

CMyLife: a maturing digital care platform

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A MATURING DIGITAL CARE PLATFORM



Lynn Verweij

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COLOFON

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CMyLife

A MATURING DIGITAL CARE PLATFORM

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Chapter 1

General introduction

Introduction

In this thesis, we focus on research regarding the implementation, evaluation, and improvement of CMyLife, a patient-centred, multi-component, digital care platform. Current practice in cancer care has shown that eHealth is beneficial in many ways for cancer patients, however, the uptake of eHealth is low in daily clinical practice and guidance for optimal implementation is lacking. Knowledge about the effect of digital care platforms on quality of care and how to improve these eHealth innovations is limited. CMyLife aims to provide chronic myeloid leukemia (CML) patients with knowledge and tools to improve their medication compliance and molecular monitoring, which could lead to increased quality of life.

Chronic myeloid leukemia

Chronic myeloid leukemia is a clonal myeloproliferative malignancy of hematopoietic stem cells. This disorder is characterized by increased proliferation of the granulocytic cell line with a normal differentiation. Diagnosis of CML is based on detection of the Philadelphia chromosome. This abnormality is formed by the t(9;22) translocation, which causes fusion of the breakpoint cluster region (BCR) gene on chromosome 22 to the Ableson1 (ABL1) gene on chromosome 9 (Figure 1) [1]. The formation of this BCR-ABL1 gene causes constitutively upregulated tyrosine kinase activity. Activity of this kinase causes downstream activation of various molecular pathways, which dysregulate adhesion, proliferation, transformation, and apoptotic behaviour of hematopoietic cells [2]. The BCR-ABL1 value is used for molecular monitoring as it is a blood value that accurately reflects the activity of the disease and thereby response to treatment [3].

Most cases of CML are diagnosed in the chronic phase of the disease [4]. Without treatment the disease progresses through three distinct phases, the chronic phase will progress via the transitional acceleration phase into a blast crisis, resembling acute leukemia [5]. Most common symptoms at diagnosis are mild, like fatigue, bleeding, or weight loss. CML diagnosis is often based on an accidental finding and in 20-50% of the cases no symptoms were experienced at diagnosis [6, 7].

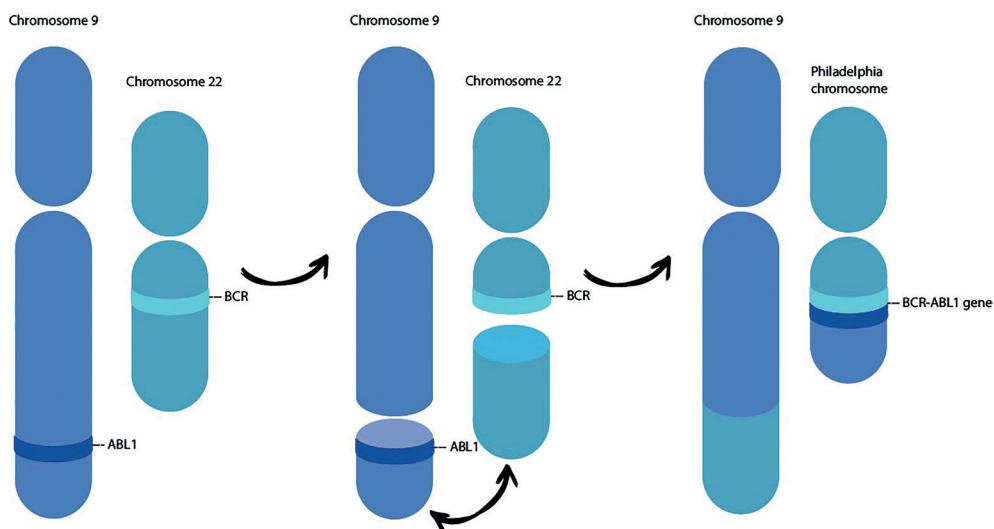


Figure 1. Reciprocal translocation between chromosomes 9 and 22 leading to formation of the Philadelphia chromosome and the BCR-ABL1 fusion gene.

Treatment

CML is the first cancer with specific knowledge on genotype, which led to a rationally therapeutic drug: a tyrosine kinase inhibitor (TKI) [8]. The first TKI, imatinib, was introduced in 2001, followed by other TKIs (nilotinib, dasatinib, bosutinib, ponatinib, asciminib) [9]. Imatinib blocks the ATP binding site of the BCR-ABL1 oncoprotein, resulting in an inhibition of the constitutively upregulated tyrosine kinase activity. Survival of patients with CML improved significantly since TKIs were used as treatment. Life expectancy of CML patients is similar to that of the general population when response to treatment is optimal [10-12]. CML became a chronic malignant disease rather than a lethal one. Most important treatment goals for CML patients are to prevent CML related death, reach a normal life expectancy, and a good quality of life [13]. Switch in TKI is recommended when patients are intolerant or when molecular milestones, described in international guidelines, are not reached [13]. Treatment-free remission is a new treatment goal, for patients who achieved a sustained deep molecular response for a sufficient period of time [13-15].

The two most important factors determining treatment success in CML care are optimal medication compliance and adequate molecular monitoring of the BCR-ABL1 values according to guidelines [16].

Optimal medication compliance

CML patients may anticipate a normal life expectancy since the advent of TKI treatment, however, low medication compliance is still a major challenge in CML care [17-19]. Mean medication compliance rates in patients with chronic myeloid

leukemia vary between 74% and 98%, only few patients were perfectly adherent with 100% intake of prescribed doses. A poor medication compliance often leads to progression of the disease and failure to achieve adequate molecular responses, which on its turn causes an increase in health care utilization and costs [20, 21]. Most common reason for intentional non-compliance was that patients suffer from adverse events of their treatment [17]. Therefore, timely recognition of adverse events by health care providers (HCPs) is essential to manage symptoms or consider switching TKI to maintain medication compliance. Previous literature has shown that HCPs overestimate their patients medication compliance and underestimate severity of adverse events of treatment [22, 23]. Also, literature shows that medication compliance is better and health care costs are reduced when monitoring disease activity is done in accordance with the guidelines [24, 25].

Adequate molecular monitoring

Adequate monitoring of BCR-ABL1 values in accordance with evidence-based guidelines is associated with reduced risk of progression and disease related mortality, since patients at risk of treatment failure can be identified timely [26]. Despite the importance of guideline adherence, literature shows that it is still suboptimal and adherence tends to be lower in hospitals treating few CML patients [26, 27]. In the Netherlands, CML patients can be treated in more than 95 hospitals. Suboptimal monitoring was reported in 26% of CML patients [27]. Previous research has shown that important reasons for physician non-adherence were lack of familiarity with the guidelines and lack of time [28].

Besides the suboptimal guideline adherence, the ageing population and therefore rising prevalence rates of chronic disease patients, among which CML patients, is another future problem [29-31]. This rising prevalence increases the pressure on health care costs and the care system together with the shortage in HCPs [29]. A Dutch report predicted that 2 million HCPs are needed in 2040 in the Netherlands, compared to only 1.4 million in 2020, hence the shortage of manpower in health care [32]. This shortage in HCPs and their limited time asks for innovative solutions [33].

There are two options in improving molecular monitoring of BCR-ABL1 values. First, to familiarize and educate all HCPs with the guidelines, however, since the amount of patients is growing this will not be sustainable as a solution on its own. Second, patients could play a more important role in guarding timely monitoring of their own BCR-ABL1 values and a shift to more involved and empowered patients should be made to enable self-management and eventually more remote care. Patient empowerment is defined by the World Health Organisation as the process through which people gain greater control over health-related decisions and

actions affecting their health [34]. The Patient Empowerment Network identified seven components which are important to empower patients and reach patient-centred care: information, health literacy, digital literacy, self-efficacy, mutual respect, shared decision making, and a facilitating environment [35].

EHealth

Provision of easy to understand and accurate information, containing relevant evidence based facts, has shown to play an important role in improving patients' self-management and empowerment [36]. EHealth could be the solution that empowers patients with tools and knowledge to play an active role in their disease process and resolve medication and monitoring problems. The CMyLife platform is co-created with and for CML patients [37]. The aim of this patient-centred, multi-component, digital care platform, is to empower CML patients and provide them with tools and knowledge to oversee and guard the process and accuracy of their treatment and thereby improve their medication compliance and molecular monitoring. This could eventually lead to increased quality of life and the opportunity of hospital-free care. The platform facilitates CML patients with a website, medication app, guideline app, and a personal health environment.

Challenges with implementation and use eHealth

Despite all benefits and the potential of eHealth, literature shows that the actual uptake of these kind of innovations is still low in both patients and HCPs and studies reported high dropout rates [38-40]. Also, guidance for implementation is lacking. Progress in the field of eHealth is accelerating, which makes implementation and evaluation of such innovations hard [41]. Implementation has shown to be more successful when innovations provide targeted and timely support including information relevant to a specific group [42]. Also, involving end users during development of eHealth showed to increase the likelihood of the innovation being implemented successfully [39, 43]. In order to keep HCPs and patients interested in using eHealth, showing evidence based added value is crucial [44]. Also, all information presented by the innovation needs to be up-to-date, to keep users interested [45]. Since eHealth innovations are continuously evolving, studies agree that systematic iterative evaluation is important to be continued after development [41, 45].

Aim and outline of this thesis

The main aim of this thesis is to explore the effectiveness of CMyLife, to investigate how to implement this digital care platform in daily clinical practice, and to find the best method to study and continuously improve such a changing tool.

The following objectives are addressed in this thesis:

- What is the best available evidence of the effect of a digital care platform on quality of care parameters such as enhancement of available information, self-efficacy, continuity of care, and patient- and health care provider–reported experiences? (**chapter 2**)
- What is the best available evidence on barriers and facilitators for implementation of digital care platforms? (**chapter 2**)
- What are barriers to and facilitators for nationwide implementation and consolidation of CMyLife, a multi-component, patient-centred, digital care platform, and which implementation activities, combined in a comprehensive implementation guide, cover these barriers? (**chapter 3**)
- What is the perceived information provision among CML patients before using CMyLife? (**chapter 4**)
- What are predicting patient factors in information perception? (**chapter 4**)
- How is the effectiveness of the CMyLife platform in terms of information provision, patient empowerment, medication compliance, molecular monitoring, and quality of life of CML patients? (**chapter 5**)
- To what extent is a participatory action research approach suited for improvement and scientific evaluation of eHealth innovations in daily clinical practice (measured by user experiences) combined with promoting patient empowerment? (**chapter 6**)

First in **chapter 2**, we focus in a systematic review on collecting the best available evidence of the effect of a digital care platform on quality of care parameters such as enhancement of available information, self-efficacy, continuity of care, and patient- and health care provider–reported experiences. Since chapter 2 shows that evidence in literature on barriers and facilitators for implementation of digital care platforms is limited, we explore barriers to and facilitators for nationwide implementation and consolidation of CMyLife, a multi-component, patient-centred, digital care platform, in **chapter 3**, and we construct a comprehensive implementation guide for launching digital care platforms in daily clinical practice. Systemic iterative evaluation of such innovations is important to be continued after initial development and implementation. Emphasizing the importance of patient information, in **chapter 4**, we conduct a cross-sectioned survey study to assess patients' evaluation of received information and information needs before CMyLife utilization and whether CMyLife as information source is used correspondingly. Additionally, we explore predicting patient factors in information perception. In **chapter 5**, we evaluate the effectiveness of CMyLife in more detail in terms of information provision, patient empowerment, medication compliance, molecular monitoring, and quality of life. Evaluation of such a dynamic set of tools in daily clinical practice is deemed tough but important to continue improvement

and further adjustments to meet patients' needs. In **chapter 6**, we aim to investigate if a participatory action research approach is suited for improvement and scientific evaluation of eHealth innovations in daily clinical practice combined with promoting sustainable patient empowerment. In **chapter 7**, we conclude this thesis with a general discussion reflecting on the results from the previous chapters and implications for future practice and research are described.

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CHAPTER 2

The effect of digital care platforms on quality of care for oncological patients and barriers and facilitators for their implementation: a systematic review

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Abstract

Background: Oncological health care services are challenged by the increasing number of cancer survivors, long-term follow-up care, and fragmentation of care. Digital care platforms are potential tools to deliver affordable, patient-centred oncological care. Previous reviews evaluated only one feature of a digital care platform or did not evaluate the effect on enhancement of information, self-efficacy, continuity of care, or patient- and health care provider-reported experiences. Additionally, they have not focused on the barriers and facilitators for implementation of a digital care platform in oncological care.

Objective: The aim of this systematic review was to collect the best available evidence of the effect of a digital care platform on quality of care parameters such as enhancement of available information, self-efficacy, continuity of care, and patient- and health care provider-reported experiences. Additionally, barriers and facilitators for implementation of digital care platforms were analysed.

Methods: The PubMed (Medline), Embase, CINAHL, and Cochrane Library databases were searched for the period from January 2000 to May 2020 for studies assessing the effect of a digital care platform on the predefined outcome parameters in oncological patients and studies describing barriers and facilitators for implementation. Synthesis of the results was performed qualitatively. Barriers and facilitators were categorized according to the framework of Grol and Wensing. The Mixed Methods Appraisal Tool was used for critical appraisal of the studies.

Results: Seventeen studies were included for final analysis, comprising 8 clinical studies on the effectiveness of the digital care platform and 13 studies describing barriers and facilitators. Usage of a digital care platform appeared to enhance the availability of information and self-efficacy. There were no data available on the effect of a digital care platform on the continuity of care. However, based on focus group interviews, digital care platforms could potentially improve continuity of care by optimizing the exchange of patient information across institutes. Patient-reported experiences such as satisfaction with the platform were considerably positive. Most barriers for implementation were identified at the professional level, such as the concern for increased workload and unattended release of medical information to patients. Most facilitators were found at the patient and innovation levels, such as improved patient-doctor communication and patient empowerment. There were few barriers and facilitators mentioned at the economic and political levels.

Conclusions: The use of digital care platforms is associated with better quality of care through enhancement of availability of information and increased self-efficacy for oncological patients. The numerous facilitators identified at the patient level illustrate that patients are positive toward a digital care platform. However, despite these favourable results, robust evidence concerning the effectiveness of digital care platforms, especially from high-quality studies, is still lacking. Future studies should therefore aim to further investigate the effectiveness of digital care platforms, and the barriers and facilitators to their implementation at the economic and political levels.

Background

Over the past few decades, the management of patients with cancer has considerably changed. Owing to earlier detection of cancer and improved treatment strategies, the number of cancer survivors has increased [1]. For this reason, patients with cancer currently require long-term follow-up care, similar to patients with chronic diseases. It is expected that the increased need of follow-up care, in combination with an overall increase of cancer patients due to an aging society, will intensify the use of health care services and increase health care costs [2]. Current health care systems cannot accommodate these increased demands and are deemed unsustainable [3, 4]. An additional problem that requires a re-evaluation of oncological health care services is the multidisciplinary, and sometimes multi-institutional, aspect of current care. This refers to the fact that cancer patients are usually cared for by multiple health care providers (HCPs), and that, as a result of centralization of complex care to high-volume centres [5], patients may receive parts of their treatment in multiple hospitals [6-9]. These aspects result in the fragmentation of cancer care [10].

The challenges facing cancer care are recognized by the World Health Organisation [11] and the Health Program of the European Union [12], and have prompted them to think of different health care structures that enable the delivery of affordable, coordinated, patient-centred oncological care. A solution in restructuring health care for oncological patients could be found in telemedicine or electronic health (eHealth). Moreover, the COVID-19 pandemic, which led to the sudden forced implementation of telemedicine, has demonstrated the potential of telemedicine and eHealth to many patients and HCPs [13]. These technologies therefore seem to be indispensable for sustainable care.

For these reasons, the time seems right to deploy eHealth much more widely in oncological care. An updated, accepted definition of eHealth is lacking, but eHealth can be perceived as an umbrella term for all digital communication and information technologies that aid in health care or health care services [14, 15]. Over the past decades, multiple eHealth interventions have been developed to support oncological care [16, 17]. The eHealth-based intervention of interest in this review is a digital care platform. We define a digital care platform as an eHealth-based tool that aims to increase coordinated and patient-centred care. A digital care platform incorporates several different features, which separately have been the subject of study elsewhere [18-21]. First, digital care platforms may provide patients with information specific to their situation. Second, they can provide an overview of the patients' personal health records, including appointments, medical results, and correspondence. Third, digital care platforms may also offer direct, secure messaging with HCPs (e.g. electronic consultation [e-Consult]). We consider these

three characteristics as key features of a digital care platform. Some additional features may include the registration of patient-reported outcome measures (PROMs), a patient forum, the possibility to exchange patient-related information between different health care institutes, and enable communication between HCPs and general practitioners. Studies on the use of eHealth-based tools and their effect on care processes have been previously described for patients with chronic diseases [22, 23]. A recent systematic review by Tighe et al [23] indicated that digital platform-like interventions such as self-management tools have a positive effect on physical activity and disease-related quality of life. A systematic review by Kooij et al [22] indicated that digital interventions had positive effects on patient confidence and HCP satisfaction, but that firm conclusions on its clinical effects could not be drawn. Studies on the use of eHealth in oncological care have reported favourable results, as it has been associated with improved patient-provider communication [24]; improved coping with cancer-related symptoms such as fatigue, depression, anxiety, and physical activity [16, 25-28]; and improved medication compliance and higher patient satisfaction [20, 27]. Some studies have also reported favourable effects on quality of life [29, 30]. However, these studies investigated the effect of only one feature of a digital care platform, for instance the registration of PROMs. Previous reviews did not study the digital care platform as a central part of the oncological health care service or the effect of digital care platforms on enhancement of information, continuity of care, or patient- and HCP-reported experiences. The effect on patient self-efficacy has only been studied for one feature of a digital care platform, namely self-management programs [25]. The outcome parameters of interest (i.e. enhancing availability of information, self-efficacy, continuity of care, and patient-reported and HCP-reported experiences) can also be placed in the Quality of Care framework provided by the Institute of Medicine [31]. The six domains of quality of care are safe, effective, patient-centred, timely, efficient, and equitable care. Enhancing availability of information is a measure of effective and equitable care, self-efficacy is a measure of patient-centred care, patient-reported and HCP-reported experiences are measures of safe and patient-centred care, and continuity of care is a measure of efficient care and arguably also timely care. Additionally, we did not identify any existing systematic reviews that focused on the barriers and facilitators that exist for the successful implementation of a digital care platform in oncological care. This is important to assess so as to adequately determine the feasibility of a digital care platform as part of routine oncological care.

The aim of this systematic review was two-fold: (1) to collect the best available evidence of the effect of a digital care platform on quality of care for oncological patients by focusing on enhancement of available information, self-efficacy,

continuity of care (including communication), and patient-reported and HCP-reported experiences; and (2) to analyse the currently reported barriers and facilitators for implementation of a digital platform in oncological health care.

Methods

Protocol and Registration

This systematic review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO; registration number CRD42020199282) [32] and was carried out according to the PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses) guidelines [33].

Search Strategy

The PubMed (Medline), Embase, CINAHL, and Cochrane Library databases were searched for the period from January 1, 2000 until May 27, 2020. Search terms used included “neoplasms” and affiliated terms combined with “patient portal” or “digital care” or “eHealth.” The aim of this search query was to provide search results on literature involving both the effect of a digital care platform on quality of care for oncological patients as well as barriers and facilitators for implementation. The exact search query is shown in Textbox 1.

Textbox 1. Search query.

(neoplasms [mesh] OR cancer* [tiab] OR tumor* [tiab] OR tumour* [tiab] OR neoplasm* [tiab] OR malignan* [tiab]) AND

("Patient Portals"[Mesh] OR "Telemedicine" [Mesh] OR Patient portal*[tiab] OR Patient platform*[tiab] OR Patient web portal*[tiab] OR Patient internet portal*[tiab] OR virtual care*[tiab] OR digital care [tiab] OR ehealth [tiab] OR e-health [tiab] OR econsult [tiab] OR e-consult [tiab])

Eligibility Criteria

Studies of interest included randomized controlled trials (RCTs), prospective studies, and retrospective cohort studies. In addition, qualitative studies in which questionnaires were distributed or stakeholders were interviewed to investigate barriers and facilitators were also included. All studies were required to generate empirical data. Studies not written in English were also screened on the condition that they presented an English abstract. A translator could translate the full text if the abstract seemed to be eligible, thus avoiding a language bias. Systematic and narrative reviews, conference abstracts, and single case reports were excluded.

For our first objective, to collect the best available evidence of the effect of a digital care platform on quality of care, studies were required to involve oncological patients ≥ 18 years old. These clinical studies had to assess the effectiveness

of a digital care platform. Although we provided our definition of a digital care platform in the introduction, considering the exploratory stage of research of digital platforms in oncological care, we suspected that there would be a rather limited number of studies investigating such an extensive digital care platform. For this reason, for inclusion in our systematic review, a digital care platform was required to have at least two of the following key features: (1) provide general information concerning the disease as education (e.g. symptoms, treatment, follow-up, prognosis); (2) provide patient-specific information concerning their medical file, such as planned appointments, treatments, and lab results; and (3) enable patients to communicate with their physician or specialized nurse via chatting, e-Consult, or email. Figure 1 depicts these and other features of a digital care platform.

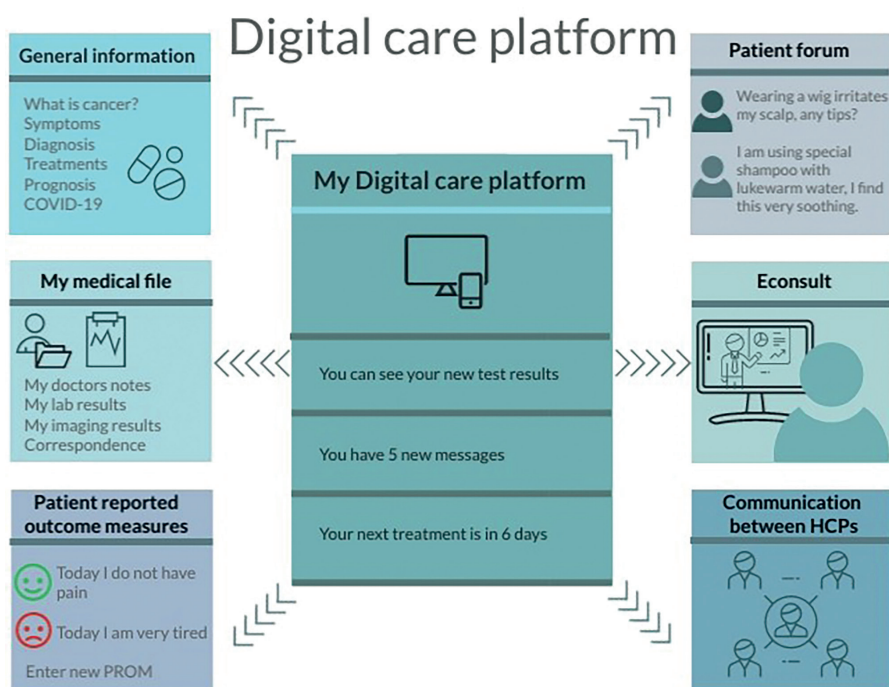


Figure 1. Explanatory illustration of a digital care platform. Studies included in this systematic review were required to investigate a digital care platform with at least two of the following features: (1) general information provision, (2) electronic patient file, or (3) electronic consult (Econsult) with health care providers (HCPs). PROM: patient-reported outcome measure.

Studies that did not involve a digital care platform with at least two of the three above-mentioned features and studies that provided insufficient or vague details concerning the digital intervention were excluded from the analysis to assess our primary objective.

For the second objective, identification of barriers and facilitators for implementation of a digital care platform in oncological care, studies were not required to involve a digital care platform that was already implemented. They could comprise studies that actually implemented a digital care platform and subsequently described the barriers and facilitators for implementation, but they could also comprise studies that identified barriers and facilitators based on a hypothetical discussion with stakeholders. In the latter case, the digital care platform in question was not yet implemented or developed.

Study Selection

Two separate reviewers (JH and LV) screened the search output on titles and abstracts using Rayyan software [34]. During this screening process, the reviewers were blinded to each other's decisions. Studies with a contradictory judgment were discussed. In case of a remaining discrepancy, senior reviewers (RH and MS) were asked to arbitrate. The full texts of the selected studies were screened for eligibility. Reference lists of studies that were included after full-text screening were checked for additional eligible studies (snowball method). In cases in which multiple eligible studies reported on the same dataset ($\geq 50\%$ overlap of sample size), we excluded the article with the shortest follow-up.

Data Extraction and Analysis

Two authors (JH and LV) extracted data using a shared template. These data included: (1) author, year of publication; (2) country; (3) study design; (4) patient population, sample size; (5) platform that was the subject of the study; (6) features of the platform; and (7) the outcome parameters, including enhancement of available information, self-efficacy, continuity of care, and patient- and HCP-reported experiences. If possible, data were pooled; otherwise, synthesis of the results was performed qualitatively.

Barriers and facilitators for implementation of digital care platforms were categorized according to the framework of Grol and Wensing [35]. This framework categorizes barriers and facilitators at six different levels: (1) innovation, which involves advantages in practice, feasibility, credibility, accessibility, and attractiveness; (2) individual professional, which concerns the awareness, knowledge, attitude, motivation to change, and behavioural routines of the involved professionals; (3) patient, which involves knowledge, skills, attitude, and compliance of the patients; (4) social context, which concerns opinion of colleagues,

culture of the network, collaboration, and leadership; (5) organisational context, which includes the organisation of the care processes, staff, capacities, resources, and structures; and (6) economic and political contexts, which involve regulations, financial arrangements, and policies. The frequency of the barriers and facilitators mentioned, and the quality of the studies were used to prioritize barriers and facilitators.

2

Critical Appraisal of Evidence

The Mixed Methods Appraisal Tool (MMAT) version 2018 was used to critically appraise the included studies [36]. The MMAT is designed to help reviewers appraise the quality of empirical studies with different methods. These include quantitative RCTs, quantitative nonrandomized trials, quantitative descriptive studies, as well as qualitative and mixed methods studies. Each category includes five different quality parameters, all requiring to be assessed by answering “yes,” “no,” or “cannot tell” (maximum total score=5). Two authors (JH and LV) independently appraised all studies. In case of disagreement, RH and MS were asked to arbitrate. Studies with a total score of 1-2 were considered to be of low quality, a study with a score of 3 was considered to be of moderate quality, and studies with total scores of 4-5 were considered high-quality studies.

Results

Search Results

The initial search generated 6789 articles. After removal of duplicates and initial screening of titles and abstracts, 52 studies remained for full-text assessment. Of these 52 studies, 17 articles met our eligibility criteria and were included in this systematic review. Figure 2 depicts the PRISMA flowchart for the study screening process.

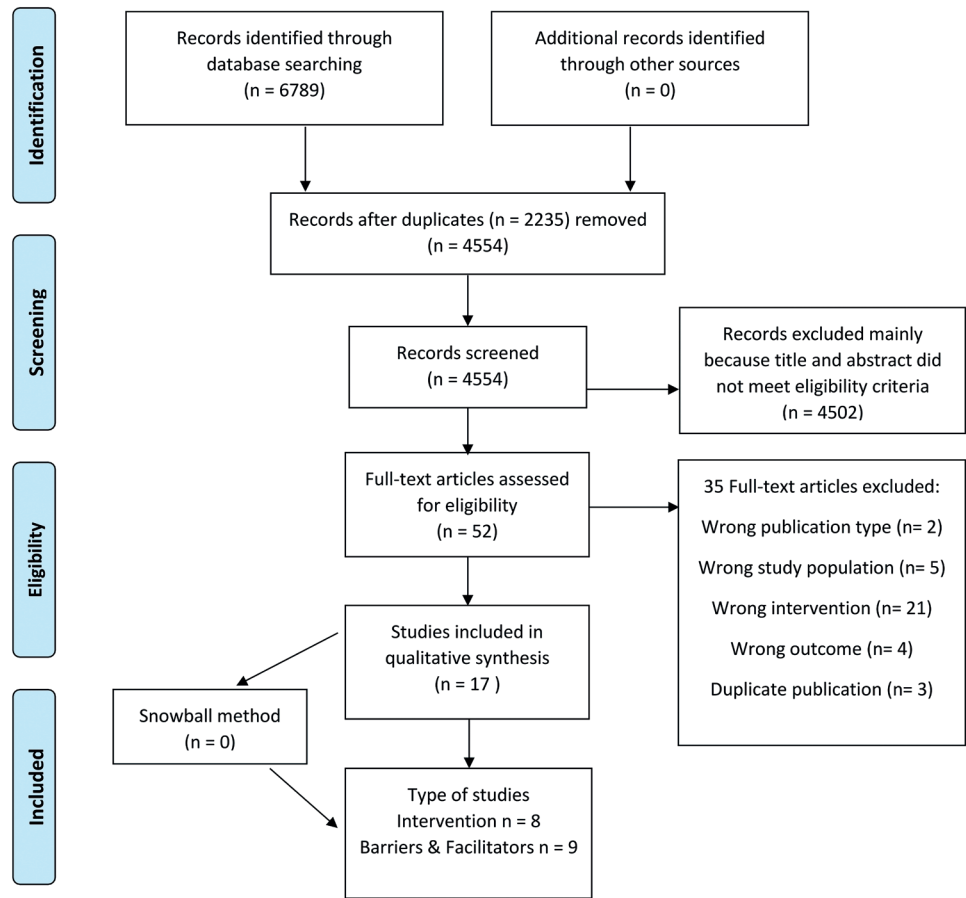


Figure 2. PRISMA flowchart.

Study Characteristics

Overview

Of the 17 included studies, eight were clinical studies that implemented a digital care platform and assessed its effect on at least one of the predefined outcome parameters [37-44]. Four of these clinical studies [39,42-44] also described barriers and facilitators for implementation. The other nine studies [45-53] only investigated barriers and facilitators for digital care platforms. None of the included studies was written in a non-English language. Table 1 and table 2 show the baseline characteristics of the clinical studies and the barrier and facilitator studies included in this review, respectively.

Table 1. Baseline characteristics of clinical studies.

Reference	Country	Study design	Patient population and sample size	Platform studied	Features of digital care platform			Outcome parameters			Q1 ^a	Q2 ^b
					General information	Access to EMR ^c	e-Consult ^d	Availability of information	Self-efficacy	COC ^e		
Baker et al [37]	US	RCT ^h	450 patients with BCA ⁱ	CHES ^j	✓	X	✓	✓	✓	X	✓	X
Børresund et al [38]	Norway	RCT	167 patients with BCA (<12 months)	Web-choice	✓	X	✓	X	✓	X	X	X
De Regge et al [39]	Belgium	Mixed methods	23 patients with metastatic kidney or bone cancer	DOP	✓	✓	✓	✓	X	X	✓	✓
Groen et al [40]	Netherlands	Feasibility study	37 patients with NSCLC ^k	MyAVL	✓	✓	X	✓	✓	X	✓	X
Gustafson et al [41]	US	RCT	257 patients with BCA (<12 months)	CHES	✓	X	✓	X	✓	X	✓	X
Kuijpers et al [42]	Netherlands	Mixed methods	92 patients with BCA (<12 months treatment)	MyAVL	✓	✓	X	✓	✓	X	✓	✓
Ruland et al [43]	Norway	Prospective cohort	103 patients with BCA (n=56) and PCA ^l (n=47)	Web-choice	✓	X	✓	✓	X	✓	✓	✓
Tiong et al [44]	Australia	Prospective pilot study	50 patients with BCA	Healthy.me	✓	X	✓	✓	✓	✓	✓	✓

^a Q1: addresses research question 1 (to collect the best available evidence of the effect of a digital care platform on quality of care for oncological patients).
^b Q2: addresses research question 2 (to analyse the currently reported barriers and facilitators for implementation of a digital platform in oncological health care).
^c EMR: electronic medical record.
^d e-Consult: electronic consult.
^e COC: continuity of care.
^f PRE: patient-reported experiences.
^g HCPE: health care provider-reported experiences.
^h RCT: randomized controlled trial.
ⁱ BCA: breast cancer.
^j CHES: Comprehensive Health Enhancement and Support System.
^k NSCLC: nonsmall cell lung cancer.
^l PCA: prostate cancer.

Table 2. Baseline characteristics of barrier and facilitator studies.

Reference	Country	Study design	Patient population and sample size	Description of platform	Q1 ^a	Q2 ^b
Alpert et al [45]	US	In-depth semistructured interviews with cancer patients and oncologists	35 cancer patients (breast n=9, haematologic n=6, gastrointestinal n=5, genitourinary n=4, lung n=3, sarcoma n=3, skin n=3, gynecologic n=2, other n=3) and 13 oncologists	Patient portals offer functional benefits to patients as they enable convenient patient access to EMR ^c data from devices such as personal computers or smartphones; they allow the ability to request medication refills, schedule appointments, and they support secure messaging	X	✓
Baudendistel et al [46]	Germany	Qualitative explorative study using focus groups	12 colorectal cancer patients, 17 physicians, and 26 other health care professionals	Patient-controlled "personal electronic health record" (PEPA) (in development)	X	✓
Ector et al [47]	Netherlands	Design thinking development study	8 CML ^d patients, 14 haematologists	CMyLife, a web-based, patient-centered intervention	X	✓
Geerts et al [48]	Netherlands	Mixed methods design: focus group and literature for patient survey, and physician survey based on literature	Patients with haematologic malignancy (questionnaire: n=204, focus group: n=6) and their physicians (questionnaire: n=13)	Not yet developed	X	✓
Gerber et al [49]	US	Qualitative study using 2 focus groups	13 nurses from a cancer center	Not yet developed	X	✓
Girault et al [50]	Canada	Questionnaire-based survey	1072 patients treated in a comprehensive cancer center	Internet-based technologies such as patient portals, websites, and applications managed by health care institutions to improve cancer care coordination	X	✓
Kildea et al [51]	Canada	Participatory stakeholder design	Focus group and survey among 361 cancer patients	Electronic patient portal accessible through smartphones (not yet developed)	X	✓
Kuijpers et al [52]	Netherlands	Focus group interviewing (9 groups)	21 BCA ^e patients, 31 lung cancer patients, and 31 health professionals	Interactive portal	X	✓
McCleary et al [53]	US	Focus group sessions and surveys	Focus group: 20 patients and family and 5 advisory council members; survey: 1019 cancer patients	Patient gateway application as patient portal: a secure, web-based database enabling patient access to their health and disease information embedded within an EMR, managed by individual health care organisations and accessible via the internet	X	✓
Kuijpers et al [42]	Netherlands	Mixed methods design: pretest-posttest design and focus group	6/92 BCA patients were included in focus group discussions; 24 health care providers were asked to fill out a questionnaire	MyAvL includes personalized educational material, overview of past and upcoming appointments, EMRs, medication overview, questionnaire concerning PROMs ^f	✓	✓

De Regge et al [39]	Belgium	Mixed method triangulation design	Interviews with 23 patients, 2 physicians, 1 nurse specialist, 2 nurse consultants, 9 nurses, and 1 psychologist	The digital oncology platform includes the individualized care path, reliable treatment-related information, contact details for the treatment team, secure conversations with the treatment team, self-registration of complaints, and a diary	✓	✓
Ruland et al [43]	Norway	Prospective cohort	103 patients with breast cancer (n=56) and prostate cancer (n=47) received questionnaires with space for additional comments and suggestions	WebChoice is an interactive electronic health application that includes personalized information, a communication tool where patients can receive support from peers or professionals, a diary, and a self-management component	✓	✓
Tiong et al [44]	Australia	Prospective pilot study	50 patients with BCA were asked to use the platform and fill out a questionnaire; 9 patients were invited for a face-to-face feedback session	Healthy.me is a secure personally controlled health management website that features the patient journey with tailored information, appointment overviews, interactive forums, and messaging with peers and private messaging with health care providers	✓	✓

^a Q1: addresses research question 1 (to collect the best available evidence of the effect of a digital care platform on quality of care for oncological patients).

