




Virtual Reality and Symptoms Management of Anxiety, Depression, Fatigue, and Pain: A Systematic Review

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Androniki Ioannou, BSc, MSc, PhD¹ ,
Evrudiki Papastavrou, MSc, PhD¹, Marios N. Avraamides, PhD^{2,3},
and Andreas Charalambous, MSc, PhD, RN^{1,4} 

Abstract

In recent years, virtual reality (VR) has become an interesting alternative to traditional exposure-based therapies for many symptoms. VR involves immersion in a computer-generated virtual environment that minimizes avoidance and facilitates emotional processing. The objective of this systematic review is to evaluate evidence on the intervention effect of VR on anxiety, depression, fatigue, and pain. The research strategy of this systematic review included three electronic databases (MEDLINE/PubMed, Cochrane Library, and ScienceDirect) based on predetermined inclusion and exclusion criteria. Published quantitative studies from 2000 to 2020 were identified, which examined the effect of VR intervention on four different symptoms related to symptoms experienced by cancer patients. Quality assessments, data extractions, and analysis were completed on all included studies. A total of 882 titles and abstracts were screened, and 23 studies were included in the review. The studies were grouped according to the symptoms: anxiety and depression, fatigue, and pain. The review showed that VR intervention is more effective compared with the control (i.e., standard care) for anxiety, depression, fatigue, and pain. VR can reduce effectively these symptoms in different contexts and diseases, including cancer. The evidence suggests that there is value in exploring this intervention as a potential crossover treatment for these symptoms in patients. This study contributes to evidence that distraction is an effective symptom management mechanism. The findings are congruent with the theoretical framework, supporting the premise that VR, as an emotion-focused distraction intervention, decreases the severity of these symptoms.

Keywords

virtual reality, anxiety, depression, fatigue, pain

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What Is Already Known About the Topic?

- Nurses use a variety of different strategies to accommodate management of physical and psychological symptoms in patients.
- Symptoms such as anxiety, depression, pain, and fatigue represent four of the most commonly reported symptoms in individuals across many diseases.
- Clinical studies provided evidence that virtual reality (VR) is a promising tool for clinical assessment and management of many symptoms.

¹Department of Nursing, Cyprus University of Technology

²Department of Psychology, University of Cyprus

³Silversky3D Virtual Reality Technologies Ltd., Nicosia, Cyprus

⁴University of Turku

Corresponding Author:

Androniki Ioannou, 3, Filippou Hatzigeorgiou, Kato Lakatamia, P.C. 2322, Nicosia, Cyprus.

Email: andronikiioannou@hotmail.com



What This Article Adds?

- VR is more effective compared with the control (i.e., standard care) for anxiety, depression, fatigue, and pain.
- Using VR decreases significantly the levels of anxiety, depression, fatigue, and pain.
- The review provided evidence on the feasibility for using VR in various inpatient medical settings.

Introduction

For many years, nurses have used a variety of different strategies to accommodate management of physical and psychological symptoms in patients. To address all the needs of the patient, clinicians must consider not only the biological impact of illness but also the psychosocial one (Humphreys et al., 2014).

It was as early as the 90s that VR has had promising applications in science and medicine, including intervention delivery (Medling, 2005; Riener & Harders, 2012; Riva et al., 2007). In more recent years, VR technology has become increasingly affordable, immersive, flexible, and portable, enabling its use in a broader range of environments, including the inpatient medical setting (Ferrer-García & Gutiérrez-Maldonado, 2012; Parsons et al., 2009).

VR is one of the strategies that have been identified as cognitive-behavioral intervention. These interventions are thought to affect symptoms by changing symptom-related thoughts, diminishing those beliefs that exacerbate symptoms, and increasing personal perceptions of control over symptoms (Anderson et al., 2006; Kwekkeboom et al., 2003, 2010; Malloy & Milling, 2010). Use of VR interventions has been studied in a wide range of medical conditions, including anxiety, depression, pain, and fatigue that represent four of the most common symptoms present in individuals in many diseases (Chirico et al., 2016; Indovina et al., 2018; Llobera et al., 2013; McCann et al., 2014; Wiederhold, 2006).

To date, there is scarcity of systematic reviews on the use of VR in the inpatient medical setting and related to symptom management. Herein, we review controlled studies evaluating the utility and efficacy of VR-based treatments for patients suffering from these four symptoms. The overall objective of study selection was to collect published peer-reviewed articles that evaluated anxiety and depression, fatigue, and pain symptoms before and after VR exposure therapy.

Virtual Reality

The term *VR* was used for the first time in 1989 by Jaron Lamier. The most popular definition of VR refers to a particular technological system, which includes a computer capable of providing interactive three-dimensional

visualization, a controller for interaction with the animations, a position tracker, and a head-mounted display (HMD) to deliver the visual output. The trackers monitor the position and orientation of the user in space and provide the information to the computer that updates in real time the images for display (Biocca, 1992; Wiederhold & Wiederhold, 2007). VR is immersive and interactive, engaging several senses simultaneously. This technology allows an individual to hear and feel stimuli that correspond with a visual image and can interact with the virtual environment and the virtual world's response in real time to those actions (Liszio et al., 2018; Yu et al., 2018).

