

Patient empowerment for cancer patients through a novel ICT infrastructure

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ABSTRACT

As a result of recent advances in cancer research and “precision medicine” approaches, i.e. the idea of treating each patient with the right drug at the right time, more and more cancer patients are being cured, or might have to cope with a life with cancer. For many people, cancer survival today means living with a complex and chronic condition. Surviving and living with or beyond cancer requires the long-term management of the disease, leading to a significant need for active rehabilitation of the patients. In this paper, we present a novel methodology employed in the iManageCancer project for cancer patient empowerment in which personal health systems, serious games, psychoemotional monitoring and other novel decision-support tools are combined into an integrated patient empowerment platform. We present in detail the ICT infrastructure developed and our evaluation with the involvement of cancer patients on two sites, a large-scale pilot for adults and a small-scale test for children. The evaluation showed mixed evidences on the improvement of patient empowerment, while ability to cope with cancer, including improvement in mood and resilience to cancer, increased for the participants of the adults’ pilot.

1. Introduction

As a result of recent advances in cancer research and “precision medicine” approaches, i.e. the idea of treating each patient with the right drug at the right time, more and more patients are being cured, or might have to cope with living with their cancer, which is increasingly considered a chronic disease [1]. Cancer as a chronic illness is among the most prevalent and expensive health problems worldwide [2]. Surviving and living with or beyond cancer is rising, for example in the United Kingdom [3] at an estimated rate of 3.2% per year. These ever-increasing numbers lead to an urgent need for cancer patients taking an

active and leading role in their rehabilitation, supported by the corresponding healthcare providers. This shift from acute to chronic care brings emphasis to self-management of cancer, where patients need to have an active and informed role in managing psychological, physical and social aspects of their health. As chronic disease management will continue to be an important component of health care, the identification of self-management processes for cancer [4] can greatly help to guide clinical practice and future research in supporting self-management efforts and integrated care.

Integrated care requires health and social care workers, from multiple professional backgrounds and different organizations, to work

Abbreviations: API, application programming interface; App, application; CDSS, clinical decision support systems; CFE, care flow engine; CFD, care flow designer; e-diary, electronic diary; eHI, eHealth intervention; GCP, guideline for good clinical practice; ICT, information and communication technology; IEO, european institute of oncology; IM, informative material; IMC, iManageCancer; iPHR, intelligent personal health record; IT, information technology; MRF, model repository framework; MHA4IMC, MyHealthAvatar for iManageCancer; mHealth, mobile health; PHIR, personal health information recommender; PHR, personal health record; SAF, smart analytical framework

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together – frequently through virtual platforms. ICT plays a vital role in supporting this team-oriented way of working [5,6], where professionals must share information about – and with – the patient in real time so as to provide high-quality, people-centred, coordinated care. This need has already been identified by several social media platforms for patients (e.g. PatientsLikeMe [7], Patient Empowerment Network [8], and CancerConnect.Com [9]), cancer specific mobile apps (e.g. Cancer Blockade, Breast Cancer Diagnosis Guide, My Cancer Manager, iCANCer, Cancer Coach, Pocket Cancer Care App, Breast Cancer Diary, Cancer.Net Mobile) and projects (e.g. p-Medicine and MyHealthAvatar projects). However, an integrated approach for collecting and integrating the currently fragmented technologies, for all involved stakeholders, such as serious games, personal health systems, decision support tools, careflow management tools etc. is still missing.

In such a context, the iManageCancer project, an EU funded project under the European Union's Horizon 2020 research and innovation programme, focused on offering effective solutions to all aforementioned areas, based on the concept of patient empowerment, and continuity of care. Continuity of care is concerned with quality of care over time. It is the process by which the patient and his/her physician-led care team are cooperatively involved in ongoing health care management toward the shared goal of high quality, cost-effective medical care [10]. The central objective of the project has been to motivate the cancer patient to take a more active role in the management of his/her disease. In so doing, the patient is to be supported by a dedicated ICT platform that offers a range of mHealth services aiming to (i) assess and improve his/her psycho-emotional status, (ii) improve his/her understanding of the disease (iii) involve more efficiently his/her family and treating physician in the disease management process.

As earlier stated, the technologies required to support integrated care are still missing [11]. As a result, a novel ICT infrastructure has been developed, designed in accordance to the needs of both the care providers and the patients, focusing on cancer self-management and on individual's wellbeing. The platform puts emphasis on monitoring and the reduction of adverse events of cancer related therapy, on tools for monitoring the psychoemotional status of the patient and on technology for self-motivation and goal setting. Since continuity of care is a central objective, the infrastructure and its services offer seamless integrating, and sharing of information amongst the members of the care team, the informal care givers and the patient her/himself.

This paper provides details on the infrastructure developed within the project, based on a co-design development process, and presents the results from its evaluation studies. More specifically, within the iManageCancer multiple apps have been developed such as the iPHR, the iManageMyHealth, the iSupportMyPatients, the Serious Games and the MyHealthAvatar4IMC offering a unique user experience to patients, doctors/researchers, family members and caregivers. In this paper, we will focus on the most novel ones, selected for extensive piloting in clinical studies:

- The **iPHR**, a personal health system for the patient with a set of novel intelligent apps such as the Personal Health Information Recommender, the alerts mechanism and a psychoemotional profiler.
- The **two serious games** developed, one for adults focusing on balancing life aspects, and one for kids focusing on social support and for patient psychological support
- The **decision support tool** enabling the definition and execution of careflow models.
- For accessing, the heterogeneous information collected by the project an effective **data management layer** ensures the persistence of all data and the integrated access to them via a semantic uplifting mechanism.

In addition, we provide short descriptions for the remaining components of the infrastructure. For supporting all these applications, an

appropriate security layer ensures granular access to information, compliant with European and national legislation. The flexibility of our approach is demonstrated by the fact that multiple, heterogeneous workflows and applications work harmonically for empowering patients. In fact, besides the individual novel components, a key novelty of the platform lies in the integration of all these tools in a unique infrastructure easily offering as a whole a vast amount of services for patients and care providers. We argue that its novelty lies in the proposed integrated technological infrastructure that enables effectively and efficiently continuity of care, it empowers patients and their relatives through an ICT based self-management service platform to better manage the cancer disease in all phases of the care continuum in collaboration with their healthcare providers. All involved participants can now be cooperatively involved sharing useful information and insights in ongoing health care management towards the shared goal of high quality medical care and improving the patient quality of life. It further allows patients, through an easy-to-use interface for mobile devices, to keep track of their health and disease status, of therapies and results of clinical interventions or tests, and to keep a health diary on personal clinical observations, such as side effects of therapies, which the patient can share with his healthcare providers. The benefits of our approach are depicted by the corresponding evaluation results collected, showing that indeed when used by adults improved coping with cancer, mood and cancer resilience.

A preliminary, abridged version of this paper presented the first version of the developed architecture [12]. The current paper extends the previous one in many ways. First, it details the final architectural specifications of the platform, showing the final components and their interactions. It focuses on the most novel ones, offering additional details for those, providing only short descriptions for the other components. In addition, it also presents the semantic layer in details and most importantly, it provides and discusses results from evaluation in the two pilots.

The rest of this paper is structured as follows: In **Section 2** we present related work and in **Section 3** we elaborate on the methods. In **Section 4**, we provide details on the technical architecture of the platform and the various layers developed. Then, **Section 5** presents results from our evaluation and **Section 6** provides a discussion on the lessons learnt and the limitations. Finally, **Section 7** concludes this paper and provides directions for future work.

2. Related work

In this section, we review similar approaches, highlighting the novelty of the developed platform. Surveys on ICT-based patient empowerment for cancer patients [13 14] have already identified several key components for patient empowerment (namely, educational services, patient-to-patient services, electronic patient outcome services, portal services and multicomponent ones) showing that IT services are important, by providing knowledge to patient empowerment. On the other hand recent research [15] has identified that for apps developed for patient empowerment of cancer patients, sources and references were absent in almost 80% of the descriptions. In addition, 20% of the apps for cancer management contained gamification elements. Furthermore, 75% of these apps was not promoting at all the communication with health providers, lacking of such functionalities. Nevertheless, a meta-review on cancer related information [16] identified that evidence exists for positive effects of ICT technology on perceived support, knowledge, and information competence of cancer patients. However, outcome effects for cancer patients are limited and show mixed evidences. In fact, in several cases, e.g. [17], evidences do not support the hypothesis that ICT tools used can indeed increase self-efficacy for coping with cancer mainly because of methodological reasons. Those surveys highlight the need for an integrated platform, developed based on a sound methodology, supporting the integration between the patients and health providers, focusing on patient

empowerment, offering clinically validated information and support, and highlight the need for evaluation of the developed technologies.

