

A mixed-methods investigation into the acceptability, usability and perceived effectiveness of active and passive virtual reality scenarios in managing pain under experimental conditions

PHELAN, Ivan, FURNESS, Penny <<http://orcid.org/0000-0003-4916-8800>>, FEHILY, Orla, THOMPSON, Andrew, BABIKER, Nathan, LAMB, Martin and LINDLEY, Shirley

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1 **Title**

2 A Mixed-Methods Investigation into the Acceptability, Usability and Perceived Effectiveness
3 of Active and Passive Virtual Reality Scenarios in Managing Pain under Experimental
4 Conditions.

5

6 **Abstract**

7 Burns patients often suffer excruciating pain during clinical procedures, even with analgesia.
8 Virtual Reality as an adjunct to pharmacological therapy has proved promising in the
9 management of burn pain. More evidence is needed regarding specific forms of Virtual
10 Reality. This mixed-method study examined the impact of active and passive Virtual Reality
11 scenarios in experimental conditions, gathering data relating to user experience, acceptability
12 and effectiveness in managing pain. Four scenarios were developed or selected following a
13 consultative workshop with burns survivors and clinicians. Each was trialled using a cold
14 pressor test with 15 University students. Data were gathered regarding pain threshold and
15 tolerance at baseline and during each exposure. Short interviews were conducted afterwards.
16 The two active scenarios were ranked highest and significantly extended participants pain
17 threshold and tolerance times compared to passive and baseline conditions. Passive scenarios
18 offered little distraction and relief from pain. Active scenarios were perceived to be engaging,
19 challenging, distracting and immersive. They reduced subjective awareness of pain, though
20 suggestions were made for further improvements. Results suggested that active Virtual
21 Reality was acceptable and enjoyable as a means of helping to control experimental pain.
22 Following suggested improvements, scenarios should now be tested in the clinical
23 environment.

24 Key words: Burn Pain, Anxiety, Wound care, Virtual Reality, Mixed Methods

25

26 **Introduction**

27 Burns patients often suffer excruciating pain during dressings change and physiotherapy,
28 even with strong analgesia¹. They are a unique group because the acute pain of treatment is
29 superimposed on the chronic background pain associated with tissue damage². Opiates are
30 used routinely for the background pain of burn injury³, but there are unpleasant side effects⁴
31 and their efficacy for procedural and anticipatory pain, such as during wound cleansing,
32 dressing change and physiotherapy⁵, has been described as limited⁶. The risks of poor pain
33 relief are physical, psychological, social and clinical. They include greater sensitivity to
34 infection, acute stress symptoms in hospital⁷, higher risk of Post-Traumatic Stress Disorder
35 (PTSD), concerns about impact on appearance⁸, and even suicide post-discharge^{9,10}, loss of
36 confidence in the care team⁵, and lower compliance with rehabilitation activities¹¹.

37 Theoretical perspectives on pain, such as Gate Control Theory and neuromatrix theory^{12, 13},
38 emphasize the role of psychological elements including perception, attention and anxiety.
39 Non-pharmacological methods of pain relief, aimed at reducing these elements (such as
40 mental imagery, hypnosis, video-watching, parental participation), have been demonstrated
41 as potentially effective through their ability to distract⁶. Virtual Reality (VR) involves an
42 artificial three-dimensional environment that is experienced by a person through sensory
43 stimuli (usually visual, auditory, and often touch) delivered by a computer and in which one's
44 actions partially determine what happens in the environment¹⁴. VR is postulated to act both
45 directly and indirectly upon pain perception, through its effects on attention, emotion,
46 concentration, and sensory involvement¹⁵. Compared with other forms of non-
47 pharmacological distractive interventions, VR makes increased demands upon the user's
48 attention¹⁶, and reduces visual and auditory cues to pain linked to anxiety and anticipatory
49 pain before and during procedures¹⁷.