Methods

Study Selection: Search Strategy, Data Sources, and Screening

A systematic literature search was conducted in the following databases: MEDLINE/PubMed, Cochrane Library, and ScienceDirect. The aim was to retrieve experimental studies of VR in inpatient medical settings and symptoms management of the four symptoms. Standard searches were performed, with keywords containing affective domains, as well as references to virtual reality exposure therapy (VRET) and the field of interest. Keywords used for the search included "Virtual Reality," "Anxiety," "Depression," "Fatigue," "Pain," and "Symptoms Management" to identify studies published between 2000 and 2020.

Study Eligibility Criteria

Inclusion/Exclusion Criteria. All studies selected for inclusion were English-language publications, which reported original empirical findings and were published in a peer-reviewed journal, between 2000 and 2020. Studies were required to have used an experimental design and focused on the efficiency or effectiveness or process of VRET on the four symptoms. The researchers excluded trials with no control or comparison group, case studies, outpatient studies, theses, or dissertations. The samples of the studies were human participants from all ages having one or more of the symptoms that were the focus of this review.

Screening. As displayed in Figure 1 (PRISMA flow diagram), the initial first search yielded 882 citations of journal articles written over the past 20 years. Two-hundred and twenty-five citations were discarded after identifying they were duplicates, and 657 more were discarded after reviewing the abstract. The researchers reviewed the remaining 68 in more detail and excluded 45 because they did not meet all the inclusion criteria, the full text was not available, or they were duplicates. The final

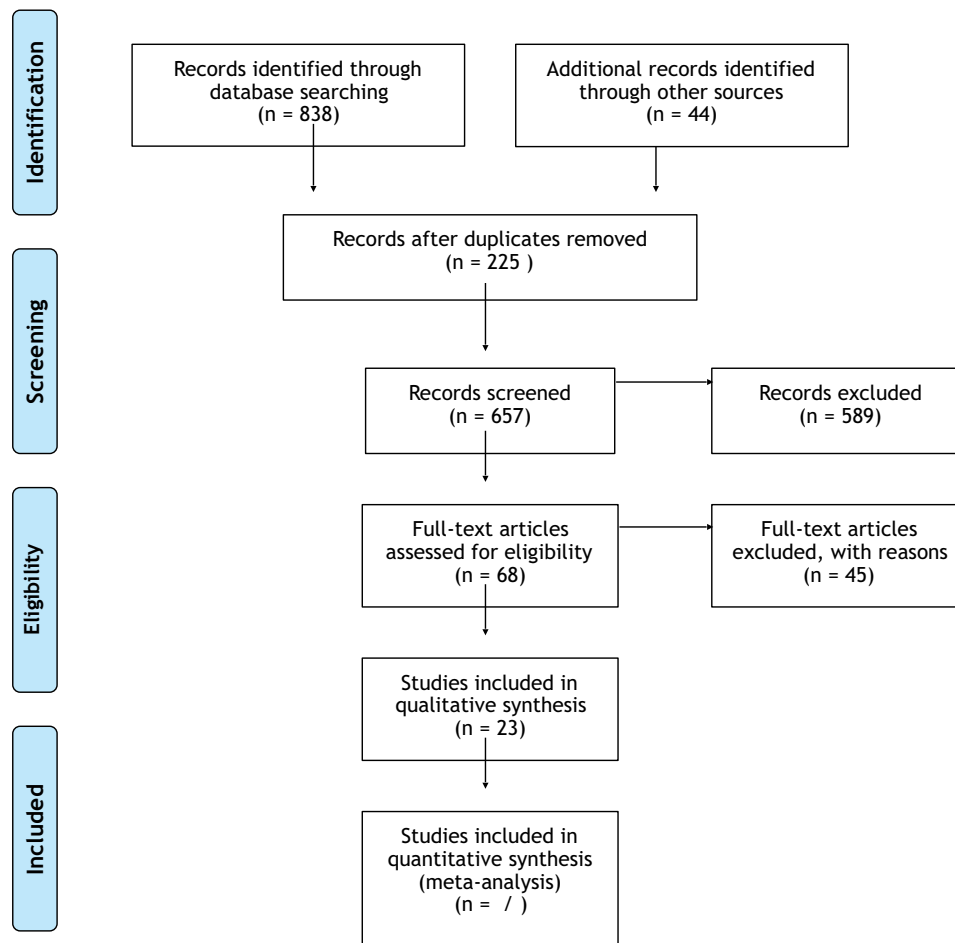


Figure 1. PRISMA 2009 Flow Diagram.

eligible for the review 23 studies were grouped based on the application of VR on the four symptoms: (a) anxiety, (b) depression, (c) fatigue, and (d) pain. These studies are described in detail in Table 1.