^b Q2: addresses research question 2 (to analyse the currently reported barriers and facilitators for implementation of a digital platform in oncological health care).

^c EMR: electronic medical record.

^d CML: chronic myeloid leukemia.

^e BCA: breast cancer.

^f PROM: patient-reported outcome measure

Study Design

Among the clinical studies, three were RCTs [37, 38, 41], two were mixed methods studies [39, 42], and three were pilot or feasibility studies [40, 43, 44] investigating the use of the platform in a small cohort. The three RCTs included 450, 167, and 257 patients, respectively, and all assessed the effectiveness of different variations of a digital care platform [37, 38, 41]. For example, Baker et al [37] assessed the effectiveness of different components of a digital care platform by comparing patient groups using a platform with information only; a platform with information and support; and a platform with information, support, and coaching. The control group did not use a digital care platform but used the internet. An example of one of the mixed methods studies is that performed by Kuijpers et al [42], in which a digital care platform was implemented in a small cohort with a postintervention questionnaire, followed by focus group discussions. Studies solely investigating barriers and facilitators were mainly qualitative in nature, with the exception of

three studies applying a mixed methods methodology [48, 51, 53] and one study using a quantitative methodology [50].

Patient Population

Breast cancer patients formed the majority of the study population of the clinical studies, with 75% of all studies including solely this patient population. The patient population was therefore mostly female, highly educated, and young (mean age 50 years) [37, 38, 42, 43]. The other studies included patients with non-small-cell lung cancer or a diverse group of cancer patients such as those with renal cell cancer and sarcoma. One study [43] included two different patient groups, namely breast cancer and prostate cancer patients, and compared the use and effectiveness of the digital care platform between these two groups. The barrier and facilitator studies (Table 2) included patients with colorectal cancer, lung cancer, breast cancer, haematological cancer, and a variety of other cancer types.

Interventions

Within the eight clinical studies, five web-based platforms were distinguished. These platforms were all web-based and were not integrated in the electronic medical record (EMR). Seventy-five percent of the studies assessed a platform that also intended to improve self-management by, for instance, symptom monitoring, physical activity advice, or self-therapy [37, 38, 40-43]. Although each digital care platform had at least two of the three predefined criteria, heterogeneity concerning the platforms was observed. For example, the digital care platform described by De Regge et al [39] enabled HCPs, including general practitioners, to read their patients' medical records from other health care centres. This allowed them to gain insight into their patients' treatment trajectory and decision-making by other involved HCPs. Other platforms such as those described by Groen et al [40] and Kuijpers et al [42] did not have this feature, and provided personalized patient education material, an overview of upcoming hospital appointments, and tailored physical activity.

Methodological Quality

Quality assessment of the included studies is shown in Table 3. Of the clinical studies, four studies were of low quality [37, 41, 43, 44], three of moderate quality [38, 39, 42], and one study was assessed as a high-quality study [40]. Regarding the barrier and facilitator studies, three studies were of low quality [49, 51, 53], one of moderate quality [48], and five were of high quality [45-47, 50, 52].

Table 3. Mixed Methods Appraisal Tool scoring of the included studies (N=17).

Reference	Qualitative		Quantitative RCTs ^a					Quantitative nonrandomized					Quantitative descriptive					Mixed methods ^b					Total score ^c			
	1.1	1.2	1.3	1.4	1.5	2.1	2.2	2.3	2.4	2.5	3.1	3.2	3.3	3.4	3.5	4.1	4.2	4.3	4.4	4.5	5.1	5.2		5.3	5.4	5.5
Clinical studies																										
Baker et al [37]	— ^d	—	—	—	—	N ^e	?	?	?	?	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	0
Børsumd et al [38]	—	—	—	—	—	?	Y ^g	Y	?	Y	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	3
Groen et al [40]	—	—	—	—	—	—	—	—	—	—	Y	Y	?	?	Y	—	—	—	—	—	—	—	—	—	—	4
Gustafson et al [41]	—	—	—	—	—	1	?	?	?	?	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Clinical studies with barriers and facilitators																										
de Regge et al [39]	Y	Y	?	N	Y	—	—	—	—	—	—	—	—	—	—	Y	Y	Y	Y	Y	?	Y	Y	Y	N	3
Kuijpers et al [42]	—	—	—	—	—	—	—	—	—	—	N	Y	N	Y	Y	—	—	—	—	—	—	—	—	—	—	3
Ruland et al [43]	—	—	—	—	—	—	—	—	—	—	Y	N	?	?	?	—	—	—	—	—	—	—	—	—	—	1
Tiong et al [44]	—	—	—	—	—	—	—	—	—	—	N	?	Y	N	?	—	—	—	—	—	—	—	—	—	—	1
Barrier and facilitator studies																										
Alpert et al [45]	Y	Y	Y	Y	Y	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5
Baudendistel et al [46]	Y	Y	Y	Y	Y	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5
Ector et al [47]	Y	Y	Y	Y	Y	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	5
Geerts et al [48]	Y	Y	?	N	?	—	—	—	—	—	—	—	—	—	—	Y	Y	Y	?	Y	Y	Y	?	?	N	3
Gerber et al [49]	Y	Y	?	?	N	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	2
Girault et al [50]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	Y	Y	?	Y	Y	—	—	—	—	—	4
Kildea et al [51]	Y	Y	?	N	?	—	—	—	—	—	—	—	—	—	—	Y	Y	?	?	?	?	?	?	?	N	1
Kuijpers et al [52]	Y	Y	?	Y	Y	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	4
McCleary et al [53]	Y	Y	?	N	?	—	—	—	—	—	—	—	—	—	—	Y	Y	?	Y	Y	?	N	?	Y	N	1

^a RCT: randomized controlled trial.^b For mixed methods studies, a score of 5.5 was required to be evaluated using category 1 and category 3 or 4.^c Total score: 0-2=low quality, 3=intermediate quality, 4-5=high quality.^d Not relevant.^e N: no.^f ? : cannot tell.^g Y: yes.

Outcome Measures

Enhancing Availability of Information

Five studies [39, 40, 42-44] reported on enhancing availability of general information on a digital care platform. In a high-quality feasibility study [40], the option to receive information was scored by patients with a mean of 7.1 (SD 1.5) on a scale of 1-10. The actual usage of information sections in the digital care platform differed among studies. One high-quality study reported the patient EMR to be the most used section of the digital care platform (mean 6.7, SD 4.7 logins during the 4-month study period) [40] and another study of moderate quality reported the opposite finding that the information section was rarely viewed (mean 0.75, SD 1.4 number of times participants consulted the information section) [39]. Needs of patients also differed, as Ruland et al [43] reported a significant difference (625 vs 271, $P=.01$) in the number of visits to the information section between breast cancer and prostate cancer patients, with breast cancer patients visiting this section more often. In this study, which was appraised as low quality, information comprehensibility of the digital care platform was rated with an overall mean score of 7.2 (SD 1.4) and usefulness was rated with a mean score of 6.5 (SD 1.7), both on a scale of 1-10 [43]. The main reasons for consulting the general disease-related information section of the digital care platform were to get help with problems and to get assurance. In addition to the information section, the platform's ability to directly communicate with a nurse was perceived as very useful, because it was perceived as easy-to-understand information. The nurses' contribution to a patient forum was reported as a trustworthy source of information [43] and was therefore highly valued by patients [44].

Self-Efficacy

Six studies investigated the effect of a digital care platform on self-efficacy [37, 38, 40-42, 44] and all of them reported positive effects. Although the effects were not significant, a clear trend toward a positive effect on self-efficacy was reported. In the RCT performed by Børøsund et al [38], a moderate-quality study, patients using a digital care platform tended to score higher on self-efficacy compared with patients in the usual care group (mean difference 8.81, range 33-297, 95% CI $[-0.92$ to 18.53 , $P=.08$). Patients reported that a digital care platform was helpful in managing their health [44]. Groen et al [40] and Kuijpers et al [42], studies with high to intermediate quality, reported that access to general disease-related information and patients' EMRs enhanced patients' knowledge of their disease and their sense of control, based on questionnaires. Two RCTs showed that using a digital care platform increased patients' perceived ability to obtain and use health care information. The digital care platform also increased their comfort and activation level of dealing with physicians and health care situations compared to

the patient group only using the internet [37, 41]. However, both of these RCTs were categorized as low quality.

Continuity of Care

None of the included clinical studies reported specifically on continuity of care as a primary or secondary outcome parameter. However, three low/intermediate-quality studies [38, 39, 43] reported on the aspect of communication between patients and HCPs and among HCPs within the platform. A questionnaire-based pilot study [43] reported that the most valued feature of the platform (i.e. Webchoice) as expressed by the study population was the ability to send messages to their HCPs. That same research group investigated the effects of their platform in an RCT and reported 40% use of the messaging service in this platform [38]. Patients perceived this feature to be useful and easy to understand. De Regge et al [39] reported that HCPs perceived the ability to exchange research results between HCPs (e.g. HCPs in other hospitals and primary care) as valuable to patient care and a means to optimize continuity of care across institutes.

Patient- and HCP-Reported Experiences

Seven studies [37-40, 42-44] reported on patient- or HCP-reported experiences. Patient satisfaction with the studied platform was considerably high in three intermediate/high-quality studies, with a mean rating of 3.9 (range 3.8-4.09) on a 1-5 scale [39, 40, 42]. A low-quality RCT that aimed to compare the effects of three different types of interventions and one control observed significantly higher patient satisfaction scores with their HCPs compared with those of the control group at 6 weeks (3.46 vs 3.17, $P=.01$) and 6 months (3.48 vs 3.28, $P=.03$) [37]. The majority of patients (75%-93%) stated that the platform was easy to use and that it was a valuable addition to their health care experience [40,42]. The most used features of the platform varied among studies, but mainly consisted of the personal medical records in intermediate/high-quality studies [39, 40, 42]. Only two clinical studies reported the experiences by HCPs. De Regge et al [39], an intermediate-quality study, reported that HCPs perceived the digital care platform as valuable compared to current care because it provides reliable, easy-to-access information for patients and because it enables the exchange of patient-related information between care providers. Despite these positive experiences, one-quarter of the physicians interviewed by Kuijpers et al [42], an intermediate-quality study, reported an increase in workload after instalment of the digital care platform, varying from a few extra minutes to more than 10 minutes per patient, for additional explanations on information made available on the platform.

Barriers and Facilitators Levels

Overview

Table 2 presents the baseline characteristics of the studies describing barriers and facilitators. Tables S1 and S2 in Multimedia Appendix 1 present all barriers and facilitators identified in the included studies. The most prominent barriers and facilitators are discussed below. Figure 3 depicts the illustrative quotations found in the studies for each level.



No quotes were found on economic and political level

Figure 3. Illustrative quotations mentioned in included studies concerning barriers (in red) and facilitators (in green) for implementation of a digital platform.

Innovation Level

Four studies [44, 46, 48, 51] described technical challenges as a possible barrier for implementation. These included software development, functionality of the website, bugs, and log-on and internet access issues. A second barrier, concerning accessibility of the innovation, was patients' unawareness of the existence of the digital care platform, which led to limited or no use of the platform [53]. Despite these barriers, three studies showed that the use of a digital care platform is feasible [40, 42, 44]. Facilitators in practice were numerous: access to general and tailored medical information [42, 45, 47-49, 52], full EMRs [39, 42, 45-48, 50-52], and educational materials [42, 47]. Moreover, the possibility to consult HCPs through interactive tools was mentioned to be a positive feature of a digital care platform that encouraged usage [43, 44, 47, 48, 50].

Individual Professional Level

The most frequently described barrier at the professional level was the concern of HCPs regarding the release of medical information on the digital care platform and the comprehensibility of medical jargon for patients [39, 45, 46, 48, 49, 51, 52]. Patients learning about a change in their health and well-being via a digital care platform was a fear expressed by all oncologists included in two studies [45, 48]. The second most frequently described barrier, described in seven studies [39, 42, 45-47, 49, 51], concerned the fear of increased workload such as an increased burden of documentation, monitoring, and direct digital communication with patients [39, 42, 45, 49].

Concerning facilitators, one study suggested that a digital care platform would not increase workload but would rather reduce workload by easing data management [46]. Another facilitator mentioned was the ability to exchange information or medical results between different HCPs, including those in primary care such as general practitioners [39, 46]. The optimization of data exchange between institutes could avoid or reduce repeated health assessments [46].

Patient Level

Three studies indicated that patients had concerns about the readability of the information (medical jargon) displayed on the digital care platform and whether medical results could be adequately understood without professional interpretation [45, 46, 48]. Some patients mentioned that this could increase anxiety [48, 52].

Facilitators at the patient level were numerous, as indicated in Table S2 of Multimedia Appendix 1. In several studies, patients and oncologists mentioned that patients having access to the platform and their EMR could better prepare them for their doctor visit and enabled them to take on an active role during

the consultation [45-47]. In addition, patients' willingness to communicate via digital resources facilitated implementation [53]. Lastly, improved patient-doctor communication was described as a facilitator, either by improved preparedness for doctor visits or by direct messaging [52].

Social Context Level

Three studies reported concerns on how a digital care platform could change the doctor-patient relationship [48] such as by increasing the patient's autonomous handling of information [46]. The digital care platform could make patients increasingly reliant on technology with decreased reliance on face-to-face communication [46, 49]. This was feared as it may negatively influence the outpatient clinic visits as patients become more focused on discussing (irrelevant) details regarding available biomedical results rather than discussing values and preferences important for a follow-up treatment [48].

The change of the doctor-patient relationship was also mentioned as a facilitator. By enabling access to medical information, patients could become more actively involved in the management of their care and feel more comfortable to interact with their HCPs during consultations [42, 45].

Organisational Context Level

Two studies mentioned the integration of the platform into existing systems as a barrier [44, 47]. This would be especially relevant in cases in which the digital care platforms were also developed for other chronic diseases [47]. Limitations in time and resources were reported as another type of barrier [44].

A clear facilitator at the organisational level was the digital care platform's ability to exchange important patient information across health care institutes. HCPs emphasized the advantage of a digital care platform in improving the cross-sectoral availability of information about the patient to HCPs who are involved in the patient's treatment. It is suggested that the digital care platform could thereby diminish information loss, be of use in emergency situations where the rapid release of medical information is vital, and avoid repeated diagnostic investigations [46]. Organisation of care could be improved as the improved availability of information promotes cross-boundary continuity of care and diminishes fragmentation of care [39, 46]. Another facilitator at the organisational level was the early introduction of the digital care platform to the patient, preferably at diagnosis [44], and sufficient instructions concerning appropriate use of the platform for patients as well as HCPs [49].

Economic and Political Context Level

Data security and protection regarding the digital care platform were concerns reported by numerous studies [46, 50, 51, 53]. During the development of the digital care platform described by Kildea et al [51], cybersecurity testing and legal issues were the most time-consuming processes. These legal issues involved the ownership of intellectual property [51] and liability [46, 51].

Secure access was therefore identified as an important facilitator for a digital care platform [48]. Another facilitator, in the economical context, was that conferred by the optimized exchange of patient information between institutes, enabled with a digital care platform, and that unnecessary repeated diagnostic procedures and health assessments could be avoided [46].

Discussion

Principal Findings

A digital care platform for oncological patients has the potential to improve quality of care through the improved availability of information and positive effect on self-efficacy. Although continuity of care was not studied as a primary outcome in the identified studies, based on focus group interviews with HCPs, a digital care platform potentially improves continuity of care by optimizing the exchange of patient information across institutes. Patient-reported experiences such as satisfaction with the platforms were considerably positive. Our barrier and facilitator analysis indicated that the majority of barriers exist at the professional level. This included a concern of increased workload for HCPs and release of unattended medical information to patients. The majority of facilitators were identified at the patient and innovation levels. The patient's ability to become more informed, empowered, and involved in their care was identified as a prominent facilitator. Another relevant facilitator, at the organisation level, is the digital care platform's potential to improve information exchange between HCPs across different institutes. This is relevant as this may improve continuity of care and diminish fragmentation of oncological care. Among the clinical studies, the majority were of low to intermediate quality. Regarding the barrier and facilitator studies, the majority were of high quality.

The positive effects of a digital care platform described in this review are consistent with prior research studying isolated features of digital care platforms [16, 29, 54]. A digital care platform seems to be a helpful medium in providing patients with general disease-related and personal information. This is a welcoming result as previous studies have described that a considerable number of patients are dissatisfied with information provision [55, 56]. Moreover, 40%-80% of all medical information provided by the HCP during a consultation is forgotten or

remembered incorrectly [57]. Therefore, the need of patients to read or reread medical information that is relevant for their situation is an important facilitator for a digital care platform. In this systematic review, we identified studies that showed positive effects on self-efficacy, but no convincing clinically significant effects. In another systematic review, which studied the effectiveness of eHealth-based self-management tools, significant yet small effects on self-efficacy were described [25]. The authors explain that the tool was able to increase self-efficacy by enabling patients to enhance participation in their care trajectory. A more recent randomized trial refuted this finding [58]. In this RCT, the effect of an eHealth-based self-management tool (Oncokompas) was investigated in 600 cancer patients. At 3 and 6 months, patients were assessed on self-efficacy with the General Self-Efficacy scale. No significant effects on self-efficacy were observed (mean difference 0.5, 95% CI -0.4 to 1.4, $P=.31$). The authors partially attributed the lack of effect to the included patient population, which mostly consisted of patients diagnosed with cancer 2 years prior to the study. The authors suggested that this population is perhaps less in need of a self-management tool to increase self-efficacy as they have more experience and “know-how” compared with their newly diagnosed peers. The hypothesis that the effect of an eHealth-based tool may vary considerably depending on the patient population is important to consider for assessing the effectiveness of a digital care platform. In our systematic review, we included studies with patients in different stages of their disease trajectory and with different cancer types, and all effects regarding self-efficacy were positive but not significant. On the one hand, this aspect can be perceived as a limitation because the heterogeneity of patients may underestimate the effect of a digital care platform. On the other hand, it is a strength as we now have an overview of the effect of a digital care platform on self-efficacy of a broad cancer patient population, thereby increasing the generalizability of our results.

Similarity with prior work concerns the limited number of studies investigating combined features of a digital care platform. During the screening process of this review, we encountered numerous studies that only investigated one feature of the platform. This finding is similar to the findings of a review by Kruse et al [20], which concluded that many studies assessed the effect of one feature of a digital care platform and that a full platform was rarely studied in clinical practice. To adequately ascribe outcomes as an effect of the intervention, it is reasonable to first study an isolated feature of a digital care platform. However, it is absolutely vital to also study the combined features in a digital care platform for two key reasons: (1) because this is likely to be the eHealth intervention that is implemented in practice, and (2) because the effect of multiple features may not be equivalent to the sum of effects of a single feature.

The fact that we assessed the effects of digital care platforms that had at least two key features can therefore be considered a strength of this review. In addition, we assessed the effect of a digital care platform on quality of care parameters such as continuity of care, and described the patient- and HCP-related experiences. Other reviews did not, and instead only assessed the effect of a digital care platform with one feature or chose to study different endpoints such as fatigue, physical activity, depression, quality of life, and self-management abilities [20, 25, 29, 30, 54, 59]. An additional strength is that we analysed barriers and facilitators for implementation. This allows for a good understanding of what is needed for successful implementation. A final strength is that the search query was quite elaborate without exclusion of non-English articles, thereby minimizing the possibility of missing valuable studies. For these reasons, this systematic review provides a comprehensive overview of the best available evidence of the effect of a digital care platform on quality of care for oncological patients.

However, this systematic review also has some limitations. First, the included clinical studies were mostly early-stage, single-arm prospective studies where feasibility and acceptability were investigated. Although we did include three studies with a more advanced research methodology (i.e. RCTs), these studies were all appraised as studies with low to intermediate quality. This makes interpretation of these RCTs quite challenging. One RCT reported a significant difference in patient satisfaction scores favouring a type of digital care platform [37]; however, the minimal difference (3.48 vs 3.28 on a 1-5 scale) puts into question the clinical relevance of this finding. A second limitation of this review concerns the heterogeneity of study designs and of the digital care platforms. Despite our predefined criteria of what a digital care platform should include, they were still quite different from each other with respect to the specific web format, options, and intended use, among other aspects. This heterogeneity precluded a pooled analysis with quantitatively measured outcome parameters. A third limitation concerns the study population and its representativeness. Three-quarters of the clinical studies included breast cancer patients. This study population mainly consists of well-educated females [60]. Indeed, 72%-73% of the breast cancer population in the studies included in this review had a college or university degree. It is plausible that a high education is an important factor for successful use of a digital care platform. For this reason, results of this review should be interpreted with caution and cannot simply be generalized to other cancer patients. A final limitation concerns the barrier and facilitator analysis. Studies included in this review almost exclusively focused on the barriers and facilitators mentioned by the end users of the platform (i.e. the patients and HCPs). Evidently, their perspectives are crucial, but barriers and facilitators proposed by other stakeholders should also be investigated, such as stakeholders with an organisational, economic, and

political background (e.g. health insurers). This latter group can provide insight into what is required to realize the structural financing of a digital care platform.

Although there is a growing body of literature that describes the positive effects of digital care platforms, high-quality studies describing the effectiveness of these platforms integrated in oncological care are currently lacking. In addition, most studies implemented a digital care platform in one target patient population such as breast cancer patients. More evidence is required concerning the desirability and use of a platform in patients with other types of cancers and education levels. More specifically, it is important to investigate whether patients with a lower level of education can benefit from digital care platforms to the same extent as their well-educated peers to avoid widened health disparities. The same applies to the patient population with limited internet access or internet skills. Studies in this review were performed in Australia, North America, and western Europe. The usefulness of digital care platforms in countries with low internet access is likely very different.

Concerning barriers and facilitators, future studies should aim to further elucidate barriers and facilitators at the organisational level and the economic and political levels. Ultimately, this is required for a digital care platform to become a successful eHealth-based tool in the improvement of quality of care for patients living with cancer.

Conclusion

Digital care platforms have a favourable effect on availability of information and enhancement of self-efficacy. Additionally, they could potentially serve as a valuable medium to improve continuity of care by optimizing communication between patients and HCPs and among HCPs. The vast majority of patients are positive about a digital care platform and its ability to meet their needs in improving the availability of information and patient involvement. Although these results are favourable, they were mostly generated by early-stage, nonrandomized studies with a specific patient population. To fully understand whether a digital care platform is able to increase quality of care by supporting the delivery of coordinated, patient-centred oncological care, more advanced studies such as RCTs are required, as well as studies investigating the barriers and facilitators at the economic and political levels.

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Supplementary material

Appendix 1

Overview of barriers and facilitators for implementation of digital care platforms extracted from the included articles

Table S1. Overview of barriers for implementation of digital care platforms extracted from the included articles

Level	Innovation	Individual professional	Patient	Social context	Organisational context	Economic and political context
Arguments	Technical challenges (38, 40, 42, 45) Not being aware of the availability of the DCP or its features (47)	Concerns about patients accessing medical results (or bad news) before meeting their HCP (33, 39, 40, 42, 43, 45, 46) Fear of increased workload (33, 36, 39–41, 43, 45) Patients would anticipate rapid communication (39, 43) Resistance to change by healthcare providers (39, 42) Concern of changing doctor-patient relationship (42) Lack awareness of the features of the DCP (39) Patients get insight in what physicians write about them (42) Medical jargon could be a problem (36, 39) HCPs do not agree to write in plain language (42) Differences in workflow and handling the DCP communications (43)	Patients not understanding medical information or medical jargon (36, 39, 40, 42, 43) Concerns about patients seeing their test results before the appointment with their physician without further explanation by the physician (39, 40, 42) Feeling obliged to prepare the appointment by studying portal information (42) Need for commitment from patients for continuation of usage (38) Differences in needs of new patients vs patients longer familiar with their disease (33, 37)	Concern of decrease in direct communication between patient and physician (40, 42, 43) Potential to widen health disparities (39)	Integration of platform in current care and other platforms (38, 41) Limitations in time and resources (38) Generational differences in dealing with data protection (40) Lack of instruction on how to use the DCP (39, 47)	Data protection, security and confidentiality and data security (40, 44, 45, 47) Legal aspect such as ownership of intellectual property, liability, contents of the patient disclaimer form (40, 45)

DCP = digital care platform, EMR = electronic medical record

Table S2. Overview of facilitators for implementation of digital care platforms extracted from the included articles.

Level	Innovation	Individual professional	Patient	Social context	Organisational context	Economic and political context
Arguments	Feasibility (34, 35, 38)	Reduced workload for professionals by easing data management (40)	Patient empowerment (36, 39, 41, 42, 46)	Patients feel more comfortable when interacting with their oncologist when they had access to the portal in advance of appointments (36, 39)	Optimization of patient information exchange between healthcare institutes increases continuity of care (33, 40)	Multiple data collections, unnecessary repeat of medical investigations and health assessments could be avoided (40)
	Visually attractive platform (36)	Feedback and advice from the HCP (36)	High use of internet based technologies, mobile phone and computer (44)			
	Educational materials (36, 41)	HCPs encouraging use of the platform (36)	Better preparation of consults and better collaboration with HCP (better patient empowerment) (39-41)	Believed that more knowledge about their condition from viewing the portal, enabled them to collaborate better with the provider (39)	Minimizing loss of information and avoiding multiple data collection and medical tests (40)	Enhancing adherence could save healthcare costs (41)
	Access to information and being able to re-read information (36, 39, 41-43, 46)	HCPs promoting forum activity (38)	Patients at home have a high information need related to understanding and dealing with cancer-related problems. (37)		Early introduction to the tool (38)	Secure and protected access to patient data (42)
	Possibility to make and change appointments online (36, 38, 42)	Physicians using plain language instead of medical jargon (42)			Frequent content updates (38)	
	Reminder for appointments (42)	Preferring electronic communication over telephone conversations, it allows nurses to discuss and research their responses before answering questions (43)	A DCP could help organize their medical information (40)		Education regarding appropriate use and expectations of a portal (43)	
	Access to the full EMR (33, 36, 39-42, 44-46) with easy-to-understand explanation (41)		Improved patient-doctor communication with a DCP because of availability of contact information of the HCPs (45) and time to directly send questions that were not asked during consult (46)			
	Forum with peer support (37, 38)	Ability to exchange research results between care providers (e.g. other hospitals and primary care) (33, 40) to avoid or reduce repeated health assessments (40)	Rapid access to important patient information, especially helpful in emergency situations (40)			
	Communication with HCP (video consulting or messaging) (37, 38, 41, 42, 44)					
	Easy access through mobile application (33, 38)					
	Improving medication management (40)					

Overview of medication list (43) and medication history with the possibility to request medication recipe (42)

Willingness to communicate via computer, indicating a comfort level with communication via a DCP (47)

Glossary of medical jargon (42)

Perceived sense of direct communication (39)

Insight into the patient-reported experiences and outcomes (41)

Better support in understanding and coping with the symptoms (41)

Improvement of guideline adherence (41)

Providing care only when medically needed or when desired by the patient (41)

Blood samples drawn at home (41)

DCP = digital care platform, EMR = electronic medical record



CHAPTER 3

A comprehensive eHealth implementation guide constructed
on a qualitative case study on barriers and facilitators
of the digital care platform CMyLife

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Abstract

Background: Substantial proliferation of eHealth has enabled a move in patient-centred cancer care from the traditional in-person care model to real-time, dynamic, and technology supported on-demand care. However, in general, the uptake of these innovations is low. Studies show that eHealth is helpful in providing patient empowerment through e.g. providing high quality and timely information, enabling self-monitoring and shared decision making, but dropout rates are high and guidance for optimal implementation is lacking.

Aim: To explore barriers to and facilitators for nationwide implementation and consolidation of CMyLife, a multi-component, patient-centred, digital care platform, and to construct a comprehensive implementation guide for launching digital care platforms in daily clinical practice.

Methods: The first qualitative case study of a digital care platform like CMyLife was performed including five focus group- and eighteen in-depth interviews with stakeholders. Data were collected using a semi-structured interview guide, based on the frameworks of Grol and Flottorp. Transcripts of the interviews were analysed and barriers and facilitators were identified and categorized according to the frameworks. An iterative process including participation of main stakeholders and using the CFIR-ERIC framework led to creating a comprehensive implementation guide for digital care platforms.

Results: In total, 45 barriers and 41 facilitators were identified. Main barriers were lack of connectivity between information technology systems, changing role for both health care providers and patients, insufficient time and resources, doubts about privacy and security of data, and insufficient digital skills of users. Main facilitators mentioned were motivating patients and health care providers by clarifying the added value of use of a digital care platform, clear business case with vision, demonstrating (cost-)effectiveness, using an implementation guide, and educating patients and health care providers about how to use CMyLife. Based on these barriers and facilitators a clear and comprehensive implementation guide was developed for digital care platforms.

Conclusion: Several barriers to and facilitators for implementation were identified, a clear overview was presented, and a unique comprehensive implementation guide was developed for launching future digital care platforms in daily clinical practice. The next step is to validate the implementation guide in other (oncological) diseases.

Background

Substantial proliferation of eHealth has enabled a move in patient-centred cancer care from traditional in-person care model to real-time, dynamic, and technology supported on-demand care [6]. An example of a basic form of eHealth is an accessible electronic medical record which provides patients with personal health information in a secured digital environment through a webbased portal [7, 8]. In this era of advanced digital technologies, eHealth is also able to offer more than just a single component [9]. One of the most extensive eHealth innovations is a digital care platform (DCP) [10]. A DCP provides patients with multiple valuable components, such as personalized education about their condition and their treatment, an overview of their personal health record, including medical results and appointments, leading to better information provision. It also offers patients a place for direct messaging with other patients and secure patient-provider messaging, leading to better communication between patients and their health care providers (HCPs) [11-13]. Additionally, it may allow patients to register patient-reported outcome measurements to monitor and manage adverse events, leading to better medication compliance [14]. Use of aforementioned, more advanced, multi-component DCPs has shown to empower patients and help to incorporate them as an equal member of their own care team [9, 11].

Despite all these benefits, and shown helpfulness in improving care of many patients, uptake of these innovations is low and studies reported high dropout rates [15-18]. Guidance for optimal implementation of eHealth is lacking and the first step to creating this is investigating barriers to and facilitators for implementation of eHealth. Previous studies have shown that there are many reasons for patients and their HCPs to use or not use eHealth. For instance, patient needs may change over the course of their disease, and different patients prefer different types of support [19]. Innovations are more likely to be used and to be successful when they provide targeted and timely support including information relevant to a specific group [20]. Involving end users during the development of eHealth showed to increase the likelihood of the technology actually being used [7, 15, 21]. Besides, implementation of eHealth often involves complex organisational change and thereby has a major impact on health care organisation [22].

A specific group of patients in which eHealth has shown to be very important are oncological patients, for example by providing better medication management, patient empowerment, and information provision [10, 23, 24]. A recent review showed that several studies evaluated barriers to and facilitators for implementation in oncological care [10]. However, these studies mostly included limited, rather simple eHealth innovations, and had limited diversity of involved stakeholders. Previous studies by Kooij et al. (2018), Cremers et al.

(2021), and Stanimirović and Vintar (2014) did evaluate barriers to and facilitators for DCP implementation, but they did not differentiate between simple forms of eHealth and more advanced multi-component innovations, they did not include stakeholders from within and outside the hospital organisation, or they did not base their results on a specific practical example [25-27]. Nevertheless, it is not clear what is needed for nationwide implementation of a multi-component DCP and little is known about appropriate specifications of such a platform in oncological care [10, 28]. Perspectives of other stakeholders with an organisational, economic and political background from outside the hospital organisation are also important to be evaluated, for example, health insurers who can provide insight in what is required to realize structural and sustainable financing of eHealth [10]. Since there is no one size fits all, the next generation of eHealth systems should develop and refine health applications acknowledging the complex and changing needs of not only patients but all stakeholders involved, from both within and outside the hospital organisation.

CMyLife is an example of a more advanced, multi-component DCP that provides patient-centred care through empowering patients which could lead to the opportunity of hospital-free care for patients with chronic myeloid leukemia (CML). The development, features, and effectiveness of the CMyLife platform are described in detail elsewhere [1, 2]. CML is a chronic, life-long malignant disease characterized by translocation of chromosome 9 and 22, leading to the BCR-ABL1 mutation, which encodes for a constitutively active tyrosine kinase [29, 30]. The treatment consists of daily oral medication (tyrosine kinase inhibitors) and if CML patients have optimal responses to the treatment their life expectancy approaches that of the general population [31, 32]. Therefore, the primary aim of CMyLife is to improve medication compliance and monitoring of the biomarker BCR-ABL1 because these factors determine treatment success [33].

Throughout the development of CMyLife the lack of implementation guidance in the field of DCPs in general, and in oncology specifically, was felt. For example, challenges in differing end user- and stakeholder needs, and behavioural and organisational resistance were encountered throughout the development and implementation phases of the various components of the DCP. The literature outlined that these issues were not specific to our context, but more universal in nature, as described above. Therefore, the research question of this study was: "What are barriers to and facilitators for nationwide implementation and consolidation of CMyLife, a multi-component, patient-centred, DCP, and which implementation activities, combined in a comprehensive implementation guide, cover these barriers?"

Methods

Design

A qualitative study including focus group- and in-depth interviews with stakeholders involved in the implementation of the CMyLife platform was performed to explore barriers to and facilitators for nationwide implementation and consolidation of CMyLife. Study participants for the interviews were recruited between August 2018 and October 2020 and included different stakeholders to reach successful implementation [34]. After the interviews, a comprehensive implementation guide for DCPs was developed in an iterative process with involvement of the multidisciplinary CMyLife project group and a national expert panel. This study was reported in accordance with the STARi and COREQ checklists [35, 36].

Setting

In the Netherlands CML is treated in eight academic hospitals and in 68 smaller peripheral hospitals. The Dutch-Belgian Cooperative Trial Group for Haematology-Oncology is established to monitor the quality of haematological care. The latest CML guidelines recommend that molecular treatment response should be measured at least every three months in the first year, and every four to six months thereafter [4]. Since CML is a chronic disease patients biomarker levels are monitored during their entire life. CML medication falls under the Dutch expensive medicine regulation and can only be prescribed by haematologists. The Dutch health care system involves mandatory health care insurance, covering all CML care which makes treatment accessible to all patients. Since CML is a rare disease treatment results differ between hospitals with high and low CML patient numbers receiving treatment [37].

The multidisciplinary CMyLife project group was formed to coordinate the process and consisted of representatives of the main stakeholders: patients, haematologists, specialized nurses, molecular biologists, and pharmacists. The DCP CMyLife is described in Box 1.

Box 1. Description of the DCP CMyLife.

The development and features of the CMyLife platform (figure 1) were described in detail elsewhere (1, 2). CMyLife facilitates CML patients with a website (www.cmylife.nl), a medication app, a guideline app, and a personal health environment (PHE). The CMyLife platform and its components are depicted below.

The **website** provides accurate and easy to understand information about CML, medication, guidelines, side effects, and the effect on daily life (work, sports, mortgage etc.). Through the website patients are enabled to communicate with specialists and other patients.

The **medication app** (3) is used to set medication alarms, register their medication intake, request for repeat medication prescriptions and read the information leaflet of the medication. In addition, patients can log the side effects they experience, which can be shared with their HCPs through their PHE.

The **guideline app** (4) enables self-monitoring of the biomarker BCR-ABL1, by sending monitoring reminders according to the Dutch CML guideline, and shows an understandable explanation of patients' BCR-ABL1 values in relation to the Dutch guideline.

Patients can save their own medical records from their electronic medical record (EMR) in their personal health environment, consisting of a Patient Knows Best portal (5). For example, they can share their side effects with their HCP in order to discuss them.

