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Virtual Reality in Health System: Beyond Entertainment. A Mini-Review on the Efficacy of VR During Cancer Treatment

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Virtual reality (VR), a computer-generated virtual environment, has been increasingly used in the entertainment world becoming a very new evolving field, but VR technology has also found a variety of applications in the biomedical field. VR can offer to subjects a safe environment within which to carry on different interventions ranging from the rehabilitation of discharged patients directly at home, to the support of hospitalized patients during different procedures and also of oncological inpatient subjects. VR appears as a promising tool for support and monitoring treatments in cancer patients influencing psychological and physiological functions. The aim of this systematic review is to provide an overview of all the studies that used VR intervention on cancer patients and analyze their main findings. Nineteen studies across nearly a thousand articles were identified that explored effects of VR interventions on cancer patients. Although these studies varied greatly in setting and design, this review identified some overarching themes. Results found that VR improved patients' emotional well-being, and diminished cancer-related psychological symptoms. The studies explored various relevant variables including different types of settings (i.e., during chemotherapy, during pain procedures, during hospitalization). Here, we point to the need of a global and multi-disciplinary approach aimed at analyzing the effects of VR taking advantage of the new technology systems like biosensors as well as electroencephalogram monitoring pre, during, and after intervention. Devoting more attention to bio-physiological variables, standardized procedures, extending duration to longitudinal studies and adjusting for motion sickness related to VR treatment need to become standard of this research field.

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In recent years, we have been experiencing a real changing world owing to the technological advances which allowed the development of new user-friendly devices in different settings and for different functions. The application of modern technology to the health field provides a fruitful breeding ground for new knowledge acquisition, and its use is bringing new important advantages. Research in pharmaceutical (Wang et al., 2014), biophysical (Linden et al., 2013), and neurological fields (Timpano et al., 2013) now can count on readily available calculating technology-based systems to predict information that previously would have remained unknown or for which years of expensive research would have been required (Foffi et al., 2013; Ciccarelli et al., 2014). In the field of surgical training, high-tech systems play an important role in coaching and allowing to gain expertise in very precise procedures avoiding the risk of training on real patients (Varshney et al., 2014). In 1990s, the increasing availability of high-performance computers with fast 3D graphics has for the first time made it feasible to perform non-trivial physical simulations—and see the results—at fully interactive speeds in a Virtual environment. Jaron Lamier used the term virtual reality (VR) for the first time in 1989. At that time, most popular definitions of VR made reference to a particular technological system. This system usually includes a computer capable of real-time animation, controlled by a set of wired gloves or other controllers, a position tracker, and using a head-mounted stereoscopic display for visual output (Biocca, 1992). Despite the VR use that is associated with immersion, all VR systems are categorized into two main categories, that is, immersive and non-immersive VR. Immersion or presence can be regarded as a variable that can influence the effects on the attention of users (Nilsson et al., 2009). Full immersion is reached by a head mounted display, which blocks the users' view of the real world and presents patients with a view of a computer-generated world instead. The helmet and headphones exclude sights and sound from the hospital environment (Hoffman, 2008). Opposite to this, a computer screen often displays non-

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immersive VR where the user is connected to the virtual world but still has the possibility to communicate with the external environment. This technology can offer to subjects a safe environment within which to carry on different interventions ranging from lifestyle intervention (Napolitano et al., 2013) the rehabilitation of discharged patients directly at home, to support hospitalized patients during different procedures and also applies to oncological inpatient subjects. VR appears as a promising tool for supporting cancer patients and monitoring neuro-physiological and biological feedback during the intervention (Fig. 1).

This manuscript provides a systematic review of the literature reporting the use of VR in therapies related to cancer patients, information on the outcomes and directions for future research.

VR on Cancer Patients

The first study about the use of VR in cancer patients was published in the February of 1999 on the journal "*Cyberpsychology & behavior*" by Oyama et al. (1999). The study showed a significant decrease of negative emotion, pain, and anxiety following VR treatment in a patient during chemotherapy infusion. After this study, many other scholars studied the efficacy of VR Intervention during cancer treatment (i.e., in order to reduce treatment-related symptoms, or pain). In particular, VR has been used during the following procedures or conditions:

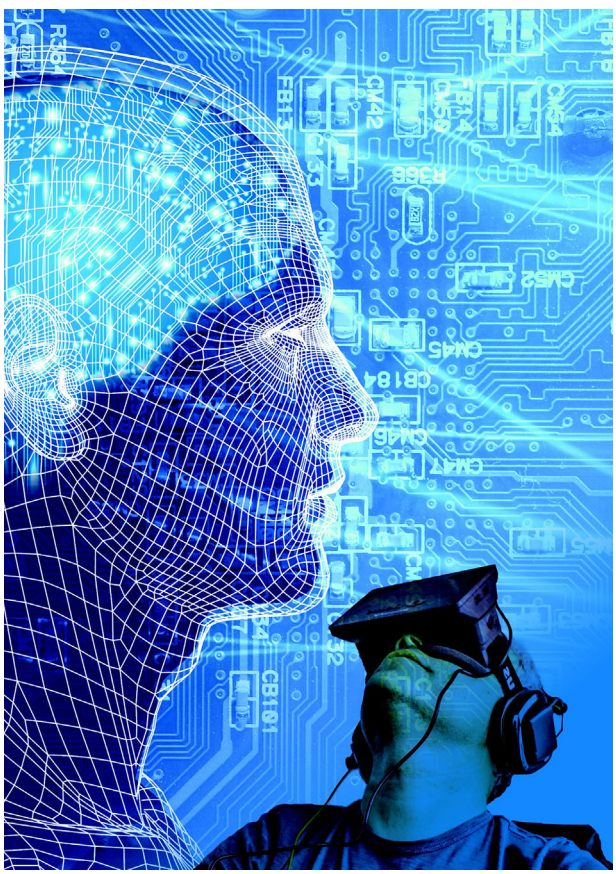

Fig. 1. Creative artwork showing neuro-physiological and biological feedback during VR intervention.

Chemotherapy

Frequently reported symptoms associated with cancer chemotherapy are nausea and vomiting (Pickett, 1991; Watson and Marvell, 1993). Other common physical and psychological symptoms associated with chemotherapy include anorexia, fatigue, and anxiety (Sarna et al., 1993; Watson and Marvell, 1993; Basch, 2010; Fisch et al., 2012). VR has been introduced during chemotherapy infusion in order to reduce the experience of acute and chronic symptoms caused both by the often toxic treatments employed in oncology care and by their underlying disease.

Painful procedures

During the course of treatment for oncological problems, the patients have often to experience painful procedures. Several psychological methods have been used successfully to reduce pain, including cognitive-behavioral procedures (Morley, 1999; Butler et al., 2000) and hypnosis (Montgomery et al., 2000; Patterson and Jensen, 2003). Also distraction is a well-established psychological intervention aimed at reducing pain (Dahlquist, 1999a,b; Powers, 1999; Blount et al., 2003). Therefore, a variety of different distraction interventions has been studied, these include deep breathing exercise, listening relaxing music, and watching a favorite video (Malloy and Milling, 2010). Because humans have finite attentional resources, a distraction task that consumes some portion of those resources is believed to leave less cognitive capacity available for processing pain (McCaul and Malott, 1984). VR has been introduced during painful procedures (e.g., Gershon et al., 2003) in order to have a more effective method to reduce pain.

Hospitalization

Another condition that can cause different levels of distress is hospitalization. Hospitalization itself can be regarded as a stressful condition because it is due to a change in health status and also because it often implies stressing conditions such as lack of autonomy, intimacy, and others. However, few researchers assessed the efficacy of therapeutic tools, such as VR, which could be capable of tackling such conditions and needs (Espinoza et al., 2012).

Variables Related to Distress

Different are the variables related to distress during cancer procedures or conditions. Psychological and Physiological are the most studied categories interested by VR intervention. Physiologic and psychological instability may increase the length of the procedure and the amount of sedation required, in case of painful procedures. Moreover, a tense patient may find it problematic to cope with treatment or collaborate with the health team, thereby adding difficulties to the procedures (Buffum et al., 2006; Pittman and Kridli, 2011; Zengin et al., 2013).

Psychological variables

The distress related to cancer treatment or condition has often been measured in terms of anxiety and depression, or in other treatment-related symptoms such as fatigue, pain, sleep disorder, time perception, subjective feeling, or mood state.

Bio-physical variables

Stress reactivity paradigms typically measure skin conductance, heart rate, respiration, muscle tension, or startle reflex to index the somato-visceral response component of fear and anxiety (Craske et al., 2009). Patients scheduled to undergo cancer

procedures or treatments are often frightened and anxious, which may influence physiologic responses, such as respiratory rate (RR), heart rate (HR), blood pressure (BP), perceptions of pain, and plasma concentrations of stress hormones (Nelson et al., 2008; Costa et al., 2010; Tan et al., 2010).

Aim of This Mini Review

Here, we provide an overview of the studies analyzing the effects of VR in relieving cancer-related symptoms.

In particular, our systematic review aims at answering these specific questions:

(1) Is VR an intervention that could support patients during cancer-related treatment?
(2) Is there a type of treatment/condition for which the VR has the best efficacy?
(3) What are the main variables on which VR operates?