To this direction multiple decision aid systems have been developed for helping patients to make informed decisions for prostate cancer screening [18] and treatment [19] and for breast cancer surgery [20], however offering simplistic support and with limited evaluation. In addition, questionnaire-based tools for systematic monitoring the mental health of cancer patients [21] and their fatigue [22] and for supporting clinical decision support, self-reporting and self-management [23] (e.g. the PROMT-Care system [24]) or for enhancing patient-physician communication (e.g. the LOOP system [25]) are currently available. Furthermore, multiple serious games have been developed for cancer. For example [26] and [27] focus on patient education for increasing drug compliance, decreasing physical side effects of chemotherapy and improving psychological status, [28] and [29] track the level of pain, and [30] promotes social integration of kids and adolescents with cancer treatment.

However, all these attempts present a highly fragmented landscape of tools for cancer management, as they focus on a very specific area neglecting the fact that cancer means living with a chronic and complex condition. Within the iManageCancer project many diverse tools have been developed, like the aforementioned ones (e.g. a decision aid that helps the patient to make informed decision on cancer screening and treatment, multiple online questionnaires available for patient profiling, multiple communication tools between the patients and with their care providers, serious games etc.). However, the developed solution goes far beyond the individual functionalities of those modules creating a whole ecosystem for the management of cancer, enabling actual integration of patients and health providers and continuity of care, finally empowering patients in collaboration with their health providers.

The limitations of the various fragmented approaches have already been identified by multiple research projects as well. For example the ACGT project [31] tried to provide a novel infrastructure for advancing the clinico-genomic trials on cancer, whereas the INTEGRATE project [32] tried to deliver solutions for advancing clinical research and enabling multidisciplinary collaboration on cancer. However, although patient empowerment was among project's objectives, the notion of the participatory aspect of the patient empowerment was not investigated. p-Medicine [33] was among the first projects to focus on patient empowerment trying to offer personalized patient services in the form of a Personal Health Record, whereas MyHealthAvatar [34] was delivering e-health infrastructures partially covering some cancer scenarios. To the best of our knowledge, there is no other available platform enabling the health and psychoemotional monitoring for cancer patients, augmenting communication with doctors, offering decision support tools and many added-value health services.

3. Methods

An overview of the research and development methodology of the iManageCancer project is shown in Fig. 1. It is consisted of four main phases:

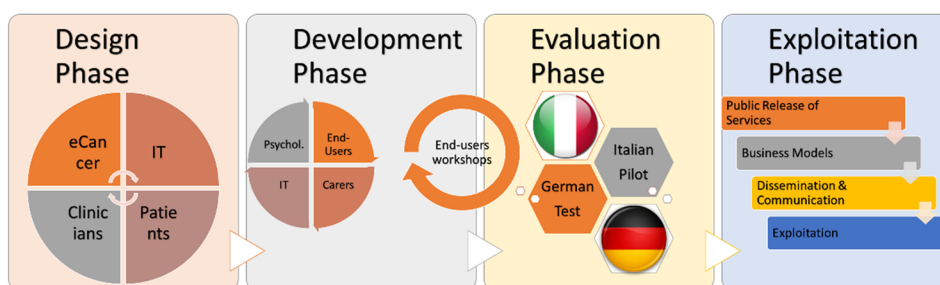


Fig. 1. Methodology of iManageCancer platform.

Design phase. In order to identify the technological solution to be developed, we initially relied on an extensive literature review on existing platforms for cancer self-management and a survey collecting the perspective from clinicians, psychologists, patients and citizens (answered by 226 adults) [36]. The survey helped us to understand on one hand the needs of citizens and patients from a platform like iManageCancer and on the other hand, to get feedback from end-users on what kind of scenarios were relevant for them. Using this information, the most important use-case scenarios were established, from an end-user perspective. In addition, three white papers from a research, publishing and consultancy group called PatientView were analyzed:

1. White paper 'What do people want from health apps?' [37].
2. White paper 'Health apps: Where do they make sense?' [38].
3. White Paper 'What do patients and carers need in health apps – but are not getting?' [39].

As a result, fourteen scenarios were created for helping patients to manage their disease in all aspects. Those scenarios were transformed into formal use cases and technical system requirements [40] and the key components were identified, required to deliver the envisaged functionalities. In the next step, these technical requirements were further validated and analyzed in order to provide input for establishing the system architecture, identifying the various components and their interactions. Same or similar requirements were summarized and merged, while some requirements were assigned to multiple components or services. Apparent conflicts were identified and resolved. Then the first version of mockups were generated. In an iterative way, led by the clinical partners, the scenarios and the respective mock-ups of the system were further refined. For this purpose, a first workshop took place for the consortium members and patient representatives, and then those results were also presented to a joint workshop with the EURECA (Enabling information re-Use by linking clinical Research and Care) project, resulting in further elaboration of the scenarios and the mockups.

Development phase. The development of the iManageCancer tools and services was based on an iterative process, which included clinicians, patients and other end-users right from the beginning of the process assigning them the responsibility to thoroughly test the usability and the functionality of the overall platform. Trying to identify whether the developed tools meet the end-users expectations, we integrated risk management activities in the software life cycle management. In addition, we adopted a software validation process based on the ISO/IEC25000 [41] series. In order to assure the quality of the desired outcome, the developed software was constantly being validated during and at the end of each development iteration. This validation was performed by internal clinicians and external patient associations, guaranteeing the effective co-design of the final solution. As such, during the development, several identified obstacles were removed in an iterative process between users and developers. For example, although there were problems with the usability of the platform at the beginning, after two development iterations usability problems were resolved.

Evaluation. The platform was developed with the objective to improve the degree of involvement of cancer patients' in their own care process. The apps and their functions support patients in getting a more active role in their healthcare pathway. Since the disease has an effect on the emotional sphere of the patient (positively or negatively), key research questions were to identify whether using the app's functions would influence patients' mood and cancer resilience and whether using the platform has an impact on patient engagement. In addition, we wanted to identify whether the platform and its services can affect patients' cognitive/attitudinal base, enabling them to increase their awareness about their condition.

To achieve these objectives, two studies have been conducted. First, a study with adult patients which was focused on evaluating the effects of the app usage among breast and prostate cancer patients, according to the objectives highlighted above; second a small-scale testing involving children, which collected anecdotal information on usability and interaction with the application through semi-structured interviews; Both studies were established during the lifetime of the project and all administrative regulations according to GCP criteria for clinical trials were successfully solved including ethical approval. Patients could be entered into the trial during the last year of the project. In the sequel, we provide more details on the two specific studies:

Pilot for adults: The objective of this study was to analyze patients' response to the usage of the iPHR app. As a preliminary evaluation, experts from the consortium used the application to report possible malfunctions or usability issues. Secondly, patients who declared using the platform were asked to respond to a usability questionnaire adapted from the Systems Usability Scale [42]: these data were used descriptively to account for the app reaching a satisfactory usability score, and were not included in further analyses. Next, the research group identified relevant constructs to analyze patients' empowerment, namely resilience, which regards the ability of people to resist and manage negative experiences and trauma; since the application is expected not only to provide entertainment and positive emotions but to help patients to exercise psychological abilities, it is possible that their resilience ability would be influenced by the continual use of the application resources. Secondly, it was considered important to evaluate changes in patients' attitudes toward cancer, in terms of their motivation and ability to confront it and to manage illness and therapy. Thirdly, the application usage, as well as the experience of the disease per se, could affect mood and emotional responses, which are an important component of perceived quality of life. For this reason, it was important to analyze patients' emotional state before and after the usage of the application (or, of the informational material in case of the control group). Finally, we wanted to see whether the application (expected group differences) or the continual experience of a disease to manage (expected pre-post differences) were associated to higher patient empowerment/engagement, namely commitment by patients towards their own care journey.