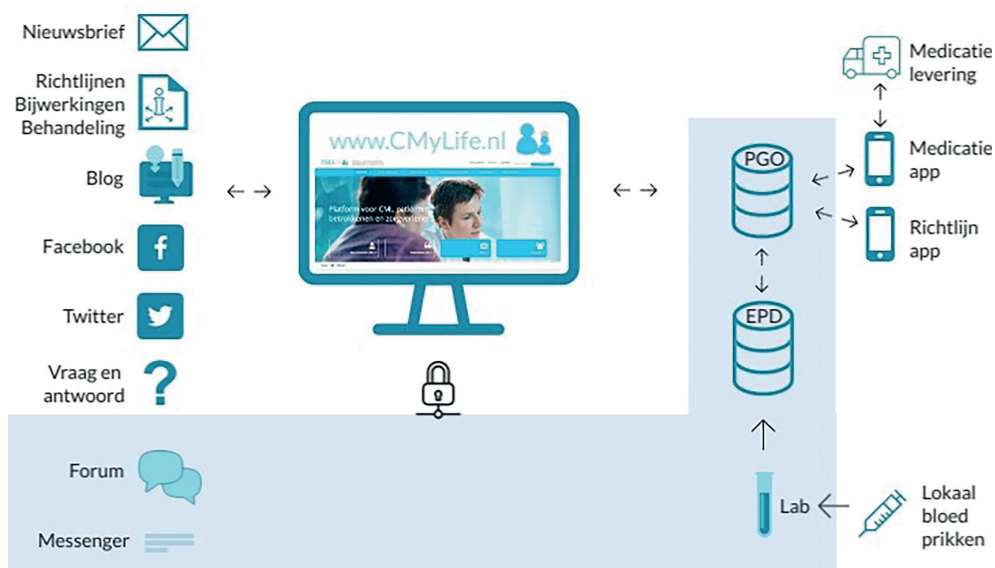


Figure 1. The CMyLife platform and its components. PHE=personal health environment, EMR=electronic medical record, all components depicted in the blue box were secured with a two-step validation with a token received via an SMS text message.

Study participants

Purposeful sampling was applied and stakeholders were approached face-to-face, via telephone, or via email to participate in this study [38]. In total, 23 interviews were performed of which five were focus group interviews with four to sixteen stakeholders of the main stakeholder groups and eighteen were individual interviews with each at least two of the additional stakeholders. Table 1 shows

an overview of the amount of participants in the (focus group) interviews. Main stakeholder groups consisted of the multidisciplinary project group, patients, haematologists, specialized nurses, and molecular biologists. The project group consisted of a policy researcher, a specialized nurse, a molecular biologist, the polyclinical pharmacist, a patient advocate of Hematon (the Dutch patient advocate association), the CMyLife project leader and the CMyLife community manager. Regarding the focus groups with haematologists and molecular biologists, researchers joined existing meetings, therefore more participants were present. The other focus groups were specially organised.

Table 1. Overview of study participants.

Focus group interviews	N	Individual interviews	N
Project group	7	Employees of pharmaceutical companies	2
Patients	6	Employees of the Netherlands comprehensive cancer organisation	2
Haematologists	16	IT-specialists	3
Specialized nurses	4	Health insurers	2
Molecular biologists	10	Policy makers	2
		Privacy officers	2
		Pharmacists	5

Data collection

Data on barriers and facilitators were collected using a semi-structured interview guide, based on the frameworks of Grol and Flottorp [39, 40], defining the barriers to and facilitators for change in health care practice at 6 different levels: (1) the innovation itself; (2) patient; (3) individual professional; (4) organisational context; (5) social context; and (6) economic and political context. Figure 2 shows a visual of the applied framework. The semi-structured interview guide was used to ensure that the main questions were asked in every interview and to have sufficient freedom to expand and ask for additional clarification on specific answers and thereby gaining in-depth understanding of how barriers and facilitators could influence implementation. Appendix 1 shows the interview guide translated from Dutch. The (focus group) interviews were held on location, which the participants preferred, or by telephone if requested, by three different interviewers (IM, RH and SR) (researchers with much experience in qualitative research), independently. No power relation between the interviewers and the interviewees was expected, therefore this did not affect the answers of the interviewees during the interviews. Informed consent was obtained before the start of each interview.

At the start of the interviews, interviewees were asked for their consent to make audio recordings of the interviews. Then, participants were informed about the background of the interviewer and CMyLife, the current situation of the platform, the duration of the interview, and the purpose of the interview. After

this, the interviewees were asked about their expected or perceived barriers to and facilitators for the nationwide implementation and consolidation of CMylife using the above mentioned semi-structured interview guide. After the interview, the interviewer gave a general summary of the interview and checked whether someone had any additional information. Finally, participants were thanked for their participation. In addition to the interviews, literature and reports about barriers to and facilitators for implementation were checked for additional barriers and facilitators for implementation.

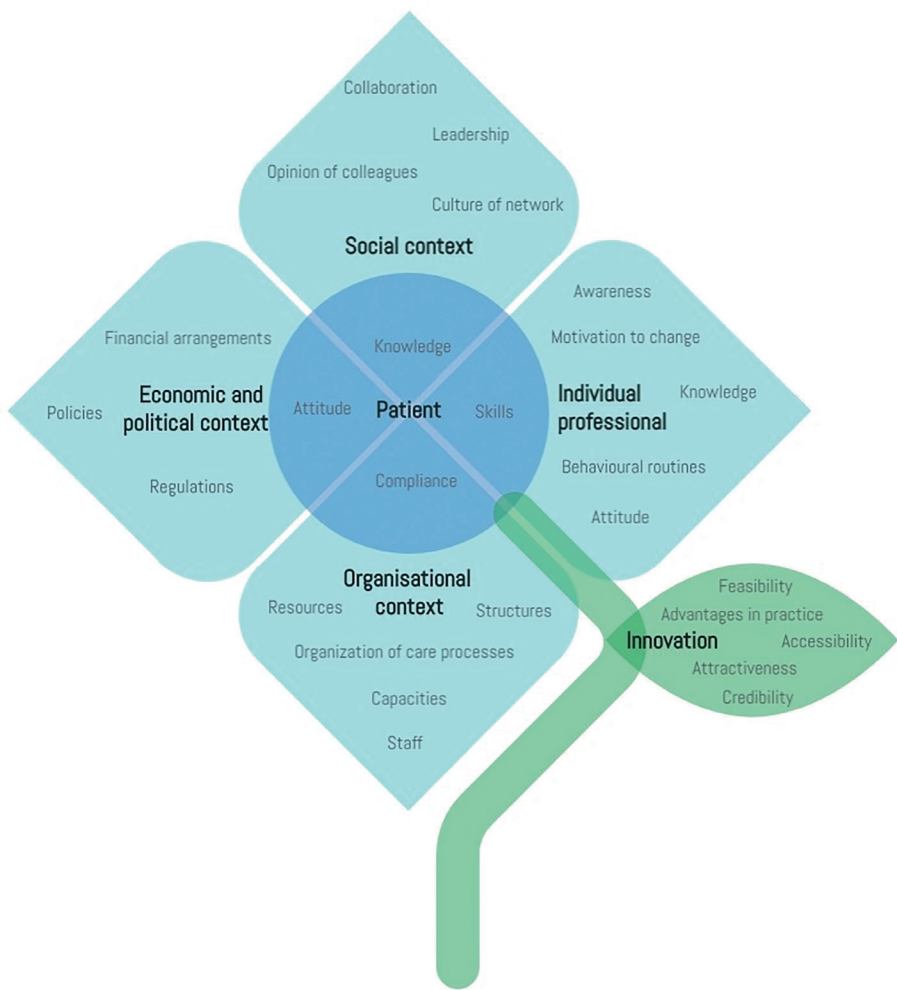


Figure 2. Barriers to and facilitators for implementation at levels of health care (39, 40).

Data analysis

First, all interviews were transcribed and all data from the interviews were anonymized. Transcripts of the interviews were qualitatively analysed by two researchers (IM and LV). They independently coded text fragments that reflected a barrier to or a facilitator for implementation of CMyLife, and then categorized them according to the above mentioned frameworks using the software programme Atlas.ti [39]. Since a pre-existing model was used for coding, the approach was deductive [41, 42]. After independently coding the transcripts, the codes were discussed between the two researchers until consensus was reached. In case of a remaining discrepancy, a third researcher was asked to arbitrate (RH). An overview of all identified barriers to and facilitators for the nationwide implementation and consolidation of CMyLife was created. To illustrate the meaning of the barriers and facilitators, quotations that were considered representative are reported in the results section. Quotations were derived from the (focus group) interviews and translated from Dutch. Creation of the implementation guide is described in detail below.

Creation of implementation guide

An iterative process including participation of the main stakeholders in the multidisciplinary CMyLife project group led to creating a comprehensive implementation guide for launching DCPs in daily clinical practice (figure 3). This process was guided by the CFIR-ERIC (Consolidated Framework for Implementation Research-Expert Recommendations for Implementing Change) Implementation Strategy Matching tool, evaluating current barriers and facilitators for implementation and matching potential actions (strategies) using facilitators to reduce barriers [43]. First, the barriers and facilitators gathered from the focus group interviews were shared and discussed. For each barrier, project group members proposed one or several potential solutions, mostly based on facilitators, and formulated matching implementation activities. Then, after the individual interviews the barriers and facilitators were again shared and discussed with the project group. They were asked if they recognized these factors and if there were any missing barriers or facilitators. Next, all gathered barriers and facilitators were plenary discussed, prioritized, and linked to matching implementation activities by the project group. Prioritization was based on what was needed to have (priority 1) versus nice to have (priority 2), and in part on what is absolutely necessary to start with (priority 1) and what can be added during the process of implementation (priority 2). Priority 3 were barriers that should be taken care of but this is beyond the control of the team implementing a DCP. Implementation experts (RH and LV) developed an implementation guide including implementation strategies using the CFIR-ERIC tool, on advise of The Netherlands Organisation for Health Research

and Development [43]. After organising, deduplicating, and generalising the first draft of the implementation guide, it was once again shared and discussed with the multidisciplinary project group and subsequently with the most important stakeholders (patients, haematologists, specialized nurses, molecular biologists, and pharmacists) in a digital expert panel meeting to come to a final version.

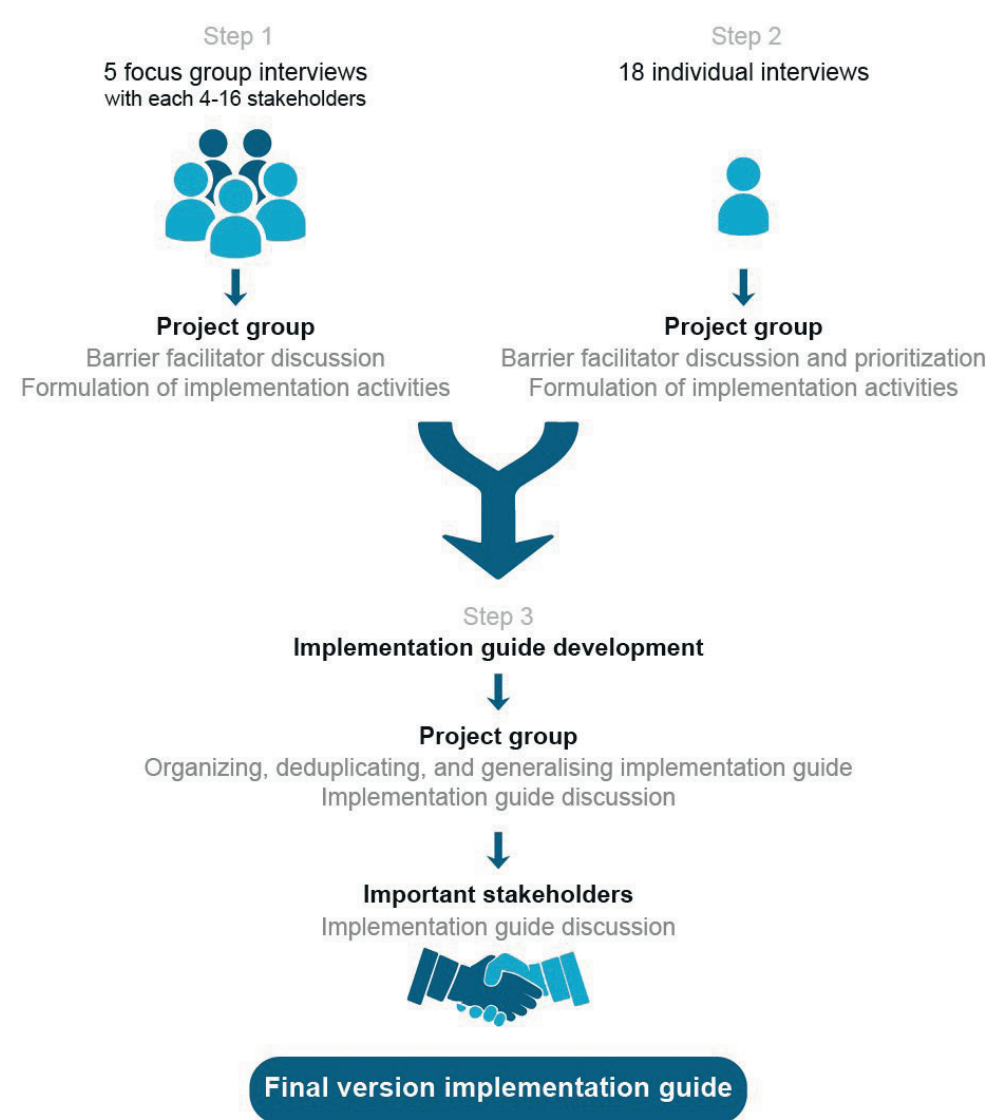


Figure 3. Summary of steps from interviews to implementation guide.

Results

Interview characteristics

In total, 61 stakeholders were interviewed in order to identify barriers to and facilitators for the nationwide implementation and consolidation of CMyLife. Twenty-three different interviews were performed of which eighteen were individual in depth interviews and five were focus group interviews. The (focus group) interviews lasted between 12 and 81 minutes.

Barriers to and facilitators for implementation of CMyLife

In total, 910 quotes were selected and 45 barriers to and 41 facilitators for implementation of CMyLife were identified. Table 2 shows an overview of all identified barriers to and facilitators for the nationwide implementation and consolidation of CMyLife, prioritization of the barriers and if barriers and facilitators were integrated in the implementation guide (in blue). Results are presented according to the six levels of the frameworks used. Barriers and facilitators in need of more explanation or barriers with first priority are presented in the text below accompanied by quotes to illustrate and clarify the barriers and facilitators. For example, the meaning of the barrier “too disease specific” is not entirely clear and needs some clarifying explanation.

Table 2. Overview of barriers to and facilitators for the nationwide implementation and consolidation of CMylife.

Barriers	Facilitators
Innovation	
• Unclearity in ownership and responsibility updates, management, and maintenance CMylife¹ • Lack of connectivity between IT-systems¹ • Too disease specific¹ • Ambiguity meeting legal and Health and Youth Care Inspectorate requirements¹ • Not user-friendly¹ • Lack of instruction for use of CMylife¹ • Not meeting requirements health insurers² • Errors, bugs CMylife² • Inadequate brand awareness² • Multiple apps is complicated² • Lack of access to internet or digital device³	• Evaluation of CMylife by group of representative end users • Connecting IT-systems • Expand CMylife to other diseases • Understandable explanations of graphs and results • Website is professional and user-friendly • Instruction PDF for use CMylife for patients and HCPs • Checklist or blueprint for implementation • Improve communication between patient and HCP • Increase brand awareness CMylife • Distant monitoring and more efficient care • Order/deliver medication from/at home
Patient	
• See no (proven) added value¹ • Doubts about data security and privacy¹ • Behavioural changes take time¹ • Differences between patients:¹ • Long stable vs. recently diagnosed¹ • Young vs. old¹ • Preference face-to-face² • Insufficient digital skills² • Patients expect fast responses²	• Emphasize benefits of CMylife • Growing motivation to use CMylife when experiencing more grip on their disease • Young patients are more ICT minded • Patients having sufficient knowledge and skills to use CMylife • Training in handling side effects, psychological aspects, and how to use CMylife • Positive attitude of patients towards CMylife: • Website/forum/blog • Reminder registration side effects • Local blood tests • Possibility to follow online courses in handling side effects/psychology/using CMylife
Individual professional	
• Lack of feedback on side effects monitoring¹ • See no (proven) added value (negative attitude)¹ • Fear of misinterpretation biomarker by patients¹ • Doubts about data security¹ • Insufficient digital skills¹ • Difficulty with changing role¹ • Preference face-to-face¹ • Opposed to centralization¹ • Time investment and costs in relation to number of patients too high¹ • Fear of loss of income by care substitution²	• Insight in side effects monitoring by patients creates awareness among HCPs • Positive attitude towards CMylife • Time saving • HCPs need to be ready for the technical revolution • Training in how to use the DCP • Enhance HCPs' knowledge about CMylife
Organisational context	
• Local blood tests are logistically complicated¹ • Integrating CMylife differs between hospitals¹ • Differences in time and resources between hospitals¹ • Patient numbers¹ • CMylife has no priority¹ • Lacking standardisation BCR-ABL1 tests¹ • Time investment and costs in relation to number of patients too high² • Integrating CMylife takes time² • IT problems have no priority² • IT problems in hospital organisation³ • Cautious policy to deliver medication at home³	• General hospitals can facilitate implementation faster • Involving someone with experience in implementation of a DCP • Appoint local project group (innovation team) • Implementation guide • One person accountable for delivery of medication at home • Clarity in who initiates the use of CMylife (patient or HCP) • Centralise care for CML patients • Sufficient time and resources available • Start implementation with frontrunners • Start implementation with hospitals with sufficient CML patients
Social context	

- Changing relationship between HCP and patients¹
- Less face-to-face¹
- Less attention to comorbidity¹
- Positive attitudes and learning from each other
- Involve all parties
- Learn from implementation in other hospitals
- Support from the board of directors
- Involve management and Ministry of Health, Welfare and Sport
- Management should provide sufficient facilities

Economic and political context

- Complexity of medical devices regulations¹
- Complexity of security and privacy law¹
- Uncertainty long-term (sustainable) and enduring financing CMyLife¹
- Fragmentation: multitude digital apps and systems²
- Lack of regulation apps and systems from government³
- Delivery of medication at home not reimbursed³
- Exchanging data electronically³
- Demonstrate (cost-)effectiveness to get health insurer interested
- Clear business case and vision
- Guarantee HCP the same income in coming years

1 First priority when implementing a digital care platform

2 Second priority when implementing a digital care platform

3 Third priority when implementing a digital care platform

Blue coloured barriers and facilitators are integrated in the implementation guide

3

Innovation: CMyLife

Barriers

Lack of connectivity between IT-systems, the innovation being too disease specific, unclarity in ownership and responsibility updates, management, and maintenance of CMyLife, and aspects of CMyLife not being user-friendly were identified as barriers on innovation level. CMyLife consisted of several systems which were not all interconnected, this hindered dataflow between systems and users of the platform had to fill in information multiple times. The innovation was only focussed on patients with CML. This is a small patient population and some hospitals only treat a few of these patients. Stakeholders also mentioned that some aspects of the innovation were not user-friendly. For example, patients mentioned that the frequency of registering side effects was too high and when they suffer from specific side effects over a longer period, they do not want to register the same side effects repeatedly. The login to CMyLife was 'a lot of hassle', patients should login multiple times (because of the lack of connectivity between IT-systems) in different ways and it did not always work.

"You should think about who is eventually owner of CMyLife and who takes care of updates and who keeps the platform going." (IT-specialist)

"Receiving a reminder for registering side effects only once a week would be better. Like, take a look back at your week which side effects did you suffer from, I would actually do that." (Patient)

Facilitators

CMyLife enabling patients to receive more efficient care and improving the communication between patients and their HCPs were mentioned as facilitators for implementation. HCPs were positive about the use of CMyLife, they agreed that the use of CMyLife made care more efficient, it saved them time and decreased waiting and travel time for patients. Patients knew their BCR-ABL1 values beforehand and were therefore able to prepare better for their consultation. Therefore, CMyLife improves the communication between the HCP and the patient. Another facilitator mentioned on innovation level was the availability of a checklist, blueprint or implementation guide before implementation, including information about connecting IT-systems, privacy and security, step-by-step what should be arranged and in what order.

“The biomarkers were good and the app shows that the patient took his medication well, yes, who are we to say that they should also physically see that patient, that is not necessary at all.” (Health insurer)

Patient

Barriers

Doubts about data security and privacy, patients not seeing a (proven) added value and differences between patients were barriers mentioned on patient level. Several stakeholders mentioned that patients feared that their personal data may end up publicly exposed. Also, differences between patients were often mentioned as a barrier to implementation. For example, using CMyLife was not a necessity for patients who were stable over a long period of time, however using CMyLife could have a great added value for patients who were recently diagnosed with CML. In addition, young patients had generally better digital skills and were more open to using DCPs compared to older patients.

“I think that contact with my health care professional is important, so I just visit four times a year.” (Patient)

Facilitators

The possibility to follow online courses in handling side effects, psychological aspects, and how to use CMyLife, and patients having a positive attitude towards CMyLife were mentioned as facilitators for implementation on patient level. Patients mentioned to be pleased with the attractiveness and the usefulness of the website, the forum and the blog. Also, they liked to receive a reminder to

register their side effects and they preferred to have their blood tested locally. Testing blood locally saved them waiting and travel time.

"I think it is possible to make sure that patients have their blood drawn at home, or somewhere near their house, and patients could only come for a consultation when their medication or biomarkers factor are not ok. This way both travel time and office hours can be saved. I think win-win-win." (Health insurer)

Individual professional

Barriers

Among others, barriers mentioned on individual professional level were insufficient digital skills and difficulty with the changing role of HCPs. Stakeholders also mentioned that time investment and costs in relation to number of patients was too high. The role of both the HCP and the patient was changing, adjusting to this new role will take time and effort. However, work pressure and understaffing hampered this process. Another mentioned barrier on individual professional level is that some HCPs preferred face-to-face communication. They wanted to prevent missing crucial things about patients' lives and possible comorbidities. Also, older HCPs tended to value personal contact more and had less digital skills.

"How interesting is your work if there is no more personal contact. It is not only important to hear about side effects but also the story around it." (Haematologist)

"Since work pressure is high and changes like this take time it is hard to get everyone cooperative with implementation." (Haematologist)

Facilitators

HCPs who were enthusiastic and positive about CMylife and who clearly understood the usefulness of CMylife facilitated the implementation of CMylife. It was important to enhance HCPs' knowledge about the benefits of the use of CMylife and how to work with DCPs. Training HCPs in the use of DCPs was also mentioned as a facilitator for implementation.

"Make the advantages that CMylife has very prominent for everyone, then it seems almost impossible not to support it as a centre." (IT-specialist)

"Keep informing people what you are doing and keep them engaged, motivation and information is essential." (Specialized nurse)

Organisational context

Barriers

Barriers on organisational context level were numerous. Time investment and costs in relation to number of patients was mentioned to be too high. Integrating CMyLife differed between hospitals, with some hospitals having enough time and resources and others not having this advantage. General hospitals were less involved with innovation and development compared to academic hospitals. Also, IT problems in the hospital organisation were a barrier to implementation, such as bad internet connection. Most of the time IT problems did not have priority in hospitals, it took time to fix these problems and good IT employees were scarce.

"I think the biggest problem is IT." (Specialized nurse)

Facilitators

Involving someone with experience during implementation of DCPs, appointing a local project group, using an implementation guide, and centralizing care were facilitators mentioned on organisational level. The implementation guide should be some sort of blue print or instructional manual about what aspects the innovation should contain and a step-by-step plan for implementation. Someone with experience in implementing the innovation could help to implement it in other hospitals and a project group including all involved stakeholders facilitated implementation.

"You have to create a project group with the important parties in your hospital and they should lead implementation." (Project group)

Social context

Barriers

On social context level the changing relationship between HCPs and patients, including less face-to-face contact and less attention for comorbidity were mentioned as barriers to the implementation of CMyLife. HCPs should allow patients to take more control over their disease and the care will be more from a distance. Also, not all HCPs agree with centralization of care for CML patients because this meant that some of them lose their CML patients.

"What I'm concerned about is that if you're going to centralize the care, some people have to let go of something and they don't want to."
(Employee IKNL)

Facilitators

Positive attitudes and learning from others was mentioned as a facilitator for implementation on social context level as well as involving all stakeholders during the process to create support. Support from colleagues, informing each other, sharing experiences and learning from each other will make a big difference in the acceptance of DCPs. Also, learning from implementation in other hospitals was mentioned as a facilitator for implementation.

"I think that raising awareness and taking our colleagues along will be the first challenge to make it land properly with other hospitals."
(Project group)

"Seeing good examples up close, that can motivate, to exchange and discuss this with each other, to really go a little deeper, to stimulate each other." (Policymaker)

Economic and political context

Barriers

The complexity of medical devices regulations, the complexity of security and privacy law, the uncertainty of long-term (sustainable) and enduring financing and the lack of regulation of apps and systems by the government were mentioned as barriers to the implementation of CMyLife. Because personal data is handled electronically in these kind of innovations the complexity of the security and privacy law was an important barrier. Before implementation all laws should be taken into

account carefully. Also, connectivity between IT-systems was a challenge because of these laws.

"It would be a shame if continuity is at stake because gaps in financing arise, sponsors might disappear at some time, then it will become very unstable, you should not want that, it would be nice if it became wider supported, also by health insurers that have an interest in it, but perhaps also clinics that can step in, but then there must also be financial benefits in return." (Employee of a pharmaceutical company)

"Before we can implement at all, I think everything around privacy and security must be arranged properly." (IT-specialist)

Facilitators

A clear business case, vision, and demonstrating (cost-)effectiveness to get health insurers interested were mentioned as facilitators for implementation on economic and political context level. CML patients are a vulnerable patient group, health insurers indicated that this is an important fact to mention in a conversation about sustainable financing and getting support from health insurers.

"The moment we see initiatives that improve patient care and it has a positive effect on costs, we are interested to play a role." (Health insurer)

"For health insurers it is very important that there is a business case behind your innovation, that is crucial for these kinds of conversations." (Health insurer)

Implementation guide

To take care of the identified barriers to implementation and use the identified facilitators for implementation an implementation guide was composed. Based on main themes returning in the interviews the implementation guide was divided in different phases of DCP implementation; development of the innovation, dissemination, continuous motivation and support, the context (here the hospital-specific context), and actual implementation and long-term and enduring financing DCP. Eventually, a clear but comprehensive implementation guide was developed for DCPs. Table 3 shows the activities of the implementation guide in combination with the type of strategy according to the CFIR-ERIC framework.

Table 3. Activities of the implementation guide for digital care platforms in combination with the strategy.

Phase of implementation	Strategy
Development innovation	
Formulate clear goal, vision, focus, and strategy	Innovation optimizing strategy
Establish a clear organisational and governance structure	
Create a clear overview of IT-system architecture	
Make data infrastructure and data flow transparent	
Ensure that the innovation complies with regulations regarding data security and privacy	Product focussed strategy
Set a clear business case	
Set a change plan and/or continuously adjust innovation based on change plan	
Give platform/apps appropriate name(s)	
Involve key stakeholders from the start and during development of the innovation	Innovation optimizing and product focussed strategy
Work intensively with end users on content, design, further development/improvement of the innovation	
Work on (further) development via short cyclical improvement, e.g. the so-called plan do check act cycle	
In the (further) development of the innovation, take diversity of patients into account	
Get the technical aspects in order and set up structure for solving bugs	Innovation optimizing strategy
Minimize the number of different IT parties involved	
Make concrete agreements with IT party(ies) about responsibility for updates and security	Cooperation promoting strategy
Involve IT/privacy officer continuously in the design, further development and improvement of the innovation	
Explore (cost-)effectiveness of the DCP	
Dissemination	
Communicate vision, focus, strategy, organisational & governance structure, system architecture, data infrastructure & data flow	Informative strategy
Communicate agreements with IT party(ies) about responsibility for updates and security with relevant stakeholders	
Promote innovation through patient conferences	
Find and use additional distribution channels that are already working well	
Communicate (cost-)effectiveness	
Continuous motivation and support of end users	
Evaluate user experiences of the innovation and provide insight into effectiveness, ensuring that stakeholders/users will see the added value of the platform	Motivation and support increasing strategy
Engage key figures and opinion leaders to provide motivation & support for innovation among stakeholders/users	
Have project team members (or rather the key figures) go to hospitals for personal approach & highlighting the benefits of DCPs	
Organise meetings with patients & health care providers (focus groups, workshops, conferences) for support	
To motivate HCPs for change (to see the need)	
Make the content of the innovation attractive to end users. For example, use an up-to-date website so that the usefulness of the DCP becomes clear	
Hospital-specific context	
In terms of IT, make sure that the 'unwieldy hospital equipment' is circumvented as much as possible so the DCP does not/barely needs to link with hospital systems	Organisational strategy
Ideally, there is a connection between electronic patient files and the innovation (when relevant)	

Inform and motivate hospital organisations about the importance of the innovation for patients; provide a fixed point of contact in the hospital who feels responsible for a smooth implementation	Informative and motivation and support increasing strategy
Emphasize that good IT facilities for implementation of the innovation are a must have for hospitals	
Actual implementation and long-term and enduring financing DCP	
Prepare and set a good blueprint/guideline for the rollout of the innovation, including the involvement of stakeholders; among other things, deal with the IT connectivity of systems, privacy & security, step-by-step plan with what needs to be arranged in a hospital before implementation and in what order, and where to go for support	Facilitating strategy
Start implementation on a small scale	
As a project team, offer temporary support for implementation; for the long term a good business model is indispensable	
Provide training for HCPs, if necessary (do not focus on the ultimate user-friendly tool because this is different for everybody) work with smart PDF including instructions	Educational strategy
When implementing with patients, provide extra support for certain groups	Motivation and support
Ensure the use of patient-reported outcome measurements data during a consultation, when patient-reported outcome measurements management is part of the DCP	increasing strategy
Integrate the DCP into the clinical pathway as much as possible	
Ensure assurance in 3 steps: start with the idea, continue to exploit innovation, build a good business case (with real-world evidence) and obtain financing for long-term and enduring financing	Market-oriented strategy

Discussion

This study presented the first qualitative case study of a DCP like CMyLife on barriers to and facilitators for nationwide implementation among various stakeholders within and outside the hospital organisation, which led to a comprehensive implementation guide for DCPs. In total, 45 barriers to and 41 facilitators for implementation of CMyLife were identified. Main barriers mentioned were a lack of connectivity between IT-systems, a changing role for both HCPs and patients, insufficient time and resources, doubt about privacy and security of data, and insufficient digital skills of patients and their HCPs. Main facilitators mentioned were motivating patients and their HCPs by clarifying the added value of the use of the DCP, a clear business case, vision, and demonstrating (cost-)effectiveness, using an implementation guide, and educating patients and HCPs about benefits and use of CMyLife. By using the barriers and facilitators we developed a comprehensive implementation guide for launching DCPs in daily clinical practice.

Kooij et al. (2018) identified barriers to and facilitators for DCP implementation facing various stakeholders within the hospital organisation, thereby had a narrower scope compared to our study [25]. Also, Kooij et al. (2018) reported differences in the included hospitals with regard to the features of the concerned DCP and the phase of DCP. Some hospitals had already provided a DCP, while others were in the middle of the implementation process or had no DCP at all. This could have caused different results from our study because expectations before implementations

and the experiences afterwards can vary among HCPs and patients [44, 45]. In our study the DCP already existed and stakeholders were familiar with its components [1, 2]. Despite these differences between our study and the study by Kooij et al. (2018), the results are quite comparable. For instance, concerning barriers to implementation, lack of time and resources and guaranteeing privacy and security were mentioned as well. Concerning the facilitators for implementation, positive attitudes, and management support (strategy plan for implementation) were also mentioned. However, our study found additional barriers and facilitators, for example, the study by Kooij et al. (2018) did not find barriers on individual professional level and facilitators on patient level whereas our study did. This is probably because they included stakeholders from hospitals with and without an implemented patient portal, this could have introduced bias into responses because some participants identified barriers and facilitators without even using a DCP and therefore had to imagine the implementation process. Like our study, Kooij et al. (2018) indicated that having an implementation guide would be a facilitator for implementation. The current study provides this practical guide for the implementation for DCPs. How translatable are the results of our DCP CMyLife, specifically developed with and for CML patients, to DCPs in general? Barriers and facilitators which are only applicable for CMyLife, for example that the platform is too disease specific (because of the small patient population) and lacking standardization of BCR-ABL1 tests are not used in the implementation guide. CMyLife comprises all features of a DCP as described in the introduction. Therefore, our developed implementation guide can be widely used for other DCPs including these features, not only national but results also seem applicable internationally. Nevertheless, the Dutch health organisation may differ from other countries, for example in universal health care coverage. This may involve differences in barriers and facilitators. To our knowledge this is the best (retrospective) display of the barriers and facilitators for nationwide implementation of CMyLife.

In a previous study by Cremers et al. (2021) an eHealth implementation guideline was developed as well, using a literature search and a two-round Delphi study among experts [26]. They presumed eHealth in general and did not differentiate between simple forms of eHealth and more advanced multi-component innovations. Contextual factors matter, there is no one size fits all and implementation guides for these digital tools will differ since implementation of a DCP is more complicated compared to implementation of single component eHealth. Our study developed an implementation guide for DCPs in particular and besides literature, stakeholder and expert opinions were based on a specific practical example. Differences between results may be caused by these differences between the studies. For example, the study by Cremers et al. (2021) states that for a successful implementation suitable patients or patient groups should be

identified to participate in the eHealth program based on predefined inclusion and exclusion criteria. Our study aims to provide all interested patients with suitable education and training to make them able to use the innovation and continue using it, as can be seen from the implementation phase; continuous motivation and support in the implementation guide. In addition to the differences between the results of the studies, results are also comparable between studies. They also mention that eHealth implementation is very complex and a variety of variables should be taken into account.

This complexity regarding national success factors in the development of eHealth interventions was also stressed by the study by Stanimirović and Vintar (2014) [27]. Their study identified the main deficiencies in eHealth implementation, they mapped a set of general success factors in the field and suggested guidelines for the effective development and implementation of eHealth projects. Again this study did not differentiate between simple forms of eHealth and a more advanced multi-component innovation, such as a DCP. For this reason results between their study and our study are not entirely comparable. For example they state that political commitment to reform and reorganisation of the clinical departments are success factors for effective development and implementation of eHealth. These factors are not mentioned in our implementation guide because they are beyond the control of the team implementing a DCP. Still, there are some agreements with our study. For example, inclusion of stakeholders and effective collaboration and promoting the use of IT, education and training.

Our study comprised several strengths and limitations. The use of semi-structured interview guides provided the interviewers with the opportunity to learn the reasons behind the answers. Semi-structured interviews allow interviewees to open up about sensitive issues and since three different interviewers performed the interviews, the use of semi-structured interview guides ensured that main questions were consistently asked in every interview and participants were given freedom to exceed on asked questions. Therefore, the use of semi-structured interviews did not restrict stakeholders in thinking outside the box when answering the questions. In our study, six patients were interviewed and 30 health care workers. This might have raised concerns that this influenced the results of the study in a way that the opinions of the health care workers were more prominently presented. However, this was not the case since this qualitative study focussed on quality and not quantity of results. The opinions of all different types of stakeholders were equally analysed (as described in the methods section). In addition, our study is the first study exploring barriers and facilitators in stakeholders from within and outside the hospital organisation, which adds insight into both perspectives.

