Systematic Review

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Comparison of the effectiveness of eHealth selfmanagement interventions for pain between oncological and musculoskeletal populations: a systematic review with narrative synthesis

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Abstract

Objectives: The aim of this systematic review is to compare the effectiveness of eHealth self-management interventions

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on pain intensity between oncological and musculoskeletal populations and to examine barriers and facilitators of the use of eHealth self-management tools.

Content: In March 2021, a systematic search of the literature was conducted using the databases PubMed and Web of Science. Studies that investigated the effect of eHealth selfmanagement interventions on pain intensity in an oncological and/or a musculoskeletal population were included.

Summary: No study was found with a direct comparison of the two populations. Of the ten included studies, only one (musculoskeletal) found a significant interaction effect in favor of the eHealth program and three (musculoskeletal and breast cancer) showed a significant time-effect of the eHealth intervention. In both populations user-friendliness of the tool was considered as a facilitator, the length of the program and the lack of an in-person session as barrier. Due to the absence of a direct comparison, no conclusion can be made on how the effectiveness differs between both populations.

Outlook: Further research should incorporate patientexperienced barriers and facilitators and there is a high need of studies making the direct comparison of the effect of an eHealth self-management intervention on pain intensity in an oncological vs. a MSK population.

Keywords: cancer; eHealth; musculoskeletal system; pain; self-management; systematic review.

Introduction

Pain is one of the most common, complex and persisting symptoms worldwide [1, 2]. Pain has a considerable impact on a person's life as it is often associated with other symptoms such as fear of movement, anxiety, sleep disturbances as well as a decrease in physical activity, social functioning and quality of life [3–6].

The ICD-11 (International classification of diseases 11th revision) classifies pain into acute and chronic pain. Other classifications, based on the established pathophysiology of pain, are prevalent in the existing literature resulting in a categorization of non-cancer vs. cancer-related pain [7]. Cancer-related pain has a prevalence of 39 % after curative cancer treatment, 55 % during cancer treatment and 66 % in advanced stages of cancer [8]. Within the non-cancer related pain group, pain associated with musculoskeletal (MSK) conditions has the highest prevalence [9, 10].

Pain is an individual experience, that is influenced by biological, social and psychological factors [11-14]. The dichotomy between cancer and non-cancer related pain is focused on the associated condition, which is only one aspect of pain. As mentioned before, psychological and social factors are also involved in the experience of pain. Which could explain why, regardless of the abovementioned categorization, there are a number of similarities as to what the best evidence for pain management is in both populations [11-13].

Patient education and exercise therapy are core concepts of chronic pain management, both in MSK-related or cancer-related pain [11-13]. In acute pain management, pharmaceuticals are recommended as first line treatment. However, due to the risk of these treatments, like opioidtolerance, there is a trend to use non-pharmacological approaches in acute pain, similar to those used in chronic pain management [15]. Next to that, clinical guidelines in both populations also emphasize the need for a more individual and patient-centered approach. In this patientcentered care, self-management interventions are highlighted due to their integration of the patient's perspective and preferences.

Self-management interventions have been proven to positively influence the wellbeing of patients with pain [16, 17]. Within the literature, there is a lack of agreement on the definition of self-management. The most used definition is: "Individual's ability to manage the symptoms, treatment, physical and psychosocial consequences and lifestyle changes inherent in living with a chronic condition". This definition has evolved to include all health conditions. Within selfmanagement, the role of the health-care provider (HCP) is regarded to be a more supportive role [18]. For the purpose of this review, we regard self-management as the patients' ability to self-manage their pain individually, without the active involvement of an HCP.

New opportunities for supporting self-management skills can be found in eHealth. EHealth describes any form of digital technology that assists health care [19]. It can

provide a solution for barriers of in-person interventions such as financial costs, time-consumption or limited access to health care facilities [20]. Despite these benefits, implementing eHealth also provides challenges on an individual. environmental and technical level [21].

The literature on the use and effectiveness of eHealth is growing. Several reviews show that these interventions are effective in the management of pain in subgroups of an MSK [22–24] as well as an oncological population [25].

The positive effect of self-management through eHealth suggests that a similar approach to pain management might be possible in both populations. However, it remains unclear how these interventions are organized and how their design compares within both oncological and musculoskeletal (MSK) populations. Next to that, the comparison of the effectiveness of these eHealth self-management interventions in these two populations has yet to be fully explored. In light of these gaps in the literature, the purpose of this review is to provide an overview of how these eHealth self-management interventions are organized in an oncological vs. a MSK population and how they compare to each other in terms of design and effectiveness.

Methods

This systematic review was registered within the International Prospective Register of Systematic Reviews (PROSPERO reference 245857) and adhered to the PRISMA statement recommendations [26].

Data sources and searches

The systematic search of the literature was conducted using the databases PubMed and Web of Science. In Table 1, the key words of this systematic search are shown, which was performed on 3rd March 2021. The search was built based on the primary research question regarding the design and the effectiveness of an eHealth selfmanagement intervention on pain intensity. Secondary, information on barriers and facilitators was extracted from the retrieved literature. However, as this was no eligibility criteria, it was not included in the search strategy.

Study selection

Original experimental trials that investigated the effect of an eHealth self-management intervention (I) on pain intensity (O) in an adult oncological or MSK population (p) were included in this review. No distinction was made between acute or chronic pain. Self-management was considered as: "The patients' ability to manage their pain individually, without the active support of an HCP."

Table 1: Key words search strategy.

