



Virtual reality as a chemotherapy support in treatment of anxiety and fatigue in patients with cancer: A systematic review and meta-analysis and future research directions

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ABSTRACT

Objective: The aim of this systematic review was to analyse the effectiveness of virtual reality intervention as an aid for treatment-related anxiety and fatigue in cancer patients undergoing chemotherapy. The term chemotherapy was assumed without distinction regarding type.

Methods: The inclusion criteria were (1) randomised controlled trials or crossover studies, (2) adult cancer patients undergoing chemotherapy, (3) treatment with VR scenarios providing distraction during chemotherapy, and (4) with pain, anxiety, fatigue, fear, or symptom distress as the measured outcomes. Articles in English, Polish, and Italian were sought. For the methodological quality assessment of risk of bias, likewise statistical analysis and meta-analysis the RevMan version 5.4 software and the Cochrane Risk of Bias Tool were used. Two authors independently analysed the following databases for relevant research articles: PubMed, Scopus, Cochrane Library, Web of Science, and Embase.

Results: From a total of 2543 records, 6 studies met the inclusion criteria for qualitative analysis. At the end of the process, 3 studies remained for quantitative analysis. The systematic review includes three randomised, controlled studies and three crossover studies with an overall sample size of 453 patients. The analysis of the primary outcomes chosen for each study revealed no significant differences between the control and experimental conditions. Moreover, an important factor influencing the results of the review and meta-analysis was the poor quality of the publications available on the topic of distraction during chemotherapy.

Conclusion: Due to the low research standards, the results do not provide an unambiguous answer to the research question. The most important limitations result from the small number of trials, the generally small sample sizes, and the differences in study design.

1. Introduction

Neoplasms seem particularly important today due to their health, psychosocial, and economic consequences. The incidence of cancer is increasing worldwide, and cancer is expected to be the leading cause of mortality after 2030.¹ Therefore, it seems necessary to take steps that will strengthen the current strategy of therapeutic management. Nowadays, innovative methods are used in addition to the standard cancer treatment methods.² The increase in the supply of targeted and

chemotherapeutic drugs, thanks to the use of new mechanisms of action, increases the effectiveness of the treatment of such types as colon, breast, stomach, ovary, and lung cancer³; unfortunately, it also affects a greater risk of fatigue, which in turn is associated with quality of life, psychological distress, and physical functioning.⁴

Fatigue is the most common cancer-related symptom, most commonly experienced by patients undergoing chemotherapy, and its prevalence is estimated at 60%–90%.^{5,6} Fatigue occurs in actively treated patients and is also a long-term effect of treatment, lasting even

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many years afterwards.⁷ It also affects the quality of life.³ An equally important component of the symptoms that influence the psychophysical state of the patient is the increased distress, anxiety, and depressive symptoms associated with both the diagnosis of cancer itself and the aggressive treatment, which contribute to limitations in everyday functioning.⁸ The prevalence of distress in cancer patients ranges from 35 % to 55 %. Depression, sadness, and lack of control over treatment decisions increase the level of anxiety and reduce the patients' quality of life.⁹ Fatigue, symptom distress, anxiety, and depression can increase the side effects of treatment and lower its effectiveness. Therefore, therapeutic interventions that increase the tolerance of treatment are crucial for the quality of life of cancer patients. Quality of life is related to the level of physical activity.¹⁰ Thus, most often, in the rehabilitation of patients treated with chemotherapy, physical exercise programmes based on endurance or resistance training are used,¹¹ likewise home exercises and relaxation techniques.¹² Recent systematic review has reported that home-based exercise interventions are feasible, and provide physiological and psychological benefits for cancer survivors.¹³ Batalik et al. included nine randomized controlled trials to identify the health benefits of home-based exercise interventions in cancer patients and survivors and to evaluate the methodological quality of the studies.¹⁴ They found a large diversity of cohorts that failed to synthesize the data, yet the results suggest that HB exercise interventions may provide multiple benefits in cardiorespiratory fitness, strength, physical activity level, HRQOL, and body composition. Thus, the investigation of new intervention approaches focused on counteracting the negative physical and/or psychological side effects of cancer treatment seems justified.

