



Digital health for optimal supportive care in oncology: benefits, limits, and future perspectives

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Abstract

Background Digital health provides solutions that capture patient-reported outcomes (PROs) and allows symptom monitoring and patient management. Digital therapeutics is the provision to patients of evidence-based therapeutic interventions through software applications aimed at prevention, monitoring, management, and treatment of symptoms and diseases or for treatment optimization. The digital health solutions collecting PROs address many unmet needs, including access to care and reassurance, increase in adherence and treatment efficacy, and decrease in hospitalizations. With current developments in oncology including increased availability of oral drugs and reduced availability of healthcare professionals, these solutions offer an innovative approach to optimize healthcare resource utilization.

Design This scoping review clarifies the role and impact of the digital health solutions in oncology supportive care, with a view of the current segmentation according to their technical features (connection to sensors, PRO collection, remote monitoring, self-management in real time...), and identifies evidence from clinical studies published about their benefits and limitations and drivers and barriers to adoption. A qualitative summary is presented.

Results Sixty-six studies were identified and included in the qualitative synthesis. Studies supported the use of 38 digital health solutions collecting ePROs and allowing remote monitoring, with benefits to patients regarding symptom reporting and management, reduction in symptom distress, decrease in unplanned hospitalizations and related costs and improved quality of life and survival. Among those 38 solutions 21 provided patient self-management with impactful symptom support, improvement of

Key message Digital solutions with ePROs and self-management can be incorporated in supportive care in oncology practice and provide benefits to: patients, e.g., reduced symptom burden and distress, increased symptom reporting, improved overall survival; healthcare professionals, with targeted patient management; payors, potentially with reduced supportive care-related costs and hospitalizations.

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QoL, usefulness and reassurance. Principal challenges are in developing and implementing digital solutions to suit most patients, while ensuring patient compliance and adaptability for use in different healthcare systems and living environments.

Conclusions There is growing evidence that digital health collecting ePROs provide benefits to patients related to clinical and health economic endpoints. These digital solutions can be integrated into routine supportive care in oncology practice to provide improved patient-centered care.

Keywords Digital therapeutics · Integrative oncology · Symptom monitoring · Self-management · Patient-reported outcomes · eHealth

Introduction

The International Agency for Research on Cancer estimated that in 2018, there were 18.1 million new cancer cases worldwide and 9.6 million cancer-related deaths [1]. A global surveillance report suggests a trend toward increased survival [2], with some cancers progressing to chronicity. However, the total burden of new cancer cases is increasing, and new therapies are generally more costly [3]. Additionally, more drugs are available in oral formulations for home administration, with reduced face-to-face surveillance by healthcare professionals (HCPs). Novel approaches for optimal patient management that allow containment of healthcare costs are urgently needed [4].

The new approaches should focus on patient-centered care with integration of tumor-directed treatment and patient-directed supportive and palliative care throughout the disease journey [5, 6]. The goals of management are to achieve improvements in not only overall survival (OS) but also patient-reported outcomes (PROs) such as quality of life (QOL) [7], fewer emergency department visits, and self-reported improvements in symptoms [7, 8].

The intensive development over recent years of therapies with novel mechanisms of action, including molecular-targeted therapies, immuno-oncology therapies, and precision radiation oncology, has transformed the oncology treatment landscape [9, 10]. These advances have increased the complexity of treatment (combination of therapies) and required modifications in the patient pathway (oral treatment intake at home versus hospitalization) to ensure quality care. The real-world toxicity profile of novel agents may not always correlate with that observed in clinical trials and may result in unanticipated toxicities [11, 12]. Increased availability of oral therapies for home administration results in less healthcare supervision during treatment, whereas the prolonged use of such treatments as long-term maintenance may be associated with the emergence of new toxicities [13]. Therefore, careful monitoring of adverse events (AEs) during self-administration of treatments at home is becoming essential to facilitate prompt intervention to reduce their severity and duration.

Patients must therefore manage symptoms and treatment-related side effects without direct medical supervision; home administration of anticancer treatments also increases the

chance of nonadherence and administration errors by patients [14]. With immunotherapeutic treatments, the timely identification of toxicities is crucial since many symptoms may improve with prompt intervention [15]. Additionally, a potential shortage in oncology services and workforce linked to the increasing cancer incidence and complexity of cancer treatments [16] has highlighted the need for new strategies to ensure that all patients receive optimal treatment and care throughout the continuum of disease.

Advances in digital communications and medical technologies have led to the digitalization of healthcare [17]. Increased access and uptake of such technologies among physicians and patients yields large amounts of potentially usable data, which, in the context of electronic health records (EHRs), forms an important part of physicians' decision-making. Self-reported data is extensively used in healthcare. Patient-level data provide real-world medical information, with opportunities for improved clinical decision-making, patient empowerment, improved health outcomes, and cost reductions [18–20]. However, patient confidentiality and compliance with local and global data privacy regulations need to be ensured.

Digital health definitions with focus on digital therapeutics

Digitalized healthcare comprises eHealth, telemedicine, telemonitoring, and digital therapeutics (Fig. 1).

The terms digital health, telehealth, and eHealth are interchangeable and are defined as the provision of healthcare services supported by telecommunications or digital technology to improve or support healthcare services. eHealth solutions can be part of each step of the healthcare process (i.e., prevention, diagnosis, decision-making, treatment/intervention, and follow-up).

Telemedicine represents medical services provided remotely to patients by HCPs using telecommunications platforms. Healthcare activities, such as patient evaluation, diagnosis, or treatment, are performed by HCPs without the need for inpatient consultation, although the legal status of such consultations varies according to jurisdiction [21].

Telemonitoring is the use of digital technology to frequently or continuously monitor patients' vital signs or any other

eHealth



Telemedicine



Telemonitoring



Digital therapeutics

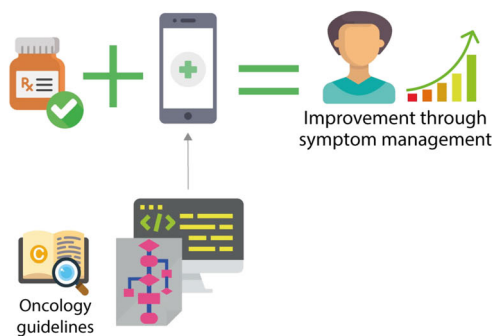


Fig. 1 Digital health definitions

symptoms. The information is assessed remotely by HCPs to inform the patient and caregivers about the actions needed for appropriate symptom management and treatment advice.

Digital therapeutics embed algorithms based on medical guidelines and best practices, which transform collected data into actionable insights, with the objective to bring value to evidence-based clinical outcomes (from clinical studies or real-world evidence). They may be used alone or in conjunction

with drugs and medicinal products, medical devices, or other therapies, to enhance and support medical treatment. According to the risk level of the embedded algorithms, the digital therapeutics may be classified as medical devices. Depending on the regulatory status, they may be used on prescription only (prescription digital therapeutics).

A further technology of relevance to the broad concept of digitalized healthcare is artificial intelligence with capabilities of machine learning, which may be defined as the use of computer algorithms to make successful predictions about future events based on past experiences [22].

From a health outcomes perspective, digital health can be grouped into solutions connected to sensors or not and that capture ePROs to allow patient monitoring only or those that allow patient monitoring and symptom management by HCPs, covering remote areas, or symptom management by the patients themselves with or without real-time decision support for self-management. Patients receive individualized guidance, from a simple recommendation to call their HCP, to a suggestion to begin a specific treatment intake.

