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Can mHealth interventions improve quality of life of cancer patients? A systematic review and meta-analysis

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ABSTRACT

mHealth can be used to deliver interventions to optimize Health-related quality of life (HRQoL) of cancer patients. In this systematic-review and meta-analysis, we explored the possible impact of health interventions delivered via mHealth tools on HRQoL of cancer patients. The systematic literature search was performed on July 20, 2019, to identify studies that evaluated the impact of mHealth intervention on HRQoL of cancer patients. We identified 25 studies (17 randomized controlled trials and 8 pre-post design studies; 957 patients) that evaluated mHealth interventions. The most commonly studied mHealth interventions included physical activity/ fitness interventions (9 studies), cognitive behavioral therapy (6 studies), mindfulness/ stress management (3 studies). In the majority of studies, mHealth interventions were associated with an improved HRQoL of cancer patients. The meta-analysis of the identified studies supported the positive effect of mHealth interventions for HRQoL of cancer patients. mHealth interventions are promising for improving HRQoL of cancer patients.

1. Introduction

mHealth technologies have become promising to improve health monitoring and delivery of health interventions. While no standardized definition has been established, the World Health Organization (WHO) defines mHealth as "*medical or public health practice that is delivered with supports of mobile phones, patient monitoring devices, and other wireless devices*" (WHO Global Observatory for eHealth, World Health Organization, 2011). The number of available mHealth applications is growing with approximately 200 new mHealth applications added to app stores each day (The Rise of mHealth Apps: A Market Snapshot [Internet], 2018). However, the lack of evidence of clinical efficacy of mHealth interventions raises valid doubts and skepticism among healthcare professionals as not all apps are developed by teams that include clinicians, adhere to treatment guidelines, or have regulatory approval (Kumar et al., 2015). Despite the lack of regulation and other potential barriers to adoption, such as concerns about privacy or inaccurate information, mHealth apps are a rising technology.

Advancement in early diagnosis, treatment strategies and life expectancy has resulted in a progressively increasing number of long-term cancer survivors (Allemani et al., 2018). Health-related quality of life (HRQoL) is a multifactorial construct that pertains to patients' perception across physical, social, mental, and functional domains. Poor HRQoL is associated with worse prognosis of cancer patients (Montazeri, 2009). Preservation of HRQoL is important in the management of cancer patients and it is commonly used as a secondary outcome measure in clinical trials (Bottomley et al., 2016).

mHealth interventions in patients with cancer is under-studied albeit high-priority area of research. We aimed to systematically review studies that investigated the possible impact of health interventions delivered via mHealth tools on the HRQoL of patients with cancer and to pool the reported results from the original studies in a meta-analysis, when feasible.

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2. Methods

A systematic review of the literature followed by a meta-analysis was implemented in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement (Moher et al., 2009).

2.1. Data sources and search strategy

The systematic search was performed on July 20, 2019, with the goal of identifying published studies that evaluated the association between mHealth intervention and HRQoL of patients with established cancer diagnosis or cancer survivors. Articles were identified from the Pubmed/ MEDLINE and Web of Knowledge databases (for details see Appendix A). Original research papers performed in humans and with their full texts available in English were considered for the review. Randomized controls trials (RCT) and observational studies were both considered for inclusion. Studies that did not provide research results in cancer patients, studies that evaluated interventions delivered via telephone (i.e., telehealth), and studies that evaluated HRQoL using non-validated scales were excluded.

2.2. Study selection and data extraction

Initial literature analysis was performed by reviewing titles and abstracts of identified papers. Literature analysis was performed by two authors (IB and AB) and disagreements were resolved via discussion. The following variables were extracted from each full text article: year and country of publication, cancer type, sample size, patients' age and gender, presence of control subjects, study design, study timing, mHealth intervention type, intervention duration, questionnaires that were used for assessment of HRQoL, study completion rate, and major study findings.

2.3. Data analysis

Two types of results were reported and analyzed separately. For studies that reported HRQoL change in the intervention group and the control group, a difference in mean scores comparing the treated arm to the control arm was calculated for each study. As for the studies that reported data on at least the treatment arm, the mean change in HRQoL was calculated in the treated arm before vs. after mHealth intervention. Both types of results were then pooled separately using the random-effects model by the DerSimonian and Laird method (DerSimonian and Kacker, 2007), which takes into account within- and between-study variances. Forest plots were used to visualize summaries of individual studies and the pooled estimates. Cochrane Q test (p-level of significance set at 0.1) along with the I^2 value (Higgins and Thompson, 2002; Huedo-Medina et al., 2006) were used to assess between-study heterogeneity. An I^2 value >50 % was generally considered to be high (Higgins et al., 2003). In an effort to minimize heterogeneity sources, pooled results were stratified by questionnaire type (EORTC global health; SH-36 General; FACT-G). When feasible, further stratification within each questionnaire type was conducted by intervention type (cognitive behavioral therapy/ behavioral change; physical activity/ fitness; social support; weight management). A new I^2 value was calculated for each subgroup. In an attempt to have an overall pooled estimate of the efficacy of mHealth on quality of life from the comparative studies that provided data on both arms, a standardized difference in means was calculated for each of these original studies and was stratified by questionnaire type. Unless otherwise specified, a two-sided p-value <0.05 was considered statistically significant. All analyses were performed using Comprehensive Meta-Analysis (version 3).

2.4. Bias and quality assessment

The quality of RCTs and pre-post design studies was assessed using the Cochrane Collaboration' risk of bias tool (Higgins et al., 2011). This tool rates 7 domains as having a low, unclear, or high risk of bias. These domains consist of sequence generation, allocation concealment, participants' and study personnel's blinding; outcome assessment blinding; outcome data completeness; selective outcomes' reporting; and other threats to validity, including intervention contamination, baseline imbalance, and carry-over effect in cross-over trials). Because there were fewer than 9–10 studies per specific outcome within each questionnaire type, publication bias assessment was not possible (Egger et al., 1997).

3. Results

Twenty-five studies evaluated the impact of different interventions delivered via mHealth on HRQoL in patients with cancer (Fig. 1 and Table 1). The majority of studies (n = 9) were from the USA, Europe (n = 8) and Asia (n = 7). Sample sizes ranged from 18 (McCarthy et al., 2018) to 409 patients (Willems et al., 2017). Mean (or median) age of study participants ranged from 17 years (Mendoza et al., 2017) to 69 years (Hong et al., 2015). The intervention duration ranged from 30 days (Graetz et al., 2018) to 12 months (Ferrante et al., 2018).

