Clinical efficacy of virtual reality for acute procedural pain management: A systematic review and meta-analysis

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Abstract

Background

Acutely painful procedures are commonplace. Current approaches to pain most often involve pharmacotherapy, however, there is interest in virtual reality (VR) as a non-pharmacological alternative. A methodologically rigorous systematic review and meta-analysis is lacking.

Methods

Following PRISMA guidelines, we searched the Cochrane Library, Ovid MEDLINE, Embase, CINAHL, ERI C, NIHR Centre for Review and Dissemination, Proquest, the System for Information on Grey Literature in Europe and the WHO International Clinical Trials Registry Platform from inception to 5 November 2017. Included studies were randomised with an experimental trial design, included a non-VR control group and examined the efficacy of VR with regards to an acutely painful clinical intervention. Bias was assessed along Cochrane guidelines, with performance bias not assessed due to the non-blindable nature of VR. We extracted summary data for maximal pain score and used standard mean difference DerSimonian-Laird random-effects meta-analysis (RevMan 5.3). This review was prospectively registered (PROSPERO CRD42017058204).

Findings

Of the 12,450 studies identified, 20 studies were eligible for the systematic review. No trials reported in sufficient detail to judge their risk of bias, and 10 studies were at high risk of bias in at least one domain. 16 studies (9 randomised controlled trials, 7 crossover studies) examining 656 individuals were included in quantitative synthesis. Pain scales were heterogeneous, but mostly employed 100-point scales. Across all trials, meta-analysis was suggestive of a -0.49 (95%CI -0.83 to -0.41, p = 0.006) standardised mean difference reduction in pain score with VR. However there was a high degree of statistical heterogeneity ($\chi^2$...
p<0.001, $I^2 = 81\%$, 95%CI for $I^2 = 70–88\%$), driven by randomised studies, with substantial clinical heterogeneity.

**Conclusion**

These data suggest that VR may have a role in acutely painful procedures, however included studies were clinically and statistically heterogenous. Further research is required to validate findings, establish cost efficacy and optimal clinical settings for usage. Future trials should report in accordance with established guidelines.

**Introduction**

The management of acute pain related to healthcare interventions remains a major global healthcare challenge[1], existing at the convergence of the consumer-driven desire for patient empowerment and physician-driven desire for better outcomes[2]. For most procedures, pharmacological approaches remain the mainstay although these have significant drawbacks including imprecise titration, narrow therapeutic windows, adverse side effects, the potential for drug misuse and cost[3]. Approaches that avoid pharmacotherapy and associated interventions such as monitoring could therefore be of benefit in a multimodal armamentarium[1].

Virtual reality (VR) is a developing technology which has garnered significant lay and medical attention as its cost and accessibility and quality have favourably converged. Briefly, virtual reality is a computer-generated depiction of an immersive environment which can be viewed through a headset[4]. By providing distraction, this approach is hypothesized to reduce pain by pharmacological-sparing means[4].

However, there is no comprehensive, high-quality systematic review that specifically assesses the efficacy of virtual reality on acutely painful healthcare interventions, nor has there been any quantitative data synthesis on this topic. We therefore conducted a systematic review and meta analysis to appraise the quality of published literature and to synthesize data for acute pain scores.

**Methods**

**Study selection, data sources and search strategy**

We defined VR as an intervention with an immersive, 3D display that excluded the external (real-world) environment. Studies were included if they were published in a peer reviewed journal, examined the effect of VR on an acutely painful clinical intervention and included a pain score as an outcome measure. Studies were excluded if there was no acutely painful clinical intervention, no non-VR control group or non-VR sequence or lacked an experimental design. This review and protocol was prospectively registered on PROSPERO (CRD42017058204).

Following PRISMA guidelines[5], we identified studies through reviews of the Cochrane Library, Ovid MEDLINE (1975–5 November 2017), Embase, CINAHL, ERIC, NIHR Centre for Review and Dissemination and Proquest (PRISMA checklist: S1 Checklist). The search strategy included the terms “virtual reality”, “simulation”, and “pain”: the full strategy is in S1 Appendix. For completeness, we searched the System for Information on Grey Literature in Europe and WHO International Clinical Trials Registry Platform. No language restrictions were applied. Non-English articles were machine translated and screened for inclusion.
Automatic de-duplication was performed in EndNote X8.1 (Clarivate Analytics, Philadelphia USA), and manually verified by an author (EC). Citation lists of included studies were hand checked to ensure completeness. Screening was performed by two authors (SF, RS) and disagreements resolved consensus discussion with a third author (EC).