50 Interest in the clinical applications of VR technology has inspired studies to explore its
51 feasibility and effectiveness in pain relief, including burn pain¹⁸. Studies have reported
52 significant reduction in both adult and child subjective procedural pain scores for VR with
53 pharmacological analgesia compared with analgesia alone^{19,20}. Qualitative findings from staff
54 and parents suggested greater relaxation and cooperation and less evidence of pain and
55 anxiety with VR, and, although immersed, patients continued to communicate well²⁰. Malloy
56 and Milling¹⁸ noted that early findings were often based on uncontrolled designs or case
57 material studies; however these outcomes are supported in three recent systematic reviews
58 (based on 9, 11 and 17 studies respectively)^{21,18,14}, which have included more recent,
59 carefully controlled studies^{22,23}. Reviews have concluded that the strongest evidence for the
60 effectiveness of VR was in the relief of pain and associated anxiety in adult and paediatric
61 burns patients^{18,14}. The downsides to VR are few: costs are falling¹⁸ and new technologies,
62 such as water-friendly VR headsets (for water-bath based wound care⁵), are becoming more
63 accessible²². Some older patients are resistant to VR, and people with pre-existing nausea or
64 a history of motion sickness tend to be excluded from research²⁴. This suggests that the VR
65 technology has its limitations and is not universally welcome or applicable; however among
66 those willing and able to use it, evidence suggests that side effects, such as nausea,
67 attributable to the VR rather than the pharmacological intervention, are rare^{22,25}.

68 Given the growing evidence for its effectiveness in reducing procedural pain, limited adverse
69 effects, reducing costs and increasing clinical applicability, immersive VR has considerable
70 value in burn pain management¹⁴. Favourable evidence is impeded by small sample sizes, but
71 is amassing and becoming more compelling², although there is scope for more work to
72 enhance the evidence-base, with larger samples and rigorous methodological approaches¹⁴.
73 Reviewers have recommended its introduction to burn care and rehabilitation²⁶, but more
74 work is required to explore the impact of varied VR environments, in different patient groups

75 and with different individuals, to ascertain the variables which moderate effectiveness¹⁸. It
76 has been suggested that VR environments may need tailoring for maximum effect²⁷. This
77 may involve designing a scenario to meet specific patient group needs, such as a ‘cold’
78 scenario for burns patients, and in children, offering a range of scenarios to suit all ages²⁰.

79 Hoffman and colleagues^{1,22} note that the degree of immersion offered by VR - the reported
80 sense of ‘presence’ - is related to the degree of VR pain reduction, a finding supported
81 elsewhere^{18, 28}. A recent study compared an immersive, active VR scenario via headset with a
82 passive pain distraction experience via bedside video and found that, although pain fell in
83 both groups, those in the experimental VR group reported a significantly greater fall²⁴.

84 However, as authors noted, it was not possible from this design to ascertain whether the
85 difference was attributable to the three-dimensional vs two-dimensional experience, the
86 active vs passive aspect, or the visual and audio variations between the two.

87 To add to the growing body of evidence, the roles played by degree of immersion and
88 tailored VR environments are fruitful areas for exploration. This study aimed to develop user-
89 informed scenarios based on either active (where the user is actively involved in the VR
90 environment) and passive VR (where the user is only watching) and compare them in
91 experimental conditions, exploring user experience, acceptability, and effectiveness in
92 distracting participants and reducing pain. The benefits of investigating VR scenarios in
93 experimental pain is that it allows greater variable control than clinical pain: each participant
94 can be administered the same pain stimulus and intervention, whereas in the clinical
95 environment, patients are likely to differ in types and levels of pain, and medical needs may
96 affect how the intervention is delivered¹⁸. Findings have shown that experimental pain ratings
97 with VR were significantly lower than with no VR²⁸⁻³⁰. However because experimental pain
98 is relatively mild, of short duration, escapable, and has no health implications, it is unclear to
99 what extent these effects can be generalised to clinical studies¹⁸, so experimental findings

100 should also be tested in the clinical arena. The study was supported by a Medical Research
101 Council Confidence in Concept grant.

102 **Aim**

103 To explore the user experience, acceptability and analgesic impact of the two active and two
104 passive VR scenarios in healthy adults under experimental pain conditions (a cold pressor
105 test), answering the following research questions:

106 - what is the impact on objective and self-rated measures of pain of each VR scenario?

107 - how do participants perceive and experience each different VR scenario?

108 The ultimate aim was to select two scenarios for improvement and later trial in the clinical
109 setting with burns patients. The University Research Ethics Committee (328-FUR) approved
110 the study.