The use of virtual reality (VR) in medicine is gaining more and more supporters, finding applications in surgery, rehabilitation, dentistry, and neurology, among other fields.¹⁵ VR also plays a special role in educating future doctors, as a virtual environment can simulate surgical procedures and support the course of complex ones. VR has also been widely adopted in the rehabilitation process.¹⁶ It has been shown to be highly effective in improving cognitive and motor functions.^{17,18} VR-based treatments for different mental health conditions have demonstrated successful results.¹⁹ A simple classification includes immersive and non-immersive virtual reality. The main difference between the two is the number of stimuli delivered to the user. Immersive technology, usually provided through a Head-Mounted Display (HMD), allows the user to be isolated from the real world and to interact in a computer-generated environment, with simultaneous involvement of different senses: vision, hearing, touch, or even smell.²⁰ Non-immersive VR is presented through a display (monitor or projector), where the user interacts with their avatar within the VR yet still perceives the external environment. Usually the infusion takes place over several hours, therefore employing VR while the patient has to sit or lie down seems to maximize the therapeutic potential. Virtual reality seems to be a new and effective tool that may distract the patient's attention from medical procedures; it can thus also contribute to improving the quality of life and reducing the undesirable effects of oncological treatment,²¹ translating into the promotion of an active lifestyle in this area among cancer patients.

Analysis of the literature suggested that the VR intervention could be an effective distraction tool during chemotherapy in both adult and pediatric patients with different cancer diagnoses,^{22–25} however revealed a lack of current meta-analyses considering the effectiveness of virtual reality interventions on anxiety and fatigue during chemotherapy. We identified only one mini-review (2016), one systematic narrative review (2021), and one meta-analysis (2019). The pooled conclusions of these reviews were that the evidence for the importance of VR interventions in reducing pain or anxiety in cancer patients undergoing medical procedures or receiving chemotherapy was inconclusive, which encouraged us to reanalyse the literature. The purpose of A mini-review by Chirico et al. was to provide an overview of studies that have used VR intervention in patients with cancer and to analyse their

main results. In the conclusion of the study, the authors identified the need for a global and multidisciplinary approach to analyse the effects of VR using new technological systems, during and after the intervention. Finally, a systematic narrative review by Chow et al. was aimed to analyse the impact of immersive VR on pain and/or anxiety in patients with cancer undergoing medical interventions. Only nine studies met inclusion criteria for review. The authors stated that further studies are necessary to investigate the effects of immersive VR as an intervention tool in cancer patients undergoing treatment.²⁶ A previous meta-analysis by Zeng et al. analysed only 3 databases and included only 1 randomized controlled trial (RCT).²⁷ Due to the publication of new RCT after the publication of this meta-analysis, it was decided to re-evaluate the effectiveness of VR-based interventions. Therefore, the aim of this study was to analyse the effectiveness of virtual reality intervention on anxiety and fatigue in cancer patients undergoing chemotherapy.

2. Methods

The study design was a systematic review including a meta-analysis and developed on the basis of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (PRISMA) guidelines.²⁸ The protocol was prospective registered in the PROSPERO database, under registration number CRD42021254460 on 07.06.2021.

2.1. Electronic search

Two authors independently analysed the following databases for relevant research articles: PubMed, Scopus, Cochrane Library, Web of Science, and Embase. The search was performed in March and April 2021. There was no time frame for publication as there was a limited number of publications on this topic. The search strategy was based on the following medical subject headings (MeSH Terms): 'Chemotherapy, Adjuvant', 'Drug Therapy', 'Virtual Reality', 'Virtual Reality Exposure Therapy', 'Smart Glasses', 'Anxiety', 'Fatigue', and 'Fear'. A full description of the search strategy is presented in the supplementary materials (see Appendix 1).

2.2. Study selection

The inclusion criteria were (1) randomised controlled trials or crossover studies, (2) adult cancer patients undergoing chemotherapy, (3) treatment with VR scenarios (immersive, non-immersive, or mixed-reality) providing distraction during chemotherapy, and (4) with pain, anxiety, fatigue, fear, or symptom distress as the measured outcomes. Articles in English, Polish, and Italian were sought. Grey literature was searched for on Google Scholar databases and in the reference lists of the articles returned. Two reviewers independently screened each abstracts using an inclusion/exclusion criteria template. All disagreements were resolved by a third researcher. The full-text quality analysis (risk of bias assessment) was then performed following the same procedures.

2.3. Outcomes

The aim of this systematic review was to analyse the effectiveness of virtual reality intervention as an aid for treatment-related anxiety and fatigue in cancer patients undergoing chemotherapy. Outcomes such as anxiety, fatigue, fear, pain, and symptom distress were analysed in controlled and experimental conditions. The experimental, VR treatment group was compared to other (traditional) care or no-intervention control groups.