**Data analysis**

Summary data was extracted by one author (PL) and confirmed by another author (EC). For parallel group randomised trials (RCTs), the Cochrane risk of bias assessment tool was used [6]. For crossover trials, a published modification of this tool was employed[7]. Two authors (PL, EC) independently assessed risk of bias, with verification by the other two authors (SF, RS). Disagreements were resolved by consensus.

The following information was extracted from each study: first author name, study location, source and number of participants, ethics approval, age, sex, study design, and virtual environment and nature of painful stimulus. The primary outcome was the mean difference in maximum self-rated pain during the healthcare intervention (with and without VR). If the study included interventions other than VR, only data relevant to pain scores with and without VR was extracted. If the study had multiple treatment periods, the first was extracted. If data were not reported in an analysable format, summary measures were reconstructed from published individual patient data, or authors approached. Where data were missing, first authors were contacted twice by e-mail at one-month intervals, and if data were still missing, senior authors were contacted similarly; if authors had moved, attempts were made to contact them at their new institutions.

It was anticipated that crossover trials would pose difficulties and thus employed Elbourne’s “ideal” method (within-individual data)[8]. In brief, correlation coefficient was sought and missing data imputed by Elbourne’s published method[8]. We used standard mean difference (SMD) DerSimonian-Laird random-effects meta-analysis (RevMan 5.3, Copenhagen) to estimate effect size on pain.

Variability within studies is reported in forest plots and incorporated into the meta-analysis (I²), and interpreted in accordance with standard guidelines[9]. To quantify uncertainty in the I² statistic, we calculated heterogeneity in I² as recommended[10] using heterogi[11] in Stata 14.2 (College Station, Texas). The calculation requires at least two degrees of freedom.

Risk of bias was assessed but other no methods to account for this were employed. *A priori*, due to the obvious nature of VR, performance bias was not assessed. Detection bias was assessed as high if an unblinded investigator assessed outcomes, low if a blinded observer assessed outcomes and unclear if self-administered instruments were used. Funnel plots were inspected for asymmetry to assess for sources of bias including publication bias[12].

**Role of the funding source**

There was no funding source for this study. All authors had full access to data and the corresponding author takes responsibility for the decision to submit to publication.

**Results**

12,450 studies were screened with 11,150 excluded, leaving 48 full text articles (Fig 1). 28 studies were excluded (predominantly because they examined non-clinical procedures), leaving 20 for qualitative synthesis.

Study characteristics are detailed in Table 1. 11 were RCTs[13–23] and 9 were crossover studies[24–32], studying 776 subjects. 10 studies were performed in the setting of burns wound care[16,18–20,25–29,32], 3 studied physiotherapy in the setting of burns[24,30,31], 5
PRISMA 2009 Flow Diagram

Records identified through database searching (n = 12,439)

Additional records identified through other sources (n = 11)

Records after duplicates removed (n = 11,198)

Records screened (n = 11,198)
96% agreement between screeners

Records excluded (n = 11,150)

Full-text articles excluded (n = 28)
Not randomised (n = 3)
Preliminary results only (n = 2)
Not VR (n = 3)
Non-clinical procedure pain (n = 20)

Studied included in qualitative synthesis (n = 20)

Studies included in quantitative synthesis (meta-analysis) (n = 16)

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.
Table 1. Included studies.