Supportive care for cancer patients definition and unmet needs

The Multinational Association of Supportive Care in Cancer defines supportive care in cancer as “the **prevention and management of the adverse effects of cancer and its treatment**. This includes management of physical and psychological symptoms and side effects across the continuum of the cancer experience from diagnosis through treatment to post-treatment care. Enhancing rehabilitation, secondary cancer prevention, survivorship, and end-of-life care are integral to supportive care.”(About MASCC. mascc.org/about-mascc. Accessed January 11, 2019). Whereas there has been significant progress in anticancer treatment, improvements for optimal supportive care are still needed at all stages of the cancer treatment pathway [5]. Currently, supportive care interventions’ assessment of patient QOL and medical outcomes remains limited, and QOL endpoints are insufficiently reported for clinical trials of novel therapies [23].

A number of evidence-based supportive care guidelines have been developed, but their implementation in routine clinical practice is suboptimal and the opportunity to improve control of symptoms is often forfeited [24]. This highlights the need for more optimal use of guidelines, for personalized and patient-centered care that is delivered in a timely manner.

Digital solutions present an opportunity to address certain unmet needs in prevention or management of adverse events in patients with cancer including (1) increased communication between patients, providers, and their communities [18]; (2) education of patients and caregivers; (3) integration of standard clinical assessments with PROs measured during routine

clinical practice; (4) help of patients in monitoring their respective conditions [18]; (5) improved patient empowerment and self-management; and (6) improved evidence from clinical trials on the basis of PRO endpoints in studies evaluating anticancer treatments and prospective evaluations of supportive care interventions and real-world efficiency of care for cancer patients.

The objectives of the present review are to evaluate the state of digital health solutions in oncology supportive care allowing collection of ePRO and focused on symptom management and to identify benefits and limitations.

Methods

Guidance of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was followed in the conduct of this study (Fig. 2).

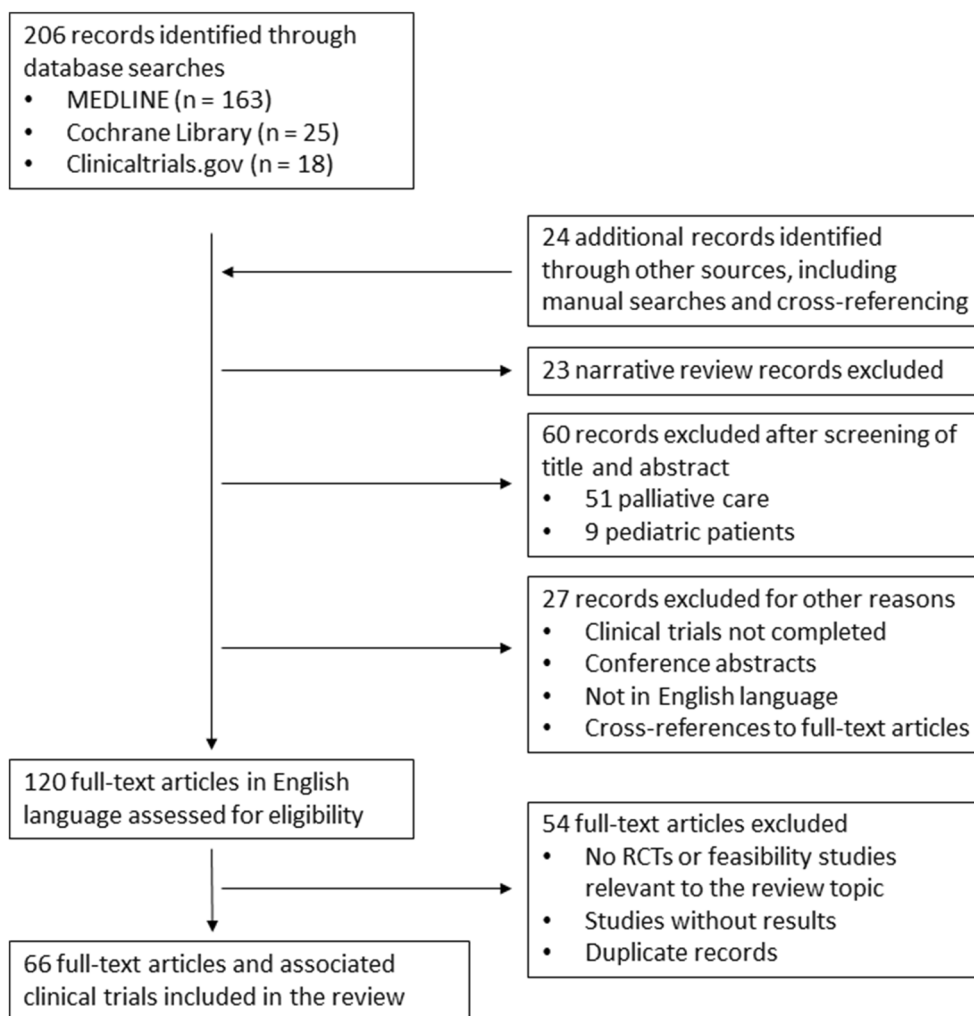
Search strategy

The MEDLINE Public Library of Medicine (PubMed) database and the Cochrane Library were explored from December 1, 2008, to November 30, 2018, for relevant studies using the following search terms: (1) MEDLINE, “cancer or oncology” AND “telehealth or eHealth” AND “symptom management” or “symptom monitoring”; (2) Cochrane Library (title abstract keywords), “cancer or oncology” AND “telehealth or eHealth” AND “symptom”. Clinicaltrials.gov search was performed using the following search strategy: “cancer or oncology” (condition or disease) AND “telehealth or eHealth” (other terms) AND “symptom” (outcomes measures).

Study eligibility criteria (inclusion/exclusion)

Screening of publication was done by 2 researchers on titles and abstracts and then full-text to ensure eligibility to the following criteria.

Fig. 2 PRISMA statement. PRISMA Preferred Reporting Items for Systematic Reviews and Meta-Analyses, RCT randomized controlled trial



Inclusion criteria Adult cancer patients, all randomized controlled trials (RCTs) or feasibility and pilot studies that evaluated the effectiveness of telehealth or eHealth solutions in supportive cancer care were eligible for inclusion in English language.

Exclusion criteria Studies involving pediatric patients and those evaluating solutions at the palliative phase were excluded.

For results retrieved from clinicaltrials.gov, not completed studies or studies without published results were excluded.

Retrieved studies were reviewed, and those evaluating solutions at palliative latest phase of cancer were removed from the analysis.

Outcomes of interest selected and assessed

Outcomes of interest were as follows for each digital solution identified: description of the digital solution including PRO for supportive care in oncology, with remote monitoring, with/without patient automated symptoms self-management, its benefits, limitations, drivers of and barriers to adoption; unmet needs; PRO data including QOL outcomes; AE incidence, severity, and management; emergency room (ER) admissions and hospitalizations; health resource utilizations; and survival outcomes including OS.

Data collection and analysis

Search results were critically analyzed by the authors for relevance to the focus of this review. Two researchers extracted the data. The authors analyzed systematically according to outcomes of interests detailed above the study results to critically discuss the impact on outcomes of the various digital solutions.

Results

A total of 206 articles have been identified through databases searches in Medline, Cochrane, and [Clinicaltrials.gov](https://clinicaltrials.gov). Twenty-four (24) additional records were provided from other sources (manual search, cross-references). We excluded narrative reviews (23), publications which titles and abstracts were about pediatric population or focused on palliative care phase of cancer (60), and other records (27) (not completed results in clinical trials, conference abstracts, not in English language, cross references to full-text articles).

Regarding the 120 selected articles, another 54 full-text articles were excluded because of absence of study results, duplicates, or design (exclusion when not a RCT nor a feasibility study).

Finally, 66 full-text articles and associated clinical trials are included in this review.