Key words	MESH-terms
Cancer OR neoplasms OR musculo- skeletal AND Online OR internet OR digital OR web OR telehealth OR mhealth OR mobile OR eHealth OR telemedicine OR technology OR app OR applica- tion AND Education OR self-management OR	Neoplasms OR musculoskeletal system AND Online system OR internet OR webbrowser OR Telemedicine OR Internet-based intervention OR educational technology OR Medical informatics applications OR mobile applications AND
self management AND Pain	Self-management OR education OR patient education as topic OR health education
	AND Pain OR cancer pain OR musculo- skeletal pain

Included articles had to be published in English, Dutch, French or German. Exclusion criteria were: pain intensity not included as outcome measure: studies in children or adolescents: studies conducted in nursing homes (because of the often more advanced disease stage in these patients) and studies including patients with metastases, palliative patients and patients with leukemia or lymphoma. When it was unclear which population was included, the author was contacted. If this information remained unclear after a time-frame of two weeks, the study was excluded. When the intervention as well as the control group was a combination of a digital and an in-person session, had active involvement of an HCP or when the eHealth was solely carried out in a clinical setting, like in a hospital, the study was also excluded. After removing duplicates, title and abstract were screened double-blinded by two independent authors (M.E. and S.V.D.). The remaining full texts were screened and conflicts were further discussed and resolved through consensus. A third reviewer (A.D.G.) was involved when conflicts were not resolved through consensus.

To screen the included articles, we made use of the software Covidence to manage our systematic review (www.covidence.org) [27].

Data extraction

Data extracted for this systematic review included: author(s), year of publication, study design, setting, continent and country of origin, sex, age, sample size, type of cancer or MSK condition, cancer stage if applicable, description of the intervention and eventual control group, method of data collection, results, pain definition and method of pain measurement, type and duration of pain and pain recall period (point, week, month, year). When applicable, barriers and facilitators for the self-management interventions were registered.

Quality assessment

Two reviewers (M.E. and S.V.D.) independently evaluated the risk of bias of included studies, using the Revised Cochrane risk-of-bias tool for randomized trials (RoB2.0). Conflicts were discussed and resolved through consensus. A third reviewer (A.D.G.) was involved when conflicts were not resolved through consensus.

Data synthesis and analysis

Because of the heterogeneity of the included studies, statistical analyses were not performed within this systematic review. This systematic review adopted a narrative description of the effect of an eHealth selfmanagement intervention on pain intensity, without distinguishing between the different questionnaires to measure pain intensity.

Results

Study search

The initial search included 2,670 articles (see Figure 1). After removing duplicates, 2,389 articles were included for title/abstract screening. After title/abstract screening, 60 articles were included for full-text screening. A total of 49 articles were excludes for various reasons. In conclusion, 11 articles, consisting of 10 individual studies, met the predefined eligibility criteria and were included in this systematic review.

Risk of bias

Figure 2 gives an overview of the assessment of risk of bias. All studies contained at least one domain with a high risk of bias, resulting in an overall high risk of bias score [28-38]. The uncontrolled have a high risk of bias on all domains except domain 5. The lack of control group results in no randomization process (D1), no concealment of assigned intervention (item 2.1 domain 2, Figure 2), important nonprotocol interventions cannot be balanced across different groups (item 2.3 domain 2, Figure 2) and as there is no comparison group we cannot assess if measurements differ between two groups (D4, Figure 2) [31-33]. Two RCTs were also scored with a high risk of bias on D1 (bias arising from the randomization process), because the allocation sequence was not concealed until participants were enrolled and assigned to the interventions [36-38], five studies with a high risk of bias on D2 (bias due to deviations from the intended intervention), because of an inappropriate or absent analyses to estimate the effect of adhering to intervention [28, 29, 35–38], and three studies with a high risk of bias on D3 (bias due to missing outcome data), due to a drop-out of more than 5% and due to a lack of evidence that the result was not biased by missing outcome data [29, 30, 37, 38].

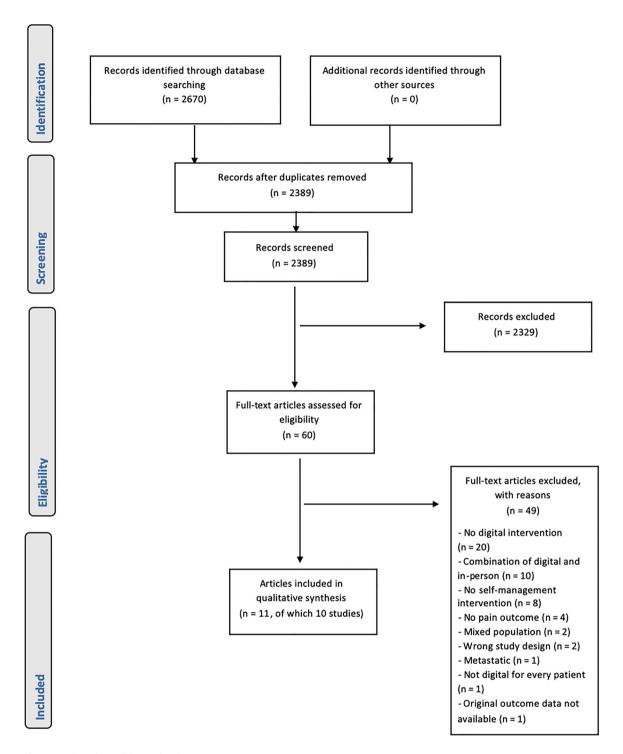


Figure 1: Flow chart of the study selection process.

Study characteristics

The study characteristics can be found in Table 2. None of the studies performed a direct comparison between the populations. Out of the 10 included studies, only two studies evaluated an oncological population, namely breast cancer [30, 31], and eight studies evaluated MSK conditions [28, 29, 32–38], including patients with knee osteoarthritis (n=1) [28], low back pain (n=2) [29, 36], overall chronic MSK pain (n=3) [32–34], fibromyalgia and chronic widespread pain (n=1) [37, 38] and patients with rotator-cuff related shoulder pain (n=1) [35].

The design of the studies with a breast cancer population were an uncontrolled clinical pilot trial [31] and an RCT [30]. Pain intensity was measured in both studies with the Patient-Reported Outcomes Measurement Information System - 29 (PROMIS-29) [30, 31]. The studies that evaluated patients with MSK-related pain consisted of two uncontrolled studies [32, 33], including one pilot study [32], and six RCTs [28, 29, 34–38], including two pilot studies [34, 35]. Pain intensity was measured with the Brief Pain Inventory (BPI) questionnaire [33, 34], a Numeric Rating Scale (NRS) [29, 32], a Visual Analogue Scale (VAS) [35, 37, 38], the Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC) [28] and with the Low Back Pain Rating Scale (LBPRS) [36].