2.4. Data extraction and management

Screening of research records was conducted by two independent reviewers, with the intervention of a third researcher in case of

disagreement. Relevant data, such as the authors, year of publication, study design, characteristics of the participants, co-interventions, sample size, type of VR-intervention, outcome measurement, and administration dates were provided in a data extraction form.

2.5. Assessment of risk of bias in the selected studies

For the methodological quality assessment of risk of bias, the software programme Review Manager (RevMan version 5.4; Nordic Cochrane Centre, Cochrane Collaboration, 2014) and the Cochrane Risk of Bias Tool²⁹ were used. The quality of the work was assessed based on bias categories: selection bias (sequence generation and allocation concealment), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective reporting), and all other biases. The risk of bias was assessed on a three-point scale, where 'low risk' stands for a low possibility of bias, 'high risk' means a high possibility of bias, and 'unclear risk' is used when the manuscript does not contain valuable information. In the case of a risk that is not described in the text, the authors were contacted in order to complete the missing data. A detailed summary of the risk of bias assessment is included in the supplementary materials (see Appendix 2). As it is not possible in most cases to blind the participants of a virtual reality intervention, it was decided to omit the domain of assessing participant

blinding (performance bias).

2.6. Data synthesis and statistical analysis

RevMan 5.4.1 was used for the statistical analysis and meta-analysis. We attempted to categorize the included interventions along two outcomes group: (1) anxiety; (2) fatigue. The Mean Difference (MD) outcome measures were used for analysis since the selected studies used this tool. Statistical heterogeneity was assessed with the I^2 statistic, with a cut-off value at 50 % and considering intervention and outcome measures. We conducted a meta-analysis based on a fixed model with a 95 % confidence interval. In the case of no data available for synthesis, an email was sent to the corresponding author. We assumed a 2-week waiting period for a response. Due to the limited number of included studies, it was not possible to perform subgroup analysis in case of high heterogeneity.

3. Results

The electronic search identified 2,543 results overall, with no additional records from the grey literature search. The following numbers were retrieved from publications in each of the databases: PubMed: 21; Scopus: 1945; Cochrane Library: 8; Web of Science: 29, and Embase:

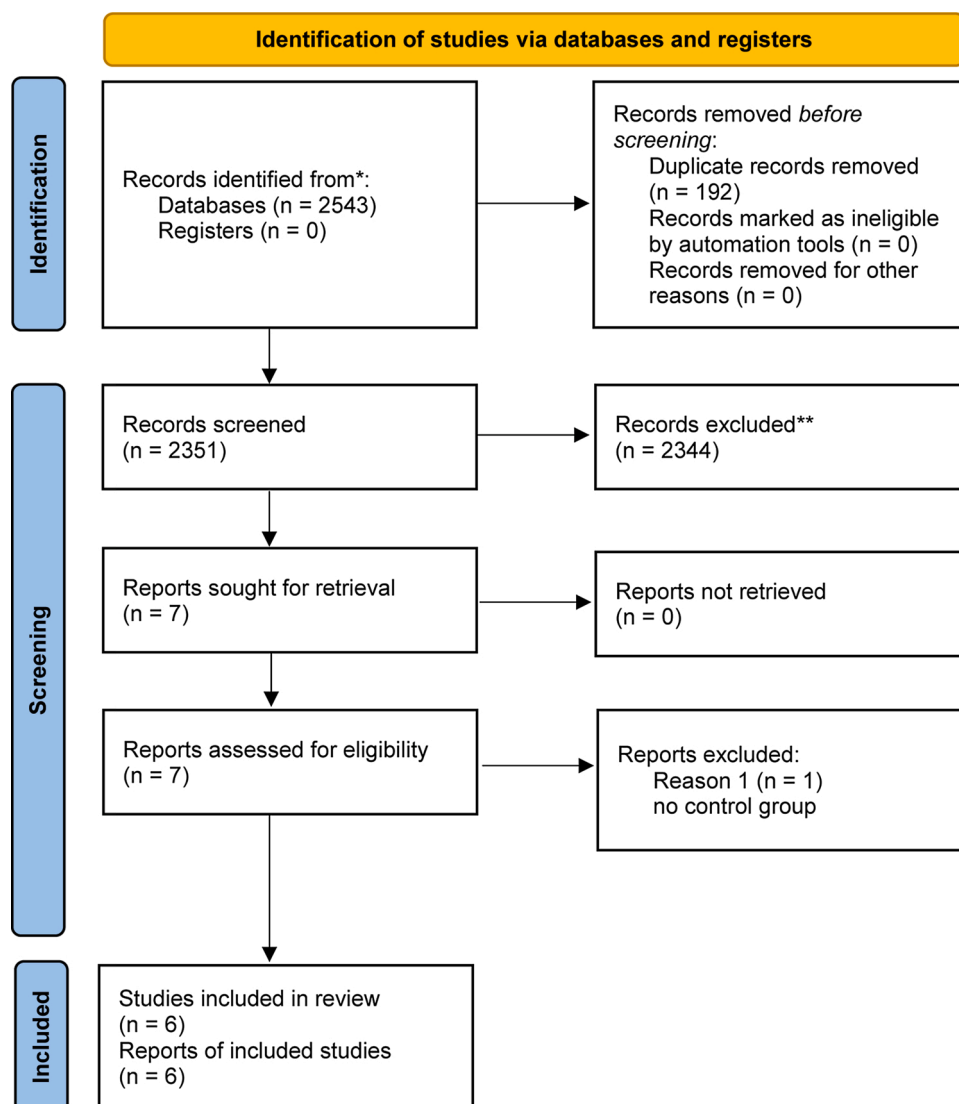


Fig. 1. Flow diagram for the study selection process.

540. The 192 duplicate records were removed, leaving a total of 2,351 abstracts for screening. At this stage, 2,344 records were excluded, and seven full-text articles were assessed for eligibility. The main reasons for rejecting abstracts were: different study design than specified in the inclusion criterion, no VR intervention during chemotherapy, different study population, inappropriate publication type. Finally, six studies met the inclusion criteria and underwent a qualitative analysis. The reason for excluding one of the full-text articles was that it lacked a standard care control group. Three studies were included in the quantitative analysis, whilst three were excluded due to insufficient data. Our attempt to contact the authors was unsuccessful. The review process presents the PRISMA flowchart (Fig. 1).

3.1. Studies included in the review

The systematic review includes three randomised, controlled studies and three crossover studies. The participants represented both sexes and were adults. The patients' age was between 18–77 years. The term chemotherapy was assumed without distinction regarding type. Different types of tumours were treated in the studies: breast cancer,^{21,22,30–33} ovarian cancer, cervical cancer,³³ cecum cancer,³³ colon cancer,^{22,33} rectal cancer³³ and lung cancer.²² Overall 506 participants were treated in the studies.

A study by Chirico et al. was the most complex, including three comparisons: an experimental group with VR, an experimental group using music therapy, and a control group with standard care.²¹ The VR intervention consisted of watching an interactive 3D video in different environments. The music therapy group received MP3 players with headphones and heard relaxing music for 20 min. For the control conditions, the medical staff followed customary procedures. Participants in this group were free to choose activities like conversation or reading during the treatment. The measured outcomes were anxiety levels, mood states, and cybersickness symptoms. The study included 94 Italian female patients.

Mohammad et al. used a 3D interactive video with different scenarios to compare with standard care procedures.³² The most important difference was the additional administration of pharmacological treatment. The standard care control group received painkillers (oral or intravenous) only for comparison. The measured parameters were pain and anxiety scores. The study included 80 Jordanian female patients.

Oyama et al. used a very extensive – for those times – VR technology for research.³³ The immersion consisted of three LCD displays, a 3D sound system, aromatherapy, and interactive pedals for movement. Patients in the experimental group were able to choose from three virtual environments. The duration of the intervention depended on that of the chemotherapy treatment. In the control group, the patients underwent no additional intervention. The primary outcomes were anxiety and depression, emotional status, subjective feelings, and fatigue. The study included 30 Japan patients.

Schneider et al. used another study design to assess the best time to use VR during chemotherapy.³⁰ The crossover study from 2003 had a small sample size. The patients were over 50 years of age, and the experimental group had to choose one of three different VR scenarios. In the control group, no other distraction interventions were used. The study included 16 American female patients

A similar study was made by Schneider et al. in 2004.³¹ As before, the patients were being treated for breast cancer. The most significant difference in study design was the participants' age. The age of the patients in the second study was between 27 and 55 years, likewise the experimental group were also able to choose one of three different VR scenarios, and the control group had no additional distraction. The study included 20 American female patients

In 2007 Schneider et al. extended the inclusion criteria to additional types of cancer.²² A total of 107 participants in the experimental group received VR distraction treatment in one of three different scenarios. The control group (n = 106) was free to choose any activity, such as

watching television, conversing, or reading during chemotherapy. The measured outcomes were symptom distress, fatigue, anxiety, and quality of distraction. The study included 213 American patients.