Data Extraction. The following data were extracted from the included studies: author, journal, country, research purpose and questions, theoretical framework, design, setting, subjects, sampling method, measurements instruments, reliability and validity, analysis, symptoms measures (anxiety, depression, fatigue, pain), outcomes of VR, and significant and nonsignificant results.

Quality Review. Each published article was reviewed for methodological quality by the research team members using the Cochrane Collaboration's tool (Table 2). The selected tool was used to assess risk of bias for randomized control trials. Although the methodological quality of the reviewed studies has been undertaken as part of this review, it was not considered as an eligibility criterion for inclusion in the review.

Results

Search Outcome

The search yielded 23 original studies that were included in the systematic review according to the predetermined inclusion criteria. Studies randomized patients to VR conditions, or randomized order of delivery of VR or standard interventions, using crossover designs. We observed that studies were heterogeneous with regard to targeted disease, VR equipment, and intervention materials. Thus, we categorized results within each of the following symptoms: anxiety and depression, fatigue, and pain management.

Overview of VR Intervention to Relieve Symptom Anxiety and Depression

Fourteen studies in total (Aminabadi et al., 2012; Dehghan et al., 2019; Gold et al., 2006; Kampmann et al., 2016; Krijn et al., 2004; Lee et al., 2015; Riva et al., 2003; Ryu et al., 2018; Schneider et al., 2003, 2004; Schneider & Hood, 2007; Shah et al., 2015; Song

Table 1. Studies Characteristics.

Study	Symptom	Type of study	Study population	N	Intervention	Tools	Main results
Delghan et al. (2019)	Anxiety	Solomon four-group randomized clinical trial	Children undergoing abdominal surgery	40 (6–12 years)	VR immersive and audio 5-minute exposure to the operating room	Yale Preoperative Anxiety Scale questionnaire (four domains including activity, vocalization, emotional expressivity, and state of apparent arousal) - m-YPAS-Preoperative anxiety, ICC- Procedural behavior rating scale	The comparison of pre- and postscores in the interventional groups by Wilcoxon test indicated a significant statistical difference in all domains except for arousals domain. Comparison of pre- and postscores among control groups showed a significant statistical difference in all domains except for emotional expressivity. Preoperative anxiety (28.3 [23.3–36.7] vs. 46.7 [31.7–51.7]; $p < .001$) and intraoperative compliance measured using ICC ($p = .038$) were lower in the gamification group than in the control group. The changes of m-YPAS scores before and after the intervention were also significantly different between the two groups (-22.5 [-29.6–14.2] vs. 0 [-20–4.2]; $p = .002$).
Ryu et al. (2018)	Anxiety	Prospective RCT	Children undergoing elective day surgery and general anesthesia	70 (5–8 years)	- VR gaming – a 5-minute VR game experiencing the preoperative experience - Conventional education regarding the preoperative process		3-day program intervention the participants had significantly lower subjective stress (X difference = 7.62, SD = 5.17, $t = 6.91$, $p < .001$), depression (X difference = 8.09, SD = 6.75, $t = 5.62$, $p < .001$), and anxiety (X difference = 5.64, SD = 4.77, $t = 5.54$, $p < .001$).
Shah et al. (2015)	Anxiety, depression	Quasi-experimental research (a single-group, pretest–posttest)	Inpatients diagnosed with major depressive disorder and bipolar disorder	22 (21–60 years)	VR DE-STRESS Program: The program comprised three daily 1-hour sessions incorporating psycho-education and VR-based relaxation practice.	DASS-21	
Lee et al. (2015)	Depression	RCT	Parkinson's disease patients	20 (65–75 years)	- Virtual reality dance exercises – control group	BDI	The depressive disorder status significantly improved in the experimental group (20.4 ± 0.9 to 18.2 ± 2.0; $p < .05$), while the depressive disorder status of the control group showed no significant improvement (21.2 ± 1.3 to 20.6 ± 1.5; $p > .05$). Compared with the control group, the depressive disorder status of the experimental group was significantly improved ($p < .05$).
Kampmann et al. (2016)	Anxiety (social)	RCT	Patients diagnosed with social anxiety disorder	60 (18–65 years)	- VRET (immersive) - iVET – waiting list	SIAS DASS-21	A significant decrease of social anxiety from pre- to post assessment for both VRET ($p = .014$; $d = 0.55$) and iVET ($p < .001$; $d = 1.14$) compared with the waiting-list control group. A significant decrease on the anxiety subscale ($p = .043$; $d = 0.47$) was observed for iVET compared with the waiting-list control group. No significant differences were found between VRET and waiting list on the anxiety subscale ($p = .135$) and depression subscale ($p = .401$) or between iVET and waiting list on the depression subscale. Participants receiving iVET, but not VRET, improved on fear of negative evaluation, speech performance, general anxiety, depression, and quality of life relative to waiting list.
Song and Park (2015)	Depression	RCT	Stroke patients	40 (40–60 years)	- VR group – ergometer training group	BDI	Both the VRG and ETG patients showed significant improvements in BDI scores after the intervention ($p < .05$). The comparison of the postintervention improvements of the two groups revealed that the VRG showed a more significant increase in BDI than the ETG.