Most studies were conducted in the USA (n=7) [28, 29, 32–34], one study in Norway [37, 38], one in Australia [35] and one in Denmark [36].

Characteristics of the eHealth Selfmanagement interventions

Details of the characteristics of the eHealth self-management interventions can be found in Table 2.

Medium

A website was the most used medium in both populations to share written material and videos. Within the studies of the musculoskeletal population, smartphone based formats were also used, ranging from an interactive game design [32], an app [33] or a mobile accessible a webpage with information [28, 29, 34-36].

Content

Similarities within the oncological studies were the modalities to facilitate self-management, namely patient education and a cognitive-behavioral approach. Comparing this to the MSK population, additional modalities including advice for physical exercise, self-report of symptoms and social support were used.

The content of educational material varied form study to study. Themes that were only seen in oncological studies was information on mind-body science [30] and specific information on late effects of oncological therapy [31]. Other educational themes that were incorporated in all studies were condition-specific information [28, 35, 36], symptom management, lifestyle changes. Themes that only occurred in the musculoskeletal population were education on pain itself [29, 32, 34] or specific instructions on a technique [33].

Concepts of cognitive behavioral therapy (CBT) were another similarity. The modalities in the oncological studies were limited to thought reframing [30], goal setting [31] or relaxation exercises [30, 31]. All these modalities were also part of the CBT in musculoskeletal populations, with the addition of meditation exercises [29], self-evaluation and



Figure 2: Risk of bias assessment.

Table 2: Characteristics of the eHealth self-management interventions.

Study	Population ^a	Group ^b	Duration ^c	Frequency ^d	Digital medium ^e	Format ^f	Content ^e
Darnall et al. [30]	ВС	I "my surgical success"	90 min	O/A	W	Video audio	CBT skills to regulate cognition, emotion, hyperarousal related to pain such as thought reframing, relaxation and attention modulation Education on mind-body science
		С		O/A	W	Written material	Education on health and nutrition in terms of recovery after surgery
Henry et al [31]	ВС	I "PROSPECT"	8 week	U/A	W	Written material video	Education on late effects of therapy, symptom management and lifestyle change
Allen et al. [28]	MSK	I "STEP-KOA"	3 month	U/A	W	Written material pictures video	Exercise recommendation stretching, strengthening and aerobic exercise with 7 levels, including progression based on WOMAC-scores
		С	9 month	Every 2 week	E-mail	Written material	Education on topics related to osteoarthritis and its management
Carpenter et al. [29]	MSK	I "Wellness Workbook"	3 week	U/A	W	Interactive format: Written material	CBT cognitive restructuring, stress management, relaxation training, mindfulness, and values-based behavioral activation Education on pain and biopsychosocial pain management
Kohns et al. [34]	MSK	C I	3 week 20– 25 min	O/A	W	Written material video	Wait-list Education on cognitive, emotional, social, and developmental processes and the neuroscience of pain Self-assessment of pain location, of signs of central sensitization and psychological factors
		С	20– 25 min	O/A	W	Written material video	Education on general health Self-assessment of health behaviors
Kristjánsdóttir et al. [37, 38]	MSK	I	4 week	U/A	S	Interactive format: Written material Audio HCP-interaction	CBT ACT exercises, Mindfulness, self-reflection, feedback on exercises and self-reflection by HCP
		С	4 week	U/A	W	Written material Audio	CBT non-interactive exercises (ACT, mindfulness)
Malliaras et al. [35]	MSK	I1	12 week	U/A	W	Interactive format: Written material Infographics Video	Exercise recommendation shoulder exercises based on best-evidence and expert consensus Education on causes of RCRSP, pain mechanisms, exercise and other treatments
		12	12 week	U/A	W	Interactive format: Written material Infographics Video HCP interaction	Exercise recommendation shoulder exercises based on best-evidence and expert consensus Education on causes of RCRSP, pain mechanisms, exercise and other treatments Telerehabilitation weekly session with a physiotherapist
		С	12 week	U/A	W	Written material Infographics	Education on rotator cuff muscles, risk factors and advice on activity-modulation
Strøm et al. [36]	MSK	I "w-SPIINA program"	1–5 week	U/A	W	Written material Video	Education on course of treatment and rehabilitation

Table 2: (continued)

Study	Population ^a	Group ^b	Duration ^c	Frequency ^d	Digital medium ^e	Format ^f	Content ^e
							CBT information and use of images to reduce anxiety, catastrophic thoughts, and misconceptions in relation to surgery Online support group self-assessment of pain and physical ability
		С			In person	Orally written material	Standard course of treatment, rehabilitation, and information
Johnson et al. [32]	MSK	I	30 day	U/A	W + S	Interactive format: Written material Game design	CBT behavioral change based on TTM: Stage-matched guidance on decisional balance, self-efficacy, processes of change and goal setting Education on stress-management, healthy sleep habits and pain coping skills Online support group self- assessment of pain symptoms
Kawi et al. [33]	MSK	I	8 min	U/A	S	Video	Instruction and demonstration on auricular point acupressure

^aBC, breast cancer; MSK, musculoskeletal; ^bI, intervention group; C, control group; ^cW, weeks, Mo, months; D, days; Min, minutes; ^dU/A, unrestricted access; O/A, one time access; eW, web-based; S, smartphone-based; fHCP, health care provider; 9CBT, cognitive behavioral therapy; WOMAC, Western Ontario & McMaster Universities Osteo-arthritis Index; ACT, acceptance and commitment therapy; RCRSP, rotator cuff-related shoulder pain; TTM, transtheoretical model.

self-reflection exercises [34], guidance on decisional balance, improving self-efficacy, and acceptance and commitment therapy [37, 38].

In the studies with a musculoskeletal population, there were some additions in content that were not prevalent in the oncological studies: self-evaluation of symptoms [36-38], instructions and recommendations for physical exercise [28, 35] and-lastly, the use of peer support [32, 36].

Within the control groups of the RCTs, two studies used another eHealth program [28, 34]. These programs consisted of education on topics related to osteoarthritis and its management [28] and of education and self-assessment on general health behaviors [34].

