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Review

Effectiveness of Digital-Based Interventions on Physical and Psychological Outcomes Among Cancer Patients: A Systematic Review and Meta-Analysis

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ABSTRACT

Objective: Evolving digital technology has paved the way for endless potentiality. Leveraging on digital technology for healthcare purposes can target cancer patients, thus improving physical and psychological symptoms. Nevertheless, there is limited consolidated evidence on the effectiveness of virtual reality (VR) and mobile applications. This review aimed to synthesize evidence concerning the effectiveness of VR and mobile-based interventions on physical (pain, fatigue, and sleep) and psychological (anxiety and depression) outcomes among cancer patients.

Methods: A comprehensive literature search was conducted on ten electronic databases, ongoing trials, and grey literature, reported between 2013 to 2023. All randomized controlled trials (RCTs) examining VR and mobile-based interventions on the physical or psychological outcomes among people with cancer were included. Two independent reviewers screened records for eligibility, appraised methodological quality, and extracted data from included studies. The Cochrane Risk of Bias tool was used for data appraisal, and a modified Cochrane data extraction form was used for data extraction. Meta-analysis and subgroup analysis were used to analyze data.

Results: In total, 43 studies were included. VR relaxation videos and game-based activities were efficacious in improving cancer-related pain. Mobile applications with educational content, symptom monitoring, relaxation videos, teleconsultation, and regular reminders contributed to positive effects on all outcomes. Mindfulness practice appeared to improve sleep quality, anxiety, and depression. Intervention effects sustained at least 6 months for all outcomes, except sleep.

Conclusions: VR and mobile-based interventions had the potential to improve pain, fatigue, sleep, anxiety, and depression at post-intervention. Future RCTs are required to further test both digital interventions on specific types of cancer on multiple research settings.

Implications to Nursing Practice: VR and mobile-based interventions can be offered in clinical settings to help cancer manage their pain, fatigue, sleep, anxiety, and depression. VR relaxation videos, game-based activities, teleconferences, mindfulness, education, and system reminders can be included.

Cancer is a leading global cause of death, with an estimated 19.3 million new cases and 10 million cancer deaths in 2020.[1] People with cancer usually encounter physical (pain, fatigue, sleep issues) and psychological symptoms (anxiety and depression).[2-4] Cancer pain encompasses various pain conditions, characteristics, and mechanisms.[5] Cancer pain is a frequent cause of emergency visits, accounting for nearly half.[6] Nevertheless, cancer pain control remains inadequate, affecting up to 50% of cancer patients, resulting in lower quality of life and problematic daily activities.[7,8]

Cancer-related fatigue (CRF) is the feeling of tiredness, occurring in nearly half of all cancer patients.[9] In comparison with fatigue in healthy individuals, CRF is more persistent, interfering daily functioning by overwhelming exhaustion and energy depletion.[9,10] CRF has a negative impact on quality of life, especially for elderly with impaired functional dependence.[11] Sleep is a vital part of human functioning, comprising of a complex multitude of processes.[12] Sleep disturbances entail difficulties in falling asleep, poor sleep quality, and increased

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Layperson Summary

What we investigated and why

Technology has been used to provide care for people with chronic illness, including cancer. The use of technology allows patients to access information anytime and anywhere. We were aware that virtual reality and mobile applications have been frequently used for healthcare purposes. Therefore, we wished to find out if such technologies could help patients with cancer manage physical problems and emotional issues. For the physical problems, we specifically looked at pain, fatigue, and sleep problems. For the emotional issues, we were interested in anxiety and depression. If the technologies could help improve the problems, we could offer them for cancer patients to use in hospital or at home.

How we did our search

We searched for research studies from 13 different databases to ascertain we obtained all relevant information. Then, we assessed the quality of the information and extracted the relevant one for analysis.

What we have found

We found 43 research studies to be included in this review. We found that virtual reality and Mobile applications can be used to improve pain, fatigue, sleep, anxiety, and depression in patients with cancer. VR relaxation videos and game-based activities helped improve cancer-related pain. Mobile applications with educational content, symptom monitoring, relaxation videos, teleconsultation, and regular reminders helped improve all outcomes. Mindfulness practice appeared to improve sleep quality, anxiety, and depression. Effects of virtual reality and mobile apps last at least 6 months for all outcomes, except sleep.

What it means

Healthcare providers may offer relaxation videos or game-based activities via virtual reality devices to cancer survivors in clinical settings. Furthermore, healthcare providers may offer educational content relating to cancer and treatments, relaxation videos, teleconsultation, and symptom monitoring using mobile applications. Mindfulness practice can be offered to help enhance sleep quality and reduce anxiety and depression.

daytime sleepiness, which affect more than half of cancer patients.[13] Sleep problems deplete morning energy, eventually diminishing quality of life.[14]

Anxiety and depression affect 10% and 35% of cancer patients respectively, signifying a huge rise compared to previous years.[15]Anxiety may progressively worsen cancer-related conditions.[16] Anxiety and depression pose difficulties in managing, controlling, and complying to treatments, leading to increased hospital stays and increased mortality rates.[17,18,19] Relationship between physical and psychological factors exist,[20] and the presence of either factors influence the severity of the other.[21,22] This warrants the need for effective interventions in managing depression and anxiety.

Conventional treatments for cancer include chemotherapy, radiotherapy and surgery.[23] Unbeknownst to some, unorthodox methods such as digital health interventions have gradually emerged in oncology.[24] Digital health interventions (such as virtual reality (VR) and mobile apps)[25] improve healthcare accessibility, quality of care, and healthcare costs.[24] VR offers multisensory lifelike experiences in individuals. According to previous reviews, VR serves as a distraction technique to divert the individual's cognitive attention away from unpleasant sensations,[26,27] potentially reducing anxiety and pain during chemotherapy.[28] This state-of-the-art technology acts as a medium for channeling visual and audio information. VR-based interventions involve educational contents,[29] relaxation videos,[26] and games,[28] among others.

Mobile applications have become a frequently operated modality throughout the world. A subset known as mobile health (mHealth) apps are widely used for such features as patient education, symptom monitoring, and medication tracking, aiding cancer self-management.[30,31,32] Furthermore, mHealth bridges gaps in accessing cancer care especially for remote patients and reducing symptom response time.[33]

Knowledge Gaps and Methodological Limitations

Although digital health interventions have become increasingly available, there is still limited evidence to support their efficacy.[34] Two systematic reviews examining the effects of VR and mobile applications were identified. However, one[35] of which did not assess sleep while another review[36] excluded anxiety and depression. Moreover, participants in the reviews mainly focused on examining cancer survivors, not cancer patients. In addition, most primary studies included in the reviews had large heterogeneity in research designs. Specifically, pooled effect sizes from combined RCTs and quasiexperimental design, might be misleading and inaccurate. Other systematic reviews had methodological issues such as unclear search strategy, the use of limited electronic databases, and questionable meta-analyses, which might lead to inconclusive findings. The summary of existing systematic reviews is presented in Appendix A. Hence, with all these limitations of current reviews, it warrants a comprehensive systematic review and meta-analysis.

Current Systematic Review

Digital health technology, particularly VR and mobile apps, are the main focus of this review given their popularity and wide usage. This systematic review aimed to; a) synthesize available evidence concerning the effect of digital health interventions on the physical (pain, fatigue and sleep) and psychological outcomes (anxiety and depression) among adult cancer patients, and b) analyse the effects of VR or mobile apps on the mentioned outcomes.

Methods

This systematic review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[37]

Eligibility Criteria

The eligibility criteria were based on the population, intervention, comparator, and outcomes (PICO) framework. We considered studies examining people aged 18 years and above with cancer diagnosis. Studies that included cancer survivors or those with cancer under remission would be excluded. Concerning interventions, we considered studies testing the effectiveness of VR and mobile apps. Intervention contents may entail, but not limited to, videos, education, symptom monitoring, and/or relaxation. Nondigital or nontechnological interventions would be excluded. Regarding comparison, we considered standard care, no interventions, or waitlisted controls.

Concerning study outcomes, studies that measured pain, fatigue, sleep, anxiety, or depression in cancer patients would be included. Randomized controlled trials (RCTs) would be considered. RCTs provide the highest level of evidence concerning the efficacy of interventions.[38,39] Primary research reported in English within 10 years (2013 to 2023) were included in this review.

Search Strategy

Formulation of search strategy encompassed a combination of keywords, index terms, truncation, proximity, and Boolean operators to ensure comprehensiveness (Appendix B). Development of the search strategy was undertaken using peer review and consultation with an experienced librarian. For published studies, ten electronic databases were searched; PubMed, Cochrane Library, Medline, Embase, PsycINFO, Cumulative Index to Nursing & Allied Health Literature (CINAHL), Web of Science, Scopus, Institute of Electrical and Electronics Engineers Xplore (IEEE Xplore) and ProQuest Dissertations & Theses Global (ProQuest). Grey literature was searched through ProQuest and Mednar. Ongoing trials were searched from the online registry of clinical trials (ClinicalTrials.gov). Reference lists of existing reviews and journals (Journal of Clinical Oncology and Journal of Clinical Nursing) were screened for additional studies.