For the adult's pilot, the inclusion criteria were a diagnosis of early stage breast or prostate cancer, age between 18 and 75, IT literacy and undergoing active oncologic treatment (surgery, chemotherapy or radiation therapy). Exclusion criteria were psychiatric comorbidities, metastatic disease, or impairments to fill questionnaires or sign the informed consent. In addition, a number of psychological states related to patients' activation/involvement in their own care were used. Specifically, the Resilience Scale for Adults [43] and the Mini-Mental Adjustment to Cancer scale (Mini-MAC) [44] have been used to analyze changes in patients' attitudes towards their own situation. Indeed, these tools analyze patients' tendency to manage their own state in a more or less functional way; as explained already, we expected that the usage of the application could have influenced patients' ability to confront with the diseases. The first tool measures resilience or the ability of adaptation in the face of significant losses, trauma or suffering, as well as the ability to find positive outcomes within adverse circumstances; this has been used to track possible changes in patients' psychological strengths

related to the use of a health management tool. Diversely, regarding the importance to analyze patient's attitude towards cancer, the Mini-MAC questionnaire [19] has been used, which includes subscales such as "avoidance" (patients' tendency to not-deal with the disease so to avoid emotional suffering), and "fighting spirit" (attitude towards actively combating the illness). This tool is useful to account for specific changes (both positive and negative) in patients' personal approach to illness and health management, which is possibly influenced by having novel technological tools to conceptualize, experience and manage illness. Additionally, the Profile of Mood States [45] has been used to investigate changes in patients' emotional state, in order to account for fine-grained aspects of the emotional reactions to the care process mediated by the tool. Finally, in order to respond to the third objective, patients' involvement in their own health was used as a primary endpoint and was measured using the Patient Health Engagement Scale [30]. This is an evidence-based measure of the patient's involvement, as an active human resource, in his or her own care process, which is a complex construct comprising cognitive (e.g., performing effective health decision-making), behavioral (e.g., adhering to therapy) and emotional aspects (e.g., being able to manage stress and illness-related negative emotions).

Patients respecting the inclusion criteria were proposed to take part in the study by one of the members of the iManageCancer team in IEO. After written informed consent, they were randomly assigned to one of the study groups (eHealth Intervention (eHI) vs. Information Material (IM); see below). Randomization was stratified by cancer site. At the beginning of the study (T0), all patients underwent a paper-based assessment that included a Case Record Form collecting socio-demographic information, disease characteristics, past and current treatments. The administration of the questionnaires described in the endpoints section the assignment to one of the study groups.

Patients in the eHealth intervention (eHI) group were given a smartphone equipped with the iManageCancer platform at T0. They could use the platform for 6–10 weeks depending on their consultation schedule. Patients assigned to the Informative Material (IM) group followed the standard care flow and were given standard informative material about their disease usually provided by the hospital. After 6–10 weeks (depending on the appointments scheduled by the clinicians), all patients underwent the same assessment as T0. Three to five months after the beginning of the study, clinical performance indices were evaluated.

Small scale test with children: In most cases, children cancer can be cured today with an overall survival rate of more than 80%. This improvement is mainly due to enrolment of children with cancer in prospective randomized clinical trials, basic research and empowering of parents of children with cancer [46]. The pilot for children aimed to evaluate the iManageCancer platform and its services in practice regarding feasibility, acceptance, usability, performance, costs, and outcome on quality of life of cancer patients. The pilot passed all regulatory bodies and ethical approval was given by the Ethical Committee of the 'Ärzttekammer des Saarlandes' (No.: 96/17, 18th July 2017). As cancer in childhood affects always the whole family, parents and their ill child were invited to take part in this pilot by giving informed consent. After registration in the iManageCancer platform parents automatically received credentials for the game for kids and access to the iMC platform. For the following 6 months, parents and children were asked to use the IMC platform and play the game for kids. At the end of the 6 months, parents were interviewed to evaluate the platform, tools and the serious game for kids.

4. Proposed model

The architecture of the iManageCancer technological infrastructure, shown in Fig. 2, was generated as a result of three development cycles and constant user interaction. It consists of five layers: a) the application layer that provides all functionality through a rich graphical user

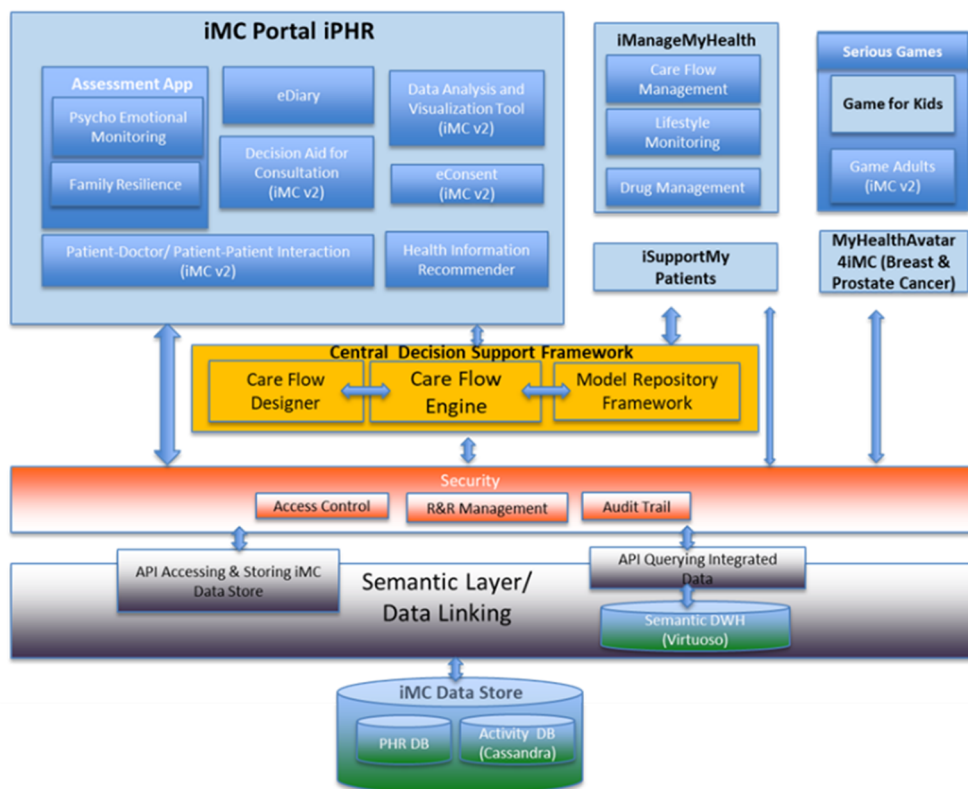


Fig. 2. The high-level architecture of the iManageCancer platform.

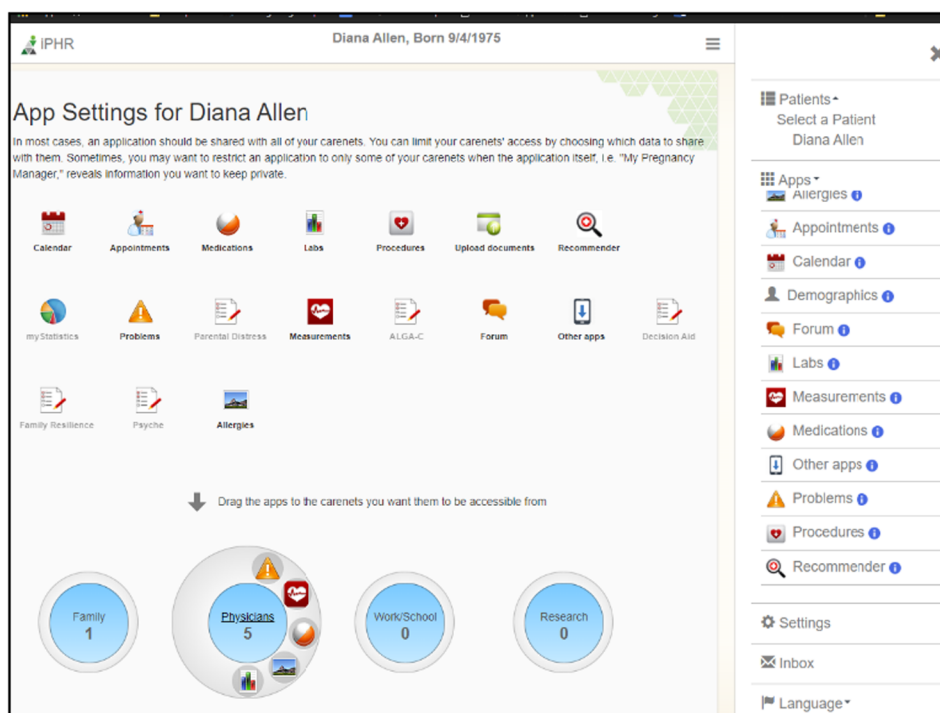


Fig. 3. Sharing available data with own networks.

interface, b) the central decision support framework enabling intelligent decision support, c) the security layer ensuring selective access to the available information, d) the semantic layer integrating all available information and the e) data storage layer enabling the persistence of all available data. Fig. 3.

