

## Original Article

# Feasibility of virtual reality-delivered pain psychology therapy for cancer-related neuropathic pain: a pilot randomised controlled trial

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## Summary

Virtual reality-delivered psychological therapies have recently been investigated as non-pharmacological management for acute and chronic pain. However, no virtual reality pain therapy software existed that met the needs of cancer patients with neuropathic pain. We created a bespoke virtual reality-delivered pain therapy software programme to help cancer patients manage neuropathic pain incorporating guided visualisation and progressive muscle relaxation techniques, whilst minimising the risk of cybersickness in this vulnerable patient population. This randomised controlled pilot study evaluated the feasibility, acceptability, recruitment rates and risk of cybersickness of this pain therapy software programme. Clinical outcomes including opioid consumption, pain severity, pain interference and global quality of life scores were secondary aims. Of 87 eligible cancer patients with neuropathic pain, 39 were recruited (47%), allocated to either the intervention (20 patients, virtual reality pain therapy software programme) or control (19 patients, viewing virtual reality videos). Four patients withdrew before the 3-month follow-up (all in the control group). Pre-existing dizziness (Spearman  $\rho$  0.37,  $p = 0.02$ ) and pre-existing nausea (Spearman  $\rho$  0.81,  $p < 0.001$ ) were significantly associated with risk of cybersickness in both groups. Patients in the intervention group reported less cybersickness, as well as tolerated and completed all therapy sessions. At 1- and 3-month follow-up, there were trends in the intervention group towards reductions in: oral morphine equivalent daily dose opioid consumption ( $-8$  mg and  $-4$  mg; vs. control:  $0$  mg and  $+15$  mg respectively); modified Brief Pain Inventory pain severity ( $-0.4$ ,  $-0.8$ ; vs. control  $+0.4$ ,  $-0.3$ ); and pain interference ( $-0.9$ ,  $-1.8$ ; vs. control  $-0.2$ ,  $-0.3$ ) scores. The global quality of life subscale from the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-C30 was not significantly changed between groups at 1 and 3 months (intervention:  $-5$ ,  $-8$ ; vs. control:  $+3$ ,  $+4$ ). This newly created virtual reality-delivered pain therapy software programme was shown to be feasible and acceptable to cancer patients with neuropathic pain. These results will aid the design of a definitive multicentre randomised controlled trial.

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## Introduction

Neuropathic pain is commonly experienced by cancer patients, with prevalence estimates ranging from 19% to 39% [1]. The causes of cancer-related neuropathic pain are varied and include: direct cancer involvement or nerve impingement by tumour growth; paraneoplastic syndrome affecting nerves; and as a complication of surgery, radiotherapy or chemotherapy. Managing this type of pain is difficult and pharmacological therapy alone often fails to achieve satisfactory analgesia. Instead, multimodal approaches including psychological interventions as complementary adjuncts are recommended [2, 3]. The goals of psychological therapy include: the reduction of experienced pain; promoting quality of life and function; and teaching self-efficacy skills that mitigate mood disturbances, disability and distress [4]. Traditionally, these therapies are delivered by clinical health psychologists in face-to-face sessions with patients.

More recently, researchers have explored the use of virtual reality as an alternative method to deliver pain psychological interventions [5]. With virtual reality, patients view a computer-generated environment using occlusive head-mounted devices, immersed in a virtual experience that replaces real-life auditory and visual inputs. Hand-held controllers enable patients to virtually interact with objects, people and graphical avatars. However, using virtual reality to provide pain psychology therapy to cancer patients presents two different challenges: a higher risk of cybersickness and the choice of psychological therapy. Cybersickness describes motion sickness-like symptoms which include: nausea; dizziness; disorientation; eyestrain; headaches; and fatigue. While cybersickness may occur with any electronic screen use, it is more common and severe with virtual reality due to the removal of external cues [6]. Predisposition to nausea in cancer patients, therefore, poses one possible limitation of virtual reality use. The second challenge is the choice of therapy. To date, most virtual reality pain studies employed distraction therapy that seeks to divert the patient's attention away from their noxious stimuli [5]. This distraction has been in the form of an interactive virtual reality game [7] or passively watching a movie clip [8]. We contend that simple distractions are not

suitable for persistent pain states, but more sophisticated psychological therapies have rarely been investigated in previous virtual reality pain studies.