111 **Methods**

112 Participants

113 Participants (aged 18 or over; English speaking) were drawn from the local student
114 population, with a target sample of 10-15 participants. Adverts with contact details were
115 placed on Campus and on University web platforms. We excluded those with self-reported
116 mental health diagnoses, migraines, nausea, pre-existing painful conditions, such as
117 Fibromyalgia, sports or hand injuries, which were likely to exacerbate or interfere with the
118 pain experience. Exclusions were explained in the information sheet, along with full details
119 of the procedure and participant rights. Informed consent was obtained from 15 volunteers.

120 Materials

121 VR Scenarios: Four scenarios were tested. Two were free-access passive scenarios and two
122 were active scenarios, which were specially developed for the study. Selection and
123 development of scenarios was informed by a prior consultative workshop with two burn
124 survivors and team members, including a games designer, two clinical psychologists with
125 expertise in burn care, an academic clinical psychologist with expertise in burn care, and an
126 academic psychologist with prior experience as a burns nurse. The University Research
127 Ethics Committee approved the workshop (PHE-298). Workshop discussions and activities
128 focused on potential positive VR environments, images, moods and words, aspects to avoid,
129 and generation of VR storyboards. For example, suggestions from the workshop included
130 '*entertainment*', '*variety*', '*immediacy*', '*novelty*' and '*laughter*', but also '*relaxing*' scenarios,
131 images related to '*cold*' and '*nature*', and sounds which '*calm*' or with a '*regular rhythm*' to
132 avoid jarring. Similarly, images related to '*heat*', '*kettles*', '*bright sun*' the colour '*red*' and
133 sounds which were '*upsetting*', '*jumpy*' '*too loud*', '*discordant*' or '*arrhythmic*' were
134 avoided.

135 The four scenarios used were named Henry, Flocker, Blindness and Basket. Henry was a pre-
136 existing passive scenario based on the birthday celebrations of a hedgehog; Flocker was an
137 active scenario developed by the games designer in which the character, controlled by the
138 user, had the tasking of rounding up and herding sheep through obstacles; Blindness was a
139 pre-existing passive scenario based on a person's story of his visual disability; Basket was an
140 energetic active scenario developed by the games designer, based on making basketball shots
141 with varied feedback to engage the user. User control in active scenarios was achieved
142 through head tracking and a simple remote device.

143 VR equipment: An Oculus Rift CV1 headset and PC were used. Experimental pain was
144 administered via a cold pressor test using an iced water tank, with water circulated to

145 maintain a temperature of 4° C, and monitored using a thermometer. This temperature
146 provides an uncomfortable experience without causing tissue damage.

147 Data Collection Booklet: The booklet collected baseline information including demographic
148 and initial pain threshold and tolerance data, pain scores for VR experience using visual
149 analogue scales, and participants' ranking of the VR scenarios after all four exposures. The
150 booklet also contained boxes for participants to add free text comments about their
151 experience, if they wished. The booklet was given to the participant for the duration of their
152 involvement, but they were assisted with its completion by the researcher.

153 Interview Schedule: Short interviews after each scenario aimed to gather further qualitative
154 comments regarding the experience (enjoyment, difficulty, appearance of, immersion in and
155 problems with scenarios, plus suggestions for improvement) and perceived impact on pain
156 and written notes were taken of participant responses.

157 Procedure

158 Trials took place on University premises. On arrival, participants were able to try out a
159 standard VR scenario for comfort and orientation before consenting.

160 Participants pain threshold and pain tolerance were recorded by placing their hand in the iced
161 water for as long as possible. Threshold was the first point at which pain was reported and
162 tolerance was the duration before pain became unbearable and the participant removed their
163 hand from the water (total time minus threshold). Participants' non-dominant hand was used
164 as the dominant hand was required to control the VR. Participants were asked to rate their
165 maximum pain on a pain scale, providing a baseline (no VR) value.

166 Scenarios were ordered differently for each participant, in case habituation effects influenced
167 pain ratings. The non-dominant hand was placed in iced water 30 seconds into the VR

168 scenario. The scenario ran until complete (approx. 5 minutes) or the participant requested to
169 stop. Tolerance timings were recorded for comparison with the baseline, following which
170 booklet and interview data were gathered. The next trial started when participants' hands
171 returned to pre-test temperature. The four trials and interview lasted around one hour in total.