We identified 17 RCTs (Willems et al., 2017; Mendoza et al., 2017; Graetz et al., 2018; Ferrante et al., 2018; Admiraal et al., 2017; Compen et al., 2018; Frensham et al., 2018; Galiano-Castillo et al., 2016; Greer et al., 2019; Ham et al., 2019; Ji et al., 2019; Kubo et al., 2019; Rosen et al., 2018; Uhm et al., 2017; Urech et al., 2018; Yang et al., 2019; Zhu et al., 2018) and 8 pre-post design studies (Børøsund et al., 2019; Cheong et al., 2018; Lozano-Lozano et al., 2019; McCarroll et al., 2015; Pappot et al., 2019; Park et al., 2019; Pope et al., 2019; Trinh et al., 2018). Nine studies (5 RCTs and 4 pre-post designs) tested physical activity / rehab / fitness interventions (Mendoza et al., 2017; Frensham et al., 2018; Galiano-Castillo et al., 2016; Ji et al., 2019; Uhm et al., 2017; Cheong et al., 2018; Lozano-Lozano et al., 2019; Park et al., 2019; Trinh et al., 2018), six studies – CBT interventions (4 RCTs and 2 pre-post designs) (McCarthy et al., 2018; Willems et al., 2017; Compen et al., 2018; Greer et al., 2019, 2019; Ham et al., 2019; Børøsund et al., 2019), three studies - mindfulness/stress management interventions (3 RCTs) (Kubo et al., 2019; Rosen et al., 2018; Urech et al., 2018), two studies - social support (1 RCT and 1 pre-post design) (Zhu et al., 2018; Pappot et al., 2019), two studies - information/psychoeducation (2 RCTs) (Graetz et al., 2018; Admiraal et al., 2017), two studies – weight management (1 RCT and 1 pre-post design) (Ferrante et al., 2018; McCarroll et al., 2015), and one study assessed a pain management intervention (1 RCT) (Yang et al., 2019).

The most commonly used HRQoL assessment questionnaires were the European Organization for Research and Treatment (EORTC; 10 studies) and the Functional Assessment of Cancer Therapy (FACT;7 studies).

The majority of studies (15 RCTs and 7 pre-post designs) found that mHealth interventions were associated with improvement in at least one domain of HRQoL of cancer patients (Willems et al., 2017; Graetz et al., 2018; Ferrante et al., 2018; Compen et al., 2018; Frensham et al., 2018; Galiano-Castillo et al., 2016; Greer et al., 2019, 2019; Ji et al., 2019; Kubo et al., 2019; Rosen et al., 2018; Uhm et al., 2017; Urech et al., 2018; Yang et al., 2019; Zhu et al., 2018; Børøsund et al., 2019; Cheong et al., 2018; Lozano-Lozano et al., 2019; McCarroll et al., 2015; Pappot et al., 2019; Park et al., 2019; Trinh et al., 2018).

3.1. Qualitative review of the studies by outcome type

3.1.1. Physical activity/ fitness

Galiano-Castillo and colleagues randomized 81 women with breast cancer to an 8-week Internet-based, tailored exercise program (*e-CUIDATE*) or to a control group that received written recommendations for

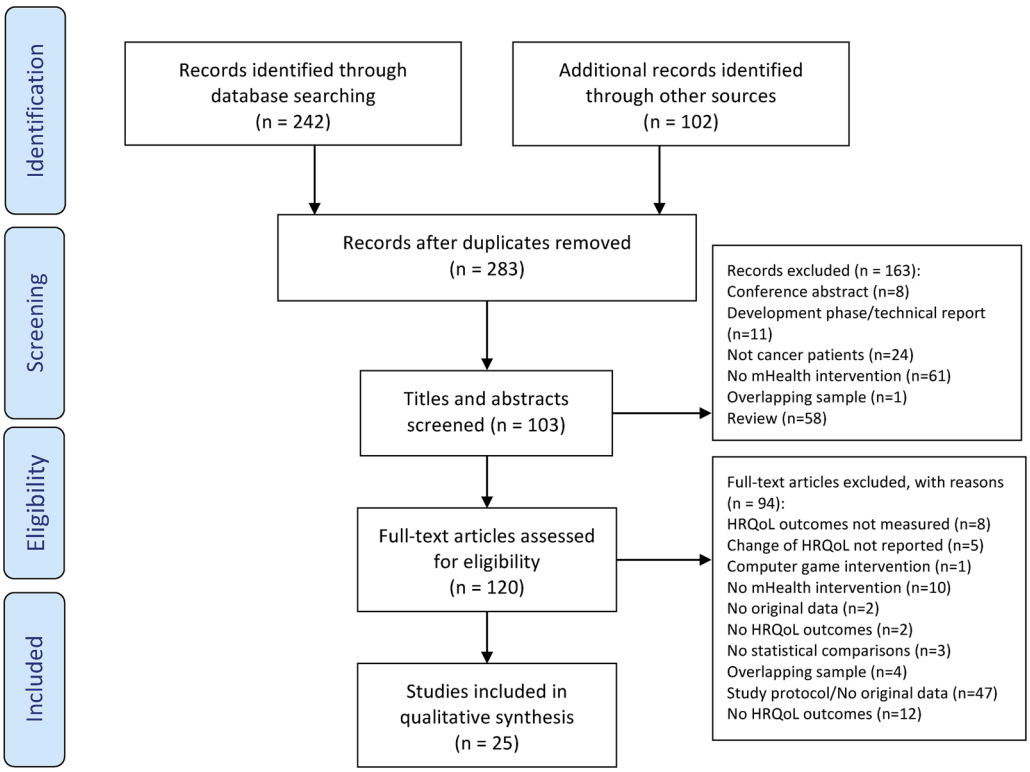

Fig. 1. PRISMA flow-chart.

exercise (Galiano-Castillo et al., 2016). The intervention was associated with improved scores on the EORTC-QLQ-C30 global health status, physical, role, and cognitive function as opposed to the control group. Uhm and colleagues (2017) randomized 356 breast cancer patients to either an mHealth regimen of aerobic and resistance training exercise program (newly developed application) coupled with a pedometer or to a control group who received an exercise brochure (Uhm et al., 2017). They found significant improvements across all EORTC QLQ-C30 and QLQ-BR 23 subscales with the exception of insomnia, appetite, constipation, body image, and sexual enjoyment domains in both the mHealth intervention and the control groups without any significant between-group differences. In another RCT, 64 patients with non-small cell lung cancer were randomized to either an mHealth personalized pulmonary rehabilitation program or a fixed exercise regimen (control group) (Ji et al., 2019). The EuroQoL visual analog scale score improved in both patient groups, without significant between-group differences. Similarly, an RCT in patients with different cancer types found improved SF-36 mental health, general health, and social functioning scores, but a worsened SF-36 bodily pain score in patients randomized to either a walking intervention (*STRIDE* online resource) or a control group, irrespective of group allocation (Frensham et al., 2018). Conversely, another RCT compared wearable physical activity tracking devices coupled with *Facebook* peer-based virtual support group (mHealth intervention group) to usual care (control group), which consisted of clinical advice on physical activity as per the providers' discretion in 59 teenagers who were cancer survivors for ≥1 year. mHealth intervention was associated with a decrease in the social functioning score (Mendoza et al., 2017).