The implemented platform follows the patient/user centered design

principles and its security mechanism is not an exception. The patient is the owner of his/her data and controls the access to the data from others such as the doctor or a friend. The platform supports authorization (using the industry standard protocol OAuth 2.0), authentication, delegation, auditing for secure access and for the communication between services and a flexible data sharing mechanism. Every patient,

registered to the platform, can upload various kinds of data. As these data are private and confidential, specific requirements for data protection have been addressed including https protocol, roles and rights management system, encrypted disk and database, while secondary usage of data is available only after consent and anonymization. The following sections describe in more detail each one of the remaining layers in detail.

4.1. The iManageCancer PHR portal

For the patients, the intelligent Personal Health Record (iPHR), is the central access point. It is accessible through all mobile devices (laptops, mobile phones, tablets etc.) and contains a collection of individual application that can be activated at will. They can be categorized as follows:

Apps for collecting health information: This category includes apps for recording and visualizing patient health information (*problems, medications, procedures, allergies, immunizations, laboratory results and measurements* apps).

Health Management apps: This category includes apps enabling the active management of health related issues and patient engagement. Such applications include an *intelligent e-diary* where all available information is visualized using timeline and calendar views, an *appointment* app for recording and reminding doctor appointments and a *documents* app for uploading existing medical documents (discharge letters, images etc.). In addition, a patient is able to actively share his information with selected persons or groups.

Intelligent apps: In this category there are multiple apps exploiting intelligence in order to provide various recommendations to patients. For example, the *Personal Health Information Recommender* [47] is a semantic [48] search engine and a recommendation system, which enables patients to search for health related information in a set of relevant documents selected carefully by domain experts. The *alerts* mechanism identifies predefined correlations between measurements, medications and laboratory results and is able to notify patients to contact their doctor if needed.

Psychoemotional apps: This category includes applications [49] that enable monitoring of the psychoemotional status of a patient through the *ALGA-C* and the *Psyche* online questionnaires, to capture the family status through the *Family Resilience Questionnaire* and the *Parental Distress* and to enable decision making through the *Decision Aid* app.

Apps for doctors and researchers: The apps in this category include apps able to provide overviews of the patient information and for analyzing the patients' data providing all necessary information to the doctor for decision-making. As such, the *Profiler* app constructs visual profiles of the patient psychoemotional status with guidelines for the doctor on how to interpret each result. Furthermore the *Smart Analytical Framework (SAF)* [50] enables cohort analysis and exploration of the available data shared with individual doctors.

4.2. The MHA4iMC and the iManageMyHealth app

The MHA4iMC app has been developed for the cancer patient empowerment, supporting the daily management of their lifestyle and promoting a healthy living. It helps patients to monitor, record and manage all their activities and physical exercises offering a unique tool for self-data collection. In addition, it focuses on patient education by providing information on potential risks, diet choices, and exercising and reduces related risks increasing their compliance with recommendations for healthy living.

The mobile application iManageMyHealth provides support for patients to successfully manage an increasing number of prescribed drugs and to generate warnings for dangerous interactions between them. The interactions of the application with other components is shown in Fig. 4, whereas the user interface is shown in Figs. 5 and 6.

The medication management app offers functionality to easily

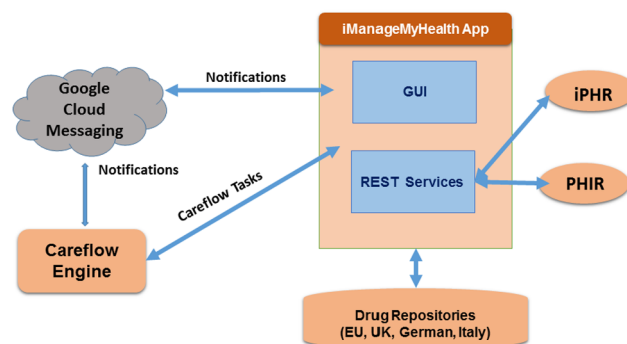


Fig. 4. ManageMyHealth app interactions.

create a medication plan including information about prescribed drug intakes like dosage, frequency, drug intake time(s) and corresponding reminders. The patient is also able to report adverse effects and outcomes that have been witnessed.

By leveraging public drug repositories, drugs in the medication plan are automatically checked if active ingredients of drugs affect each other when administered together. The interaction can be antagonistic or synergistic. Antagonistic means that the drug's effect is reduced whereas synergistic means that it is increased. In some cases, drug interactions can lead to a new effect that the individual drugs do not produce. As such, the app provides information on these interactions and supplementary functionality to view the drug taking history, and to get structured information about a drug like instruction leaflet.

The drugs in the medication plan can be also scanned for contraindications due to patient's reported diseases and health status. For example, some medications might only cause adverse events in people with specific allergies, in case of pregnancy, diabetes, high blood pressure etc. Additionally, the app performs quality checks, e.g. if the dosage for the patient is correct according to age and weight data as recorded in the patient's profile.

The multifunctional app also allows patients to record measurement values when using medical devices for blood pressure, weight, and temperature monitoring. Devices from specific vendors can be directly connected with the smartphone via Bluetooth Low Energy protocol. The measurements are stored in the local database and optionally in the iManageCancer data store using the security infrastructure of the platform. They can be viewed as graphs on the smartphone and on the iManageCancer portal as well.

The patient can edit his profile information, access the own records on the iManageCancer platform. Further to this, he can take pictures of his paper based clinical documents and add them to the own health profile and get additional information on terms that he does not understand. The medical documents can be optionally synchronized with the iManageCancer portal.

4.3. Serious games

iManageCancer focused on implementing two serious games, one for adults and one for children.

For adults: The serious game for adults, shown in Fig. 7, has the objective to educate patients on healthy lifestyle in an entertaining way. The game has to do with balancing between the different aspects of life for virtual characters in the game. As such, the patients can understand how the choices they make regarding lifestyle, diet and exercising affects their well-being and are able to translate these key lessons in their individual life. The app is communicating with the iManageCancer platform for capturing statistics, whereas at the same time offline playing is also supported. In addition, the players can exchange comments and score on social networks. Fig. 8.

For kids: "Boosters" is a serious game for children and adolescent.

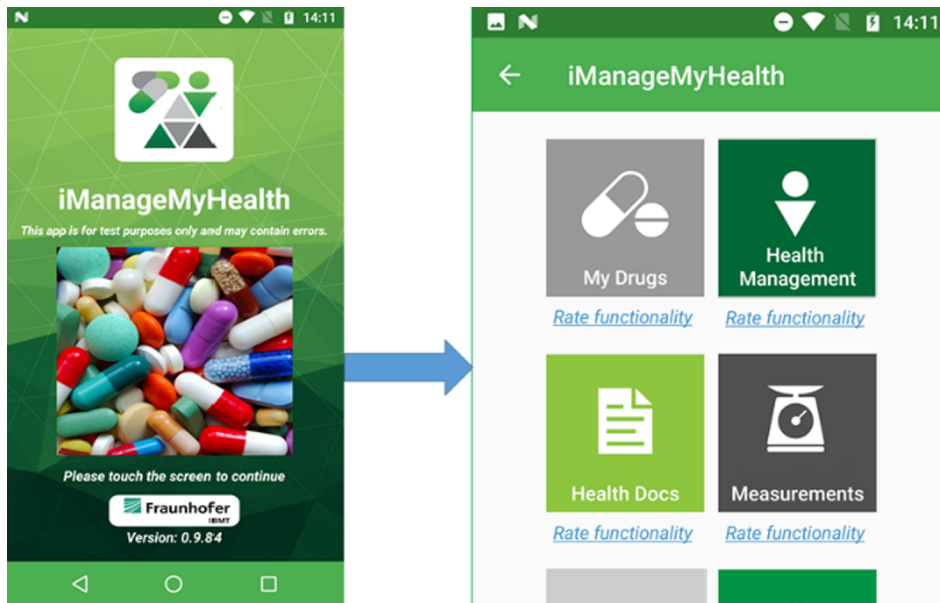


Fig. 5. Start page and main menu.