Delivery

Two studies compared an individual intervention to one with support of an HCP [35, 37, 38]. In one study, the non-HCP supported group consisted of non-interactive CBT exercises [37, 38] and in the other of education on rotator cuff muscles, risk factors and advice on activity-modulation [35].

Duration

The duration of the interventions varied between a video of 8 min to a program of 3 months, with most interventions being around the one-month duration.

The effect of an eHealth self-management intervention on pain intensity

Oncological population

One RCT, reporting on post-operative pain after curative breast cancer surgery, found no significant interaction effect in pain intensity (p time x group=0.53) [30]. However, a significant decrease in pain intensity over time was seen within the intervention group (p=0.0002) which received pain education and CBT in comparison to the control group, who received general health information [30].

The uncontrolled trial, that used an education intervention cancer-specific symptom management after curative treatment, found that none of the symptoms significantly improved in the group of patients who reported pain as their primary symptom. However, in the large cohort of the sample, which consisted of patients with a primary complaint of pain or fatigue or insomnia, significant decrease in pain intensity over time at eight weeks follow-up was shown (p<0.001) [31].

MSK population

Of the six RCT's [28, 29, 34-38], only two RCTs reported a significant difference in treatment effects between groups [34, 36], one in favor of the experimental group [34], one in favor of the control group. [36].

Kohns et al. [34] observed a significant decrease in pain intensity in the intervention group (eHealth: biopsychosocial pain education) in comparison with the control group (eHealth: general health education) at one month follow-up (p time x group=0.024), but not at 10 months follow-up (p time x group=0.434) [34]. The other RCT, studying post-operative pain in patients after lumbar fusion surgery, reported a significant difference in leg pain two days after surgery within the control group (usual treatment) (p time x group=0.01), vs. the eHealth group, who received education on the treatment and rehabilitation, CBT, learned self-assessment of pain and physical ability and had access to an online support group [36].

One uncontrolled pilot trial reported a significant decrease over time in all pain outcomes after 30 days of selfmanagement intervention [32]. This pilot study included CBT, pain education, an online support group and selfassessment of symptoms.

Other studies [28, 29, 33, 35, 37, 38] did report results in favor of the eHealth intervention, albeit non-significant. Details of the includes studies can be found in Table 3.

Experienced barriers and facilitators

Only two of the 10 studies specifically asked about barriers and facilitators for the use of an eHealth self-management intervention through an interview [33] and an online guestionnaire [32].

In a mobile program for chronic MSK pain, patients reported that the program was too long, that is was unclear how they had to answer some of the questions, that the design of the program was confusing, that they got the idea of not getting new information by the program and that there was a lack of audio and video fragments [32]. However, they all liked the content and information and found the program easy to use [32]. After using the Auricular Point Acupressure Smartphone app, barriers were that the screen on their smartphone was too small to look at the videos (n=4), they had to watch the videos multiple times to know where the ear point locations are situated (n=5) and five persons reported to prefer a face-to-face training session [33]. They also reported that the eHealth intervention was user friendly and that it empowered them to come to self-management [33].

Discussion

No study was found that made a direct comparison between both populations when examining the design or effects of an eHealth self-management intervention. Concerning the effectiveness, only two studies in an MSK population, reported a significant difference between the control and intervention group [34, 36], with only one in favor of the self-management intervention [34]. Looking at the clinical trials that only reported on time effect, two breast cancer studies reported a significant decrease in pain intensity over time [30, 31], as well as one MSK study [32]. However, with no control group, these time-effects have little value in proving effectiveness. Additionally, these effects were not very long lasting. The other included studies reported no significant difference over time or between groups [28, 29, 33, 35, 37, 38].

The high risk of bias and several other factors of the included studied hinder firm conclusions on the effect of an eHealth self-management intervention on pain intensity within these populations.

First, different measurement methods of pain intensity were used. Because of the subjectivity and complexity of pain, it is important to select the most sensitive and accurate outcome measure [39]. The VAS is considered as the 'gold standard' for measuring pain intensity as it is universal in application, simple and quick to administer and easily understood by the patient [40].

Second, according to the biopsychosocial model, pain has many influencing factors which are unique to the individual [41]. Different pain mechanisms can be present and psychological and social factors vary in each person. Due to the individuality of pain, a more tailored approach to the individual might be more applicable and group research might not be able to represent the effect on the individual adequately.

Lastly, studies on acute and chronic pain management were included. Two studies used a pre-operative intervention for acute post-operative pain relief and showed inconclusive evidence. The study with a breast cancer population [30] found a beneficial time effect in the group with education on mind-body science but found no difference in comparison to the control group who received general health information, both delivered through eHealth. In contrast, the study in low back pain patients [36] who underwent spinal fusion surgery, reported a beneficial effect in favor of the usual treatment-control group over the group who also received an additional eHealth program. Although, this finding was only present in one outcome, namely immediate leg pain 2-3 days after surgery. The absence of pre-operative pain in breast cancer patients might offer an explanation. Providing education, regardless if it is specific on pain or more general, might decrease anxiety around surgery resulting in a lower pain intensity post-operatively. This finding might contribute to the trend

 Table 3: Effect of an EHealth self-management intervention on pain intensity.