A pre-post study used a mobile application and a wearable device that included a rehabilitation exercise program and information on the disease and treatment of 102 colorectal cancer patients undergoing chemotherapy (Cheong et al., 2018). After 12 weeks, there was an improvement in the EORTC symptoms of fatigue and nausea/ vomiting. A study in lung cancer patients found that physical rehabilitation program delivered via a mobile application was associated with improved scores on the ERTC-QLQ-C30 role, emotional and social functioning, fatigue, appetite, and diarrhea symptom subscales (Park et al., 2019). Another pre-post study found that the 12-week intervention that included a Web-based application combined with wearable accelerometer and activity tracker was associated with improved emotional well-being domain of the FACT-G (Trinh et al., 2018). Finally, a healthy eating and physical activity feedback app (BENECA) administered to 80 overweight or obese breast cancer patients improved global health perception, physical, emotional, cognitive and social functioning domains, in addition to fatigue dyspnea and insomnia symptom severity, as evaluated by the EORTC-QLQ-C30 questionnaire (Lozano-Lozano et al., 2019).

3.1.2. *Weight management*

In an RCT of African American breast cancer survivors, all study participants received a physical activity tracker (Fitbit Charge) and were randomized to either an intervention (commercially available *Spark-People* app) or a waitlist control (Ferrante et al., 2018). When compared to the control group, the intervention group participants achieved a significantly greater improvement in the HRQoL at 6 months as measured by the Quality of Life in Adult Cancer Survivors Scale (QLACS) scale, albeit the difference was not statistically significant at 3 months. In a pre-post design study of 50 overweight or obese breast or endometrial cancer, survivors tested a "beta" healthcare provider version of Web and mobile based application *LoseIt!* (Boston, MA) (McCarroll et al., 2015); there were no significant differences in FACT-G scores at 4 weeks when compared to baseline.

3.1.3. *Cognitive behavioral therapy (CBT)*

In women with incurable cancer and with elevated anxiety symptoms, a tablet-delivered CBT program (intervention) and health education program (control group) delivered via tablet computers were associated with a significant improvement in the FACT-General questionnaire scores, yet without a statistically significant between-group differences (Greer et al., 2019). Ham and colleagues found a similar

Table 1
Studies that evaluated the association of mHealth interventions with HRQoL of cancer patients.

Ref.	Country	Population	Sample size / Gender / Age	Study design	Intervention / number of patients	Control group / number of patients	Intervention duration	Health related quality of life measures	Completion rate	Major findings
Physical activity / fitness (9 studies)										
(Galiano-Castillo et al., 2016)	Spain	Breast cancer	81 / all women	RCT	Internet-based, tailored exercise program (e-CUIDATE) / n = 40	Written recommendations for exercise / n = 41	8 weeks	EORTC QLQ-C30	94%	Intervention group had improved scores for global health status, physical, role, cognitive functioning, relative to control group
(Uhm et al., 2017)	Korea	Breast cancer	356 / all women/ 50 ± 9 years	RCT	Podometer and app to provide information and monitoring / n = 179	Exercise brochure / n = 177	12 weeks	EORTC-QLQ-C30 and EORTC QLQ-BR 23	95 %	Improvement of HRQoL in both groups, without between group differences
(Ji et al., 2019)	Republic of Korea	Non-small cell lung cancer	64 / 70 % men/ range: 20–80	RCT	Personalized pulmonary rehabilitation program (efil breath) / n = 32	Fixed exercise / n = 32	12 weeks	EuroQol- 5D and VAS	67 %	Improved EurQoL-VAS score in both groups without between-group differences
(Frensham et al., 2018)	Australia	Different types of cancer	91 / 52 % women / 29–86 years	RCT	Waking intervention (STRIDE, Steps Toward Improving Diet and Exercise) online resource	Waitlist-control	12 weeks	SF-36	100%	Improved mental health, social functioning, and general health in both groups; yet, an increase in bodily pain in both groups
(Mendoza et al., 2017)	USA	Different cancer types	59 / 59 % girls / 17 ± 2 years (range: 14–18)	RCT	Wearable physical activity tracking device (Fitbit Flex) and peer-based virtual support group (Facebook group) / n = 29	Usual care / n = 30	10 weeks	PedsQL 4.0 Generic Core and Cancer Module	Days wearing tracking device: 71.5 %, Facebook group engagement: 89.7 %	Intervention was associated with decreased score on PedsQL social functioning scale.
(Cheong et al., 2018)	South Korea	Colorectal cancer	102 / 41 % women/ 58 ± 12 years	Pre-post	Wearable device and application that included rehabilitation exercise program and information on their disease and treatment	None	12 weeks	EORTC-C30	74 %	Improved EORTC symptoms of fatigue and nausea/vomiting.
(Park et al., 2019)	Republic of Korea	Lung cancer	90 / 54 % women / 55.1 ± 8.7 years	Pre-post	App delivered physical rehabilitation program (Smart Aftercare app)	None	12 weeks	EORTC QLQ-C30	90%	Improved role, emotional and social functioning, fatigue, appetite, diarrhea
(Trinh et al., 2018)	Canada	Prostate cancer	46 / all men / 73.2 ± 7.3 years	Pre-post	Accelerometer, wrist-worn activity tracker and Web based application	None	12 weeks	FACT-General	91 %	Improved emotional well-being
(Lozano-Lozano et al., 2019)	Spain	Breast cancer (Overweight/ obese)	80 / all women / age 59 ± 9 years	Pre-post	Healthy eating and physical activity feedback app (BENECA)	None	8 weeks	EORT QLQ-C30	73 %	Improved global health, physical, emotional, social and cognitive functioning, fatigue, dyspnea, insomnia
Cognitive behavioral therapy / behavioral change (6 studies)										
(Greer et al., 2019)	USA	Incurable cancer (patients with high anxiety)	145 / 74 % women / mean age: 56 ± 11 years	RCT	CBT (tablet based)	Health education program	12 weeks	FACT-G	–	QOL improved in both patient groups.
(Ham et al., 2019)	South Korea	Different cancer types	63 / 52 women / age range 20–65 years	RCT	Mobile-application-based CBT (*HARUToday*) / n = 21	Waitlist control group (n = 21) and attention control group (n = 21)	10 weeks	SF-36	73 %	No significant changes in SF-36 score
(Compen et al., 2018)	Netherlands	Different cancer types and	245 / 86 % women / 51.7 ± 10.7 years	RCT		Treatment as usual and Face-to-Face	8 weeks	SF-12 (mental and	70 %	Both eMBCT and face-to-face MBCT improved