Study Selection

The PRISMA flow diagram[40] provided as a guidance for study selection. Search results were exported to EndNote 20.[41] Removal of duplicates were performed digitally and manually. Two reviewers conducted a joint pilot test on screening of six to eight studies to ensure consistency.[42] During the first round of screening, both reviewers (CCG & XMG) independently examined the titles and abstracts according to the eligibility criteria. Following this, the full texts of those who fulfilled the criteria or had an uncertain eligibility status were screened to determine inclusion. Disagreements between the reviewers were resolved by consulting a third reviewer (PKY).

Data Extraction

Extraction of data was based on a modified version of Cochrane data extraction form,[43] which two reviewers independently piloted before actual data were extracted. The extracted data were eligibility criteria, study characteristics, population demographics (age, gender, and cancer type), content of intervention (type, duration, and providers), type of control groups, outcome measurements (mean, standard deviation, and total values), and results (Appendix C). Authors of studies with missing data would be contacted and requested for the missing data.

Risk of Bias Assessment

Risk of bias for each included study was assessed by two independent reviewers (CCG & XMG) using the Cochrane's Risk of Bias tool (ROB 1).[44] The ROB comprises six domains of bias; selection, reporting, performance, detection, and attrition. Judgement for each domain was assigned as either 'high', 'low' or 'unclear' depending on the information provided by the study (Appendix D). A pilot test of the ROB 1 tool on six studies was carried out to set a benchmark in judgment before proceeding with the actual assessment. Any disagreements in evaluation between the reviewers are resolved by consulting a third reviewer (PKY). Risk of bias graph and summary figures were then generated for a summarized overview.

Data Synthesis

RevMan Web was used to perform statistical analysis.[45] A random-effects meta-analysis was performed given heterogeneity of intervention contents and platforms.[46] The included studies had different measurements for continuous data, which prompted the use of standardized mean differences (SMD).[47] SMD with its 95% confidence interval were used as an effect measure of continuous outcomes, with interpretations as small ($d = 0.2$), medium ($d = 0.5$), or large effects ($d = 0.8$).[48] Dichotomous outcomes were accounted for through the use of risk ratio (RR) and its corresponding 95% CI.[49] RR of 1 is indicative of intervention inefficiency, while values of more than 1 signify an increased likelihood of an event occurrence from the intervention.[49]

Heterogeneity across effect sizes was assessed using Cochran's Q test and I^2 statistic with interpretation values of likely irrelevant (0% to 40%), moderate heterogeneity (30% to 60%), substantial heterogeneity (50% to 90%), and considerable heterogeneity (75% to 100%).[50] Outliers that may have occurred from differing participant demographics, intervention methods, and outcome measurements would be evaluated through sensitivity analysis.[51] Diversity in treatment effects across studies would be examined using subgroup analysis.[50] Egger's test via funnel plot asymmetry was conducted to investigate for any skewed effect indicating publication bias.[52]

Overall Quality of Evidence

The overall quality of evidence of the RCTs in this review was appraised using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach[53] through GRADEpro GDT software.[54] GRADE involves factors that either lead to a rating up or rating down of the evidence, additionally, the certainty of evidence includes high (very confident that true effect is close to estimated effect), moderate (moderately confident that true effect is probably close to estimated effect), low (true effect may be different from estimated effect), and very low (true effect is likely different from estimated effect).[55]

Results

Search Summary

A comprehensive search yielded 24,144 records and duplicates were removed, leaving 284 articles for full-text screening. Next, 241 articles were excluded with reasons listed (Appendix H). Finally, 43 articles were included as presented in the PRISMA flow diagram (Appendix E).

Characteristics of Included Studies

A total of 43 RCTs (Appendix F) involving 4,266 patients were conducted in 16 countries. RCTs had two-arm (n = 37), three-arm (n = 5), and four-arm (n = 1) designs. Digital technology included VR (n = 10) and mobile application (n = 33). Cancer types encompassed breast cancer (n = 28) and others (n = 50). Study outcomes entailed pain (n = 22), fatigue (n = 15), sleep (n = 16), anxiety (n = 24) and depression (n = 18). Comparison groups used customary protocol (n = 13), conventional intervention (n = 5), waitlisted (n = 3), no intervention (n = 1), and usual care (n = 21). The summary of participant characteristics and interventions is presented in Appendix G

Quality Appraisal

Most RCTs were rated as low risk due to selection bias (random generation), selective bias, and attrition bias (Appendix I). However, only seven RCTs were rated low risk on selection bias (allocation concealment) and performance bias. Two studies reported other biases including nonresponse rate and institutional bias, whereas the rest had none identified.

Effects of Digital Interventions on Pain

Meta-analysis was conducted on 19 studies that measured pain at postintervention. Results suggested considerable heterogeneity of effect size ($I^2 = 93\%$, $\chi^2 = 263.60$, $P < .00001$) and; therefore, the pooled effect will not be emphasized. Subgroup analyses were then conducted to explore sources of heterogeneity.

Subgroup analysis based on digital technology suggested no statistically significant difference in effect sizes across the subgroups ($\chi^2 = 3.94$, $P = .05$) (Appendix J). Given high heterogeneity, the pooled effect size of each subgroup was not emphasized, and individual effect sizes were examined instead. As such, the VR subgroup produced a range of larger effect sizes (−3.05 to 0.05) than those of the mobile subgroup (−1.36 to 1.07). Three RCTs in the VR subgroup and two in the mobile subgroup had large effect sizes.

Subgroup analysis based on intervention contents showed statistically significant subgroup differences ($\chi^2 = 13.90$, $p < 0.1$) (Fig. 1). The relaxation video subgroup had the largest effect size range (−3.05 to 0.05), followed by game-based activity (−1.15 to −0.63) and reminder subgroup (−1.36 to −0.50). Such intervention contents were promising in lowering pain among cancer patients. Nevertheless, another subgroup based on assessment points showed no significant difference across the subgroups (Appendix K).

Effects of Digital Interventions on Fatigue

Meta-analysis was conducted on 12 studies that measured fatigue at postintervention. Results suggested considerable heterogeneity ($I^2 = 92\%$, $\chi^2 = 139.45$, $P < .00001$). Subgroup analysis based on digital technology suggested no significant difference in effect sizes across the subgroups ($\chi^2 = 0.20$, $P = .65$) (Appendix L). As heterogeneity was high, individual effect sizes were examined instead. The VR subgroup produced a range of larger effect sizes (−2.74 to −0.30) than those of the mobile app subgroup (−2.05 to 0.35). One RCT in the VR subgroup and five in the mobile subgroup had large effect sizes.

Subgroup analysis based on intervention contents (Fig. 2) showed significant subgroup differences ($\chi^2 = 25.12$, $P = .0001$). Specifically, interventions with large effect sizes (SMD > 0.80) encompassed VR relaxation videos and mobile applications with education, symptom monitoring, teleconsultation, and reminders.

Moreover, subgroup analysis, according to assessment points, revealed statistically significant differences across the subgroups ($\chi^2 = 21.34$, $P < .0001$) (Appendix M). The long-term follow-up subgroup (> 6 months) had the largest effect size range (−2.27 to 0.35) than other subgroups.

Effects of Digital Interventions on Sleep

Fourteen studies measured sleep at postintervention and results suggested substantial heterogeneity ($I^2 = 69\%$, $\chi^2 = 41.83$, $P < .0001$). Subgroup analysis according to digital technology indicated no significant difference in effect sizes across the subgroups ($\chi^2 = 1.34$, $P = .25$) (Appendix N). As heterogeneity was high, individual effect sizes were examined. The Mobile App subgroup produced a range of larger effect sizes (−2.30 to 0.22) than those of the VR subgroup (−0.09 to 0.16). Two RCTs in the mobile app subgroup had large effect sizes.

Subgroup analysis conducted according to intervention contents (Fig. 3) showed no significant subgroup differences ($\chi^2 = 3.62$, $P = .61$). Interventions with large effect sizes (SMD > 0.80) used mobile applications with education, symptom monitoring, teleconsultation, mindfulness, and reminders.

Another subgroup analysis was conducted according to assessment points and no significant subgroup differences were observed across the subgroups ($\chi^2 = 2.76$, $P = .10$) (Appendix O). The short-term assessment (< 3 months) subgroup had the largest effect size range (−2.12 to 0.12) than other subgroups. Findings suggested that the effects of intervention, specifically mobile apps, improved sleep for a short period (<3 months).

Effects of Digital Interventions on Anxiety

Meta-analysis was conducted for 22 studies that measured anxiety at postintervention. Results suggested considerable heterogeneity ($I^2 = 95\%$, $\chi^2 = 461.66$, $P < .00001$). Subgroup analysis based on digital technology showed significant difference in effect sizes across the subgroups ($\chi^2 = 6.88$, $P = .009$) (Appendix P). Due to high heterogeneity, individual effect sizes were examined. The VR subgroup produced a range of larger effect sizes (−8.72 to −0.41) than those of the mobile subgroup (−2.68 to 0.72). Four RCTs in the VR subgroup and five in the Mobile App subgroup had large effect sizes.

