for her commitment and expertise in our close collaboration and joint conceptual work on the statistical analyses, which were essential to this research. I would also like to thank Anna Burns-Gebhart for her valuable support in the transcription and coding of the qualitative focus group data, and Dr. med. Marvin Mergen for his assistance in organizing and conducting the focus group sessions. I am further grateful to Christina Karamanidou, PhD, for the always inspiring and productive collaboration within the MyPal project, and to Vassilis Koutkias, PhD, whose vision and leadership laid the groundwork for the project. His untimely passing was a great loss to the scientific community, and I remain deeply grateful for his contribution and inspiration.

I would also like to thank the members of the Department of Pediatric Oncology and Hematology at Saarland University for providing a supportive and inspiring research environment. I am grateful to my colleagues, Dr. rer. nat. Yvonne Braun and Dr. rer. med. Stefan Theobald, for our daily collaboration, their collegial support, and the stimulating discussions that enrich my work.

Finally, I extend my deepest gratitude to my family and friends for their unwavering support and encouragement throughout this journey. Their faith in me provided the strength and motivation to persevere until the completion of this thesis.

Publications to Date

Project-Related Publications (MyPal)

- **Meyerheim M**, Karamanidou C, Payne S, Garani-Papadatos T, Sander A, Downing J, Stamatopoulos K, Ling J, Payne C, Scarfò L, Lokaj P, Maramis C, Graf N (2021) MyPal-Child study protocol: an observational prospective clinical feasibility study of the MyPal ePRO-based early palliative care digital system in paediatric oncology patients. BMJ Open 11:e045226. https://doi.org/10.1136/bmjopen-2020-045226
- **Meyerheim M**, Burns-Gebhart A, Mirzaie K, Garani-Papadatos T, Braun Y, Graf N (2021) Challenges and Pitfalls for Implementing Digital Health Solutions in Clinical Studies in Europe. Front Digit Health 3:730680. https://doi.org/10.3389/fdgth.2021.730680
- Hoffmann S, Schraut R, Kröll T, Scholz W, Belova T, Erhardt J, Gollmer D, Mauck C, Zacharioudakis G, **Meyerheim M**, Bonotis P, Kakalou C, Chatzimina M, Karamanidou C, Sander A, Didi J, Graf N, Natsiavas P (2021) AquaScouts: ePROs Implemented as a Serious Game for Children With Cancer to Support Palliative Care. Front Digit Health 3:1–10. https://doi.org/10.3389/fdgth.2021.730948
- Mirzaie K, Burns-Gebhart A, **Meyerheim M**, Sander A, Graf N (2022) Emotion Regulation Flexibility and Electronic Patient-Reported Outcomes: A Framework for Understanding Symptoms and Affect Dynamics in Pediatric Psycho-Oncology. Cancers (Basel) 14:3874. https://doi.org/10.3390/cancers14163874
- Garani-Papadatos T, Natsiavas P, **Meyerheim M**, Hoffmann S, Karamanidou C, Payne SA (2022) Ethical Principles in Digital Palliative Care for Children: The MyPal Project and Experiences Made in Designing a Trustworthy Approach. Front Digit Health 4:730430. https://doi.org/10.3389/fdgth.2022.730430
- **Meyerheim M**, Burns-Gebhart A, Mirzaie K, Dokutur S, Sander A, Graf N (2022) Clinical Impressions of Electronic Patient-Reported Outcomes in Paediatric Oncology Based on Single Case Reports in the MyPal Project (EAPC2022 Abstract Book). Palliat Med 36:111. https://doi.org/10.1177/02692163221093145
- **Meyerheim M**, Burns-Gebhart A, Mirzaie K, Dokutur S, Sander A, Graf N (2023) Insights into the Introduction of an ePRO-based Digital Health Platform in Paediatric Oncology – Focus Group Results from the Clinical MyPal-CHILD Study (EAPC2023 Abstract Book). Palliat Med 37:66. https://doi.org/10.1177/02692163231172891
- Bonotis P, **Meyerheim M**, Kakalou C, Scarfo L, Natsiavas P, Karamanidou C (2025) Enhancing Healthcare Professionals' Adherence to the MyPal Project Digital Health Intervention Protocol Through Quick Reference Guides. In: Andrikopoulou E, Gallos P, Arvanitis T, Austin R, Benis A, Cornert R, Panagiotis C, Dejaco A, Dusseljee-Peute L, Mohasseb A, Natsiavas P, Nakkas H, Scott P (eds) Intelligent Health Systems – From Technology to Data and Knowledge: Proceedings of MIE 2025 (Stud Health Technol Inform). IOS Press, Amsterdam, pp 283–287
- Chatzikonstantinou T, Vasilopoulou M, Kyrou D, Karakatsoulis G, Argyropaidas P, Besikli-Dimou S, Bonotis P, Chatzimina M, Didi J, Dimosthenous C, Garani-Papadatos T, Hoffman S, Kakalou C, Kazantzaki E, Kiefer S, Koumakis L, Ling J, Maramis C, **Meyerheim M**, Payne C, Papangelou C, Payne S, Pontikoglou C, Reston R, Ryblom H, Sander A, Schera F, Smedby KE, Zacharioudakis G, Chatzidimitriou A, Doubek M, Stavroyianni N, Ghia P, Papadaki HA, Rosenquist R, Graf N, Natsiavas P, Stamatopoulos K, Karamanidou C, Scarfò L (2025) Assessing an eHealth Intervention on Quality of Life in Patients With Chronic Lymphocytic Leukemia and Myelodysplastic Syndromes: The MyPal Randomized Controlled Trial. JCO Oncol Pract OP2500087. https://doi.org/10.1200/OP-25-00087
- Kyrou D, Bonotis P, Kakalou C, Vasilopoulou M, Scarfò L, **Meyerheim M**, Sander A, Arpáš T, Kazantzaki E, Maramis C, Karamanidou C (2025) Perceptions and Needs of Stakeholders Regarding MyPal Project's Electronic Patient-Reported Outcome App: Cross-Sectional Qualitative Focus Group Study. JMIR Cancer 11:e57388. https://doi.org/10.2196/57388