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Table 1 (*continued*)

Ref.	Country	Population	Sample size / Gender / Age	Study design	Intervention / number of patients	Control group / number of patients	Intervention duration	Health related quality of life measures	Completion rate	Major findings
		psychological distress			Internet-based mindfulness-based cognitive therapy (eMBCT)	mindfulness based cognitive therapy (MBCT)		physical scales)		mental health, but not physical health compared to usual care.
(Willems et al., 2017)	Netherlands	Different cancer types	409 (who completed) / 81 % women / 56 years	RCT	Web-based intervention according to CBT /PST principles	Waiting list control / n = 231	6 months	EORTC QLQ-C30	89%	Intervention was associated with improved emotional and social functioning
(Børøsund et al., 2019)	Norway	Different cancer types	25 / 84 % women / mean 48 years (range: 34–71)	Pre-post	App-based cognitive-behavioral stress management (*Stress Proffen*)	None	8 weeks	SF-36	67 % completed at least 7 out of 10 modules	Significant improvement of physical, general health, vitality, and emotional aspects of QoL,
(McCarthy et al., 2018)	USA	Breast cancer	18 / all women / 57.7 ± 6.5 years	Pre-post	CBT for insomnia intervention via Internet videoconference	None	6 weeks	EORTC QLQ-C30	100%	Global EORTC QLQ-C30 improved after intervention
Mindfulness / stress management (3 studies)										
(Kubo et al., 2019)	USA	Different cancer types (receiving chemotherapy)	Cancer patients: 97 / 69 % women / median: 59 years	RCT	Commercially available mindfulness program / n = 54	Waitlist/ n = 43	8 weeks	FACT-G and CQOLC	74 % of patients and 84 % of caregivers	Improved emotional well-being and overall well-being in intervention group but not in control group
(Rosen et al., 2018)	USA	Breast cancer (diagnosed ≤5 years)	112 / all women / 52 ± 10 years	RCT	Commercially available mobile app-delivered mindfulness training / n = 57	Waitlist / n = 55	8 weeks	FACT-B	66 %	Intervention group was associated with improved QoL in mHealth but not control group
(Urech et al., 2018)	Switzerland	Newly diagnosed with different cancer types	112	RCT	Web-based stress management program (STREAM) / N = 65	Waitlist / n=64	8 weeks	FACIT-Fatigue	83 %	Quality of life was significantly higher after the intervention relative to controls
Social support (2 studies)										
(Zhu et al., 2018)	China	Breast cancer (receiving chemotherapy)	114 / all women / 47 ± 8 years	RCT	App-based breast cancer-support program / n = 57	Care as usual / n = 57	12 weeks	FACT-B	91.2 %	Less deterioration in FACT-B scores within 3 months when compared to control group; but no significant differences at 6 months.
(Pappot et al., 2019)	Denmark	Adolescents and young adults with different cancers	20 / 70 % female / 25 years	Pre-post	App symptom diary, communication network and information	None	6 weeks	EORTC QLQ-C30	–	Significant increase in global HRQOL after app use in a subgroup pf patients who were post active cancer treatment
Information / psychoeducation (2 studies)										
(Graetz et al., 2018)	USA	Gynecological cancer (bilateral salpingo-oophorectomy surgery)	26 / all women / 55 years	RCT	Postoperative instructions and real-time symptom monitoring + reminders / n = 14	App only, no reminders / n = 15	30-day follow-up	SF-12	93%	In the mHealth intervention group, there was improvement in mental health but decrease in the physical health score (differences not statistically significant)
(Admiraal et al., 2017)	Netherlands	Breast cancer patients after chemotherapy	136	RCT	Web-based tailored psychoeducational program (ENCOURAGE) / n = 70	Control (regular visits to a medical specialist) / n=69	12 weeks	EORT QLQ-C30 and BR23	79%	No between group effects
Weight management (2 studies)										
(Ferrante et al., 2018)	USA	Breast cancer (African Americans)	35/ all women / 62 ± 9 years	RCT	Intervention (SparkPeople) plus activity tracker (Fitbit Charge) / n = 18	Waitlist - Fitbit only) / n = 17	12 months	QLACS	97.1 %	Only intervention group was associated with improved QoL.

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Table 1 (*continued*)

Ref.	Country	Population	Sample size / Gender / Age	Study design	Intervention / number of patients	Control group / number of patients	Intervention duration	Health related quality of life measures	Completion rate	Major findings
(McCarroll et al., 2015)	USA	Breast and endometrial cancer (overweight/ obese)	50 / all women / mean: 58 ± 10years	Pre-post	Web- and mobile-based weight-loss application (LoseIt!)	None	4 weeks	FACT-G	70 %	No changes in HRQoL.
Pain management (1 study)										
(Yang et al., 2019)	China	Different types (patients with cancer pain)	58 / 34 % women / 51 ± 9 (intervention), 54 ± 9 (control)	RCT	Mobile phone app providing continuous treatment information and feedback (Pain Guard) / n = 31	Traditional pharmacologic treatment / n = 27	4 weeks	EORT QLQ-C30	100%	Intervention group patients scored higher on cognitive, social and emotional functioning, sleeping disturbances, nausea and vomiting, constipation, fatigue, pain and global QoL domains

EORTC BR23, breast cancer questionnaire; EORTC QLQ-C30, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; EORTC QLQ-BR23 Quality of Life Questionnaire Breast Cancer Module 23; PedsQL, Pediatric Quality of Life Inventory; HRQoL, Health related quality of life; MBCT, mindfulness based cognitive therapy; RCT, randomized control trial; SF-36, 36-Item Short Form Health Survey, QLCAS, Quality of Life in Adult Cancer Survivors; VAS, visual analog scale.

between-group improvement of the SF-36 total score in cancer patients randomized to either a mobile-application-based CBT (*HARUToday*), a waitlist control group, or an attention control group (Ham et al., 2019). Another RCT found that cancer patients randomized to either an Internet-based mindfulness-based cognitive therapy or a face-to-face mindfulness based cognitive therapy had improved mental health, but not physical health, when compared to cancer patients who received treatment as usual (Compen et al., 2018). Finally, Willems and colleagues found cancer patients with similar baseline EORTC QLQ-C30 scores, randomized to a Web-based intervention according to CBT along with problem-solving therapy principles or to a waitlist control, had improved emotional and social functioning when compared to waitlist controls (Willems et al., 2017).

