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Virtual Reality for Pain Management to Tackle the Opioid Crisis

Sudarshan Ramanan[1] and Ajay S. Yekkirala[2]

[1]Boston University Academy, Boston, MA, USA
[2]Blue Therapeutics, Waltham, MA, USA

ABSTRACT

The opioid crisis is a serious public health issue of epidemic proportions, building over the past decades. Prescription opioid abuse is one of the key sources of this issue. While pain is usually managed using pharmacological approaches, such as opioids, they produce several unwanted side effects – including respiratory depression and addiction – non-pharmacological approaches can be significant with minimal or no side effects. Recent developments in technology, such as Virtual Reality (VR), show considerable promise for main-stream adoption as one of the non-pharmacological interventions. Preventing a patient's transition from acute to chronic pain is one instance where VR can presumably be effective. However, challenges remain due to the inherent subjectivity and lack of clear baselines in clinical intervention studies. Here, we review recent studies on the application of VR as a treatment for acute and chronic pain management to primarily understand key technical challenges faced by VR. The secondary goal of this work is to identify possible options to tackle some of the key challenges. Design considerations emerge as one critical component in improving patient engagement.

Introduction

Opioids are potent analgesics that are still the standard of care to manage pain in clinical settings (HHS, 2019). However, controlling their use for managing pain and minimizing the morbidity and mortality associated with its misuse and abuse, is the biggest challenge faced in the healthcare system. Indeed, the ongoing opioid crisis lies at the intersection of two substantial public health challenges — reducing the burden of suffering from pain and containing the rising toll of the harms that can result from the use of opioid medications, according to HHS. Between 1999 and 2017, more than 700,000 people have died from drug overdose. Roughly 21-29% of patients who were prescribed opioids for chronic pain misuse them (Centers for Disease Control and Prevention, 2020).

According to the American Psychiatric Association, the criteria for Opioid Use Disorder (OUD) includes – a) consumption of opioids in larger amounts or longer than intended and b) persistent desire or unsuccessful efforts to control or cut down opioid use (Schuckit, 2016). While the use of a pharmacological approach (drug use) starts with the objective to manage pain, the very use of drugs makes patients vulnerable to slip into opioid addiction, which is a form of substance use disorder (SUD). Thus, this becomes a vicious cycle resulting in serious economic repercussions for the healthcare system and compromises the quality of life for the patient (White House Report, 2017). Based on its duration, pain is classified into two main types- acute and chronic. The lack of adequate attention and care can

transition a person from acute to chronic state and hence increase incidence of opioid use and potentially its misuse (Glare et al., 2019). In the fight against opioid misuse, it is important that the gateways or pathways that cause this slippery slope are understood and addressed.

Based on type and severity of pain, it is commonly treated via drugs (pharmacological), non-medications (non-pharmacological), or a combination of these two methods (HHS, 2019). For most clinical indications, pharmacological approaches have been the mainstay. However, the risks associated with imprecise titration, narrow therapeutic window, adverse side effects, the potential for drug misuse, and cost have driven patients and doctors to explore alternative non-pharmacological interventions. For any intervention to be effective and achieve mainstream adoption, the degree of treatment success on recovery (efficacy) and quality of life post-treatment are critical (Makin, 2019). Of the many non-pharmacological treatment types, Virtual Reality (VR) has shown considerable promise, especially due to recent advancements in gaming technologies and lower hardware costs (Delshad et al., 2018). Since 2018, there has been a strong surge in the number of studies that focus on VR as used in pain management. Despite such extensive research work, significant challenges still remain for mainstream adoption of this technology (Ventola, 2019).

The goals of this work are to understand the current state of VR application for pain management, identify key challenges, and offer perspectives on improvement. This paper provides a brief background on pain management and its common treatment types, before attempting to evaluate recent studies on VR-based interventions to treat pain. It systematically reviews the latest progress on this topic following a meta-analysis style of review. It focuses on the efficacy, key challenges, and opportunities for improvement in VR, which are critical for its mainstream adoption in pain management to mitigate the opioid crisis.