To meet these challenges, we created a bespoke software programme to help manage cancer-related neuropathic pain. This programme was informed by design principles that specifically minimised cybersickness. The chosen therapies were guided pain visualisation and progressive muscle relaxation, which are well-regarded interventions commonly recommended by pain psychologists in the management of cancer pain [9–11]. To test our software programme, we conducted this randomised controlled pilot study with primary aims to assess: the feasibility of recruitment and data collection; rate of withdrawals; acceptability; and cybersickness rates. Secondary aims were clinical outcomes including: opioid consumption; pain scores; and quality of life. These outcomes would be included in a definitive trial of effectiveness of our software programme in the management of neuropathic pain in cancer patients.

## Methods

This single-centre, prospective, pilot randomised controlled trial was approved by the South Western Sydney Local Health District Human Research Ethics Committee and conducted between February 2020 and December 2021.

Cancer patients met their oncologist at their regular outpatient appointment in the Cancer Therapy Centre, Liverpool Hospital, Sydney, Australia. If the treating oncologist or palliative care physician diagnosed symptoms of neuropathic pain caused by cancer or interventions for their cancer, the patient was invited to meet an independent study researcher. Patients were eligible for study inclusion if they: were adult patients aged  $\geq 18$  y; were functionally independent in most activities of daily living with an Eastern Cooperative Oncology Group Performance Status score  $\leq 2$ ; and had sufficient English language proficiency to complete written questionnaires and to understand instructions and explanations provided during virtual reality therapy. Patients with psychological or psychiatric illness not stabilised with therapy or medications were excluded.

After providing written informed consent, eligible patients had data collected on their characteristics and cancer diagnosis. Opioid use was recorded as average daily doses of all opioid analgesics over the previous week and doses were standardised to a single oral morphine equivalent daily dose (oMEDD) using the Australian and New Zealand College of Anaesthetists opioid conversion calculator [12]. Severity of neuropathic pain was assessed using the self-reported version of the Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) questionnaire [13]. Current pain levels, and known risk factors for development of chronic pain, were self-assessed using the modified Brief Pain Inventory (mBPI), depression anxiety and stress scale and pain catastrophising scale, included in the Australian English version 2.0 of the Electronic Persistent Pain Outcomes Collaboration [14]. Baseline functional self-assessment was performed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core (QLQ-C30, version 3.0, 2001). This 30-item tool is a standardised quality of life assessment for cancer patients in international clinical trials, divided into 15 subscales [15].

We created a bespoke virtual reality-delivered software programme that taught pain self-efficacy to patients using progressive muscle relaxation and guided pain visualisation techniques. In muscle relaxation, patients are taught how to identify tensed muscle groups in their arms, legs, shoulders and neck, and to then relax this tension. In pain visualisation, patients are taught to attenuate their pain within an imaginary mind space. Our research team health psychologists converted their face-to-face protocols into a computerised version and incorporated this into the software programme. We created captivating computer avatars to enhance the level of visual, auditory and tactile interactions within the virtual reality environment (Fig. 1).

For example, a computer-generated, anatomically correct human body highlighted the deltoid and biceps muscles of the proximal arm, asking the patient to localise tension before guiding the patient in a scripted relaxation exercise. In the pain visualisation therapy, an angry, fiery ball symbolised the patient's neuropathic pain, evoking imagery of burning and shooting. Patients are then led through a scripted exercise that teaches how to subdue the pain as represented by the computer character. Each session of relaxation and visualisation took 30 min to complete. These therapies were coded using deliberate design philosophies that sought to minimise cybersickness. These include reducing the need to excessively move the user's head and arm movements within the virtual reality environment; avoiding abrupt scenery changes that exaggerate a sense of motion; avoiding unnecessary movements of computer characters that forces users to rapidly eye track; and integrating calming music. As an example in the pain visualisation therapy, the angry pain character always returns to a position within a forward 60° cone such that the patient can use minimal head and arm movements to interact.

Patients in the control arm were instead asked to view a selection of short documentaries and videos specifically filmed in a virtual reality format for viewing through a virtual reality headset. These publicly available videos were selected from the dedicated virtual reality channel on YouTube. In their 30 min session, patients could choose from any of the following: a documentary on jaguars in Brazil, a documentary on the Apollo 11 moon landing, an animated cartoon in a snow environment and a car review (see online Supporting Information Appendix S1 for links to these).