Subgroup analysis according to intervention contents (Fig. 4) showed no significant subgroup differences ($\chi^2 = 12.42$, $P = .13$). Interventions with large effect sizes (SMD > 0.80) used VR relaxation videos and mobile applications with education, symptom monitoring, teleconsultation, and mindfulness. These suggest that such intervention contents had the likelihood of reducing anxiety among cancer patients. Nevertheless, subgroup analysis, according to assessment points, revealed no significant difference across the subgroups ($\chi^2 = 0.08$, $P = .96$) (Appendix Q).

Effects of VR and Mobile-Based Interventions on Depression

Meta-analysis was conducted for 15 studies that measured depression at postintervention. Results suggested considerable heterogeneity ($I^2 = 90\%$, $\chi^2 = 138.46$, $P < .00001$). Subgroup analysis based on digital technology suggested no significant difference in effect sizes across the subgroups ($\chi^2 = 1.33$, $P = .25$) (Appendix R). Due to high heterogeneity, individual effect sizes were examined. The VR subgroup produced a range of larger effect sizes (−5.84 to 0.21) than those of the mobile app subgroup (−1.29 to 1.04). One RCT in the VR subgroup and two in the mobile app subgroup had large effect sizes. These suggested that the use of VR and mobile apps can reduce depression among cancer patients.

Subgroup analysis conducted according to intervention content (Fig. 5) showed no significant subgroup differences ($\chi^2 = 7.72$, $P = .36$). Interventions with large effect sizes (SMD > 0.80) used VR relaxation videos and mobile applications with education, symptom monitoring, teleconsultation, and mindfulness. However, subgroup analysis, according to assessment points, revealed no significant differences across the subgroups ($\chi^2 = 0.14$, $P = .93$) (Appendix S).

Publication Bias

Funnel plots with the standard error were plotted against SMD for the relevant outcomes (Appendix T), and asymmetry was observed. The plots suggested the existence of publication bias.[56] Nonetheless, the comprehensive search for published and unpublished studies might minimize the publication bias.

Overall Quality of Evidence

GRADE approach evaluated the overall certainty of the evidence. All domains except indirectness were rated as serious or very serious due to unclear description of randomization methods and allocation concealment, no blinding of participants, attrition issue, considerable heterogeneity, wide CIs, and strong suspicion of publication bias from funnel plot asymmetry.[57] The resulting certainty for all the outcomes was appraised as very low quality (Appendix U).

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. mean difference IV, Random, 95% CI
9.1.1 Education								
Yang et al., 2019	21.4548	25.9037	31	50	26.0947	27	2.3%	-1.08 [-1.64 , -0.53]
Seven et al., 2022	6.66	16.57	20	24.16	28.85	20	2.1%	-0.73 [-1.37 , -0.09]
Huggins et al., 2022	16	21.2	36	29.2	24.7	37	2.4%	-0.57 [-1.04 , -0.10]
Di & Li 2018	3.12	8.36	65	8.24	11.75	67	2.6%	-0.50 [-0.84 , -0.15]
Liao et al., 2022	6.72	4.83	57	8.91	4.94	57	2.5%	-0.45 [-0.82 , -0.07]
Park et al., 2021	10.6	12.8	75	17.9	22.1	73	2.6%	-0.40 [-0.73 , -0.08]
Zhou et al., 2020	1.63	2.6	55	2.36	2.1	48	2.5%	-0.30 [-0.69 , 0.09]
Peng et al., 2020	2.5	1.2	152	2.8	1.1	150	2.7%	-0.26 [-0.49 , -0.03]
Vos et al., 2021	8.1	16.4	127	6.7	14.3	134	2.7%	0.09 [-0.15 , 0.33]
Schuit et al., 2022	29.4	27.3	60	24.2	27.1	62	2.5%	0.19 [-0.17 , 0.55]
Somers et al., 2016	3.32	1.89	15	2.05	1.95	15	2.0%	0.64 [-0.09 , 1.38]
Wu et al., 2021	86.14	8.84	43	76.68	8.66	43	2.4%	1.07 [0.62 , 1.52]
Subtotal (95% CI)			**736**			**733**	**29.3%**	**-0.19 [-0.46 , 0.07]**
Heterogeneity: Tau² = 0.18; Chi² = 66.48, df = 11 (P < 0.00001); I² = 83%								
Test for overall effect: Z = 1.42 (P = 0.16)								
9.1.2 Symptom Monitoring								
Sun et al., 2017	2.2	0.5	25	2.95	0.59	21	2.1%	-1.36 [-2.01 , -0.71]
Yang et al., 2019	21.4548	25.9037	31	50	26.0947	27	2.3%	-1.08 [-1.64 , -0.53]
Seven et al., 2022	6.66	16.57	20	24.16	28.85	20	2.1%	-0.73 [-1.37 , -0.09]
Huggins et al., 2022	16	21.2	36	29.2	24.7	37	2.4%	-0.57 [-1.04 , -0.10]
Öztürk & Kutlutürkan 2021	16.07	12.41	28	24.71	18.7	29	2.3%	-0.54 [-1.06 , -0.01]
Liao et al., 2022	6.72	4.83	57	8.91	4.94	57	2.5%	-0.45 [-0.82 , -0.07]
Park et al., 2021	10.6	12.8	75	17.9	22.1	73	2.6%	-0.40 [-0.73 , -0.08]
Zhou et al., 2020	1.63	2.6	55	2.36	2.1	48	2.5%	-0.30 [-0.69 , 0.09]
Fjell et al., 2020	25.45	39.19	69	33.48	39.75	71	2.6%	-0.20 [-0.53 , 0.13]
Vos et al., 2021	8.1	16.4	127	6.7	14.3	134	2.7%	0.09 [-0.15 , 0.33]
Schuit et al., 2022	29.4	27.3	60	24.2	27.1	62	2.5%	0.19 [-0.17 , 0.55]
Bacorro et al., 2018	2.77	2.78	39	2	2.88	37	2.4%	0.27 [-0.18 , 0.72]
Subtotal (95% CI)			**622**			**616**	**29.1%**	**-0.37 [-0.61 , -0.13]**
Heterogeneity: Tau² = 0.13; Chi² = 45.47, df = 11 (P < 0.00001); I² = 76%								
Test for overall effect: Z = 3.02 (P = 0.003)								
9.1.3 Relaxing Videos								
Menekli et al., 2022	3.32	0.7	69	5.26	0.56	70	2.4%	-3.05 [-3.54 , -2.55]
Bani Mohammad & Ahmad 2019	0.33	0.82	40	4.84	2.57	40	2.2%	-2.34 [-2.92 , -1.77]
Fabi et al., 2022	21.4	28.4	22	20.1	19.9	22	2.2%	0.05 [-0.54 , 0.64]
Subtotal (95% CI)			**131**			**132**	**6.8%**	**-1.78 [-3.60 , 0.03]**
Heterogeneity: Tau² = 2.49; Chi² = 64.89, df = 2 (P < 0.00001); I² = 97%								
Test for overall effect: Z = 1.93 (P = 0.05)								
9.1.4 Game-Based Activity								
Basha et al., 2021	40.33	10.33	30	53.67	12.45	30	2.3%	-1.15 [-1.70 , -0.60]
Feyzioğlu et al., 2020	1.53	1.35	19	2.56	1.82	17	2.1%	-0.63 [-1.31 , 0.04]
Subtotal (95% CI)			**49**			**47**	**4.4%**	**-0.93 [-1.43 , -0.43]**
Heterogeneity: Tau² = 0.04; Chi² = 1.36, df = 1 (P = 0.24); I² = 27%								
Test for overall effect: Z = 3.64 (P = 0.0003)								
9.1.5 Mindfulness								
Wang et al., 2022	2.6	1.3	51	3.2	1.5	52	2.5%	-0.42 [-0.81 , -0.03]
Zhou et al., 2020	1.63	2.6	55	2.36	2.1	48	2.5%	-0.30 [-0.69 , 0.09]
Somers et al., 2016	3.32	1.89	15	2.05	1.95	15	2.0%	0.64 [-0.09 , 1.38]
Subtotal (95% CI)			**121**			**115**	**7.0%**	**-0.12 [-0.62 , 0.37]**
Heterogeneity: Tau² = 0.13; Chi² = 6.48, df = 2 (P = 0.04); I² = 69%								
Test for overall effect: Z = 0.49 (P = 0.62)								
9.1.6 Teleconsultation								
Sun et al., 2017	2.2	0.5	25	2.95	0.59	21	2.1%	-1.36 [-2.01 , -0.71]
Yang et al., 2019	21.4548	25.9037	31	50	26.0947	27	2.3%	-1.08 [-1.64 , -0.53]
Liao et al., 2022	6.72	4.83	57	8.91	4.94	57	2.5%	-0.45 [-0.82 , -0.07]
Park et al., 2021	10.6	12.8	75	17.9	22.1	73	2.6%	-0.40 [-0.73 , -0.08]
Zhou et al., 2020	1.63	2.6	55	2.36	2.1	48	2.5%	-0.30 [-0.69 , 0.09]
Somers et al., 2016	3.32	1.89	15	2.05	1.95	15	2.0%	0.64 [-0.09 , 1.38]
Wu et al., 2021	86.14	8.84	43	76.68	8.66	43	2.4%	1.07 [0.62 , 1.52]
Subtotal (95% CI)			**301**			**284**	**16.4%**	**-0.27 [-0.82 , 0.28]**
Heterogeneity: Tau² = 0.48; Chi² = 60.12, df = 6 (P < 0.00001); I² = 90%								
Test for overall effect: Z = 0.96 (P = 0.34)								
9.1.7 Reminders								
Sun et al., 2017	2.2	0.5	25	2.95	0.59	21	2.1%	-1.36 [-2.01 , -0.71]
Yang et al., 2019	21.4548	25.9037	31	50	26.0947	27	2.3%	-1.08 [-1.64 , -0.53]
Di & Li 2018	3.12	8.36	65	8.24	11.75	67	2.6%	-0.50 [-0.84 , -0.15]
Subtotal (95% CI)			**121**			**115**	**7.0%**	**-0.93 [-1.47 , -0.39]**
Heterogeneity: Tau² = 0.16; Chi² = 6.74, df = 2 (P = 0.03); I² = 70%								
Test for overall effect: Z = 3.37 (P = 0.0007)								
Total (95% CI)			**2081**			**2042**	**100.0%**	**-0.45 [-0.65 , -0.25]**
Heterogeneity: Tau² = 0.37; Chi² = 382.10, df = 41 (P < 0.00001); I² = 89%								
Test for overall effect: Z = 4.48 (P < 0.00001)								
Test for subgroup differences: Chi² = 13.90, df = 6 (P = 0.03), I² = 56.8%								