Study ID ^a	Inclusion and exclusion criteria	Patient characteristics ^b Age: mean (SD or range)	Intervention ^c (more information within Table 3)	Outcome measures ^d	Results ^e
Darnall et al. RCT (pilot) USA (N-A) [30]	Inclusion criteria (1) Women scheduled for lumpectomy or mastectomy Exclusion criteria (1) Inability to complete study procedures (2) Lack of access to internet and phone (3) Pregnancy (4) Ongoing pain or disability-related legal claim	 Total 68 Sex F Breast cancer Intervention group (n=36): Age 51.27 (SD not reported) Control group (n=32): Age 61.16 (SD not reported) 	Intervention group (n=36): Before surgery: "My surgical success" Control group (n=32): Before surgery: Digital general health education	collection Questionnaire/ interview Tools used for data collection PROMIS (of last 7 day): Pain in- tensity subscale Times of data collection T0: Baseline T1: 2 weeks after surgery T2: 4 weeks T3: 8 weeks	Mean (SEM) Within groups Intervention T0: 1.47, SEM=0.12 T4: 1.98, SEM=0.10 p=0.0002 ^a Control T0: 1.75, SEM=0.13 T4: 1.86, SEM=0.10 p=0.4191 Between groups Intervention vs. Control I: 1.73, SEM=0.09 C: 1.81, SEM=0.09 p=0.53
Henry et al. UT (pilot) USA (N-A) [31]	Inclusion criteria 1. Women with a history of stage 0–3 breast cancer 2. Reporting pain, fatigue or trouble sleeping 3. Completed all indicated surgery, radiation therapy, and chemotherapy at least 3 months before enrolment 4. If endocrine therapy was prescribed, patients had to have initiated treatment at least 3 months before enrolment 5. Access to and be able to operate a computer with internet access 6. Be able to read and understand English 7. Report one of the following: - 4 of 10 to the question, "how tired did you feel in the past week?" - Yes to the question, "did you have trouble sleeping in the past week?" - 4 of 10 to the question, "what was your average pain in the past week?" Exclusion criteria A diagnosis of obstructive sleep apnea or restless leg syndrome that was currently	 Sex F Age 58.0 (SD 10) Breast cancer (I–III) (B) Cohort of pain as primary complaint Total 19 (at T1: 16) Sex F Age 57.2 (SD 10.2) 	Intervention: "PROSPECT" cancer-specific symptom management	T4: 12 weeks Method of data collection Questionnaire Tools used for data collection PROMIS-29: Sub- scale pain in- tensity Times of data collection T0: Baseline T1: 8 weeks	(A) Mean T0: 3.62 T1: 2.66 Difference mean (SD) T0-T1: -0.89 ± 1.7 p<0.001 ^a (B) Mean T0: 4.9 T1: 4.4 Difference mean (SD) T0-T1: -0.5 ± 1.8 p=0.44

Table 3: (continued)

Study ID ^a	Inclusion and exclusion criteria	Patient characteristics ^b Age: mean (SD or range)	Intervention ^c (more infor- mation within Table 3)	Outcome measures ^d	Results ^e
Allen et al. RCT USA (N-A) [28]	Inclusion criteria (1) Veterans with a diagnosis of knee osteoarthritis (2) Self-reported joint pain ≥3/10 in a knee with osteoarthritis during the past 2 weeks Exclusion criteria (1) Cooccurring rheumatic conditions (2) Recent completion of PT for knee osteoarthritis (3) Health conditions that would make unsupervised exercise unsafe	- Total n=345 - Sex M/F (292/53) - Age 60.0 (SD 10.3) - Knee osteoarthritis	Intervention group (n=230): STEP-KOA, step 1: Exercise program Control group (n=115): Educational materials	Method of data collection Interview Tools used for data collection WOMAC: Pain subscale Times of data collection T0: Baseline T1: 3 months	Mean difference (range) Within groups Intervention T0-T1: -1.0 (-1.5 to -0.5) Control T0-T1: -0.1 (-0.7 to 0.5) Between groups: Mean difference T1 I-C: -0.9 (-1.7 to -0.1)
Carpenter et al. RCT USA (N-A) [29]	Inclusion criteria (1) ≥40 years (2) Non-cancer related lower back pain for at least 6 months (3) Average pain ≥4/10 for the past week (4) Access to a computer with audio capabilities, an internet connection, and a working email account (5) Could read and write in English (6) Not participated in a multidisciplinary program or CBT for chronic pain within the past three years Exclusion criteria See inclusion criteria	 Total 164 (at baseline) Sex M/F (27 %/83 %) Age 42.5 (SD 10.3) Chronic low back pain 	Intervention group (n=70): "Wellness Workbook" Control group (n=71): Wait-list control group, after 3 weeks access to wellness workbook	Method of data collection Questionnaire Tools used for data collection NRS (of the last 7 day): - Average - Highest - Lowest Times of data collection T0: Baseline T1: 3 weeks after start intervention T2: 6 weeks after start intervention	T1: 3.3 + 1.9 T2: /
	Inclusion criteria	Total 104Sex M/F/O (26/76/2)	Intervention (n=51): PPN self-evaluation	Method of data collection	T1: p=0.784 Mean (SD) Within groups

Table 3: (continued)