In order to make sure that this exploration of barriers to and facilitators for the nationwide implementation of CMyLife will lead to quality improvement of the platform, it is important that the content of CMyLife gets improved accordingly and expanded to other cancer types. Future research is required to determine whether the implementation guide is actually useful in the implementation of a DCP and to determine the validity of this implementation guide in other (oncological) diseases. In addition, it needs to be validated and recalibrated regularly to increase its potential to facilitate implementation and the next step after successful implementation is investigating what is a necessity to establish sustained use of DCPs among patients and their HCPs.

Conclusion

The aim of the present research was to explore barriers to and facilitators for the nationwide implementation and consolidation of the CMyLife platform, leading to a comprehensive implementation guide for launching DCPs in daily clinical practice. This research has shown that the nationwide implementation of a DCP is a complex process. Main barriers were lack of connectivity between information technology systems, changing role for both HCPs and patients, insufficient time and resources, doubts about privacy and security of data, and insufficient digital skills. Main facilitators mentioned were motivating patients and HCPs by clarifying the added value of use of the DCP, clear business case with vision, demonstrating (cost-)effectiveness, using an implementation guide, and educating patients and HCPs about the use of CMyLife. Based on these barriers and facilitators a strategic and comprehensive implementation guide was developed as this study and previous studies asked for. Future research should be undertaken to confirm the practical utility and explore whether this implementation guide actually facilitates implementation of DCPs.

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Supplementary material

Appendix 1

Interview guide CMyLife e-Clinics

1. Format focus group interviews CMyLife

Background CMyLife platform

CMyLife has two main goals:

- Give patients control of their CML care; this requires optimal patient information
- Organize hospital free care

Why put 'control in the hands of the patients'?

- The patient can then ensure that his/her blood levels are checked on time (and receives his/her blood result on time).
- Patient knows how to act after receiving his/her blood results.
- Patient receives feedback on his medication intake (insight into the relationship between his/her medication intake and his/her blood value).
- Patient can make his/her complaints known and receive feedback on them.
- Patient is provided with all the information that the care provider wants to provide him/her.

How is that organized: with the help of digital tools (website CMyLife, medication app & guideline app, BCR-ABL charts and personal health environment), feedback from health care providers and the CMyLife support desk for patients and health care providers.

Why hospital-free care?

- Patient is free to visit the hospital.

How is that organized: process change in each hospital via local blood tests, delivery of medication, video consultation by the hospital's specialized nurse.

Situation at the Radboudumc

In the Radboudumc CMyLife e-clinics has already been partially implemented (website & apps are available, local blood tests, delivery of medication and video consultation (now also by haematologists) are possible).

However, implementation of CMyLife e-clinics in other Dutch hospitals will not happen automatically. A first step to realize implementation in other Dutch

hospitals is to make an inventory of barriers and facilitators among people who have contributed to the implementation at Radboudumc, the CMylife project group. This inventory takes place with the use of a focus group interview and is carried out in the context of the ZonMw action research.

Structure and purpose of the focus group interviews

As indicated above, we initially organize a focus group discussion with the CMylife project group. This will allow us to get a better picture of the experiences with the implementation of CMylife e-clinics and of possible barriers and facilitators for implementation. The goal is to hear as many experiences as possible without striving for consensus or saturation. In addition to the group discussion with the project group, the project members who cannot attend the focus group discussion will be interviewed separately (a second focus group may be planned). The previous inventory of 'stakeholders' who have a role in national implementation, from the project group meeting on ..., is supplemented from the group discussion and the additional discussions. In a second interview round, focus group and/or individual interviews are planned with them.

3

2. Performance interviews

Practical issues

- Arrange space or room to perform the interviews
- Create+sent invitation letter for participants
- Create+sent information to participants (important to have a factsheet about the apps)
- Working (recording) equipment
- Arrange and fill out Informed consent forms
- Provide short questionnaires on participants background characteristics, pens and paper to create nametags.

Points of attention in advance

- The interviewer must have a good idea of the distribution of the topics in her/his head;
- During the conversation it is important to verify whether it is the opinion of a respondent and possibly reflect on the aforementioned opinions;
- When a participant does not express his opinion or to a lesser extent, the interviewer tries to stimulate a respondent with previously inventoried opinions.
- Asking questions, trying to understand the participant's perspective;

- Do not defend or explain;
- Listen to whether the respondent answers the question, be alert;
- Do not move on to the next topic too quickly, but take breaks after a participant has said something;
- Ask for additional information. Example questions can be:
 - o Can you explain that further?
 - o Can you give me an example of what you mean?
 - o What else can you say about it?
 - o Tell us more?
 - o Is there anything else?
 - o Would you like to describe what you mean?
 - o I don't quite understand
 - o Are there any other insights?

FOCUS GROUP TOPICS

- Broad: barriers and facilitators of the national implementation of CMyLife e-clinics based on the 6 domains of the Grol & Wensing model (innovation itself, individual professionals, patient, social setting, organisational context, economic & political context (financing or legislation & regulations)
- Zoom in on: the significance of CMyLife e-clinics for the way of working as a health care provider
- Zoom in on: the significance of CMyLife e-clinics on the relationship and communication with the patient
- Zooming in on: the attitude of health care professionals and how to influence
- Zoom in on: dealing with digital skills of patients and health care professionals

3. Protocol focus group CMyLife e-clinics

WELCOME + THANK FOR PARTICIPATION + ASK PERMISSION FOR AUDIO RECORDING

INTRODUCTION

- Introduction of our research concerning CMyLife e-clinics
- Emphasize confidentiality and voluntariness, as well as confidentiality of recording and data processing
- Propose to tutor each other during the interview and whether there is any objection to this
- Time indication, mention break
- Are there any questions before we start?

INDIVIDUAL INTRODUCTION

Introductory question

CMyLife is largely implemented at the Radboudumc. The next step is implementation in other hospitals, on the way to national implementation and consolidation. If you look at that, what barriers do you expect? What are factors that can facilitate implementation?

We will discuss this on the basis of the 6 domains of the Grol & Wensing framework (innovation itself, individual professional, patient, social setting, organisational context, economic & political context (financing or legislation & regulations)). your first reaction to this question?

With regard to CMyLife, by this we mean all parts, so both the parts needed for 'patient in control' and the parts needed for 'hospital-free care'.

TOPICS

- o Topic: CMyLife / eHealth apps

Which barriers do you expect, in relation to the implementation of CMyLife in other hospitals, ***in the field of CMyLife, the innovation itself?***

- What barriers have you experienced at Radboudumc in the field of innovation itself?
- What barriers do you expect in other centres? Do you expect differences between the different types of hospitals (UMCs, large peripheral, small peripheral)?

What are facilitators for the implementation of CMyLife in other hospitals, ***in the field of CMyLife, the innovation itself?***

- What is working well in the Radboudumc?
- Does this apply to CMyLife as a whole? Or does this apply to certain parts?

Examples:

- Accessibility of CMyLife
- Attractiveness of CMyLife
- Ease of use of CMyLife (clear, easy to master, operation)
- To what extent CMyLife is consistent with daily routines
- Credibility of CMyLife content
- To what extent CMyLife can be useful for work
- To what extent CMyLife can contribute to productivity
- What is needed (what needs to change) in the area of innovation itself to facilitate implementation in other hospitals?

o Topic: Individual professional

Which barriers do you expect, in relation to the implementation of CMylife in other hospitals, ***in the field of individual professional?***

- What barriers have you experienced at Radboudumc in the field of innovation itself?
- What barriers do you expect in other centres? Do you expect differences between the different types of hospitals (UMCs, large peripheral, small peripheral)?

What are facilitators for the implementation of CMylife in other hospitals, ***in the field of individual professional?***

- What is working well in the Radboudumc?
- Does this apply to CMylife as a whole? Or does this apply to certain parts?

Examples:

- Knowledge regarding the implementation of an eHealth innovation
- Attitude towards the implementation of an eHealth innovation, e.g. do you expect to use it?
- Motivation regarding the implementation of an eHealth innovation, e.g. What is your prediction that you will use CMylife in the coming months?

What is needed (what needs to change) in the field of the **individual professional** to facilitate implementation in other hospitals?

o Topic: Patient

Which barriers do you expect, in relation to the implementation of CMylife in other hospitals, ***in the field of the patient?***

- What barriers have patients experienced in the Radboudumc?
- What barriers do you expect in other hospitals for patients?

What are facilitators for the implementation of CMylife in other hospitals, ***in the field of the patient?***

- What is working well in the Radboudumc?
- Does this apply to CMylife as a whole? Or does this apply to certain parts?

Examples:

- Patient knowledge about using an app
- Patients' skills to use an app

- Patients' attitudes towards an app
- To what extent is CMyLife understandable for patients

What is needed (what needs to change) in **the patient field** to facilitate implementation in other hospitals?

- o Topic: Social context

Which barriers do you expect, in relation to the implementation of CMyLife in other hospitals, **the social context area**

- What barriers did you experience in the social setting area in the Radboudumc?
- What barriers do you expect in other hospitals in the field of social setting?

What are facilitators for the implementation of CMyLife in other hospitals, **in the social context area?**

- What is working well in the Radboudumc?
- Does this apply to CMyLife as a whole? Or does this apply to certain parts?

Examples:

- Opinion of colleagues; do you expect people whose opinions you value to think you should start using CMyLife?
- Culture within the organisation; Do you expect your employer/colleague(s) to be/are helpful when using CMyLife?
- Cooperation

What is needed (what needs to change) in **the social context area** to facilitate implementation in other hospitals?

- o Topic: Organisational context

Which barriers do you expect, in relation to the implementation of CMyLife in other hospitals, **in organisational context?**

- What barriers did you experience in organisational context in the Radboudumc?
- What barriers do you expect in other hospitals in organisational context?

What are facilitators for the implementation of CMyLife in other hospitals, **in the field of organisational context?**

- What is working well in the Radboudumc?
- Does this apply to CMyLife as a whole? Or does this apply to certain parts?

Examples:

- Organisation of care processes
- Staff
- Resources
- Need for support
- Differences between different health care institutions

What is needed (what needs to change) in **the organisation context** to facilitate implementation in other hospitals?

o Topic: economic and political context

Which barriers do you expect, in relation to the implementation of CMyLife in other hospitals, ***in economic and political context?***

- What barriers did you experience in economic and political context at the Radboudumc?
- What barriers do you expect in other hospitals in economic and political context?

What are facilitators for the implementation of CMyLife in other hospitals, ***in economic and political context?***

- What is working well in the Radboudumc?
- Does this apply to CMyLife as a whole? Or does this apply to certain parts?

Examples:

- Financial arrangements
- Laws and regulations
- Policy
- ownership

What is needed (what needs to change) in **economic and political context** to facilitate implementation in other hospitals?

o Topic: Significance of CMyLife for the way of working as a HCP
Question: what does CMyLife mean for the work and way of working?

For example, think of:

- How a doctor or nurse takes notes
- Additional tasks
- Discuss it with colleagues

- Difference with colleagues
- Consequences: quality of care, efficiency, financial, communication, patient management, control and transparency of information?
- Change of conversation between you and the patient, added value?
- o Topic: Significance of CMyLife on patient relationship and communication
Question: what does CMyLife mean for patient communication?
- o Topic: Significance of CMyLife for the attitude of health care professionals and how to influence
Question: what attitude is needed by health care professionals for the use of CMyLife and how can this be influenced?
- o Topic: Significance of using CMyLife for the digital skills of patients and health care professionals
Question: What does the use of CMyLife require from the digital skills of patients and health care professionals?

4. Closing the (focus group) interview

- General summary + check if someone has a reaction or addition
- Last question: did we miss something?
- Thank you for the input!
- Complete the interview

→Turn of recording equipment!



CHAPTER 4

Filling the gaps of patient information needs
and information perception in chronic myeloid leukemia
with the patient-physician co-produced
web-based platform CMyLife

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Abstract

Background: For patients with chronic myeloid leukemia, a web-based platform CMyLife was developed. Its aim is to enhance patient empowerment, by adequate information provision, among others. Before evaluating its effect, information provision and needs in current care were assessed.

Objective: To assess patients' evaluation of received information and information needs before CMyLife utilization and whether this information source is used correspondingly. Additionally, we explored predicting patient factors in information perception.

Patient involvement: CMyLife platform was developed with active patient participation.

Methods: We conducted a cross-sectional survey among 203 CML patients before launch of the CMyLife platform, using validated questionnaires on information provision and predictive factors. We focused on website utilization during the first 3 years, using Google Analytics. Regression analyses were performed to determine influence of patient factors on information perception.

Results: Global perceived information provision was scored 42.8 (0–100). Information on other services such as rehabilitation and psychological support, and effects of treatment on sexuality showed room for improvement. One out of 3 knew where to find useful health information online. But more information was desired by 36% of them. Age ≥ 65 years, time since diagnosis and low education were negatively associated with this need. Pages on medication and side effects were visited the most.

Discussion: To fill the gap in perceived provision and needs, information should be adjusted more to the individual in content, manner and timing. Age, time since diagnosis, and educational level are of influence in perceived information, and specific needs within these groups should be further explored.

Practical value: CMyLife provides reliable and up-to-date information for low eHealth literacy skilled patients concerning multiple topics indicated by patients.

Background

Information seeking among cancer patients is common [3, 4]. Current rates of internet use among cancer patients are ranging from 60% to 80.8% and are increasing over time [3, 5-7]. Seeking information does not equal finding it, let alone use it. Patients require a certain level of eHealth literacy, which is defined as “the ability to seek, find, understand, and appraise health information from electronic sources and apply the knowledge gained to addressing or solving a health problem” [8]. In a Dutch study, only 50% of subjects could complete an assignment to find certain health related information online, and only 35% was able to use that information for personal benefit [9]. Elderly and subjects with lower education experienced more difficulties.

Reported negative effects of patients’ unmet information needs include lower satisfaction with care and worse illness perception [10-13]. Reported advantages encompass less anxiety and fear, improvements in quality of life, therapy adherence, psychological well-being, satisfaction and engagement in decision-making, daily functioning, and pain management [14-18].

In cancer patients in general, the most frequent information needs identified concern side-effects and treatment [19-22]. Studies on information needs in patients with haematological malignancies are scarce, despite the increasing prevalence [23-25]. Reported satisfaction with information rates vary from 52% to 67% [26]. Basic information was desired, with a higher need for medical (e.g. regarding diagnosis, curability, treatment options, and prognosis) than psychosocial information. Information concerning effects of socio-economic status, education, or coping on information needs among patients with haematological malignancies is lacking.

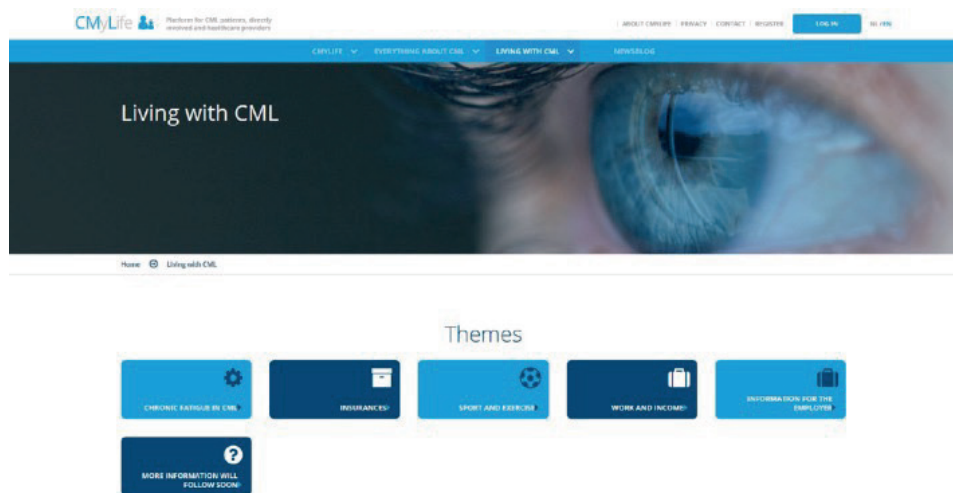
Chronic myeloid leukemia (CML) is a haematological malignancy caused by a chromosome translocation, resulting in a constitutively active protein, a so called tyrosine kinase, generating an increased proliferation of mature blood cells. Due to the advent of tyrosine kinase inhibitors (TKIs), survival in CML patients approximates that of the general population although without cure of the chronic malignant disease itself [27]. Information needs, therefore, can differ from other haematological malignancies with worse survival outcomes. Comparable to chronic non-malignant diseases, patients’ treatment adherence despite numerous adverse effects and physicians’ guideline adherence are paramount in CML care. Nonetheless, suboptimal adherence rates are reported and emphasize the importance of patient education [17, 18, 28-30]. Information regarding disease, therapy and management of adverse events is essential in improving therapy adherence [17]. Even if patients eventually qualify for discontinuation of TKI therapy after achievement of a sustained molecular response, information

provision remains important and needs are still reported, e.g. regarding trial results, withdrawal effects, risks and opportunities of stopping, and monitoring [31, 32]. Studies regarding information provision in CML patients are actually limited to one study concerning information needs on TKI treatment [33].

Box 1. Description of the CMylife platform.

In 2016, the web-based platform CMylife (www.cmylife.com) was launched on a national information day on CML for patients and has been freely accessible ever since. Patients are made aware of the existence of CMylife by the patient advocacy group Hematon and their health care professionals. Moreover, CMylife is one of the first Dutch hits in online search engines when searching for CML.

CMylife has been developed with aid of active patient participation. It comprises multiple features; such as smartphone applications containing an easy to understand version of the national CML guideline [1], medication intake and symptom logs, insights in lab results, a secured patient forum, a news blog and a website providing information on all sorts of CML related topics. Examples of these topics are: diagnosis and treatment of CML, adverse events of medication, and life with CML – i.e. work and income, mortgage and insurance, fatigue, sports (figure below).



Patients can register an account online to gain access to the secured patient forum and emails with newsletters and updates. Additional registration for a personal electronic health record on CMylife, which can be connected to some hospital systems, is possible after an identity check based on name, date of birth, postal code, and citizen service number.

The objective of CMylife platform is to enhance patient empowerment by providing patients with knowledge and tools to take lead in their own care process. It is run by a committed and multidisciplinary project team, including patients and HCPs. Recently, the concept has been extended for other haematological malignancies such as chronic lymphocytic leukemia and myeloproliferative neoplasms as well. A more detailed description of the development of CMylife can be found elsewhere [2].

To improve patients' disease knowledge, the type and amount of information provision should meet the needs and desires of the individual [34, 35]. Moderating factors should be taken into account such as age, educational level, cancer type,

time since diagnosis, and treatment. In case internet is the preferred information source, is the desired information subsequently found online by patients, and once found online, does that information match the readability and eHealth literacy level of that particular patient?

The web-based platform CMyLife is an intervention aimed at improving patient information and comprehension in CML patients [2] (Box 1). Patients are made aware of the existence of CMyLife by the patient advocacy group Hematon and their health care professionals. Besides, CMyLife is one of the first Dutch hits in online search engines when searching for CML. Before evaluation of CMyLife's effect on information provision, it is important to assess patients' evaluation of information provision in current CML care, before CMyLife's launch, and whether the information on CMyLife, after its launch, is used correspondingly. That is, if information provision on a specific topic is perceived to be insufficient, is information regarding this topic obtained from CMyLife?

Also, are there predicting factors, patient-or disease-related (e.g. demographics, treatment, time since diagnosis, quality of life, patient empowerment, eHealth literacy), in information perception? In this study we aim to assess perceived information provision, compare this with CMyLife's utilization and explore predicting factors in information perception.

4

Methods

Design

To assess perceived information provision and information needs in patients with CML, we conducted a cross-sectional survey among CML patients before the launch of the CMyLife platform, using validated questionnaires. After CMyLife's launch we focused on the web activity of the information pages on CMyLife during the first 3 years (2017–2019). With the web activity data we could examine if CMyLife's content was used correspondingly to the reported information provision in the questionnaires.

Participants

Patients were asked to participate by their HCP during routine visits at 7 participating hospitals (including 4 university centres). Hospitals, spread over the Netherlands, were invited to participate per letter. Patients who received TKI therapy, were about to start, or had just continued TKI therapy, were considered eligible. Patients received a package containing information on the study, contact information of the investigator, an informed consent form, and a return envelope.

They were able to take their time thinking about participation, discussing it with others. Moreover, the informed consent form stated explicitly that their decision would not affect their treatment. After written consent was obtained, paper questionnaires were sent per mail by HCPs, including a stamped envelope addressed to the investigators. Patients familiar with CMylife or with a history of an hematopoietic stem cell transplantation were excluded. Familiarity was left to patients' judgement as it was inquired at the informed consent form. The study was approved by the Radboudumc institutional ethics committee.

Data collection

Questionnaires

The survey-questionnaire concerned the outcome measurement information perception and needs, and information on the following predictive factors: demographics, CML disease course, and validated questionnaires on patient empowerment, eHealth literacy and quality of life (QoL).

Information perception and needs were measured with the EORTC QLQ-INFO25 questionnaire and comprised four information subscales: perceived information provision about the disease, medical tests, treatment, and other care services, and 8 individual items [36]. Except for four dichotomous items, items were rated on a 4-point Likert scale. Linear transformation as described above was used as well, with higher scores representing a higher level of information received, desire for more information and greater satisfaction.

Patient empowerment was defined as the individual knowledge, skills, and confidence for managing patient's own health and health care, and was measured with Patient Activation Measure-13 (PAM13) [37]. Again, scores on a 4-point Likert scale were transformed in a 0–100 range, which corresponds with one of four levels of patients activation (level 1 representing the lowest activation and 4 the highest).

Self-perceived eHealth literacy was assessed with eHealth Literacy Scale (eHEALS) [8], comprising 8 items on a 5-point Likert scale. Scores were summed to range from 8 to 40, higher scores represent higher self-perceived eHealth literacy.

QoL was assessed with EORTC QLQ-C30 and CML specific EORTC QLQ-CML24 questionnaires [38], [39]. They comprised 14 (1 global, 5 functioning and 8 symptom) and 6 subscales (symptom burden, impact on mood, impact on daily life, and satisfaction with care and information, body image and satisfaction with social life), respectively. Linear transformation to standardized scores ranging from 0 to 100 was used per EORTC scoring manual [40]. Higher scores represent a higher level of functioning, a higher level of symptoms/impairment, or a higher level of satisfaction.

User data

To analyse CMyLife web activity, we used Google Analytics to collect user data from January 2017 until January 2020. These data included user demographics and location, kind of device used, and behavioural information: pages per session, transitions between pages, and duration of time on specific site. All collected data were anonymous, on account of Google Analytics privacy terms and conditions.

Patients can register an account online to gain access to the secured patient forum and emails with newsletters and updates. Additional registration for a personal electronic health environment on CMyLife, which can be connected to some hospital systems, is possible after an identity check based on name, date of birth, postal code, and citizen service number.

Analysis

Descriptive statistics were used for baseline characteristics. In addition to mean scores from 0 to 100 on the EORTC QLQ-INFO25, the proportion of patients that perceived to receive no information at all on a specific subject was reported as well.

Reliability analysis (Cronbach's α) was used to assess internal consistency of the EORTC QLQ-INFO25 questionnaire subscales. We used univariate analyses to test the relation between EORTC QLQ-INFO25 subscales as dependent variable and the following sociodemographic and clinical characteristics as independent variables: gender, age (<65 years versus ≥ 65 years), treatment hospital (academic versus non-academic), educational level (low versus high: university and upper secondary education versus compulsory education), perceived health rating (poor-fair versus good-excellent), therapy (TKI versus TFR, in case of TKI therapy: first-line TKI versus subsequent lines), time since diagnosis (years) and, scores on the PAM13, eHEALS, EORTC QLQ-C30 subscale global functioning and EORTC QLQ-CML24 subscale symptom burden. Variables with $P < 0.20$ in the univariate analysis on the subscales of EORTC QLQ-INFO25 were selected for the multivariate regression analyses. Logistic regression analyses were performed with the dichotomous dependent variables of the EORTC QLQ-INFO25 regarding the wish for more information and wish for less information.

Pearson or Spearman correlation was used to test collinearity among independent variables. In case of strong correlation ($r > 0.6$), only the most clinically relevant variable was included. Multicollinearity was tested with the variance inflation factor. Analyses were performed with SPSS (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY).

Descriptive statistics were used for CMyLife web traffic.

Results

Patient and disease characteristics

A total of 219 patients completed the questionnaire. After exclusion of 16 patients (familiarity with CMyLife $n=11$; stem cell transplantation $n=5$), a total of 203 participants remained. Baseline characteristics of survey participants are summarized in Table 1. Most patients were aged ≥ 55 years (66.2%) and 45.2% were male. TKI treatment was discontinued in 19%. Of the patients receiving TKI therapy, almost 40% received first-line TKI. Median years since CML diagnosis was 6 (range 0–22, SD 5.3). The majority of questionnaires was received the first 2 weeks after they were sent, however, the exact time of return was not registered.

Table 1. Baseline characteristics

	%	(n)
Age (years)		
18-24	1.5	(3)
25-34	4.0	(8)
35-44	6.1	(12)
45-54	22.2	(44)
55-64	28.3	(56)
65-74	26.3	(52)
≥ 75	11.6	(23)
Sex		
Male	45.2	(89)
Female	54.8	(108)
Educational Level		
University education	10.2	(20)
Upper secondary education	28.6	(56)
Compulsory education	56.6	(111)
Other	4.6	(9)
TKI therapy		
Imatinib	32.8	(64)
Nilotinib	16.9	(33)
Dasatinib	19.0	(37)
Bosutinib	8.7	(17)
Ponatinib	3.6	(7)
Discontinued TKI therapy	19.0	(37)
First-line TKI therapy	39.0	(78)
Hospital		
University medical center	78.7	(155)
Non-university medical center	21.3	(42)
Perceived health rating		
Excellent	7.6	(15)
Very good	14.7	(29)
Good	48.7	(96)
Fair	27.4	(54)
Poor	1.5	(3)

Questionnaires

Regarding EORTC QLQ-INFO25, internal consistency based on the current data was good ($\alpha=0.80-0.91$). Mean global score was 42.8 (SD 18.2). On a scale from 1 (not at all) to 4 (very much), satisfaction with the amount of information provided was 2.79. Information on other services (i.e. help outside of the hospital, rehabilitation and psychological services) was rated especially low (Table 2).

Table 2. Mean scores on perception of information provision, quality of life, patient activation and eHealth literacy (EORTC QLQ-INFO25, EORTC QLQ-C30, EORTC QLQ-CML24, PAM13 and eHEALS, respectively).

EORTC-QLQ-INFO 25	N	Mean (SD)
Information on the disease (items 31-34)	197	56.2 (21.4)
Information on tests (items 35-37)	197	63.8 (23.6)
Information on treatment (items 38-43)	196	48.9 (21.1)
Information on other services (items 44-47)	196	16.7(22.0)
Global score (all items)	198	42.8 (18.2)
Satisfied with amount of information on a scale from 1 (not at all) to 4 (very much).	196	2.79 (0.76)
EORTC-QLQ-C30		
Global health status/ QoL	197	76.6 (17.3)
Physical functioning	199	83.7 (17.0)
Role functioning	198	78.8 (26.2)
Emotional functioning	197	83.4 (22.1)
Cognitive functioning	197	81.7 (21.3)
Social functioning	197	84.9 (21.2)
Fatigue	198	31.4 (25.1)
Nausea and vomiting	198	7.9 (15.3)
Pain	198	18.1 (24.1)
Dyspnoea	198	19.5 (25.8)
Insomnia	197	23.5 (27.7)
Appetite loss	197	9.1 (18.9)
Constipation	193	8.1 (17.6)
Diarrhoea	196	11.4 (22.4)
EORTC-QLQ-CML24*		
Symptom burden	198	22.8 (15.5)
Impact on worry/mood	65	16.1 (15.2)
Impact on daily life	59	17.4 (17.5)
Satisfaction with care and information	60	67.8 (33.7)
Body image problems	63	19.0 (27.9)
Satisfaction with social life	62	66.1 (34.9)
Patient Activation Measure-13 (PAM13)		% (N)
Level 1		11.7 (21)
Level 2		20.1 (36)
Level 3		47.5 (85)
Level 4		20.7 (37)
eHealth Literacy (eHEALS)	N	Mean (SD)
Total score	187	25.6 (8.3)

*Regarding the system missing in all subscales except symptom burden: we have compared scores on the symptom burden subscale between the system-missing group (all other subscales system-missing) and the non-missing group (not all subscales system-missing): mean difference 1.2 score, $p=0.13$. This suggests that the scores of the non-missing group on the other five subscales are representative for both groups.

The proportion patients that in their perception received no information (i.e. scored 1 on Likert scale) on different care locations was 71.1%. Regarding information on rehabilitation possibilities, psychological support, effects of treatment on sexual activity, and aspects of dealing with the disease at home, the percentages of patients that perceived to have received no information were 71.0%, 62.8%, 60.2% and 54.1%, respectively. About a third (28.5% and 35.9%, respectively) reported to receive no information on the effect of treatment on social and family life, nor on patient organisations. Almost a quarter (23.6%) received, in their perception, no information on the positive and negative effects of various TKIs. The majority (72.7%) received written information, of whom 72.2% searched for additional information on the internet. More information was desired by 35.9%.

Mean score on the global health scale of the EORTC QLQ-C30 was 76.6 (SD 17.3), the symptom scales fatigue, insomnia, dyspnoea, and pain scored the highest with mean scores of 31.4 (SD 25.1), 23.5 (SD 27.7), 19.5 (SD 25.8) and 18.1 (SD 24.1), respectively (Table 2). Mean score of the symptom burden scale of the EORTC QLQ-CML24 was 22 (SD 15.5). Satisfaction with care and information was rated 19.0 (SD 27.9) and impact on daily life 17.5 (SD 17.5). On the PAM13, almost a third of the patients scored level 1 or 2 (11.7% and 20.1%, respectively). Regarding eHealth literacy, a third of the patients reported to know which, where and how to find useful health information and only a quarter reported to be able to tell high quality health resources from low quality health resources on the internet.

When more information was desired ($n=70$), the most reported subjects were: management of adverse events (in general and by patient self), current updates and information on CML in general, meaning of blood tests, terminology, long-term effects of disease and medication, prognosis, pregnancy and effect on work and sexuality. When less information was desired ($n=7$), no specific subjects were mentioned, the only 2 reports were "information of treating physician was good" and "too much information at the same time".

Determinant analysis

Multivariate linear regression and logistics regression analyses showed that age ≥ 65 years (OR 0.24, $p<0.01$), lower education (OR 0.37, $p<0.05$) and more time since diagnosis (OR 0.56, $p<0.05$) were negatively associated with the wish for more information (Table 3). TKI therapy was associated with higher perceived levels of receiving information on tests (β 0.98 $p<0.05$). Years since diagnosis was negatively associated with perceived information on disease (β -0.29 $p<0.01$) and treatment (β -0.25 $p<0.05$). Higher scores on the PAM13 were associated with higher perceived levels of receiving information on disease (β 0.28 $p<0.05$), tests (β 0.26 $p<0.01$), treatment (β 0.39 $p<0.01$), other services (β 0.40 $p<0.01$), and global score (β 0.45 $p<0.01$). No significant effect of PAM13 score on wish

for either more or less information was found. A higher score on eHEALS was negatively associated with the wish for less information (OR 0.18, $p < 0.05$). QoL scores were not associated with EORTC QLQ-INFO25 subscales.

Table 3. Standardized betas (β) of multivariate linear regression and odds ratios (OR) of logistic regression analyses evaluating the association of independent variables with the information provision subscales.

N.B. Considering the strong correlation between the QoL subscale from EORTC QLQ-C30 and symptom burden subscale from EORTC QLQ-CML24 ($r = -0.6$), only QoL was used in analyses.

	Disease (β)	Tests (β)	Treatment (β)	Other Services (β)	Global (β)	More info OR (95% CI)	Less info OR (95% CI)
Sex							
Male	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Female	0.013	0.38	1.3	0.00	0.63	0.84 (0.37-1.90)	0.12 (0.01-1.98)
Age							
Under 65 years	Ref	Ref	Ref	Ref	Ref	Ref	Ref
65 years and older	0.70	0.72	0.66	0.48	0.61	0.24 (0.10-0.61)**	4.47 (0.22-41.16)
Treatment hospital							
Academic	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Non-academic	-0.22	0.48	-1.34	-2.1	-1.18	1.11 (0.38-3.34)	2.33 (0.12-46.16)
Education							
High	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Low	-0.35	-0.11	0.33	-0.85	-0.27	0.37 (0.14-0.96)*	0.59 (0.03-10.31)
Health Rating							
Good-excellent	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Poor-fair	-0.75	-0.60	-1.11	-0.32	-0.94	1.78 (0.64-4.99)	1.21 (0.06-23.23)
Therapy							
TFR	Ref	Ref	Ref	Ref	Ref	Ref	Ref
TKI	0.24	0.97 *	0.37	-0.32	0.25	2.10 (0.68-6.43)	1.41 (0.03-60.26)
Line TKI therapy							
First-line TKI	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Subsequent-line TKI	0.87	0.94	0.76	0.99	0.96	1.10 (0.45-2.57)	0.35 (0.01-9.31)
Years since diagnosis	-0.29 **	-0.25 *	-0.11	-0.02	-0.17	0.56 (0.35-0.90)*	0.84 (0.21-3.33)
PAM13 score	0.28*	0.26 **	0.40**	0.41 **	0.45 **	0.71 (0.44-1.16)	3.84 (0.68-21.67)
QoL (EORTC-QLQ-C30)	0.06	0.16	0.09	0.13	0.12	0.74 (0.45-1.21)	0.28 (0.06-1.21)
eHEALS score	0.15	0.029	0.05	0.01	0.05	0.96 (0.60-1.55)	0.18 (0.04-0.93)*

* $P < 0.05$. ** $P < 0.01$.

User statistics

In 2017, CMylife had 6 334 visitors and 338 registered user accounts. On average, 5.2 pages were visited per session. Mean time spent per page was 46 s. For 2018, numbers were as follows: 9 159 visitors, 472 registered accounts, 4.1 page visited per session, mean session duration of 2.7 min and 53 s per page. For 2019, number were 14 448, 625, 4.6, 2.9 min, and 55 s, respectively.

Most visited pages after the homepage were pages containing the patient forum and information on the disease CML, CML research, and adverse events of medication in 2017 (Table 4). This remained roughly the same in 2018 and 2019, the small difference explained by the advent of a news blog. View rates for pages regarding life with CML are shown in Table 5.

Table 4. Mean visits per month of CMylife webpages in the year 2017, 2018 and 2019.

Year	Title of webpage (/Subpage)	Mean visits/month		
		2017	2018	2019
	Homepage	1458	907	1184
	Newsblog	75	193	213
	Patient forum	102	111	124
	Diagnosis of CML	50	83	113
	What is CML?	135	187	260
	What is CML/ Symptoms	80	81	157
	What is CML?/ CML video	33	30	136
	Medication and side effects	137	171	211
	CML Treatment	63	92	138
	CML research	92	73	88
	CML guideline	80	84	86
	Living with CML/ Fatigue	79	71	127
	Living with CML/ Sports & Movement	37	41	63
	Living with CML/ Work & Income	34	29	44
	Living with CML/ Mortgage	27	28	30

Table 5. Mean visits per month of the pages life with CML for the years 2017, 2018 and 2019.

	Views 2017	Views 2018	Views 2019
Video – Life with CML	33	31	38
Fatigue	154	89	135
Mortgage and insurances	27	28	35
Sport and exercise	37	41	45
Work and income	34	30	33
Information for employer	N/A	4	25

N/A: not applicable, page was developed in 2018.

For all three years, pages on fatigue and medication adverse events were the only pages with an average time spent of more than 2 min. Electronic devices used to visit CMylife in 2017 and 2018 was in about 53% a desktop and 33% a mobile

phone, in 2019 this was more equally distributed. Tablets were used in 12–14% in all 3 years.