(continued)

Table 1. Continued.

Study	Symptom	Type of study	Study population	N	Intervention	Tools	Main results
Krijn et al. (2004)	Anxiety (acrophobia)	Prospective RCT	Patients diagnosed with acrophobia	37 (22) (40–60 years)	- VRET with an HMD (immersive) - VRET – a computer automatic virtual environment- No intervention	Acrophobia Questionnaire (Anxiety in height situations)	VRET was more effective than no treatment on patient with acrophobia. Univariate analysis showed that there was not a significant time-effect: AQ-Anxiety: $F(1, 20) = 0.346$; $p = .563$, but there was significant interaction effect between time and condition, $F(4, 23) = 7.304$; $p = .012$, to anxiety related to height. They also experienced less presence and anxiety in the virtual environment used in Session 1 when compared with patients who completed VRET.
Riva et al. (2003)	Anxiety, depression	RCT	Patients with eating disorders	36 (women, 18–50 years)	ECT: 15 sessions of Virtual Reality for Eating Disorders Modification— (immersive virtual environment), 14 virtual environments used by the therapist during a 50-minute session CBT: 15 sessions of group sessions aimed at improving assertiveness and motivation to change and 10 biweekly individual sessions whose target behaviors for change were eating behavior (dietary restraint and binge eating) as well as self-esteem and related problems. - Virtual reality distraction (immersive)	STAI (Italian version)BDI II	State Anxiety (STAI X2) significantly decreased in both ECT (mean score before treatment, 49.44; after: 36.77; $p = .018$) and nutritional groups conditions (before: 49.77; after: 38.77; $p = .013$), while no significant changes were evidenced in CBT and in the waiting-list conditions. Depression levels (BDI) significantly decreased in both ECT (before: 22.23; after: 8.11; $p = .008$) and CBT (before: 20.55; after: 12.11; $p = .050$); however, complete remission of depressive symptoms was observed only in the ECT group.
Schneider et al. (2003)	Anxiety, fatigue	RCT – crossover design	Breast cancer women	16 (50–77 years)	-	Revised PF SSAI	There was a significant difference in the SAI for Adults ($p = .10$, 15 df) scores immediately following the chemotherapy treatment when subjects used the VR intervention. There were no significant changes in any of the measures of symptom fatigue, or anxiety 2 days later. There was a trend toward lower scores with the VR condition.
Schneider et al. (2004)	Anxiety, fatigue	RCT – crossover design	Breast cancer women	20 (27–55 years)	VR as a distraction intervention during one session of chemotherapy (immersive)	The SAI for Adults The Revised PFS	Mean state anxiety scores were lower following the use of the virtual reality, but no significant differences were found ($p = .230$). Highest level of fatigue occurring 2 days after chemotherapy treatments and the lowest level of fatigue (X score = 1.85) immediately following chemotherapy treatment when the participants used the VR. No significant changes in any of the measures of fatigue, or anxiety 2 days later, but a trend toward lower scores existed with the VR condition.

(continued)

Table 1. Continued.

Study	Symptom	Type of study	Study population	N	Intervention	Tools	Main results
Schneider & Hood (2007)	Anxiety, fatigue	RCT – crossover design	Breast, colon, or lung cancer patients	123 (32–78 years)	VR headset during an IV chemotherapy treatment (immersive)	-Revised PFS-SAI	Significant ($p < .01$) Pearson correlations were found between Presence Questionnaire and Revised PFS (-0.296) and SAI for Adults (-0.308), suggesting that higher levels of interaction with VR were related to lower levels of symptom distress. Individuals who received the VR during their first chemotherapy treatment had significantly less anxiety, compared with the control condition during the second chemotherapy treatment. The level of fatigue in the exercise group showed a dramatic decrease, from 6.7 points to 4.9 points ($p > .001$), while almost no changes were noted in the control group. Pain scores were determined to be lower in Groups 1 and 2. Although there was no difference between the Groups 1 and 2, a statistically significant difference was found between Groups 1 or 2 and Group 3 based on all pain scores.
Cho & Sohng (2014)	Fatigue	Nonequivalent control group pretest–post-test design	Hemodialysis patients with end-stage renal failure	46 (45–70 years)	- Virtual reality exercise program (nonimmersive)	Visual Analogue Scale for Fatigue (0–10)	
Gerçekler et al (2018)	Pain	Prospective RCT	Children during phlebotomy	121 (7–12 years)	Group 1: VR (cartoon videos) Group 2: external cold and vibration Group 3: control - VR (video glasses and local infiltration; 5 ml solution of lidocaine 2%) - Local infiltration (5 ml solution of lidocaine 2%) control group	- Wong–Baker FACES scale (0–10)	
JahaniShoorab et al. (2015)	Pain	RCT	Primiparous parturient women having labor for episiotomy repair	32 (18–43 years)	- VR (cartoon video) immersive -No VR	Numeric Pain Rating Scale (0–100 scale)	There were statistically significant differences between the pain score during episiotomy repair in both groups ($p = .038$).
Aminabadi et al. (2012)	Pain, anxiety	Single-blind crossover clinical trial study	Children during dental procedures	120 (4–6 years)	-VR (cartoon video) immersive -No VR	Wong–Baker FACES Pain Rating Scale Faces version of the Modified Child Dental Anxiety Scale Screen for Child Anxiety Related Disorders questionnaire	There was a significant decrease in pain perception ($p < .001$) and state anxiety scores ($p < .001$) with the use of virtual reality eyeglasses during dental treatment.
Schmitt et al. (2011)	Pain	RCT – within-subjects (crossover design)	Hospitalized pediatric burn inpatients undergoing painful physical therapy	54 (6–19 years)	Virtual reality exposure (immersive) SnowWorld game for 5 days	GRS assessing separate components of pain (cognitive, affective, sensory)	On Study Day 1, subjects reported significant decreases (27%–44%) in pain ratings during virtual reality. GRS assessments on Study Day 1 of cognitive pain (44% reduction), affective pain (32% reduction), and sensory pain (27% reduction) were significantly lower ($p < .05$ for each paired comparison) in the adjunctive virtual reality condition than in the control condition. The analgesia and affect improvements were maintained with repeated virtual reality use over multiple therapy sessions.
Maani et al. (2011)	Pain	Within-subject experimental design	U.S. soldiers burned in combat attacks involving explosive devices in Iraq or Afghanistan	12 (20–29 years)	- Immersive VR SnowWorld - No VR intervention	Questions and rating scales (0–10)	Patients reported significantly less pain when distracted with VR. Worst pain (pain intensity) dropped from 6.25 of 10 to 4.50 of 10. Pain unpleasantness ratings dropped from moderate (6.25 of 10) to mild (2.83 of 10). "Time spent thinking about pain" dropped from 76% during no VR to 22% during VR.