A detailed description of the selected studies is presented in Table 1.

3.2. Excluded studies

One study was excluded after the full-text screening. The results presented by Spencer et al.³⁴ were insufficient to compare them to the rest of the data, due to the lack of a standard care control group.

3.3. Risk of bias of the studies

Fig. 2 shows the risk of bias in the studies included in the review.

- **Random sequence generation (selection bias):** Two studies^{32,33} had a low risk of bias. The authors described in detail the random component of the sequence-generation process. Three studies^{22,30,31} were assessed as having an unclear risk of bias, as no information about the randomisation process was provided. One²¹ of the studies had no randomised control group and was assessed as a high risk of selection bias.
- **Allocation concealment (selection bias):** Two studies^{21,33} had a high risk of this bias because the recruitment for the control group was started separately from that of the experimental group and the allocation was based on the order in which participants joined the study. As there was no information about procedures for allocation concealment, four studies^{22,30–32} were assessed as having an unclear risk of bias.
- **Blinding of outcome assessment (detection bias):** In one study²¹ the data analyst was not blinded, so the risk of bias was judged as high. Five studies,^{22,30–33} due to a lack of information about assessors' blinding, were judged as having an unclear risk.
- **Incomplete outcome data (attrition bias):** Four studies^{21,22,31,32} were assessed as having a low risk of bias because no missing data were found, or the purpose behind excluding the participants was justified. Only one study³³ had a high risk of bias because of the imprecise reason for exclusion. One study³⁰ was judged to have an unclear risk of attrition bias, due to missing information about incomplete outcome data.
- **Selective reporting (reporting bias):** Five studies^{21,22,31–33} were judged to have a low risk of bias. The studies' protocols were available and the published reports included all expected outcomes, or the studies' protocols were unavailable but it was clear that the published reports included all expected outcomes. One study,³⁰ due to a lack of information was assessed as having an unclear risk of bias.
- **Other bias:** Four studies^{22,30–32} were judged to have a low risk of other bias because no additional biases were found. Two of the studies^{21,33} were judged to have an unclear risk because of the low overall quality of research and the lack of relevant information.

3.4. Effects of intervention

Three studies with an overall sample size of 357 patients were analysed for anxiety levels during the chemotherapy procedure. As the outcome measurement in those studies was performed according to the State Anxiety Inventory (SAI) for adults, the analysis was performed using MD with a fixed-effect model. The meta-analysis showed no significant differences between the two treatment conditions. These studies were too heterogeneous to be pooled ($I^2 = 92\%$), as presented in Fig. 3. Presumably, the high heterogeneity was due to the VR technology used.

Four studies^{22,30,31,33} examined fatigue levels in patients, however, we were unable to conduct a meta-analysis due to lack of data. Only the Schneider 2007 study presented pre-post data. Unfortunately, when we sent a request for data from the 2003 and 2004 papers, we were

Table 1
Characteristics of the selected studies.