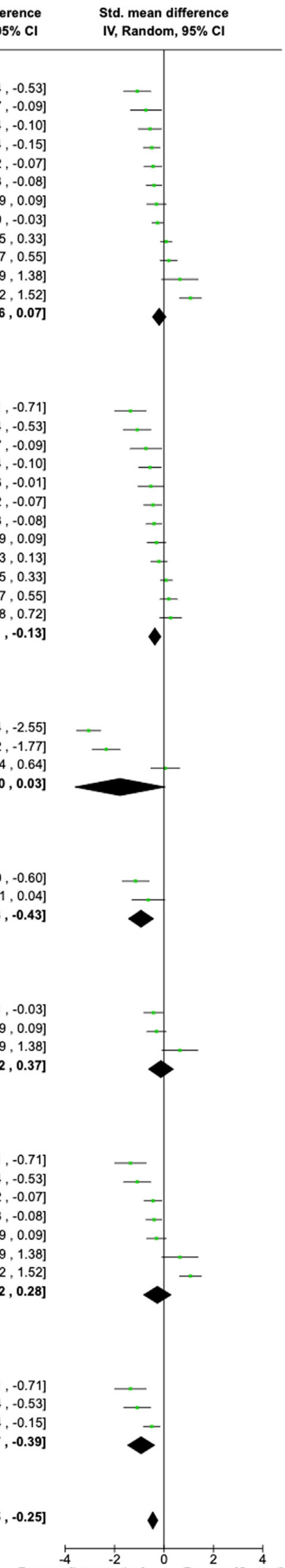
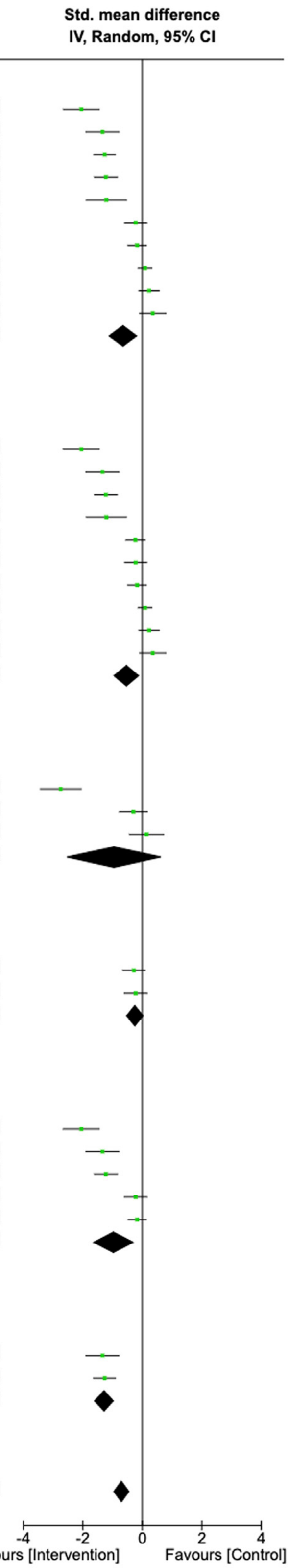


FIG 1. Subgroup analysis of intervention contents on pain.

	Intervention			Control				Std. mean difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
9.2.1 Education								
Wang et al., 2022* (1)	2.51	0.54	32	4.62	1.34	31	2.9%	-2.05 [-2.67 , -1.43]
Yang et al., 2019	37.2884	8.6346	31	55.5564	17.3991	27	3.0%	-1.34 [-1.92 , -0.77]
Di & Li 2018	22.14	12.54	65	38.64	13.32	67	3.3%	-1.27 [-1.64 , -0.89]
Liao et al., 2022	19.86	3.63	57	24.09	3.21	57	3.2%	-1.23 [-1.63 , -0.82]
Seven et al., 2022	12.77	12.1	20	38.33	26.6	20	2.8%	-1.21 [-1.89 , -0.53]
Zhou et al., 2020	2.29	2.23	55	2.82	2.51	48	3.2%	-0.22 [-0.61 , 0.17]
Park et al., 2021	22.9	16.6	75	26.3	21.9	73	3.3%	-0.17 [-0.50 , 0.15]
Vos et al., 2021	17.2	19.5	126	15.5	17.6	133	3.4%	0.09 [-0.15 , 0.34]
Schuit et al., 2022	44.4	28.6	60	37.9	27.7	62	3.3%	0.23 [-0.13 , 0.59]
Huggins et al., 2022	45.8	26.3	36	37.2	22	37	3.1%	0.35 [-0.11 , 0.81]
Subtotal (95% CI)			**557**			**555**	**31.4%**	**-0.65 [-1.12 , -0.19]**
Heterogeneity: Tau² = 0.50; Chi² = 120.60, df = 9 (P < 0.00001); I² = 93%								
Test for overall effect: Z = 2.76 (P = 0.006)								
9.2.2 Symptom Monitoring								
Wang et al., 2022* (1)	2.51	0.54	32	4.62	1.34	31	2.9%	-2.05 [-2.67 , -1.43]
Yang et al., 2019	37.2884	8.6346	31	55.5564	17.3991	27	3.0%	-1.34 [-1.92 , -0.77]
Liao et al., 2022	19.86	3.63	57	24.09	3.21	57	3.2%	-1.23 [-1.63 , -0.82]
Seven et al., 2022	12.77	12.1	20	38.33	26.6	20	2.8%	-1.21 [-1.89 , -0.53]
Fjell et al., 2020	48.83	35	69	57.09	35.51	71	3.3%	-0.23 [-0.57 , 0.10]
Zhou et al., 2020	2.29	2.23	55	2.82	2.51	48	3.2%	-0.22 [-0.61 , 0.17]
Park et al., 2021	22.9	16.6	75	26.3	21.9	73	3.3%	-0.17 [-0.50 , 0.15]
Vos et al., 2021	17.2	19.5	126	15.5	17.6	133	3.4%	0.09 [-0.15 , 0.34]
Schuit et al., 2022	44.4	28.6	60	37.9	27.7	62	3.3%	0.23 [-0.13 , 0.59]
Huggins et al., 2022	45.8	26.3	36	37.2	22	37	3.1%	0.35 [-0.11 , 0.81]
Subtotal (95% CI)			**561**			**559**	**31.5%**	**-0.54 [-0.95 , -0.13]**
Heterogeneity: Tau² = 0.39; Chi² = 97.84, df = 9 (P < 0.00001); I² = 91%								
Test for overall effect: Z = 2.56 (P = 0.01)								
9.2.3 Relaxing Videos								
Chirico et al., 2020	13.5	0.578	30	15.029	0.525	34	2.8%	-2.74 [-3.44 , -2.05]
Uslu & Arslan 2023	13.67	8.39	33	16.09	7.53	33	3.1%	-0.30 [-0.79 , 0.19]
Fabi et al., 2022	38.4	30	22	34.8	18.8	22	2.9%	0.14 [-0.45 , 0.73]
Subtotal (95% CI)			**85**			**89**	**8.8%**	**-0.95 [-2.53 , 0.62]**
Heterogeneity: Tau² = 1.85; Chi² = 43.67, df = 2 (P < 0.00001); I² = 95%								
Test for overall effect: Z = 1.18 (P = 0.24)								
9.2.4 Mindfulness								
Wang et al., 2022	2.9	1.3	51	3.3	1.5	52	3.2%	-0.28 [-0.67 , 0.11]
Zhou et al., 2020	2.29	2.23	55	2.82	2.51	48	3.2%	-0.22 [-0.61 , 0.17]
Subtotal (95% CI)			**106**			**100**	**6.5%**	**-0.25 [-0.53 , 0.02]**
Heterogeneity: Tau² = 0.00; Chi² = 0.05, df = 1 (P = 0.83); I² = 0%								
Test for overall effect: Z = 1.80 (P = 0.07)								
9.2.5 Teleconsultation								
Wang et al., 2022* (1)	2.51	0.54	32	4.62	1.34	31	2.9%	-2.05 [-2.67 , -1.43]
Yang et al., 2019	37.2884	8.6346	31	55.5564	17.3991	27	3.0%	-1.34 [-1.92 , -0.77]
Liao et al., 2022	19.86	3.63	57	24.09	3.21	57	3.2%	-1.23 [-1.63 , -0.82]
Zhou et al., 2020	2.29	2.23	55	2.82	2.51	48	3.2%	-0.22 [-0.61 , 0.17]
Park et al., 2021	22.9	16.6	75	26.3	21.9	73	3.3%	-0.17 [-0.50 , 0.15]
Subtotal (95% CI)			**250**			**236**	**15.6%**	**-0.97 [-1.63 , -0.31]**
Heterogeneity: Tau² = 0.51; Chi² = 45.78, df = 4 (P < 0.00001); I² = 91%								
Test for overall effect: Z = 2.89 (P = 0.004)								
9.2.6 Reminders								
Yang et al., 2019	37.2884	8.6346	31	55.5564	17.3991	27	3.0%	-1.34 [-1.92 , -0.77]
Di & Li 2018	22.14	12.54	65	38.64	13.32	67	3.3%	-1.27 [-1.64 , -0.89]
Subtotal (95% CI)			**96**			**94**	**6.2%**	**-1.29 [-1.60 , -0.98]**
Heterogeneity: Tau² = 0.00; Chi² = 0.04, df = 1 (P = 0.83); I² = 0%								
Test for overall effect: Z = 8.05 (P < 0.00001)								
Total (95% CI)			**1655**			**1633**	**100.0%**	**-0.70 [-0.95 , -0.46]**
Heterogeneity: Tau² = 0.45; Chi² = 355.00, df = 31 (P < 0.00001); I² = 91%								
Test for overall effect: Z = 5.60 (P < 0.00001)								
Test for subgroup differences: Chi² = 25.12, df = 5 (P = 0.0001), I² = 80.1%								