Materials and Methods

Design

This study was performed using the guidelines set out by the preferred reporting items for systematic reviews (Moher et al., 2009)

Search strategy

The search undertaken aimed to retrieve from the literature all articles related to the use of VR in oncological patients during cancer treatments.

A broad search was performed using Scopus database in the date range from January 1993 to December 2013. Search terms included a combination of "VR" and "VR" with "oncology" or "cancer." Once the main articles were identified, a second search was carried out using the citations within each article, to supplement the already mentioned search terms.

Study eligibility criteria

Original research articles ranging from January 1993 to December 2013, describing the use of VR during cancer treatments, were included in the review. Non-English-language studies were excluded.

Study selection and data extraction

Studies that arose from the search terms were assessed for further evaluation via abstract review, duplicates were removed. The research results showed in total 803 potentially relevant articles. After a screening of the titles, a total of 700 articles were eliminated, the remaining 103 studies were examined by abstract review, of these 73 articles were excluded and of the remaining 30 studies, a further 11 were excluded following full-text review. All the excluded studies did not meet the eligibility criteria.

The number of studies excluded is very high and it is due to different reasons: firstly, there is a broad use of VR tools in oncological care in order to train Medical Doctors, furthermore, some studies analyzed the use of VR intervention for home-based care, but these lie outside the aim of this review.

Various data were extracted from each study, these included number of participants, age of patients, experimental design, treatment/condition, psychological variables, biological variables, used instrument, data analyses, main results, time of VR intervention (Table 1).

Synthesis

Due to the heterogeneity of methodological and analytical strategies across studies, a meta-analysis was considered not to be feasible. Therefore, we planned a narrative analysis in the first instance, to allow for a comprehensive approach to description and interpretation. The unit of analysis for the review was the entire series of published articles reported from the data set (hereafter referred to as "study").

Results

Search outcome

Thus, the 19 original studies that were included in the systematic review followed the inclusion criteria, Figure 2 shows all the papers examined in the search process.

Overview of findings of included studies

The main results from studies are grouped based on the treatment/condition where VR was applied (during chemotherapy, during painful procedures, during hospitalization).

In order to clarify the results, we divided the selected studies depending on the setting in which the VR intervention was carried out. (During chemotherapy infusion; painful procedures or during hospitalization).

Overview of VR intervention to relieve symptom distress of chemotherapy infusion

Of all the 19 studies reviewed, 8 (Kaneda and Jatsumata, 1999; Schneider and Workman, 1999; Oyama et al., 2000; Schneider et al., 2000,2003, 2004, 2011; Schneider and Hood, 2007) evaluated the efficacy of a VR intervention in order to relieve patients' symptom distress due to chemotherapy treatment. All of these found a reduction of patients' distress in terms of cancer-related symptoms, it was detected a significant decrease in anxiety, distress, and fatigue immediately after chemotherapy sessions with VR. In particular, Schneider et al.

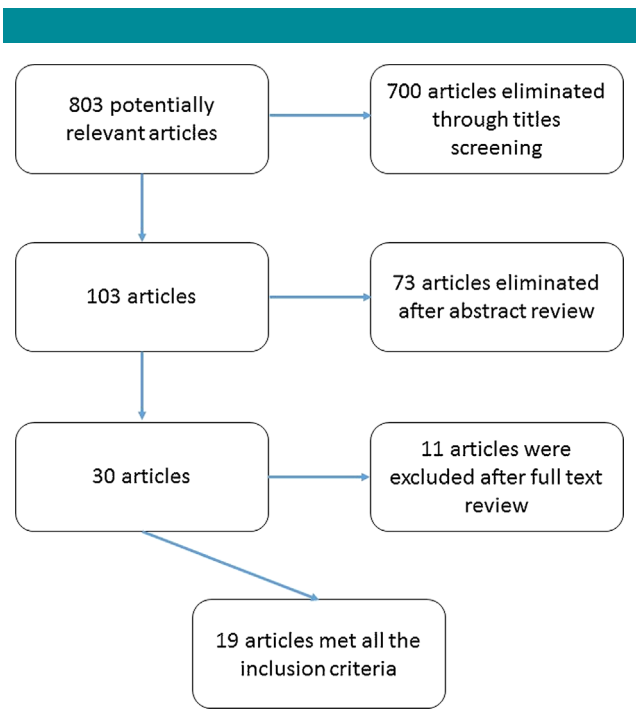

Fig. 2. Flow of information through the different phases of the systematic review.

(2011), in her studies, also focused her attention on time perception showing that VR alters time perception during chemotherapy sessions, so it became a more tolerable procedure.