STUDY ID	STUDY DESIGN	PARTICIPANTS	VR ENVIRONMENT	INTERVENTIONS	OUTCOMES	CONCLUSION
Chirico et al. 2020	RCT	Women aged 18–70 years with breast cancer undergoing chemotherapy	Immersive VR	1. Experimental Group I – virtual Reality - device: Vuzix Wrap 1200 VR - watching an interactive 3D video in different environments - scenarios: exploring an island, walking through a forest, observing different animals, climbing a mountain, and swimming in the sea - 5–10 min of getting accustomed to the VR system → chemotherapy with 20 min of VR 2. Experimental Group II – music therapy - beginning 5 min after the start of chemotherapy - 20 min of relaxing music - an MP3 player with headphones 3. Control Group – standard care - for the control conditions, nurses and medical staff followed customary procedures; the patients were free to choose different activities during treatment, including conversation and reading	1. Primary outcomes: - anxiety levels (State Anxiety Inventory [SAI] for adults) - mood states (short version of Profile of Mood States [SV-POMS]), which evaluates tension, depression, anger, vigour, fatigue, and confusion) - cybersickness symptoms (Virtual Reality Symptom Questionnaire [VRSQ])	Both VR and MT seem to be useful interventions for alleviating anxiety and improving mood states in breast cancer patients during chemotherapy. The VR intervention seems more effective than MT in relieving anxiety, depression, and fatigue.
		1. Experimental Group I (n = 30) 2. Experimental Group II (n = 30) 3. Control Group (n = 34)				
Mohammad et al. 2019	RCT	Women aged 30–70 years with breast cancer undergoing chemotherapy	Immersive VR	1. Experimental Group – virtual reality + morphine - device: HMD with headphones - watching an interactive 3D video in different environments + headphones - scenarios: deep sea diving ‘Ocean Rift’ or sitting on the beach with the ‘Happy Place’ track - The scenarios were assessed in a pilot study to determine whether they were comfortable and clear → the patients wore a head-mounted display with headphones → the VR exposure session ended at the peak time of painkiller efficacy 2. Control Group – standard care - standard care, including only pharmacological interventions (oral or intravenous morphine)	1. Primary outcomes: - pain (VAS 0–10) - anxiety (SAI for adults)	This study suggests that immersive VR is promising as an effective distraction intervention for managing pain and anxiety among breast cancer patients. Using immersive VR as an adjuvant is more effective than morphine alone in relieving pain and anxiety.
		1. Experimental Group (n = 40) 2. Control Group (n = 40)				
Oyama et al. 2000	RCT	Patients aged 29–73 years with different cancers undergoing chemotherapy	Immersive VR	1. Experimental Group – Bedside Wellness System - device: 3 LCD displays + 3D sound system (headphones and speakers were available) + aromatherapy + movement assistance mode - three virtual worlds were available (lake, forest, and country town) - VR duration: the length of the BSW intervention depended on the length of the chemotherapy 2. Control Group – standard care	1. Primary outcomes: - anxiety and depression (HADS) - emotional status (facial scale) - subjective feelings: on a scale of 1 (not at all) to 5 (very much) for a set of nine goals classified as positive and negative states. Positive goals were ‘relaxed’, ‘refreshed’, ‘calm’, and ‘vivid’. Negative goals were ‘tense’, ‘depressed’, ‘unpleasant’, ‘sleepy’, and ‘tired’. - fatigue (Cancer Fatigue Scale and VAS)	Bedside Wellness System intervention is an effective way to treat fatigue and emesis. This virtual reality system is a new therapeutic method that can be used in palliative medicine.
		1. Experimental Group (n = 15) 2. Control Group (n = 15)				

(continued on next page)

Table 1 (continued)

STUDY ID	STUDY DESIGN	PARTICIPANTS	VR ENVIRONMENT	INTERVENTIONS	OUTCOMES	CONCLUSION
Schneider et al. 2003	Crossover study	Women aged 50–77 years with breast cancer undergoing chemotherapy	Immersive VR	- chemotherapy without additional intervention 1. Experimental Group – virtual reality - device: Sony PC Glasstron PLM-S700 - three different scenarios: ‘Titanic®’, ‘World of Art®,’ and ‘Oceans Below®’ 2. Control Group – standard care	1. Primary outcomes: - fatigue (Revised Piper Fatigue Scale [PFS]) - anxiety (SAI for adults) - symptom distress (Symptom Distress Scale [SDS])	The hypothesis that VR could mitigate chemotherapy-related symptom distress as a distraction intervention was partially supported. While there were no significant changes in any of the measures of symptom distress, fatigue, or anxiety after two days, there was a trend towards lower scores with the VR condition.
Schneider et al. 2004	Crossover study	Women aged 27–55 years with breast cancer undergoing chemotherapy	Immersive VR	- chemotherapy without distraction intervention 1. Experimental Group – virtual reality - device: Sony PC Glasstron PLM-S700 - three different scenarios: sea diving, walking through an art museum, or solving a mystery 2. Control Group – standard care	- symptom distress (SDS) - anxiety (SAI for adults) - fatigue (Revised Piper Fatigue Scale [PFS])	The distraction intervention decreased symptom distress, was well received, and was easy to implement in a clinical setting. The results suggest that virtual reality can be used to manage symptoms.
Schneider et al. 2007	Crossover study	Patients aged 32–78 years with different cancer types undergoing chemotherapy	Immersive VR	- chemotherapy without distraction intervention 1. Experimental Group – virtual reality - device: i-Glasses® SVGA head-mounted display - four different scenarios: sea diving, walking through an art museum, solving a mystery, or exploring ancient worlds 2. Control Group – standard care - the subjects were free to participate in any activities they chose during treatment, such as watching television, conversing with others, or reading	1. Primary outcomes: - symptom distress (Adapted Symptom Distress Scale 2 [ASDS-2]) - fatigue (Revised PFS) - anxiety (SAI for adults) - distracting quality (Presence Questionnaire [PQ] and Evaluation of Virtual Reality Intervention)	The findings support the notion that using VR can help make chemotherapy treatments more tolerable, but clinicians should not assume that the use of VR will improve chemotherapy-related symptoms.