Footnotes

(1) "Effects of a WeChat-based multimodal psychoeducational intervention on psychological well-being and quality of life in acute leukaemia patients"

FIG 2. Subgroup analysis of intervention content on fatigue.

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. mean difference IV, Random, 95% CI
9.3.1 Education								
Yang et al., 2019	11.8752	25.9037	31	60.7151	13.0474	27	2.8%	-2.30 [-2.97 , -1.63]
Chung et al., 2022	15.63	10	21	23.82	6.09	16	2.7%	-0.94 [-1.63 , -0.25]
Sarlak et al., 2023	12.57	3.437	33	14.66	2.495	33	3.3%	-0.69 [-1.19 , -0.19]
Peng et al., 2020	12.7	3.3	152	14.6	3.9	150	3.9%	-0.52 [-0.75 , -0.30]
Di & Li 2018	6.13	16.58	65	13.14	20.11	67	3.7%	-0.38 [-0.72 , -0.03]
Seven et al., 2022	38.33	29.16	20	50	42.57	20	2.9%	-0.31 [-0.94 , 0.31]
Zhou et al., 2020	2.46	2.32	55	2.76	2.36	48	3.6%	-0.13 [-0.51 , 0.26]
Vos et al., 2021	16.4	23.4	126	16.5	22.3	133	3.9%	-0.00 [-0.25 , 0.24]
Park et al., 2021	24	25.9	75	23.9	30	73	3.7%	0.00 [-0.32 , 0.33]
Huggins et al., 2022	32	31.1	36	28.3	29.2	37	3.4%	0.12 [-0.34 , 0.58]
Schuit et al., 2022	32.2	28.1	60	25.8	29.8	62	3.7%	0.22 [-0.14 , 0.58]
Subtotal (95% CI)			**674**			**666**	**37.6%**	**-0.39 [-0.68 , -0.09]**
Heterogeneity: Tau² = 0.19; Chi² = 64.23, df = 10 (P < 0.00001); I² = 84%								
Test for overall effect: Z = 2.59 (P = 0.010)								
9.3.2 Symptom Monitoring								
Yang et al., 2019	11.8752	25.9037	31	60.7151	13.0474	27	2.8%	-2.30 [-2.97 , -1.63]
Seven et al., 2022	38.33	29.16	20	50	42.57	20	2.9%	-0.31 [-0.94 , 0.31]
Öztürk & Kutlutürkan 2021	21.43	28.99	28	31.03	34.42	29	3.2%	-0.30 [-0.82 , 0.23]
Fjell et al., 2020	34.78	44.39	69	40.85	45.03	71	3.7%	-0.14 [-0.47 , 0.20]
Zhou et al., 2020	2.46	2.32	55	2.76	2.36	48	3.6%	-0.13 [-0.51 , 0.26]
Vos et al., 2021	16.4	23.4	126	16.5	22.3	133	3.9%	-0.00 [-0.25 , 0.24]
Park et al., 2021	24	25.9	75	23.9	30	73	3.7%	0.00 [-0.32 , 0.33]
Huggins et al., 2022	32	31.1	36	28.3	29.2	37	3.4%	0.12 [-0.34 , 0.58]
Schuit et al., 2022	32.2	28.1	60	25.8	29.8	62	3.7%	0.22 [-0.14 , 0.58]
Subtotal (95% CI)			**500**			**500**	**30.9%**	**-0.25 [-0.57 , 0.07]**
Heterogeneity: Tau² = 0.19; Chi² = 46.98, df = 8 (P < 0.00001); I² = 83%								
Test for overall effect: Z = 1.53 (P = 0.13)								
9.3.3 Relaxing Videos								
Fabi et al., 2022	32.2	35.3	22	34.9	23	22	3.0%	-0.09 [-0.68 , 0.50]
Czech et al., 2022	6.22	3.46	9	5.71	2.36	7	2.0%	0.16 [-0.83 , 1.15]
Subtotal (95% CI)			**31**			**29**	**5.0%**	**-0.02 [-0.53 , 0.48]**
Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 1 (P = 0.67); I² = 0%								
Test for overall effect: Z = 0.09 (P = 0.93)								
9.3.4 Mindfulness								
Chung et al., 2022	15.63	10	21	23.82	6.09	16	2.7%	-0.94 [-1.63 , -0.25]
Wang et al., 2022	3.6	1.4	51	4.3	1.9	52	3.6%	-0.42 [-0.81 , -0.03]
Zhou et al., 2020	2.46	2.32	55	2.76	2.36	48	3.6%	-0.13 [-0.51 , 0.26]
Subtotal (95% CI)			**127**			**116**	**9.9%**	**-0.41 [-0.80 , -0.03]**
Heterogeneity: Tau² = 0.06; Chi² = 4.17, df = 2 (P = 0.12); I² = 52%								
Test for overall effect: Z = 2.09 (P = 0.04)								
9.3.5 Teleconsultation								
Yang et al., 2019	11.8752	25.9037	31	60.7151	13.0474	27	2.8%	-2.30 [-2.97 , -1.63]
Zhou et al., 2020	2.46	2.32	55	2.76	2.36	48	3.6%	-0.13 [-0.51 , 0.26]
Park et al., 2021	24	25.9	75	23.9	30	73	3.7%	0.00 [-0.32 , 0.33]
Subtotal (95% CI)			**161**			**148**	**10.1%**	**-0.76 [-1.85 , 0.33]**
Heterogeneity: Tau² = 0.87; Chi² = 38.00, df = 2 (P < 0.00001); I² = 95%								
Test for overall effect: Z = 1.37 (P = 0.17)								
9.3.6 Reminders								
Yang et al., 2019	11.8752	25.9037	31	60.7151	13.0474	27	2.8%	-2.30 [-2.97 , -1.63]
Di & Li 2018	6.13	16.58	65	13.14	20.11	67	3.7%	-0.38 [-0.72 , -0.03]
Subtotal (95% CI)			**96**			**94**	**6.5%**	**-1.32 [-3.20 , 0.57]**
Heterogeneity: Tau² = 1.78; Chi² = 24.81, df = 1 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 1.37 (P = 0.17)								
Total (95% CI)			**1589**			**1553**	**100.0%**	**-0.42 [-0.61 , -0.23]**
Heterogeneity: Tau² = 0.23; Chi² = 196.55, df = 29 (P < 0.00001); I² = 85%								
Test for overall effect: Z = 4.23 (P < 0.0001)								
Test for subgroup differences: Chi² = 3.62, df = 5 (P = 0.61), I² = 0%								

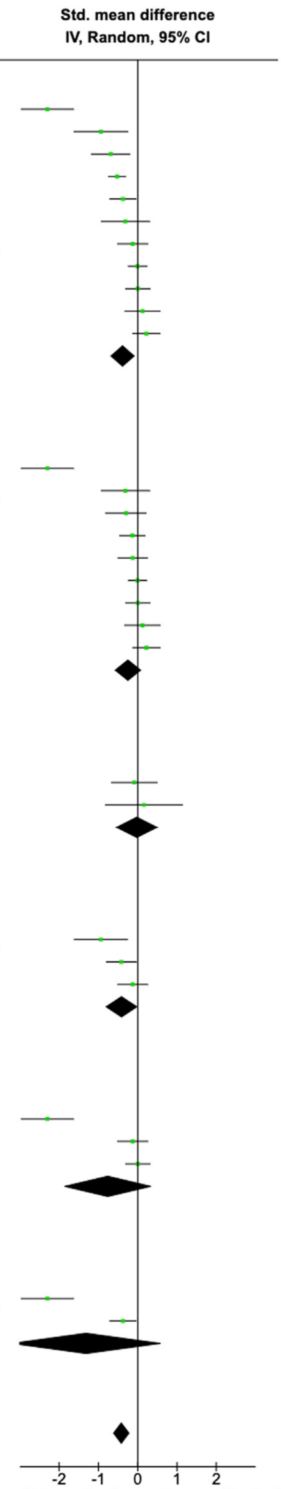


FIG 3. Subgroup analysis of intervention contents on sleep.