Study ID ^a	Inclusion and exclusion criteria	Patient characteristics ^b Age: mean (SD or range)	Intervention ^c (more information within Table 3)	Outcome measures ^d	Results ^e
Kohns et al. RCT (pilot) USA (N-A) [34]	 Diagnosis of low back pain and/or fibromyalgia for at least 3 months English-speaking Exclusion criteria The presence of other serious disease or impairment Clear evidence of significant structural damage likely causing their pain Being considered for interventional spine procedures or surgery Use of illicit drugs Serious mental illness 	•	intervention Control (n=53): General health education	Questionnaire Tools used for data collection BPI (last 7d): mean of: - Current pain - Highest pain - Lowest pain - Average pain Times of data collection T0: Baseline T1: 1 month	Intervention T0: 4.98 ± 1.54 T1: 4.03 ± 0.18 T2: 4.46 ± 0.23 Control T0: 4.50 ± 1.73 T1: 4.60 ± 0.17 T2: 4.21 ± 0.23 Between groups Intervention vs. control T1: p=0.024 ^a T2: p=0.434
Kristjánsdóttir et al. RCT Nor- way (EU) [37, 38]	Inclusion criteria (1) Female (2) ≥18 year (3) Participating in the inpatient multidimensional rehabilitation program for chronic pain (4) Chronic widespread pain for more than 6 months (5) Being able to use a smartphone Exclusion criteria (1) Participating in another research project at the rehabilitation centre (2) Not being diagnosed with a profound psychiatric disorder	 Total 135 (112 completed the intervention) F Age 43.33 (SD 11.18) Fibromyalgia + chronic widespread pain 	Intervention group (n=68): Self-help pain management material Control group (n=48): An interactive CBT-intervention + HCP interaction + self-help pain management material	T2: 10 months Method of data collection Questionnaire Tools used for data collection VAS Times of data collection T1: Baseline, af- ter inpatient rehabilitation program T2: Completion smartphone intervention (4 weeks) T3: 6 months af- ter T1 T4: 12 months after T1	Within groups Mean (SD) intervention T1: 52.99 ± 21.27 T2: 50.56 ± 23.37 T3: 58.45 ± 22.46 T4: 55.85 ± 2.73 Control T1: 53.07 ± 22.20 T2: 54.14 ± 24.06 T3: 51.96 ± 23.76 T4: 56.28 ± 28.24 Mean difference (range) Intervention T2-T3: -0.99 (-7.48 to 5.50) (p=0.76) T2-T4: 5.82 (-1.26 - 12.90) (p=0.10) Control T2-T3: 1.11 (-3.9 to 6.16) (p=0.66) T2-T4: 0.61 (-7.0 to 8.24) (p=0.87) Between groups Effect size T2: -0. (p=0.49)
Malliaras et al. RCT (pilot) Australia (O) [35]	 Inclusion criteria (1) Shoulder pain mainly around the area shown in the photos (2) Shoulder pain brought on by moving your arm above head 	 Total 36 Sex F/M (32/4) Age 53.9 (SD 12.0) Rotator cuff-related shoulder pain 	Intervention group (n=12) (1) Advice only (2) Advice with recommended care (n=12) Control group (n=24) (3) Advice with recommended care and telerehabilitation (n=12)	Method of data collection Questionnaire Tools used for data collection VAS: Worst pain last 7 days Times of data	T3: 0.28 (p=0.22) Mean (SD) <i>Within groups</i> Intervention Advice only: T0: 56.8 ± 17.9 T1: 55.7 ± 22.2 T2: 41.8 ± 23.1 Recommended

Table 3: (continued)

Study ID ^a	Inclusion and exclusion criteria	Patient characteristics ^b Age: mean (SD or range)	Intervention ^c (more information within Table 3)	Outcome measures ^d	Results ^e
Strøm et al. RCT Denmark (EU) (36]	(3) Ability to lift arm to the height of 90 degrees of elevation Exclusion criteria (1) 18 year (2) Shoulder pain for less than 3 months (3) Prior surgery for their currently most symptomatic shoulder (4) Another complaint more troubling than their shoulder (5) Diagnosis by a health professional of frozen shoulder, arthritis, a labral tear, instability (6) Shoulder pain a result of a shoulder dislocation (7) Shoulder pain made worse by neck movement (8) Severely depressed (9) Taking recreational drugs, oral steroids or blood thinning medications (10) Angina, heart problems, or severe middle abdominal or upper back pain (11) History of cancer (12) Recent dizziness, blurred vision, slurred speech, difficulty swallowing, falls, or unsteadiness (13) Recent seizure Inclusion criteria (1) Patients scheduled for first-time elective one-three level lumbar spine fusion: Instrumented posterolateral fusion (PLF) or transforaminal interbody fusion (TLIF) (2) Attending baseline visit 1–5 weeks prior surgery Exclusion criteria (1) 18 (2) Patients with psychotic disease, schizophrenia or other psychotic disorder (3) Inability to communicate in Danish	- Total 99 - Sex M/F (35/64) - Age 54 (29–79) - Low back pain - Spondylolisthesis: n=35 - Degenerative disease: n=64	Intervention group (n=48): - W-SPIINA program + standard course of treatment Control group (n=51): - Standard course of treatment, rehabilitation, and information (starting 1–5 week before surgery)	collection T0: Baseline T1: 6 weeks T2: 12 weeks T2: 12 weeks Method of data collection Questionnaire Tools used for data collection LBPRS Times of data collection T0: Baseline (1–5 week before surgery) T1: 2 days after surgery T2: 3 months T3: 6 months	Care T0: 51.6 ± 22.4 T1: 41.5 ± 22.2 T2: 44.8 ± 28.1 Control Recommended care and telerehabilitation T0: 59.7 ± 21.1 T1: 31.9 ± 23.1 T2: 28.1 ± 25.6 Median (IQR) Within groups Back pain-back pain right now Intervention T1: 6 (5-7) T0-T1: 1 (2-0) T2: 3 (1-5) T0-T2: -2 (-1 to -4) T3: 3 (2-4) T0-T3: -3 (-1 to -4) Control T1: 5 (3.5-7) T0-T1: 0 (-2 to T2: 3 (1-4) T0-T2: -3 (-1 to

Table 3: (continued)

Study ID ^a	Inclusion and exclusion criteria	Patient characteristics ^b Age: mean (SD or range)	Intervention ^c (more infor- mation within Table 3)	Outcome measures ^d	Results ^e
	(4) Patients without an				T3: 3 (1-5)
	internet connection				T0-T3: -2 (-1
					to -4)
					Between groups
					Between group
					difference
					p-value
					T1: p=0.42
					T2: p=0.38
					T3: p=0.51
					Within groups
					Back pain–the
					worst back pain
					within the last
					14 days
					Intervention
					T1: 9 (8–10); 1 (2–
					T2: 6 (3–8); –2 (–4
					to 0)
					T3: 5 (3–7); –3 (–4
					to 0)
					Control
					T1: 9 (8–10)
					T0-T1: 1 (2-0)
					T2: 5 (2-8)
					T0-T2: -3 (-5 to (
					T3: 5 (2-7)
					T0-T3: -3 (-5 to 0
					Between groups
					Between group
					difference
					p-value
					T1: p=0.78
					T2: p=0.24
					T3: p=0.59
					Within groups
					Back pain–media
					back pain within
					the last 14 days
					Intervention
					T1: 6 (5-7)
					T0-T1: 0 (1 to -1)
					T2: 3 (2-5)
					T0-T2: -2 (-0.5
					to -3.5)
					T3: 3 (2-5)
					T0-T3: -2 (-1
					to -4)
					Control
					T1: 8 (5-8)
					T0-T1: 0 (1 to -1)
					T2: 3 (1.5–5)
					T0-T2: -3 (-1

Table 3: (continued)