| Source           | Population (age range, years or mean ± std dev, females: males) | N   | Procedure                  | Setting     | Pain outcome measures | Virtual reality environment, headset type, interaction method | Main findings for VR group versus control group |
|------------------|-----------------------------------------------------------------|-----|-----------------------------|-------------|-----------------------|-------------------------------------------------------------|------------------------------------------------|
| **Randomised controlled trials** |                                                                  |     |                             |             |                       |                                                             |                                                |
| Gershon 2004     | 7–19, 29:30                                                     | 59  | Port access                 | USA, outpatient | VAS, CHEOPS [33]   | Virtual Gorilla, interactive game, HMD via PC, joystick     | No difference in self-rated VAS*, parent VAS or nurse-rated VAS, lower nurse-rated CHEOPS, |
| Gold 2006        | 8–12, 8:12                                                     | 20  | Peripheral intravenous cannula | USA, outpatient | FPS-R [34], Wong-Baker FACES [35] | Street Luge, interactive game, HMD via laptop, inertial tracking, | No difference in child-rated FPS-R* or child-rated Wong-Baker FACES |
| Gold 2017        | 10–21, 72:71                                                   | 143 | Venepuncture                 | USA, outpatient | VAS, CAS, FPS-R | Bear Blast, interactive game, HMD-mounted phone, gaze tracking, | After controlling for baseline pain, no difference in self-rated VAS or CAS, but lower self-rated FPS-R* |
| Guo 2015         | 18–65, 13:85                                                   | 98  | Hand injury wound care      | China, outpatient | VAS | Afanda, non-interactive video, HMD via computer | Lower self-rated VAS* after dressing |
| JahaniShoorab 2015 | 18–34, 30:0                                               | 30  | Episiotomy repair           | Iran, inpatient | NPRS | Dolphins and Whales, non-interactive video, HMD via blu-ray player, gaze-tracking | Lower NRPS* during skin repair (rater not stated) |
| Jeffs 2014       | 10–17, 9:19                                                   | 28  | Burns wound care            | USA, outpatient | APPT-WGRS [36] | SnowWorld, interactive game, HMD via PC, trackball | Lower estimated self-rated APPT-WGRS* |
| Kipping 2012     | 11–17, 13:28                                                  | 41  | Burns wound care            | Australia, inpatient | VAS, FLACC | Chicken Little/Need for Speed, interactive game, HMD via PC, joystick | No difference in adolescent or caregiver reported VAS, but reduction in nurse-rated FLACC at dressing removal^ |
| Konstantatos 2009 | 18–80, not stated                                        | 88  | Burns wound care            | Australia, inpatient | VAS | Virtual Medicine, non-interactive video, HMD via DVD player | Higher self-rated VAS* in VR group |
| Sander Windt 2002 | 10–19, 14:16                                              | 30  | Lumbar puncture             | USA, inpatient | VAS | Escape, non-interactive video, HMD (PC/DVD not stated) | Lower self-rated VAS^ |
| Walker 2014      | 18–70, 0:43                                                   | 43  | Rigid cystoscopy            | USA, outpatient | VAS | SnowWorld, interactive game, HMD (PC not stated), trackball | No difference in self-rated VAS* or proceduralist-rated discomfort VAS |
| Wolitzky 2005    | 7–14, 8:12                                                   | 20  | Port access                 | USA, outpatient | VAS, CHEOPS | Virtual Gorilla, interactive game, HMD via PC, joystick | No differences in VAS* (rater unclear), reduction in first-author rated CHEOPS |
| **Crossover**    |                                                                  |     |                             |             |                       |                                                             |                                                |
| Carrougher 2009  | 29–57, 4:35                                                   | 39  | Burns physiotherapy         | USA, inpatient | GRS | SnowWorld, interactive game, HMD (PC not stated), keyboard | Reduction in worst self-rated GRS* |
| Chan 2007        | 6.5±2.3, 1:7                                                  | 8   | Burns wound care            | Taiwan, inpatient | FACES | Ice Cream Factory, interactive game, HMD via PC, mouse | Reduction in self-rated FACES* |
| Das 2005         | 5–18, 3:6                                                    | 9   | Burns wound care            | Australia, inpatient | FACES | Custom game, interactive game, HMD via PC, mouse | Reduction in self-rated FACES^ |
| Hoffman 2008     | 9–40, 0:11                                                   | 11  | Burns wound care            | USA, inpatient | GRS | SnowWorld, interactive game, HMD via PC, joystick, interactive | Reduction in self-rated GRS* |

(Continued)
further studies concerned needle-related procedures (largely venous access) [13–15, 21, 23], and 2 examined minor surgical procedures [17, 22]. Studies were predominantly conducted in English speaking countries (USA (n = 12), Australia (n = 3), South Africa (n = 1)). 11 trials were performed in the inpatient setting, and the remainder were outpatient studies. Pain measurement instruments were heterogeneous, but mostly employed 100-point scales. 10 studies demonstrated high risk of bias in at least 1 domain (Tables 2 and 3). No trials reported in sufficient detail that their risk of bias could be sufficiently assessed across all

Table 1. (Continued)

| Source          | Population (age range, years or mean ±std dev, females: males) | N | Procedure            | Setting               | Pain outcome measures | Virtual reality environment, headset type, interaction method | Main findings for VR group versus control group |
|-----------------|-----------------------------------------------------------------|---|----------------------|-----------------------|----------------------|---------------------------------------------------------------|------------------------------------------------|
| Maani 2011      | 20–27, 0:12                                                     | 12| Burns wound care     | USA, inpatient        | GRS                  | SnowWorld, interactive game, HMD via laptop, mouse           | Reduction in self-rated GRS^                      |
| McSherry 2017   | 38.4±15.5, 5:13                                                 | 18| Wound care (various) | USA, inpatient        | VNS[37]              | SnowWorld, interactive game, HMD via laptop, mouse           | Reduction in self-rated VNS^                      |
| Morris 2010     | 23–54, 3:8                                                     | 11| Burns physiotherapy  | South Africa, outpatient | NPRS                | Chicken Little, interactive game, HMD via PC, joystick       | Reduction in self-rated NPRS^                     |
| Schmitt 2011    | 6–19, 10:44                                                    | 54| Burns physiotherapy  | USA, inpatient        | GRS                  | SnowWorld, interactive game, HMD via laptop, keyboard/mouse | Reduction in self-rated GRS^                     |
| Van Twillert 2007 | 8–65, 7:12                                                  | 19| Burns wound care     | Netherlands, inpatient | VAT                  | SnowWorld, interactive game, HMD (PC not stated), keyboard/mouse | Reduction in self-rated VAT^                     |