Overview of VR intervention as distraction intervention during painful procedures

Of all the 19 studies screened for this overview, 6 (Wint et al., 2002; Gershon et al., 2003, 2004; Wolitzky et al., 2005; Windich-Biermeier et al., 2007; Nilsson et al., 2009;) evaluated the efficacy of VR as a distraction intervention during painful procedures, of which, one was a case study (Gershon et al., 2003). Three of these studies (Gershon et al., 2003, 2004; Wolitzky et al., 2005) found a significant reduction of pain (measured by the authors or by the nurse with not self-reported instruments) during VR-assisted procedure. In other two studies, the pain/distress scores tended to be lower for the patients post-VR treatment (Wint et al., 2002) or a not increasing effect of pain was reported, compared with the patients who did not use VR (Nilsson et al., 2009). Only one study did not find any evidence of pain reduction; however, this was not the aim of the authors (Windich-Biermeier et al., 2007).

Overview of the effects of VR intervention during hospitalization

Four studies evaluated the effects of VR in promoting emotional well-being in inpatients hospitalized with a cancer diagnosis. All the studies demonstrated different improving effects in the emotional status of patients in terms of lowering cancer-related symptoms (i.e., anxiety, depression, and fatigue) (Oyama et al., 1999; Espinoza et al., 2012), improving positive emotions as well as reducing negative emotions. (i.e., joy, sadness, relax, stress, anxiety, vigor) (Li et al., 2011; Baños et al., 2013).

Psychological variables

All the studies evaluated the efficacy of VR on different psychological variables with different measures (see Table 1). All the studies found a significant difference on these variables or lower but not significant distress when using a VR intervention on patients. Among the most studied variables were state anxiety, which was analyzed through a specific measure in 14 of 19 studies, and the evaluation of the symptoms related to cancer or treatment, which were most measured with different symptom distress scales and that showed the most significant reduction effects.

Bio-physiological variables

Seven of all 19 (Oyama et al., 1999; Gershon et al., 2003, 2004; Klosky et al., 2004; Schneider et al., 2004; Wolitzky et al., 2005; Nilsson et al., 2009) studies evaluated different bio-physiological variables comparing VR intervention and no VR condition (in crossover design or control group). All the studies took into account the pulse rate as a measure of arousal. A minority of the studies, two of the eight (Oyama et al., 1999; Klosky et al., 2004), also evaluated various measures like blood pressure, ECG, pattern of respiration, blood flow volume under a fingernail.

Four of these eight studies found significant differences in pulse rate, showing lower heart rate in the VR group compared with the control group. All these four studies evaluated the effect of VR in painful procedures (Gershon et al., 2003, 2004; Klosky et al., 2004; Wolitzky et al., 2005).

Discussion

Patients diagnosed with cancer must undergo frequent procedures under conditions that influence their physical and psychological state.

This review identified 19 studies exploring the effects of VR during cancer-related treatments. These studies have contributed to our understanding of the efficacy of VR in reducing various cancer-related symptoms in different contexts.

Although studies varied greatly in setting and design, this review identified some overarching themes in addressing the questions presented in the introduction.

Is VR an intervention that could support patients during cancer-related treatment?

Yes, all the studies showed a reduction of the principal psychological variables related to stress conditions or to cancer. Implementing VR during the different phases of cancer treatment could support patients reducing their distress; moreover, the patients do not need any kind of training to use VR, which is without risk for the patient and very inexpensive for the Health Institution.

Is there a type of treatment/condition where the VR has the best efficacy?

VR has been used principally during specific procedures (e.g., chemotherapy) as a complementary therapeutic tool having direct influence on patients' distress as well as analgesic effect (during painful procedures). Furthermore, the use of VR seems to have important positive effects in inpatients during their hospitalization relieving distress that frequently occurs during this phase of the treatment.

An overall analysis shows that VR seems to have the best efficacy during chemotherapy; however, there were more studies evaluating this condition than pain procedures and hospitalized patients.

What are the main variables on which VR operates?

VR primarily operates on psychological variables showing a reduction of perceived distress. Indeed, in almost all of the studies that also evaluated physiological variables, a significant reduction of bio-physiological parameters related to distress was demonstrated, specifically in heart rate reduction.

Limitations of the studies

This review included studies that were very heterogeneous in study design as well as theoretical background and approach. The principal difference between studies was the use of different patients (in terms of age, number of subjects), instruments (self-reported VS not-self reported), and analyses.

During studies of painful procedures, results showed a reduction of pain; however, these studies did not use-self reported measure, the researcher or a nurse collected the measures, they were not blind of the subject's condition, often being one of the authors.