High specification computer hardware was used to run the software programme and virtual reality control



**Figure 1** Screenshots of the guided pain visualisation (left) and progressive muscle relaxation (right) therapies included in our virtual reality-delivered pain software programme.

protocols: Core i7-8750H powered gaming laptop running at 2.2GHz (Intel Corp, Mountain View, CA, USA); 16 gigabytes memory; dedicated multithread graphics core (GeForce GTX 1060, NVIDIA Corp, Santa Clara, CA, USA); and optimised to power an Oculus Rift S (Meta Platforms, Menlo Park, CA, USA) virtual reality headset and hand-held controllers. This allowed the virtual reality software to be run with high resolution audio and graphics, create a fully immersive 360° realistic environment, experience zero lag and react with seamless responses to patient inputs.

As the study commenced soon after the SARS-CoV-2 pandemic, we brought in the infection control and social distancing protocols. A commercially available gel pad standoff was inserted over the foam pads on the virtual reality headset, allowing for easier cleaning using a neutral disinfectant surface wipe. All surfaces on the virtual reality headset and hand controllers were similarly disinfected. Patients wore surgical disposable hats and masks to further act as aerosol and contact barriers, as did researchers. Recruitment occurred in an isolated room with only one patient and one researcher. Hand sanitiser use was encouraged and freely available.

Patient characteristics, cancer diagnosis, S-LANSS, oMEDD, baseline mBPI, depression anxiety and stress scale, pain catastrophising scale and QLQ-C30 questionnaires were completed by each patient after recruitment. Subsequently, each patient was allocated randomly using a computer-generated sequence, with allocation in blocks of 4, to either intervention or control groups. Patients received three 30-min sessions of intervention or control therapy within a 4-week period after group allocation. All sessions were performed in the Cancer Therapy Centre. Patients in the intervention group were encouraged to continue to use the muscle relaxation and pain visualisation techniques they learnt outside of the sessions and over the next 3 months. Patients could not be blinded to their group allocation but were separated from other patients to prevent contamination. All patients completed an acceptability questionnaire on the severity of the three most reported side-effects of virtual reality use: nausea, dizziness and eyestrain. Patients scored severity using a 0–10 Likert scale, with 0 representing no symptoms and 10 representing severe symptoms. The acceptability questionnaire was completed before virtual reality use to measure presence of pre-existing symptoms and after virtual reality use. Ability to tolerate the virtual reality headset for each 30-min session was reported as yes/no. A free text box allowed for extra information or feedback. Feasibility was measured by: comparing the actual number of patients recruited compared with the potential number of eligible patients;