Total n 776

VAS, visual analogue scale; CHEOPS, Children’s Hospital of Eastern Ontario Pain Scale; FPS-R, Faces Pain Scale Revised; Wong-Baker FACES; CAS, colored analogue scale, NPRS, numeric pain rating scale; APPT-WGRS, adolescent pediatric pain tool word graphic rating scale; GRS, graphical rating scale; VNS, verbal numeric scale; VAT, visual analogue thermometer; HMD, head mounted device; PC, personal computer; DVD, digital video disc.

* denotes meta-analysed outcome.

^ data unavailable for meta-analysis.

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Table 2. Bias assessment for randomised controlled trials.

|                | Randomisation sequence generation | Allocation concealment | Performance bias | Detection bias | Attrition bias | Selective reporting |
|----------------|----------------------------------|------------------------|------------------|----------------|----------------|--------------------|
| Gershon 2004   | +                                | ?                      | n/a              | ?              | +              | -                  |
| Gold 2006      | ?                                | ?                      | n/a              | ?              | +              | +                  |
| Gold 2017      | +                                | +                      | n/a              | ?              | +              | ?                  |
| Guo 2015       | ?                                | ?                      | n/a              | ?              | +              | +                  |
| JahaniShoorab 2015 | ?                         | ?                      | n/a              | ?              | +              | +                  |
| Jeffs 2014     | +                                | +                      | n/a              | +              | +              | -                  |
| Kipping 2012   | +                                | ?                      | n/a              | ?              | +              | +                  |
| Konstantatous 2009 | +                       | ?                      | n/a              | ?              | +              | =                  |
| Sander-Windt 2002 | ?                        | ?                      | n/a              | ?              | +              | +                  |
| Walker 2014    | +                                | ?                      | n/a              | ?              | +              | ?                  |
| Wolitzky 2005  | ?                                | ?                      | n/a              | ?              | +              | -                  |

Legend: — high risk of bias; + low risk of bias; ? unclear risk of bias.

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domains. No trials were prospectively registered and only four studies\cite{17,19,20,31} mentioned CONSORT\cite{38} reporting guidelines. Incomplete reporting or selective reporting was judged at unclear or high risk of bias in 9 studies.

All trials had short follow up periods and thus attrition bias was generally low. 9/20 studies did not adequately describe their randomisation sequence generation, and 9/11 randomised trials did not describe their allocation concealment in sufficient detail to be assessable.

Data were generally not reported in sufficient detail for detection bias to be assessable, and only one study was assessed at low detection bias risk.

One trial\cite{26} used a crossover design where pain was assessed as being at high risk of being different between baseline and intervention, and was therefore excluded from analysis. No crossover trials specifically reported carry-over effects.

Three further studies were excluded from meta-analysis due to missing data (one group of authors did not respond, one group had destroyed data in accordance with legislation retention requirements, and one group could not provide data due to workload constraints (personal communications)). The meta-analysis therefore consisted of 16 studies for meta-analysis: 9 RCT and 7 crossover, involving 656 individuals (Fig 2).

Statistical heterogeneity\cite{6} was high for RCTs (n = 9, $\chi^2 p < 0.001$, I^2 88%, 95%CI for I^2 80–93%), low for crossover studies but with a wide confidence interval for I^2 (n = 6, $\chi^2 p = 0.79$, I^2 20%, 95%CI for I^2 0–64%) and considerable overall (n = 16, $\chi^2 p < 0.001$, I^2 81%, 95%CI for I^2 70–88%). The relatively low number of studies available limited the assessment of the funnel plot. However, no evidence of asymmetry was seen on visual inspection and in particular studies were not absent from the bottom right corner, which would have suggested publication bias (S1 Fig\cite{12,39}).

Meta-analysis of all studies was suggestive of a beneficial effect for VR, with a standardised mean difference pain score reduction of -0.49 (95%CI -0.83 to -0.14, p = 0.006)(Fig 2).