Digital health solutions in oncology

The review results outlining the status of clinical evidence regarding digital health solutions that collect ePRO for supportive care in oncology are summarized in Table 1 [7, 8, 25–86]. These 38 digital solutions can be classified into 2 main categories: the first, 17 digital solutions based on PRO collection only, and the second, 21 digital solutions providing also self-management. The key findings are summarized according to outcome.

Clinical evidence for adoption of digital solutions

Clinical evidence for digital health solutions evaluated in feasibility or randomized controlled studies are also summarized in Table 1 [7, 8, 25–86].

Drivers and barriers to usage

From the patient perspective, some of the key factors identified for the uptake of the digital tools included the following:

- (1) Ease of use [30, 38, 44, 51, 53, 55, 64, 80];
- (2) Reassurance [28, 30, 41, 48, 49, 55, 59, 70];
- (3) High usability and usefulness [37, 42, 44, 58, 62, 74];
- (4) Improved communication with HCPs [27, 29, 30, 53, 58] www.owise.uk;
- (5) Correct generation of system alerts and fast response to alerts [28, 70, 80];
- (6) Patient empowerment [29, 30, 69]; and
- (7) The convenience of real-time reporting of symptoms [28, 37];

One study evaluating the extent of patient use of a Web-based intervention reported that reduction of cancer symptom distress was a key driver of uptake, with use of the intervention resulting in a significant reduction in distress score [47].

Conversely, some of the barriers for adoption encountered by patients were as follows:

- (1) Problems with technology or connectivity [48, 49, 69, 80];
- (2) Limited usefulness [29, 30, 71];
- (3) Lack of clarity of the language used [29, 30]; and
- (4) Generation of false alerts [69].

Whereas higher education level, current employment, and low levels of social support have been associated with uptake, lower education level and non-working status may be barriers to accessing interventions [47, 84].

Table 1 Description of digital solutions for supportive care in oncology with remote monitoring with/without patient automated symptoms self- management

Digital solutions description		Study type ^a	N	Tumor type/inclusion criteria	Results	Patients	HCPs	Reference
Name	Remote symptom monitoring (mobile, web, phone based)	Symptom management with patient automated self-management						
ASyMS [©]	Yes Mobile phone-based Rate the severity and bother of each symptom (CTCAE based) through 10 specific chemotherapy-related symptoms questionnaires (i.e. nausea, vomiting, diarrhea, constipation, hand-foot syndrome, mucositis, paresthesia, flu-like symptoms, fatigue, and pain).	Yes ^b Mobile phone-based Patients will immediately receive automated, evidence-based self-care advice on the basis of their symptom reports	112	Breast, lung, colorectal receiving CT	- Significantly less fatigue in the intervention group and less hand-foot syndrome in the control group - Improved communication with HCPs; improved symptom management; reassuring	- Useful for symptom management		Kearney [25]; Maguire [26], McCann [27]
			16	Lung receiving RT	- Less anxiety and drowsiness; improved self-care efficacy - Real-time symptom reporting; reassuring; fast HCP response to alerts - Feasible. Easy to use, reassuring; increased health awareness and empowerment; improved execution of self-care activities; improved communication with HCPs and family/friends; improved AE management - System limitations: inadequate grading scale for AEs; unclear language; limited AEs; less beneficial for patients with few AEs; inaccurate AE reporting by patients to avoid generating alerts	- <i>Positive</i> : generation of real-time alerts; self-care advice - <i>Negative</i> : questionable clinical use of alerts; increased workload		Maguire [28]
			17	Hematologic receiving CT				Breen [29]
			222	Hematologic receiving CT				Breen [30]
		Feasibility to assess the ASyMS technological readiness before the RCT (Maguire [32])	64/	Breast, colorectal, hematologic receiving first-line CT	- Feasible. High compliance in all countries and all cancer types	- Technical issues with the Web-based platform. Resolved with additional training of physicians - Modifications in ASyMS: longer time frame to provide feedback; changes in symptom algorithm		Furlong [31]

Table 1 (continued)

Digital solutions description		Study type ^a	N	Tumor type/inclusion criteria	Results		Reference
Name	Remote symptom monitoring (mobile, web, phone based)				Symptom management with patient automated self-management	Patients	
Automated voice response (AVR) system	Yes Phone-based Symptom management toolkit, completed a baseline interview. Symptoms questionnaires about: fatigue, pain, insomnia, poor appetite, constipation, nausea/vomiting, anxiety, cough, depression, diarrhea, mouth sores, shortness of breath, peripheral neuropathy, difficulty remembering, and weakness.	Yes (Paper-based information for symptom management; phone-based calls for adherence management) Weekly AVR calls	RCT in progress	1108	Breast, colorectal, hematologic receiving first-line CT Solid tumor	- ASyMS not feasible in 2 centers due to organizational issues: lack of staff and technology connectivity - - Symptom severity decreased similarly in all groups. No difference in adherence to oral chemotherapy treatment between groups	Maguire [32] Spoelstra [33]
AWARE	Yes Phone-, wearable sensor-, and Fibit-based passive data collection and PROs: pain, fatigue, feeling disconnected from others, trouble concentrating or remembering things, feeling sad or down, feeling anxious or worried, not enjoying things, feeling irritable, shortness of breath, numbness or tingling, nausea, and poor appetite.	No Fibit-based passive data collection and PROs)	Feasib. (Passively collected data vs PROs)	14	Gastrointestinal receiving CT	- Feasible; passively collected data during CT correlated with PRO scores with high accuracy	Low [34]
Biocnect	Yes Web-based app Weekly self-scoring of 13 common patient symptoms among which: fever, shivers, a brutal asthenia, a decrease in urine volume, an important breathlessness, pain when swallowing, or blood in mouth, prolonged febrile neutropenia	No ^b	Feasib.	41	Cancer patients receiving CT associated with ≥ 20% overall risk of febrile neutropenia	- Feasible; high usability; high compliance; high satisfaction - Fewer unplanned hospitalizations and reduced cost of hospitalization for neutropenia compared with a historical cohort	Denis [35]
BREATH (Breast Cancer E-Health system)	Yes Web-based	Yes Web-based (No therapist involved)	RCT (Usual psychological)	150	Breast cancer survivors who had completed	- Significantly less distress and clinically significant	Van den Berg [36]

Table 1 (continued)

Digital solutions description		Study type ^a	N	Tumor type/inclusion criteria	Results		Reference
Name	Remote symptom monitoring (mobile, web, phone based)				Patients	HCPs	
	Symptom management with patient automated self-management						
	Distress reporting with cognitive behavioral therapy and include information, assignment (48 tasks, or homework), assessment (10 self-tests followed by automated feedback), and video	care + BREATH vs Usual psychological care)		surgery + adjuvant CT and/or RT	improvement in the BREATH arm		
Cankado	Yes Web-based app Symptoms self-reporting and alert function to the patient	RCT	822 participants (CHAPLIN)	Metastatic non-squamous NSCLC or extensive-stage SCLC		NCT03911219	
Care Expert	Yes Web-based. Three supportive functions: continuous communication, reinforcement of self-driven agency, and cooperative agency with a sense of being looked after	Feasib.	4	Breast receiving outpatient CT	- High usability and usefulness; high patient satisfaction related to the system's reliability and real-time reporting function	Ventura [37]	
CHOICE	Yes Web-based Global symptom distress reporting and provides information that is personalized and interactively tailored to patients' specific needs, and that patients can share knowledge and experience to better manage their own care (assessment component, self-management information, communication, diary).	Feasib.	52	Various	- Easy to use - Availability of PROs before clinical visits led to higher congruence in addressing the symptoms during consultation	Ruland [38]	
		Feasib.	65 nurses; 12 physicians	N/A			- High usefulness by nurses and physicians; higher use among nurses
		RCT (availability of PRO data vs No PRO data before consultation)	145	Patients starting antileukemia or -lymphoma treatment	- PRO data availability before visits led to 1) addressing more symptoms during consultation; 2) significant decrease of symptom distress; 3) significant reduction in need for symptom management support	Ruland [40]	
COMPASS (Capturing and Analyzing Sensor and Self-Report Data for Clinicians and Researchers)	Yes Smartphone-based app and wearable heart rate monitor device-agnostic eHealth technology platform that can passively and remotely monitor multiple domains of function and PROs Passive monitoring of patients' health status	Feasib.	3 patients; 10 HCPs	Cancer patients and HCPs	- Feasible; reassuring; highest interest in symptom monitoring	Lucas [41]	- Feasible; highest interest in monitoring of vital signs and medication adherence