(continued)

Table 1. Continued.

Study	Symptom	Type of study	Study population	N	Intervention	Tools	Main results
Kipping et al. (2012)	Pain	Prospective RCT with a parallel group design	Adolescents undergoing burn wound care and nursing staff	41 (11–17 years)	-VR immersive - Distraction (TV, stories, music, caregivers) or no distraction	VAS	For adolescent self-report of pain, mean pain scores were higher for the SDG compared with the VRG in both dressing removal and application; however, these differences were not statistically significant. Nursing staff reported a statistically significant reduction in pain scores during dressing removal and significantly less rescue doses of Entonox given to those receiving VR, compared with those receiving standard distraction. For all other pain outcomes and length of treatment, there was a trend for lower pain scores and treatment times for those receiving VR, but these differences were not statistically significant. Observed reductions in all GRS in pain unpleasantness (31%), time spent thinking about pain (37%), and worst pain experienced (27%) in VR conditions.
Carrougier et al. (2009)	Pain	RCT – crossover design	Inpatient with a mean total burn surface area burn of 18%	39 (21–57 years)	Virtual reality exposure (immersive)	GRS (0–100)	Thirteen of 19 patients reported clinically meaningful (33% or greater) reductions in pain during VR distraction. No side effects were reported. No correlations were found between the reduction in pain ratings and patient variables such as age, sex, duration of hospital stay, or percentage of (deep) burns. There was no significant reduction of anxiety ratings.
van Twillert et al. (2007)	Pain, anxiety	Experimental within-subject design	Burn patients	19 (8–65 years)	-Immersive VR SnowWorld game -Distraction television, music, nonmedical conversation, and distraction by a child-care worker	Pain: visual analog thermometer; Anxiety: STAI (Dutch edition)	Responses from the Faces Pain Scale–Revised indicated a fourfold increase in affective pain within the control condition; by contrast, no significant differences were detected within the VR condition. Significant associations between multiple measures of anticipatory anxiety, affective pain, IV pain intensity, and measures of past procedural pain provided support for the complex interplay of a multimodal assessment of pain perception.
Gold et al. (2006)	Pain, anxiety	RCT	Children, their parents, and nurses during MRI or CT and IV placement	20 (8–12 years)	-VR distraction using Street Luge Immersive - Standard of care (topical anesthetic) with no distraction	Wong–Baker FACES Pain Rating Scale; Faces Pain Scale–Revised	The average pain scores (from the Faces Scale) for pharmacological analgesia only was 4.1 (SD = 2.9), while VR coupled with pharmacological analgesia, the average pain score was 1.3 (SD = 1.8). Although VAS pain scores were not statistically different between the two groups ($p = .77$), VAS scores tended to be lower in the VR group (median VAS of 7.0, range 0–48) than in the control group (median VAS of 9.0, range: 0–59). Seventy-seven percent of subjects in the experimental group said the VR glasses helped to distract them from the LP.
Das et al. (2005)	Pain	RCT – crossover design	Children undergoing burn dressing changes	9 (5–18 years)	Virtual reality game (immersive)	Faces Pain Scale	
Wint et al. (2002)	Pain	RCT	Adolescents with cancer undergoing LPs	30 (10–19 years)	- VR glasses and watched a video	VAS (0–100)	