informed that the raw data from this study were missing. We did not receive a response to our request for data from Oyama et al., thus it was not possible to pool the data.

4. Discussion

This systematic review with meta-analysis was designed to assess the effectiveness of VR distraction during chemotherapy in cancer patients compared to standard care procedures. The analysis of the primary outcomes chosen for each study revealed no significant differences between the control and experimental conditions; however, it is worth noting that articles following modern publication standards and much more advanced technology^{21,32} showed promising results. It can be assumed that the technology used in 2007²² was markedly different from the studies of the past two years, which we believe distorted the results of the meta-analysis. The review of included papers identified two groups of studies in terms of the length of the intervention. In three papers,^{21,32,33} the exposure time was between 15 and 20 min, while in Schneider’s papers,^{22,30,31} the VR exposure time was between 45–90 min. Moreover, an important factor influencing the results of the review and meta-analysis was the poor quality of the publications available on the topic of distraction during chemotherapy. The appearance of CONSORT standards in 2010 made a large impact on the quality of publications, which is confirmed by the quality assessment of the studies included in this review. It is worth continuing research in this direction in order to be able to better assess the use of VR as a distractor in various medical fields, not only in oncological treatment. Although the results do not show a statistically significant benefit of using VR, the review

supports the need for research in this area. Scientists should focus on examining larger patient groups and standardising the methodology.

The results of this systematic review with meta-analysis are in line with previous results considering a mini-review,³⁵ narratives review²⁶ and meta-analysis,²⁷ suggested that virtual reality is an effective tool for distraction in pain management and stressful medical procedures in cancer patients, which may also lead to the minimisation of other emotional side effects. A meta-analysis by Zeng et al. showed that VR-based interventions had positive effects on reducing symptoms of anxiety (SMD = −3.03; 95 % CI −6.20 to 0.15). However, the authors noted a very high heterogeneity ($I^2 = 95$ %) rendering the results unreliable. The overall results favoured a VR-based intervention to reduce fatigue and pain levels, but only fatigue symptoms reached statistical significance (MD = −2.50; 95 % CI −5.97 to −0.99; $I^2 = 16$ %).

Mental well-being is an important factor in oncological rehabilitation, as it impacts the progress of physical rehabilitation. Oncological patients are exposed to stress and anxiety related to their diagnosis, treatment, hospitalisation, and prognosis; therefore, it is important to reduce unpleasant experiences at every stage of the disease. It has also been proven that stressed patients tolerate therapy less well and are less cooperative with medical staff.³⁶ In our opinion, the results suggesting the effectiveness of VR as an anxiety-reducing method are based on the distraction mechanism. It has been proven that distraction has a different mechanism of action than placebo. According to Buhle et al. placebo and distraction provide two distinct pathways to pain relief.³⁷ The authors conducted an fMRI analysis that suggests distraction effectively inhibits pain processing in the brain, while placebo may not have a significant effect on pain processing. It can be assumed that

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Chirico et al. 2020	+	+	+	+	+	+
Mohammad et al. 2019	+	?	?	+	+	?
Oyama et al. 2000	+	-	?	-	+	+
Schneider et al. 2003	?	?	?	?	?	?
Schneider et al. 2004	?	?	?	+	+	?
Schneider et al. 2007	?	?	?	+	+	?

Fig. 2. Summary of the risk of bias analysis.

pain-relief effect during chemotherapy, results in reduced anxiety. Such a hypothesis was confirmed in by our team in a previous meta-analysis on virtual reality interventions for needle-related procedural pain, fear, and anxiety.³⁸ Statistically significant benefits of using VR were shown in children’s pain scores, where VR significantly decreased symptoms (n = 3204 patients, MD = -2.85; 95 % CI -3.57, -2.14, for the Wong-Baker Faces Pain Rating Scale and n = 2240 patients, MD = -0.19; 95 % CI -0.58, 0.20, for the Faces Pain Scale—Revised). However, it is worth emphasizing that VR is not the only method of distraction.