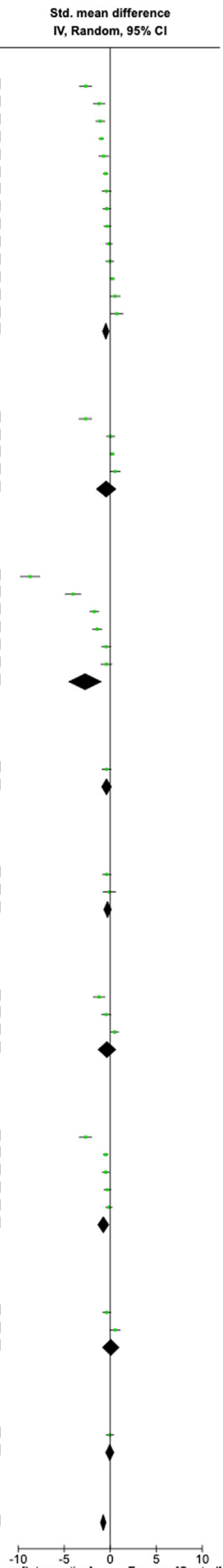
Discussion

This review investigated the effect of digital interventions (VR and mobile apps) on pain, fatigue, sleep, anxiety and depression among adult patients with cancer. The interventions showed positive improvements in the outcomes at postintervention. Intervention contents, including VR relaxation videos, game-based activities, reminders, teleconsultation, education, and symptom monitoring, had the potential to improve study outcomes. Additionally, our results suggested favorable outcomes for the long-term use of the interventions.

Intervention Platforms

VR and mobile-based intervention had the potential to improve pain, fatigue, sleep, anxiety, and depression postintervention. Three VR studies[58-60] demonstrated effective pain reduction, which was consistent with previous reviews.[26,61-63] A possible explanation for

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Std. mean difference IV, Random, 95% CI
9.4.1 Education								
Wang et al., 2022* (1)	11	1.72	32	16.29	2.16	31	2.5%	-2.68 [-3.37 , -1.99]
Ham et al., 2019	43.29	9.12	21	54.62	9.32	21	2.5%	-1.21 [-1.87 , -0.54]
Ghanbari et al., 2021	90.66	13.84	38	106.92	15.94	39	2.7%	-1.08 [-1.56 , -0.60]
Peng et al., 2020	9.8	2.2	152	12.4	3.1	150	2.8%	-0.97 [-1.20 , -0.73]
El-Jawahri et al., 2023	3.54	2.92	25	5.64	2.88	28	2.6%	-0.71 [-1.27 , -0.16]
Sui et al., 2020	5	2.84	100	6.69	4.01	100	2.8%	-0.48 [-0.77 , -0.20]
Gao et al., 2022	36.13	8.18	30	39.83	9.77	30	2.7%	-0.41 [-0.92 , 0.11]
Kim et al., 2018	40.6	3.6	34	42	3.8	38	2.7%	-0.37 [-0.84 , 0.09]
Ackermann et al., 2022	1.3	2.1	49	2.4	4.5	51	2.7%	-0.31 [-0.70 , 0.09]
Zhu et al., 2018	9.93	2.72	57	10.29	2.46	57	2.8%	-0.14 [-0.51 , 0.23]
Fang et al., 2021	5.64	4.33	42	5.85	3.84	41	2.7%	-0.05 [-0.48 , 0.38]
Vos et al., 2021	17.9	21	125	13.8	18.4	133	2.8%	0.21 [-0.04 , 0.45]
Greer et al., 2020	82.25	26.95	23	67.78	27.55	25	2.6%	0.52 [-0.05 , 1.10]
Foley et al., 2016	4.9125	4.5681	13	2.3933	2.7452	26	2.5%	0.72 [0.03 , 1.40]
Subtotal (95% CI)			**741**			**770**	**37.4%**	**-0.48 [-0.82 , -0.14]**
Heterogeneity: Tau² = 0.36; Chi² = 126.56, df = 13 (P < 0.00001); I² = 90%								
Test for overall effect: Z = 2.76 (P = 0.006)								
9.4.2 Symptom Monitoring								
Wang et al., 2022* (1)	11	1.72	32	16.29	2.16	31	2.5%	-2.68 [-3.37 , -1.99]
Bacorro et al., 2018	0.77	1.74	39	0.71	1.9	37	2.7%	0.03 [-0.42 , 0.48]
Vos et al., 2021	17.9	21	125	13.8	18.4	133	2.8%	0.21 [-0.04 , 0.45]
Greer et al., 2020	82.25	26.95	23	67.78	27.55	25	2.6%	0.52 [-0.05 , 1.10]
Subtotal (95% CI)			**219**			**226**	**10.6%**	**-0.45 [-1.49 , 0.59]**
Heterogeneity: Tau² = 1.06; Chi² = 63.70, df = 3 (P < 0.00001); I² = 95%								
Test for overall effect: Z = 0.84 (P = 0.40)								
9.4.3 Relaxing Videos								
Menekli et al., 2022	28.68	3.83	69	66.23	4.69	70	2.1%	-8.72 [-9.81 , -7.62]
Chirico et al., 2020	37.444	1.684	30	43.941	1.5	34	2.3%	-4.04 [-4.91 , -3.17]
Bani Mohammad & Ahmad 2019	37.68	3.8	40	50.13	9.32	40	2.6%	-1.73 [-2.25 , -1.21]
Uslu & Arslan 2023	29.3	7.21	33	41.12	9.19	33	2.6%	-1.41 [-1.96 , -0.87]
Zhang et al., 2023	38.07	9.45	30	42.23	9.43	30	2.6%	-0.43 [-0.95 , 0.08]
Fabi et al., 2022	33.4	9.3	22	37.2	9	22	2.6%	-0.41 [-1.01 , 0.19]
Subtotal (95% CI)			**224**			**229**	**14.8%**	**-2.74 [-4.48 , -1.00]**
Heterogeneity: Tau² = 4.58; Chi² = 228.76, df = 5 (P < 0.00001); I² = 98%								
Test for overall effect: Z = 3.09 (P = 0.002)								
9.4.4 Educational Video								
Gao et al., 2022	36.13	8.18	30	39.83	9.77	30	2.7%	-0.41 [-0.92 , 0.11]
Subtotal (95% CI)			**30**			**30**	**2.7%**	**-0.41 [-0.92 , 0.11]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.55 (P = 0.12)								
9.4.5 Mobile Games								
Kim et al., 2018	40.6	3.6	34	42	3.8	38	2.7%	-0.37 [-0.84 , 0.09]
Kim et al., 2018* (2)	18.7	10.7	15	19.7	7.7	15	2.5%	-0.10 [-0.82 , 0.61]
Subtotal (95% CI)			**49**			**53**	**5.1%**	**-0.29 [-0.68 , 0.10]**
Heterogeneity: Tau² = 0.00; Chi² = 0.38, df = 1 (P = 0.54); I² = 0%								
Test for overall effect: Z = 1.47 (P = 0.14)								
9.4.6 Mindfulness								
Ham et al., 2019	43.29	9.12	21	54.62	9.32	21	2.5%	-1.21 [-1.87 , -0.54]
Zhang et al., 2023	38.07	9.45	30	42.23	9.43	30	2.6%	-0.43 [-0.95 , 0.08]
Rocamora González et al., 2022	6.9	3.5	35	5.2	3.4	41	2.7%	0.49 [0.03 , 0.95]
Subtotal (95% CI)			**86**			**92**	**7.9%**	**-0.36 [-1.30 , 0.58]**
Heterogeneity: Tau² = 0.61; Chi² = 18.32, df = 2 (P = 0.0001); I² = 89%								
Test for overall effect: Z = 0.75 (P = 0.45)								
9.4.7 Teleconsultation								
Wang et al., 2022* (1)	11	1.72	32	16.29	2.16	31	2.5%	-2.68 [-3.37 , -1.99]
Sui et al., 2020	5	2.84	100	6.69	4.01	100	2.8%	-0.48 [-0.77 , -0.20]
Zheng et al., 2022	2.84	2.61	50	4.5	4.06	50	2.7%	-0.48 [-0.88 , -0.08]
Ackermann et al., 2022	1.3	2.1	49	2.4	4.5	51	2.7%	-0.31 [-0.70 , 0.09]
Zhu et al., 2018	9.93	2.72	57	10.29	2.46	57	2.8%	-0.14 [-0.51 , 0.23]
Subtotal (95% CI)			**288**			**289**	**13.5%**	**-0.75 [-1.33 , -0.17]**
Heterogeneity: Tau² = 0.39; Chi² = 42.88, df = 4 (P < 0.00001); I² = 91%								
Test for overall effect: Z = 2.55 (P = 0.01)								
9.4.8 Reminders								
Kim et al., 2018	40.6	3.6	34	42	3.8	38	2.7%	-0.37 [-0.84 , 0.09]
Greer et al., 2020	82.25	26.95	23	67.78	27.55	25	2.6%	0.52 [-0.05 , 1.10]
Subtotal (95% CI)			**57**			**63**	**5.3%**	**0.06 [-0.82 , 0.93]**
Heterogeneity: Tau² = 0.33; Chi² = 5.60, df = 1 (P = 0.02); I² = 82%								
Test for overall effect: Z = 0.13 (P = 0.90)								
9.4.9 Decision-Making								
Fang et al., 2021	5.64	4.33	42	5.85	3.84	41	2.7%	-0.05 [-0.48 , 0.38]
Subtotal (95% CI)			**42**			**41**	**2.7%**	**-0.05 [-0.48 , 0.38]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.23 (P = 0.82)								
Total (95% CI)			**1736**			**1793**	**100.0%**	**-0.76 [-1.05 , -0.47]**
Heterogeneity: Tau² = 0.77; Chi² = 610.69, df = 37 (P < 0.00001); I² = 94%								
Test for overall effect: Z = 5.11 (P < 0.00001)								
Test for subgroup differences: Chi² = 12.42, df = 8 (P = 0.13), I² = 35.6%								