Discussion and conclusion

Discussion

In our study, before the use of the CMyLife platform, a below average mean global score on the EORTC QLQ-INFO25 was reported. Satisfaction with amount of information provided was rated slightly above average. Written information was provided in most cases, though a substantial group desired to receive more information. Information provision on other services, such as help outside of the hospital, rehabilitation and psychological services, was rated particularly low. More than half of the patients reported to have received no information on psychological support, dealing with the disease at home, or effects on sexuality. Older age, duration since diagnosis, and lower educational level were negatively associated with a need for more information. Also, higher patient activation was associated with higher reported levels of received information and higher eHealth literacy was negatively associated with a need for less information, respectively. Regarding CMyLife's traffic, information pages concerning medication and side effects were visited most frequently. Pages on fatigue and side effects were visited the longest. Although information provision on other services was reported low, pages regarding these subjects were visited moderately.

Direct comparison of our results with other CML populations or haematological malignancies is difficult due to the paucity in studies. The one study regarding information on TKI treatment supports our reported need for information on side effects [33]. Symptom scales fatigue, insomnia and dyspnoea in our study were scored high compared to cancer patients in general [41], yet in line with CML literature [42, 43]. These scores, together with side effects being the main reason of intentional non-compliance in CML, emphasize the need for improvement [44-46].

Compared to other malignancies, perceived information scores vary among type of cancer, although they are roughly comparable on the subscales disease, tests, treatment and global score [47-50]. In all these studies information on other services was scored the lowest of all subscales. Still, even compared to these rates, the score on other services was remarkably low in our study. In contrast, need for more information was reported the lowest in our study. Nevertheless, this concerned more than a third of the patients and their needs should be explored. eHealth literacy was negatively associated with the need for less information. This shows that the difference in information needs in patients with a lower eHealth

literacy and more eHealth literate patients should be explored to meet the needs of both groups.

A variety in (mobile) interventions aimed at meeting cancer patients' information needs have been developed, yet their effect in clinical trials have not yet been established [51-54]. Few other, non-RCT, studies reported variable information needs, usage of information sections, and page visits among different cancer types [55-58]. Patient involvement in developing interventions is therefore indispensable [58]. When interviewed about their needs most cancer patients in general reported a need for informational features that would help them in self-management of their cancer [59]. Besides, in qualitative studies, patients do report a perceived added value of information provision platforms. The way we measure information provision itself could be one of the reasons a beneficial effect is not established in clinical trials. Other factors include, among others, the scarcity in studies regarding information needs in minorities (based on ethnicity, socioeconomic status and/or age) and a mismatch in readability level between the patient and provided information.

Possible explanations for higher information needs in younger patients comprise a difference in disease perception and knowledge [60], more active participation [61], and less difficulty processing and remembering information [62, 63]. Younger patients might prefer looking for additional information online when it suits them, while older patient might prefer information supplied by their HCP [64]. The role of educational level could be explained by a higher patient activity in more educated patients and the familiarity they might have with using the Internet or books for information-seeking, compared to lower educated patients [65]. Besides, the latter might ask fewer questions and experience greater difficulty in communicating preferences [66]. Reasons that a shorter time since diagnosis was associated with more information needs might be that these patients are new to all information and want to learn about their disease. In contrast to patients who are diagnoses a longer time ago who are already familiar with this information [4, 16, 67, 68].

Regarding CMyLife's traffic, pages on basic medical information (e.g. CML, treatment, symptoms) were visited the most and information on living with CML less often. This confirms the need for basic information with a higher need for medical than psychosocial information [26]. As to low perceived information provision on other services, however, one could have expected that pages concerning life with CML would have been visited more often. Considering the limited eHealth literacy rates, the pages could have been too difficult to find, or there may be a gap in needs and information provided.

A more passive role is reported to be associated with lower perceived information provision [36, 47, 69]. Most patients in our study scored a high

activation level (i.e. level 3 or 4), in other words, are taking action and control in their own care process or is maintaining this behaviour. Higher PAM13 scores were positively associated with almost all information perception subscales. Still, a third scored level 1 or 2, e.g. tend to be passive and feel overwhelmed by, and lack knowledge and confidence to manage their own health [37]. Patient activation is also a strong predictor for seeking and using health information, more than functional health literacy [70]. Therefore, we do not know whether CMyLife was used by less activated patients. CMyLife's aim is to enhance patient empowerment and to provide patients with tools to do so, we should focus more on this group of patients and further explore their needs in future research.

The continuous registration of new user accounts on CMyLife over the years implicates that there is a need for such an intervention. CMyLife has potential to enhance information provision, although there are a few improvements to be made. First, information should be more adjusted to the individual. Age, time since diagnosis, and educational level are of influence in perceived information, and specific needs within these groups should be further explored and processed in CMyLife. To date, some determinants such as treatment and disease phase (i.e. chronic phase) are incorporated in CMyLife, though other important factors such as health literacy, educational level, and age are not. Second, content of information should be expanded. Substantial proportions of patients in this study did not recall to receive any information on patient organisations, effects of treatment on social and family life, and effects on sexual life, and not all of these topics are currently covered by CMyLife. Again, patient-tailored information provision is crucial to ensure patients know where to find it and how to use it.

Last, adjustment of information does not only apply to the provided content, as well as its timing, as another contributing factor to the gaps in information provision may be recall of information. Of the medical information provided during consultations is 40–80% either forgotten or remembered incorrectly [71]. This is worsened by anxiety, which can be expected in cancer patients [71, 72]. In haematological cancer patients, 20–28% reported inadequate on recall of information, information overload, insufficient opportunity to ask questions, and inadequate information provision about managing anxiety associated with a procedure or treatment [35]. A solution could be the provision of information in a sequential or repetitive manner. For instance, patients receive references to information sources a few hours or even days after consultation, which can be sent by mail, email, text message or by a web-based platform such as CMyLife, based on patients' preferences. Consequently, patients can choose themselves when and whether they retrieve information, in what amount and on which subject.

Limitations of our study mainly relate to the generalizability of our results. User data derived from Google Analytics are aggregated data and it remains of

question whether they truly are a measure for user behaviour. Time spent on a page does not equal time spent actually reading the page. Furthermore, recall bias could have occurred when filling out the questionnaires. Finally, except for the symptom burden scale, there are some system missing on the EORTC QLQ-CML24 questionnaire. However, when comparing means on non-missing items between the groups (system missing versus non-missing) there was no statistical difference, so no selection had occurred.

Conclusion

Information provision in current Dutch CML care is suboptimal. Although satisfaction with information provided was rated about average, information perception concerning disease and treatment-related topics in relation to everyday life was rated low and extra information was desired by more than a third of patients. Older age, lower education, and duration since diagnosis were negatively associated with this desire. A considerable proportion of patients had a low patient activation level, hesitating to manage their own health and lacking knowledge and confidence to do so. Patient-centred strategies to improve information provision should focus on this group to enhance patient empowerment. Furthermore, many patients searched for additional information online, even though they reported low rates of having the know-how where to find useful health information and how to distinguish high and low quality information sources. This implies a need for an understandable and trustworthy information source, such as the CMylife platform. Patients need to find it though, and references by HCPs and/or patient organisations are important. Information on the platform is actively used by patients. Though its content comprises many topics, this study shows room for improvement to further adjust content to patients' needs and preferences. Evaluation processes such as described in this study are dynamic and continue to improve the adjustment of the platform to the patient, in order to achieve patient-centredness where the patient is able to choose the amount, topics, time, and manner of information provision.

Practice implications

CMylife has the potential of improving information provision in current CML care, although there is room for improvement. Online information seeking is common and patients report to have difficulties in finding current, good-quality, and reliable information. HCPs may facilitate patient adoption by browsing through CMylife together during consultation and supply the patient with a leaflet for at home. CMylife could serve as a dynamic information source, which can be used complementary to the information provided by hospitals. As the fear for an increased workload is one of the major reported barriers in HCP adoption

of such platforms [73-76], an appointment following consultation with an on-site specialized e-nurse to support patients' use may facilitate patient adoption as well. CML represents only a small share of the haematological malignancies. Hence, the current extension to an adapted digital care platform for patients with other haematological malignancies (e.g. myeloproliferative neoplasms, chronic lymphocytic leukemia) could, once constructed, make it more time-worthy for HCPs to invest effort in CMyLife.

To truly tailor information provision to patients, research and innovations should focus on gaining insights in information needs of the individual patient, in a longitudinal manner during the disease course. Frequent assessments should take place, with options to log them, so patients can prepare their consultation and provide HCPs an overview of their desires, comparable to the increasing assessment of other patient reported outcomes such as experienced symptoms and disease burden.

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CHAPTER 5

Effectiveness of digital care platform CMyLife for patients with chronic myeloid leukemia: results of a patient-preference trial

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Abstract

Background: Two most important factors determining treatment success in chronic myeloid leukemia (CML) are adequate medication compliance and molecular monitoring albeit still being suboptimal. The CMyLife platform is an eHealth innovation, co-created with and for CML patients, aiming to improve their care, leading to an increased quality of life and the opportunity of hospital-free care.

Objective: To explore the effectiveness of CMyLife in terms of information provision, patient empowerment, medication compliance, molecular monitoring, and quality of life.

Methods: Effectiveness of CMyLife was explored using a patient-preference trial. Upon completion of the baseline questionnaire, participants actively used (intervention group) or did not actively use (questionnaire group) the CMyLife platform for at least 6 months, after which they completed the post-intervention questionnaire. Scores between the intervention group and the questionnaire group were compared with regard to the within-subject change between baseline and post-measurement using Generalized Estimating Equation models.

Results: At baseline, 33 patients were enrolled in the questionnaire group and 75 in the intervention group. Online health information knowledge improved significantly when actively using CMyLife and patients felt more empowered. No significant improvements were found regarding medication compliance and molecular monitoring, which were already outstanding. Self-reported effectiveness showed that patients experienced that using CMyLife improved their medication compliance and helped them to oversee their molecular monitoring. Patients using CMyLife reported more symptoms but were better able to manage these.

Conclusions: Since hospital-free care has shown to be feasible in time of the COVID-19 pandemic, eHealth-based innovations such as CMyLife could be a solution to maintain the quality of care and make current oncological health care services more sustainable.

Background

To meet the growing burden of chronic diseases, the World Health Organisation reported that health care systems must reorganize and that innovative approaches are essential [1]. Cancer has become a notable proportion of these chronic diseases, as life expectancy of oncology patients has increased substantially due to new technologies, earlier diagnosis and better treatments [2, 3]. An example of such an oncologic chronic disease is chronic myeloid leukemia (CML). CML is characterized by translocation of chromosome 9 and 22, leading to the BCR-ABL1 mutation, which encodes for a constitutively active protein e.g. tyrosine kinase [4, 5]. Since tyrosine kinase inhibitors (TKIs) have been used as treatment the life expectancy of CML patients has increased. It approaches that of the general population, if patients have optimal responses to the treatment [6, 7].

The two most important factors determining treatment success are patients' medication compliance and adequate molecular monitoring of BCR-ABL1 values according to evidence-based guidelines [8]. The BCR-ABL1 value is a disease-specific biomarker that accurately reflects the course of the disease and treatment response [8]. This monitoring of disease activity in accordance with guidelines is associated with a reduced risk of progression and mortality [9], improved TKI adherence [10], and lower health care costs [11]. Treatment-free remission has become an additional treatment goal, where TKI treatment can be safely discontinued without relapsing [12]. However, guideline adherence is still suboptimal and tends to be lower in hospitals, which are less experienced in treating CML patients [9, 13]. Hence, patients could play an important role in guarding their own molecular values.

This shift to more involved and empowered patients, and ultimately to hospital-free care, needs a patient-centred approach, based on eHealth [14–18]. eHealth could provide patients with tools to oversee and guard the progress and accuracy of their treatment. If they have any questions they could get in touch with their health care provider (HCP) to monitor their treatment. Therefore, eHealth could be a promising medium for patients to easily monitor their molecular levels from home. Besides, eHealth enables patients to monitor their medication compliance, provides patients with access to care efficiently, enables interactive patient-provider communication, and helps them to access and understand medical information more readily [17, 18]. Hence, eHealth seems to have considerable potential and added value, as it may give patients the chance to get sufficient information and care from home and only visit the hospital when necessary. Feasibility of eHealth platforms is extensively investigated, but insight into their effectiveness in haematological malignancies is scarce.

CMyLife is an example of such an eHealth innovation and was co-created with and for CML patients [19]. CMyLife aims to provide CML patients with tools and knowledge to control their care process and improve their medication compliance and molecular monitoring. This could eventually lead to increased quality of life and opportunity of hospital-free care. The aim of this study is to explore the effectiveness of the CMyLife platform in terms of information provision, patient empowerment, medication compliance, molecular monitoring, and quality of life of CML patients.

Methods

Design

A patient-preference trial was performed in order to gain insights into the effectiveness of CMyLife in terms of information provision, patient empowerment, medication compliance, molecular monitoring of BCR-ABL1 values, and quality of life of CML patients. Patients could choose between actively or not actively using CMyLife, including a pre- and post-measurement. The study period lasted from July 2019 to October 2020. Given the nature of this study and the low impact on participants, the Medical Research Involving Human Subjects Act (Dutch: WMO) does not apply, as confirmed by the institutional Medical Ethical Committee 'CMO Regio Arnhem-Nijmegen'. The trial was registered at ClinicalTrials.gov at 22/10/2020 (registration number: NCT04595955).

Study population

HCPs approached their patients (who visited them for an appointment within the study period) for participation in this study in five academic and seven large non-academic hospitals, spread over the Netherlands. In addition, participants were recruited through the website of the Dutch patient advocate association, called Hematon, and via the CMyLife website [20]. Upon participation in the study, all participants signed informed consent. The study population consisted of patients in chronic phase CML who were treated with first or second line TKIs. Patients treated with second line TKIs were only allowed to participate if they had switched TKIs as a result of intolerance, not because of treatment failure. Patients were excluded if they were in treatment-free remission, in acceleration phase, in blast crisis, or if pregnancy was planned in the study period.

Patient preference was leading in determining group enrolment. Patients who agreed to actively use CMyLife for at least 6 months were enrolled in the treatment group; patients who did not were enrolled in the questionnaire group. Active use in the intervention group comprised receipt of adequate support from the CMyLife-team. The support consisted of an instruction package and a

kick-off workshop to inform patients about how, when, and why they could and should use CMyLife. The CMyLife-team was reachable for questions during the day and offered all users to help them install the platform. Also, the CMyLife-team gathered feedback from users about if their support was adequate. Patients in the questionnaire group were aware of the existence of CMyLife and the website remained accessible for them. However, they received no support. After enrolment participants received a written baseline questionnaire by mail. Upon completion of the baseline questionnaire, participants actively used (intervention group) or did not actively use (questionnaire group) CMyLife for at least 6 months, after which they completed the post-intervention questionnaire.

Intervention

Development and features of the CMyLife platform were described in detail elsewhere [19]. CMyLife facilitates CML patients with a website, medication app, guideline app, and a personal health environment. All data were secured and conform the General Data Protection Regulation. In accordance with the Dutch security guideline (NEN7510), features containing data from the hospital's electronic health record (for example, laboratory results) were secured with a two-step validation with a token received via an SMS text message.

The **website** provides accurate and easy to understand information about the disease, medication, guidelines, side effects, and the effect on daily life (work, sports, mortgage etc.). It is provided with a question and answer functionality, where patients can receive answers from specialized haematologists and pharmacists. In addition, patients (in the intervention group) can communicate with other patients (in the intervention group), to share information or ask questions (via a password protected forum).

The **medication app** [21] is used to optimize medication compliance and supports patients in preparing the consultation with their HCP by allowing patients to set medication alarms, register their medication intake, request for repeat medication prescriptions and read the information leaflet of the medication they are taking. In addition, they can log side effects they experience, which can be shared with their HCPs through their personal health environment. The medication app also includes an option that enables patients to record the consultation with their HCPs.

The **guideline app** [22] displays scheduled blood checks and appointments with haematologists, sends monitoring reminders, and shows an understandable explanation of patients' BCR-ABL1 values and of the Dutch treatment guidelines. This enables patients to compare their values to the guideline's targets, and when they differ, act accordingly.

Patients can save their own medical records in their **personal health environment**, consisting of a Patient Knows Best portal [23]. They can determine which information they store and with whom they share it (adjustable by turning off or on their informed consent). For example, they can share side effects with their HCPs in order to discuss them.

Data collection

At baseline, all participants completed a survey containing patient characteristics (i.e. sociodemographics, CML related information) and Dutch translated and validated questionnaires (Appendix 1) exploring the effectiveness of CMyLife in terms of information provision, patient empowerment, medication compliance, molecular monitoring and quality of life. Six months later, patients completed the post-intervention questionnaire containing the same validated questionnaires. The postintervention questionnaire of patients in the intervention group included additional questions about self-reported effectiveness. Regarding information provision, familiarity with CML related concepts (Philadelphia chromosome, BCR-ABL1, tyrosine kinase inhibitor, remission, log reduction (for BCR-ABL1), haematological response/remission, cytogenetic response/remission, molecular response/remission, major molecular remission, complete cytogenetic remission, treatment-free remission, Hematon) was rated on a scale from 1 to 6. Information provision, eHealth literacy (patients' ability to find and evaluate online health information), patient empowerment and medication compliance were measured using the validated questionnaires EORTC QLQ-INFO25 [24], eHealth Literacy Scale (eHEALS) [25], Patient Activation Measure (PAM) [26–28], and the Medication Adherence Rating Scale (MARS) [29, 30], respectively. The MARS was supplemented with patients' self-reported effectiveness on medication compliance in the post-measurement of patients in the intervention group. Adequate molecular monitoring was measured using the frequency of hospital visits in the past 12 months and was supplemented with patients' self-reported effectiveness on their molecular monitoring in the post-measurement of patients in the intervention group. Appendix 2 describes questions and interpretation of the self-reported effectiveness on medication compliance and molecular monitoring. Quality of life and disease-specific quality of life were measured using the EORTC QLQ-C30 [31], and the EORTC QLQ-CML24 [32], respectively. Table 1 shows an overview of outcomes with corresponding measures used in this study.

Table 1. overview of outcomes and corresponding measures used.

Outcome	Measure
Information provision	Familiarity with CML related concepts EORTC QLQ-INFO25 ^a [24]
eHealth literacy	eHealth Literacy Scale [25]
Patient empowerment	Patient Activation Measure [26-28]
Medication compliance	Medication Adherence Rating Scale [29, 30] Self-reported effectiveness on medication compliance ^b
Molecular monitoring	Frequency of hospital visits in the past twelve months Self-reported effectiveness on molecular monitoring ^c
Quality of life	EORTC QLQ-C30 ^d [31] EORTC QLQ-CML24 ^e [32]

a European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Information 25-item,

b Questions and interpretation of self-reported effectiveness on medication compliance is described in appendix 2,

c Questions and interpretation of self-reported effectiveness on molecular monitoring is described in appendix 2.

d European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30-item,

e European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Chronic Myeloid Leukemia 24-item.

Analysis

Measurements processed anonymously, and analyses were performed with SPSS version 25 (IBM Corp). Descriptive statistics were used to describe basic features of participants. Attrition bias was evaluated by comparing patient characteristics between baseline and post-measurements. The EORTC QLQ-INFO25, eHEALS, PAM, MARS, EORTC QLQ-C30, and EORTC QLQ-CML24 were scored according to their manuals. In addition, all individual items on EORTC QLQ-INFO25 and EORTC QLQ-CML24 were analysed to get better insight in information gaps in CMyLife and in symptoms and problems of CML patients to improve CMyLife. Effectiveness of CMyLife was evaluated by comparing scores between the intervention and questionnaire group with regard to within-subject change between baseline and post-measurement using Generalized Estimating Equation models. If basic characteristics differed significantly between groups, P-values were corrected. Except for self-reported effectiveness, all differences shown in the results are referring to differences between intervention and questionnaire groups with regard to within-subject change between baseline and post-measurement.

Results

Patient characteristics

In total, 116 CML patients applied to participate in this study. Four patients dropped out, and four patients were excluded (stopped or never used TKIs). At baseline, 33 patients were enrolled in the questionnaire group and 75 in the intervention group. After 6 months, 29 patients filled in the post-intervention questionnaire and four patients did not return their answers (88% response) in the questionnaire group. During the six-month study period, eight patients in the intervention group stopped their participation. After 6 months, 57 patients filled in

the post-intervention questionnaire and ten patients did not return their answers (85% response). Figure 1 shows the flowchart of the study. Attrition bias between pre- and post-measurements was evaluated and not detected. Table 2 summarises patient characteristics. In the questionnaire group, 64% were female, and 64% were aged ≥ 65 . In the intervention group, 38% were female, and 40% were aged ≥ 65 . The percentage of patients that used CMyLife before participating in this study was comparable between groups. Gender, age, education, and whether patients had previously been treated with TKIs differed significantly between groups (Table 2). Therefore, the P-values were corrected for these characteristics.

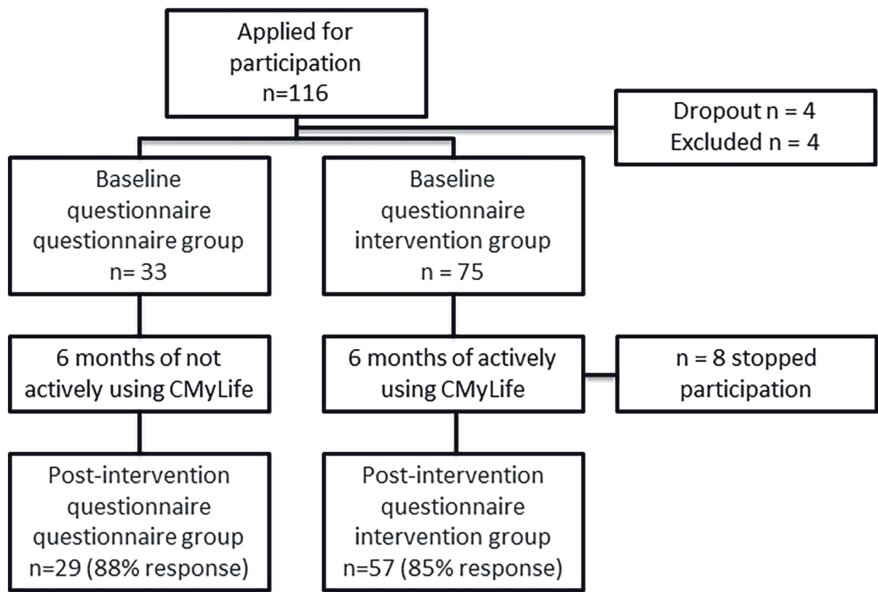


Figure 1. Flowchart study population.

Information provision

During the study period, patients in the intervention group became significantly more familiar with patient association Hematon compared to patients in the questionnaire group ($P = .023$). For the other concepts, no statistically significant differences were found between the groups. However, in the intervention group, a clear trend towards better familiarity with disease related concepts was seen (Appendix 3).

Table 3 shows the percentage of patients who reported to receive no or little information on all individual information items. After the study period, information on “additional help outside the hospital” scored significantly better in the intervention group ($P = .025$). Several items showed a trend towards better information provision in the intervention group when compared to the questionnaire group (e.g. diagnosis, extent spread, possible causes of the disease, and expected effects and possible side effects of treatment). Table 3 also shows scores on perceived information provision on different EORTC scales. There was no significant difference between the two groups although all information scales show a trend towards better information provision in the intervention group.

Table 2. Baseline characteristics for CML patients.

Baseline characteristics	Questionnaire group (n=33)	Intervention group (n=75)	P-value
Gender, n (%)			.013
Male	12 (36.4)	46 (62.2)	
Female	21 (63.6)	28 (37.8)	
Age (years), n (%)			.022
18-64	12 (36.4)	44 (60.3)	
65 and older	21 (63.6)	29 (39.7)	
Education level, n (%)			.000
High ^a	10 (30.3)	39 (52.7)	
Middle ^b	7 (21.2)	26 (35.1)	
Low ^c	16 (48.5)	9 (12.2)	
Years since diagnosis, (mean $\pm$ SD)	6.7 $\pm$ 5.2	6.3 $\pm$ 6.2	.724
Previously used CMyLife, n (%)			.915
Yes, website	12 (36.4)	25 (33.3)	
Yes, medication app/ guideline app/otherwise	6 (18.2)	16 (21.3)	
No, not yet	14 (42.4)	31 (41.3)	
Currently used TKI, n (%)			.327
Yes, imatinib	16 (45.7)	44 (60.3)	
Yes, Otherwise ^d	16 (45.7)	29 (39.7)	
Previously treated with TKI, n (%)			.007
Yes	20 (62.5)	25 (34.2)	
No	11 (37.5)	48 (65.8)	
Hospital visits in the past 12 months, n (%)			.186
Zero	0 (0.0)	2 (2.7)	
1 time	3 (9.1)	2 (2.7)	
2 times	0 (0.0)	6 (8.1)	
3 times or more	30 (90.8)	64 (86.5)	

^a High education level: higher vocational education, academic education.

^b Middle education level: secondary vocational education, higher general secondary education, pre-university education.

^c Low education level: primary education, lower general secondary education, preparatory secondary vocational education.

^d Mostly dasatinib and nilotinib.

Table 3. Percentage of CML patients who perceived to receive no or little information per item of the EORTC QLQ-INFO25 and mean scores (SD) on information provision scales of the EORTC QLQ-INFO25, questionnaire vs intervention group.

Percentage of cml patients who perceived to receive no or little information about:	Questionnaire group			Intervention group		
	Pre (n=33) %	Post (n=29) %	Δ	Pre (n=75) %	Post (n=57) %	Δ
The diagnosis of your disease	30.3	31.0	0.7	26.4	17.9	-8.5
The extent (spread) of your disease	42.4	55.2	12.8	41.9	33.9	-8
The possible causes of your disease	68.8	65.5	-3.3	64.9	55.4	-9.5
Whether the disease is under control	18.2	17.2	-1	17.6	12.5	-5.1
The purpose of any medical tests you have had or may undergo	27.3	31.0	3.7	20.3	16.1	-4.2
The procedures of the medical tests	24.2	24.1	-0.1	23.0	16.4	-6.6
The results of the medical tests you have already received	18.2	10.3	-7.9	12.2	9.1	-3.1
The medical treatment	18.2	13.8	-4.4	13.5	9.1	-4.4
The expected benefit of the treatment	30.2	27.6	-2.6	18.9	9.1	-9.8
The possible side-effects of your treatment	54.5	35.7	-18.8	51.4	27.3	-24.1
The expected effects of the treatment on disease symptoms	48.5	34.5	-14	41.9	27.3	-14.6
The effects of the treatment on social and family life	87.9	72.4	-15.5	81.1	72.7	-8.4
The effect of the treatment on sexual activity	83.9	82.8	-1.1	90.5	88.9	-1.6
Additional help outside the hospital	90.9	93.1	2.2	97.2	85.5	-11.7
Rehabilitation services	90.9	92.9	2	94.5	87.3	-7.2
Aspects of managing your illness at home	93.9	86.2	-7.7	87.7	85.5	-2.2
Possible professional psychological support	93.8	96.6	2.8	84.9	78.6	-6.3
Different locations of care	84.4	93.1	8.7	89.0	85.5	-3.5
Things that you can do to help yourself get well	75.0	78.6	3.6	78.1	78.2	0.1

EORTC QLQ-INFO25 scales ^a	Questionnaire group			Intervention group		
	Pre (n=33) Mean (SD)	Post (n=29) Mean (SD)	Δ	Pre (n=75) Mean (SD)	Post (n=57) Mean (SD)	Δ
Information about						
Disease	58.8 (24.1)	57.2 (22.5)	-1.6	57.1 (21.1)	63.2 (20.6)	6.1
Medical tests	71.7 (24.2)	67.8 (20.6)	-3.9	69.7 (22.5)	70.0 (22.2)	0.3
Treatments	48.1 (18.4)	53.8 (21.7)	5.7	50.2 (19.1)	55.4 (18.1)	5.2
Other services	12.4 (18.1)	13.2 (19.7)	0.8	16.4 (18.6)	22.3 (25.6)	5.9

Different location of care facilities	18.7 (25.3)	10.3 (20.1)	-8.4	16.9 (24.3)	20.0 (30.5)	3.1	.052
How to help yourself	29.2 (31.4)	29.8 (30.5)	0.6	30.6 (26.5)	33.3 (30.1)	2.7	.513
Received written information	68.8 (47.1)	67.9 (47.6)	-0.9	70.3 (46.0)	71.4 (45.6)	1.1	.884
Received cd/video	6.06 (24.2)	10.3 (31.0)	4.24	5.48 (22.9)	7.14 (26.0)	1.66	.538
Satisfaction with amount of information	43.4 (25.7)	41.4 (21.2)	-2	38.4 (23.4)	36.4 (20.6)	-2	.865
Wish to receive more info	33.3 (47.9)	31.0 (47.1)	-2.3	45.9 (50.2)	22.8 (42.3)	-23.1	.106
Wish to receive less info	66.7 (47.9)	69.0 (47.1)	2.3	54.1 (50.2)	77.8 (42.0)	23.7	.105
Helpfulness of information	31.3 (26.3)	34.5 (26.4)	3.2	31.1 (21.8)	32.1 (22.2)	1	.222
Global score	46.3 (16.1)	46.7 (17.0)	0.4	47.1 (15.9)	51.2 (16.5)	4.1	.161

P-value shows the difference between intervention and questionnaire with regard to the within-subject change between baseline and post-measurement.

Δ= difference between pre- and post-measurements.

^a Scores between 0-100, higher scores indicate more/better information and satisfaction.

Table 4. Mean scores (SD) on eHealth Literacy (eHEALS) a per item questionnaire vs intervention group.

Item	Questionnaire group			Intervention group			Corrected P-value
	Pre (n=33) Mean (SD)	Post (n=29) Mean (SD)	Δ	Pre (n=75) Mean (SD)	Post (n=57) Mean (SD)	Δ	
I know what health resources are available on the Internet	4.03 (0.67)	3.86 (0.79)	-0.17	3.73 (0.97)	3.95 (0.77)	0.22	.076
I know where to find helpful health resources on the Internet	4.03 (0.73)	3.79 (0.83)	-0.24	3.77 (1.04)	4.04 (0.69)	0.27	.032
I know how to find helpful health resources on the Internet	3.88 (0.82)	3.83 (0.85)	-0.05	3.85 (0.92)	4.04 (0.69)	0.19	.424
I know how to use the Internet to answer my health questions	3.67 (0.82)	3.79 (0.68)	0.12	3.69 (0.98)	3.95 (0.70)	0.26	.543
I know how to use the health information I find on the Internet to help me	3.48 (0.94)	3.59 (0.73)	0.11	3.46 (1.00)	3.77 (0.76)	0.31	.464
I have the skills I need to evaluate the health resources I find on the Internet	3.69 (1.03)	3.86 (0.79)	0.17	3.58 (0.97)	3.96 (0.76)	0.38	.437
I can tell high-quality from low-quality health resources on the Internet	3.47 (1.05)	3.69 (0.89)	0.22	3.46 (1.05)	3.84 (0.89)	0.38	.703
I feel confident in using information from the Internet to make health decisions	3.31 (1.15)	3.36 (0.91)	0.05	3.26 (1.10)	3.71 (0.89)	0.45	.110

P-value shows the difference between intervention and questionnaire with regard to the within-subject change between baseline and post-measurement.

Δ= difference between pre- and post-measurements.

^a Scores between 0-5 with higher scores indicating better eHealth literacy.

eHealth Literacy

Table 4 shows mean scores on eHealth literacy. Results from the eHEALS showed that both groups had comparable competences before the study period. After the study period, patients’ knowledge on where to find helpful health resources on the internet was significantly improved in the intervention group ($P=.032$). Furthermore, the intervention group showed a trend towards better eHealth literacy after the study period.

Patient empowerment

Figure 2 shows scores on patient empowerment. At baseline, 40% of patients in the questionnaire group did not believe in their own role in treating their CML or did not have trust or knowledge to take action (level 1-2). After the study period, 35% of them was level 1 or 2. For the intervention group, these rates were 43% and 26%, respectively.

Moreover, there was no significant difference in the standardized activation score between the intervention and the questionnaire group ($P=.139$). In the intervention group, a trend towards increased patient empowerment was observed. The mean PAM score of the questionnaire group increased from 60.5 (SD=14.6) to 62.6 (SD=13.2) whereas the intervention group increased from 58.5 (SD=13.7) to 64.0 (SD=12.4).

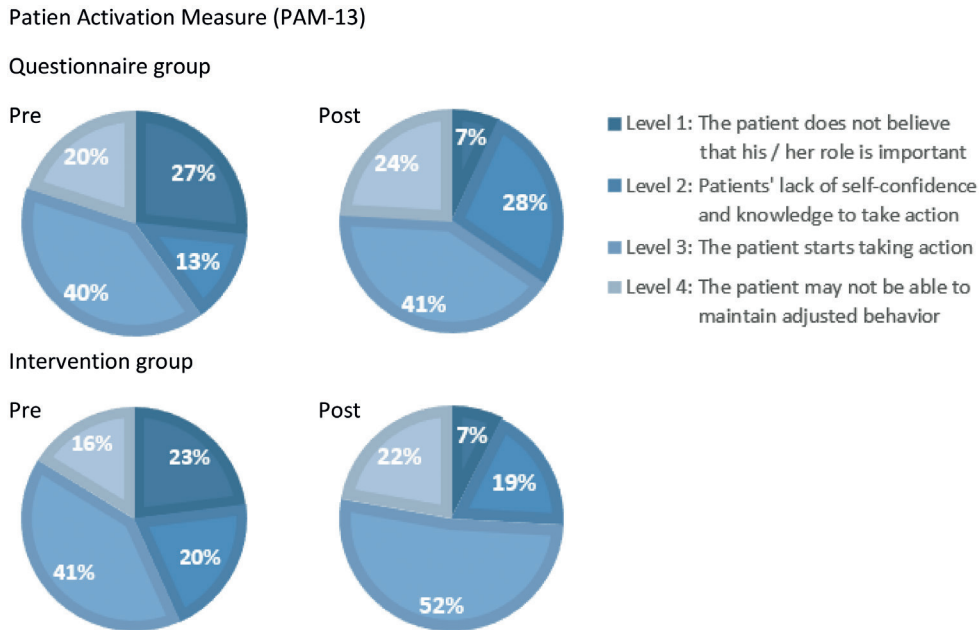


Figure 2. Patient empowerment levels (PAM13 NL) questionnaire vs intervention group.

Medication compliance

No statistical difference was found in mean total score of patients' medication compliance between groups ($P=.922$). Mean total score of the questionnaire group increased from 5.3 ($SD=0.92$) to 5.4 ($SD=1.00$) whereas the intervention group increased from 5.4 ($SD=0.54$) to 5.5 ($SD=0.82$) after using CMylife. Patients' self-reported effectiveness showed that 34.2% of patients in the intervention group reported that due to using the medication app they knew better why taking their medication properly is important. Additionally, 47.4% felt more motivated to take medication properly and 28.9% had started to think differently about how important it is. Using the medication app stimulated 21.0% of patients to search for help if necessary, it improved medication compliance of 42.1% of patients, and 52.7% of them felt less insecure about it.

Molecular monitoring according to guidelines

In the questionnaire group, 90.8% of patients visited the hospital three times or more at baseline versus 86.2% in the post-measurement. In the intervention group, these rates decreased from 86.2% to 78.9%. No statistical differences were found between the groups ($P=.685$). In the self-reported effectiveness questionnaire, 44.0% of patients in the intervention group indicated that they were more aware of when they needed to get their BCR-ABL1 values checked, and 20.0% felt less insecure about it after using the guideline app. In addition, 20.0% of patients felt more motivated to get their BCR-ABL1 values checked timely when using the guideline app, and it stimulated 32.0% to contact their HCP if their response to treatment was not sufficient according to guidelines. Forty percent of patients knew when treatment response was good and 20.0% of patients started to think differently about how important it is to get their BCR-ABL1 values checked in time. Lastly, 32.0% of patients reported to have more insight into their BCR-ABL1 values and its course.