172 Analysis

173 To explore the differences between the VR scenarios a repeated-measures ANOVA or
174 Friedman's test was conducted if the data violated parametric assumptions, with significance
175 set at $p \leq 0.05$. A Kruskal-Wallis test was conducted to analyse the differences between the
176 types of VR (e.g. active, passive, and control), again with significance set at $p \leq 0.05$. Post-hoc
177 analysis was conducted with a Bonferroni correction made. All analysis was conducted using
178 IBM SPSS Statistics Version 24 for Windows (IBM United Kingdom Limited, Hampshire,
179 UK). Qualitative booklet and interview data were analysed for content, identifying common
180 patterns and terms in the data.

181 Results

182 Participants were 10 men and 5 women, ranging in age from 18 – 49 (mean 25).

183 Table 1 presents descriptive results for each the four scenarios, presented by rank, alongside a
184 summary of qualitative comments.

185 TABLE 1 HERE

186 The four scenarios were clearly differentiated by rank, with Basket the most popular.
187 Qualitative comments indicated that, although participants enjoyed the professional
188 appearance of the two passive scenarios, which were already in the public domain, their lack
189 of personal involvement limited impact on pain and distraction. These latter elements were

190 better in the two active scenarios developed by the team, but shortcomings in the appearance
191 sometimes jarred and reduced their effectiveness.

192 Pain Threshold

193 Pain threshold was the point in seconds from the start of the VR scenario at which pain was
194 reported. There was a statistically significant difference in threshold times depending upon
195 the VR scenario that a participant was exposed to, $\chi^2(4) = 15.80$, $p=0.003$. Significant
196 differences in threshold for pain were found between Baseline (median 26 secs) and three VR
197 scenarios: Flocker (median 55 secs, $Z = -2.94$, $p=0.003$), Blindness (median 33 secs, $Z = -$
198 3.18 , $p=0.001$) and Basket (median 59 secs, $Z = -2.81$, $p=0.005$). No other significant
199 threshold differences were found.

200 Pain Tolerance

201 Pain tolerance was the point at which the participant withdrew their hand from the cold water.
202 There was a statistically significant difference in tolerance times depending upon the VR
203 scenario that a participant was exposed to, $\chi^2(4) = 33.67$, $p<0.001$. Significant differences in
204 tolerance of pain were found between baseline (median 57 secs) and Henry (median 300 secs,
205 $Z = -2.93$, $p=0.003$), Flocker (median 300 secs, $Z = -2.85$, $p=0.004$) and Basket (median 300
206 secs, $Z = -2.93$, $p=0.003$). Tolerance of pain was found to be significantly different between
207 Blindness (median 194 secs) and Henry ($Z = -3.20$, $p=0.001$), Flocker ($Z = -3.23$, $p=0.001$)
208 and Basket ($Z = -3.17$, $p=0.002$), but other tolerance differences were not significant.
209 Blindness was the only scenario during which participants were unable to tolerate pain for the
210 full 5 minute test duration.

211 Maximum pain

212 Maximum pain was the score (from 0-100) given by participants to their worst pain after each
213 scenario. Significant differences in maximum reported pain were found between VR
214 scenarios ($F(2.36, 32.98) = 7.06, p=0.002$), but post hoc tests revealed these were only
215 between Henry and Blindness (means 52.53 and 65.27 respectively, $p<0.001$).

216 Immersion and Enjoyment

217 Both immersion and enjoyment were rated out of 10. Significant differences in immersion
218 scores were found between VR scenarios, $\chi^2(3) = 18.02, p<0.001$. Immersions scores were
219 significantly higher in the Henry (median 8, $Z = -2.81, p=0.005$), Flocker (median 8, $Z = -$
220 $2.79, p=0.005$), and Basket (median 8, $Z = -3.19, p=0.001$) VR scenario compared to the
221 Blindness scenario (median 6). Significant differences in enjoyment scores were found
222 between VR scenarios, $\chi^2(3) = 14.31, p=0.003$. Enjoyment scores were significantly higher in
223 the Henry (median 8, $Z = -2.83, p=0.005$), Flocker (median 8, $Z = -2.70, p=0.007$), and
224 Basket (median 8, $Z = -2.90, p=0.004$) VR scenarios compared to the Blindness VR scenario
225 (median 5).

226 Comparisons between types of VR

227 Types of VR were active (Basket and Flocker scenarios), passive (Henry and Blindness
228 scenarios), and control (baseline test). There was found to be a significant difference between
229 the threshold scores depending upon the type of VR, $\chi^2(2) = 16.00, p<0.001$. Post hoc
230 analysis found that pain threshold scores were significantly lower in the control condition
231 (mean, 25 secs, $U=135.00, p=0.012$) and passive scenarios (mean 43.57 secs, $U=44.50,$
232 $p<0.001$) than the active VR scenarios (mean 69.05). There was no significant difference
233 between the control and passive threshold scores ($U=95.50, p=0.02$).