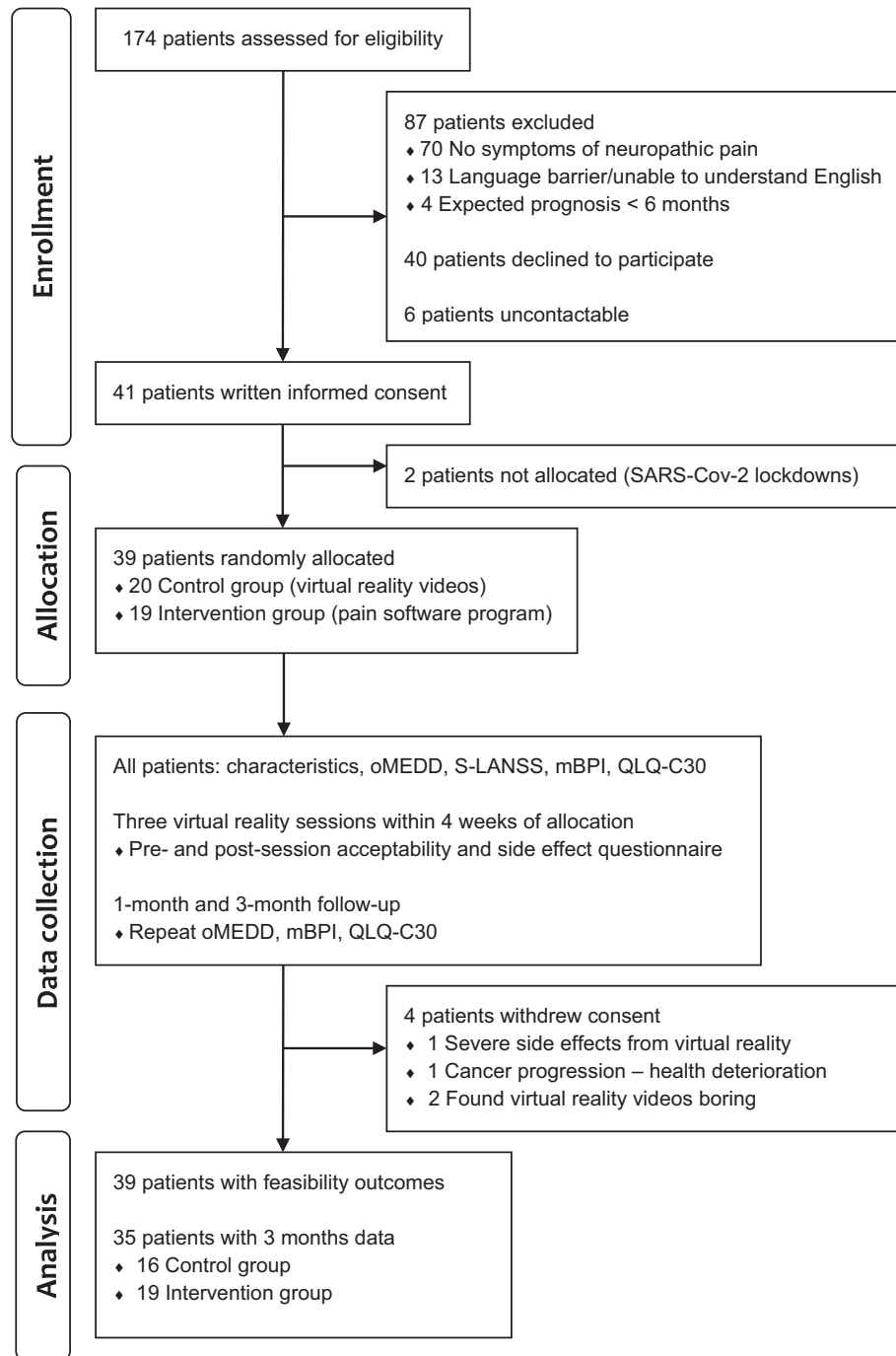
rate of withdrawals; and number lost to follow-up including the reasons for this.

Clinical endpoints were oMEDD, pain scores (mBPI pain severity and pain interference subscales where higher values are associated with more severe pain and more functional interference) and quality of life (QLQ-C30, global quality of life subscale) at 1 and 3 months after completing intervention or control sessions. The study flow diagram and endpoint measurements are shown in Fig. 2.

To our knowledge, no previous studies have reported feasibility of full immersion, interactive virtual reality as a therapeutic modality for cancer patients. Consequently, we selected a convenience sample size of 40 patients to answer this study's primary aims of feasibility of recruitment, acceptability and risk of cybersickness side-effects. Data were analysed using the Kolmogorov–Smirnov test for normality and results reported as mean (SD) or median (IQR [range]). The proportion of patients in each group with feasibility and acceptability outcomes, and frequency of virtual reality-associated side-effects, were analysed using Fisher's exact test. Severity of virtual reality side-effects was analysed using the Kruskal–Wallis H test for ordinal Likert data between the intervention and control groups over the three sessions of virtual reality, while the Friedman test was used to compare within group changes over the three sessions. Association between pre-existing symptoms and presence of side-effects after virtual reality use was analysed using Spearman correlation. Mean change in opioid consumption, pain severity, pain interference and global quality of life subscale from baseline to 1 and 3 months were analysed using repeated measures ANCOVA, with baseline measurements as the covariate; noting that this study is not powered to detect significant changes in these treatment outcomes. Analysis was performed using SPSS version 24 (IBM Corp, Armonk, NY, USA). Statistical significance was determined by two-tailed analysis with  $p < 0.05$ .

## Results

During the study period, 174 patients presented to the cancer outpatient clinics and were screened for eligibility (Fig. 2). Of these, 50% of patients did not meet inclusion criteria (87 patients: 70 due to no evidence of concurrent neuropathic pain; 13 due to insufficient English proficiency; and 4 with estimated prognosis  $\leq 6$  months). Of the remaining patients, 46 (53%) were not recruited (40 patients declined participation and 6 were uncontactable). Written informed consent was obtained from 41 patients but two were not allocated as non-critical research ceased due to a prolonged SARS-CoV-2 lockdown in Sydney (June–October 2021), leaving a total of 39 patients included.