The Challenge of Dealing with Pain

The International Association for the Study of Pain (IASP) defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. However, there are no objective measures for accurately gleaning how much pain a person perceives (Johnson, 2019). This further poses a major challenge in diagnosis. To help patients report the intensity of pain they experience, various quantitative and qualitative mechanisms, such as numerical rating scales (NRS) and visual analog scales (VAS), are being used (Jacques, 2020). Broadly, based on the intensity and nature of the pain, it can be classified into two main types - acute and chronic. Acute pain commonly results from disease, inflammation, or injury to tissues, such as broken bone, burn, fall, and dental work, and may usually last up to 3 months. This type of pain can be easily diagnosed and treated. On the other hand, chronic pain is believed to be a result of a chronic disease condition similar to diabetes or asthma and it lasts for more than 6 months. It is important that the pain is managed and conditions are treated. For example, constant exposure to intense pain and stress during medical and nursing procedures, can pose the risk of extended hospitalization. This can also transition a patient from an acute to chronic pain state. The exact mechanisms underlying the acute to chronic pain transitions are still unclear and is an ongoing topic of research (Glare et al., 2019). For example, chronic, postsurgical pain, occurring in approximately 10% of patients who have surgery, typically begins as acute postoperative pain that is difficult to control, but it soon transitions into a persistent pain condition. However, current studies have led to a stronger understanding of opioid-induced hyperalgesia and the use of more effective and safer opioid-sparing analgesic regimens. Indeed, it is now imperative that pain is managed by a non-pharmacological method as part of opioid-sparing repertoire (Schuckit, 2016). This is one of the primary drivers for this work.

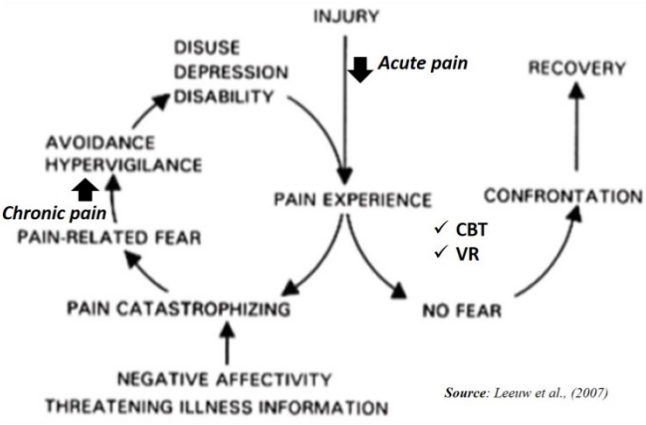

Figure 1. Fear Avoidance Model (adapted from Leeuw et al., 2007)

Fear also plays an important role in developing pain. The fear-avoidance model (**Figure 1**) for example describes how individuals develop chronic, musculoskeletal pain as a result of avoidant behavior based on fear (Leeuw et al., 2007). Many non-drug-based pain treatment approaches, such as cognitive behavioral therapy (CBT), distraction, and virtual environment-based therapies, have been found effective in treating fear avoidance and helping prevent chronic conditions.

Pain Treatments

Pain treatments can be categorized into one of the two following types based on what is involved in the treatment process.

a) *Pharmacological:* These are predominantly medication or drug-based treatments. Different types of medications are available for managing acute or chronic pain, which range from over-the-counter products to prescription medications. They mostly fall into one of the following categories: Narcotic (Opioids) Analgesics, Muscle Relaxants, Non-steroidal Anti-inflammatory Drugs (NSAIDs), Selective Norepinephrine Reuptake Inhibitors (SNRIs), Tricyclic Antidepressants, and Anticonvulsants (Pain Management Centers of New England, 2020). Of these, the opioid medications are the most effective due to their analgesic effects predominantly by binding to mu-opioid receptors. Mu-opioid receptors are densely concentrated in brain regions that regulate pain perception including pain-induced emotional responses (amygdala), and in brain reward regions that underlie the perception of pleasure and well-being. However, the same medications contribute to opioid addiction (Yekkirala et al., 2017). The rewarding effects of opioids play a major role in the risks of opioid diversion, overdose, and addiction.

b) *Non-Pharmacological*: These are non-medication-based therapies and include physical modalities, behavioral approaches, interventional approaches, and patient education. Examples include cognitive-behavior therapy (CBT), acceptance and commitment therapy (AACT), relaxation therapy, mindfulness-based stress reduction and hypnosis, Virtual Reality, and music therapy (HHS, 2019).