A single-arm pre-post design study (2019) in 25 survivors of different cancers found that an 8-week app-based cognitive behavioral stress management intervention (*Stress Proffen* app) improved the perception of physical aspects, emotional aspects, vitality, and general health aspects of the HRQoL, as measured with the SF-36 questionnaire (Børøsund et al., 2019). Another small study in 18 breast cancer patients found that CBT for insomnia intervention delivered via Internet videoconference on a computer was associated with an improved EORTC QLQ-C30 global health status score (McCarthy et al., 2018).

3.1.4. Mindfulness

Mindfulness mediation or stress management mHealth interventions in cancer patients were studied in 3 RCTs (Kubo et al., 2019; Rosen et al., 2018;Urech et al., 2018). In cancer patients receiving chemotherapy, patients who received a commercially available mindfulness app (*Headspace*) intervention delivered over an 8-week period reported a significant improvement in the FACT-G emotional well-being and the overall well-being dimensions (Kubo et al., 2019). In another study, breast cancer patients were randomized to either an 8-week intervention using a commercially available mindfulness training app (*Headspace*) or the waitlist control group. There were improved FACT-B scores in the mHealth intervention group, but not in the control group (Rosen et al., 2018). In an RCT of patients with different cancer types, a web-based stress management program was associated with higher improvement in FACIT-F scores relative to the waitlist control (Urech et al., 2018).

3.1.5. Social support

One study in 114 breast cancer patients receiving chemotherapy randomized patients to either an app-based support program (mHealth intervention group) or to usual care (control group), which comprised a health supportive care during chemotherapy as inpatients. Women in the mHealth intervention group experienced significantly less deterioration in the total FACT-B scores at 3 months when compared to the control group; however, FACT-B scores at 6 months were not different between the two groups (Zhu et al., 2018). Another pre-post study in adolescent and young adults with cancer found a significant improvement in global HRQoL after 6 weeks of mHealth intervention, which included symptom diary, communication network, and information (Pappot et al., 2019).

3.1.6. Information

Twenty-six women undergoing bilateral salpingo-oophorectomy for suspected gynecological cancer received some app-based postoperative instructions and real-time symptom monitoring and were randomized to either receive reminders (intervention group) or not (control group) (Graetz et al., 2018). At 30-day follow-up, women in the intervention group reported improved mental health but decreased physical health as measured by the SF-12 Mental Health and Physical Health questionnaires, respectively, when compared to controls; however, these differences were not statistically significant. Another RCT in women with breast cancer randomized women to either a Web-based tailored psychoeducational program (ENCOURAGE) or to standard care, which included regular visits to a medical specialist. Despite the reported

improvements of HRQoL in both study groups, there was no statistically significant difference between the 2 groups (Admiraal et al., 2017).

3.1.7. Pain management

Yang and colleagues (2019) randomized 58 patients with different cancer types to either receive an mHealth app providing continuous treatment information and feedback (*Pain Guard*) or to a control group who received a traditional pharmacologic treatment (Yang et al., 2019). At 4-week of follow-up, compared to the control group, patients in the intervention group scored significantly higher on the EORTC QLQ-C30 emotional, cognitive, and social functioning domains as well as sleep, nausea/vomiting, constipation, fatigue and pain symptoms scales, and global QoL domain.

3.2. Meta-analysis

Sixteen studies reported scores on the EORTC QLQ-C30 Global Health Status (8 studies and 9 patient cohorts; 669 patients), SF-36 (3 studies; 89 patients) and FACT-G (4 studies; 199 patients) before and after mHealth intervention (Table 2). The overall pooled results showed a statistically significant improvement of EORTC QLQ-C30 Global Health Status (mean difference: 8.48; 95 %CI: 4.16; 12.8; I^2: 92.3 %; p-heterogeneity <0.01; Fig. 2) and SF-36 (mean difference: 15.4; 95 %CI: 5.30; 25.5; I2: 88.1 %; p-heterogeneity <0.01) scores, but not the FACT-G scores (mean difference: -0.03; 95 %CI: -0.19; 0.13; I^2: 85.9 %; p-heterogeneity <0.01) after the mHealth intervention. Pooled results stratified by mHealth intervention type are presented in Table 2.

Six studies reported scores on the EORTC QLQ-C30 Global Health Status (3 studies; 394 patients in the intervention group and 430 controls), SF-36 (2 studies; 67 patients in the intervention group and 66 controls) and FACT-G (1 study; 40 patients in the intervention group and 32 controls) before and after mHealth intervention in both mHealth intervention and control arms. The overall pooled estimate on the efficacy of mHealth on quality of life from studies that provided data on both arms, the pooled standardized difference for all questionnaire types was statistically significant (standardized mean difference: 0.28; 95 % CI: 0.03; 0.53; 6 studies; I2: 61.4 %; p-heterogeneity: 0.02); however, further stratification by questionnaire type led to non-statistically significant results with few studies in each subgroup (Table 3 and Fig. 3).

Table 2
Summary of the main pooled effect estimates (95 % CI) of studies comparing mHealth to control with data on at least the treatment arm, stratified by 1) questionnaire type and 2) intervention type.

Questionnaire type	Pooled effect estimate for HRQoL	Studies reporting data on at least the treatment arm; # of studies	I^2%; P-heterogeneity
EORTC QLQ-C30 (Overall)*	Mean difference (95 % CI)	8.48 (4.16, 12.8); n = 9	92.3 %; p < 0.01
By mHealth intervention type:			
Cognitive		11.9 (2.76, 21.0); n = 2	96.0%; p < 0.01
PA/ fitness		7.05 (1.47, 12.6); n = 5	94.0 %; p < 0.01
Social support		9.06 (-1.29, 19.4); n = 2	86.8 %; p < 0.01
p-interaction		*p-int:0.67*	
SF-36 (Overall)*	Mean difference (95 % CI)	15.4 (5.30, 25.5); n = 3	88.0%; p < 0.01
By mHealth intervention type:			
Cognitive		13.2 (0.73, 25.7); n = 2	89.9%; p < 0.01
PA/ fitness		19.5 (2.35, 36.7); n = 1	NA
p-interaction		*p-int: 0.56*	
FACT-G (Overall)	Mean difference (95 % CI)	−0.03 (-0.19, 0.13); n = 4	85.9 %; p < 0.01
By mHealth intervention type:			
Cognitive		0.04 (-0.31, 0.38); n = 1	NA
Mindfulness			
PA/ fitness		0.30 (-0.02, 0.62); n = 1	NA
Weight management		−0.11 (-0.43, 0.21); n = 1−0.32 (-0.63, -0.01); n = 1	NA
p-interaction		*p-int:0.05*	NA

CI: confidence interval; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; FACT-G: Functional Assessment of Cancer Therapy-General; HRQol: Health-related quality of life; NA: not applicable; SF-36: Medical Outcomes Study 36-Item Short Form.