Footnotes
(1) "Effects of a WeChat-based multimodal psychoeducational intervention on psychological well-being and quality of life in acute leukaemia patients"
(2) "The Effects of a Serious Game on Depressive Symptoms and Anxiety in Breast Cancer Patients with Depression: a Pilot Study Using Functional MRI"

FIG 4. Subgroup analysis of intervention contents on anxiety.

	Intervention			Control				Std. mean difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
9.5.1 Education								
Wang et al., 2022* (1)	12.88	2.21	32	16.29	2.98	31	3.5%	-1.29 [-1.83 , -0.74]
Ham et al., 2019	15.9	8.89	21	25.81	10.72	21	3.2%	-0.99 [-1.63 , -0.34]
Peng et al., 2020	10.1	2.8	152	11.2	2.2	150	4.2%	-0.44 [-0.66 , -0.21]
Sui et al., 2020	5.22	2.77	100	6.55	3.42	100	4.1%	-0.43 [-0.71 , -0.15]
El-Jawahri et al., 2023	4.76	3.64	25	6.29	3.63	28	3.5%	-0.41 [-0.96 , 0.13]
Ackermann et al., 2022	1.1	2	49	2.2	4.7	51	3.9%	-0.30 [-0.69 , 0.09]
Fang et al., 2021	5.64	3.52	42	5.93	4.08	42	3.8%	-0.08 [-0.50 , 0.35]
Zhu et al., 2018	12.75	1.57	57	12.58	2.15	57	4.0%	0.09 [-0.28 , 0.46]
Kim et al., 2018	15.7	3.7	34	14.9	5.2	38	3.7%	0.17 [-0.29 , 0.64]
Foley et al., 2016	2.365	2.4917	13	0.6073	1.0196	26	3.1%	1.04 [0.34 , 1.75]
Subtotal (95% CI)			**525**			**544**	**37.1%**	**-0.27 [-0.56 , 0.01]**
Heterogeneity: Tau² = 0.15; Chi² = 42.41, df = 9 (P < 0.00001); I² = 79%								
Test for overall effect: Z = 1.89 (P = 0.06)								
9.5.2 Symptom Monitoring								
Wang et al., 2022* (1)	12.88	2.21	32	16.29	2.98	31	3.5%	-1.29 [-1.83 , -0.74]
Bacorro et al., 2018	0.91	1.8	39	0.79	2.15	37	3.8%	0.06 [-0.39 , 0.51]
Subtotal (95% CI)			**71**			**68**	**7.3%**	**-0.60 [-1.92 , 0.72]**
Heterogeneity: Tau² = 0.84; Chi² = 13.93, df = 1 (P = 0.0002); I² = 93%								
Test for overall effect: Z = 0.90 (P = 0.37)								
9.5.3 Relaxing Videos								
Chirico et al., 2020	10.286	0.759	30	14.559	0.689	34	2.0%	-5.84 [-7.00 , -4.69]
Zhang et al., 2023	11.13	6.01	30	14.1	7.18	30	3.6%	-0.44 [-0.96 , 0.07]
Czech et al., 2022	8.11	6.17	9	7	5.51	7	2.4%	0.18 [-0.81 , 1.17]
Fabi et al., 2022	6.4	3.9	22	5.6	3.4	22	3.4%	0.21 [-0.38 , 0.81]
Subtotal (95% CI)			**91**			**93**	**11.4%**	**-1.42 [-3.44 , 0.59]**
Heterogeneity: Tau² = 4.04; Chi² = 89.18, df = 3 (P < 0.00001); I² = 97%								
Test for overall effect: Z = 1.38 (P = 0.17)								
9.5.4 Mobile Games								
Kim et al., 2018* (2)	18.9	10.2	15	21.6	6	15	3.0%	-0.31 [-1.03 , 0.41]
Kim et al., 2018	15.7	3.7	34	14.9	5.2	38	3.7%	0.17 [-0.29 , 0.64]
Subtotal (95% CI)			**49**			**53**	**6.8%**	**0.01 [-0.44 , 0.46]**
Heterogeneity: Tau² = 0.02; Chi² = 1.24, df = 1 (P = 0.26); I² = 20%								
Test for overall effect: Z = 0.05 (P = 0.96)								
9.5.5 Mindfulness								
Ham et al., 2019	15.9	8.89	21	25.81	10.72	21	3.2%	-0.99 [-1.63 , -0.34]
Zhang et al., 2023	11.13	6.01	30	14.1	7.18	30	3.6%	-0.44 [-0.96 , 0.07]
Rocamora González et al., 2022	4.9	3.9	35	4.1	3.4	41	3.7%	0.22 [-0.23 , 0.67]
Subtotal (95% CI)			**86**			**92**	**10.6%**	**-0.37 [-1.05 , 0.30]**
Heterogeneity: Tau² = 0.28; Chi² = 9.66, df = 2 (P = 0.008); I² = 79%								
Test for overall effect: Z = 1.09 (P = 0.28)								
9.5.6 Teleconsultation								
Wang et al., 2022* (1)	12.88	2.21	32	16.29	2.98	31	3.5%	-1.29 [-1.83 , -0.74]
Zheng et al., 2022	2.86	2.8	50	4.58	4.39	50	3.9%	-0.46 [-0.86 , -0.07]
Sui et al., 2020	5.22	2.77	100	6.55	3.42	100	4.1%	-0.43 [-0.71 , -0.15]
Ackermann et al., 2022	1.1	2	49	2.2	4.7	51	3.9%	-0.30 [-0.69 , 0.09]
Zhu et al., 2018	12.75	1.57	57	12.58	2.15	57	4.0%	0.09 [-0.28 , 0.46]
Subtotal (95% CI)			**288**			**289**	**19.4%**	**-0.44 [-0.80 , -0.09]**
Heterogeneity: Tau² = 0.13; Chi² = 17.32, df = 4 (P = 0.002); I² = 77%								
Test for overall effect: Z = 2.43 (P = 0.02)								
9.5.7 Reminders								
Kim et al., 2018	15.7	3.7	34	14.9	5.2	38	3.7%	0.17 [-0.29 , 0.64]
Subtotal (95% CI)			**34**			**38**	**3.7%**	**0.17 [-0.29 , 0.64]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.73 (P = 0.46)								
9.5.8 Decision-Making								
Fang et al., 2021	5.64	3.52	42	5.93	4.08	42	3.8%	-0.08 [-0.50 , 0.35]
Subtotal (95% CI)			**42**			**42**	**3.8%**	**-0.08 [-0.50 , 0.35]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.35 (P = 0.73)								
Total (95% CI)			**1186**			**1219**	**100.0%**	**-0.40 [-0.62 , -0.17]**
Heterogeneity: Tau² = 0.30; Chi² = 187.08, df = 27 (P < 0.00001); I² = 86%								
Test for overall effect: Z = 3.44 (P = 0.0006)								
Test for subgroup differences: Chi² = 7.72, df = 7 (P = 0.36), I² = 9.3%								