Study ID ^a	Inclusion and exclusion criteria	Patient characteristics ^b Age: mean (SD or range)	Intervention ^c (more information within Table 3)	Outcome measures ^d	Results ^e
					T3: 4 (2-5)
					T0-T3: -2 (-1
					to -4)
					Between groups
					Between group
					difference
					p-value
					T1: p=0.79
					T2: p=0.26
					T3: p=0.98
					Within groups
					Leg pain–leg pair
					right now
					Intervention
					T1: 3 (2-6)
					T0-T1: 1 (3-2)
					T2: 2 (0-5)
					T0-T2: -2 (-5 to
					T3: 1 (0-5)
					T0-T3: -2.5 (-5 to
					0)
					Control
					T1: 2 (0-4)
					T0-T1: 3 (5-0)
					T2: 1 (0-3)
					T0-T2: -3 (-5
					to -1)
					T3: 1 (0-4)
					T0-T3: -3 (-5
					to -1)
					Between groups
					Between group
					difference
					p-value
					T1: p=0.01 ^a
					T2: p=0.17
					T3: p=0.38
					Within groups
					Leg pain–the wor
					leg pain within th
					last 14 days
					Intervention
					T1: 7 (6-9)
					T0-T1: 1 (0-3)
					T2: 3 (1–7)
					T0-T2: -1.5 (-4 to
					0)
					T3: 4 (1–8)
					T0-T3: -2 (-4 to -
					Control
					T1: 7.5 (5.5-9)
					T0-T1: 1.5 (0-4)
					T2: 1 (0-5)
					T0-T2: -2 (-4 to (
					T3: 2 (0-6)

Table 3: (continued)

Study ID ^a	Inclusion and exclusion criteria	Patient characteristics ^b Age: mean (SD or range)	Intervention ^c (more information within Table 3)	Outcome measures ^d	Results ^e
Johnson et al. UT (pilot) USA (N-A) [32]	Inclusion criteria (1) ≥18 year (2) Veteran status (3) Having a chronic MSK pain rating ≥4/10 (4) Having pain for more than 3 months Exclusion criteria Currently undergoing treatment with a psychologist, psychiatrist, or other mental health professional for a condition such as bipolar disorder, anxiety, or substance abuse	 Total 69 (44 at follow-up) Sex M/F (56/13) Age 50.3 (SD 12.0) Chronic MSK pain 	Intervention: Health eRide program	Method of data collection Questionnaire Tools used for data collection NRS (last 7d): Right now Usual level Best level Worst level Times of data collection TO: Baseline T1: After 30202Fdays	T0-T3: -2(-4 to 0) Between groups Between group difference p-value T1: p=0.40 T2: p=0.73 T3: p=0.62 Within groups Leg pain-median leg pain within the last 14 days Intervention T1: 5 (5-7) T0-T1: 0 (-2 to 0) T2: 2 (1-5) T0-T2: -3 (-5 to -1) T0-T3: -2 (-5 to -1) Control T1: 5 (3-7) T0-T1: 0 (1 to -2) T2: 1 (0-3) T0-T2: -3 (-5 to -1) T3: 1 (0-5) T0-T3: -3 (-5 to 0) Between groups Between groups Between groups Between group difference p-value T1: p=0.20 T2: p=0.55 T3: p=0.51 Mean (SD) Pain now T0: 5.8 ± 2.1 T1: 5.0 ± 2.0 T0-T1: p=0.002a Usual pain past week T0: 6.8 ± 1.6 T1: 5.4 ± 1.9 T0-T1: p=0.001a Best pain past week T0: 4.9 ± 2.1 T1: 4.0 ± 2.1 T0-T1: p=0.002a Worst pain past week T0: 4.9 ± 2.1 T1: 4.0 ± 2.1 T0-T1: p=0.002a Worst pain past week T0: 8.3 ± 1.4

Table 3: (continued)

Study ID ^a	Inclusion and exclusion criteria	Patient characteristics ^b Age: mean (SD or range)	Intervention ^c (more information within Table 3)	Outcome measures ^d	Results ^e
Kawi et al. UT USA (N-A) [33]	Inclusion criteria (1) ≥18 year (2) Able to read and write English (3) Chronic MSK pain for at least 3 months (4) An average intensity of pain >4 on an 11-point numerical pain scale for the previous week (5) Smartphone user (6) Able to apply pressure to the seeds taped on their ears Exclusion criteria Any allergy to latex (tapes used on ear points)	- Total 30 - Sex F/M (25/5) - Age 54 (SD 12.49) - Chronic MSK pain	Intervention: Auricular point acupressure instructions	Method of data collection Questionnaire Tools used for data collection BPI (last 7 day) I: Current pain Highest pain Lowest pain Average pain Times of data collection T1: Baseline T2: Immediately	Mean (SD) T1: 7.2 ± 1.8 T2: 4.7 ± 2.86 T3: 5.0 ± 2.67
	(6) Able to apply pressure to the seeds taped on their ears Exclusion criteria Any allergy to latex (tapes used	I			 Average pain Times of data collection T1: Baseline

^aEU, Europe; N-A, Nord-America; O, Oceania; UT, uncontrolled trial; RCT, randomized controlled trial; ^bM, male; F, female; MSK, musculoskeletal; ^cHCP, health care provider; CBT, cognitive behavioral therapy; PPN, pain psychology and neuroscience; dWOMAC, Western Ontario and McMasters Universities Osteoarthritis Index; PROMIS-29, Patient-Reported Outcomes Measurement Information System—29; VAS, Visual Analogue Scale; BPI, Brief Pain Inventory; NRS, Numeric Rating Scale; LBPRS, Low Back Pain Rating Scale. eIQR, interquartile range (25th and 75th percentile); SD, standard deviation; *=p<0.05.

of adding pre-operative education as part of post-operative pain management.

Only one study in a **chronic pain** population found a significant result between groups [34]. Most interventions for chronic pain management target reconceptualization of pain and behavioral changes [42, 43]. As this takes time, it might be that the follow-up length was too short to see a possible effect.