Note. VR = virtual reality; RCT = randomized control trial; m-YPAS = Modified Yale Preoperative Anxiety Scale; ICC = induction compliance checklist; DASS = Depression Anxiety Stress Scale; BDI = Beck Depression Inventory; VRET = virtual reality exposure therapy; IVET = in vivo exposure therapy; SIAS = Social Interaction Anxiety Scale; HMD = head-mounted display; STAI = State-Trait Anxiety Inventory; PFS = Piper Fatigue Scale; SAI = State Anxiety Inventory; GRS = graphic rating scale; VAS = Virtual Analog Scale; MRI = magnetic resonance imaging; CT = computerized tomography; IV = intravenous; LP = lumbar puncture; CBT = Cognitive Behavioral Therapy; AQ = Acrophobia Questionnaire; VRG = Virtual Reality Group; SDG = Standard Distraction Group; ETG = Ergometer Training Group.

Table 2. Quality Assessment of Selected Researches.

Study	Selection bias		Selection bias Allocation concealment	Performance bias Blinding of participants and personnel ^a		Detection bias Blinding of outcome assessment ^a	Attrition bias Incomplete outcome data ^a	Reporting bias Selective reporting	Other bias Anything else ideally prespecified
	Random sequence generation	Allocation concealment							
Dehghan et al. (2019)	-	+	+	?	?	?	+	+	+
Ryu et al. (2018)	+	+	+	+	+	+	+	+	+
Shah et al. (2015)	+	+	+	- (informed about the study aim)	- (informed about the study aim)	- (informed about the study aim)	+	+	+
Lee et al. (2015)	+	-	+	+	?	?	+	+	-
Kampmann et al. (2016)	+	+	+	+	+	+	+	+	+
Song and Park (2015)	-	+	+	- (informed about the study aim)	- (informed about the study aim)	- (informed about the study aim)	+	?	-
Krijn et al. (2004)	-	?	?	?	?	?	-	+	-
Riva et al. (2003)	+	+	+	+ -	+	+	?	+	-
Schneider et al. (2003)	+	+	+	- (informed about the study aim)	- (informed about the study aim)	- (informed about the study aim)	+	+	+
Schneider et al. (2004)	+	+	+	- (informed about the study aim)	- (informed about the study aim)	- (informed about the study aim)	+	+	+
Schneider & Hood (2007)	+	+	+	?	?	- (informed about the study aim)	-	-	-
Cho & Sohng (2014)	-	-	-	+	+	-	+	+	+
Gerçeker et al (2018)	+	+	+	+	+	+	+	+	-
JahaniShoorab et al. (2015)	-	+	+	- ? (informed about VR)	- ? (informed about VR)	+	+	+	-
Aminabadi et al. (2012)	+	+	+	-	+	+	+	+	-
Schmitt et al. (2011)	+	?	?	+	+	+	-	+	-
Maani et al. (2011)	-	+	+	-	-	-	+	+	-
Kipping et al (2012)	+	+	+	-	-	-	+	+	-
Carrougner et al.(2009)	+	+	+	-	-	-	+	+	+
van Twillert et al. (2007)	+	+	+	-	-	-	-	+	-
Gold et al. (2006)	+	+	+	+	+	+	+	+	-
Das et al. (2005)	+	+	+	- (informed about the study aim)	- (informed about the study aim)	- (informed about the study aim)	+	+	-
Wint et al. (2002)	+	+	+	+	+	+	+	+	-

Note. VR = virtual reality.

^aAssessments should be made for each main outcome or class of outcomes.

+ indicates low risk of bias; - indicates high risk of bias; ? indicates unclear risk of bias.

& Park, 2015; van Twillert et al., 2007) evaluated the efficiency of a VR intervention on relieving anxiety and depression. All of these studies found a statistically significant reduction on patients' anxiety with the exception of the study by van Twillert et al. (2007), who evaluate anxiety before and after burn wound change after the use of VR. Four of the studies (Lee et al., 2015; Riva et al., 2003; Shah et al., 2015; Song & Park, 2015) had a decrease in the depression level of patients following the use of the VR intervention. In particular, in the study by Ryu et al. (2018), where they used a gaming VR intervention in children undergoing elective day surgery and general anesthesia, findings showed that children who used VR gaming had lower pretreating anxiety than those who did not use VR. Krijn et al. (2004) explored that VR was more effective compared with control in patients with acrophobia, while Aminabadi et al. (2012) explored whether VR can help children reduce their anxiety during dental procedures. Song and Park (2015) demonstrated that the group with the intervention showed more significant improvement in their depression state after the intervention than the group without VR intervention. Moreover, Schneider et al. (2003, 2004) and Schneider & Hood (2007) found that VR decreased the mean state of anxiety in cancer patients during the chemotherapy session.