None of the identified studies touted a robust research design and sample size (Table 1), and studies with larger sample sizes failed to utilize controls (i.e., Schneider et al., 2011).

Only few studies made also a bio-physiological evaluation. This becomes important because the HR reductions attributed to the experimental interventions, if validated in additional studies, could represent an important advantage of VR intervention, due to having no additional cost to hospitals, ease of delivery, and avoidance of medical risk.

TABLE 1. Studies selected and data extraction

Author	N	Age	Experimental design	Setting	VR method	Psychological variables	Biological variables	Used instruments	Analyses	Main results	Time of intervention
Schneider et al. (1999)	12	17-Oct	Pre- and post-test and 48–52 h post-intervention for three chemotherapy treatments	During chemotherapy	Immersive	Symptom distress, anxiety, nausea, and vomiting	None	Symptom distress Scale,(Mc Corkle and Young, 1978) STAI for children (Spielberger, 1970), Single item for nausea and vomiting with VAS	ANOVA test for pre-, post-test, and 48–52 h after	Post-hoc analysis using paired *f*-tests demonstrated that the measurement following the second chemotherapy treatment when subjects used the VR intervention was different ($P = 0.02$) than the other three. A significant difference was found also in scores for the SDS ($P = 0.01$) before and after the second chemotherapy.	NS (throughout the treatment)
Kaneda et al. (1999)	10	16–70	Pre- and post-test	During chemotherapy	Immersive	Anxiety and nausea	None	Observation and interview	NS	Nausea and vomiting during chemotherapy improved for all patients. The majority of patients also reported lower anxiety levels as they focused their attention on the movie.	120 min
Oyama et al. (2000)	15 vs. 15	29–73	Pre- and post-test for two infusion of chemotherapy	During chemotherapy	Immersive on bedside	Anxiety and depression, emotional status, subjective feelings, cancer fatigue	None	HADS (Kugaya et al, 1998) to evaluate psychological status, emotional status with a facial scale, cancer fatigue Scale (Okuyama et al, 2000); Subjective feelings rated on a likert scale from 1 to 5 "how are you: relaxed, refreshed, calm, vivid, tense, depressed, unpleasant, sleepy and tired	*t*-Test or nonparametric test if normality was not indicated	Pre-test analysis: There was a significant difference($P < 0.05$) on fatigue score in the second trial between VR vs. control group. Intervention group showed less fatigue; Post-test analysis: Intervention group feel less "tense," less "tired"(subjective feeling questionnaire) and less fatigued (VAS score). Pre- and post-test between the two groups: In the first trial, "tense" ($P = 0.05$) improved. In the second trial, the HADS ($P < 0.05$), face scale	20 min

(*Continued*)

TABLE 1. (*Continued*)

Author	N	Age	Experimental design	Setting	VR method	Psychological variables	Biological variables	Used instruments	Analyses	Main results	Time of intervention
										($P < 0.05$), and physical fatigue ($P < 0.05$) scores were improved. This suggests that the second trial the VR had a stronger effect on patients than the first trial. Repeating the procedure seems to strengthen the power of the treatment. The VR group had a lower emesis level, especially on the third and fourth days after the first trial and the third and fifth days after the second trial. The VR group had a decrease in the emesis level after the second trial, while the control group had an increased level.	
Schneider et al. (2000)	11	17-Oct	Post-test evaluation	During chemotherapy	Immersive	Evaluation of virtual reality intervention (comfort, distraction effects, overall evaluation etc.)	None	Open-ended questionnaire to evaluate the intervention reported in the original article	Descriptive analyses	Descriptive findings support the clinical use of VR as a distraction intervention. Responses to the subjective evaluation suggest also that the intervention was well received.	Throughout the administration of chemotherapy (ranging from 40 to 120 min)
Schneider et al. (2003)	16	50–77	Pre-, Post-test and 48–52 h post-treatment. VR intervention group vs. control group. patients randomly assigned to receive the VR treatment during either their first chemotherapy treatment or during their next chemotherapy treatment.	During chemotherapy	Immersive	Fatigue, anxiety, cancer symptom, time perception	None	Piper fatigue scale PFS (Piper et al, 1998), STAI (Spielberger, 1983), Symptom distress scale SDS (Mc Korkle And Young, 1978), Open-ended questionnaire (reported in the original article)	*t*-Test	There was a significant difference in STAI score immediately following the chemotherapy treatment when subjects used the VR intervention ($P < 0.10$, 15 df). Mean SDS and PFS scores were lower following the use of the VR, but no significant differences were found. The average amount of time women thought that they used VR was 43 min, significantly less ($P < 0.001$) than the actual mean recorded time of 78 min.	Mean 78 min
Schneider et al. (2004)	20	27–55	Crossover, one pre-test and two post-test measures (immediately	During chemotherapy	Immersive	Symptom distress, fatigue, and anxiety	Pulse rate	SDS (McKorkle and Young, 1978), STAI (Spielberger, 1983), revised PFS (Piper et al, 1998),	*t*-Test	Results of analysis using paired *t*-test demonstrated that a significant difference existed in the SDS	45–90 min