Table 1 (continued)

Digital solutions description		Study type ^a	N	Tumor type/inclusion criteria	Results		Reference
Name	Remote symptom monitoring (mobile, web, phone based)				Symptom management with patient automated self-management	Patients	
eCO (eCediranib/Olaparib)	Yes Smartphone-based app. Blood pressure monitor linked to the app via Bluetooth and diarrhea symptom management	Yes ^b Smartphone app and phone-based	16	Patients with recurrent ovarian cancer enrolled in a phase II study of cediranib/olaparib (NCT 02345265)	- Feasible. High usability; high compliance; feeling of improved team-based supportive care, allowed rapid provider response and positive overall patient experience - Hypertension and diarrhea events reported at a similar frequency via eCO and by HCPs in the study database.	-	Liu [42]
eDiary	Yes Smartphone-based app Electronic daily symptom diary: severity ratings of pain, nausea, vomiting, fatigue, and sleep, other selected physical sequelae and selected descriptors of their mood	No	10	Adolescents and young adults with various types of cancer receiving CT	- Feasible; high usefulness; high compliance; few technical issues; very easy to use	-	Baggott [44]
ESRA-C (Electronic Self-report Assessment-Cancer)	Yes Web-based Self-report symptom and quality of life	Yes Web-based Self-care education and customized coaching on how to report concerns to clinicians	752	Various. Patients starting CT or RT	- Reduced symptom distress in the intervention arm; higher benefit in > 50-year-old patients. Significantly more patients in the intervention arm reported symptoms and HRQOL during clinic visits - Higher use by patients starting RT - Reduced symptom distress in the intervention arm	- No difference in clinicians' responses between arms	Berry [45], Berry [46]
The Health Buddy® System	Yes Phone-based tele-messaging Daily response to symptom management algorithms using a simple telehealth messaging device	Yes ^b Phone-based tele-messaging Support provided to patients	374 39; 44	Various. Patients starting CT or RT who used the tool voluntarily Newly diagnosed H&N	- Feasible, well-accepted, reassuring - System limitation: land-based phone line required - Significant improvement in QOL and lower symptom burden posttreatment. No significant improvement in social and emotional well-being - Well accepted, few technical issues	- Well accepted	Berry [47] Head [48, 49]
		RCT	80				Pfeifer [50]

Table 1 (continued)

Digital solutions description		Study type ^a	N	Tumor type/inclusion criteria	Results		Reference
Name	Remote symptom monitoring (mobile, web, phone based)				Symptom management with patient automated self-management	Patients	
Home-based telehealth service	Yes PC/phone/tablet-based videoconferencing	Yes PC/phone/tablet-based videoconferencing	30	H&N after CT or RT	- Reduced number and duration of appointments until discharge - Easy to use; good audio/visual quality; high satisfaction	- Easy to use; good audio/visual quality; high satisfaction; allowed for adequate clinical assessment	Collins [51]
HRQOL in routine oncology practice	Yes Touchscreen computers Symptoms, depression scale and HRQOL questionnaire	Feasib. (Home-based telehealth rehabilitation vs Clinic-based rehabilitation) RCT (Patient-reported HRQOL vs No reporting)	286 patients; 28 oncologists	Various	- Improved HRQOL in intervention arm. No difference in patient-management efficiency - Improved patient-HCP communication - Significantly fewer severe symptoms and symptom interference in the IVR + clinical alerts group - Easy to use IVR system, better rates in the IVR + clinical alerts group	- Mostly rated by oncologists as “very useful” or “quite useful”	Velikova [52]
Interactive voice response (IVR) system	Yes Phone-based Patients rated symptoms twice weekly for 4 weeks via automated telephone calls. (11-point scale), 5 targeted symptoms met or exceeded a preset severity threshold. Symptoms and severity thresholds were chosen in consultation with the thoracic surgery staff.	No ^b (email-based alert to HCPs in study arm) Email alert was forwarded to the patient’s clinical team for response if any of a subset of symptoms	79	Primary lung or lung metastases scheduled for thoracic surgery	- Technologically easy to implement		Cleeland [53]
IVR system	Yes Phone-based Called twice weekly by the IVR system and asked to rate the intensity of their pain and other symptoms	Pilot	60	Breast- and cancer-related pain	- Significantly greater decrease in moderate to severe pain; improvement in sleep disturbance and drowsiness	- Rated as only somewhat useful by physicians	Anderson [56]
Interaktor	Yes Web-based app Daily symptom assessment (HRQOL model) 1) regular assessment of self-reported symptoms, 2) connection to a monitoring web-interface, 3) risk assessment models for alerts, 4) continuous access to evidence-based self-care advice	Yes ^b Self-care advice Two levels of alerts to the HCP	150 150	Prostate (NCT02477137) Breast (NCT02479607)			Langius-Eklöf [54]
	Yes Smartphone-based app Daily symptom assessment (HRQOL model)	Yes ^b Web-based Self-care advice Two levels of alerts to the HCP	6	Patients with pancreatic cancer after pancreaticoduodenectomy	- Reassuring; high compliance; easy to use		Gustavell [55]

Table 1 (continued)

Digital solutions description		Study type ^a	N	Tumor type/inclusion criteria	Results		Reference
Name	Remote symptom monitoring (mobile, web, phone based)				Symptom management with patient automated self-management	Patients	
KAIKU®	Yes Web-based app Self-assess patient side effects QoL and free text collecting PROs on early adverse effects of radiotherapy and on health-related quality of life	No ^a	5	H&N	- Improved patient-HCP communication - Improved follow-up of patients	-	Peltola [57]
MeQoL	Yes Smartphone-based app Daily recording of degree of perceived distress, pain intensity, weekly QoL assessment, short-form 8; Minimal Documentation System.	No	40	Patients with solid cancer with at least monthly appointments in outpatient clinic	- Feasible; high usability; beneficial; would use again; high compliance	- Feasible; high usability; would use again	Benze [58]
MOOVOCARE™	Yes Web-based app Weekly self-scored patient symptoms (weight, weight variation, appetite loss, weakness, pain, cough, breathlessness, depression, fever, face swelling, lump under skin, voice changing, blood in sputum)	No ^a Web-mediated follow up, weekly report and self-reported symptoms automatically triggered an alert sent to the oncologist by e-mail when predefined criteria were fulfilled.	42	Patients with surgical excision, complete response, or non-progressive lung carcinoma	- Feasible; reassuring; reduced anxiety; high compliance - Relapses detected 5 weeks earlier with Moovocare than usual planned visits with Moovocare. High compliance	-	Denis [59]
		Moovocare (prospective) vs Routine surveillance (retrospective) RCT	98				Denis [60]
			121	Non-progressive advanced lung	- Significantly improved OS and better performance status at relapse with Moovocare	-	Denis [61]
		Pooled analysis of 4 prospective studies (including Denis [69, 71]) vs Routine surveillance RCT	300	Lung/various	- Significantly improved OS with Moovocare	-	Denis [62]
NCI PRO-CTCAE (STAR)	Yes Web-based (Weekly email prompt of symptom monitoring, 12 symptoms: appetite loss, constipation, cough, diarrhea, dyspnea, dysuria, fatigue, hot flashes, nausea, pain, neuropathy, and vomiting.)	No ^b STAR triggered e-mail alerts to nurses whenever a patient-reported symptom worsened by ≥ 2 points or reached an absolute grade ≥ 3	766	Advanced solid tumors. Patients receiving outpatient CT	- Significantly improved HRQoL; fewer ER visits; longer time on CT. Greater clinical improvements among patients without prior computer experience	-	Basch [8]
NCI PRO-CTCAE	Yes	No ^b			- Significantly increased OS	-	Basch [7] Basch [63]