3.3. Study bias

The main source of bias for RCTs was the absence of or unclearly defined blinding procedures of study participants or personnel for intervention or control group allocation (Appendix B). Due to the paucity of studies in each of the subgroups, publication bias was not feasible to conduct.

4. Discussion

mHealth interventions are promising for improving the HRQoL of patients with cancer. The strongest evidence currently exists for physical activity/ fitness interventions, followed by CBT, and mindfulness. The evidence is more limited for weight management, health information, social support, and pain management mHealth interventions.

The majority of studies explored the effect of physical activity/ fitness mHealth interventions on the HRQoL of cancer patients. While 4 pre-post design studies (Cheong et al., 2018; Lozano-Lozano et al., 2019; Trinh et al., 2018) found that mHealth physical activity/ fitness intervention improved HRQoL in cancer patients, only 1 RCT (Galiano-Castillo et al., 2016) out of the 4 RCTs (Frensham et al., 2018; Galiano-Castillo et al., 2016; Ji et al., 2019; Uhm et al., 2017) demonstrated superiority of mHealth-delivered physical activity intervention over the control group. Surprisingly, another RCT found a negative impact of the mHealth intervention on the social functioning aspect of HRQoL (Mendoza et al., 2017). Physical activity is important in patients with established cancer diagnosis and is associated with longer patient survival, lower cancer recurrence rate, better treatment adherence, reduced fatigue symptom severity, and improved HRQoL (Courneya et al., 2007; Ibrahim and Al-Homaidh, 2011; Meyerhardt et al., 2009; Rock et al., 2012; Schmitz et al., 2010). Physical activity of at least 150 min per week and strength exercises at least 2 times per week are recommended for patients with cancer (Rock et al., 2012). However, fewer than 10 % of cancer patients remained physically active during the treatment and only up to 30 % of patients engaged in physical activity after cancer treatment (Garcia and Thomson, 2014). Smartphone apps can help increase physical activity, especially exercise programs that are shorter than 3 months, that do not include diet interventions and have social features (Tong and Laranjo, 2018). mHealth interventions promoting physical activity had a high retention rate exceeding 67 % across selected studies. Further studies exploring mHealth possibilities to promote physical activity in cancer patients are encouraged.

Obesity is associated with increased site-specific and overall mortality of cancer patients (Parekh et al., 2012; Calle et al., 2003; Wolin et al., 2010; Chan et al., 2014). The international Reach Out to Enhance Wellness (RENEW) trial of 641 long-term colorectal, breast, and prostate cancer survivors found that diet-exercise intervention with telephone

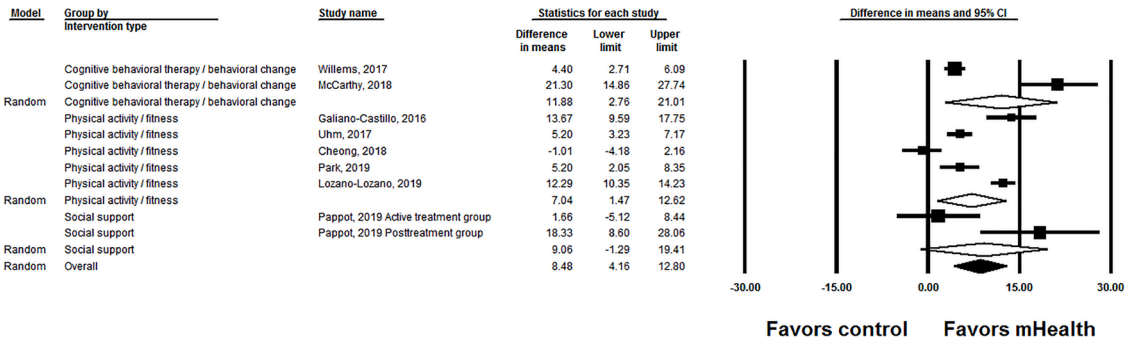

Fig. 2. Forest plot denoting pooled mean difference comparing the change in the EORTC QLQ-C30 Global Health Status score before vs. after intervention mHealth intervention stratified by mHealth intervention type.
Black squares reflect the mean difference in HRQoL in the mHealth arm of each study. Horizontal lines denote 95 % CIs. The centre of the clear diamonds represent the pooled mean difference for each subgroup from the random-effects model (D + L). The width of the diamond denotes the 95 % confidence interval. The canter of the black diamond denotes the overall mean difference of all studies. Study weights are from the random-effects analysis (D + L). Pooled estimates from the random-effects analysis (D + L) are shown based on 9 studies (n = 669 participants).

counseling was associated with better HRQoL at 1 year as measured with the SF-36 physical functioning subscale when compared to waitlist controls (Demark-Wahnefried et al., 2012). We identified one RCT that reported improvement in HRQoL with an mHealth weight management intervention (Ferrante et al., 2018), while another pre-post study did not find an impact of Web and mobile mHealth interventions on HRQoL (McCarroll et al., 2015). These findings suggest that mHealth weight management interventions might improve HRQoL of cancer patients but remain to be further explored.

Mindfulness is a psychological state of being aware in the present moment and without judgment. Mindfulness-based interventions are structured 8-week programs that consist of group programs and individual practices. Mindfulness has a broad range of positive mental effects (Sedlmeier et al., 2012) and has been shown to be effective for depression, anxiety, pain, distress, and QoL improvement (Goyal et al., 2014; Buchholz, 2015). In patients with cancer, traditional mindfulness-based interventions have been associated with numerous positive mental health effects. They have also been shown to improve HRQoL in patients with cancer (Carlson et al., 2016; Henderson et al., 2012). Regarding mindfulness mHealth interventions, the three RCTs (Kubo et al., 2019; Rosen et al., 2018; Urech et al., 2018) in our systematic review demonstrated results in favor of the these tools compared to the controls. mHealth holds promise to effectively deliver mindfulness interventions for cancer patients and should be further exploited. Also, smartphones can enable a more precise measurement of the intervention effect using passively gathered information from the smartphone (for example, digital phenotyping), regardless whether the intervention was delivered via a smartphone or not. Digital phenotyping could potentially allow to objectively evaluate and monitor the possible impact of mHealth interventions on patient's functional and cognitive functioning domains that are important aspects of HRQoL (Cote et al., 2019, 2017; Onnela, 2020).