Further Publications

- Panagiotidou F, Masouros D, **Meyerheim M**, Georgiadi E, Graf N, Soudris D, Stamatakos G (2022) Virtual instances or avatars of a nephroblastoma digital twin: creating a performance efficient architecture for the clinical adaptation of the Nephroblastoma Oncosimulator. In: Virtual Physiological Human (VPH) Conference: Digital Twins for Personalized Treatment Development and Clinical Trials. 6-9 September, Porto, Portugal, p 136
- Mergen M, **Meyerheim M**, Graf N (2023) Reviewing the current state of virtual reality integration in medical education – a scoping review protocol. Syst Rev 12:97. https://doi.org/10.1186/s13643-023-02266-6
- Mergen M, **Meyerheim M**, Graf N (2023) Towards Integrating Virtual Reality into Medical Curricula: A Single Center Student Survey. Educ Sci 13:477. https://doi.org/10.3390/educsci13050477
- Mergen M, Graf N, **Meyerheim M** (2024) Reviewing the current state of virtual reality integration in medical education - a scoping review. BMC Med Educ 24:788. https://doi.org/10.1186/s12909-024-05777-5
- Laupichler MC, Aster A, **Meyerheim M**, Raupach T, Mergen M (2024) Medical students' AI literacy and attitudes towards AI: a cross-sectional two-center study using pre-validated assessment instruments. BMC Med Educ 24:401. https://doi.org/10.1186/s12909-024-05400-7
- Wen S, Theobald S, Gangas P, Borja Jiménez KC, Merks JHM, Schoot RA, **Meyerheim M**, Graf N (2024) A practical guide to apply AI in childhood cancer: Data collection and AI model implementation. EJC Paediatr Oncol 4:100197. https://doi.org/10.1016/j.ejcped.2024.100197
- Kockwelp P, **Meyerheim M**, Valkov D, Mergen M, Junga A, Krüger A, Marschall B, Holling M, Risse B (2024) VR-based Competence Training at Scale: Teaching Clinical Skills in the Context of Virtual Brain Death Examination. Proc ACM Hum-Comput Interact 8:1–31. https://doi.org/10.1145/3664635
- **Meyerheim M**, Panagiotidou F, Georgiadi E, Soudris D, Stamatakos G, Graf N (2025) Exploring the in silico adaptation of the Nephroblastoma Oncosimulator to MRI scans, treatment data, and histological profiles of patients from different risk groups. Front Physiol 16:1465631. https://doi.org/10.3389/fphys.2025.1465631
- Junga A, Bozdere P, Hätscher O, Scherzer S, Schmidle P, Schulze H, Pielage L, Kockwelp P, **Meyerheim M**, Mergen M, Risse B, Marschall B, Glückselig T, Ungru K, Schmitz M, Akbal M, Sassen C, Schwarz J, Wagner F (2025) Rethinking interaction design - special implications for interaction concepts in medical education using virtual reality. Virtual Real 29:98. https://doi.org/10.1007/s10055-025-01180-7
- Mergen M, Will L, Graf N, **Meyerheim M** (2025) Feasibility study on virtual reality-based training for skin cancer screening: Bridging the gap in dermatological education. Educ Inf Technol 30:5251–5282. https://doi.org/10.1007/s10639-024-13019-w

Curriculum Vitae

Aus datenschutzrechtlichen Gründen wird der Lebenslauf in der elektronischen Fassung der Dissertation nicht veröffentlicht.