In practice, however, effective treatments often involve a combination of these two types of treatments, which are often called multi-modal treatments (Cuomo et al., 2019).

The Promise of Virtual Reality

Virtual Reality (VR) refers to the interactions between an individual and a computer-generated environment, stimulating multiple sensory modalities, including visual, auditory, or haptic experiences. (Cornick, 2014). When a VR environment is immersive, it consumes cognitive and attentional resources through sensory input, which limits pain-processing capabilities. A proposed mechanistic theory of VR suggests that by stimulating the visual cortex while engaging other senses, VR acts as a distraction to limit the user's processing of nociceptive stimuli (Li et al., 2011). Distraction is a process in which attention is directed away from the nociceptive stimuli and changes the quality and quantity of pain, as perceived by the patient. The user's perception of immersive reality which leads to the feeling of "presence" (one's sense of being in the virtual world), is facilitated by the use of head-mounted displays (HMDs, in goggles or headsets), wall projectors, and/or gloves fitted with sensors or touch-sensitive motors along with additional user interaction mechanisms such as joysticks. Combination of the advancements in the field of digital therapeutics, the decline in gaming gadget prices, and the increased pressure to identify ways to minimize opioid use have contributed to a growing interest within the scientific community. In fact, within the past 10 years, there has been a steady increase in the number of studies on Virtual Reality as a treatment for clinical conditions, including acute and chronic pain management. **Figure 2** shows the number of articles which have been published on topics of "virtual reality" and "pain" since 2010. Particularly, the surge in the number of publications within the past 3 years, clearly demonstrates the scientific community's interest and the dire need for better clinical solutions. Among these, many works also focused on meta-analysis and systematic reviews on previous studies to overcome difficulties in performing large-scale randomized controlled trials (Ahn, 2018). These meta-analysis and systematic reviews (represented in solid black in **Figure 2**) followed recommended guidelines to help minimize study biases and improve their quality. These studies provide valuable insight into the state of VR on pain management.

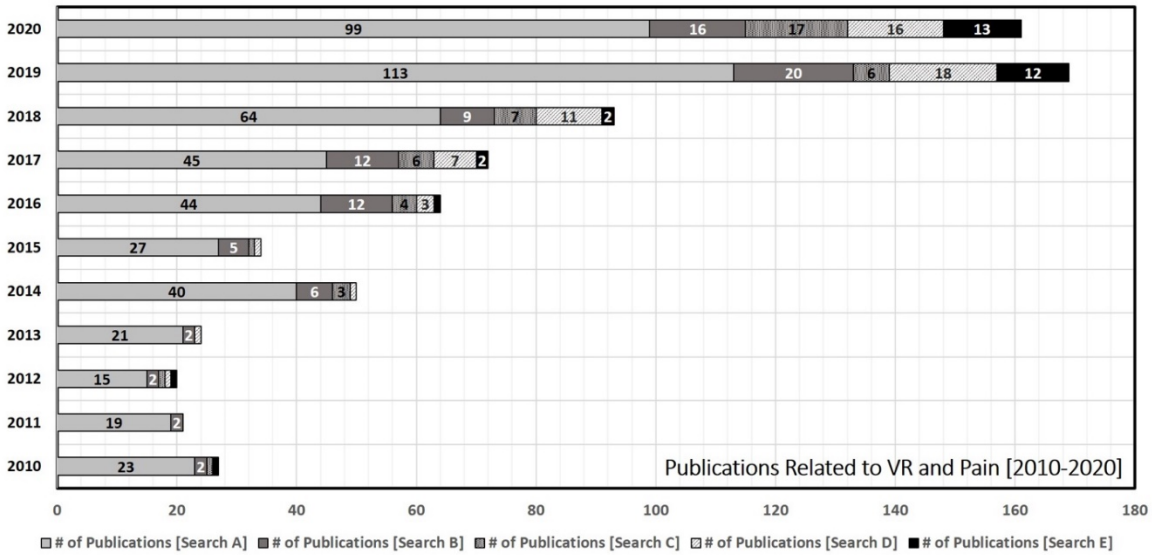

Figure 2. Publications Related to VR and Pain (2010-2020)