(*Continued*)

TABLE 1. (*Continued*)

Author	N	Age	Experimental design	Setting	VR method	Psychological variables	Biological variables	Used instruments	Analyses	Main results	Time of intervention
			and post-48 h), VR group vs. control group					the evaluation of virtual reality intervention (open-ended questionnaire), time perception		($P = 0.095$) and PFS ($P = 0.040$) scores immediately following the chemotherapy treatment when subjects used the virtual reality intervention. Mean state anxiety scores were lower following the use of the virtual reality, but no significant differences were found ($P = 0.230$). Paired *t*-tests indicated no significant changes in any of the measures of symptom distress, fatigue, or anxiety two days later, but a trend toward lower scores existed with the virtual reality condition. Although the mean length of time for an IV chemotherapy treatment with virtual reality was 67 min, the mean time estimated by the participants was 42 min. This difference in time perception was significant at the $P < 0.001$ level	
Schneider et al. (2007)	123	32–78	Crossover, one pre-test and two post-test measures (immediately and post-48 h), VR intervention group vs. control group	During chemotherapy	Immersive	Distraction; cancer-related symptom distress (ASDS), anxiety and fatigue	None	Presence questionnaire (Witmer and Singer, 1998), adapted symptom distress scale −2 (Rhodes et al., 2000), STAI (Spielberger, 1983), PFS (Piper et al., 1998). Evaluation of virtual reality intervention	Mixed models	Patients had an altered perception of time ($P < 0.001$) when using the VR. A significant crossover effect was present ($P = 0.03$) for time 2 to time 1 change. Among those who received VR first, the time 2 to time 1 difference (−3.34) was significant at 0.01.	45–90
Schneider et al. (2011)	137	27–78	Pre- vs. post-test. crossover, patients were randomly assigned to receive VR distraction intervention	During chemotherapy	Immersive	Anxiety, fatigue, time perception,	None	STAI (Spierberger, 1983), PFS (Piper et al., 1998).	Multiple regression of all variables on time perception measured as the sum (positive or negative) of difference between elapsed	All the patients underestimated time elapsed, breast Cancer patients are whose underestimated more than other cancer patients the time elapsed ($P < 0.01$)	62 min

(*Continued*)

TABLE 1. (*Continued*)

Author	N	Age	Experimental design	Setting	VR method	Psychological variables	Biological variables	Used instruments	Analyses	Main results	Time of intervention
			during the first or second treatment and standard care with no distraction during the alternate treatment						and perceived time		
Wint et al. (2002)	30 (17 vs. 13)	19-Oct	VR intervention group vs. control no VR intervention	During lumbar puncture	Immersive	Pain, sedation level	None	VAS to evaluate pain, sedation assessment scale (an institutional scale used in the hospital of the study), Open-ended questionnaire to determine VR experience (reported in the original article)	Mann–Whitney test	Not significant difference, but pain tended to be lower for the VR group	64 min
Gershon et al. (2003)	1	8	Case study, crossover repeated measures: A-B-C-A where A was a "no intervention" B was a "not VR intervention" C was a "VR intervention"	During port access	Immersive	Anxiety, pain.	Child pulse rate	Multidimensional Anxiety scale for children (MASC) (Mark, 1997), VAS to evaluate pain and anxiety filled by child, nurse, and parents. Child behavior checklist filled by parents (Achenbach, 1991), Children Hospital of Eastern Ontario Pain Scale filled by nurse (McGrath et al., 1985).	NS	The nurse reported much lower ratings on both pain and anxiety during the VR condition than the other conditions. Parent ratings of pain and anxiety decreased steadily during the first three conditions, with the lowest ratings during the VR condition. The ratings of both pain and anxiety by the parent remained at the same level during the return to the A condition. The patient's pain ratings were lowest during the VR distraction and his anxiety rating was the lowest during the non VR condition. The patient's pulse rate was lowest during the VR condition	5–10 min
Gershon et al. (2004)	59	7–19	VR intervention vs. no VR intervention vs. control	During port access	Immersive	Anxiety and pain distress	Pulse rate	VAS to evaluate pain and anxiety filled by nurse and parents	ANOVA	Children in the VR distraction condition had a significantly lower pulse rate than children in the control condition ($P < 0.05$). Lower ratings of pain evaluated	5–10 min