Overview of VR Intervention to Relieve Symptom Fatigue

Of the 23 studies selected for this overview, 4 studies (Cho & Sohng, 2014; Schneider et al., 2003, 2004; Schneider & Hood, 2007) evaluated the efficiency of VR on fatigue. Three of these studies (Cho & Sohng, 2014; Schneider et al., 2004; Schneider & Hood, 2007) found a statistically significant reduction in symptom fatigue during VR assisted procedure, while the study by Schneider et al. (2003) did not report any statistically significant change of fatigue. Two studies (Schneider et al., 2004; Schneider & Hood, 2007) with cancer patients demonstrated a statistically significant difference in fatigue (i.e., reduction) immediately after chemotherapy treatment when subjects used the VR intervention. Cho and Sohng (2014) in their study with hemodialysis patients with end-stage renal failure found a statistically significant decrease of fatigue at the intervention group with VR exercise program, while almost no changes were noted in the control group.

Overview of VR Intervention Effects of Pain

As shown in Table 1, VR is used for acute pain management in inpatient populations more commonly than for chronic pain. The review yielded 11 studies (Aminabadi et al., 2012; Carrougher et al., 2009; Das et al., 2005;

Gerçeker et al., 2018; Gold et al., 2006; JahaniShoorab et al., 2015; Kipping et al., 2012; Maani et al., 2011; Schmitt et al., 2011; van Twillert et al., 2007; Wint et al., 2002) that evaluated efficacy of VR on painful procedures. Six studies (Carrougher et al., 2009; Das et al., 2005; Kipping et al., 2012; Maani et al., 2011; Schmitt et al., 2011; van Twillert et al., 2007) used VR as a distraction intervention during wound changes of burn injuries in children and adults, while the others used VR during or after painful procedures. All studies found statistically significant reductions of pain rates during and after using VR procedure, with the exception of the study by Kipping et al. (2012) where no statistically significant changes between VR group and control group were found. In the other studies using VR for other painful procedures, such as dental procedures, intravenous placement, and lumbar puncture, the results showed that pain scores were lower in the VR groups compared with the control groups (Aminabadi et al., 2012; Gerçeker et al., 2018; Gold et al., 2006; Wint et al., 2002). Furthermore, many positive changes were recorded on secondary end point measurements such as emotional unpleasantness, time spent thinking about pain, and worst pain experience (Carrougher et al., 2009; Maani et al., 2011).

Discussion

In contrast with previous reviews of case reports and observational evidence, the present review focused on experimental studies that describe applications of VR technology on symptom management. Data from 23 eligible studies provided insights into four current medical applications of the VR system: anxiety, depression, fatigue, and pain management. These studies have contributed to our better understanding of the efficiency of VR in reducing these symptoms in different contexts and diseases, such as neurophysiological (Motl et al., 2009) or especially on cancer (Brown & Kroenke, 2009; So et al., 2009). The findings of this systematic review are congruent with those of previous researches, and reviews that suggest that VR can be used to effectively manage symptoms (Chirico et al., 2016; Dascal et al., 2017; Hoffman et al., 2000; Wint et al., 2002). Although studies varied greatly in terms of the contextual setting and the method of intervention, this review identified some overarching themes in addressing the research questions presented in the Introduction section.

Anxiety and Depression

The use of VRET for clinical purpose on anxiety and depression has been investigated empirically for many years. The VR has been used as a tool to deliver exposure therapy, psychoeducation, and relaxation therapy

in people suffering from one or both of these symptoms. The results of four independent meta-analyses enhance the conclusion that such interventions lead to significant decreases in anxiety- and depression-related symptoms (Morina et al., 2015; Oprüş et al., 2012; Parsons & Rizzo, 2008; Powers & Emmelkamp, 2008). All the studies with a primary focus on anxiety and depression that were included in this review demonstrated an important decrease on the anxiety and depression levels in patients. These results contributed to the preceding evidence showing that the use of VR as an intervention in clinical settings has important positive effects on depression and anxiety level.

Fatigue

Fatigue is a major problem and concern for many patients with diseases such as cancer, stroke, renal failure, autoimmune disorders, and lung disease (chronic obstructive pulmonary disease) to name a few. In a cross-sectional descriptive study with 148 randomly recruited prostate cancer patients in active treatment, the aim was to explore cancer-related fatigue and its impact on quality of life (Charalambous & Kouta, 2016). The results demonstrated that fatigue is a common symptom among patients with advance prostate cancer undergoing treatment. This was supported by the high levels of fatigue reported in this sample with almost two thirds of the patients (66.9%) reporting fatigue as a problem. Findings from this study show that VR could be a potential tool to secure better fatigue levels for all patients. Moreover, findings also identified a relationship between higher levels of presence in the virtual environment and lower levels of fatigue and anxiety. However, there are limited number of studies that have been undertaken to measure VR effectiveness on fatigue. This stresses the need for additional longitudinal studies in this context.