In post-hoc per-procedure subgroup analysis, VR had no effect for minor surgical procedures (SMD -0.65, -1.48 to 0.18, p = 0.13) or burns wound care (SMD -0.46, -1.36 to 0.44, p = 0.31)(S2 Fig). There appeared to be a favourable effect for VR on pain in needles (SMD -0.66, 95%CI -0.56 to -0.04, p = 0.02), and in burns physical therapy (SMD -0.53 95%CI -0.81

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**Table 3. Bias assessment for crossover trials.**

|                | Appropriate crossover design | Adequate randomisation | Carry-over effect | Unbiased data | Allocation concealment | Detection bias | Performance bias | Incomplete outcome data | Selective outcome reporting |
|----------------|------------------------------|------------------------|-------------------|---------------|------------------------|---------------|-----------------|------------------------|-----------------------------|
| Carroughe 2009 | +                            | ?                      | ?                 | +             | ?                      | n/a           | +               | +                      | +                           |
| Chan 2007      | +                            | +                      | ?                 | +             | ?                      | n/a           | +               | +                      | +                           |
| Das 2005       | -                            | +                      | ?                 | +             | ?                      | n/a           | -               | -                      | ?                           |
| Hoffman 2008   | +                            | ?                      | ?                 | +             | ?                      | n/a           | +               | +                      | +                           |
| Maani 2011     | +                            | ?                      | ?                 | +             | ?                      | n/a           | +               | +                      | +                           |
| McSherry 2017  | +                            | +                      | ?                 | +             | +                      | n/a           | +               | +                      | +                           |
| Morris 2010    | +                            | +                      | ?                 | +             | ?                      | n/a           | +               | +                      | +                           |
| Schmitt 2011   | +                            | +                      | ?                 | +             | ?                      | n/a           | -               | -                      | +                           |
| Van Twillert 2007 | +                      | ?                      | ?                 | +             | ?                      | n/a           | -               | +                      | +                           |

Legend:— high risk of bias; + low risk of bias;? unclear risk of bias.

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| Study or Subgroup          | Virtual reality | Control | Std. Mean Difference IV, Random, 95% CI |
|---------------------------|----------------|---------|----------------------------------------|
| Gershon 2004              | 13.2           | 22      | -0.12 [-0.71, 0.48]                    |
| Gold 2006                 | 1.8            | 10      | -0.27 [-1.15, 0.61]                    |
| Gold 2017                 | 1.4            | 70      | -0.31 [-0.64, 0.02]                    |
| Guo 2015                  | 26.3           | 49      | -1.93 [-2.41, -1.45]                   |
| JahaniShoorab 2015        | 16.7           | 15      | -1.11 [-1.89, -0.34]                   |
| Jeffs 2014                | 38.4           | 10      | 0.69 [-0.28, 1.65]                     |
| Konstantatos 2009         | 37             | 43      | 0.59 [0.10, 1.09]                      |
| Walker 2014               | 59             | 22      | -0.26 [-0.86, 0.34]                    |
| Woltzky 2005              | 12             | 10      | -0.68 [-1.58, 0.23]                    |
| Total (95% CI)            | 249            | 253     | -0.39 [-0.96, 0.18]                    |

Heterogeneity: Tau² = 0.65; Chi² = 6.67, df = 8 (P < 0.00001); I² = 88%
Test for overall effect: Z = 1.34 (P = 0.18)

| Study or Subgroup          | Virtual reality | Control | Std. Mean Difference IV, Random, 95% CI |
|---------------------------|----------------|---------|----------------------------------------|
| Carrougher 2009           | -0.5378        | 0.2307  | -0.54 [-0.99, -0.09]                   |
| Chan 2007                 | 0.4396         | 0.5079  | 0.44 [-0.56, 1.44]                     |
| Hoffman 2008              | -1.0562        | 0.4612  | -1.06 [-1.96, -0.15]                   |
| Maani 2011                | -0.7677        | 0.4259  | -0.77 [-1.60, 0.07]                    |
| Morris 2010               | -0.6701        | 0.4407  | -0.67 [-1.53, 0.19]                    |
| Schnitt 2011              | -0.5011        | 0.1956  | -0.50 [-0.88, -0.12]                   |
| Van Twillert 2007         | -1.0776        | 0.3497  | -1.08 [-1.76, -0.39]                   |
| Total (95% CI)            | 154            | 154     | -0.61 [-0.88, -0.33]                   |

Heterogeneity: Tau² = 0.03; Chi² = 7.54, df = 6 (P = 0.27); I² = 20%
Test for overall effect: Z = 4.33 (P < 0.0001)