(*Continued*)

TABLE 1. (*Continued*)

Author	N	Age	Experimental design	Setting	VR method	Psychological variables	Biological variables	Used instruments	Analyses	Main results	Time of intervention
										by the nurse, and reduced behavioral indices of distress for the VR condition.	
								Children Hospital of Eastern Ontario Pain Scale filled by nurse (Mc Grath et al., 1985).			
Wolitzky et al. (2005)	23	7–14	VR condition vs. no VR condition. Pre-test and during procedure	During port access	Immersive	Axiety and pain	Pulse rate	How I feel questionnaire (Spielberger et al., 1970),	MANOVA and qualitative analysis	Significant differences on CHEOPS with VR condition experienced less pain and anxiety during the procedure ($P < 0.05$). Also significant lower Pulse rate for the children in VR condition ($P < 0.05$). Children in the VR condition also recalled significantly more actions in their narratives ($P < 0.05$), elaborated more, and tended to mention more thoughts and emotions	NS
								VAS to evaluate pain and anxiety filled by nurse and parents			
								Facial analogue scale to evaluate child pain			
								Children Hospital of Eastern Ontario pain scale (McGrath et al., 1985)			
Windich-Biermeier et al. (2007)	50	5–18	Intervention vs. control group. Pre, During, and after procedure	During port access	Immersive	Pain, fear, distress	None	Colored assessment scale (McGrath et al., 1996) to evaluate Pain, Glasses fear scale (an analogue scale made with glasses filled with different levels of liquid); fear also was scored by the parent before and after the procedure, and the SC nurse before, during, and after	Non parametric analyses were used because the distribution of scores. Mann–Whitney U test differences in self-reported levels of pain and fear and observed fear and distress. Spearman's Rho to evaluate the relationship between self–assessed pain and	Change on distress and on fear from beginning to during the procedure as rated by the nurse was significantly improved ($P < 0.05$) from during-to-after the procedure in the intervention vs. comparison group. IPQ content analysis showed ($P < 0.05$) that most of participant of the intervention group than the comparison, current poke was "better." More parent in the	45–64

(*Continued*)

TABLE 1. (*Continued*)

Author	N	Age	Experimental design	Setting	VR method	Psychological variables	Biological variables	Used instruments	Analyses	Main results	Time of intervention
								the procedure The observational scale of behavioral distress completed by nurses during procedure (Elliot et al., 1987) Investigator developed IV Poke Questionnaire for subjects and parents assessed their experience during venipuncture/ port access.	fear as well as observed fear and distress. The level of agreement between self and observed measure was calculated by Cohen index. Content analysis of the IPQ	intervention than in the comparison group believed that the current venous port access was better or much better than their child's last venipuncture ($P = 0.007$). All the parents of intervention group (100%) said that the distracter was effective in diverting their child's attention."	
Klosky et al. (2004)	79	2–7	Intervention vs. modified control group	During RT simulation	Not immersive	Distress and pain	Heart rate and physiological arousal	Observation scale of behavioral distress (Elliot et al., 1987), STAI (Spielberger et al., 1983)	ANOVA	Intervention group had lower HR rate from baseline to simulation during the initial phase and during the total treatment ($P < 0.05$)	7 min
Nilsson et al. (2009)	42 (21 vs. 21 control)	5–18	Intervention vs. control group. Pre, During, and after procedure	During venipuncture and port devices	Not immersive	Pain	Pulse rate	Color analogue scale and facial affective scale (McGrath et al., 1996) self reported by children to assess pain. Not self reported "face, legs, activity, cry, and consolability scale" (Merkel et al., 1997) collected from a nurse. Semi structured interview about the use and satisfaction of VR	Quantitative: U tests for differences between levels of pain. Wilcoxon test signed rank test the differences in the different timing (CAS, FAS e FLACC). Heart rate analyzed with *t*-test for independent group and paired *t*-test for comparison over time. Qualitative: content analysis	Quantitative data: FLACC score increased significantly in the control group and not in the intervention group. Qualitative and quantitative analysis: who were satisfied showed a significant decrease of pain after the procedure	NS
Oyama et al. (1999)	22	33–75	Pre- and post-test and each days for 4 days after intervention	Hospitalized patients	Immersive	Anxiety and depression, fatigue,	ECG, blood pressure and respiration and blood flow volume under a fingernail	HADS (Zigmond and Snaith, 1983); The fatigue scale (developed for the study), Vas to evaluate Fatigue, A questionnaire on the impression of the system. Subjective ratings on a set of adjectives (relaxed, refreshed, calm, vivid, strained, depressed,	NS	Less fatigue post-test scores ($P < 0.05$). Increase of positive emotions after intervention and decreasing of negative emotions. ($P < 0.05$). Most patients became more animated after VR intervention	6–7 min