Quality of life

Table 5 shows scores of the EORTC QLQ-C30 and EORTC QLQ-CML24 questionnaires. On the scales of the EORTC QLQ-C30 no significant differences between the pre- and post-measurement of the groups were reported. Regarding the EORTC QLQ-CML24, during the study period, individual items showed that patients in the intervention group had a significant increase in experiencing treatment as burdensome, compared to patients in the questionnaire group ($P=.043$) (Table 5). Also, on the scales of the EORTC QLQ-CML24, a significant decrease was reported on impact on daily life ($P=.043$) and an increase in symptom burden ($P=.013$) in the intervention group compared to the questionnaire group (Table 5).

Table 5. Mean scores (SD) from the EORTC QLQ-C30 and the EORTC QLQ-CML24 scales and percentage of patients experiencing moderate to severe burden of disease specific complaints (EORTC QLQ-CML24): questionnaire vs intervention group.

	Questionnaire group			Intervention group			
Scales	Pre (n=33) Mean (SD)	Post (n=29) Mean (SD)	Δ	Pre (n=75) Mean (SD)	Post (n=57) Mean (SD)	Δ	Corrected P-value
EORTC QLQ-C30 ^a							
Global health status/ QoL	75.0 (15.5)	69.8 (19.0)	-5.2	75.3 (18.9)	75.7 (19.6)	0.4	.317
Functioning							
Physical functioning	82.2 (15.9)	84.8 (15.2)	2.6	86.8 (16.4)	87.3 (15.4)	0.5	.482
Role functioning	76.3 (23.9)	81.6 (23.7)	5.3	75.5 (28.4)	79.8 (26.1)	4.3	.968
Emotional functioning	81.3 (17.4)	79.3 (20.6)	-2	83.6 (18.2)	82.7 (19.8)	-0.9	.700
Cognitive functioning	87.9 (16.8)	89.1 (16.8)	1.2	85.6 (18.6)	83.9 (20.4)	-1.7	.417
Social functioning	82.8 (25.5)	87.4 (15.8)	4.6	83.1 (23.0)	86.0 (20.1)	2.9	.626
Symptoms							
Fatigue	33.3 (19.4)	28.7 (22.7)	-4.6	33.3 (28.4)	30.4 (26.4)	-2.9	.377
Pain	20.7 (25.4)	19.0 (23.9)	-1.7	14.4 (24.4)	14.0 (24.2)	-0.4	.516
Nausea and vomiting	9.09 (17.2)	9.20 (15.2)	0.11	7.21 (13.0)	9.06 (14.8)	1.85	.537
Insomnia	28.3 (30.2)	31.0 (33.3)	2.7	19.4 (26.5)	23.4 (25.9)	4	.690
Dyspnoea	21.9 (23.4)	19.5 (24.4)	-2.4	14.4 (24.7)	14.0 (23.5)	-0.4	.589
Loss of appetite	16.2 (29.0)	16.1 (26.2)	-0.1	6.31 (18.9)	5.26 (15.2)	-1.05	.940
Constipation	16.7 (22.4)	9.52 (17.8)	-7.18	4.05 (13.5)	7.02 (18.6)	2.97	.064
Diarrhoea	20.2 (31.1)	18.5 (29.7)	-1.7	20.1 (25.3)	21.1 (28.6)	1	.332
Financial difficulties	8.08 (16.7)	5.75 (12.8)	-2.33	6.31 (20.4)	5.26 (15.2)	-1.05	.720
EORTC QLQ-CML24 ^a							
Impact on daily life	16.0 (15.2)	18.4 (19.1)	2.4	19.2 (17.1)	15.0 (15.8)	-4.2	.043
Symptom burden	25.6 (15.2)	22.5 (16.2)	-3.1	20.6 (12.4)	21.6 (13.2)	1	.013
Impact on worry/mood	21.1 (20.8)	25.9 (22.5)	4.8	15.4 (13.9)	20.0 (18.5)	4.6	.671
Body image problems	28.1 (26.9)	20.7 (24.3)	-7.4	20.1 (27.2)	22.8 (29.7)	2.7	.052
Satisfaction with care and information	77.4 (24.9)	77.8 (17.3)	0.4	72.4 (32.0)	74.2 (30.9)	1.8	.871
Satisfaction with social life	67.7 (28.7)	64.4 (25.1)	-3.3	63.9 (33.2)	59.6 (33.2)	-4.3	.844
	Questionnaire group			Intervention group			
Moderate to severe burden of following complaints (EORTC QLQ-CML24):	Pre (n=33) %	Post (n=29) %	Δ	Pre (n=75) %	Post (n=57) %	Δ	Corrected P-value
Abdominal pain or cramps	9.4	3.4	-6	8.1	10.5	2.4	*
Dry mouth	21.9	27.6	5.7	12.2	19.3	7.1	.538
Worry about change in weight	12.5	6.9	-5.6	5.4	7.1	1.7	.365
Skin problems	31.3	24.1	-7.2	14.9	19.3	4.4	.170
Headache	3.1	6.9	3.8	4.1	7.0	2.9	.910
Aches or pains in muscles or joints	37.5	32.1	-5.4	25.7	33.9	8.2	.080
Hair loss	15.6	3.4	-12.2	5.4	3.5	-1.9	.254
Excessive sweating	19.4	10.3	-9.1	14.9	10.5	-4.4	.527

Acid indigestion or heartburn	9.4	13.8	4.4	8.1	8.9	0.8	.805
Drowsiness	15.6	3.4	-12.2	12.2	12.5	0.3	.072
Oedema	21.9	17.2	-4.7	16.2	12.3	-3.9	.946
Frequent urination	28.1	17.2	-10.9	29.7	19.3	-10.4	.639
Problem with eyes	28.1	20.7	-7.4	18.9	19.6	0.7	.479
Muscle cramps	37.5	34.5	-3	24.3	24.6	0.3	.433
Emotional ups and downs	12.5	13.8	1.3	9.6	14.3	4.7	.259
Worry about future health	28.1	20.7	-7.4	12.7	14.0	1.3	.137
Difficulty living a normal life because I got tired quickly	21.9	13.8	-8.1	17.8	15.8	-2	.529
Worry about infection	12.5	27.6	15.1	4.1	19.6	15.5	.373
Dissatisfied with my body as a result of illness or treatment	25.0	13.8	-11.2	15.5	17.5	2	.073
Burdensome treatment	16.1	20.7	4.6	19.2	5.3	-13.9	.043
Social support was needed	0.0	3.4	3.4	5.5	5.3	-0.2	*
Satisfied with the care	89.3	96.3	7	80.6	83.0	2.4	.278
Satisfied with the information	90.3	86.2	-4.1	76.8	83.6	6.8	.280
Satisfied about the quality of my social life	78.1	69.0	-9.1	68.5	63.2	-5.3	.668

P-value shows the difference between intervention and questionnaire with regard to the within-subject change between baseline and post-measurement.

Δ= difference between pre- and post-measurements.

*Scores between 0-100; higher scores on the functioning scales indicate better quality of life, higher scores on the symptom scales indicate more/more severe symptoms. Higher scores on daily life, symptom burden, worry/mood and body image problems, indicates higher impact, higher scores on satisfaction indicate more satisfaction.

**P*-value could not be determined due to limited number in participants.

Discussion

Principal results and comparison with prior work

This is the first patient directed preference trial, including a before-after measurement, to explore the effectiveness of CMyLife on information provision, patient empowerment, medication compliance, molecular monitoring, and quality of life of CML patients. Overall, active use of CMyLife showed a clear trend towards improvement of all above-mentioned components except quality of life. The quality of life questionnaire showed a slight increase in patients' burden of symptoms but simultaneously a decrease on impact on daily life.

Both familiarity with CML related concepts and perceived information provision showed positive trends in patients that actively used CMyLife and information on additional support outside the hospital improved significantly. Especially information provision on direct disease related concepts, such as diagnosis, treatment, tests, and side effects, showed a positive trend towards better information provision, although the percentage of sufficiently informed patients stayed unchanged low in other items. Content of CMyLife should be adjusted according to patients'

information needs to improve information provision. Previous literature emphasized the beneficial effects of adequate information provision in cancer patients [33-37]. Perceived information provision in patients with other malignancies varied although it is roughly comparable [38-40].

In addition to information provision, CMylife significantly improved patients' knowledge on where to find online health information. Literature shows that only half of cancer patients have knowledge and capability to access and differentiate the high amount of web-based information [41]. Results showed that active use of CMylife improved eHealth literacy among CML patients and helped them become a well-informed partner in health care. Especially during the COVID-19 pandemic for instance, it is important for CML patients to stay accurately informed. Accurate and reliable information should be provided rapidly to these patients since almost 40% of them reported to be substantially concerned about the coronavirus [42]. CMylife had been a great medium to provide patients with this timely information [43].

Patient empowerment was increased in our study, albeit not significant. Patients who are more empowered in taking control of their own disease could believe in their abilities to optimize their medication compliance and oversee their molecular monitoring. Other interactive patient portals, such as one for breast cancer survivors and one for lung cancer patients, showed a decrease in patient activation, although not directly comparable due to a difference in study population, content and features [44, 45]. Perhaps no significant increase in patient empowerment was found because of limited sample size, because the outcome measure is not responsive enough to detect an effect, or because actual usage was not strong enough. Therefore, future studies should take actual usage into account when investigating patient empowerment.

Our study showed extremely high medication compliance rates. Pre-intervention, these rates were reported as almost 100% and did not significantly change post-intervention. In literature, medication compliance rates vary from 19% to 98%, probably due to heterogeneity in adherence measurement methods and study populations [46, 47]. Only small proportions of patients were perfectly adherent. Patients in our study were very strict in taking their medication because they are very motivated for taking care of their disease, and therefore, participated in this patient preference study. As MARS is a rather general measure it is not possible to determine whether patients take their medication on all prescribed moments. Therefore, a more objective and specific tool to measure medication compliance should be used in the future. The well-known medication event monitoring system is an example of such an adequate measure, it provides an objective and reliable measure of medication compliance [48, 49]. Nevertheless,

self-reported effectiveness shows patients to be more motivated and medication compliant when using the medication app.

Our study results show that frequency of hospital visits was not significantly affected by CMyLife. Remarkably, hospital visits decreased in both groups, probably due to the COVID-19 pandemic, during which routine care was deliberately postponed and digital care was stimulated. CMyLife enabled CML patients to continue their care digitally without any delay or interruption. CMyLife gave patients opportunity to replace in-person visits by video consultations, which decreased the risk of exposing them to COVID-19 [50]. Self-reported effectiveness showed that by using the guideline app, patients felt more motivated to undergo testing on scheduled time, and they gained more insights in their obtained results and disease course. Importance of patient empowerment is further emphasized by suboptimal guideline adherence rates by HCPs [51]. CMyLife could be a great medium for accurate surveillance of treatment-free remission in CML patients.

None of the EORTC QLQ-C30 scales showed significant differences in quality of life between the questionnaire and intervention group. Scores in our study are roughly comparable to cancer patients in general [52]. The EORTC QLQ-CML24 scales showed a significant decrease of impact on daily life and a significant increase in symptom burden. Using CMyLife with logging their side effects could have made patients more aware of their symptoms. On the other side the concurrent decrease in impact suggests that patients were better able to self-manage their symptoms. In CML, adverse events are the main reason of intentional non-adherence, so timely recognition and management by HCPs is important [53-56]. Yet, HCPs tend to underestimate severity of patients' symptoms [57]. Patient reported outcomes (PROs) are essential in patient-centred care, and its advantages as well as the necessity for routine PRO assessment in clinical practice are well described, not only in CML, but other malignancies too [57-61]. CMyLife provides a platform for this assessment.

Future improvements

Despite promising potential of CMyLife, there is still room for improvement. In the future, content of CMyLife should be adjusted according to changing patients' information needs. This requires a dynamic improvement process, where patients' needs are measured routinely and content of CMyLife is adjusted accordingly. In addition to the information gap, PRO assessment combined with personalized feedback should be properly integrated in the CMyLife platform together with proper monitoring of molecular levels and medication adherence to enhance self-management aiming at the ultimate goal of true patient-centred care. HCPs will not become entirely redundant as monitoring and follow-up for adverse events

and late effects of TKI treatment, albeit from a distance, is still required but their role is changing in coaching the patient.

Strengths, limitations and future research

In our study a number of strengths and limitations are recognized. First, our results are strengthened by the presence of a questionnaire group. Despite the limited sample size and the sample being a convenience sample, it encompasses an adequate, nationwide, representation of Dutch CML patients. Our preference-based design has advantages compared to randomised controlled trials (RCTs). EHealth users should be motivated in order to actually use the innovation. Patients with a strong preference for one of the arms who refuse randomisation may be absent in RCTs. Also, literature shows high dropout and nonresponse rates in studies evaluating the effectiveness of eHealth using RCTs. When randomising patients to use or not use an eHealth innovation, bias will be introduced. Not all patients in the intervention group wanted to use the innovation and patients in the control group could have wanted to use the intervention but were not allowed to. Absence, dropout, and nonresponse of patients affects generalisability of study results, which is not the case in a preference based design [62–64]. Allocation of patients to use or not use eHealth randomly is therefore not ethical and should always be done in agreement with patients. However, when using a non-randomised design, unknown and uncontrolled confounders could be present [65]. Access to the CMylife website for patients in the questionnaire group was not denied, this could have caused underestimation of the effects of the platform. Although as many covariates as possible were taken into account in our analysis, some factors should be focus of future studies in order to minimize confounding effects. For example, no data of CMylife utilization were collected, nor how patients' use other information and communication resources aside from CMylife. Lastly, communication between patients could not have been prevented since patients in the intervention group met in small groups during workshops. Also, part of the platform was that patients in the intervention group were enabled to communicate with other patients in the intervention group, to share information or ask questions via a password protected forum. However, communication between the intervention group and the questionnaire group was very unlikely since the groups did not meet each other and had no contact information of each other. Therefore, we do not think this could have affected results.

Conclusion

Aim of CMylife is to provide hospital-free virtual care, by giving CML patients tools and know-how to self-manage their disease. Results of our study suggest that

although more symptoms were reported, patients were better able to manage their symptoms. Knowledge on where to find online health information was improved significantly and, albeit not significant, they felt more empowered. Beneficial effects on medication compliance and molecular monitoring were experienced by patients, which is paramount in patient-centred care. CMyLife provides patients with information, tailored in amount and content and in a timely manner. However, we found room for improvement in content of information provision by expanding topics, adjusted to patients' information needs. Personalized information based on PROs assessed in CMyLife such as symptoms experienced, and quality of life could further enhance self-management. An iterative process of assessing patients' needs and further adjustment of CMyLife is required to keep care patient-centred, fit CMyLife into future perspectives, and put patients in lead of their disease process. Since hospital-free care has shown to be feasible in time of the COVID-19 pandemic, eHealth-based innovations such as CMyLife could be a solution to maintain quality of care and make current oncological health care services more sustainable.

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Supplementary material

Appendix 1

Validated questionnaires with scores and internal consistency

The EORTC QLQ-INFO25 (scores between 0-100 with higher scores indicating more/better information and satisfaction) (internal consistency of $\alpha=0.74-0.89$).

The eHealth Literacy Scale (eHEALS) (scores between 0-5 with higher scores indicating better eHealth literacy) (internal consistency of $\alpha=0.93$).

The Patient Activation Measure (PAM) (level 1-4 and scores between 0-100 with higher levels and scores indicating better patient activation) (internal consistency of $\alpha=0.88$).

The Medication compliance Rating Scale (MARS) (scores between 5-25 with lower scores indicating better medication compliance) (internal consistency of $\alpha=0.76$).

The EORTC QLQ-C30 (scores between 0-100, higher scores on the functioning scales mean better quality of life, higher scores on the symptom scales mean more/more severe symptoms) (internal consistency of $\alpha=0.65-0.92$).

The EORTC QLQ-CML24 (scores between 0-100, higher scores on daily life, symptom burden, worry/mood and body image problems, means higher impact, higher scores on satisfaction mean more satisfaction) (internal consistency of $\alpha=0.66-0.83$).

Appendix 2

Self-reported effectiveness on medication compliance and molecular monitoring questions and interpretation

The influence of the medication app on medication adherence	Completely disagree	Disagree	Neutral	Agree	Completely agree
When using the medication app I know better why it is important to take medication properly	☐	☐	☐	☐	☐
The medication app makes me more aware of the importance to take medication properly	☐	☐	☐	☐	☐
The medication app motivates me to take medication properly	☐	☐	☐	☐	☐
The medication app encourages to seek help (if necessary) to take medication properly	☐	☐	☐	☐	☐
The medication app has improved my medication adherence	☐	☐	☐	☐	☐
The medication app makes me feel less insecure about my medication adherence	☐	☐	☐	☐	☐

The influence of the guideline app on guideline adherence	Completely disagree	Disagree	Neutral	Agree	Completely agree
I have more insight into my BCR-ABL1 value and its course	☐	☐	☐	☐	☐
I know better whether my treatment is working	☐	☐	☐	☐	☐
I know better when to have my BCR-ABL1 value checked	☐	☐	☐	☐	☐
The guideline app makes more aware of importance of checking BCR-ABL1 value in time	☐	☐	☐	☐	☐
The guideline app motivates to have BCR-ABL1 value checked in time	☐	☐	☐	☐	☐
The guideline app clearly shows me what my BCR-ABL1 values mean	☐	☐	☐	☐	☐
The guideline app encourages to contact HCPs if treatment response is not sufficient	☐	☐	☐	☐	☐
The guideline app makes me feel less insecure about my BCR-ABL1 values	☐	☐	☐	☐	☐

For the interpretation of the results completely disagree and disagree were grouped and completely agree and agree were grouped.

Appendix 3

Patients' familiarity with CML related concepts questionnaire vs intervention group

Not (at all) familiar with undermentioned concepts:	Questionnaire group			Intervention group			Corrected P-value
	Pre (n=33) %	Post (n=29) %	Δ	Pre (n=75) %	Post (n=57) %	Δ	
Philadelphia chromosome (t9;22)	25.1	20.7	-4.4	12.3	8.9	-3.4	*
BCR-ABL1	20.0	7.4	-12.6	12.3	5.3	-7	.323
Tyrosine Kinase Inhibitor	33.3	29.6	-3.7	26.0	8.9	-17.1	.054
Remission	40.0	40.7	0.7	30.6	18.5	-12.1	.177
Log reduction (for BCR-ABL1)	62.1	63.0	0.9	57.5	49.1	-8.4	.440
Haematological response/remission	46.7	48.1	1.4	44.4	32.1	-12.3	.218
Cytogenetic response/remission	69.0	66.5	-2.5	59.2	50.9	-8.3	.360
Molecular response/remission	67.9	59.3	-8.6	47.2	34.5	-12.7	.879
Major Molecular Remission (MMR)	67.9	61.6	-6.3	60.6	50.0	-10.6	.794
Complete Cytogenetic Remission (CCyR)	72.4	57.7	-14.7	63.4	55.6	-7.8	.265
Treatment-free Remission (TFR)	82.1	65.4	-16.7	68.1	49.1	-19	.639
Hematon	44.8	34.6	-10.2	42.3	18.2	-24.1	.023

P-value shows the difference between intervention and questionnaire with regard to the within-subject change between baseline and post-measurement.

Δ= difference between pre- and post-measurements.

*P-value could not be determined due to limited number of participants.



CHAPTER 6

Participatory Action Research:
method to improve, implement, and evaluate a real-life
digital care platform

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Abstract

Background: It is unclear how to evaluate a continuously changing eHealth tool on its improvement and implementation in daily practice. A digital care platform, CMyLife, provides patient-centred care by empowering patients with chronic myeloid leukemia, focussing on making medication compliance insightful, discussable, and optimal, and achieving optimal control of the biomarker BCR-ABL1. The aim of this study was to investigate to what extent a participatory action research approach was suited for improvement and scientific evaluation of eHealth innovations in daily clinical practice (measured by user experiences) combined with promoting patient empowerment.

Methods: The study used iterative cycles of planning, action, and reflection, whereby participants' experiences (of patients, health care providers, the CMyLife-team, and app suppliers) with the platform determined next actions. Codesign workshops were the foundation of this cyclic process. Also, patients filled in two sets of questionnaires for assessing experiences with, the actual use of, and influence of CMyLife after three and at least six months. Data collected during the workshops were analysed using content analysis, often used for making a practical guide to action. Descriptive statistics were used to characterize the study population in terms of CML related information and socio-demographics, and to describe experiences with, and the actual use of the digital care platform CMyLife.

Results: Codesign workshops provided insights that contributed to the improvement, implementation, and evaluation of CMyLife and empowered patients with chronic myeloid leukemia. For example, simplification of language, and improvement of user-friendliness of functionalities. Results of the questionnaires indicated that a. the platform improved information provision, b. use of the medication app improved patients' medication compliance, c. use of the guideline app improved patients' guideline adherence, and d. patients felt more empowered when using the platform.

Conclusions: Participatory action research approach is suited to scientifically evaluate digital care platforms in daily clinical practice on its improvement, implementation, and patient empowerment. We advise to systemic iteratively evaluate users' needs and wishes to keep care patient-centred and keep the innovation up-to-date and valuable to its users.

Background

The World Health Organisation recognizes the challenges facing the growing burden of chronic diseases and cancer care [1]. Prevalence of patients with chronic diseases is increasing, a large shortage in healthcare professionals (HCPs) is predicted, and healthcare costs are rising [2-4]. Innovative approaches, like eHealth, could enable the delivery of sustainable, affordable, patient-centred oncological care [1]. Therefore, a transition to patient-centred models of care in which cancer patients or survivors play an active role in their care process is needed to be future proof.

As part of this patient-centred approach, improvement of patient empowerment is paramount [5, 6]. The World Health Organisation defines patient empowerment as “a process through which people gain greater control over decisions and actions affecting their health” [7]. Research has shown that innovations aimed at improving patient empowerment have a positive effect on care experiences and health outcomes [6]. For example, more empowered patients have better treatment compliance, perform regular self-monitoring at home, and obtain more efficient care. Besides patient empowerment, eHealth could also improve tailored information provision, enable management of medication intake and adverse events more readily, and eventually decrease healthcare utilization by substituting regular care [8-12]. This shows that the benefits of eHealth are considerable and multidimensional [13].

Implementation of eHealth is deemed tough since the progress in the field of eHealth is accelerating [13, 14]. Studies agree that systematic iterative evaluation of such innovations is important to be continued after development [13-15]. Information presented by eHealth innovations needs to be up-to-date or the innovation loses value and credibility among HCPs and patients [14]. It is crucial to show evidence based added value of the innovation in order to keep HCPs and patients interested in sustained use [12, 16, 17]. The question is, which scientific method could best serve this purpose of evaluating effectiveness, feasibility, and usefulness of such a changing tool in daily clinical practice. Participatory action research (PAR) seems to suit this purpose since improvement and evaluation go hand in hand. PAR is defined by Baum et al. (2006) as research that seeks to understand and improve the world by changing it. It includes iterative cycles of planning, action, and reflection, whereby participants collect and analyse data, and determine what actions should follow. The process of PAR should empower participants and lead to increased self-control. [18]. PAR helps to gather feedback relatively quickly about what works and what does not work. However, the PAR approach for eHealth in the field of oncology is rarely described in the literature.

Our study is the first to evaluate and improve a patient-centred digital care platform, using a PAR approach.

The digital care platform CMyLife provides patient-centred care by empowering patients with chronic myeloid leukemia (CML) [12, 19, 20]. CML is a haematological malignancy caused by a chromosomal translocation that gives rise to constitutively active tyrosine kinase protein (BCR-ABL1) [21]. Since the advent of oral administered tyrosine kinase inhibitors (TKIs), survival in CML patients approximates that of the general population, permitted that patients have optimal responses to the treatment [22]. In order to achieve optimal responses to treatment, medication compliance and guideline adherence are two determining factors. CMyLife aims to provide CML patients with tools and knowledge to take a more active role in their care process and improve their medication compliance and molecular monitoring, which could ultimately lead to an increased quality of life and the opportunity of more remote care. Main features of CMyLife are: a website, apps to monitor medication compliance and control of biomarker levels, and a personal health environment. The first version of CMyLife, developed in close cooperation with patients using a design thinking approach, was launched in 2016 and has been freely accessible ever since [19]. However, as mentioned above, evaluation of such a continuous evolving tool in daily clinical practice is deemed challenging but important.

This PAR involved patients in the effort to improve their own health, focussing on making medication compliance insightful and discussable for shared decision making and improve it, and achieve optimal control of the biomarker levels (guideline adherence). We studied to what extent a PAR approach was suited for improvement and scientific evaluation of eHealth innovations in daily clinical practice (measured by user experiences) combined with promoting patient empowerment.

Methods

Design

A participatory action research design was used to improve, implement, and evaluate the digital care platform CMyLife and promote patient empowerment. The study lasted from May 2018 to October 2020 and used iterative cycles of planning, action, and reflection, whereby participants' experiences with the platform determined actions. Depending on the input of users and interim results, aims, research methods, and actions were adjusted. Given the nature of this study and the low impact on study participants, the Medical Research Involving Human Subjects Act (Dutch: WMO) does not apply, as confirmed by the institutional

Medical Ethical Committee 'CMO Regio Arnhem-Nijmegen' [dossier no. 2016-2291].

Setting

In the Netherlands CML treatment is organised in eight academic hospitals and in 68 smaller non-academic hospitals. Patients' biomarker levels are monitored during their entire life. The latest evidence based CML guidelines recommend that molecular treatment response should be measured at least every three months in the first year after diagnosis, and every four to six months from that time forward [27]. Only medical specialists (e.g. haematologists) can prescribe CML medication since it pertains the Dutch expensive medicine regulation. Health care insurance which covers all CML care, is mandatory in the Dutch health care system, hence treatment is accessible to all patients. Treatment results differ between hospitals with high and low CML patient numbers receiving treatment because CML is a rare disease [23]. The CMylife digital care platform (DCP), developed using a design thinking methodology, aims to provide CML patients with tools and knowledge to self-monitor their disease process, interpret, and act on it [19]. The DCP CMylife is described in Box 1.

Box 1. Description of digital care platform CMylife.

Intervention

CMylife consists of multiple features comprising a website [24], a personal health environment (PHE), and two apps to monitor medication compliance and guideline adherence, called the medication app, and the guideline app. All data were secured conform the General Data Protection Regulation and in accordance with the Dutch security guideline (NEN7510). Features containing data from the hospital's electronic medical record (EMR) (i.e. biomarker levels) were secured with a double authentication procedure. The platform stimulates patients to get their medication delivered at home and do local blood tests. The **website** provides accurate and easy to understand information about living with CML (medication, guidelines, side effects, and the effect on daily life). The website enables patients to communicate with specialists and other patients through a forum. Patients' **personal health environment** consists of a Patient Knows Best portal [25]. Patients can save their medical records, for example side effects, from their EMR in their PHE and share this with their HCP. The **medication app** [26] is used to improve medication compliance. The app aims to make patients medication compliance insightful and easy to share and discuss with their HCPs. It is also possible to set medication reminders, request for repeat medication prescriptions, read the information leaflet of the medication, and log their side effects (which they can share with their HCPs through their PHE). To reach optimal monitoring of the biomarker BCR-ABL1 (guideline adherence) the **guideline app** [27] was developed with patients. This app sends reminders when it is time for patients to get their biomarker levels checked in accordance with to the Dutch CML guideline. It also shows a visual and understandable explanation of the patients' BCR-ABL1 values in relation to the Dutch guideline. Therefore, this app gives patients control over their own guideline adherence and enables them to contact their HCP if treatment goals are not reached.

Study population

During this PAR patients, HCPs, the CMyLife-team (responsible for supporting users of the digital care platform), and app suppliers were involved during the entire process. Included patients were in chronic phase CML and treated with first or second-line TKIs. Patients who were treated with second-line TKIs were only allowed to participate if they had shifted from first line to second-line TKIs as a result of intolerance (not because of treatment failure). Patients in treatment-free remission, acceleration phase, blast crisis, or if pregnancy was planned during the study period were excluded from this study because this could influence study results. Patients were obtained from 20 different hospitals spread over the Netherlands (five academic hospitals and fifteen non-academic hospitals) via their HCPs, the CMyLife website, or the patient advocacy group Hematon. HCPs were obtained from 12 different hospitals spread over the Netherlands (five academic hospitals and seven non-academic hospitals). The number of patients and HCPs per cycle is shown in figure 1. The CMyLife-team comprised 4 project staff members (who were in continuous contact with patients, HCPs, and app suppliers), the CMyLife program manager, a physician with eHealth expertise, a patient, a specialized nurse, a researcher, and a research assistant. Patients were supported in using CMyLife by an instruction package and a kick-off workshop. Patients and HCPs were provided with adequate support by the CMyLife-team in using CMyLife and they were informed about when to use the platform and the benefits of using it. The CMyLife-team was reachable for questions during the day and offered all users to help them install the platform. Also, the CMyLife-team gathered feedback from users during workshops. App suppliers had to meet the General Data Protection Regulations, Medical Devices Regulations, and had to work in accordance with the Dutch security guideline (NEN7510). They were in continuous contact with the CMyLife-team for improving the apps. All participants signed informed consent before participation.

Data collection

Further development of the CMyLife platform was established using an iterative cyclic process including codesign workshops and questionnaires (described in figure 1). The codesign workshops were the foundation of the iterative process. Additionally, patients using the CMyLife platform filled in two sets of questionnaires. The medication app was an already existing app; therefore, the aim was to further develop and adjust it to the wishes and needs of CML patients. The guideline app was developed entirely for CML patients during this PAR.

Codesign workshops

A total of three types of workshops were planned based on codesign activity methods, comprising of feedback workshops, kick-off workshops, and end-workshops. Experiences of patients were collected during the codesign workshops, including testing of the apps, oral discussions, short questionnaires, and (focus group) interviews. The process of walking through the experiences of participants with the apps helped to guide and focus improvements and adjustments of the platform [28]. Results of the workshops gave input for the actions that should be undertaken. When determining new actions, patients, HCPs, and the CMyLife-team were involved and eventually app suppliers were consulted. Workshops were facilitated by members of the CMyLife-team. All discussions were audio-recorded, and notes were collected with the consent of all workshop participants. Facilitators of the workshops used semi-structured guides for each workshop to guide the discussion. The guides were used to ensure the overall sense of direction throughout the activities but had sufficient freedom to expand and ask for additional clarification on specific topics and thereby gaining in-depth understanding. Participants were divided into smaller groups during the workshops. The use of smaller groups ensured that all participants were able to contribute [29, 30]. All workshops included a short questionnaire about the use and quality of the apps, which gave participants, who were uncomfortable discussing topics in a group setting, the possibility to give feedback. Also, participants were asked about the quality of the workshops on a scale from 1 to 5 (the higher the score the better).

Questionnaires

After three and six months of using CMyLife participants filled in the first and second questionnaire. The first questionnaire contained questions about patient characteristics, users' perceptions on the instruction package, contact with the CMyLife-team, the kick-off workshop, the website, and the medication app. The second questionnaire contained questions about participants' use of delivering medication, use of local blood tests, use of CMyLife, users' perceptions on the influence of CMyLife (on several aspects: patient empowerment, medication compliance, guideline adherence, information provision), the usability of CMyLife, experiences with CMyLife, and with the guideline app. The second questionnaire was more extensive compared to the first one because patients then had more experience with the different components of CMyLife. Also, the first questionnaire zoomed in on the medication app since this was an already existing app and the second questionnaire zoomed in on the guideline app since patients needed time to use the newest version of the app.

Analysis

Data collected during the workshops were analysed using content analysis, which is often used for making a practical guide to action [31]. During the workshops content of the apps was discussed orally and questionnaires were filled in. Results were analysed by researchers and discussed with the CMyLife-team and app suppliers to improve the apps. All measurements of the questionnaires were processed anonymously, and analyses were performed using SPSS version 25 (IBM Corp). Descriptive statistics were used to characterize the study population in terms of CML related information and socio-demographics, and to describe experiences with, and the use of the digital care platform CMyLife. The features of CMyLife were graded on a scale from one to ten. The influence of different features of CMyLife was scored with a grade from one to three, these numbers were converted to sum scores. A higher sum score indicates more influence on the mentioned aspect.

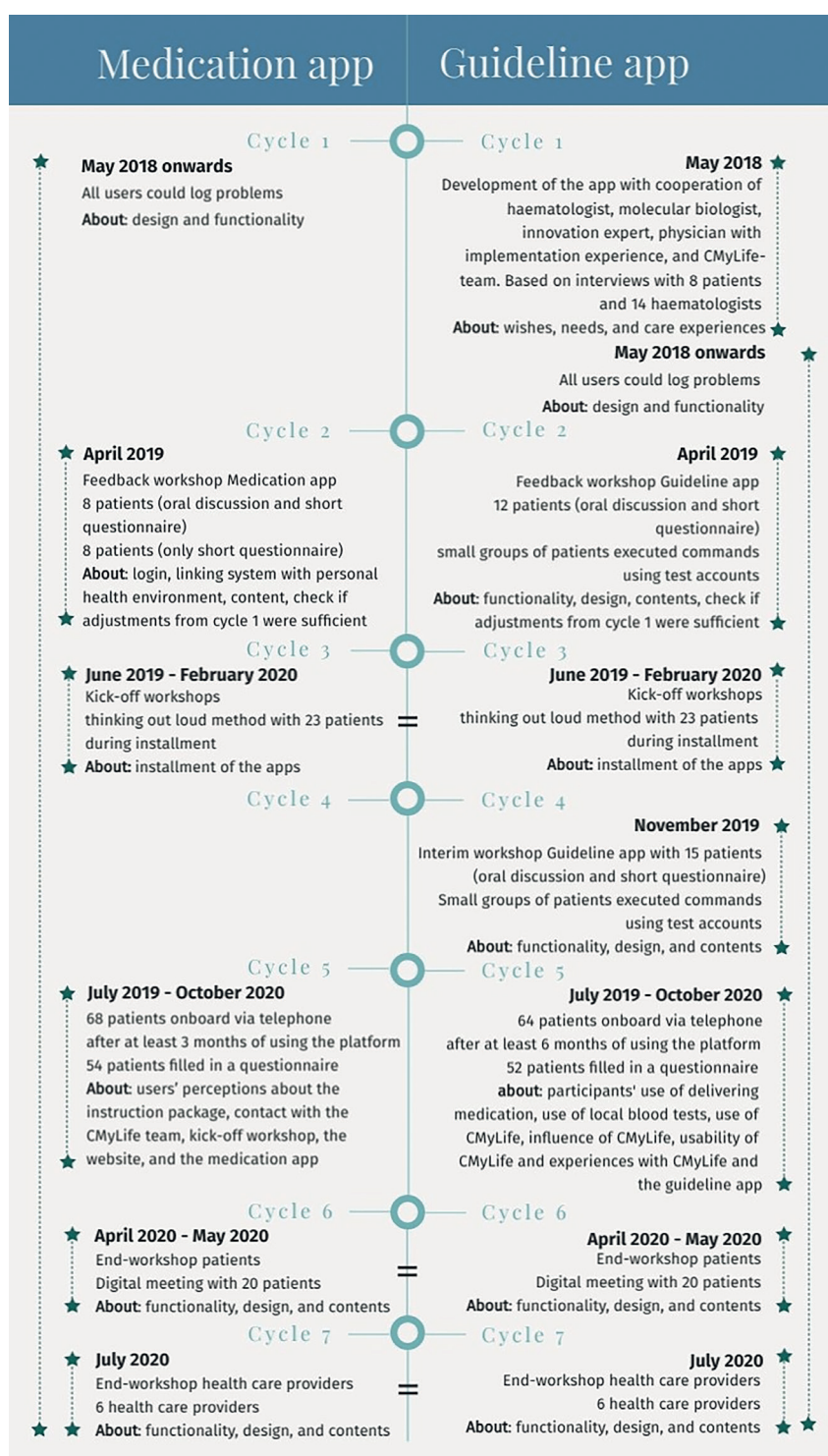


Figure 1. Description of iterative cyclic process of the participatory action research.