**Figure 2** Study flow diagram. oMEDD, oral morphine equivalent daily dose on average in the previous week; S-LANSS, Self-reported Leeds Assessment of Neuropathic Symptoms and Signs questionnaire; mBPI, modified Brief Pain Inventory; QLQ-C30, Quality of Life Questionnaire-Core 30.

Patient characteristics, opioid consumption, pain and quality of life scores were not significantly different between the intervention and control groups at baseline (Table 1).

The tolerability of the virtual reality headset, feasibility of follow-up and frequency and type of side effects after virtual

reality use are reported in Table 2. The proportion of patients reporting side effects, as well as the type and severity of side effects, did not show a statistically significant difference between groups. This was also the case within groups for repeated virtual reality use, but they were less in the software

**Table 1** Patient characteristics in the intervention (virtual reality-delivered pain software programme) and control (virtual reality video) groups. Values are mean (SD), number (proportion) or median (IQR [range]).

	Intervention n = 19	Control n = 20
Age; y	56 (8)	63 (11)
Sex; female	11 (58%)	14 (70%)
Eastern Cooperative Oncology Group Performance Status score	1 (1–1 [0–1])	1 (1–1 [0–2])
Cancer diagnosis		
Colorectal	6 (32%)	9 (45%)
Lung	2 (10%)	7 (35%)
Breast	8 (42%)	4 (20%)
Other	3 (16%)	0 (0%)
S-LANSS score	11 (5)	12 (6)
Depression anxiety and stress scale	18 (5–32 [0–50])	12 (6–20 [2–42])
Pain catastrophising scale	18 (7–38 [2–51])	9 (3–30 [0–46])
oMEDD; mg	0 (0–23 [0–155])	0 (0–24 [0–126])
Baseline mBPI pain severity	4.9 (1.1)	4.4 (1.9)
Baseline mBPI pain interference	4.7 (2.4)	4.1 (2.7)
Baseline QLQ-C30 with subscales:		
Global quality of life	62 (25)	55 (20)
Physical functioning	69 (19)	69 (23)
Role functioning	49 (34)	54 (31)
Emotional functioning	68 (30)	79 (23)
Cognitive functioning	58 (34)	67 (34)
Social functioning	58 (31)	59 (34)
Fatigue	56 (26)	57 (27)
Nausea/vomiting	10 (13)	9 (13)
Pain	69 (30)	58 (30)
Dyspnoea	19 (30)	28 (41)
Insomnia	40 (33)	62 (38)
Appetite Loss	25 (31)	33 (38)
Constipation	16 (28)	23 (31)
Diarrhoea	9 (19)	15 (25)
Financial difficulties	23 (37)	27 (33)

S-LANSS, Self-reported Leeds Assessment of Neuropathic Symptoms and Signs questionnaire; oMEDD, oral morphine equivalent daily dose on average in the previous week; mBPI, modified Brief Pain Inventory; QLQ-C30, Quality of Life Questionnaire-Core 30.

programme group. For one control patient, the side-effect (severe headache) was severe enough to withdraw from the study and two control patients were unable to tolerate the

headset and did not complete one of their virtual reality sessions. Two other control patients withdrew citing boredom with the video content, whereas there were no withdrawals in the intervention group (Fig. 2 and Table 2). Pre-existing symptoms before virtual reality use were significantly associated with side effects after virtual reality use for all three sessions and for patients in either group: pre-existing dizziness, Spearman  $\rho$  0.37 ( $p = 0.02$ ); and pre-existing nausea, Spearman  $\rho$  0.81 ( $p < 0.001$ ).