234 There was found to be a significant difference between the tolerance scores depending upon
235 the type of VR, $\chi^2(2) = 11.15$, $p=0.004$. Post hoc analysis found that tolerance scores were
236 significantly higher in the active VR scenario (mean 224.37 secs) compared to the control
237 (mean 122.33 secs, $U=105.00$, $p=0.002$). There was no significant difference found between
238 active and passive VR scenarios (passive mean 173.17, $U=311.50$, $p=0.03$) or control and
239 passive VR scenarios ($U=152.50$, $p=0.08$). There was found to be no significant difference in
240 maximum pain scores between any of the scenarios, $\chi^2(2) = 3.74$, $p=0.15$.

241 **Discussion**

242 Results suggested that, compared to baseline, participants' threshold for and tolerance of pain
243 was best in the two active scenarios, Flocker and Basket. There were no significant
244 differences between these two in maximum pain. Active scenarios significantly extended
245 threshold time compared with both baseline and passive scenarios. Blindness emerged as
246 least effective in controlling pain, and least enjoyable and immersive. Qualitative comments
247 suggested that the content in Henry was perceived to be intended more for children.

248 This study goes some way towards meeting existing recommendations for research into VR¹⁸,
249 such as the suggestion to explore fun and presence as variables which contribute to the
250 effectiveness of VR. Our findings offer some insight into these aspects. Qualitative data
251 suggested that VR, especially where the person was actively involved and competing to gain
252 high scores, was fun. Active VR was ranked higher and gave a greater sense of presence and
253 immersion than passive alternatives. This study didn't compare VR with other interventions
254 for pain, such as hypnosis and CBT, but these are exceptional rather than standard in clinical
255 settings. While these other non-pharmacological distraction techniques are effective, there is
256 wide variability in their use and two thirds of European Burn Centres have reported
257 dissatisfaction with their current analgesia strategies³¹. A recent systematic review showed

258 that non-pharmacological interventions are rarely used in practice³². More could be done to
259 reduce procedural pain, and VR could play a vital role.

260 Results demonstrated that active VR technology was positively received and evaluated under
261 experimental pain conditions. However, the small sample may have contributed to the non-
262 significant results between active and passive scenarios in tolerance and maximum pain. The
263 feasibility of VR within a Burns Unit should now be tested, ideally with inpatients, whose
264 pain may be most acute. Previous work has focused on an outpatient samples³³, with minor
265 injuries or at a later stage of care. Clinical trials are also essential to assess the burden, costs
266 and benefits of new treatments^{34, 35} and to ensure support systems are in place to facilitate
267 their integration into the care setting beyond the end of a research project³⁴. If VR proved as
268 effective in managing perceived pain in clinical settings as was demonstrated under
269 experimental conditions, it may have positive impact on opiate analgesia use, whose side
270 effects include respiratory depression, constipation, sedation, nausea³⁶⁻³⁸. VR could also be
271 used to promote earlier mobilisation after burns²⁶ by allowing patients and clinicians to focus
272 on mobilisation and recovery of full movement, rather than on pain.

273 A strength of our study was user involvement. In developing and selecting scenarios, the
274 potential for a targeted VR environment was discussed between a range of stakeholders,
275 including clinicians and two previous burns patients. Inclusion of burns survivors in
276 designing or conducting research was recommended in a recent report on priorities for burn
277 rehabilitation research²⁶. Some VR studies report considering the applicability to their group
278 of a particular intervention²⁰, and others used specifically designed software²², but few report
279 details of user involvement in the design or decision-making process. Existing evidence has
280 little to say about the aspects which may prove either problematic or useful in VR for burns,
281 so these discussions were novel in helping develop our scenarios. It went some way towards

282 the tailoring suggested by previous literature²⁷. Clinical testing will allow us to explore this
283 aspect further.