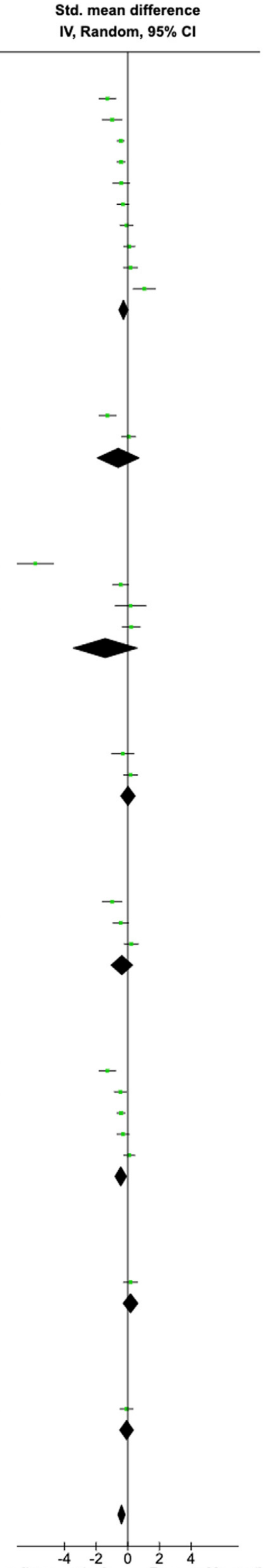


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FIG 5. Subgroup analysis of intervention contents on depression.

pain reduction is that VR display imitated visual and task distractors to draw users' attention away from the pain, substituting as a nonpharmacological method for analgesia.[64,65] Furthermore, two mobile app studies[66,67] showed effective pain reduction, which aligns with previous reviews.[68,69] Mobile apps offer many functions and contents encompassing education, reminders, and real-time monitoring of pain with subsequent adjustment of medication dosage according to the reported pain severity.

Effects of Digital Interventions on Fatigue

In our review, only one VR study[70] showed effective fatigue reduction, consistent with previous reviews.[26,71] The study used a single VR application lasting for a short time, whereas other included studies used either multiple sessions or longer intervention durations.[70] VR is known to induce cybersickness, a condition that occurs due to discrepancies between vestibular inputs and option flow information, causing disorientation.[72] Cybersickness may contribute to fatigue, and this may be a reason for conflicting results in our review. Nonetheless, five mobile app studies showed effective fatigue reduction.[67,73-76] Essential intervention contents entailed education, symptom monitoring, teleconsultation, and reminders.

Effects of Digital Interventions on Sleep

Mobile app interventions, in two RCTs, had positive effects on sleep. A possibility is that one RCT curated contents specifically for sleep improvement.[77] Furthermore, the mobile apps in another RCT helped reduce pain levels.[67] As a result, patients might feel more comfortable, therefore enabling them to sleep better. Unfortunately, there were no other similar reviews that measured sleep; hence, no comparisons can be made. Interestingly, no VR studies showed favorable results for sleep. This can be attributed to an underlying mechanism of VR whereby individuals are kept awake for the entirety of intervention duration. Thus, sleep improvements were not expected.

Effects of Digital Interventions on Anxiety

Both interventions had large range of effect sizes for anxiety. Four VR studies in our review showed effective anxiety reduction, consistent with previous reviews.[26,61-63,71,78] A possible explanation is that the distraction capability of VR in taking control of users' attention might provide an unorthodox method for anxiolytic effects.[64,65] Four mobile app studies displayed[76,79-81] effective anxiety reduction, agreeing with a previous review.[82] Specifically, the mobile apps provided psychoeducation to cancer patients, such as recognizing anxiety symptoms, which increased their awareness.[76,79,80] Moreover, relaxation techniques were offered, allowing thought and emotional management, thereby contributing to anxiety reduction.[80]

Effects of Digital Interventions on Depression

Last, digital interventions helped improve depression. One VR study[70] displayed effective depression reduction, coinciding with a previous review.[62] Again, an underlying mechanism of VR concerned the creation of alternate reality to keep users' mind away from the real world, hence improving their psychological state of mind. Two mobile app studies[76,80] showed effective improvement in depression, aligning with previous reviews.[82,83] The mobile apps provided psychoeducation, relaxation techniques, symptom awareness, and management of thoughts and emotion.

Intervention Contents

Current findings of intervention content showed significant subgroup differences for pain and fatigue. The VR studies mainly involved relaxation videos and games that promote physical activity,[59,84] while only one study[85] played education-related videos for patients before receiving treatment. Most mobile app studies provided educational content and symptom monitoring, but two involved playing games.[86,87]

Intervention contents play a major role in improving study outcomes. Particularly, studies that generated large effect sizes on pain reduction involved VR relaxation videos, game-based activity, and reminders. Furthermore, game-based activity helped promote physical activities that users had to perform, acting as physical rehabilitation, thereby reducing pain levels. Reminders consisted of notifications for timely consumption of painkillers and performance of other activities like pain diary, ultimately contributing to reduction of pain levels.

Intervention contents that were effective on fatigue reduction encompassed VR relaxation videos, teleconsultation, education, and symptom monitoring. Teleconsultation via mobile apps minimizes transportation time to the hospital, which might help reduce fatigue among cancer patients. Furthermore, one RCT[75] provided symptom-specific recommendations, which included fatigue, while the mobile app used in the study[73] had various modules such as rehabilitation information, which most presumably improved fatigue levels.

Effects of Digital Interventions at Follow-Up Assessments

Findings of subgroup analysis conducted according to posttest follow-up showed significant subgroup differences for fatigue. Follow-up subgroup ($>$ 6 months) for fatigue had the largest range of effect size compared to subgroups (3 to 6 months and $<$ 3 months) subsequently. Particularly, Liao et al. 74 was the focal study that produced such findings. A possible explanation is that the population in the study had completed their cancer treatment; hence, their baseline fatigue levels were high. Overtime, naturally occurring effects along with the use of the mobile app might have synergistically caused a larger decline in fatigue levels compared to Huggins et al,[88] in which the study population had yet to undergo treatment. Therefore, their fatigue levels are not expected to deviate vastly from baseline. There were no previous reviews involving mobile apps that conducted a subgroup analysis of follow-up duration for fatigue. Despite the lack of comparison, current findings suggest a positive outlook for prolonged sustainability of the interventions on fatigue.

Pain, sleep, anxiety, and depression outcomes showed no significant subgroup differences, indicating that the intervention effects were similar for these symptoms, regardless of the duration. A previous review on pain[68] aligned with the current findings, but there were no existing reviews that conducted such subgroup analysis for the other outcomes.

Limitations

This review has some limitations. Generalizability of the results is limited as most studies had mixed cancer types and intervention contents resulting in heterogeneity. There were also limited number of studies for VR intervention outcomes (sleep), subgroup analyses of intervention contents and posttest follow-up, affecting the ability to make meaningful finding interpretations.[89] Only English-language published articles were also included; omitting possible relevant studies in different languages contributes to publication bias. Finally, the review outcomes had a rating of very low quality in the GRADE assessment, which indicates little confidence in the results.[90]

Implications to Clinical Practice

Our findings have implications to clinical practice (Appendix V). Healthcare institutions may consider implementing VR and mobile apps as a nonpharmacological approach to reduce physical and psychological symptoms among cancer patients. In fact, these modalities can be used as supplementary add-ons to the individual's care management which may result in further amelioration of their symptoms and overall condition. As an example, cancer patients can put on VR headsets[70] or use mobile apps during treatment or evaluation procedures. Intervention contents may include VR relaxation videos, game-based activities, and reminders, which are useful in reducing pain. Teleconsultation, education, and symptom monitoring can be integrated into an interventions to minimize cancer-related fatigue, anxiety, and depression. Mobile applications with mindfulness practice can be offered to improve sleep quality, anxiety, and depression.

Recommendations to Future Research

Future research may find possible ways of blinding and allocation concealment to prevent a potential Hawthorne effect, thereby reducing the risk of bias and producing higher-quality findings. As most included studies had populations of mixed cancers and intervention contents, future trials should focus on specific cancers and intervention contents to obtain a holistic understanding of the effectiveness of VR and mobile apps for the general cancer population.

Conclusion

Overall, this review suggested that VR and mobile-based intervention improved pain, fatigue, anxiety and depression. However, the effects of VR on sleep remain inconclusive. At follow-up, the interventions made small improvements only in physical symptoms although this should be interpreted with caution as only a handful of included studies had repeated posttest measurements. As there are no similar reviews that have yet to conduct a subgroup analysis of cancer types, future trials should seek to address this knowledge gap to potentially obtain results generalizable to the general cancer population. As only English studies were included, future reviews should broaden their search for studies of different languages for inclusiveness and prevent possible publication bias. The very low-quality outcomes in GRADE assessment probe more future studies to be conducted in similar settings along with added ways to reduce the risk of bias. Last, as perpetual improvements in digital health interventions are progressively made, its future implementations in health care can undoubtedly improve the quality of cancer patients' lives.

Declaration of competing interest

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

CRediT authorship contribution statement

Chun Chong Goh: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Xi Meng Gan:** Writing – review & editing, Investigation, Data curation. **Piyanee Klainin-Yobas:** Writing – review & editing, Writing – original draft, Methodology, Conceptualization.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.soncn.2024.151796.

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