Table 1 (continued)

Digital solutions description		Study type ^a	N	Tumor type/inclusion criteria	Results		Reference
Name	Remote symptom monitoring (mobile, web, phone based)				Symptom management with patient automated self-management	Patients	
NOONA	Web- or AVR system-based (ePRO, 30 PRO-CTCAE) Self-report symptoms and physical functioning using the PRO-Core system weekly	500 in PROSPECT (NCT 01515787)	Locally advanced rectal cancer	- High compliance; few technical difficulties (e.g., patient log-in issues and slow internet connectivity)	-	NCT03459352	
	Yes Web-based software; can be integrated to wearable devices (www.noona.com) AE questionnaire: symptoms and distress prompted once per month and one week prior to any medically indicated oncology clinic visit.	Yes Web-based Recommendation to contact care team if required	Feasib. study in progress RCT final visit of 765 follow up by phone or Noona	Gastrointestinal Early breast cancer	- 40% of the patients preferred phone - 30% Noona while 30% considered both modalities equally good. - For patient choosing Noona easiness to contact. No difference in quality of life, symptoms or patient satisfaction between the modalities. Compliance was 98%	-	https://ascopubs.org/doi/abs/10.1200/JCO.2018.36.15_suppl.e18883
OASIS (Oncology Associated Symptoms and Individualized Strategies)	Yes Web-based app (https://oasis.nursing.uiova.edu/AboutOasis) Monitoring platform to track symptom distress with educational information about cancer symptoms	Feasib. In progress	Adult potential system users from rural areas	- Easy to use; relevant content (patients and caregivers)	-	Gilbertson-White [64]	
	Yes Web-based PROMs completion targeting OOL domains	Yes Web-based app Provide self-management strategies for symptoms	56 patients; 57 caregivers; 9 HCPs	-	- Feasible; easy to use; relevant content		
Oncokompas	Yes Web-based PROMs completion targeting OOL domains	Feasib.	HCPs specialized in H&N cancer	-	- <i>Positive</i> : Favorable attitude of HCPs toward the eHealth application - <i>Negative</i> : Complex structure	Duman-Lubberding [65]	
	Yes Web-based PROMs completion targeting OOL domains	Feasib. Tailored advice and personalized referral to supportive care options based on PROM scores and expressed preferences.	11	-	- Feasible; high adoption and usage rates; good satisfaction with positive NPS	Duman-Lubberding [66]	
		Feasib.	Breast cancer survivors who had completed surgery ± CT and/or RT	- High adoption and usage rates; good satisfaction but negative NPS - Improved patient activation but no difference in patient-HCP communication	-	Melissant [67]	
		RCT in progress (Oncokompas vs Wait-list control)	Breast, colorectal, H&N cancer, or lymphoma survivors	-	-	Van der Hout [68]	

Table 1 (continued)

Digital solutions description		Study type ^a	N	Tumor type/inclusion criteria	Results	Reference
Name	Remote symptom monitoring (mobile, web, phone based)	Symptom management with patient automated self-management			Patients	HCPs
OWise	Yes Web-based app Physical and psychological symptom registration. Information regarding type of breast cancer. Diary and calendar. Question to ask to doctor.	Yes Web-based app Personalized information and support	Feasib.	Breast	- Symptom reporting was the least-used feature; improved patient-HCP communication - Increased well-being of patients	www.owise.uk
Oxford Telemedicine System	Yes Mobile app Patients were asked to enter twice a day their temperature and symptoms: nausea, vomiting, mucositis, diarrhea/bowel movements and hand-foot syndrome(CTCAE-based)	Yes ^{b,c} Mobile-based Self-care advice on their phone, directly related to their symptom. Nurses respond to alerts	Feasib.	Colon receiving adjuvant CT	- Reassuring; fast HCP response to alerts; patient empowerment. Overall correct generation of clinical alerts, with few false alerts generated due to missing data and poor connectivity to network - Feasible with amber alerts generated correctly; reassuring, feeling of less “bothersome” to HCPs; high compliance	Capable and confident with the system; no work overload due to alerts Capable and confident with the system; no work overload due to alerts
Pharmacist-run tele-oncology service for CINV monitoring	Yes Phone-based SMS system Patients’ CINV symptoms were monitored through short message service	Yes ^b Phone-based SMS system SMS advice and call from pharmacists for uncontrolled situation	Pilot	Colon receiving capecitabine	- Feasible and confident with the system; no work overload due to alerts	Larsen [70]
Phone- or Web-based system	Yes Phone- or Web-based Depression and pain follow-up	Yes ^b Phone- or Web-based Centralized telecare management by a nurse-physician specialist team coupled with automated home-based symptom monitoring by interactive voice recording or internet	Feasib.	Cancer patients receiving single-day moderate to highly emetogenic chemotherapy ^d	<i>Positive:</i> Feasible; rated highly useful; high compliance <i>Negative:</i> Dissatisfaction of patients who did not experience CINV; debatable usefulness	Yap [71]
Phone- or Web-based system	Yes Phone- or Web-based Depression and pain follow-up	Yes ^b Phone- or Web-based Centralized telecare management by a nurse-physician specialist team coupled with automated home-based symptom monitoring by interactive voice recording or internet	RCT	Various (solid and hematologic). Patients with cancer-related pain and depression	- Significant improvement in depression and pain severity; improved HRQOL, anxiety; fewer hospital days and ER visits; no difference in disability days, physical symptoms and healthcare/co-intervention use	Kroenke [72, 73]
Remote monitoring and treatment (RMT) application	Yes Phone-based Severity of and change in self-reported symptoms, well-being, and daily physical activity And wearable sensor-based with: (1) a symptom and physical activity monitoring (S&PAM) system, and (2) a	No Information accessible both for patients and HCPs via a Web portal	Feasib.	Primary lung cancer patients scheduled for curative lung resection	- Feasible; good usability, usefulness, and satisfaction	<i>Positive:</i> Favorable perception of the exercise program <i>Negative:</i> Low HCP perception of the added value of the symptom monitoring system

Table 1 (continued)