284 These results have helped us make decisions regarding further development and selection of
285 scenarios for the clinical trial. The two active scenarios are being developed and improved for
286 use in the clinical setting. However, the experimental findings suggest that neither Blindness
287 nor Henry is likely to prove suitable for the clinical setting. Blindness was ineffective in pain
288 control, so it would be unethical to offer this as an intervention with patients. Henry was
289 more effective but too brief for use in painful procedures such as dressing changes and
290 participants saw it as more suited to children. Alternative forms of passive VR will be chosen
291 for trial. Trials with larger clinical samples and using controlled approaches are
292 recommended by reviewers in the area³². However, our experience suggests that future trials
293 would also be wise to consider mixed methods as inclusion of qualitative responses enables
294 nuanced aspects of the experience to be monitored.

295

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300 added later].

301 **References**

- 302 1. Hoffman HG, Patterson DR, Magula J, et al. Water-friendly virtual reality pain control
303 during wound care. *Int J Clin Psychol* 2004;60(2):189-95.
- 304 2. Pardesi O, Fuzaylov G. Pain Management in Pediatric Burn Patients: Review of Recent
305 Literature and Future Directions. *J Burn Care Res* 2017;38:335-47.
- 306 3. Patterson DR, Sharar SR. Burn Pain. In JD Loeser, SH Butler, CR Chapman et al. (eds.)
307 *Bonica's management of pain*. Philadelphia: Lippincott Williams and Wilkins; 2001, pp. 780-
308 787.
- 309 4. Cherny N, Ripamonti C, Pereira J. et al. Strategies to manage the adverse effects of oral
310 morphine: an evidence-based report. *J Clin Oncol*, 2001;19:2542-54.
- 311 5. Edwards J. Managing wound pain in patients with burns using soft silicone dressings.
312 *Wounds* 2011;7(4):1-4
- 313 6. Hoffman HG, Patterson DR, Carouger GJ et al. Effectiveness of Virtual Reality-Based
314 Pain Control With Multiple Treatments. *Clin J Pain* 2001;17:229-235.
- 315 7. Stoddard FJ, Saxe G, Ronfeldt H et al. Acute stress symptoms in young children with
316 burns. *J Am Acad Child Adolesc Psychiatry* 206;45:87-93.
- 317 8. Macleod R, Shepherd L, Thompson AR. Posttraumatic Stress Symptomatology and
318 Appearance Distress Following Burn Injury: An Interpretative Phenomenological Analysis.
319 *Health Psychol* 2016;35(11):1197-1204.
- 320 9. Berger MM, Davadent M, Marin C, et al. Impact of a pain protocol including hypnosis in
321 major burns. *Burns* 2010;36:639-46.

- 322 10. Mahar PD, Wasiak J, O'Loughlin CJ et al. Frequency and use of pain assessment tools
323 implemented in randomized controlled trials in the adult burns population: a systematic
324 review. *Burns* 2012;38:147-54.
- 325 11. Richardson P, Mustard L. The management of pain in the burns unit. *Burns* 2009;35:921-
326 36.
- 327 12. Melzack R. Pain and the neuromatrix in the brain. *J Dent Educ* 2001;65:1378-1382.
- 328 13. Melzack R. Evolution of the neuromatrix of pain. The Prithvi Raj Lecture: presented at
329 the third World Congress of World Institute of Pain, Barcelona 2004. *Pain Pract* 2005;5:85-
330 94.
- 331 14. Garrett B, Taverner T, Masinde W et al. Rapid Evidence Assessment of immersive
332 Virtual Reality as an Adjunct Therapy in Acute Pain Management in Clinical Practice. *Clin J*
333 *Pain* 2014;30(12):1089-1098.
- 334 15. Gold JI, Belmont KA, Thomas DA. The neurobiology of virtual reality pain attenuation.
335 *Cyberpsychol Behav* 2007;10:536-544.
- 336 16. Hoffman HG, Prothero J, Wells M et al. Virtual chess: the role of meaning in the
337 sensation of presence. *J Hum-Comput Interaction* 1998;10:251-263.
- 338 17. Hoffman HG, Patterson DR, Carougher GJ. Use of virtual reality for adjunctive treatment
339 of adult burn pain during physical therapy: a controlled study. *Clin J Pain* 2000;16(3):244-
340 250.
- 341 18. Malloy KM, Milling LS. The effectiveness of virtual reality distraction for pain reduction:
342 A systematic review. *Clin Psychol Rev* 2010;30:1011-1018.