Results

Participant characteristics - iterative cycles

Patients, HCPs, the CMyLife-team, and app suppliers were involved during this PAR. Included patients were diverse; gender, age, first- or second-line TKIs, years since diagnosis, digital skills, and education varied (characteristics are mentioned below). Numbers of participants for each cycle are depicted in figure 1. Below, results of the PAR are described for the different components of the CMyLife platform. These results show that the iterative cycles of planning, action, and reflection, led to evaluation of participants' experiences with the digital care platform CMyLife, which eventually determined actions that improved the platform, in particular regarding content and functionality of features.

Patient characteristics – questionnaires

After three months of using CMyLife, 67 questionnaires were sent of which 54 were completed (80.6% response). After six months of using the platform, 64 questionnaires were sent of which 52 were completed (one patient deceased) (81.3% response), three questionnaires were partially completed. Figure 2 shows the flow chart of the questionnaires during the PAR. Table 1 summarises patient characteristics with majority of users being male, aged below 65, and did use CMyLife before the study period.

Table 1. Baseline characteristics for CML patients who filled in the questionnaires after 3 (n=54) and 6 (n=52) months of using CMyLife.

Baseline characteristics	After 3 months CMyLife (n=54)	After 6 months CMyLife (n=52)
Gender, n (%)		
Male	35 (66.0)	33 (63.5)
Female	18 (34.0)	19 (36.5)
Age (years), n (%)		
18-64	34 (65.4)	35 (68.6)
65 and older	18 (34.6)	16 (31.4)
Education level, n (%)		
High ^a	25 (47.2)	28 (53.8)
Middle ^b	23 (43.4)	18 (34.6)
Low ^c	5 (9.4)	6 (11.5)
Years since diagnosis, (mean ± SD)	5.5 (5.7)	5.9 (6.4)
Currently used TKI, n (%)		
Yes, imatinib	30 (57.7)	31 (60.8)
Yes, Otherwise ^d	22 (42.3)	20 (39.2)
Previously treated with TKI, n (%)		
Yes	19 (40.4)	16 (34.8)
No	28 (59.6)	29 (63.0)

^aHigh education level: higher vocational education, academic education. ^bMiddle education level: secondary vocational education, higher general secondary education, pre-university education. ^cLow education level: primary education, lower general secondary education, preparatory secondary vocational education. ^dMostly dasatinib and nilotinib.

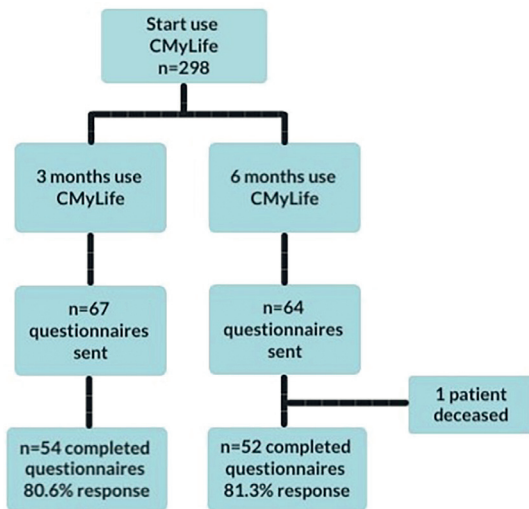


Figure 2. Flow chart questionnaires.

Instruction package

All results from the first questionnaires are shown in appendix 1. Most prominent and relevant results are described in text below. Results show that 79.6% of patients found the instruction package (very) usable and 81.5% of them found it (very) understandable. Installing the apps was successfully done by 81.5% of the patients with the help of the instruction package or the CMylife-team. Patients graded the instruction package with a 7.1 out of ten. The instruction package was clear and complete, and the explanation and support was good. In addition to the positive points of the components evaluated, tips were gathered too. Language of the instruction package was still too difficult for some patients; they would have liked it to be more simple. Also, they indicated that a version for android and apple, and an English version would be an improvement since the first version was only in Dutch.

Contact with the CMylife-team

In addition, 92.6% of the patients thought contact with the CMylife-team for installing the apps was (very) pleasant. Patients mentioned that the contact with the CMylife-team was result-oriented, and time was not an issue. Members of the CMylife-team were reported to be very helpful, friendly, patient, and knowledgeable. Tips for contact with the CMylife-team were contact at night and more frequent initiative to check the situation. Patients mentioned they would have liked it if there was more room for personal attention during the workshops and they want to know more clearly what the CMylife-team wants to know from the users.

Kick-off workshop

Positive points mentioned by participants about the kick-off workshop were: presence of a haematologist, contact with fellow patients, informativeness, usefulness, and the small setup. Moreover, 92.9% of the patients who attended the kick-off workshop reported that they thought that the workshop was (very) informative. The mean grade of the kick-off workshop was 8.2 out of ten.

Website

Regarding the use of the website, information about the disease was used by 73.7%. All patients would recommend the website to other people with CML. In addition, 97.4% of the patients agreed that language use was (very) understandable. Patients liked to see more information about research, pregnancy, dealing with side effects and stopping treatment on the website. Especially new CML patients liked that there is a website with reliable, clear, comprehensive, information focussed on CML patients, including actual subjects like COVID-19 and summaries of medication and its side effects. They liked the forum to read stories of fellow patients. In contrast, some patients report to become anxious and worried by the forum. In addition, patients who are diagnosed with CML for a longer period and are stable are less interested in using CMylife compared to newly diagnosed patients.

Medication app

The medication app was used by 72.2% of the patients who filled in the first questionnaire, of which 64.1% used the app daily. With 84.6% of the patients logging medication intake moments, this was the most used component of the medication app. Last, 76.9% of the patients reported they would recommend using the medication app to other people with CML. The reminder function, simplicity and clarity of the app, and inventory management were mentioned as positive points of the medication app. Some patients did not see the added value of the medication app and reported that the menu structure was not clear. Patients would have liked to see their medication compliance over a longer period in the app. Also, some side effects were missing (mental complaints, dizziness and neuropathies in feet and hands) and some functionalities did not work optimally.

Medication delivery and local blood tests

All results from the second questionnaires are shown in appendix 2. Most prominent and relevant results are described below. Half of the patients had their medication delivered at home, of which 11.5% via the medication app. Blood was still drawn at the treating hospital in 82.7% of the patients.

CMyLife

Only 5.8% of the patients did not use the CMyLife platform in the past 6 months. Patients indicated that information on the CMyLife website had the most positive influence on their knowledge about CML, degree of control over their disease, and insight in side effects/complaints. The System Usability Scale shows mean scores of 65.3 and 60.0 for the medication app and the guideline app, respectively.

Results showed that 47.9% of the patients learned something new about the disease because of using CMyLife. For example, about the heredity, course of the disease, origin of the disease, experiences with diverse medication, and effects of COVID-19. In addition, 45.8% of the patients learned something new about treatment of the disease because of using CMyLife. For example, medications' mechanism of action, research and new medication, treatment-free remission, and switch in TKIs. Also, 35.4% of the patients learned something new about side effects and complaints because of using CMyLife. Examples of new information were; not being the only one experiencing certain side effects, how others deal with side effects, and experiences of other patients.

Figure 3 shows percentages of patients who (completely) agreed, (completely) disagreed or were neutral towards statements about the influence, use, and functionality of features of CMyLife. Knowledge about the disease and treatment increased in 67.3% and 75.5% of the patients, respectively. CMyLife made 45.9% of the patients more confident because they gained insights in their side effects and the use of the medication app made 52.7% of the patients feel less insecure about their medication compliance. The PHE felt like a reliable and central place to store their personal health data for 59.4% and 54.8% of the patients, respectively. Furthermore, 44.0% of the patients reported that they knew better when to get BCR-ABL1 values checked, and that the guideline app is a handy tool for this purpose. Logging side effects and entering medication in the PHE was (very) easy for 42.4% of the patients and entering BCR-ABL1 values in the PHE was (very) easy for 30.3% of them. Linking the guideline app and the medication app to patients' PHE was experiences to be (very) easy for 39.4% and 24.3% of the patients, respectively.

Guideline app

Of all patients who filled in the second questionnaire after at least six months of using CMyLife 48.1% used the guideline app. In addition, 36.0% of these patients used the app monthly and 84.0% of them would recommend using the app to other people with CML. Positive points of the guideline app were simplicity and clarity of the app, clear messages, confidence boost, insights in BCR-ABL1 values and overview of disease course, and information about the next moment of a blood check. Linking the guideline app with other apps is a tip from several patients.

Some patients also mentioned that the guideline app should be more user-friendly and sometimes the app is not up-to-date.

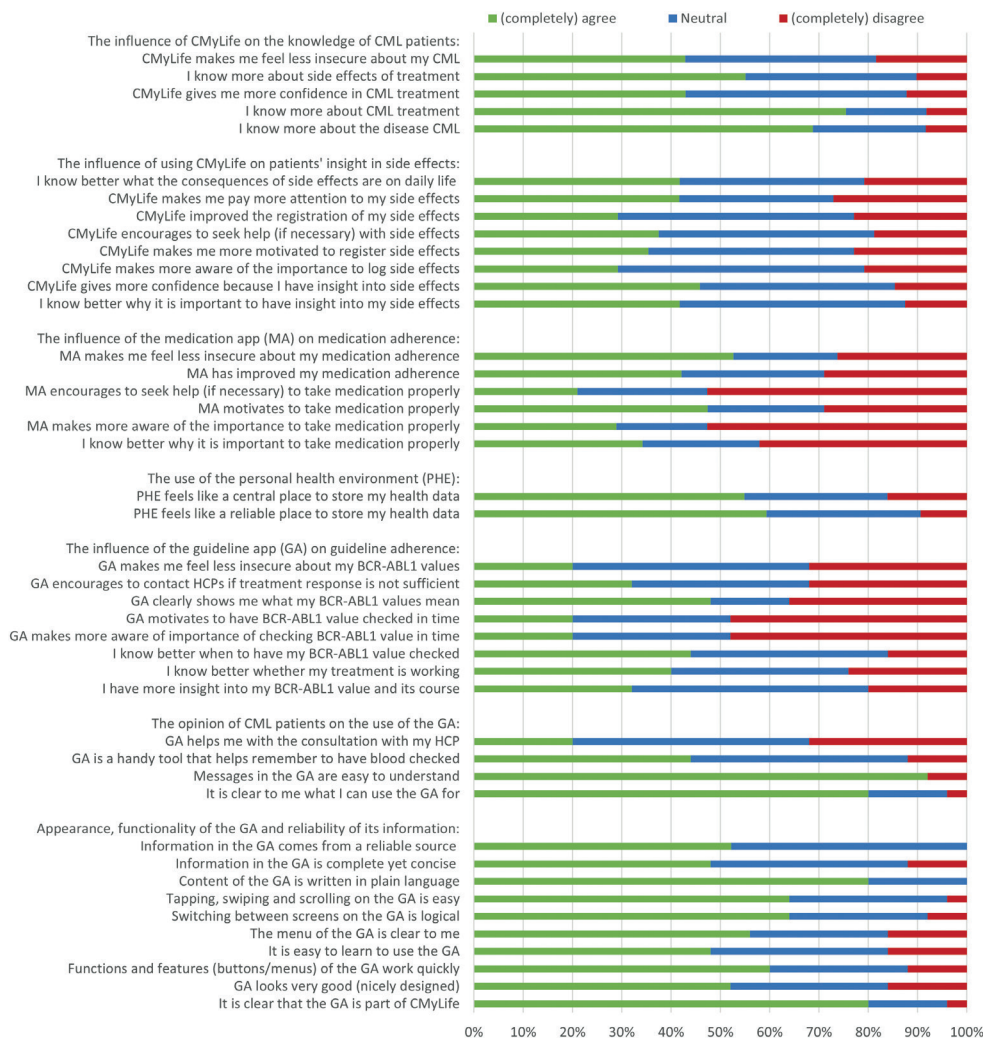


Figure 3. Percentages of patients who (completely) agreed, (completely) disagreed or were neutral towards statements about the influence, use, and functionality of features of CMylife. Abbreviations: medication app (MA), personal health environment (PHE), guideline app (GA).

Discussion

General findings

Results showed that the iterative cycles of planning, action, and reflection, whereby participants' experiences with the real-life digital care platform CMylife determined actions, helped to evaluate, improve, and implement the platform. Also, results showed that the platform improves patients' knowledge about their disease and its treatment, use of the medication app improved patients' medication compliance, patients know better when to have their BCR-ABL1 values checked, and patients felt more empowered when using the platform. Therefore, participatory action research is suited for improvement and evaluation of eHealth innovations in daily clinical practice, which goes hand in hand with promoting patient empowerment since patients felt more empowered.

Comparison with previous research

EHealth innovations play a substantial role in shaping health care systems, but until innovations are "fit for purpose", the risk of failing implementation is high and challenges of evaluating these complex interventions are recognised [13, 32]. Several studies suggested that to gain most from eHealth innovations it is important to match the innovation with what is needed in practice, to work together with relevant stakeholders in all stages of the project, and to do continuous systematic evaluations of the changing tools [13-15, 33]. However, it is hard to choose a proper methodology that serves these purposes. Randomized controlled trials, the golden standard of testing a hypothesis, are not a possible method to evaluate eHealth since it is simply not possible to blind patients whether they participate in the intervention group (using eHealth) or in the control group (not using eHealth). Also, it would not be ethical to withhold patients from using something that benefits their health.

Participatory action research seemed to suit the purpose of bridging the gap between basic scientific methods and clinical practice [34]. Action research produces knowledge, like conventional quantitative and qualitative research methodologies, but also combines it with action and reflection cycles [35]. PAR focusses on involving users during the action research [36]. A review by Oberschmidt et al. (2022) aimed to provide more knowledge on best practices and lessons learned from action research studies in eHealth [37]. The review focussed on a variety of eHealth innovations, ranging from electronic medical records, health information systems, and mental health services to telemonitoring and health promotion and education, which differs a lot from our multi-component, digital care platform [37]. Also, target groups of the included studies are various. Only three studies focussed on patients with cancer. Despite their variation in target groups and

included eHealth innovations they state that their recommendations are not exclusively related to eHealth and maybe relevant for other fields. Their most important recommendations include paying attention to training of stakeholders' skills and confidence, and the different roles and tasks of researchers. They also highlight the need for frequent reflection and understandable dissemination suiting the target group. Therefore, the target group should be involved and informed properly about the innovation and the research.

In our study, participants were provided with an instruction package, which helped them to use the platform. Also, during the workshops patients were guided and trained by the CMyLife-team in using the platform and evaluating it. Attention was not necessarily paid to the different roles of researchers as described by Oberschmidt et al. (2022) [37]. For example, fostering a welcoming environment for all stakeholders was paid attention to by the CMyLife-team. Therefore, this did not limit our study. Also, frequent reflection of the changes of previous cycles, the process, and the current status of the platform were accurately performed as depicted in figure 1. At last, Oberschmidt et al. reported that researchers of action research need to communicate findings to the academic world and inform the target group about the project in ways that suit users' needs [37]. In our study, researchers communicate findings to the academic world, however, informing the target group is done by the CMyLife-team.

Strengths and limitations

A PAR approach has several strengths for the evaluation, improvement, and implementation of a real-life digital care platform called CMyLife and empowering CML patients. It is a unique approach to a particular context as it revolves around wishes and needs within a particular group of people in daily clinical practice. Our PAR aimed to improve empowerment as well as evaluate it [38]. End users of the CMyLife platform have not only been involved in the development and implementation of CMyLife, but they are also involved in each step of the improvement process to establish true patient-centred care. End users provided unique and completing perspectives based on their own experiences [39]. PAR enables to evaluate constantly evolving innovations. This PAR involved both qualitative (e.g. interviews) and quantitative (e.g. questionnaires) research methods to evaluate the DCP, which is another strength of this study.

Regarding limitations of our PAR approach, participants commitment constitutes the foundation on which PAR can emerge. It requires participants to dedicate time, to be open-minded, to accept a degree of uncertainty and to be interested in the process. All our study participants were willing to use CMyLife and patients with low literacy were absent. This may overestimate the results

of the questionnaires, limiting generalizability to the larger population of CML patients.

Future perspectives and research directions

It is important that systematic iterative evaluation of eHealth innovation, like CMyLife, is continued after development and implementation [13-15]. Also, such innovations should be continuously adapted to keep information up-to-date. Without these continuous evaluation of the innovation it loses value and credibility among clinicians and patients [14]. CMyLife included users from the beginning of the project and will never stop involving them in the improvement and the platform will continue to be evaluated, adapted, and improved. This study describes the first period of the platform from May 2018 to October 2020, the platform has been improved a lot at the end of this study period compared to the beginning. Eventually, information gathered through the DCP, maybe used for guideline development. Involving data derived from patient reported outcome measures in the guideline development process could help to create personalised guideline development [40-42]. This should first be investigated in future studies before it can be implemented.

Conclusion

We showed that a participatory action research approach is ideally suited for improvement and scientific evaluation of eHealth innovations in daily clinical practice combined with promoting patient empowerment. Results support that intensive involvement of patients in a PAR approach enables continuous improvement and evaluation of DCPs in daily clinical practice combined with promoting patient empowerment. Systemic iterative evaluation of users' needs and wishes, is required to keep care patient-centred and keep the innovation up-to-date and valuable for its users. Since it is not possible to blind patients or withhold patients from using such an effective digital tool, PAR is ideally suited to still evaluate and improve quality of their care.

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Supplementary material

Appendix 1

Results from the first questionnaire after CML patients used the CMylife platform for three months (n=54)

Instruction package	
Usability (very) usable % (n)	79.6% (43)
Language use (very) understandable % (n)	81.5% (44)
Layout/design (very) appealing % (n)	40.7% (22)
Grade instruction package mean (SD)	7.1 (1.0)
Successfully installed the apps	
Using instruction package % (n)	29.6% (16)
Without instruction package % (n)	14.8 % (8)
With the help of the CMylife-team % (n)	51.9% (28)
With the help of family/acquaintances % (n)	3.7% (2)
Contact CMylife-team for instalment (very) pleasant % (n)	92.6% (50)
Grade contact CMylife-team mean (SD)	8.4 (0.9)
Kick-off workshop	
Attended, yes % (n)	51.9% (28)
What did you think of the workshop (very) informative % (n)	92.9% (26)
Grade starters workshop mean (SD)	8.2 (0.9)
Website	
Use website % (n)	70.4 (38)
Mainly uses question & answer % (n)	34.2 (13)
Mainly uses the forum % (n)	44.7 (17)
Mainly uses information % (n)	73.7 (28)
Mainly uses the news blog % (n)	23.7 (9)
Mainly uses video consultations % (n)	2.6 (1)
Findability information (very) good % (n)	89.5 (34)
Content (very) good % (n)	100.0 (38)
Usability (very) useful % (n)	89.5 (34)
Language use (very) understandable % (n)	97.4 (37)
layout/design (very) appealing % (n)	71.1 (27)
Recommend to other people with CML % (n)	100.0 (38)
Grade website mean (SD)	7.7 (0.9)
Medication app	
Use Medication app % (n)	72.2 (39)
Last used	
Today % (n)	66.7 (26)
Last week % (n)	10.3 (4)
> a week , < month ago % (n)	10.3 (4)
> a month ago % (n)	10.3 (4)
How long have you been using the Medication app	
Less than 1 month % (n)	2.6 (1)
Between 1-3 months % (n)	46.2 (18)
Between 3-6 months % (n)	15.4 (6)
At least 6 months % (n)	30.8 (12)
How often did you use the Medication app	
Daily % (n)	64.1 (25)
Few times a week % (n)	7.7 (3)
Few times a month % (n)	7.7 (3)
Monthly % (n)	7.7 (3)

Top 5 most used components of the Medication app	
1. Enter medication intake moments	84.6 (33)
2. Enter personal medication	61.5 (24)
3. CMyLife module on	41.0 (16)
4. Set medication reminders	41.0 (16)
5. Inventory management	35.9 (14)
Ease of use (very) good % (n)	
71.8 (28)	
Layout/design (very) appealing % (n)	
48.7 (19)	
Comprehensibility information (very) understandable % (n)	
74.4 (29)	
Misses side effects % (n)	
12.8 (5)	
Recommend to other people with CML % (n)	
76.9 (30)	
Use in preparation of consult with health care provider % (n)	
23.1 (9)	
Grade Medication app <i>mean (SD)</i>	7.6 (1.3)

Appendix 2

Results from the second questionnaire after CML patients used the CMyLife platform for six months (n=52)

Delivered CML medication at home	
No %(n)	53.8 (28)
Yes, via the Medication app %(n)	11.5 (6)
Yes, directly via the pharmacy %(n)	23.1 (12)
Yes, other %(n)	15.4 (8)
Where was your blood drawn in the past 6 months?	
In hospital of treatment %(n)	82.7 (43)
At my own GP practice %(n)	3.8 (2)
At a consultation hours supporting GP diagnostic centre %(n)	1.9 (1)
At the thrombosis service %(n)	3.8 (2)
At home %(n)	0.0 (0)
No blood was drawn in the past 6 months %(n)	0.0 (0)
Other %(n)	11.5 (6)
Did you use CMyLife in the past 6 months?	
Yes, the website %(n)	69.2 (36)
Forum %(n)	52.8 (19)
Question & answer %(n)	11.1 (4)
News blog %(n)	58.3 (21)
Information about CML %(n)	86.1 (31)
other %(n)	2.8 (1)
Yes, the Medication app %(n)	69.2 (36)
Yes, the Guideline app %(n)	46.2 (24)
Yes, the personal health environment %(n)	63.5 (33)
Yes, other %(n)	1.9 (1)
No, not yet %(n)	5.8 (3)
Features of CMyLife that influence my knowledge about CML and its treatment	
Information on the website %(n)	76.9 (40)
Forum %(n)	32.5 (13)
Question & answer %(n)	7.5 (3)
News blog %(n)	50.0 (20)
Information about CML %(n)	85.0 (34)
Other %(n)	5.0 (2)
The Medication app %(n)	25.0 (13)
The Guideline app %(n)	17.3 (9)
The personal health environment %(n)	25.0 (13)
None of the above %(n)	13.5 (7)
Other %(n)	1.9 (1)
Features of CMyLife with the most influence on knowledge	
Information on the website (sum score)	102
The Medication app (sum score)	61
The personal health environment (sum score)	60
The guideline app (sum score)	44
Using CMyLife gave me	
More control over my CML %(n)	26.9 (14)
Less control over my CML %(n)	1.9 (1)
No difference %(n)	61.5 (32)

Features of CMylife that influence the degree of control over CML	
Information on the website %(n)	23.1 (12)
Forum %(n)	41.7 (5)
Question & answer %(n)	8.3 (1)
News blog %(n)	75.0 (9)
Information about CML %(n)	91.7 (11)
Other %(n)	0.0 (0)
The Medication app %(n)	13.5 (7)
The Guideline app %(n)	11.5 (6)
The personal health environment %(n)	15.4 (8)
None of the above %(n)	0.0 (0)
Other %(n)	0.0 (0)
Features of CMylife with the most influence on degree of control over CML	
Information on the website (sum score)	24
The Medication app (sum score)	20
Het PGO (Persoonlijke Gezondheidsomgeving) (sum score)	18
The guideline app (sum score)	11
Features of CMylife that influence insight in side effects/complaints	
Information on the website %(n)	51.9 (27)
Forum %(n)	44.4 (12)
Question & answer %(n)	11.1 (3)
News blog %(n)	40.7 (11)
Information about CML %(n)	74.1 (20)
Other %(n)	7.4 (2)
The Medication app %(n)	23.1 (12)
The Guideline app %(n)	15.4 (8)
The personal health environment %(n)	21.2 (11)
None of the above %(n)	21.2 (11)
Other %(n)	11.5 (6)
Features of CMylife with the most influence on insight in side effects/complaints	
Information on the website (sum score)	79
The personal health environment (sum score)	55
The Medication app (sum score)	48
The guideline app (sum score)	43
System Usability Scale Medication app mean (min-max)	
	65.3 (30.0-100.0)
Personal health environment	
Use Personal health environment %(n)	65.4 (34)
To enter BCR-ABL1 value %(n)	82.4 (28)
To enter medication %(n)	44.1 (15)
To Log side effects/symptoms %(n)	41.2 (14)
To keep a log %(n)	8.8 (3)
To enter measurements %(n)	17.6 (6)
Link with other apps, medication app and the guideline app %(n)	11.8 (4)
Did you use the personal health environment to give others insight in your health data?	
No %(n)	57.7 (30)
Yes %(n)	5.8 (3)
Guideline app	
Use Guideline app %(n)	48.1 (25)
How long have you been using the Guideline app	
Less than 1 month %(n)	4.0 (1)
Between 1-3 months %(n)	12.0 (3)
Between 3-6 months %(n)	56.0 (14)
At least 6 months %(n)	16.0 (4)
How often did you use the Guideline app?	
Daily %(n)	0.0 (0)
Few times a week %(n)	8.0 (2)
Weekly %(n)	8.0 (2)
Few times a month %(n)	28.0 (7)
Monthly %(n)	36.0 (9)
Other %(n)	20.0 (5)
Recommend to other people with CML %(n)	84.0 (21)
Use in preparation of consult with health care provider %(n)	32.0 (8)
Grade Guideline app mean (SD)	7.0 (1.2)
System Usability Scale Guideline app mean (min-max)	
	60.0 (37.5-97.5)



CHAPTER 7

General discussion

This thesis focused on research on digital care platforms (DCPs), in particular the CMyLife platform. We aimed to implement CMyLife in daily clinical practice, explored its effectiveness, and investigated the best method to study and continuously improve such a changing DCP while enhancing patient empowerment. In this final chapter we first summarize results, then reflect on main findings of the conducted studies in light of recent literature, and finally we discuss implications for daily clinical practice and future research directions.

Main findings

What is known about implementation and effect of DCPs (chapter 2)

- Usage of a DCP appeared to enhance the availability of information and self-efficacy of cancer patients.
- Most barriers for implementation were reported on professional level and most facilitators on patient level. Little is known about barriers and facilitators for implementation of DCPs on economic and political levels.
- Robust evidence concerning the effect of DCPs on quality of care is still lacking.

Influencing factors of implementation (chapter 3)

- 45 barriers and 41 facilitators for implementation of CMyLife were identified. Main identified barriers were lack of connectivity between information technology systems, changing role for both health care providers and patients, insufficient time and resources, doubts about privacy and security of data, and insufficient digital skills of users. Main identified facilitators were motivating patients and health care providers by clarifying the added value of using a digital care platform, clear business case with vision, demonstrating (cost-) effectiveness, using an implementation guide, and educating patients and health care providers about how to use CMyLife.
- Based on these barriers and facilitators we developed a clear and comprehensive implementation guide for launching DCPs in daily clinical practice.

The effectiveness of CMyLife (chapter 4 & 5)

- Before implementation and development of CMyLife we found that global perceived information provision was scored 42.8 (0-100) and 36% of CML patients desired more information. This need was negatively associated with patients above 65 years of age, time since diagnosis and low education. Only one out of three patients knew where to find useful health information online. **(chapter 4)**
- After implementation of CMyLife we found a trend towards better information provision when using CMyLife and knowledge on where to find online health

information was improved significantly. Also, patients felt more empowered. Self-reported effectiveness showed that patients experienced that using CMyLife improved their medication compliance and helped them to oversee their molecular monitoring. Although patients reported more symptoms when using CMyLife, they were better able to manage these. (**chapter 5**)

Improvement and scientific evaluation of eHealth innovations in daily clinical practice (chapter 6)

- Using a Participatory Action Research (PAR) approach we evaluated CMyLife in daily clinical practice on its improvement, implementation, and patient empowerment while involving users.
- During iterative cycles of planning, action, and reflection (codesign workshops were the foundation of this cyclic process) we found several points of improvement which lead to enhancement of the DCP.
- Results from questionnaires showed that the platform improved information provision, medication compliance, guideline adherence, and patients felt more empowered. Therefore, we showed that PAR is suited to scientifically evaluate DCPs in daily clinical practice.

Discussion of the main findings learned

Lessons learned

Below we reflect on main findings of the conducted studies in light of recent literature. We discuss what lessons we learned during the studies, like factors influencing eHealth usage, how generalizable our results are to other forms of eHealth, and what recent literature says about the completeness of our DCP.

Factors influencing eHealth usage

Since there is no one-size-fits-all, we do not aim to suit everyone in the same way but we aim to provide patients with tools to decide when and in what manner they would like to use the platform. Research has shown that patients who had been diagnosed in the past 5 years were much more interested in using an app compared to patients who were diagnosed at least 6 years ago [1]. This emphasized that patients need the greatest support right after diagnosis. Also, younger patients have shown to use health apps more and are more interested in doing so compared to older patients [2, 3]. These factors should be taken into account when developing an innovation like CMyLife [4]. Patients in our studies showed to have concerns about data protection and security regarding sharing their data in the apps. Previous research shares these concerns and data security should therefore be taken into account from the start of development of a DCP

[5]. Also, our research has shown that it would be favourable if all features are incorporated in one app instead of multiple apps like CMyLife. Since the DCP is continuously being improved, the CMyLife team is working on this.

As mentioned in **chapter 1 and 6**, the rising prevalence of chronic disease patients increases not only the pressure on health care costs but also on the care system with a shortage in health care providers (HCPs) [6-9]. The percentage of people working in health care in the Netherlands has increased since the 70s from seven to fifteen percent. In 2020, one in seven working people is working in health care, in 2040 this will be one in four to provide in care demand [8, 9]. We learned that DCPs, like CMyLife, could deliver tools to enable delivery of sustainable, affordable, patient-centred oncological care. Future research should focus on investigating whether quality of care is retained when comparing this eHealth assisted remote care to usual care.

Generalizability

All our results are based on research regarding a DCP, which is a comprehensive form of eHealth. A definition of eHealth: “eHealth is an emerging field in the intersection of medical informatics, public health and business, referring to health services and information delivered or enhanced through the Internet and related technologies. In a broader sense, the term characterizes not only a technical development, but also a state-of-mind, a way of thinking, an attitude, and a commitment for networked, global thinking, to improve health care locally, regionally, and worldwide by using information and communication technology [10].”

As defined in **chapter 2**, a DCP is a form of eHealth that incorporates several components, like disease specific information, patients’ personal health records (appointments, laboratory results), secure messaging, registration of patient-reported outcomes, and a forum. A review by Kruse et al. (2015) concluded that many studies assessed the effect of just one feature of a DCP and that a full platform was not often studied in clinical practice [11]. Whether our research is translatable to other forms of eHealth is debatable. Since a DCP is more complicated compared to other more simple forms of eHealth, like an electronic medical record (EMR), implementation of a DCP may be different too. When implementing a more simple form of eHealth and using an implementation guide some things should be taken care of like with implementing a DCP, for example involving stakeholders from the start of development and exploring (cost-)effectiveness of the innovation. However, some steps could be skipped, for example having a connection between electronic patient files and ensuring the use of patient-reported outcome measurements data during a consultation are not applicable with implementing all sorts of eHealth innovations. Also, effectiveness of a DCP is different compared to other forms of eHealth because it is dependent on the features it incorporates. To assign effect

outcomes to an intervention, it is justifiable to first study an isolated feature of a DCP. However, it is essential to also study the combination of features, because the sum of single features may not be similar to the effect of multiple features combined. For example, literature shows that multi-component forms of eHealth are most effective for improving quality of life in breast cancer patients [12].

Features of a digital care platform for CML patients

Important questions are; did our DCP contain the right features for our patient group and what could we have done differently? We think our DCP contains all components CML patients asked for, since the DCP was co-created with CML patients and we acted on results from the PAR and started with a qualitative study both researching the needs, wishes, and opinions from stakeholders. A recent study aimed to investigate the current and future role of apps as a means of supporting patients with CML [1]. This international, questionnaire-based study shows that CML patients have a relatively low awareness of and use of CML specific eHealth innovations. Also, 94.1 percent of participants showed to be interested in using an app to help them manage their CML. This shows an unmet need of CML patients for appropriate innovation. CML patients in the Netherlands are provided with such a comprehensive DCP and studies in previous chapters show their appreciation. The study by Khadam et al. (2022), emphasizes the importance of spreading CMylife internationally [1]. Currently the CMylife-team is working on expanding certain parts of CMylife with other languages to make spreading possible.

Khadam et al. (2022) also asked participants what potential features they desired in a new CML-specific app. A drug interaction checker appeared to be the feature of greatest interest to the patients. According to their findings our DCP is quite complete except for the drug interaction checker and a generic diary to track lifestyle changes and feelings. Our platform contains all other mentioned features, which were all shown to be desired a lot.

Previous research showed that drug-drug interactions are a real problem with tyrosine kinase inhibitors (TKIs) and it is important to provide CML patients with tools and knowledge to promote self-management [13, 14]. In addition to only drug-drug interaction checker, participants in the study by Khadam et al. (2022) also expressed interest in an interaction checker for substances other than drugs such as foods, vitamins and herbal remedies to further aid self-management [1]. Our platform does not contain such an interaction checker nor a generic diary. Our findings, however, did not show a desire for such features. Maybe Khadam et al. (2022) did find these results since they particularly asked if patients desired these features in an app. However, it would be a good idea to further investigate whether such features would be of added value for the users of CMylife.

Methodological considerations

In this part of the discussion we focus on methodological considerations we encountered during and after the conducted studies in this thesis. Because the use of RCTs for evaluating eHealth is not the best practice, we discuss other methods to evaluate eHealth and iteratively continue this after development. Also, we discuss frameworks used in our study.

RCTs are not the golden standard for evaluating eHealth

There exists a disagreement on how to evaluate eHealth. Randomized controlled trials (RCTs) are seen as the golden standard for assessing evidence-based effectiveness. Most researchers still consider that RCTs are superior to other types of evidence [15]. When using an RCT, blinding of patients is important to avoid confounders and bias but this is not possible when using eHealth [16]. Also, it is questionable whether an RCT is the right fit for exploring the effectiveness of eHealth innovations since participants should be motivated in order to use it. Patients who have a strong preference for one of the arms may refuse randomization at all, or dropout, or not respond when randomized into the other study-arm, or they will just not do what they have to concerning the intervention, which introduces bias. All these factors may influence generalizability of study results [17]. Literature shows high dropout and non-response rates in studies evaluating the effectiveness of eHealth using RCTs.

An example of such a study is performed by Schuit et al. (2022), who did an RCT to investigate the efficacy of their eHealth intervention on patient activation, general self-efficacy, and health related quality of life [18]. In their study 219 patients were found to be eligible, of which eventually 138 completed the baseline questionnaire. This is a response rate of 63% and of the patients in the intervention group, only 74% used the innovation as intended. This means that one fourth of patients who were randomized into a group using an eHealth innovation was not interested in doing so. They did not find significant differences between patients who used the innovation as intended versus those who did not regarding patient activation, general self-efficacy, and health related quality of life. Therefore, other methodologies for investigating effectiveness of eHealth should be explored. We used a patient-preference trial to explore the effectiveness of CMylife. At baseline, our study found a response rate of 93 percent, which is really high compared to other randomized studies. The downside of using a non-randomised design is that unknown and uncontrolled confounders could influence study results [19]. Also, patients of the questionnaire group in our study (**chapter 5**) had access to the CMylife website, which could have caused underestimate of the effects of CMylife. If data on actual utilization of the features of CMylife were collected and data on patients' use of other information and communication resources besides CMylife,

results could be corrected for this to minimize confounding effects. However, we expect that this underestimation is little, since patients in the questionnaire group only had access to information on the website and not to the other features of the platform.