Pain

The findings of experimental studies within the context of pain experience showed that VR distraction is an effective nonpharmacologic intervention for reducing pain from undergoing unpleasant medical procedures (acute or chronic), as well as the pain associated with burn injury care in adult and pediatric patients. According to the theory of pain management, decreased pain can be achieved by blocking the information of pain via analgesics drugs or by creating some sort of distraction that deviates the focus of the brain on pain (Gershon et al., 2004; Parsons et al., 2009). Many side effects can be caused by the medical analgesics such as nausea, increased length of hospitalizations, and inadequate pain alleviation (Teeley et al., 2012). These

traditional pharmacotherapies can be supplemented (or even replaced in some cases) by VR as a particularly useful pain distraction intervention. Furthermore, our results coincide with those of preceding studies that VR has been reported to be an effective modality to decrease pain during burn care (Gershon et al., 2004). A systematic review of nine studies by Morris et al. (2009) found that VR coupled with standard analgesia was effective in reducing pain during burn care in eight of the nine studies. Last, but not least, Indovina et al. (2018) in their systematic review using Virtual Reality as a Distraction Intervention to Relieve Pain and Distress During Medical Procedures stated that VR has proven to be effective in reducing procedural pain, as almost invariably observed even in patients subjected to extremely painful procedures, such as patients with burn injuries undergoing wound care, and physical therapy. Moreover, VR seemed to decrease cancer-related symptoms in different settings, including during chemotherapy. VR could promise a useful alternative way of reducing the pain with minimal side effects or one that could enhance standard pain management.

Although the use of VR in the majority of the studies included in this review showed a very positive effect on the specific symptoms of interest, it is possible that some confounding factors might have affected the effectiveness of VR. The researches therefore completed a thorough check of the included studies based on the quality assessment tool. Variables that have been considered included the type of images on VR that seems to work better, the best type of the devices, the interaction with the environment, and finally considering the differentiating of the sense of presence between immersive and nonimmersive VR. This assessment highlighted the fact that the tools utilized in these studies for evaluating the symptoms were different. However, all tools were valid and reliable to measure the symptoms and have previously used in clinical studies. According to the assessment, VR interventions that were game based were found more effective in children as a means to distract them from the hospital environment and the medical procedures. Adults showed a preference toward more natural and relaxing environments and requested to have variety of choices in terms of the virtual environments they could experience (sea, mountains, and adventures). Furthermore, the duration of the intervention varied from study to study, and this variation appeared to be related to the target symptom. For example, Dehghan et al. (2019) used VR for 5 minutes only to reduce anxiety in children scheduled for operation, and in Shah et al. (2015), the intervention lasted 1 hour over 3-day period to reduce anxiety and depression. Both studies demonstrated a positive effect of VR on reducing anxiety and depression. Therefore, further studies are needed to validate the effective time of the VR intervention. Furthermore, the devices that

were used in the studies were also different. In the more recent studies where the latest technology of VR was used, participants mentioned that the images and the sense of presence were very realistic, and the interaction was more efficient by using more advanced special controllers (e.g., gloves, remote control). Finally, participants did not report any motion sickness or any unusual symptoms during the use of VR, which means VR is safe and does not cause any side effects.

The studies we reviewed have several strengths. The majority of the studies reviewed employed a randomized control trial's design, offering the highest level of evidence on the effectiveness of the VR interventions tested. The specific content of interventions was fairly consistent within each category. Moreover, a wide variety of patients were studied, including inpatients and outpatients, patients receiving treatment and those who had completed it, as well as individuals with various diagnoses and stages of disease.

This review included studies that were very heterogeneous in study design as well as theoretical background and the way the intervention was conducted. The principal differences between studies were the use of different disease, instruments, and analysis. Some of the studies required the presence of symptoms as an inclusion criterion, reducing the possibility of floor effects in these trials. Furthermore, sample sizes used in most trials were small to moderate ($N < 50$). Specific types (immersive, nonimmersive) and doses (duration, frequency, virtual environment) of VR intervention varied across studies.

Future Research

As the results of this review showed, future studies of VR should be undertaken in the context of medical inpatients with larger samples and assessed over time to investigate long-term effects. This intervention has the potential to be effective for patients with a variety of diagnoses and across a wide range of ages. However, although most VR studies are done only in hospital settings, some health professionals point out that VR should also be promoted as a home-based technique. Another issue that needs to be considered is the sense of independence and self-improvement promoted by VR at the home setting for users to be able to implement the VR intervention without supervision and on demand, allowing a sense of control over the symptoms and on the overall disease.

Conclusion

As VR technology expands and becomes more usable, effective, and safe, budget concerns give way to ability for greater impact. The majority of patients were very satisfied, and in most cases, patients state that experience

with VR was fun, immersive, and enjoyable, with not a lot of side effects, considering that they would definitely use VR again. Studies varied in terms of quality, but we observed no relationship between study quality and key findings. The findings of this study agree with those of previous research that suggest that VR can be used to manage symptoms. The use of VR in medical fields is relatively novel and promising. It is highly interactive, flexible, tailored to the individual, and applicable to people varying in age, sex, and medical disorders. As technology improves and costs are reduced, VR will play a major role in the future of health care.

Authors' Note

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ORCID iDs

Androniki Ioannou  <https://orcid.org/0000-0002-3343-8768>
 Andreas Charalambous  <https://orcid.org/0000-0003-4050-031X>

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