Literature Review and Methodology

In this systematic review, we performed an additional meta-analysis. The meta-analysis style of review, in general, aims to summarize quantitative data from a pre-defined set of studies to make claims about what is known or not known in a given area (Pigott et al, 2020). Such studies synthesize the quantitative results from earlier studies using various statistical methods to improve data quality and reduce risk of bias. The primary objective of our work was to explore the fundamental questions: how effective is VR in pain management and what challenges are prevalent that require further attention? This is to inform appropriate study designs for future studies and interventions.

As part of this work, various meta-analysis or systematic reviews reported between 2018 and July of 2020 were reviewed and analyzed for their key goals, intervention approaches, study designs and conditions, and reported outcomes. Key word searches were done on terms such as "virtual reality" AND "pain" present in title or abstract, which yielded 392 articles published since 2015. For the scope of the current work, focus was given to earlier meta-analysis or systematic review works on chronic and acute pain that were published in peer reviewed journals. Searched databases included Google scholar, PubMed, and PubMed Central. Citations, retracted articles, patents, conference abstracts as well as individual dissertations were excluded. Additionally, to obtain more reliable results, this meta-analysis was restricted to studies that relied on randomized controlled trials (RCTs), which usually have a high-level of evidence. This yielded 12 publications, which met the study criteria and were analyzed as part of this review work. Primary findings of past meta-analysis work in scope for this study are summarized in **Table 1**. Key databases, scope of their search, primary goals of the study, pain conditions, pain measurement mechanisms, interventions details, and primary findings by the authors were closely reviewed and analyzed.

Discussion

Analysis of the meta-analysis works listed in **Table 1** shows that there are encouraging results as well as concerns that are impediments in the effective use of VR for pain management. The underlying clinical studies included in scope for these listed works were a mix of randomized control (RCT) and non-random or pre-post intervention (quasi-experimental design) trials, which included 8 - 150 patients, in age groups ranging from 8 to 85 years. Pain conditions range from acute pain as a result of mild injury to chronic pain resulting from serious trauma. Patient reported pain pre- and post-VR exposure sessions, which varied from 5 through 90 minutes, were mainly mostly tracked using the Visual Analog Scale (VAS), Numeric Rating Scale (NRS), and in some cases using the McGill Pain Questionnaire (MPQ). A variety of VR gadgets, which widely differ in their design, performance, and features, were used in these interventions. While some of the studies involved the use of expensive products like ProView family of HMDs, other studies relied on screen time using DVD players. Studies have shown that there is a strong dependency on the type of VR systems used on patient's perceived experience on pain and immersion (Grassini et al., 2020). For example, in a recent study focused on presence and self-efficacy, users indicated a higher sense of spatial presence and immersion while using VR HMD than when using desktop VR (Yu Shu et al., 2019).

Despite the diversity in the study design, such as underlying pain conditions and interventions, some common themes emerge from these meta-analysis studies. While VR qualitatively helps in pain management, there is minimal consensus on its efficacy. Key benefits of VR therapy cited include the following: a) VR therapy reduces acute pain

condition (Mallari et al., 2019 and Chuan et al., 2020), (b) Its use in perioperative period could effectively relieve postoperative pain (Ding, et al., 2020 and Georgescu et al., 2019), c) VR distraction providing immersive environments wherein patients interact with the virtual scenario appear most effective (Eijlers et al, 2019 and Chuan et al., 2020), and d) VR use is effective for short-term pain relief in both acute and chronic pain (Pourmand et al., 2018 and Luo, 2019). These studies also cited serious limitations, which broadly fall under following themes: 1) Lack of systematic protocols in VR intervention, 2) Significant heterogeneity in study populations, pain conditions, and pain reporting mechanisms used in those underlying studies, 3) Limited number of studies for overcoming biases, and 4) Lack of blinded participant groups and intervention delivery, which are critical for minimizing bias and improving data quality. It is important to note that VR as a technology in intervention studies makes it difficult to blind study participants.