There were reductions in opioid consumption in the intervention group; however, the mean change in oMEDD dose was small and not significant at 1 month (intervention group  $-8$  mg, control group  $0$  mg,  $p = 0.52$ ) and 3 months (intervention group  $-4$  mg, control group  $+15$  mg,  $p = 0.34$ ). Mean change in global quality of life did not favour the intervention group but was similarly small and not statistically significant at either 1 month (intervention group  $-5$  (19), control group  $+3$  (21),  $p = 0.53$ ) and 3 months (intervention group  $-8$  (20), control group  $+2$  (21),  $p = 0.62$ ). Mean change in pain severity levels at 1 month (intervention group  $-0.4$  (1.2), control group  $+0.4$  (1.5),  $p = 0.02$ ) and 3 months (intervention group  $-0.8$  (2.0), control group  $-0.3$  (1.6),  $p = 0.10$ ) showed a trend in larger reductions in the intervention group. Mean change in pain interference similarly showed a larger reduction for the software programme group at 1 month (intervention group  $-0.9$  (1.5), control group  $-0.2$  (2),  $p = 0.40$ ) and 3 months (intervention group  $1.8$  (2.7), control group  $-0.3$  (2.0),  $p = 0.14$ ) (Table 3).

## Discussion

This prospective randomised pilot study demonstrated feasibility of recruitment of cancer patients using virtual reality to manage neuropathic pain. The bespoke software programme was designed to deliver guided visualisation and progressive muscle relaxation pain psychological therapies in a high fidelity, highly immersive virtual reality environment. This study provided the first data on the incidence of side-effects, tolerability of virtual reality use in this patient population, and effect size of clinical outcomes, which are necessary to assist in designing future trials.

Virtual reality as a modality to treat pain is relatively new, with the first description of virtual reality-delivered interventions appearing in 2000 [16]. Using virtual reality has multiple advantages: highly immersive distractions can temporarily reduce experienced pain; improve mood; and bring excitement and fun. With reducing costs of commercially available headsets, virtual reality-based programmes can be accessed by a wider audience and treatment can occur at home as outpatients [17]. We have

**Table 2** Tolerability of virtual reality headset, feasibility of follow-up and frequency and type of side-effects in the intervention and control groups. Values are number (proportion) or median (IQR [range]).

	Intervention n = 19	Control n = 20	p value
Tolerability of virtual reality headset	19 (100%)	18 (90%)	0.49
Feasibility to complete			
1-month follow-up	19 (100%)	17 (85%)	0.23
3-month follow-up	19 (100%)	16 (80%)	0.11
Virtual reality-associated side-effects during any session			
Nausea	4 (21%)	5 (25%)	1.00
Dizziness	4 (21%)	4 (20%)	1.00
Eyestrain	4 (21%)	8 (40%)	0.30
Severity of virtual reality-associated side-effects (0–10 Likert scale)			
Nausea session 1	0 (0–0 [0–3])	0 (0–0 [0–5])	0.37
Nausea session 2	0 (0–1 [0–5])	0 (0–0 [0–1])	0.15
Nausea session 3	0 (0–0 [0–5])	0 (0–0 [0–7])	1.00
Dizziness session 1	0 (0–0 [0–3])	0 (0–0 [0–3])	0.61
Dizziness session 2	0 (0–1 [0–6])	0 (0–0 [0–3])	0.19
Dizziness session 3	0 (0–0 [0–1])	0 (0–0 [0–6])	0.49
Eyestrain session 1	0 (0–0 [0–1])	0 (0–2 [0–5])	0.04
Eyestrain session 2	0 (0–0 [0–7])	0 (0–1 [0–4])	0.95
Eyestrain session 3	0 (0–0 [0–10])	0 (0–0 [0–4])	0.35
Within group severity of side-effect comparisons between sessions; p value			
Nausea	0.26	0.37	
Dizziness	0.08	0.67	
Eyestrain	0.78	0.25	

**Table 3** Opioid consumption, pain scores and quality of life at 1 and 3 months for intervention and control groups. Values are median (IQR [range]) or mean (SD) and with significance testing on mean changes from group baselines.

	Intervention group	Control group	p value
One-month follow-up			
oMEDD; mg	0 (0–19 [0–155])	0 (0–38 [0–126])	0.52
Pain severity of mBPI	4.5 (1.6)	4.5 (2.2)	0.02
Pain interference of mBPI	3.7 (2.4)	4.1 (2.9)	0.40
Global quality of life subscale of QLQ-C30	57 (18)	57 (18)	0.53
Three-month follow-up			
oMEDD; mg	0 (0–15 [0–230])	0 (0–51 [0–246])	0.34
Pain severity of mBPI	4.1 (2.1)	3.8 (2.7)	0.10
Pain interference of mBPI	2.8 (2.7)	3.8 (3.7)	0.14
Global quality of life subscale of QLQ-C30	54 (25)	56 (24)	0.62

oMEDD, oral morphine equivalent daily dose on average in the previous week; mBPI, modified Brief Pain Inventory; QLQ-C30, Quality of Life Questionnaire-Core 30.

since systematically reviewed the use of virtual reality for management of pain and anxiety in cancer patients [18], finding that while these benefits potentially exist, the quality of evidence for efficacy was low. We similarly reviewed studies using virtual reality in peri-operative medicine, acute and chronic non-cancer pain and identified problems with

lack of blinding, low immersion experiences from early generation virtual reality hardware and inactive control groups that possibly magnified the beneficial effects of virtual reality [5].