Further reflection on the results of our team’s meta-analysis may be worthwhile at this point. We anticipated different results while planning the present study because the previous literature reviews conducted by our team revealed the significant importance of VR technology in psychiatry and rehabilitation.^{15,16,18,19} Moreover, in our research conducted under the supervision of Prof. Joanna Szczepańska-Gierach, we examined the effectiveness of the TierOne VR system in reducing anxiety and depression in cardiovascular disease, pulmonology, and elderly patients.³⁹⁻⁴² The results of these clinical trials conducted by our team confirmed the helpfulness of VR in improving the mental condition of patients. However, certain conditions must be met. The meta-analysis revealed that it is not enough to show nice landscapes to patients in VR goggles in order to achieve a therapeutic effect. None of the VR systems in the analysis used therapeutic factors such as breathing exercises,

relaxation, mindfulness, or elements of psychotherapy. Surprisingly, for many years no visualisations were used as a therapeutic method to strengthen the work of the immune system according to the assumptions of Carl Simonton’s therapy.

Nevertheless, knowing the capabilities of immersive VR systems and being aware of the rapid development of this technology, it seems clear that soon interdisciplinary teams of specialists including 3D graphic designers, physicians, and psychotherapists will develop new solutions to effectively support the treatment of oncology patients. It is only a matter of time in our opinion, and we hope that the conclusions from this review will help in the design of appropriate clinical trials devoid of methodological flaws, which will objectively verify the effectiveness of the modern therapeutic methods being developed. An important direction of further development is to enable patients to continue their therapy at home, as the treatment does not end when the patient leaves the oncology ward. Therefore, producers of VR systems should consider home versions for a tablet or smartphone to continue therapy after cancer treatment has ended. The COVID-19 pandemic has demonstrated the importance of remote treatment systems when in-person patient–doctor contact is not possible. The research conducted over the years has shown that patients are as satisfied with this form of treatment as with traditional, face-to-face interventions.^{43,44} This area of mental health care – telemental health – is currently the most widely used option of telemedicine. This technology has gained the greatest popularity and effectiveness in the treatment of depression, anxiety disorders, and post-traumatic stress disorder.^{45,46} Therefore, VR technology supplemented by telemental health projects has the potential to increase the efficiency of health care.

This study has some limitations that need to be addressed. Firstly, the included studies involved small sample sizes, highlighting the need to develop trials with larger population size. Secondly, although our primary outcomes were related to the assessment of fatigue, only one study²² reported comprehensive data, whereas three studies^{30,31,33} included partial data, which precluded performing a meta-analysis.

5. Conclusions

The most important limitations result from the small number of trials, the generally small sample sizes, and the differences in study design. Due to the low research standards, the results do not provide an unambiguous answer to the research question. Large methodological discrepancies in the articles led to a high level of heterogeneity. Also, the sample size was insufficient to objectively assess the effectiveness of virtual reality in this area. It is impossible to draw any conclusions about the efficacy of a virtual reality distractor for cancer patients, due to the overall lack of methodological quality and statistical power observed in the current literature.

Author contributions

Conceptualization, S.R., J.S-G., I.M.; methodology, S.R., O.C., A.W., P.K.; investigation, S.R., O.C., A.W., P.K., J.S-G., I.M; writing—original draft preparation, S.R., O.C., A.W., J.S-G., I.M.; writing—review and editing, S.R., O.C., A.W., P.K., J.S-G., I.M. All authors have read and agreed to the published version of the manuscript.

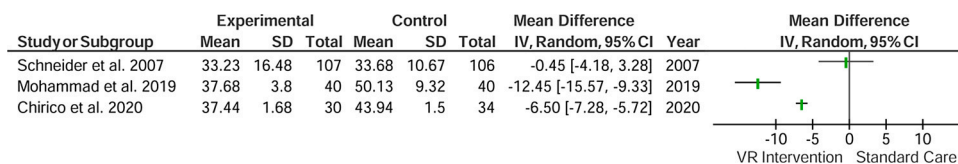


Fig. 3. Comparison of VR treatment and standard care, according to anxiety (SAI). SD: standard deviation; 95 % CI: 95 % confidence interval.

Data availability statement

The data presented in this study are available on request from the corresponding author.

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Declaration of Competing Interest

The authors declare no competing interests.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.ctim.2021.102767>.

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