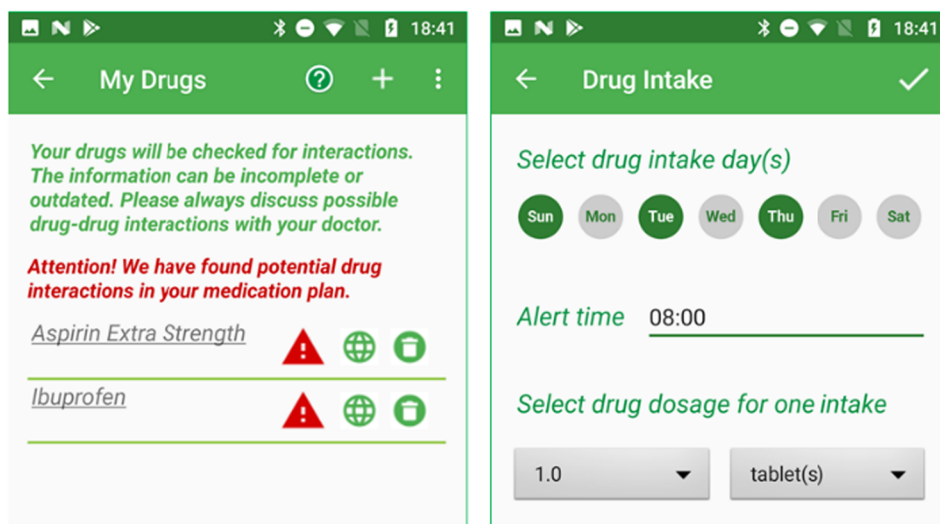


Fig. 6. Medication plan and drug intake times.



Fig. 7. Serious game for adults.

The game combines the elements of a classical shooter game and a match game (like “Candycrush”) with social aspects. The screenshot in Fig. 7 shows a scene from the shooter game.

The game is developed for the two most important operating systems of mobile devices, iOS and Android. It can be played on both smartphones and tablets. In the shooter game, the players travel with their vessel through the human body and fight various types of virtual cancer cells using multiple weapons gained by their supporters. The different weapon types are aligned with the different therapeutic options available in cancer treatment.

As such, the game sends out the message that patients themselves can play an active role in the combat against cancer – and that weapons do exist. Also, social aspects are included in the game, as family members and friends can act as the player’s supporters, who send to them extra weapons, extra damage shields and – simply, but maybe most importantly - attention. An important finding that came out from the evaluation activities of the serious games is that there is a need to have a deeper understanding of the game’s target, so a child-friendly tutorial mode was added.

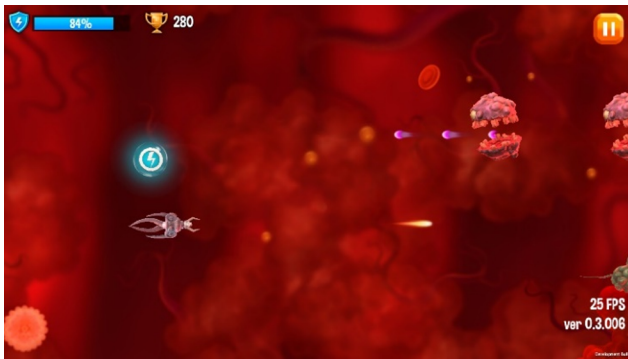


Fig. 8. Serious game for kids.

4.4. The decision support tool

Clinical decision support systems (CDSS) cover a wide range of health applications spanning across health economics, adverse events alerts and patient satisfaction. Main objective of CDSS is to improve the healthcare quality while the most recent approaches focus on the information [51] and intervention [52] delivery to the appropriate person at the right time, during the healthcare process. Another discipline of CDSS is to fill the gap between clinical research and practice acting as knowledge mediator of the research findings to the clinical care setting.

The decision support layer of iManageCancer platform provides a central point for clinical decision support for the health providers able to offer appropriate guidance based on the presented results, as shown in Fig. 9. The iManageCancer CDSS takes advantage of state of the art clinical knowledge, patient/personal data, and healthcare delivery models in order to support patients and clinical experts in the decision making process for treatment choices and management of side effects. The iManageCancer CDSS currently includes the following apps: the iManageMyHealth, the iSupportMyPatients, the Care Flow Engine (CFE), the Care Flow Designer (CFD) and the Model Repository Framework (MRF).

The execution of the (formal) disease management pathways, also called care flows [53], is delivered by the CFE. CFE has been the result of a co-design process between clinical domain experts and informaticians. It provides an intuitive user interface as formal disease management workflows [54] and uses rules that operate on patient's health information to deliver appropriate treatment paths. The iManageCancer CFE is a highly innovative technological output of the

project that follows a patient catered approach and supports the co-management of his/her health. The care flows follow the Business Process Model and Notation 2.0 (BPMN) while for the execution the open source platform Activiti (<https://www.activiti.org/>) has been deployed.

Furthermore, the system is integrated with the Model Repository Framework (MRF) [55] and can invoke predictive models tuned for identification of optimal treatment plans. The MRF framework (Fig. 10) supports a variety of multi-scale models such as combined community-developed models (e.g. the St. Gallen risk model) and knowledge models from relevant research (e.g. Oncosimulator [56], MinePath [57], microRNA model [58]) in the oncology domain. Fig. 11

With the help of the CFD, experts can design new Care Flow models, involving time triggered tasks and predictive models and can deploy them as executable workflows in the CFE. The care flows are interfaced to a user's mobile application providing recommendations for the optimal management of cancer in various aspects such as fatigue, pain or the monitoring of chemotherapy.

The iManageCancer platform is a service-oriented, modular infrastructure providing a high degree of autonomy and automation and the designing of meaningful care flow diagrams is not an exception. The iManageMyHealth and iSupportMyPatients apps provide clients that use the care flows for their execution, and can process tasks for the healthcare provider and the patient by the CFE.

Care flow models take also into account self-assessment data from the patient and their clinicians. Specialized questionnaires dedicated to health assessment and measurement tasks have been integrated into the iManageMyHealth app. Data from the different sources is compiled and advice is given as information tasks or linked with the personal medical information recommender [59] that provides high quality public internet resources on cancer.

The iSupportMyPatients app supports the healthcare professionals who can download and process tasks for their patient's. iSupportMyPatients and iManageMyHealth apps are integrated with the CFE enabling them to receive notifications about tasks assigned.

4.5. Data management & semantic layers

To enable effective and efficient data access to all information collected through the various applications and tools a data management infrastructure has been set up [60,61]. It consists of the data lake, the iMC semantic core ontology and a set of data integration tools. These will be described in detail in the sections to follow.

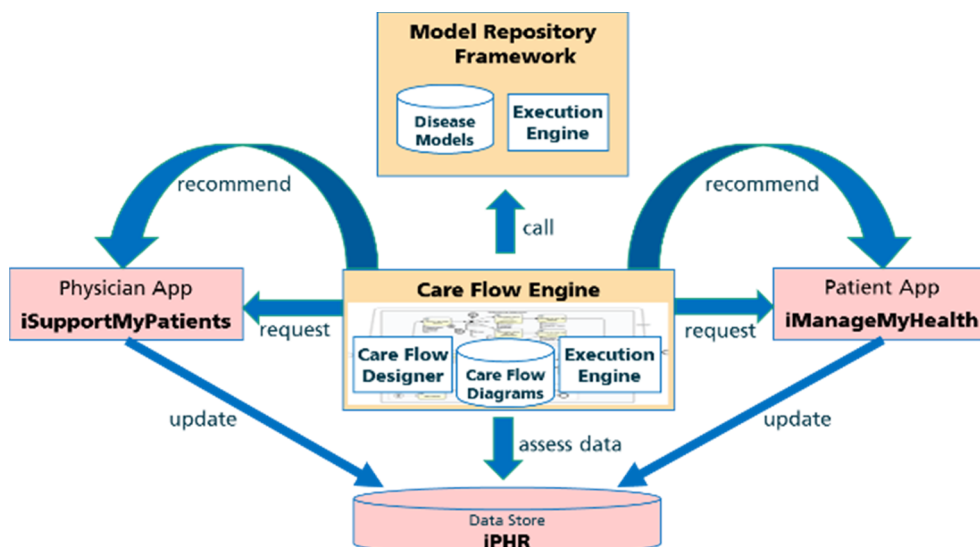


Fig. 9. The iManageCancer care flow decision support layer.