Digital solutions description		Study type ^a	N	Tumor type/inclusion criteria	Results	Reference
Name	Remote symptom monitoring (mobile, web, phone based)	Symptom management with patient automated self-management		Patients	HCPs	
SIS.NET (System for Individualized Survivorship Care)	web-accessible exercise program (WEP) with remote supervision by a physiotherapist Yes Web-based survey Scheduled cancer related visits to clinic. Online health questionnaires + evaluation of self-reported symptoms Short Form Health Survey (SF-36) and the 8-item Personal Health Questionnaire Depression Scale (PHQ-8), medical conditions, family history, Memorial Symptom Assessment Scale	No Notification to nurse practitioner, symptoms followed by phone as necessary	100	Breast cancer survivors	- More "new" or "changed" symptoms reported in the SIS.NET arm. No significant differences between arms in healthcare resource utilization Nurses addressed 74% of reported new or changed patients' symptoms within 3 days. Reasons for delayed response: 1) system malfunction; 2) problems contacting patients by phone	Whelock [75]
SyMon-L IVR system	Yes Phone-based Patients completed questionnaires and symptom surveys via interactive voice response weekly: fatigue, poor appetite, difficulty breathing, and treatment side effects, pain, cough, shortness of breath	No ^b (Email-based alert to HCPs in study arm) Patients' clinically significant symptom scores generated an email alert to the site nurse for management	153	Advanced lung	- No difference between groups in reducing symptom burden or in HRQOL - Feasible; high patient satisfaction and compliance in both groups	Yount [76]
SymptomCare@Home (SCH)	Yes Phone-based (land line) Patient has to call the automated telephone symptom-monitoring system daily: fatigue, pain, trouble in sleeping, nausea, vomiting...	Yes ^a Web-based decision support-symptom management system; phone-based (land line) immediate automated algorithms-based self-care -management tailored to the reported symptom prevalence and severity, coaching and HCP follow-up	358	Cancer patients receiving CT	- Monitoring and reporting of 11 symptoms - Significantly lower symptom severity, fewer days of moderate and severe symptoms - Fewer days of moderate and severe CT-induced peripheral neuropathy	Mooney [77] Kolb [78]
Telehealth self-management program for pain and fatigue	Yes Phone-based (telephone, text messaging) Reporting of distress related to pain and fatigue	Yes Paper-based with phone follow-up Self-management strategies	750	Cancer patients receiving CT	-	NCT 02779725
Telemonitoring system (Philips Healthcare)	No ^b Care team alert in case of severe symptom or abnormal blood telecommunication hub	No ^b Care team alert in case of severe symptom or abnormal blood	40	Cancer patients with previous patient-reported pain and/or fatigue	- Not feasible; low patient adoption Positive: Easy to use; acceptable to patients; high compliance rate;	Rocque [79] Nimako [80]

Table 1 (continued)

Digital solutions description		Study type ^a	N	Tumor type/inclusion criteria	Results		Reference
Name	Remote symptom monitoring (mobile, web, phone based)				Symptom management with patient automated self-management	Patients	
TRSC (Therapy-Related Symptom Checklist for Adults) and TRSC-C (for children)	Patients were asked to analyze their own blood (capillary) and to enter temperature and symptoms and severity (based on CTCAE) for fatigue, nausea, vomiting, diarrhea, sore throat, rash and pain	vs Hospital laboratory standard)	282 adults; 385 children	Various	overall correct generation of clinical alerts - <i>Negative</i> : Difficulty of device use; measurements not performed as planned. However, good clinical correlation between the system and laboratory standard - High satisfaction - High satisfaction; no increase in costs	Williams [81]	
Web-based app for management of postoperative symptoms	Yes Web-based with interactive voice response telephone Data collection through questionnaires. Conversational data collection, short response phrases indicating understanding of the reported symptom, use of open-ended questions, directed questions, review of symptoms at designated stages	Feasib. (App vs App + reminders [email or SMS])	35	Patients with gynecologic cancer scheduled for open surgery	- Feasible; high recruitment and completion rates; higher use in the app + reminder arm - For HRQOL, higher mental health scores and lower physical health scores in the app + reminder arm - Symptom distress significantly lower in WebChoice arm. Better self-efficacy, HRQOL, depression, and social support with WebChoice - Use of WebChoice in 63.6% of patients. Higher usage associated with a high level of computer experience and lack of comorbidities	Graetz [82]	
WebChoice	Yes Web-based application (www.communicatetools.org). Patients could monitor their symptoms, problems, and priorities for support in physical, functional, and psychosocial dimensions	RCT (WebChoice vs Information sheet with public cancer-related websites) Post hoc analysis of RCT (Ruland [45])	325	Breast and prostate	- WebChoice vs usual care: Reduced symptom distress, anxiety, and depression; - IPPC vs usual care: Reduced depression with IPPC	Ruland [83]	
	Yes Appropriate individually tailored information and self-management activities + access to other reliable Web sources, e-forum for group discussion with other patients, e-communication with expert cancer nurses	RCT (IPPC vs WebChoice vs usual care)	167	Breast	- WebChoice vs usual care: Reduced symptom distress, anxiety, and depression; - IPPC vs usual care: Reduced depression with IPPC	Børnsund [85]	

Table 1 (continued)

Digital solutions description		Study type ^a	N	Tumor type/inclusion criteria	Results	Reference
Name	Remote symptom monitoring (mobile, web, phone based)	Symptom management with patient automated self-management			Patients	HCPs
Web portal for physical activity and symptom tracking	Yes Web-based and linked to a wearable activity monitor device Collection of PROs and symptom information, symptom and health related QoL tracking	Yes Web-based Provision of educational material, and individualized coaching messaging. Remote monitoring of physical activity for patient and clinician	49	Various	- Feasible. Highest compliance when access to Web portal was accompanied by weekly activity reports and personalized coaching messaging	Marthick [86]

^a For RCTs, the digital health tool was compared with usual care, unless otherwise specified

^b System alerts to HCPs generated if clinically relevant symptoms were reported

^c Red alerts for severe side effects; amber alerts for less-severe symptoms

^d Defined by the National Comprehensive Cancer Network antiemesis guidelines v.1.2011.AE, adverse event

ASyMS Advanced Symptom Management System, CINV chemotherapy-induced nausea and vomiting, CT chemotherapy, CTCAE Common Terminology Criteria for Adverse Events, EHR electronic health record, ER emergency room, Feasib, feasibility, H&N head and neck, HCP healthcare professional, HRQOL health-related quality of life, IPPC internet-based patient-provider communication, misc. miscellaneous, N/A not applicable, NCI National Cancer Institute, NPS net promoter score, OS overall survival, PC personal computer, PROs patient-reported outcomes, PROMs patient-reported outcome measures, RCT randomized controlled trial, RT radiotherapy, SMS short message service

Fewer studies have assessed the feasibility of digital solutions from the HCP perspective. The most important reasons for adoption reported by HCPs were the usability and usefulness of the tool [26, 38, 52, 58], and the most commonly reported barrier was problems with technology or connectivity [31, 75].

Interestingly, while some tools were perceived as a burden due to increased workload [28], others did not impact the working time of HCPs [69, 85].

Impact on clinical assessment

Most studies presented ePRO data, including symptom distress and burden, pain, depression, and adherence.

A meta-analysis of 9 studies reported a statistically significant benefit for digital interventions in patients with cancer-related fatigue, with moderate benefits also observed for QOL and depression [45].

Several studies showed a significant reduction compared with usual care in symptom-related distress on the basis of measures that included Short-Form (SF)-36, Memorial Symptom Assessment Scale (MSAS), Symptom Distress Scale-15 (SDS-15), and Functional Assessment of Cancer Therapy-Head & Neck Scale (FACT-HN) [36, 40, 45, 47, 50, 78, 85]. Symptom benefit was observed in conjunction with automated home or Web-based symptom self-management systems.

Studies also reported a reduction in depression [73, 85], symptom severity [33, 53], pain [43, 56, 73, 77], and need for symptom management support [40].

An RCT enrolling 766 patients with solid tumors receiving outpatient chemotherapy demonstrated that self-reporting of 12 common cancer-related symptoms led to significant improvement in QOL, as measured by the EuroQol EQ-5D Index [8].

Two studies used the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC-QLQ-C30) for QOL assessment [43, 52]. One of these used the EORTC-QLQ-C30 and the Hospital Anxiety and Depression Scale (HADS) as an intervention, with a larger proportion of patients who reported these measures to their oncologists showing clinically meaningful improvements in QOL compared with a control group, despite no detectable changes in patient management [52].

An RCT evaluating the impact of an internet-based exercise intervention reported significant improvement in EORTC-QLQ-C30 scores for global health status, physical, role, and cognitive functioning, together with improvements in pain severity on the Brief Pain Inventory compared with control [43].