- 343 19. Farrar JT, Portenoy RK, Berlin JA et al. Defining the clinically important difference in
344 pain outcome measures. *Pain* 2000;88:287-294.
- 345 20. Das DA, Grimmer KA, Sparnon AL et al. (2005) The efficacy of playing a virtual reality
346 game in modulating pain for children with acute burn injuries: A randomised controlled trial.
347 *BMC Pediatrics* 2005;5:1.
- 348 21. Morris LD, Louw QA, Grimmer-Somers K. The Effectiveness of Virtual Reality on
349 Reducing Pain and Anxiety in Burn Injury Patients: A Systematic Review. *Clin J Pain*
350 2009;25(9):815-26.
- 351 22. Hoffman HG, Patterson DR, Seibel E et al. Virtual Reality Pain Control During Burn
352 Wound Debridement in the Hydrotank. *Clin J Pain* 2008;24(4):299-304.
- 353 23. Mott J, Bucolo S, Cuttle L et al. The efficacy of an augmented virtual reality system to
354 alleviate pain in children undergoing burns dressing changes: A randomised controlled trial.
355 *Burns* 2008;34:803-8.
- 356 24. Tashjian VC, Mosadeghi S, Howard AR et al. Virtual Reality of Management of Pain in
357 Hospitalized Patients: Results of a Controlled Trial. *JIMR Health* 2017;4(1):e9
- 358 25. Jones, T., Moore, T., Choo, J. The impact of virtual reality on chronic pain. *PLoS ONE*
359 2016;11(12):e0167523.
- 360 26. Schneider JC. Rehabilitation Research Priorities: The Next 10 Years. *J Burn Care Res*
361 2017;38:e635-e637.
- 362 27. Hua Y, Qiu R, Yao W et al.. The Effect of Virtual Reality Distraction on Pain Relief
363 During Dressing Changes in Children with Chronic Wounds on Lower Limbs. *Pain Manage*
364 *Nurs* 2015;16(5):685-691.

- 365 28. Dahlquist LM, McKenna KD, Jones KK et al. Active and passive distraction using a
366 head-mounted display helmet on cold pressor pain in children. *Health Psychol* 2007;26:794-
367 801.
- 368 29. Hoffman HG, Seibel EJ, Richards TL et al. Virtual reality helmet display influences the
369 magnitude of virtual reality analgesia. *J Pain* 2006;7:843-850.
- 370 30. Patterson DR, Hoffman HG, Palacios AG et al. Analgesic effects of posthypnotic
371 suggestions and virtual reality distraction on thermal pain. *J Abnorm Psychol* 2006;115:834-
372 841.
- 373 31. Retrouvey H, Shahrokhi S. Pain and the Thermally Injured patient - A Review of Current
374 Therapies. *J Burn Care Res* 2015;36:315-323.
- 375 32. Sheffler M, Koranyi S, Meissner W et al. Efficacy of non-pharmacological interventions
376 for procedural pain relief in adults undergoing burn wound care: A systematic review and
377 meta-analysis of randomized controlled trials. *Burns* 2017.
- 378 33. Ford CG, Manegold EM, Randall CL et al. Assessing the feasibility of implementing low-
379 cost virtual reality therapy during routine burn care. *Burns* 2017,
380 <https://doi.org/10.1016/j.burns.2017.11.020>.
- 381 <https://doi.org/10.1016/j.burns.2017.11.019>.
- 382 34. Markus LA, Willems KE, Maruna CC et al. Virtual reality: Feasibility of implementation
383 in a regional burn center. *Burns* 2009;35:967-69.
- 384 35. Morris LD, Louw QA, Crous LC. Feasibility and potential effect of a low-cost virtual
385 reality system on reducing pain and anxiety in adult burn injury patients during physiotherapy
386 in a developing country. *Burns* 2010;36:859-64.

- 387 46. Christie MJ, Connor M, Vaughan CW et al. Cellular actions of opioids and other
388 analgesics: implications for synergism in pain relief. *Clin Exp Pharmacol Physiol*
389 2000;27:520-3.
- 390 37. Rittner HL, Roewer N, Brack A. The clinical (ir)relevance of opioid-induced immune
391 suppression. *Curr Opin Anaesthesiol* 2010;23:588-92.
- 392 38. Maani CV, Hoffman HG, Fowler M et al. Combining ketamine and virtual reality pain
393 control during severe burn wound care: one military and one civilian patient. *Pain Med*
394 2011;12:673-8.
- 395