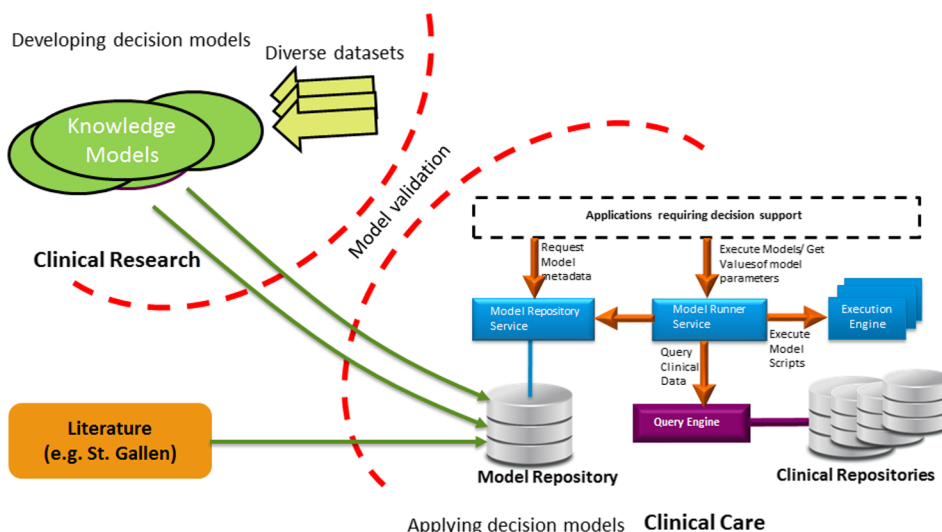


Fig. 10. The models repository framework.

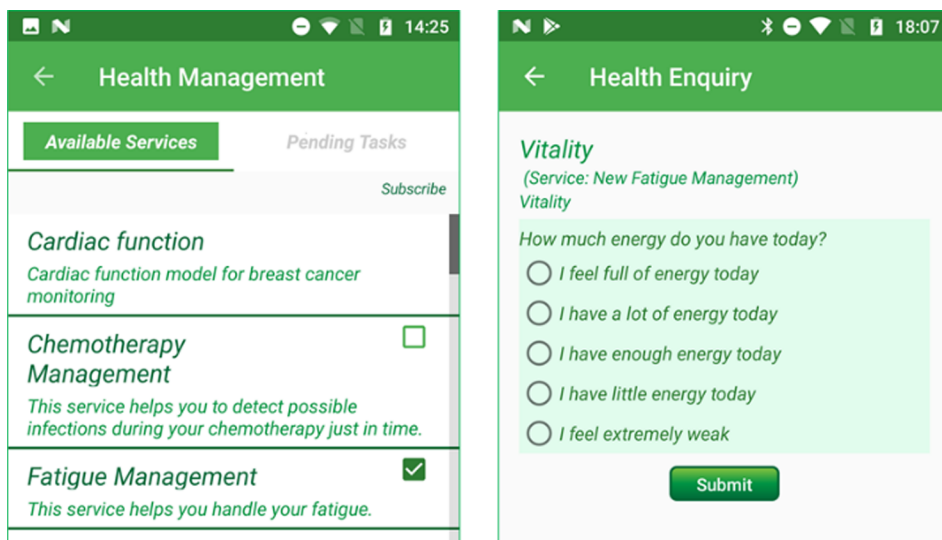


Fig. 11. iManageMyHealth app, care flows (left) and questionnaires (right).

5. The data lake.

The bottom layer of the data management infrastructure is an instantiation of the data lake. In this data lake multiple, heterogeneous databases exist offering different options for managing and accessing the stored data. For example various components use relational databases (e.g iPHR), that offer SQL-based APIs, others might use NoSQL databases (e.g. MHA4IMC) that offer CQL-based APIs etc. In addition, a triple store is available storing individual data sources such as drug interactions and selected integrated information resulted from the data integration tools.

6. The IMC semantic core ontology

For conceptually modeling the cancer domain and capturing all relevant data, the iManageCancer project reuses and extends the MyHealthAvatar Ontology Suite [34]. The resulting ontology consists of 48 subontologies, most widely used in the health domain integrated through mapping relationships. Based on this ontology all available data can be mapped to appropriate terms from this ontology and eventually integrated using the data integration tools.

7. Data integration tools

The data integration tools can get the mappings [35] between the iMC Semantic Core Ontology and the data sources and enable transparent access to them through a SPARQL endpoint. In addition, the used tools can materialize the integrated information to be further stored in the available triple store. As such, we can both access always the latest information, sacrificing execution time or access the data through their integrated instance available in the triple store, sacrificing access to the latest data. Both approaches are used in the iManageCancer project depending on the various requirements of the tools.

As SPARQL is not a common language to be used by developers, multiple APIs have been implemented on top for accessing the integrated information. In addition, direct access to the data lake is also possible, using additional data access APIs.

8. Evaluation results

In this section we report the evaluation results for the one main pilot and then for the small-scale study with children.

Table 1
Characteristics of the pilot for adults (missing responses excluded).

	Group	Men	Women
Tot recruited		47	88
Age – mean (SD)		61.6 (5.35)	51.4 (8.07)
Residence – N (%)	Intra Region	16 (37.1)	45 (62.5)
	Extra Region	26 (62.8)	27 (37.5)
Education – N (%)	No diploma	5 (10.9)	13 (14.9)
	Diploma	31 (67.4)	44 (55.2)
	B.A./M.A	10 (21.7)	26 (29.9)
Marital Status – N (%)	Married	39 (84.8)	55 (63.2)
	Never married	0 (0)	18 (20.7)
	Divorced/separated	6 (13)	11 (12.6)
	Widowed	1 (2.2)	3 (3.5)
Occupation – N (%)	Employed	21 (42.6)	55 (63.2)
	Self-employed	13 (28.3)	11 (12.6)
	Manager	3 (6.5)	3 (3.4)
	Retired	8 (17.4)	9 (10.3)
	Unemployed	1 (2.2)	9 (10.3)

8.1. Pilot for adults

In the pilot for adults, 135 patients were recruited: 88 women with breast cancer and 47 men with prostate cancer. The characteristics of the sample are shown in Table 1.

During the 6–10 weeks in which the patients tested the platform, they reported some common issues or useful comments for the improvement of applications. The most significant problems were the technical difficulties in using the app, due to internal bugs in the apps and to some patients’ lack of smartphone knowledge. Patients also reported issues in managing two smartphones, their own and the project one in addition, and in finding the time to use all the apps. A few patients also stated that they could not use the app because of the stress caused by the platform constant reference to cancer.

The results from the usability evaluation for adult patients that followed are shown in Fig. 12. Some key observations are that 90% of the patients agreed on that the platform is an added value for the hospital, 54% of the patients rated the platform in general above average and 67% of the users agreed that the system was easy to use. Finally, 74% of the users found the various features of the platform useful. Overall, the usability evaluation showed that the system was relatively easy to use and comprehend with interesting functionality, offering a benefit to the health organizations.

For what regards usage frequency, participants had more accesses (both total and mean) to the iPHR app in the first weeks, while accesses decreased in the last weeks of the intervention (see Table 2). It is important to consider that the usage data showed an inconsistent pattern,

Table 2
Number of accesses to the application by adult participants per week.

week	Total accesses per week	Accesses per patient (mean)
1	597	4.59
2	84	0.65
3	55	0.42
4	57	0.44
5	21	0.16
6	18	0.14
7	29	0.22
8	12	0.09
9	23	0.18
10	2	0.02

with patients having accesses to the application more times in the first weeks and less accesses in the last ones: future studies may explore the causes of such a decreasing beyond a typical “novelty effect”, which are not necessarily negative (e.g., the patients interiorized soon the abilities promoted by the app), as well as its influences on final results. Table 3

Mixed design analyses of variance have been conducted on all the dependent variables, with Group (Experimental vs. Control) as the between subjects factor, and Time (Pre vs. post intervention) as the within subjects factor. Resilience measures did not lead to significant differences between the groups. Mini-MAC showed meaningful differences: specifically, subscales “fighting spirit”, “anxious preoccupation”, and “avoidance” reduced in the experimental group after the iManageCancer intervention; “fatalism”, instead, reduced in both groups.

Also POMS measures showed significant results, related to differences between pre and post intervention evaluations: both groups resulted more angry, more confused, more depressed, more indolent, more anxious but also more active/vigorous after the intervention (see Table 2 for results and mean values).

Finally, also the PHE scale detected a change in level of engagement after the intervention in both groups (see Table 2 for results and mean values).