Many of the limitations observed in these studies can be overcome by increasing patient sizes in RCTs, standardization of the intervention protocols, and moving from subjective to objective pain and immersion measurements. For example, studies have shown that biophysical parameter measurements, such as heart rate variability (HRV) and skin conductance using sensor-based pain monitoring technologies, can help measure pain objectively (Naranjo-Hernández et al., 2020). Though research on the immersion process is still in its infancy, the degree of immersion has been found to be a critical factor in improving the target patient engagement (Servotte et al., 2020). The level of immersion can be enhanced by taking a closer look at 5 key VR characteristics, which are presence, interactivity, social interactions, customization, and embodiment illustrated in **Figure 3** (Won et al., 2017). "Presence" is the sheer subjective experience of being in an environment as if it were real. The sense of presence can be improved by high fidelity systems, which are a combination of high-end hardware and software applications (Chuan et al, 2020). "Interactivity" is the ability to engage the user with the system in order to enhance user experience. Systems built with skill-building features in applications, characterized by dynamic feedback to the patient as opposed to simple distraction features, will help improve this (Ahmadpour et al., 2020).

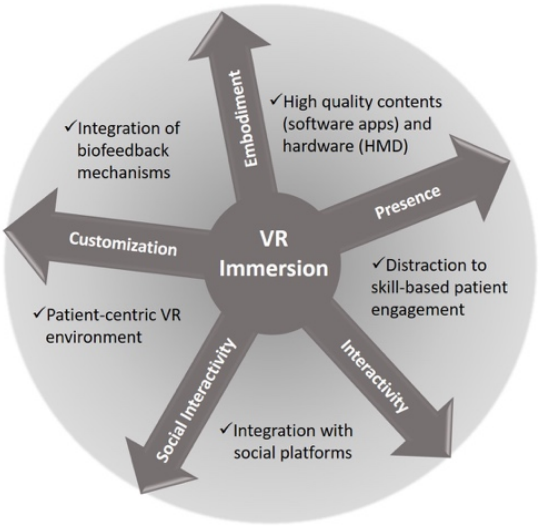

Figure 3. VR Design Considerations for Higher Immersion

"Social interaction" is the capability that helps a patient interact with their family and friends. A recent pilot study has reported higher tolerance for pain when participants interacted with their loved ones (Hwang et al., 2020). "Customization" is the ability to choose a VR environment based on a patient's conditions and choices. It can be realized by personalizing the VR scenes and ambience based on patient's age group, physical conditions, and ethnic backgrounds (Eijlers et al., 2019). "Embodiment" is defined as the sense of having a body, which can be considered to be both the subject and object of medical science and practice (Marta et al., 2019). The use of body trackers, such as hand trackers, are found to help patients track their real-life movements represented by the movements of their avatars in virtual reality. Specifically, studies have shown that personalized avatars can significantly increase the body ownership and feel of presence and thus the immersion (Waltemate et al, 2018). Recent developments in the field of biomedical engineering, such as the OpenButterfly platform, have already started building dynamically controllable environments to meet various needs identified in this work (Powell et al., 2020).

Conclusion

Virtual Reality is a powerful, non-pharmacological technique in treating acute pain conditions and limit patients slipping into chronic pain conditions. The strong surge in the number of studies focused on VR intervention for pain management since 2018 is a direct indication of the significant promise this technology holds in treating pain, which in turn is a necessary step in the fight against the opioid crisis. Intervention studies done to-date are mostly vague on efficacy due to the lack of systematic protocols and heterogeneity in study conditions and methodological biases inherent in the observations. Future studies should focus on enhancing the level of immersion by taking a closer look at the design considerations surrounding VR and biofeedback mechanisms highlighted in this work to improve objectivity in pain and immersion measurements.