**Overall effect**

| Study or Subgroup          | Virtual reality | Control | Std. Mean Difference IV, Random, 95% CI |
|---------------------------|----------------|---------|----------------------------------------|
| Carrougher 2009           | -0.5378        | 0.2307  | -0.54 [-0.99, -0.09]                   |
| Chan 2007                 | 0.4396         | 0.5079  | 0.44 [-0.56, 1.44]                     |
| Gershon 2004              | -0.1157        | 0.3018  | -0.12 [-0.71, 0.48]                    |
| Gold 2006                 | -0.2687        | 0.4497  | -0.27 [-1.15, 0.61]                    |
| Gold 2017                 | -0.3123        | 0.1683  | -0.31 [-0.64, 0.02]                    |
| Guo 2015                  | -1.9319        | 0.2463  | -1.93 [-2.41, -1.45]                   |
| Hoffman 2008              | -1.0562        | 0.4612  | -1.06 [-1.96, -0.15]                   |
| JahaniShoorab 2015        | -1.1145        | 0.3964  | -1.11 [-1.89, -0.34]                   |
| Jeffs 2014                | 0.6858         | 0.4917  | 0.69 [-0.28, 1.65]                     |
| Konstantatos 2009         | 0.5892         | 0.2205  | 0.59 [0.16, 1.02]                      |
| Maani 2011                | -0.7677        | 0.4259  | -0.77 [-1.60, 0.07]                    |
| Morris 2010               | -0.6701        | 0.4407  | -0.67 [-1.53, 0.19]                    |
| Schnitt 2011              | -0.5011        | 0.1956  | -0.50 [-0.88, -0.12]                   |
| Van Twillert 2007         | -1.0776        | 0.3497  | -1.08 [-1.76, -0.39]                   |
| Walker 2014               | -0.2594        | 0.3065  | -0.26 [-0.86, 0.34]                    |
| Woltzky 2005              | -0.6774        | 0.4629  | -0.68 [-1.58, 0.23]                    |
| Total (95% CI)            | 100.0%         | 100.0%  | -0.49 [-0.83, -0.14]                   |

Heterogeneity: Tau² = 0.38; Chi² = 78.24, df = 15 (P < 0.00001); I² = 81%
Test for overall effect: Z = 2.74 (P = 0.006)

Fig 2. Meta-analysis of the efficacy of virtual reality in acutely painful procedures.

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to -0.26, p < 0.001, although these subgroups enrolled limited numbers of patients (227 and 104 participants respectively).

Statistical heterogeneity assessment was often limited by the relatively few studies present, and reflected in wide I² confidence intervals. For minor surgical procedures (n = 2 studies), some heterogeneity was present (χ² p = 0.09, I² 66%, 95% CI for I² not calculated as too few studies), and for burns wound care (n = 7 studies), there was considerable heterogeneity (χ² p < 0.001, I² 92%, 95% CI for I² 85–95%). Though the χ² test indicated no evidence of heterogeneity for needles (n = 4 studies, χ² p = 0.79, I² 0%, 95% CI for I² 0–85%) or for burns physical therapy (n = 3 studies, χ² p = 0.94, I² 0%, 95% CI for I² 0–90%), the confidence intervals for I² were broad.

Discussion

This systematic review appraises the efficacy of virtual reality for acutely painful clinical procedures, finding that studies were generally at high risk of bias. In meta-analysis, VR appeared to reduce pain in comparison with control, and in post-hoc analysis, the benefit was limited to burns physical therapy and needles.

Applying published, well-accepted criteria, 10/20 studies were at high risk of bias in one or more domain, and no trial reported completely enough for their risk of bias to be completely evaluated. No studies were prospectively registered, and the risk of incomplete or selective outcome reporting was unclear or high in 9 studies. Only four studies reported according to CONSORT guidelines[38].

Meta-analysis indicated a positive effect of VR (SMD -0.49, 95% CI -0.83 to -0.41, p = 0.006) on pain, although the strength of this finding was limited by significant clinical and statistical heterogeneity. Statistical heterogeneity was generally high. This was likely due at least in part to differences in differences in study design and study populations, as well as small study numbers. We chose random-effects meta-analysis to synthesize data in this setting. Although the overall effect may be interpreted by convention as a 'medium' effect size[40], benefits appear to differ across different procedural subtypes, with no statistically significant evidence for burns wounds care or minor surgical procedures. Positive effects were driven by needles studies and burns physical therapy studies, raising the possibility that the effect of VR may vary according to study population and clinical scenario. Subgroup analyses were based on small numbers of studies. Importantly, the results of this systematic review and meta-analysis are based on less than 1,000 patients in total, with post-hoc subgroup analyses, so findings require confirmation. Before widespread clinical usage of VR can be recommended, large methodologically rigorous studies validating and extending these findings are required.

This study has limitations. VR is a non-blindable intervention that creates methodological issues in bias assessment. Performance bias is un-assessable, and detection bias is difficult to assess, thus we a priori defined risk categories. Measures to reduce detection bias can include using independent assessors for study outcomes[6], however, this may be logistically difficult and in paediatric subjects particularly, the patient is at risk of un-blinding the assessor. No crossover studies assessed for carryover effects. However, it seems likely that VR would be reversible and short lived and thus unlikely that VR would have a persistent effect in this clinical context. In addition, study populations were heterogenous, and the precise nature of the hardware and software employed in the VR intervention varied.