Previous studies have explored virtual reality use in non-cancer peripheral neuropathies [19] and neuropathy

after spinal cord injury [20, 21]. To our knowledge, our study is the first investigating the use of virtual reality in cancer-related neuropathic pain. This study has several strengths. Our software programme was specifically designed for this study in consultation with pain health psychologists and delivered cognitive behavioural therapies that are in common use for pain management. In contrast, previous studies typically co-opted generic videos or games, relying on distraction for pain relief. We measured outcomes at time periods more consistent with management of persistent pain states, whereas previous studies measured early outcomes which may give a higher benefit to the virtual reality intervention [5]. The presence of nausea and dizziness before virtual reality use was shown to be a significant risk factor for cybersickness. To mitigate this, our software design principles included minimising the need for patients to move their heads to look at virtual objects, reducing the speed of characters moving in the simulation and ensuring transitions were not abrupt. These strategies to reduce cybersickness appear to have been successful, as all patients in the intervention group were able to tolerate wearing the headset and none withdrew from the study. This is compared with two patients who were unable to tolerate the headset and three patients withdrawing in the control group. Lastly, we deliberately chose a control with virtual reality exposure to allow blinding of data collectors to group allocation, which was identified as a major risk of bias in previous studies. [5].

There are some limitations to the study. Recruitment commenced in February 2020 and was impacted by the SARS-CoV-2 pandemic, especially due to city-wide lockdowns in 2020 and again in 2021, forcing the cessation of non-critical research activity. In between lockdowns, many immune compromised cancer patients were reluctant to participate and this is reflected in the recruitment rate. Furthermore, an element of selection bias may have occurred, as perhaps healthier or less worried cancer patients were more willing to be included. We anticipate that future studies would not be as negatively affected with reduced likelihood of social restrictions used to control the pandemic. Control group patients watched a curated selection of videos made for virtual reality, but this choice impacted on an increased risk of cybersickness and a lack of interest. Future studies should incorporate a different approach, such as giving patients a choice of their videos from the entire library or interactive virtual reality game. This study was a planned as a pilot feasibility study and our sample size was convenience-based and not powered for the clinical outcomes evaluated. We therefore cannot conclusively report on the trend in reductions in pain scores

or the lack of change between groups for quality of life and opioid use. This contrasts with the very large improvement observed in a recent trial of virtual reality distraction therapy for neuropathic pain associated with spinal cord injury where numerical pain rating scales reduced from 5.3 to 2.2, with an effect size 0.80 [20]. The pain scales were, however, recorded immediately after the virtual reality intervention and not during longer follow-up, as occurred in our study. This study also did not assess uptake of the pain interventions included in the software programme, or whether patients continued to utilise these pain management strategies over the ensuing months, which will be an important contributory factor in outcomes. A future trial would also benefit from the virtual reality interventions spread out more temporally to improve uptake and retention by patients, rather than the condensed 4-week time period used in this study. Nonetheless, the trends in outcomes in our pilot data are encouraging and suggest modest clinical efficacy.

In summary, our virtual reality-delivered pain software programme was found to be feasible and acceptable for the intended patient population of cancer patients, with fewer reported side effects and greater equipment tolerance compared with the control group who watched virtual reality distraction videos. We attribute this to purposeful design choices that reduced the risk of cybersickness. We incorporated guided visualisation and progressive muscle relaxation techniques as non-pharmacological pain therapies for neuropathic pain. This pilot study collected data appropriate to designing and planning a definitive multicentre randomised controlled trial to investigate this novel intervention.

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## Supporting Information

Additional supporting information may be found online via the journal website.

**Appendix S1.** Examples of videos filmed in a virtual reality format for viewing through a virtual reality headset.