Results from the adult pilot, showed a complex pattern, especially regarding participants’ emotional response to diagnosis and treatment. Specifically, according to POMS measures, participants experienced an increase in negative emotions and physiological state; being spread across the whole sample, these changes in mood are probably related to the disease process and to the late emergence of side effects of medical therapy. However, at the same time, Mini-mental subscales were able to capture differences between groups. Those are, reduction in “Fighting spirit” coupled with reduction in “Anxious preoccupation” in experimental group if compared with the control one. This may be explained

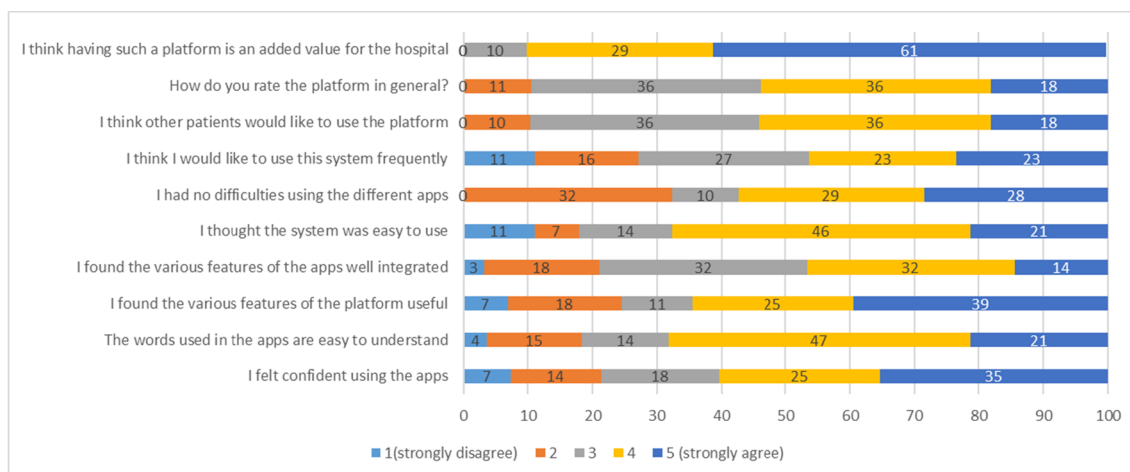


Fig. 12. The results (percentages) from the usability evaluation through the adapted SUS questionnaire.

Table 3

Results of the mixed design ANOVAs on the dependent variables (Mini-MAC, POMS, PHE scale); * < 0.05 ; ** < 0.01.

Questionnaire	Assessed dimensions		Pre-Intervention	Post-Intervention	Pre-Post comparison		η^2	Group comparison		η^2
			M (SD)	M (SD)	F(df)	p		F(df)	p	
Mini-MAC	Fighting Spirit	Experimental	15.7 (2.7)	14.6 (2.3)	2.96 (1.93)	0.089	0.031	6.08 (1.93)	0.015*	0.061
		Control	15.01 (3.5)	15 (2.2)						
	Preoccupation	Experimental	16.8 (4.2)	15.4 (3.5)	2.79 (1.93)	0.098	0.029	5.37 (1.93)	0.023*	0.055
		Control	15.6 (5.4)	15.7 (4.1)						
	Avoidance	Experimental	11.1 (2.7)	10.3 (2.4)	2.83 (1.93)	0.096	0.03	3.79 (1.93)	0.054	0.039
		Control	10.2 (3.1)	10.2 (2.1)						
Fatalism	Experimental	9.5 (2.0)	9.3 (1.9)	4.10 (1.93)	0.046*	0.042		n.s.		
	Control	10.3 (2.2)	9.8 (1.9)							
POMS	Anger	Experimental	4.6 (4.5)	9.9 (3.9)	150 (1.89)	0.000**	0.62		n.s.	
		Control	4.9 (5.2)	10 (4.5)						
	Confusion	Experimental	8.7 (5.4)	13.2 (5.3)	110.6 (1.89)	0.000**	0.55		n.s.	
		Control	8.3 (5.9)	13.2 (4.9)						
	Depression	Experimental	9.3 (9.8)	23.1 (9.1)	265.2 (1.89)	0.000**	0.74		n.s.	
		Control	9.8 (11.6)	24.1 (11.0)						
	Indolence	Experimental	6.3 (5.1)	14.1 (5.8)	333.4 (1.89)	0.000**	0.79		n.s.	
		Control	6.9 (5.9)	14.1 (5.5)						
	Vigor	Experimental	16.3 (5.9)	22.9 (5.5)	193.5 (1.89)	0.000**	0.68		n.s.	
		Control	14.9 (6.8)	22.3 (6.5)						
	Anxiety	Experimental	9.4 (6.8)	14.3 (5.3)	105.2 (1.89)	0.000**	0.54		n.s.	
		Control	9.2 (7.0)	15.7 (6.5)						
PHE	Engagement	Experimental	5.1 (1.2)	5.4 (1.2)	4.62 (1.94)	0.034*	0.047		n.s.	
		Control	4.8 (1.5)	5.0 (1.4)						

by considering the interesting result involving Mini-Mental-Avoidance, which reflects patients' tendency to "not-think" (not cope with) cancer diagnosis and its expected effects on future life. Indeed, Avoidance was reduced in experimental group as well; this could be an indication that, thanks to the tools offered by the intervention, the patients in the experimental group were able to deal with the experience of cancer sooner than their control counterparts. For this reason, they were less prone to "fight" the disease but also less anxious. This is in accordance with the patient engagement journey as described by the PHE scale and the theoretical model behind it [62]; indeed, as patients are evolving through a more complex representation of the disease and of their life with the illness, emotional experience is more dramatic than immediately after the diagnosis, when the first evaluations of psychological variables were performed. However, when the application is available, they have more occasions to deal with the disease (not "avoiding it") and reduce anxious preoccupation. This is yet another important result, showing that patients helped by the app have less tendency to feel anxious about the illness. In this sense, it is possible to sustain that the iManageCancer ICT infrastructure succeeded in augmenting patients' knowledge and in complexifying their representation of the disease (first objective). Regarding the other objectives of the study, mood and emotions appear only partially influenced by the availability of the application, while patient engagement seems, at the present time, independent of the application.

Future studies on the platform should include the analysis of the emotional responses at more advanced phases of patient engagement, to explore whether the application was useful to improve subjective quality of life too.

8.2. Small scale testing with children

In this small scale testing the goal was to enroll 23 families with children with cancer (setting a confidence level of 95% with a confidence interval (margin of error) of 20% to get results reflecting a population of 1800 patients that represents the whole population of children with cancer in Germany per year. In addition, a higher number of children was unrealistic to recruit in the timeframe of the iManageCancer project, as cancer in childhood is a rare disease with only 50 new cases diagnosed within one year at the Saarland University. However only fifteen patients were finally enrolled. This is

because some of them refused to give informed consent (5), were transferred to another hospital (1) or died within four weeks after diagnosis (2).

All families went through a semi-structured interview by a medical doctoral student. This interview included the following topics:

1. Questions regarding the process for signing the informed consent.
2. Questions regarding the usability of the platform.
3. The level of satisfaction by using the platform.
4. Whether they had to report any non-technical problems.

According to the collected reviews, the patients reported that the process for signing the informed consent was in many cases too long (3 days on average) and in some cases, they were overwhelmed by the amount of information offered by the platform. In addition, some families complained about further stress caused by the additional time required to use the platform and its IT tools at a time in which they were confronted with the cancer diagnosis. Specifically for the pilot in children, parents were worried for not been successful in the shooter game for killing cancer cells; it created additional emotional stress to them and negatively influenced their acceptance of the serious game. Many parents were also anxious about storing and sharing personal health data, which also influenced the usage of the platform, an issue that is regularly reported as a factor-influencing acceptance of eHealth and mHealth services [63].

9. Discussion and limitations

Significant advances have been made in cancer care, so that even when cure is not possible, many cancers can be controlled and managed for long periods of time. The progress in diagnosis and treatment results in more cancer survivors, and many strategies have been proposed to support this population [64]. Many physicians and practitioners consider patients being treated for some types of cancer as living with a chronic condition. Nevertheless, most of the strategies are based on group activities and tutoring, while the ICT-based systems of self-management provide in most of the cases only electronic questionnaires. The proposed ICT framework, of self-management, for patients with and after cancer, provides a broader pallet of tools with the aim to facilitate continuity of care and to enable increased patient

empowerment.

Our evaluation results demonstrate that ICT self-management tools for cancer can improve the psychoemotional status of the patient and reduce distress, a finding that is in line with available evidence [65].