Table 3
Summary of the main pooled effect estimates (95 % CI) of studies comparing mHealth to control with data on both the treatment and the control arms stratified by 1) questionnaire type and when feasible 2) intervention type.

Questionnaire type	Pooled effect estimate for HRQoL	Studies reporting data on **both arms**; # of studies	I^2 %; P-heterogeneity
EORTC QLQ-C30 Global Health Status (Overall)*	Mean difference (95 % CI)	3.66 (-0.94, 8.26); n = 3	81.5%; p < 0.01
SF-36 (Overall)*	Mean difference (95 % CI)	15.4 (5.30, 25.5); n = 3	0%; p: 0.49
FACT-G (Overall)	Mean difference (95 % CI)	5.86 (0.77, 11.0); n = 1	NA
All combined (Overall)	SMD (95 % CI)	0.28 (0.03, 0.53); n=6	61.4 %; p: 0.02
EORTC QLQ-C30 Global Health Status		0.27 (-0.06, 0.59); n = 3	80.7 %; p < 0.01
SF-36		0.17 (-0.32, 0.66); n = 2	0%; p: 0.50
FACT-G		0.54 (-0.14, 1.21); n = 1	NA
p-interaction		*p-int:0.68*	

CI: confidence interval; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30; FACT-G: Functional Assessment of Cancer Therapy-General; HRQol: Health-related quality of life; NA: not applicable; SF-36: Medical Outcomes Study 36-Item Short Form; SMD: standardized mean difference.

Two RCTs found that mHealth CBT intervention was associated with a higher post-CBT HRQoL when compared to patients who did not receive an mHealth CBT intervention (Willems et al., 2017; Compen et al., 2018). Two pre-post design studies also showed improvements in the HRQoL of patients with mHealth interventions (McCarthy et al., 2018; Børøsund et al., 2019). CBT is a structured form of psychotherapy that helps to cope with negative emotions by changing thoughts and behavior (Daniels, 2015; Hofmann et al., 2012). A growing number of studies have documented numerous positive effects of CBT in patients with cancer that include decreased psychological distress, pain (Tatrow and Montgomery, 2006), depression, fear of cancer recurrence (van de Wal et al., 2017), and improvement in the HRQoL. Barriers of wider implementation of CBT training in clinical cancer care include limited institutional and system resources, patient preference for pharmacotherapy, and lack of interest and/or motivation (Wiebe and Greiver, 2005). Mobile apps could potentially help enhance wider adoption of CBT by patients (Aguilera and Muench, 2012; Lan et al., 2018). However, commercially available CBT apps do not foster patient-physician relationship; therefore, they should be adapted to healthcare systems and patient/physician needs before fostering their wider adoption in healthcare and by cancer patients (Lan et al., 2018).

Findings regarding the effectiveness of mHealth-delivered information and psychoeducation interventions on the HRQoL of cancer patients are conflicting (Graetz et al., 2018; Admiraal et al., 2017). However, mHealth information interventions for perioperative care of cancer patients could be a valuable tool to deliver patient-tailored, disease-stage, and treatment specific information about cancer care, but delivered information should be carefully balanced to the context of patient health literacy and disease gravity (Fotis, 2017).

One RCT and another pre-post study found that mHealth social support program was associated with an improved HRQoL of cancer patients (Zhu et al., 2018; Pappot et al., 2019; Cella et al., 1993).

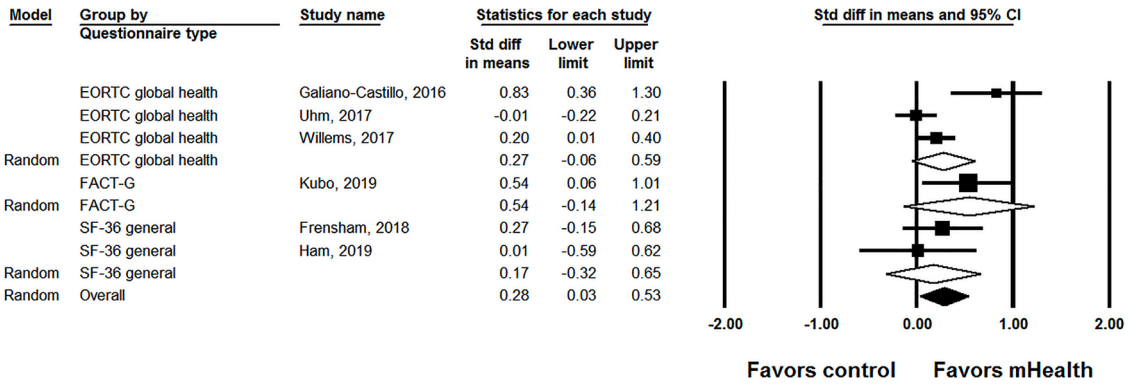

Fig. 3. Forest plot denoting pooled standardized mean difference comparing the change in HRQoL in mHealth vs. control in all the studies that provided data on both mHealth intervention and control arms. Results are stratified by questionnaire type.
Black squares reflect the standardized mean difference in HRQoL comparing mHealth to control of each study. Horizontal lines denote 95 % CIs. The center of the clear diamonds represents the pooled mean difference for each subgroup from the random-effects model (D + L). The width of the diamond denotes the 95 % confidence interval. The center of the black diamond denotes the overall standardized mean difference of all studies. Study weights are from the random-effects analysis (D + L). Pooled estimates from the random-effects analysis (D + L) are shown based on 6 studies (501 participants in the mHealth intervention group and 528 controls). The I2 and P values for heterogeneity are reported in Table 3 for the overall estimate and for each subgroup. D + L, DerSimonian.

Perceived social support is an important determinant of life satisfaction, better mood symptoms, and better perceived HRQoL of patients with cancer (Leuteritz et al., 2018; Yoo et al., 2017). Coping strategies of cancer patients are important for the HRQoL of cancer patients (Nipp et al., 2016) and can mediate the relationship between social support and HRQoL (Zhou et al., 2010). In a systematic review, seeking for social support was identified as a major coping strategy of patients with cancer (Mehrabi et al., 2015). Therefore, social support delivered via mHealth interventions can be well accepted by cancer patients allowing them to optimize their HRQoL. mHealth tools should be further explored to enhance social support in patients with cancer.