We treated VR as a homogenous intervention, although the VR environments and hardware used differed. Even if individual patient data were available, it is unlikely that we would have sufficient statistical power to separate differences between different VR types given significant confounding would exist due to study design, population, and procedure type.
Strengths of our study include a clear clinical question, prospectively registered protocol, thorough search strategy, and the use of high-quality, standardised assessment criteria with more than one assessor at each stage of the review process. We deliberately restricted our selection criteria to clinical studies that were pertinent to our clinical question to maximise external validity. No prior reviews have specifically addressed the clinical question we sought to assess. Existing reviews have not employed a systematic methodology[4], located fewer studies[41], have not performed quantitative data synthesis[42,43], or have focused on special populations[44]. The conclusion of our risk of bias assessment is broadly similar to Garrett[4], inasmuch as we found few trials to be at low risk of bias. The conclusions of our meta-analysis are broadly similar but of a lesser magnitude to Kenney[41], who found a large effect size for VR for painful stimuli in a different group of studies.

Conclusion

In summary, there is early evidence to suggest that VR is effective for burns physical therapy and needles. However, the quality of the underlying evidence is limited and statistically heterogeneous. Thus, prior to widespread adoption of VR, there is a need for further, high-quality studies to validate findings. Trials should be prospectively registered, and reporting should be along CONSORT guidelines to minimise bias. Further studies could include cost-efficacy outcomes, and investigate the role of VR in other acutely painful procedures.

Supporting information

S1 Checklist. PRISMA checklist.

S1 Appendix. Search strategy. Search executed on 5 November 2017.

S1 Fig. Funnel plot.

S2 Fig. Post-hoc procedural type meta-analysis.

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References

1. Upp J, Kent M, Tighe PJ. The Evolution and Practice of Acute Pain Medicine. Pain Med. 2013; 14: 124–144. https://doi.org/10.1111/pme.12015 PMID: 23241132

2. Tighe P, Buckenmaier CC, Boezaart AP, Carr DB, Clark LL, Herring AA, et al. Acute Pain Medicine in the United States: A Status Report. Pain Med Malden Mass. 2015; 16; 1806–1826.

3. Frieden TR, Houry D. Reducing the Risks of Relief—The CDC Opioid-Prescribing Guideline. N Engl J Med 2016; 374: 1501–1504. https://doi.org/10.1056/NEJMp1515917 PMID: 26977701

4. Garrett D, Liberati A, Tetzlaff J, Altman DG, Group TP. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLOS Med. 2009; 6: e1000097. https://doi.org/10.1371/journal.pmed.1000097 PMID: 19621072

5. Higgins JPT, Altman DG, Tetzlaff J, Moher D, Oxman AD, et al. The Cochrane Collaboration’s tool for assessing risk of bias in randomised trials. BMJ. 2011; 343: d5928. https://doi.org/10.1136/bmj.d5928 PMID: 22008217

6. Ding H, Hu GL, Zheng XY, Chen Q, Threapleton DE, Zhou ZH. The Method Quality of Cross-Over Studies Involved in Cochrane Systematic Reviews. PLOS ONE. 2015; 10: e0120519. https://doi.org/10.1371/journal.pone.0120519 PMID: 25867772

7. Elbourne DR, Altman DG, Curtin F, Worthington HV, Vail A. Meta-analyses involving cross-over trials: methodological issues. Int J Epidemiol. 2002; 31: 140–149. PMID: 11914310

8. Gershon J, Zimand E, Pickering M, Rothbaum BO, Hodges L. A pilot and feasibility study of virtual reality as a distraction for children with cancer. J Am Acad Child Adolesc Psychiatry. 2004; 43: 1243–1249. https://doi.org/10.1097/01.chi.0000135621.23145.05 PMID: 15381891

9. Gold JI, Kim SH, Kant AJ, Joseph MH, Rizzo AS. Effectiveness of virtual reality for pediatric pain distraction during i.v. placement. Cyberpsychology Behav Impact Internet Multimed Virtual Real Behav Soc. 2006; 9: 207–212. https://doi.org/10.1089/cpb.2006.9.207 PMID: 16640481

10. Guo C, Deng H, Yang J. Effect of virtual reality distraction on pain among patients with hand injury undergoing dressing change. J Clin Nurs. 2015; 24: 115–120. https://doi.org/10.1111/jocn.12626 PMID: 24899241

11. JahaniShoorab N, EbrahimzadehZagami S, Nahvi A, Mazloum SR, Golmakani N, Talebi M, et al. The Effect of Virtual Reality on Pain in Primiparity Women during Episiotomy Repair: A Randomized Clinical Trial. Iran J Med Sci. 2015; 40: 219–224. PMID: 25999621