In another study of a Web-based intervention, the addition of self-care instructions and communication coaching to Electronic Self-report Assessment–Cancer (ESRA-C) of

symptoms and QOL resulted in significant increase in reporting fatigue, pain, and physical function issues. However, differences between groups in symptom distress reported by patient did not reach significance [46].

Finally, a report found benefit for patient QOL, including increased symptom identification and management, and improved functional status following electronic collection of Therapy-Related Symptom Checklist for Adults (TRSC) [81].

Impact on survival

A prospective study compared survival in patients with lung cancer who were assigned to weekly symptom self-reporting via a Web application intervention for early detection of relapse with a retrospective group of control patients [60]. Median OS was improved for the patients assigned to the intervention compared with the historical control arm.

Survival outcomes were also reported in 2 RCTs. A single-center trial reported that integration of ePROs into the routine care of patients with metastatic cancer led to increased survival compared with usual care [7]. At a median follow-up of 7 years, median OS was 31.2 months (95% CI, 24.5–39.6) in the group that provided self-report of 12 common symptoms, with severe or worsening symptoms triggering an email alert and follow-up care by a nurse practitioner with escalation as needed. In comparison, median OS in the group assigned to usual care was 26.0 months (95% CI, 22.1–30.9; difference, 5 months; $P = .03$). In patients with advanced lung cancer, a multicenter study reported that intervention involving a Web-based follow-up algorithm to assess weekly patient symptom self-reports compared with routine follow-up resulted in median OS of 19.0 (95% CI, 12.5–noncalculable) and 12.0 months (95% CI, 8.6–16.4), respectively ($P = .001$) [61]. In addition, the performance status at first relapse was 0 to 1 for 76% of patients in the intervention arm compared with 33% in the control arm (2-sided $P < .001$); anticancer treatment was considered to be optimal in 72% and 33%, respectively (2-sided $P < .001$). In the final OS analysis for this study, median OS was 22.5 months in the intervention group and 14.9 months in the control group (hazard ratio, 0.59 [95% CI, 0.37–0.96]; $P = .03$) [87].

Impact on ER admissions, hospitalizations, and healthcare resource utilization

The effect of digital solutions on the number of ER visits, hospital days, or utilization of healthcare resources is not commonly evaluated in clinical studies. Some solutions, involved in patient monitoring providing or not providing feedback for self-management, have been associated with a reduction in ER visits, unplanned hospitalizations, and hospital days [8, 35, 73]. Additionally, use of a telehealth system for rehabilitation of patients with head and neck cancer following chemo-

radiotherapy resulted in fewer and shorter appointments until discharge compared with usual care and was accompanied by a significant cost-reduction for patients, specifically in travel costs [51]. On the contrary, one study using a Web-based intervention that included review by a nurse practitioner found no differences compared with control with respect to healthcare resource use, including oncology-related appointments, number of physician visits, or medical tests [75]. The effect of digital solutions on overall healthcare costs needs further assessment [8, 35, 73, 75].

Clinical benefits and limitations of the digital solutions for stakeholders

Benefits and limitations of introducing a patient-management solution in oncology, according to stakeholders of digital

solutions in the healthcare system, are summarized in Table 2 and illustrated in Fig. 3. These benefits and limitations were identified in the selected publications and from the authors experience and opinion. Lots of benefits have been identified of important impact on all stakeholders (patients, physicians, caregivers, nurses, healthcare system, pharmaceutical company), with limitations related to technical dealing, regulatory constraints, costs, and changes in practices.

Discussion

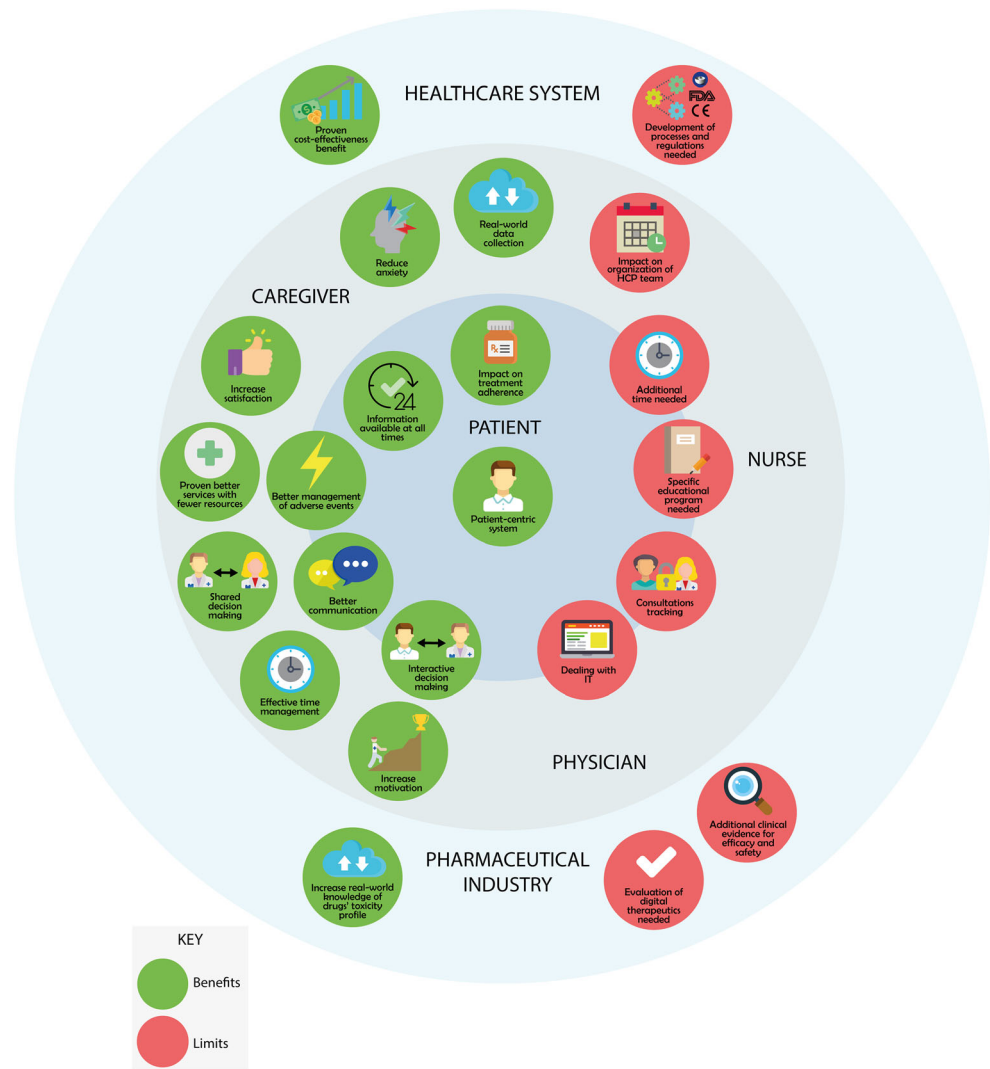
Although the clinical benefits of remote patient monitoring have been demonstrated in clinical trials [7, 62], achieving optimal supportive care requires strategies that go beyond ePRO apps/systems. Such benefits are not obtained solely

Table 2 Benefits and limitations of digital healthcare solutions for stakeholders