Pain is experienced by over 80 % of cancer patients, should be appropriately diagnosed, and is usually managed with pharmacological approaches that can be associated with an elevated risk of adverse events, such as opioid addiction (Jost and Roila, 2008). mHealth pain management interventions can improve the HRQoL of cancer patients (Yang et al., 2019), indicating that mHealth interventions can help manage cancer related pain and therefore should be explored in future studies.

In the majority of studies, HRQoL was evaluated using EORTC and FACT questionnaires that were specifically designed for cancer patient population, and were validated and widely used for assessment of HRQoL in patients with cancer (Cella et al., 1993; Aaronson et al., 1993; Luckett et al., 2011; Nolte et al., 2019). The use of widely accepted and validated instruments is an important strength of the identified studies, reinforcing the reliability and reproducibility of their findings. Only a fraction of the reviewed studies used generic HRQoL instruments, such as SF-36 (Ware and Sherbourne, 1992) and SF-12 (Ware et al., 1995) that are also commonly used in cancer patients; however, future studies examining the impact of mHealth interventions on the HRQoL of cancer patients should consider using cancer specific HRQoL instruments.

The meta-analysis of the identified studies supported the positive effect of various mHealth interventions on the HRQoL of cancer patients. A recent meta-analysis (7 studies, 1220 patients) found that internet based psycho-educational interventions were associated with improved fatigue and depression symptoms, but the effect of distress and HRQoL was not significant (Wang et al., 2020). Our study results should be interpreted with caution given heterogeneity of studies included in the meta-analysis in patient populations and mHealth interventions. Nevertheless, our findings support that mHealth interventions can help improve the HRQoL of cancer patients or prevent it from deteriorating, a phenomenon that is often inevitable given the progressive course of the disease (Basch et al., 2016; Bunevicius et al., 2020; Giesinger et al., 2011).

The COVID-19 pandemic further underscores the clinical significance of mHealth interventions for cancer patients given the high risk of COVID-19 related complications in patients with established cancer diagnoses and receiving active cancer treatment (Kuderer et al., 2020). Notably, a delay in care for these cancer patients places them at an elevated risk for potentially avoidable complications (Maringe et al., 2020). COVID-19 pandemic has resulted in an explosion in digital healthcare adoption and consumption (Hollander and Carr, 2020; Keesara et al., 2020); therefore, it is expected that the ongoing pandemic will place even more emphasis on remote cancer patient care using mHealth solutions.

This review study had limitations. The included studies were heterogenous in study design (RCTs vs. single-arm studies), sample size, types of mHealth interventions, cancer types, and methods of HRQoL assessment. Furthermore, we focused on publications in English and therefore did not capture non-English publications. Our results cannot be generalized to telemedicine interventions that consist of information and communication technologies that are administered by healthcare professionals as opposed to mHealth interventions that are used by patients and do not require any clinician's intervention. Despite these limitations, our study had several strengths. To our knowledge, this was the first systematic review and meta-analysis on this novel topic that included a large number of studies and an overall large number of patients with cancer who tested a myriad of mHealth interventions. A meticulous assessment of study quality for the different primary studies included in our review allowed us to identify the biases and weaknesses in the current literature and to provide useful recommendations for future studies. Despite the inherent above-mentioned heterogeneity, we tried our best to subgroup the results not only by questionnaire type, but also by intervention type, in order to pool the results of the original studies that provided such data. Additionally, we standardized the pooled effect estimated when combining different questionnaire types to further attenuate the heterogeneity issue.

5. Conclusion

The available evidence strongly suggest that mHealth interventions hold promise for improving the HRQoL of patients with cancer. At present, the strongest evidence exists for physical activity/ fitness interventions, followed by mindfulness and CBT interventions. Data are more limited for health information, social support, weight management, and pain management mHealth interventions. The majority of studies were RCTs, but their results remain to be replicated. While the market of mHealth interventions is rapidly expanding, rigorous studies

with focus on the efficacy of mHealth interventions are essential prior to considering their implementation in the existing physician-patient relationship. Ideally, mHealth interventions could be tailored to individual needs of cancer patients and be adaptive considering longitudinal changes of physical and cognitive functioning that are often inevitable given cancer progression and cancer-treatment side effects.

Declaration of Competing Interest

The authors report no declarations of interest.

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Appendix A. Search terms

Database	Search terms
Pubmed	(mobile health[MeSH Terms] OR "mobile application"[Text Word] OR "mobile app"[Text Word] OR "mobile health"[Text Word] OR "mobile health app"[Text Word] OR "mhealth"[Text Word]) AND (cancer[MeSH Terms] OR "cancer"[Text Word]) AND (quality of life[MeSH Terms] OR "quality of life"[Text Word] or "health related quality of life" [Text Word]) **RESULTS: 242 articles on 10/17/2019**
Clarivate Analytics	Date of Clarivate Analytics database search: October 17, 2019 TS=("quality of life" OR "health related quality of life") AND TS = ("cancer") AND TS=("mobile health" OR "mobile application" OR "mobile app" OR "mobile health app" OR "mhealth") **RESULTS: 102 articles on 10/17/2019**

Appendix B. Risk of Bias Assessment Tool for RCTs and pre-post studies

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Incomplete outcome data	Selective outcome reporting	Other sources of bias
Galiano-Castillo et al., 2016	+	?	+	+	+	+
Uhm et al., 2017	+	?	?	+	+	+
Ji et al., 2019	+	?	?	+	+	+
Frensham et al., 2018	+	?	–	+	+	+
Mendoza et al., 2017	?	?	–	+	+	+
Cheong et al., 2018	–	–	–	+	+	+
Park et al., 2019	–	–	–	+	+	+
Trinh et al., 2018	–	–	–	+	+	+
Lozano-Lozano et al., 2019	–	–	–	+	+	+
Kubo et al., 2019	+	?	+	+	+	+
Rosen et al., 2018	+	?	+	+	+	+
Urech et al., 2018	+	?	+	+	+	+
Greer et al., 2019	+	?	?	+	+	+
Ham et al., 2019	+	+	?	+	+	+
Compen et al., 2018	+	?	+	+	+	+
Willems et al., 2017	+	?	–	+	+	+
Børøsund et al., 2019	–	–	–	+	+	+
McCarthy et al., 2018	–	–	–	+	+	+
Zhu et al., 2018	+	?	+	+	+	+
Pappot et al., 2019	–	–	–	+	+	+
Graetz et al., 2018	+	+	+	+	+	+
Admiraal et al., 2017	+	–	–	+	+	+
Yang et al., 2019	?	?	+	+	+	+
Ferrante et al., 2018	+	+	?	+	+	+
McCarroll et al., 2015	–	–	–	+	+	+

Key: "+" – low risk of bias; "- "high risk of bias; "?" – unclear risk of bias.

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