Study Limitation

This review relied on previous reviews published on the indicated search topics since 2018 in PubMed, PubMed Central, and Google Scholar and excluded conference proceedings as well as other direct clinical studies. It is important to note that the randomized trial studies provide the highest level of evidence because they contain the least amount of bias while meta-analyses increase bias.

Table 1. Meta-Analysis Summary

Author	Work Type and Scope	Primary Study Goal	Pain Conditions	Intervention Details	Primary Findings / Outcomes
Eijlers et al. (2019)	**Type:** Meta-analysis. **DB**s: EMBASE, MEDLINE, CENTRAL, PubMed, Web of Science, and PsycINFO	Determine if virtual reality (VR) is effective in reducing pain and anxiety in	**Pain source**: Burn, oncological care and venous access; Pain and anxiety	**Study designs covered:** RCTs (crossover and parallel) **VR Use**: I-glasses 920HR, nVisor SX, ProView	VR is an effective tool to diminish patient-reported pain; VR interventions for pain and anxiety were potentially more efficacious for

	Search Term: VR+ Children+ adolescents **Study Size**: 17 **Patient Size**: 8 to 143 **Patient Age**: 4 to 19 **Study Quality Assessment:** Delphi List for RCT	pediatric patients undergoing medical procedures.	**Pain scale**: VAS	XL50, eMagin z800, intervention during- restorative treatment, chemotherapy, lumber puncture, MRI, and post burn physiotherapy	younger than for older children; VR distraction is possibly more effective than other distraction interventions during medical procedure; There was a difference in effect of VR for different medical procedures
Mallari et al. (2019)	**Type:** Meta-analysis. **DBs**: PubMed, CINAHL, Trip Database searches done: 2007-2018 **Search Term**: "Virtual reality AND distraction", "Virtual reality AND pain", and "Virtual reality AND analgesia **Study Size**: 20 **Patient Size**: 6 to 98 **Patient Age**: 18-70 **Study Quality Assessment:** PEDro tool	To compare the effectiveness of VR in reducing acute and chronic pain in adults compared to standard care without VR	**Pain source**: (Acute) Pain related to burns and medical procedures; musculoskeletal, neuropathic, mixed musculoskeletal, and neuropathic or unspecified chronic pain conditions **Pain scale**: VAS, NRS	**Study Design**: RCT Parallel **VR Use**: Oculus Rift (Dk2); Samsung Galaxy S5+ Gear, for 6 - 20 min, during and after the procedures	VR is an effective tool in reducing acute pain both during and after a VR intervention, and that VR is especially effective in mitigating medical procedure related pain (MPRP)
B.Chi et al., (2019)	**Type**: Systematic Review **DB:** MEDLINE, PubMed, CINAHL, EMBASE, and PsycINFO. **Search Terms**: spinal cord injury, tetraplegia, quadriplegia, or paraplegia with "virtual reality" (2007-2018) **Study Size**: 9 **Patient Size**: 150 **Patient Age**: 20-50 **Study Quality Assessment:** Spinal Cord Injury Research Evidence	Systematic review to investigate the effect of VR therapy on SCI-associated neuropathic pain	**Pain source**: Spinal cord injury (SCI) **Pain Scale**: NRS, VAS, McGill pain questionnaire (MPQ)	**Study Design:** RCT, pre-post studies **VR Use**: Varied protocols; 10-min session to 33 sessions of 90 min each over a 6-month period; VR therapy methods such as virtual walking, VR-augmented training, virtual illusion, and VR hypnosis	VR therapy could reduce SCI-associated neuropathic pain; Clinical trials evaluating VR therapy as standalone and/or adjunct therapy for neuropathic pain in SCI patients are warranted