A key lesson learnt from the implementation and evaluation activities of reported in this manuscript is that usability is a major key to success and that technology pilots should only start when the relevant tools have reached a high maturity level. However, in order to reach this maturity level constant involvement of all stakeholders is required and co-design with the end-users is very important.

Another key lesson is that 'One-size-fits-all'-approach does not work for cancer. A platform of multiple services must be further personalised to individual needs, to reduce the burden of patients to deal with its functionality. Some patients might not have the digital literacy required to use them, they might have different priorities and the burden of the disease/therapy might be too high to try new approaches. In addition, although we expected that serious games would be very attractive for kids, we had not foreseen the additional stress that would induce to them in some cases.

In addition, results demonstrated that the psycho-emotional state of patients in the first months after the diagnosis tend get more negative (depressed, angry). Future tools may be used not only to give patients activities and stimuli, but also affordances to express their own experience of the lived illness, so that their emotional and attitudinal response to diagnosis and treatment would be understood more clearly [66,67].

Furthermore, pilots should be constructed in a way that they assess only one (or a few) intervention(s) for the specific cancer group, and the specific phase of the treatment they are designed for. Standardized clinical guidelines are required to advice patients how to cope with monitored findings.

Finally, we have to mention that the limited participation in the small-case study. This fact did not allow us to make a statistically significant analysis of the effects that serious games have on patients' ability and resilience to cope with the disease. Nevertheless, it has proven to be a very useful intervention, in that it enabled us to discover the negative effects it had on the patients due to the increased emotional stress induced to the patients. As the platform will be used in further projects, the pilot for children will continue to seek answers on how serious games will be able to benefit cancer patients, if such benefits, do actually exist.

10. Conclusions

Studies have shown that up to two thirds of cancer patients experience substantial physical, psychological and social problems due to the disease and treatment [68]. Support from healthcare and social services is often inappropriate, and patients report high levels of unmet needs following treatment and even a long time after [69]. One key such, currently unmet, need is the effective support of continuous and integrated care [70]. In this paper, we presented the elements of a novel a novel ICT infrastructure developed and employed for supporting integration of care and empowering cancer patients to take better part in the management of their disease. We presented in detail the various

Appendix

The user scenarios were developed in an iterative process with all stakeholders. The following Fig. A1 gives a schematic overview of the selected user scenarios together with the responsible stakeholders, whereas the interested reader is forwarded to the relevant deliverable to see them in their full detail¹. All scenarios translated in use cases and built as tools/apps.

technological components developed and their integration in a unique, modular platform. The platform was tested on two sites with the involvement of cancer patients, a large-scale pilot for adults and a small-scale test for children. The results of these pilot activities are presented and discussed in detail.

A key conclusion from our work is that the platform has been shown to be effective in integrating all involved stakeholders through a multicomponent ICT platform, ensuring continuity and consistency of clinical management, including providing and sharing information and care planning, coordinating the care required by the patient. The work reported in this manuscript provides additional evidence indicating that continuity is valuable and important to both doctors and patients. It not only enables health doctors to have an improved relationship with their patients but also enables them to work more effectively and, most importantly, results in improved clinical outcomes, a finding that is in line with prior published evidence [71].

Additional key findings from the large-scale pilot demonstrate mixed evidence regarding improvements for patient empowerment due (i) to lack of time and (ii) effects of treatment that induced stress and psychological problems. Nevertheless coping with cancer, including mood and cancer resilience, improved for the trial arm using the platform. Regarding the small-scale testing in the pilot for children it was not possible to demonstrate any impact on distress in parents with children with cancer, due to the limitations on the number of patients enrolled. Nevertheless, users recognized the usability and the usefulness of the developed platform.

CRedit authorship contribution statement

Haridimos Kondylakis: Conceptualization, Methodology, Writing - original draft. **Anca Bucur:** . **Chiara Crico:** Data curation, Validation. **Feng Dong:** . **Norbert Graf:** Data curation, Validation. **Stefan Hoffman:** Writing - review & editing. **Lefteris Koumakis:** Visualization, Writing - review & editing. **Alice Manenti:** Data curation, Validation. **Kostas Marias:** Supervision. **Ketti Mazzocco:** Data curation, Validation. **Gabriella Pravettoni:** Supervision. **Chiara Renzi:** Data curation, Validation. **Fatima Schera:** Writing - review & editing. **Stefano Triberti:** Data curation, Validation, Writing - review & editing. **Manolis Tsiknakis:** Supervision, Writing - review & editing. **Stephan Kiefer:** Supervision, Writing - review & editing, Project administration.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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¹ http://imanagecancer.eu/download_file/62/294.

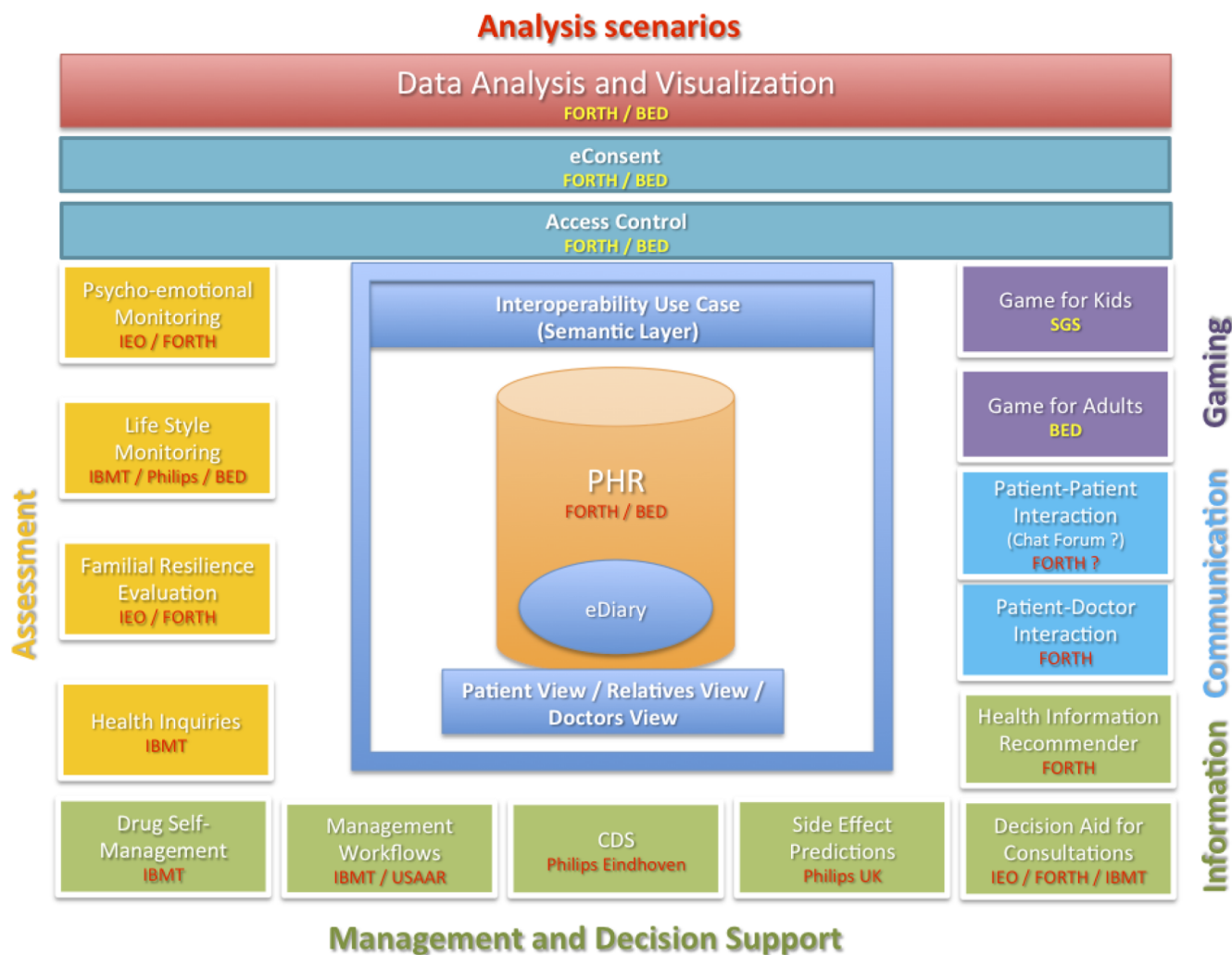


Fig. A1. Schematic overview of selected user scenarios giving also the responsible stakeholders for each of the scenarios.

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