Iterative evaluation

Implementation of eHealth is deemed tough since the progress in this field is accelerating and a method for evaluating effectiveness, feasibility, and usefulness of a changing digital tool in daily clinical practice is necessary [20, 21]. Previous research agrees on the importance of systematic iterative evaluation of innovations like DCPs to be continued after development to create an optimal fit between the DCP and patients' needs [20, 21]. In **chapter 6**, we showed that PAR serves this purpose. PAR revolves around wishes and needs within a particular group of people in daily clinical practice. Therefore, end users of CMylife have been involved in the development and implementation of CMylife and also in each step of the improvement process to establish true patient-centred care. Results of our study supported that intensive involvement of patients in a PAR approach enabled continuous improvement of DCPs and evaluation in daily clinical practice combined with promoting patient empowerment. Participants' commitment constitutes the foundation of a PAR approach. It requires participants to dedicate time, to be open-minded, to accept a degree of uncertainty and to be interested in the process. This may limit the generalizability of study results since certain users of the platform were not involved. Our study contained only participants who were willing to use CMylife. Participants with a low literacy were absent. These patients should be actively included in such studies to incorporate their wishes and needs in a DCP.

In addition, since the aim of CMylife is to provide patients with a multi-component digital care platform that empowers them to manage their disease optimally and facilitates patient independence, self-management, and self-efficacy. In order to be sure that this goal is reached patient empowerment should be monitored. What is the best way to do so? Previous research shows that eHealth innovations aiming at fostering patient empowerment can only succeed when HCPs are willing to engage in this patient-HCP partnership and when patients are willing to be more responsible for their own health management [22]. Patient empowerment should be monitored regularly as the DCP is continuously evolving and improving. Objective measures like the patient activation measure, used in **chapter 5**, could be used to do so once in a while [23-25]. In addition to an objective measure, it is important what patients feel and experience and a subjective measure is also important in true patient-centred care. Patients could be asked in interviews or questionnaires on how they feel about the influence of the DCP on

empowerment. Examples of such questionnaires are the patient perceptions of empowerment scale [26] and the Multidimensional health locus of control scale, measuring patients' perceived control [27].

Frameworks used

In **chapter 3** our semi-structured interview guide was based on the frameworks of Grol and Flottorp [28, 29]. Also, during analysis of the (focus group) interviews we used the frameworks to categorize barriers and facilitators. These are frameworks to define barriers to and facilitators for change in health care practice, like the implementation of a DCP. Using these frameworks, we were able to create an overview of barriers and facilitators, not only focused on innovation and end user factors, but also focused on social context factors, organisational context factors and economic and political context factors. However, these frameworks are not particularly aimed at the implementation of a digital innovation. A new framework, called the NASSS framework, is specially developed for studying non-adoption, abandonment and challenges to scale-up, spread and sustain technology-supported change efforts in health and social care [30, 31]. A lot of domains of the frameworks we used correspond to the domains in the NASSS framework. Grouping of the domains is a little different but the content is comparable. For example the first domain of the NASSS framework is condition, that contains sub-domains about the nature of the condition and comorbidities. In our study, comorbidities were a subject of discussion during the interviews, however, we accommodated this to the individual professional level, since HCPs wanted to prevent missing crucial things about patients' lives and comorbidities. Also, the nature of the condition sub-domain in the NASSS framework is divided under the patient and the innovation levels in our used frameworks. Therefore, probably no barriers to and facilitators for the implementation of a DCP were missed since the used frameworks were not particularly aimed at digital innovations. It might be useful to investigate whether using such a framework as the NASSS, specially designed for digital innovation implementation, is better when implementing a DCP compared to proven and accepted frameworks that are not focussed on digital innovations.

Implications for clinical practice and future research directions

Finally, we discuss implications for daily clinical practice and future research directions. We especially focus on how a DCP could suit all patients, including the ones with limited health literacy, how structural and sustainable finance could be reached for DCPs, and the implications of DCP regarding big data and patient reported outcomes.

Suiting all patients

Most important is that patients' needs are taken into account when implementing and improving eHealth. Just providing patients with tools and knowledge in order to improve patients' care may not be enough, since approximately 36% of the Dutch population has limited health literacy [32]. Guidance in the use of eHealth should be provided since the existence of a tool may not be enough for these patients. eHealth literacy is defined as "the ability to seek, find, understand, and appraise health information from electronic sources and apply the knowledge gained to addressing or solving a health problem" [33]. As mentioned in **chapter 4**, only a third of the CML patients in the study population knew which, where, and how to find useful health information. We did not focus on this in our research but this group of patients probably needs specific features to be able to use the DCP properly. Focus of future research must therefore be to involve not only the motivated and involved patients with improvement of CMyLife, but also patients with limited health literacy to develop these features. Also, previous research has shown that it is important to make digital health care information understandable and accessible, support patients in using the DCP, improve their abilities, and make the innovations correspond with the desires and wishes of patients with limited health literacy [32]. However, this is still a challenge since this group of patients is hard to reach. This emphasizes that there is no one-size-fits-all and innovations should provide tools and knowledge for all patients including those with limited health literacy. This way care is personalized and patients can decide themselves when and in what manner they use the platform and how they want to be supported in doing so.

Reaching structural and sustained financing

Financing of eHealth mostly depends on project-based sourcing, which makes structural and sustainable financing a challenge. A lot of benefits of eHealth are long-term, which takes a considerable amount of time before an investment is returned. As mentioned in **chapter 3** health insurers stated that to get eHealth reimbursed it is important to prove cost-effectiveness and that there is a clear business case behind the innovation. Therefore the lack of evidence concerning cost-effectiveness can be a problem. The value of the eHealth innovations should not only be evaluated money wise but also in terms of time and effort. Recent studies showed that better adherent patients and HCPs which is a goal of CMyLife, result in cost saving [34-36]. Economic evaluations of innovations improving quality of care of CML patients remain scarce. A previous study investigated cost-effectiveness of therapeutic drug monitoring (improving dose management) [37]. Results showed that impact of therapeutic drug monitoring is modest but cost-effective. Since CMyLife not only improves medication compliance but also

other outcomes, as described in **chapter 5**, it is important to investigate cost-effectiveness.

Big data

Besides all benefits that CMylife offers patients, eHealth also generates a large amount of data which provides opportunities that should be explored. Big data analytics is a growing area with the ability to provide insight in health care [38]. Using big data, predictive algorithms could be developed to identify patients at risk of treatment failure, adverse events, low medication compliance, low guideline adherence, and many more. Big data can also enhance personalization of the delivery of information. Adjusting information to patients' preferences does not only apply to the content but also the timing of information. Literature shows that a contributing gap in information provision may be recall of information since a large proportion of patients forgets or incorrectly remembers the medical information provided during a consultation [39]. A DCP like CMylife could provide patients with preferred information in a timely manner. Applicability of the actual use of big data should be explored in future research.

Patient Reported Outcomes

Previous studies have reported underestimation of symptom severity by HCPs [40, 41]. Incorporating a feature to register side effects in DCPs has shown to enhance side effect management [42, 43]. In addition to patients gaining insight into their side effects themselves, patient-reported outcomes measures (PROMs) assessment has also shown to improve communication between patients and their HCPs [44]. Routinely reporting of PROMs through a DCP offers a multitude of opportunities. PRO data give patients and HCPs the opportunity to discuss side effects during consultations. Also, PROs derived from real life are hardly taken into account in the process of guideline development, despite their considerable influence on shared decision making during the consultation and on treatment outcomes [40]. Experience must be gathered about the application and integration of different types of knowledge, like PRO data, into guideline development [45]. It is important to investigate stakeholders opinions concerning incorporation of PROM data into guideline adjustment to personalize treatment guidelines before actual implementation. We do not criticize the current process of guideline development but it may be time to renew the understanding of what is the best evidence for different clinical problems.

Recommendations for future research

Improving the DCP

- Explore what the right features of a DCP are in order to serve the needs of specific patient groups.
- Investigate what is the best method to educate patients and HCPs in how and why to use CMyLife and how to reach not only the motivated and involved patients with CMyLife, but also patients with for example limited health literacy.
- Prove cost-effectiveness of CMyLife by comparing usual care with CMyLife supported (more remote) care to reach sustainable financing for DCPs.

Methodologies

- What is the best method to evaluate the effectiveness of eHealth and what is the best way to measure patient empowerment, combining objective and subjective measures.
- Investigate if CMyLife could serve as an example for evaluating a DCP while using a dynamic feedback loop for improvement and validate the implementation guide of chapter 3 in other (oncological) diseases.
- Study if using a framework especially designed for digital innovation implementation is better when implementing a DCP compared to proven and accepted frameworks that are not focussed on digital innovations.

Other research possibilities produced by DCPs

- Explore applicability and possibilities of the use of big data.
- Investigate what stakeholders opinions are about incorporating PRO data into guideline development to personalize treatment guidelines and explore other possibilities of routinely reporting of patient-reported outcomes.
- Gather experiences with the application and integration of different types of knowledge, like PRO data, into guideline development.

Final conclusion

Health care systems must reorganize and innovative approaches are essential to meet the growing burden of chronic diseases. A shift to more involved and empowered patients, and ultimately to more remote care, needs a patient-centred approach. EHealth innovations like CMyLife enable the delivery of sustainable, affordable, patient-centred oncological care while maintaining quality of care. CMyLife provides patients with tools to oversee and guard the progress and accuracy of their treatment. We described the implementation and evaluation

of CMyLife, a multi-component digital care platform and provided guidance for implementation and evidence for rather new methods for continuous evaluation of eHealth. This iterative process of assessing patients' needs in clinical practice and improving CMyLife must be continued to keep care patient-centred and fit CMyLife into future perspectives. CMyLife is currently being expanded to other haematological malignancies (chronic lymphocytic leukemia, myeloproliferative neoplasms, multiple myeloma, malignant lymphoma) and in other languages (French, German, English). Opportunities using big data and PROs generated by eHealth should be explored. EHealth use provides us with plenty opportunities and challenges for future research.

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CHAPTER 8

Summary

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About the author

Summary

Digital innovations like CMyLife have the potential to improve cancer care. The uptake of such eHealth innovations is still low in daily clinical practice and guidance for optimal implementation is lacking. Also, knowledge about the effect of digital care platforms (DCPs) on quality of care and how to improve these innovations in daily clinical practice is limited. As described in **chapter 1** there is room for improvement in CML care, since medication compliance and guideline adherence are suboptimal, which are important factors in determining treatment success. Therefore, the patient-centred, multi-component, DCP, CMyLife aims to provide CML patients with tools and knowledge, to improve medication compliance and guideline adherence, to enhance patient empowerment and eventually to reach better quality of life and more remote care. This thesis focussed on research regarding implementation, evaluation, and improvement of CMyLife.

Implementation of digital care platforms and its effect on quality of care

In **chapter 2** we did a systematic review to collect the best available evidence of the effect of a DCP on quality of care parameters such as enhancement of available information, self-efficacy, continuity of care, and patient- and health care provider-reported experiences. Additionally, barriers and facilitators for implementation of DCPs were analysed. The PubMed (Medline), Embase, CINAHL, and Cochrane Library databases were searched for the period from January 2000 to May 2020 for studies assessing the effect of a DCP on the predefined outcome parameters in oncological patients and studies describing barriers and facilitators for implementation. Synthesis of the results was performed qualitatively. Barriers and facilitators were categorized according to the framework of Grol and Wensing. The Mixed Methods Appraisal Tool was used for critical appraisal of the studies. Seventeen studies were included for final analysis, comprising 8 clinical studies on the effectiveness of a DCP and 13 studies describing barriers and facilitators for implementation. Usage of a DCP appeared to enhance the availability of information and self-efficacy. There were no data available on the effect of a DCP on the continuity of care. However, based on focus group interviews, DCPs could potentially improve continuity of care by optimizing the exchange of patient information across institutes. Patient-reported experiences such as satisfaction with the platform were considerably positive. Most barriers for implementation were identified at the professional level, such as the concern for increased workload and unattended release of medical information to patients. Most facilitators were found at the patient and innovation levels, such as improved patient-doctor communication and patient empowerment. There were few barriers and facilitators mentioned at the economic and political levels. The numerous facilitators identified at the

patient level illustrate that patients are positive toward a DCP. However, despite these favourable results, robust evidence concerning the effectiveness of DCPs, especially from high-quality studies, is still lacking.

Implementation of CMyLife and an implementation guide

In **chapter 3** we explored barriers to and facilitators for nationwide implementation and consolidation of CMyLife, a multi-component, patient-centred, DCP, and constructed a comprehensive implementation guide for launching DCPs in daily clinical practice. This qualitative case study of CMyLife, was performed including five focus group- and eighteen in-depth interviews with stakeholders. Data were collected using a semi-structured interview guide, based on the frameworks of Grol and Flottorp. Transcripts of the interviews were analysed and barriers and facilitators were identified and categorized according to the frameworks. An iterative process including participation of main stakeholders and using the CFIR-ERIC framework led to creating a comprehensive implementation guide for DCPs. In total, 45 barriers and 41 facilitators were identified. Main barriers were lack of connectivity between information technology systems, changing role for both health care providers and patients, insufficient time and resources, doubts about privacy and security of data, and insufficient digital skills of users. Main facilitators mentioned were motivating patients and health care providers by clarifying the added value of use of a DCP, clear business case with vision, demonstrating (cost-) effectiveness, using an implementation guide, and educating patients and health care providers about how to use CMyLife. Based on these barriers and facilitators a clear and comprehensive implementation guide was developed for DCPs.

Effectiveness of CMyLife

In **chapter 4** we assessed patients' evaluation of received information and information needs before introduction of CMyLife and whether this information source is used correspondingly after introduction. Additionally, we explored predicting patient factors in information perception. We conducted a cross-sectional survey among 203 CML patients before launch of the CMyLife platform, using validated questionnaires on information provision and predictive factors. We focused on website utilization during the first 3 years, using Google Analytics. Regression analyses were performed to determine influence of patient factors on information perception. Global perceived information provision was scored below average, 42.8 (0–100). Before the introduction of CMyLife, information on other services such as rehabilitation and psychological support, and effects of treatment on sexuality showed room for improvement. One out of three knew where to find useful health information online, but more information was desired by 36% of them. Age ≥ 65 years, time since diagnosis and low education were negatively

associated with this need. After introducing CMyLife, results showed that pages on medication and side effects were visited the most. To fill the gap in perceived provision and needs, information should be adjusted more to the individual in content, manner, and timing.

In **chapter 5** we explored the effectiveness of CMyLife in terms of information provision, patient empowerment, medication compliance, molecular monitoring, and quality of life, using a patient-preference trial. Upon completion of the baseline questionnaire, participants actively used (intervention group) or did not actively use (questionnaire group) the CMyLife platform for at least six months, after which they completed the post-intervention questionnaire. Scores between the intervention group and the questionnaire group were compared with regard to the within-subject change between baseline and post-measurement using Generalized Estimating Equation models. At baseline, 33 patients were enrolled in the questionnaire group and 75 in the intervention group. Online health information knowledge improved significantly when actively using CMyLife and patients felt more empowered. No significant improvements were found regarding medication compliance and molecular monitoring, which were already outstanding. Self-reported effectiveness showed that using CMyLife improved patients' medication compliance and helped them to oversee their molecular monitoring. Patients using CMyLife reported more symptoms but were better able to manage these.

Evaluate and improve a continuously changing tool

In **chapter 6** we aimed to investigate whether a participatory action research approach is best suited for scientific evaluation of eHealth innovations in daily clinical practice on improvement, implementation, and patient empowerment. We used iterative cycles of planning, action, and reflection, whereby participants' experiences (of patients, health care providers, the CMyLife-team, and app suppliers) with the platform determined next actions. Codesign workshops were the foundation of this cyclic process. Also, patients filled in two sets of questionnaires for assessing experiences with, the actual use of, and influence of CMyLife after three months and after at least six months. Data collected during the workshops were analysed using content analysis, often used for making a practical guide to action. Descriptive statistics were used to characterize the study population in terms of CML related information and socio-demographics, and to describe experiences with, and the actual use of the DCP CMyLife. Codesign workshops provided insights, for example, simplification of language, and improvement of user-friendliness of functionalities that contributed to the improvement, implementation, and evaluation of CMyLife and empowered patients with CML. Results of the questionnaires indicated that a. the platform improved information

provision, b. use of the medication app improved patients' medication compliance, c. use of the guideline app improved patients' guideline adherence, and d. patients felt more empowered when using the platform. Therefore, participatory action research approach is suited to scientifically evaluate DCPs in daily clinical practice.

Discussion

In **chapter 7** we summarize results, reflect on main findings of the conducted studies in light of recent literature, and finally we discuss implications for daily clinical practice and future research directions.

Samenvatting

Digitale innovaties, zoals het CMyLife zorgplatform, hebben de potentie om de zorg voor mensen met kanker te verbeteren. CMyLife is een digitaal zorgplatform met als doel de zorg voor mensen met chronische myeloïde leukemie (CML) te verbeteren. Het gebruik van dergelijke eHealth innovaties in de dagelijkse klinische praktijk is echter nog te laag en advies en begeleiding voor een optimale implementatie ervan ontbreekt. Ook is de kennis over het effect van digitale zorgplatforms op de kwaliteit van zorg en hoe deze innovaties in de dagelijkse klinische praktijk toetsbaar de zorg kunnen verbeteren beperkt. Zoals beschreven in **hoofdstuk 1** is er ruimte voor verbetering in de huidige zorg voor mensen met CML. Belangrijke factoren voor het succes van de behandeling met (dure) specifieke medicijnen, zoals medicatietrouw en richtlijnadherentie, zijn namelijk suboptimaal. Het CMyLife platform, bestaande uit meerdere componenten, beoogt de medicatietrouw en richtlijnadherentie te verbeteren en de regie van de patiënt te vergroten. Daarmee krijgen patiënten een betere kwaliteit van leven met meer hybride zorg, dus meer zorg op afstand. In dit proefschrift hebben we ons gericht op onderzoek naar implementatie, evaluatie en verbetering van het CMyLife platform.

Implementatie van digitale zorgplatforms en effect op kwaliteit van zorg

In **hoofdstuk 2** hebben we een systematisch review uitgevoerd om het best beschikbare bewijs te verzamelen van het effect van een digitaal zorgplatform op verschillende parameters voor kwaliteit van zorg. Deze betreffen verbetering van beschikbare informatie, zelfredzaamheid, continuïteit van zorg en door zowel patiënten als zorgverleners gerapporteerde ervaringen. Daarnaast zijn belemmerende en bevorderende factoren voor de implementatie van dit soort digitale zorgplatforms geanalyseerd. De databases PubMed (Medline), Embase, CINAHL en Cochrane Library werden doorzocht over de periode van januari 2000 tot mei 2020. De focus lag op studies die het effect van een digitaal zorgplatform op de vooraf gedefinieerde uitkomstparameters bij oncologische patiënten beoordelen en studies die belemmerende en bevorderende factoren voor implementatie ervan beschrijven. De resultaten uit de verschillende studies werden kwalitatief samengevat. Belemmerende en bevorderende factoren werden gecategoriseerd volgens het framework van Grol en Wensing. De Mixed Methods Appraisal Tool werd gebruikt voor de kritische beoordeling van de kwaliteit van de studies. Zeventien studies werden geïncludeerd voor de uiteindelijke analyse, waaronder 8 klinische studies naar de effectiviteit van de digitale zorgplatforms en 13 studies die belemmerende en bevorderende factoren beschrijven. Het gebruik van een digitaal zorgplatform bleek de beschikbaarheid van informatie

en de zelfredzaamheid van patiënten te vergroten. Er waren geen gegevens beschikbaar over het effect van een digitaal zorgplatform op de continuïteit van de zorg. Resultaten uit focusgroep interviews lieten echter wel zien dat digitale zorgplatforms de continuïteit van zorg zouden kunnen verbeteren door de uitwisseling van patiëntinformatie tussen instellingen te optimaliseren. Patiënt-gerapporteerde ervaringen, zoals tevredenheid met het platform, waren aanzienlijk positief. Het merendeel van de belemmerende factoren voor de implementatie van digitale zorgplatforms werden vastgesteld op professioneel niveau, zoals bezorgdheid over een verhoogde werkdruk en het "onbewaakt" vrijgeven van medische informatie aan patiënten. Het merendeel van de bevorderende factoren werden gevonden op het niveau van de patiënt en op het niveau van innovatie (dat wil zeggen het digitale zorgplatform), zoals een verbeterde communicatie tussen patiënt en arts en een verbeterde zelfredzaamheid van de patiënt. Op economisch en politiek niveau werden weinig belemmerende en bevorderende factoren gevonden. De talrijke bevorderende factoren die op het niveau van de patiënt werden vastgesteld, tonen aan dat patiënten positief staan tegenover een digitaal zorgplatform. Ondanks deze gunstige resultaten ontbreekt het echter nog steeds aan degelijk bewijs voor de effectiviteit van digitale zorgplatforms, met name door het gebrek aan studies van hoge kwaliteit. Wel laat literatuur gunstige resultaten zien in studies naar losse onderdelen van een digitaal zorgplatform, zoals bijvoorbeeld een elektronisch patiëntendossier.

Implementatie van CMyLife en een implementatiegids

In **hoofdstuk 3** onderzochten we belemmerende en bevorderende factoren voor landelijke implementatie en consolidatie van het CMyLife platform en stelden we een uitgebreide implementatiegids op voor het invoeren van digitale zorgplatforms in de dagelijkse klinische praktijk. Deze kwalitatieve studie werd uitgevoerd met vijf focusgroep- en achttien diepte-interviews met betrokkenen in de zorg voor CML patiënten. De gegevens werden verzameld aan de hand van semigestructureerde interviews, gebaseerd op de frameworks van Grol en Flottorp. Transcripties van de interviews werden geanalyseerd en belemmerende en bevorderende factoren werden geïdentificeerd en gecategoriseerd volgens de frameworks. Een iteratief proces met deelname van de belangrijkste betrokkenen en het gebruik van het CFIR-ERIC framework leidde tot een uitgebreide implementatiegids voor invoering van digitale zorgplatforms in de dagelijkse klinische praktijk. In totaal werden 45 belemmerende en 41 bevorderende factoren geïdentificeerd. De belangrijkste belemmerende factoren waren het gebrek aan verbindingen tussen ICT-systemen, de veranderende rol van zowel zorgverleners als patiënten, onvoldoende tijd en middelen van zorgverleners, twijfels over de privacy en veiligheid van gegevens en onvoldoende digitale vaardigheden van gebruikers. De belangrijkste

bevorderende factoren waren het motiveren van patiënten en zorgverleners door de toegevoegde waarde van het gebruik van een digitaal zorgplatform te verduidelijken, een duidelijke business case met visie te stellen, het aantonen van (kosten)effectiviteit, het beschikbaar stellen van een implementatiegids en het voorlichten van patiënten en zorgverleners over het gebruik van CMylife. Op basis van deze belemmerende en bevorderende factoren is een duidelijke en uitgebreide implementatiegids voor digitale zorgplatforms ontwikkeld.

Effectiviteit van CMylife

In **hoofdstuk 4** onderzochten we hoe CML-patiënten, vóór de introductie van CMylife, de informatievoorziening beoordeelden en hoe CMylife na introductie werd gebruikt gedurende de eerste drie jaar (met behulp van Google Analytics). Daarnaast onderzochten we met een regressieanalyse welke patiëntfactoren gerelateerd waren aan verhoogde informatiebehoeften. We voerden een dwarsdoorsnede onderzoek uit onder 203 CML-patiënten vóór de introductie van CMylife, met gevalideerde vragenlijsten over informatievoorziening en voorspellende factoren. De globale informatievoorziening scoorde onder het gemiddelde, namelijk 42,8 op een schaal van 0 tot 100. Vóór de introductie van CMylife ontbrak het vooral aan informatie over voorzieningen als revalidatie, psychologische ondersteuning en effecten van de behandeling op seksualiteit. Een kwart van de patiënten gaf aan geen informatie te hebben ontvangen over de positieve en negatieve effecten van de medicatie. Een op de drie wist waar men online nuttige gezondheidsinformatie kon vinden en ruim een derde van hen wenste meer informatie te verkrijgen. Een leeftijd boven de 65 jaar, langere tijd sinds diagnose en lager opleidingsniveau waren negatief geassocieerd met meer behoefte aan extra informatie. Na invoering van CMylife bleek uit de gebruikersdata van de website dat pagina's over medicatie en bijwerkingen het meest werden bezocht. Om de kloof tussen de ervaren voorziening en de behoeften te dichten dient de informatie op CMylife qua inhoud, manier van aanbieden en timing beter op het individu worden afgestemd.

In **hoofdstuk 5** onderzochten we de effectiviteit van CMylife op het gebied van informatievoorziening, zelfredzaamheid van de patiënt, medicatietrouw, monitoring van bloedwaardes en kwaliteit van leven. Patiënten mochten kiezen of zij CMylife wilden gebruiken of niet. Na het invullen van een vragenlijst aan het begin van het onderzoek gebruikten deelnemers CMylife gedurende minimaal zes maanden actief (interventiegroep) of niet actief (vragenlijstgroep), waarna zij opnieuw een vragenlijst invulden. De kennis van online gezondheidsinformatie verbeterde significant bij actief gebruik van CMylife en patiënten voelden zich meer zelfredzaam. Er werden geen significante verbeteringen gevonden met betrekking tot medicatietrouw en het monitoren van bloedwaardes, die ook al heel

goed waren. Echter, volgens de patiënten zelf verbeterde hun medicatietrouw door het gebruik van CMyLife en hielp het hen de monitoring van hun bloedwaardes te overzien. Patiënten die CMyLife gebruikten, meldden meer bijwerkingen van hun medicijnen, maar ze waren beter in staat deze te beheersen.

Een voortdurend veranderende tool evalueren en verbeteren

In **hoofdstuk 6** onderzochten we of participatief actieonderzoek geschikt is om eHealth-innovaties in de dagelijkse klinische praktijk wetenschappelijk te evalueren op het gebied van verbetering, implementatie en zelfredzaamheid van patiënten. We gebruikten herhaalde cycli van planning, actie en reflectie, waarbij de ervaringen van betrokkenen (patiënten, zorgverleners, het CMyLife-team en app-leveranciers) met het platform de volgende acties bepaalden. Codesign-workshops (workshops in samenwerking met gebruikers) vormden de basis van dit cyclische proces. Ook vulden patiënten twee sets van vragenlijsten in om hun ervaringen met het gebruik van en de invloed van CMyLife na drie maanden en na minstens zes maanden te beoordelen. Codesign-workshops leverden inzichten op die bijdroegen aan de verbetering, implementatie en evaluatie van CMyLife en die CML patiënten meer regie gaven in hun ziekteproces. Voorbeelden hiervan zijn de vereenvoudiging van taal en verbetering van de gebruiksvriendelijkheid van functionaliteiten zoals de medicatie app en de richtlijn app. Resultaten van de vragenlijsten laten zien dat a. het platformgebruik de informatievoorziening verbetert, b. het gebruik van de medicatie app de medicatietrouw van patiënten verbetert, c. het gebruik van de richtlijn app het monitoren van bloedwaardes van patiënten verbetert, en d. patiënten zich meer zelfredzaam voelen door het gebruik van het platform. Dit laat zien dat participatief actieonderzoek geschikt is om een voortdurend veranderend digitaal zorgplatform in de dagelijkse klinische praktijk wetenschappelijk te verbeteren, implementeren en evalueren.

Conclusie

In **hoofdstuk 7** vatten we de resultaten samen, reflecteren we op de belangrijkste bevindingen van de uitgevoerde studies in het licht van recente literatuur en tot slot bespreken we implicaties voor de dagelijkse klinische praktijk en toekomstige onderzoeksrichtingen. EHealth innovaties zoals CMyLife maken duurzame, betaalbare, patiëntgerichte zorg mogelijk zonder de kwaliteit van de zorg te verliezen. CMyLife biedt patiënten tools om de voortgang en nauwkeurigheid van hun behandeling te overzien en te bewaken. Het proces van herhaalde evaluatie van de behoeften van patiënten en het verbeteren van CMyLife moet worden voortgezet om de zorg patiëntgericht te houden en CMyLife in te passen binnen toekomstperspectieven.

Research data management

Radboud Institute for Health Sciences endorse the importance of facilitating reuse of research data as underlined by the FAIR principles, which are guidelines to enhance and improve Findability, Accessibility, Interoperability and Reuse of research data. The data obtained and described in this thesis are archived in accordance with the FAIR principles. Data in this thesis resulted from human studies (chapter 3-6). However, given the nature of this study and the low impact on participants, the Medical Research Involving Human Subjects Act (Dutch: WMO; Wet medisch-wetenschappelijk onderzoek met mensen) does not apply, as confirmed by the institutional Medical Ethical Committee 'CMO Regio Arnhem-Nijmegen' (dossier no. 2016-2291). All studies in this thesis were conducted in accordance with the Declaration of Helsinki. This research was partly supported by The Netherlands Organisation for Health Research and Development (ZonMw) [Project no. 51 6006001]. All data were secured and conform the General Data Protection Regulation and conform the Dutch standard for the safe and reliable exchange of health data between patients and health care providers (MedMij). Also, Features of CMyLife containing data from the hospital's electronic health record were secured with a two-step authentication procedure, which is in accordance with the Dutch security guideline (NEN7510).

Participants were obtained via health care providers, the CMyLife website, or the patient advocacy group Hematon. We have used focus group interviews, interviews, and surveys as methods for data collection. Upon participation in our studies, all participants signed informed consent. In case of qualitative research (chapter 3 and 6) participants provided informed consent for audio recording of the interviews and transcripts of audio recordings were anonymized, before used for data analysis. Paper versions of informed consent forms were stored in a closed cabinet on the department of IQ Health care and digital versions were stored on the Radboudumc haematology department server in a separate protected folder, apart from the folder in which research data was stored. This folder was only accessible for the research team. In addition, all survey studies were anonymous in order to ensure privacy of respondents. By using encrypted and unique individual subject codes we warranted the privacy of participants. The names of participants coupled to this unique code were stored separately from study data again on the protected folder apart from the research data. After completing the project, the document which connects ID codes to the personal data of participants will be erased. The original and anonymous raw data will be kept and archived and the syntaxes and data-adjustments will be saved so that the study may reliably be replicated with the same results. Raw and processed data is stored on the Radboudumc haematology department server in project folders, in SPSS, ATLAS.

ti, or Microsoft Excel. When possible, raw and processed data will be stored in the Digital Research Environment (DRE). Data will then be shared via the DRE in the DANS EASY repository. All data will be kept for at least 10 years (14 April, 2023).

The servers of the Radboud University Medical Centre adhere to all requirements of data protection, among which are password protection, protection against viruses, malware and access by unauthorized persons, protected servers, backup procedures, a secure digital mailing system and a secure out-of-office working environment. The Radboud University Medical Centre only works with legally obtained software applications, which are routinely maintained by internal personnel.

PhD portfolio of Lynn Verweij

Department: **Haematology**

PhD period: **15/04/2020-14/04/2023**

PhD Supervisor(s): **Prof. dr. N.M.A. Blijlevens, Prof. dr. R.P.M.G. Hermens**

PhD Co-supervisor(s): **Dr. G.I.C.G. Ector**

Training activities	Year	ECTS
Courses		
BROK	2018	1.5
RIHS- Introduction course	2020	0.5
RIHS PhD introduction course	2020	0.75
Journal club implementeren en evalueren	2020	0.1
Plannen en organiseren	2020	0.3
RU – Digital tools	2020	0.1
RU – Scientific Writing for PhD candidates	2020	3.0
Journal club implementeren en evalueren	2020	0.1
Workshop Arbeidsmarkt oriëntatie	2021	0.1
Workshop CV en motivatiebrief	2021	0.1
RU – Design and illustration	2021	0.9
Workshop LinkedIn	2021	0.1
RU – Effective Writing Strategies	2021	2.7
Workshop boost your writing skills	2022	0.1
Radboudumc – Scientific integrity	2022	0.7
RU – The art of Finishing Up	2022	0.4
Seminars & Lectures		
RIHS – webinar publishing in open access	2020	0.1
Webinar 'Science & communication: social media for scientists'	2020	0.1
Webinar 'Organisation Theory for Implementation Science (OTIS)'	2020	0.1
Research integrity round	2021	0.1
Research integrity round	2022	0.1
Conferences & Symposia		
New Frontiers Symposium	2020	1.0
Online CaRe Symposium	2020	0.1
Research integrity symposium	2020	0.1
Congres Kanker en Leven	2021	1.0
Annual John Goldman E-Conference on Chronic Myeloid Leukemia (virtual - poster)	2021	1.25
New Frontiers Symposium	2021	1.0
MASCC annual meeting supportive care in cancer (virtual - poster)	2021	1.25
PhD Retreat	2022	1.0
MASCC annual meeting supportive care in cancer (Toronto, Canada - poster)	2022	1.25
Annual John Goldman Conference on Chronic Myeloid Leukemia (Mandelieu-la-Napoule, France - poster)	2022	1.25
PhD Retreat	2022	1.0
Total		22.15

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Submitted papers

- Verweij L.**, Metsemakers S.J.J.P.M., Ector G.I.C.G., Rademaker P., Bekker C.L., van Vlijmen B., van der Reijden B.A., Blijlevens N.M.A., Hermens R.P.M.G. Participatory Action Research: method to improve, implement, and evaluate a real-life digital care platform.

Poster presentations

- Effect of Digital Care Platforms on Quality of Care for Oncological Patients and Barriers and Facilitators for Their Implementation: Systematic Review. Multinational association of supportive care in cancer annual meeting, June 2021, Virtual.
- Effectiveness of the digital care platform CMylife for patients with chronic myeloid leukemia. Annual John Goldman Conference on Chronic Myeloid Leukemia, October 2021, Virtual.
- A comprehensive eHealth implementation guide constructed on a qualitative case study on barriers and facilitators of the digital care platform CMylife. Multinational association of supportive care in cancer annual meeting, June 2022, Virtual, Toronto, Canada.

Participatory Action Research: method to improve, implement, and evaluate a real-life digital care platform. Annual John Goldman Conference on Chronic Myeloid Leukemia, October 2022, Mandelieu-la-Napoule, France.

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About the author

Lynn Verweij was born on November 30th, 1995 in Nijmegen, the Netherlands. After graduating from pre-university education at Mondial College (VWO) in Nijmegen in 2014, she developed a special interest in the health care process, particularly regarding malignant diseases. Therefore, she chose to study a three-year Bachelor program and a two-year Master program in Biomedical sciences at the Radboud University in Nijmegen. During the Master program, she completed two scientific internships. In 2017 she did her epidemiology internship at the department of Health Evidence about the association between body composition and survival in renal cell carcinoma. In 2019, she did her communication profile internship at the department of IQ health care about the effect of CMyLife on the medication compliance, guideline adherence, quality of life, and patient empowerment for patients with chronic myeloid leukemia. The second internship was under supervision of prof. dr. Rosella Hermens. After successfully completing the internship, the last supervisor mentioned that prof. dr. Nicole Blijlevens and herself were looking for a PhD student to conduct research regarding the effect and implementation of the CMyLife platform. The ball started rolling and in April 2020 Lynn started with her PhD trajectory at the department of haematology. Most part of her PhD she was working from home because of the COVID-19 pandemic. After successfully finishing the PhD trajectory, Lynn will continue working on the CMyLife projects at A.T. TWINTEY, the company collaborating with Radboudumc to improve the care of patients with haematological diseases and create sustainable change in health care.