	(SCIRE), PEDRo, D and B scores				
Georgescu et al., (2020)	**Type:** Meta-analysis **DB:** PubMed, EMBASE, the Cochrane Library, and PsycINFO **Search Terms**: Virtual reality, game, interface, immersion, virtual reality exposure therapy, pain, burn, wound, and injuries **Study Size:** 27 **Patient Size**: 8-70 **Patient Age:** Children, Adults **Study Quality Assessment:** Risk of Bias (RoB)	To assess the efficacy and safety of VR-based psychological interventions for pain associated to medical procedures	**Pain source:** Dental, burn, wound procedures **Pain Scale**: VAS, GRS	**Study Design:** RCTs (crossover and parallel) **VR Use**: VR + pharmacological treatments	VR-based interventions reduced pain for patients undergoing medical Procedures; Adjunct VR therapy for pain management in hospitalized patients could reduce costs.
Chuan et al., (2020)	**Type:** Narrative Review **DB:** Medline; PubMed and PsychINFO **Search Term**: virtual reality AND (analgesia OR pain) **Study Size**: 18 **Patient Size**: 20-98 **Patient Age**: 18-75 **Study Quality Assessment**: Cochrane risk of bias assessment tool	To evaluate clinical studies that used virtual reality in adult patients for management of acute and chronic pain	**Pain Source:** Acute and Chronic pain conditions such as- hand trauma surgery, postoperative wound dressing changes, First stage labor, Stage 1–4 breast cancer patients. Post-surgical chronic pain, Cervical lumbar spine pain **Pain Scale**: VAS, NRS	**Study Design:** RCT (unblinded), Crossover RCT, Observational **VR Use:** GearVR, Samsung, Oculus Rift; 30 min of a single instance of virtual reality exposure, for 3 weeks	Higher fidelity software provided more analgesia than lower fidelity and better than non-virtual reality controls; Degree of virtual reality immersion is more effective than the same content delivered by traditional two- dimensional television screens
Ahmad et al., (2020)	**Type**: Meta-Analysis **DB**: EBSCO, Science Direct, MEDLINE, EMBASE, PubMed,	To summarize and evaluate the methodological quality	**Pain Source:** Chemotherapy, port access/venipuncture	**Study Design:** RCT and quasi-experimental design (8 studies)	VR intervention may be beneficial for the management of pain and anxiety in patients

	Scopus, and CINAHL's DB from 1999 - 2018 **Search Term**: virtual reality, environment, pain, anxiety, cancer-related pain, cancer-anxiety, patients with cancer, malignancy, carcinoma, and tumor **Study Size**: 13 **Patient Size**: 11-132 **Patient Age**: 5-85 **Study Quality Assessment:** Downs and Black quality checklist	of primary studies on the virtual reality (VR) technology for the management of pain and anxiety among patients with cancer, and to analyze the effectiveness of VR in the reviewed studies	Procedure **Pain Scale**: VAS, NRS	**VR Use**: 3-5 minutes during painful procedures, from 45-90 minutes during chemotherapy infusions, and for around 30 minutes during hospitalization and the follow-up from 0-48 hours after the end of the VR intervention	with cancer; Compared with standard care, VR plus standard care was more effective in reducing pain and anxiety in patients with cancer.
Chan et al., (2018)	**Type:** Meta-Analysis **DB:** MEDLINE, Embase, CINAHL, ERIC, NIHR **Search Term:** virtual reality, simulation, and pain **Study Size**: 20 **Patient Size**: 11-132 **Patient Age**: 5-80 **Study Quality Assessment:** Manual	A systematic review and meta-analysis to appraise the quality of published literature and to synthesize data for acute pain scores	**Pain Source:** Peripheral intravenous cannula, port access, injury from burn wounds, episiotomy, and repair **Pain Scale**: VAS, NPRS, GRS, VNS, VAT	**Study Design:** RCT and Crossover **VR Use:** Interactive games, HMD via laptop, blue-ray and DVD players	VR is effective for burns physical therapy and needles
Pourmand et al., (2018)	**Type:** Review **DB:** PubMed **Search term:** virtual reality pain, 5-year span **Study Size:** 28 **Patient Size:** 25-74 **Patient Age:** N/A **Study Quality Assessment:** NR	To evaluate the use of virtual reality (VR) therapies as a clinical tool for the management of acute and chronic pain	**Pain Source:** Acute and chronic pains from fibromyalgia, phantom limb pain, and regional specific pain from past injuries and illnesses	**Study Design:** Randomized controlled trial (RCT) and Crossover **VR Use:** HMDs (Oculus Rift Dk2), videos	Study demonstrates the potential for VR distraction therapy to provide effective analgesia for patients experiencing varied pain across many settings