Stakeholder	Benefits	Limitations
Patients	<ul style="list-style-type: none"> - Promote patient-centricity - Direct communication with HCPs - Closer involvement in the decision-making process - Impact on treatment-adherence - Information from clinical visits always available - Relevant disease- and treatment-related information always available - Less recourse to generic Web consultation without scientific content 	<ul style="list-style-type: none"> - Difficulty in dealing with technology - Need for specific education and training - Time-consuming - Uncomfortable asking clinicians for permission to record clinical visits - Depersonalization
Physicians	<ul style="list-style-type: none"> - Improved communication with patients - Shared decision-making by involving patients in the process - Real-world data collection in real time - Optimal management of toxicities in real time • Increased motivation thanks to visible improvements - Effective time-management • Time saving in the analyses of patients' data • Contact patients only when clinically relevant situations occur - Focused supportive care - Less healthcare resource utilization 	<ul style="list-style-type: none"> - Difficulty in dealing with technology - Need for specific training to ensure engagement - Time dedicated outside of consultation hours - Changes in the organization of HCP teams - Difficulty in changing usual practices of symptom management
Nurses	<ul style="list-style-type: none"> - Effective time-management • Time saving in the analyses of patients' data • Contact patients only when clinically relevant situations occur - Increased quality of services with less healthcare resource utilization - Improved patient-nurse communication 	<ul style="list-style-type: none"> - Difficulty in dealing with technology - Need for specific training to ensure engagement - Time dedicated to educating and inform patients and caregivers - Additional time allocated outside patients' visits
Caregivers	<ul style="list-style-type: none"> - Reduced burden and anxiety - Increased satisfaction 	<ul style="list-style-type: none"> - Difficulty in dealing with technology - Need for specific education and training
Healthcare system	<ul style="list-style-type: none"> - Impact of preventive care in healthcare costs. Cost-effectiveness benefits • Reduction in ER visits, wait time in ER, transportation costs • Reduction in unplanned visits and hospitalizations • Impact on the working time of physicians, nurses, ER personnel • Reduction in medication cost • Prevention and treatment of AEs more consistent with guidelines 	<ul style="list-style-type: none"> - Need for development of processes and regulations for homologation of digital solutions by regulatory agencies - Formation and training of dedicated teams for evaluation - Delays in cost-effectiveness analyses for the implementation of reimbursement policies, resulting in impeded access to patients
Pharmaceutical industry	<ul style="list-style-type: none"> - Real-world data and increased knowledge of the toxicity profile of drugs - Development of plans for improved management of AEs - Expedited approval of drugs when filing in combination with digital solutions 	<ul style="list-style-type: none"> - Additional studies with the drug + digital solution combination needs to be performed, to generate clinical evidence of efficacy and safety to support filing: increased time and cost

AE adverse event, *ER* emergency room, *HCP* healthcare professional

Fig. 3 Benefits and limitations of digital solutions in the healthcare system. FDA US Food and Drug Administration, HCP healthcare professional, IT information technology



through the assessment of outcomes of interest but also through appropriate management in response to assessments. Even if benefits have been confirmed in the setting of RCTs, there is a need to continue to evaluate ePRO efficacy and efficiency in real-world conditions, with ongoing assurances of data security and privacy, to provide relevant information for optimal self-management.

Several factors need to be considered for a high-quality symptom self-management system. Guidance from the treating physician is critical. Electronic self-reported assessment tools for cancer-related symptoms and QOL can increase communication between patients and HCPs and promote discussion that is focused on symptoms and QOL. Digital tools that give advice to patients on the reporting of symptoms to HCPs have been shown to increase symptom reports by patients during visits. However, these have not been shown to impact practitioner responses, indicating that guideline adherence and commitment by the medical team is also needed. The collection of information regarding related clinical symptoms

and the medication received requires integration with electronic real-time monitoring of symptoms into oncologists' routine clinical practice. When real-time monitoring is used, beneficial outcomes in terms of symptom management have been identified [88], with the potential for further optimization when structured patient education or practitioner-/nurse-led symptom counseling is in place. Optimization of digital tools requires integration with the patients' EHRs, thereby allowing continuity in the flow of patient-related data and the healthcare support systems.

Digital health solutions need to be integrated into the patient pathway and in healthcare team practices for optimal supportive care in oncology in line with appropriate guidelines. How this integration is implemented is debatable, with consideration given as to whether the digital tool is merged into current healthcare systems in a gradual or disruptive manner. The European Society for Medical Oncology (ESMO) has developed a Magnitude of Clinical Benefit Scale (ESMO-MCBS) to assess the extent of the clinical benefit from new and effective



Fig. 4 Ideal digital health solution

anticancer therapies measuring improvement in survival, disease-free survival, response, grade 3–4 toxicities, and QOL measures [89]. MCBS-based assessment of the digital tools as part of anticancer therapies and the use of MCBS for the development of clinical guidelines would ease this integration.

There are challenges in the development of a digital solution for supportive care of cancer patients. Setting up and conducting clinical trials for the evaluation of digital tools is a long process, especially because digital solutions need to be quickly available for evaluation in real-world settings. The principal difficulties are in developing and implementing a solution to fit the needs of all or most patients, while achieving the necessary patient compliance to change with the new digital tool and integrate it into care and maintaining enough adaptability for its use in different regulatory systems and healthcare centers. Implementation may be associated with challenges in staff having to deal with new technologies, accepting and adapting to changes, and the potential for

reorganization of multidisciplinary teams/treatment centers. Maintenance of the device may also introduce complexity since device utility is dependent on updates in accordance with relevant guidelines, as well as drug safety information, approval of new drugs, and the use of different drugs from the same class. Oncologic therapy is by its nature complex, with sequential phases, and device utility will need to reflect the use of different antitumor regimens, including radiotherapy and radio-chemotherapy, and combination of drugs. Uptake of the technology may be dependent on oncologist perceptions of patients' willingness to adopt new technologies, as well as the actual willingness of patient subgroups, particularly elderly patients, to embrace digital solutions. Finally, digital solutions should be perceived as facilitators of in-person communication between patient and practitioner.

This review offers elements for scoping digital solution based on feasibility studies on limited level of evidence or still limited numbers of patients evaluated on RCT.

Outlook for the future

Several clinical studies have already demonstrated reliability, feasibility, and clinical value (various symptoms, QOL, and OS) with efficacy of ePRO collection through digital solutions. The ideal digital solution in the setting of supportive care in oncology would present with the following characteristics (Fig. 4): it would be user-friendly, intuitive, and engaging to meet the immediate needs of the end-users; it would also be efficient at processing and delivering relevant information to provide supportive care as its principal aim. In thinking about its place in the supportive care setting, the ideal digital solution is not intended as a replacement for the practitioner; rather, its intended value would be in providing additional information that is appropriate to the care of the patient and the specific issues associated with their disease in real time. This information would be sufficiently detailed but not overcomplicated and presented in a language the patient understands in order to be accessible by the patient for effective symptom self-management [90]. The digital solution would maintain existing expectations regarding patient confidentiality and data privacy [91], cybersecurity, compliance with regulatory requirements, and being updated according to the most recent evidence-based practice. It would be operational throughout the entire course of the disease and for all anticancer treatments. Its built-in flexibility would enable adaptation of the digital tool to all territories, institutions, and centers and to all different care needs according to whether treatment is delivered in the community or at a regional center, such that it also serves patients who live in remote areas. It would be customizable to adapt to the needs of the individual patient. It would have a seamless connection with HCPs' systems. Integration with patients' EHR would allow for rapid follow-up and intervention as appropriate by HCPs in response to system alerts triggered by patient reports of clinically relevant events. It would have a high level of acceptance both by HCPs and patients, allowing its complete adoption and full integration in the patient pathway and in routine clinical practice. For digital solutions with proven clinical and cost benefits, reimbursement policies would be in place to ensure availability for implementation through defined market access programs. Finally, the ideal digital solution would not only provide the means for patient self-management of anticancer treatment-related symptoms but would also provide psychosocial support and improve QOL. Although a single system would not be able to address all needs—treatment adherence, symptom management, alignment with guidelines, medication reminders, medical and nutritional information, resources for social support, and coping strategies—it is important that digital tools find common ground, with solutions offered to address key challenges in the setting of supportive care in cancer.

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