(*Continued*)

TABLE 1. (*Continued*)

Author	N	Age	Experimental design	Setting	VR method	Psychological variables	Biological variables	Used instruments	Analyses	Main results	Time of intervention
								displeased, sleepy and tired)			
Espinoza et al. (2012)	33	41–85	Pre- and Post-test with four session of treatment	Hospitalized patients	Not immersive	Anxiety, depression, happiness. Emotional state physical discomfort	None	HADS adapted version (Tejero et al., 1986), Fordyce questionnaire (Fordyce, 1988), VAS to evaluate emotions (joy, sadness, anxiety relax and vigor + a general + the perception of change after the treatment), VAS to evaluate physical Discomfort	*t*-Test for mean difference	Significant reduction in anxiety and depression levels, and significant increases in happiness levels after intervention. Improvements were found in emotional state and physical discomfort after each session. Positive emotions increased and negative emotion decreased after each session ($P < 0.05$)	30 min
LI et al. (2011)	122 (52 vs. 70 control group)	8–16	Pre- and post-test (baseline on admission and post-test after 7 days of hospitalization)	Hospitalized patients	"PlayMotion" system is a device that transforms ordinary walls, floors, and ceiling into wildly interactive, virtual playgrounds	Anxiety and depression	None	Children state anxiety level (Li & Lopez, 2007) and Children depressive symptom CES DC (Weissman et al., 1980)	ANOVA test	Children in the experimental group reported statistically significant fewer depressive symptoms than children in control group on day 7.	30 min
Baños et al. (2013)	19	29–85	Pre- and Post-test with four session	Hospitalized patients	Not immersive	Mood, physical disconfort, stisfaction	None	Visual analog scale to evaluate mood and physical discomfort; Visual analog scale to evaluate also satisfaction with the intervention; satisfaction with intervention scale (adapted version of Borkovec and Nau, 1972), open-ended questions	*t*-Test	Statistically significant differences were only detected in the second session (increases in general mood ($P < 0.001$) and relaxation ($P < 0.05$) and a decrease in sadness ($P < 0.003$) and the fourth session increase in joy ($P < 0.009$).	30 min

Strauss (1995) indicates that a gap in VR literature is that authors neglect to mention any adverse reactions. In our sample, only few studies (Schneider et al., 1999, 2000, 2004; Baños et al., 2013) evaluated the motion sickness effect, or its related symptoms (i.e., dryness of the eyes, headache). This is an important issue because it could represent an hurdle toward VR implementation in the standard care of distress of cancer patients. These knowledge gaps need to be remedied and results need to be extended to additional target populations.

Conclusions

The diagnosis, treatment, and long-term management of cancer patients can present an individual with a multitude of stressors (Philip et al., 2013). During these different phases, patients may experience financial strains, difficulty in maintaining interpersonal relationships, physical symptoms, and emotional distress. In the last 2 decades, researchers have (i) shown high prevalence levels of distress that require attention by care providers (Boyes et al., 2009; Brintzenhofe-Szoc et al., 2009); (ii) identified determinants of distress (Sanson-Fisher et al., 2000); (iii) revealed that treatment-induced reduction of distress may enhance life expectancy (Giese-Davis et al., 2011); and (iv) developed and evaluated a variety of interventions for distress reduction and symptom management (Soellner and Keller, 2007; Jacobmson and Jim, 2008; Moyer et al., 2009; Wolfgang and Afaf, 2012).

Nineteen studies across nearly a thousand articles were identified that explored effects of VR interventions on cancer patients. These studies found that VR improved patients' emotional well-being, and diminished cancer-related psychological symptoms. They explored various relevant variables including different types of settings (i.e., during chemotherapy, during pain procedures, during hospitalization). Studies used a variety of approaches and designs, although the majority of studies used quantitative approaches, two combined both qualitative and quantitative methodologies without significant richer inference than the others.

The abatement of distress is central to oncological care, and this is especially true in the specific contexts of the studies analyzed. More interdisciplinary research, grounded in appropriate theoretical frameworks, is needed to explore inherent complexities in these settings. A more global approach to study the effects of VR could rely on the latest technology advancements that provide new systems like biosensors as well as "electroencephalogram" monitoring during procedures, which could help to speed up research in this field, with all the modern bio-techs.

Future studies need to devote more attention to bio-physiological variables, standardized procedures, extending duration to longitudinal study, and adjusting for motion sickness related to VR treatment.

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