			Pain Scale: VAS, self-report questionnaires		
Ding et al., (2020)	**Type:** Meta-Analysis **DB:** PubMed (Medline), Embase, Web of Science, Cochrane Controlled Register of Trials (CENTRAL), Proquest, Scopus, CNKI, WanFang, and Sinomed [2013-2019] **Search Terms**: virtual reality, VR, immersi*, distract*, postoperative period, after surgery, follow* surgery, follow* operati*, pain and analgesi* **Study Size**: 8 **Patient Size**: 30-182 **Patient Age**: 20-78 **Study Quality Assessment:** Cochrane risk of bias tool	To explore the effects of VR on relieving postoperative pain	Knee, dental, spine surgery **Pain Scales**: VAS, NRS	**Study Design:** RCTs **VR Use:** before, after and during surgery for 5-60 min duration	VR intervention during perioperative period could effectively relieve postoperative pain
Wittkopf et al., (2019)	**Type:** Systematic Review **DB:** Medline (Ovid), PsychInfo, CINAHL, Cochrane library and Web of Science **Search Terms:** NR **Study Size:** 13 **Patient Size**: 9-90 **Patient Age**: 18-65 **Study Quality Assessment:** The Cochrane Risk of Bias and National Heart, Lung, and Blood Institute tools	To evaluate the effect of immersive and non-immersive interactive virtual reality on pain perception in patients with a clinical pain condition	**Pain Source:** Chronic neck, low-back pain, Ankylosing, Spondylitis, breast cancer, post-spinal cord injury **Pain Scale**: VAS, NRS, McGill Pain Questionnaire	**Study Design:** RCTs, pre-test post-test without control groups. **VR Use:** Xbox 360 Kinect – games, Wii games	There is not enough evidence to judge the effectiveness of the use of virtual reality for the management of pain

De Araújo et al., (2019)	**Type:** Systematic Review **DB:** PubMed, BVS, Web of Science, Cochrane Central, and Scielo databases (Jan, 1980 to May 1, 2019) **Search Terms:** virtual reality OR virtual reality immersion therapy OR virtual reality therapy OR reality therapy OR game(s)AND spinal cord injury(ies) OR spinal cord trauma OR paraplegia OR tetraplegia. **Study Size:** 25 **Patient Size**: 6-45 **Patient Age**: 18-65 **Study Quality Assessment:** PEDro scale	To investigate the possible benefits and efficacy of VR-based rehabilitation in individuals with Spinal Cord Injury (SCI)	**Pain Source:** Spinal Cord Injury (SCI) **Pain Scale:** VAS	**Study Design:** RCT, non-randomized, Non-blinded, cross-sectional **VR Use:** VR driving simulator, CyberGlove + 3D, Nintendo Wii, iPad2, Mobile prototype of the YouKicker system for 1 – 60 minute sessions	Overall, the studies reported a beneficial effect of VR therapy alone or VR associated with conventional rehabilitation; Initial evidence of VR to improve motor function, motor skills, balance, and aerobic function and to reduce the pain level was observed
Luo et al., (2019)	**Type:** **DB:** PubMed, EMBASE, and the Cochrane Central Register of Controlled Trials (till Feb, 2018) **Search Terms:** Virtual Reality, Pain Management, Virtual Reality Exposure Therapy, Burn, wound care, Physical Therapy Modalities **Study Size:** 13 **Patient Size**: 8-88 **Patient Age**: 5-65 **Study Quality Assessment:** The Cochrane Risk of Bias	Study to verify the pain-reducing efficacy of virtual reality among burn patients undergoing dressing change or physical therapy	**Pain Source:** Burns **Pain Scale:** NR	**Study Design:** RCT **VR Use:** Snow-World with Spider-World, with HMD during dressing change	The application of VR coupled with analgesics is safe and effective in reducing all four components of pain during burn patients' dressing change and physical therapy sessions

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