The focus of this review was the effect of the interventions on pain intensity, which is only one aspect within the complexity of pain. When considering other pain-related outcomes in the included studies, assessments included outcomes related to the impact of pain on a patients daily activities and functioning (e.g. pain interference, pain disability) and other outcomes related to pain experience (e.g. pain-related beliefs, pain catastrophizing and pain coping).

In the first category of outcomes related to the impact of pain on daily functioning, only one study, including a MSK population, reported a significant effect on pain interference [34] and two studies, also including a MSK population, reported a significant effect on pain disability [32, 37]. In contrast, some significant effects were found on pain-related beliefs [29, 31] and pain catastrophizing [29] in

both populations. In the studies that include an MSK-populations, there were significant effects on additional pain-related outcomes such as pain coping [32], psychological/brain attributions and readiness for pain self-management [34].

Despite the positive effects in other pain-related outcomes, there was a consistent lack of transfer to pain intensity. Additionally, some studies reported an effect on outcomes related to pain experience, but not on the outcomes related to a patients daily activities and functioning. Future research is required to explore the interaction between these different outcomes and to determine how eHealth self-management interventions should be tailored to address this interaction. Lastly, it would be of interest to take other health-related outcome measures, like quality of life, into account when looking at the effect of an eHealth self-management intervention.

Barriers and facilitators

Very limited information was provided on barriers and facilitators for the use of an eHealth self-management intervention. Previous literature on barriers and facilitators of an eHealth intervention identified three themes: individual, environmental and organizational, and technical barriers [44]. To our knowledge, there yet exists no valid tool that inventories barriers and facilitators. Tools that are often used are user satisfaction questionnaires or interviews. Future research should focus on developing valid research methods to identify the experienced barriers and facilitators of an eHealth intervention.

Recommendations

The findings of this review indicate that design characteristics are similar in both populations. Despite the limited amount of included studies, a high risk of bias and a high amount of heterogeneity between the different eHealth self-management interventions, some cautious recommendations on design of eHealth self-management support programs can be made. In both populations, targeted education was used, be it on pain itself or more conditionspecific education [30, 31, 34-36]. Targeted education appears to be more beneficial then only providing general information such as information on surgical treatment [36] or instructions on a technique [33]. Contemporary pain science education has already been proven to be a successful intervention in pain mediation in oncological and MSK pain populations. All studies reporting significant effects contained at least one aspect of CBT, suggesting that this might be an important modality [30-32, 34, 36]. At the same time, other studies who also implemented CBT as part of their intervention, found no significant results [29, 37, 38]. CBT comprehends multiple strategies with the aim of behavior change [42]. No clear similarities were seen in which elements were effective. We hypothesize that the combination of elements is likely more important than the isolated elements.

In line with the existing literature on positive effects of peer support to promote health behavior, the included studies who used a form of social support similarly showed beneficial effects [32, 36]. Previous literature shows that higher levels of pain have been associated with a decrease in social support [45]. Because of this vulnerability, social support should be facilitated and eHealth can provide an easier way to engage with other patients for example through online support groups. Although, this addition of social support into the intervention was only used within the MSK studies, previous research has shown that a low level of social support has a negative predictive effect on pain, inflammation and depression after breast cancer treatment [46]. Therefore, we recommend the use of social support in both populations.

Some studies made the comparison of an individual and an HCP-supported eHealth intervention, resulting in a better outcome on pain intensity for the HCP-supported group, albeit not significant [35, 37, 38]. Another benefit of HCP-support is a higher adherence to the intervention [47]. A barrier that was reported in one study, was the lack of in-person sessions, indicating that patients have a need for additional support of HCPs when using eHealth interventions.

Limitations and strengths

A first limitation is the large heterogeneity in how the outcome measure of interest, i.e. pain intensity, is assessed, making a meta-analysis impossible.

A second limitation concerns the high risk of bias of the included studies. To investigate the effectiveness of an intervention, RCTs have a higher level of evidence then uncontrolled trials. However, due to the limited available studies in the oncological population, we decided to also include uncontrolled trials. To depict the risk of bias in a uniform way, the same scoring tool was used for both study designs. However, this leads to a high risk of bias of the uncontrolled trials as this design contains only one group. Within the RCT studies, the lack of a well-designed control group is a first contributor to the high risk of bias. Second, a high amount of drop-out was found in the included studies and third, most studies did not use an appropriate analysis to correct for the bias due to missing outcome data. EHealth self-management interventions are often paired with a low adherence and a high drop-out [47]. Participants might not be motivated enough to follow the complete program due to the lack of feedback and personal interaction with an HCP [47]. Lastly, we also included pilot studies, the lack of an appropriate sample size leads to statistical underpowered studies. Because of the reasons mentioned above, the reported results should be interpreted with caution.

A strength of this systematic review is that we included both MSK-and cancer-related pain, resulting in a broad overview. Another important strength of this systematic review is that we only included studies where at least the intervention or control group existed of an individual eHealth intervention with no active interference of an HCP. This differs from the already existing reviews of Hernandez-Silva et al. (2018) and Thurnheer et al. (2019), both systematic reviews found beneficial effects of eHealth self-management interventions in pain management and Thurnheer et al. (2019) reported that eHealth interventions are well liked by both the patients and the health care providers [16]. These findings are in contrast with the low

evidence retrieved in the present review and suggests the importance of the active role of HCPs in supporting selfmanagement. Consequently, this systematic review provides an overview of the sole effect of an eHealth selfmanagement intervention without the need for a health care provider on pain intensity.

Conclusions

The aim of this review was to look at the comparison of the effect of an eHealth self-management intervention on pain intensity in oncological vs. MSK populations. This review is innovative as it looks at self-management without the active involvement of HCPs. Overall, the available literature is limited and the included studies are too heterogenous to make a valid conclusion on the comparison of the two population groups. Regarding each separate population, the evidence is still preliminary, due to the lack of sound RCT's. However, lessons can be learned from both populations. Education, aspects of cognitive behavioral therapy and social support seem universally applicable, regardless of population.

Further research should incorporate experienced barriers and facilitators and there is a high need of studies making the direct comparison of the effect of an eHealth self-management intervention on pain intensity in an oncological vs. a MSK population.

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