12. Jeffs D, Dorman D, Brown S, Files A, Graves T, Kirk E, et al. Effect of Virtual Reality on Adolescent Pain During Burn Wound Care. J Burn Care Res. 2014; 35: 395–408. https://doi.org/10.1097/BCR.000000000000019 PMID: 24823326

13. Kipping B, Rodger S, Miller K, Kimble RM. Virtual reality for acute pain reduction in adolescents undergoing burn wound care: A prospective randomized controlled trial. Burns. 2012; 38: 650–657. https://doi.org/10.1016/j.burns.2011.11.010 PMID: 22348801

14. Konstantatos AH, Angliss M, Costello V, Cleland H, Stafrace S. Predicting the effectiveness of virtual reality relaxation on pain and anxiety when added to PCA morphine in patients having burns dressings changes. Burns. 2009; 35: 491–499. https://doi.org/10.1016/j.burns.2008.08.017 PMID: 19111995

15. Sander Wint S, Eshelman D, Steele J, Guzzetta CE. Effects of distraction using virtual reality glasses during lumbar punctures in adolescents with cancer. Oncol Nurs Forum. 2002; 29: E8–E15. https://doi.org/10.1188/02.ONF.E8-E15 PMID: 11845217
22. Walker MR, Kallingal GJS, Musser JE, Folen R, Stetz MC, Clark JY. Treatment Efficacy of Virtual Reality Distraction in the Reduction of Pain and Anxiety During Cystoscopy. Mil Med. 2014; 179: 891–896. https://doi.org/10.7205/MILMED-D-13-00343 PMID: 25102532

23. Wolitzky K, Fivush R, Zimand E, Hodges L, Rothbaum BO. Effectiveness of virtual reality distraction during a painful medical procedure in pediatric oncology patients. Psychol Health. 2005; 20: 817–824. https://doi.org/10.1080/14768320500143339

24. Carrougher GJ, Hoffman HG, Nakamura D, Lezotte D, Soltani M, Leahy L, et al. The Effect of Virtual Reality on Pain and Range of Motion in Adults With Burn Injuries: J Burn Care Res. 2009; 30: 785–791. https://doi.org/10.1097/BCR.0b013e3181b485d3 PMID: 19692911

25. Chan EA, Chung JW, Wong TK, Lien AS, Yang JY. Application of a virtual reality prototype for pain relief of pediatric burn in Taiwan. J Clin Nurs. 2007; 16: 786–793. https://doi.org/10.1111/j.1365-2702.2006.01719.x PMID: 17402961

26. Das DA, Grimmer KA, Sparnon AL, McRae SE, Thomas BH. The efficacy of playing a virtual reality game in modulating pain for children with acute burn injuries: A randomized controlled trial [ISRCTN87413556]. BMC Pediatr. 2005; 5. https://doi.org/10.1186/1471-2431-5-1 PMID: 15745448

27. Hoffman HG, Patterson DR, Seibel E, Soltani M, Jewett-Leahy L, Sharar SR. Virtual reality pain control during burn wound debridement in the hydrotank. Clin J Pain. 2008; 24: 299–304. https://doi.org/10.1097/AJP.0b013e318164d2cc PMID: 18427228

28. Maani CV, Hoffman HG, Morrow M, Maisers A, Gaylord K, McGhee LL, et al. Virtual Reality Pain Control During Burn Wound Debridement of Combat-Related Burn Injuries Using Robot-Like Arm Mounted VR Goggles: J Trauma Inj Infect Crit Care. 2011; 71: S125–S130. https://doi.org/10.1097/TA.0b013e31822192e2 PMID: 21795888

29. McSherry T, Atterbury M, Gartner S, Helmold E, Searles DM, Schulman C. Randomized, Crossover Study of Immersive Virtual Reality to Decrease Opioid Use During Painful Wound Care Procedures in Adults: J Burn Care Res. 2017; 1. https://doi.org/10.1097/BCR.0000000000000589 PMID: 28570305

30. Morris LD, Louw QA, Crous LC. Feasibility and potential effect of a low-cost virtual reality system on reducing pain and anxiety in adult burn injury patients during physiotherapy in a developing country. Burns J Int Soc Burn Inj. 2010; 36: 659–664. https://doi.org/10.1016/j.burns.2009.09.005 PMID: 20022431

31. Schmitt YS, Hoffman HG, Blough DK, Patterson DR, Jensen MP, Soltani M, et al. A randomized, controlled trial of immersive virtual reality analgesia, during physical therapy for pediatric burns. Burns. 2011; 37: 61–68. https://doi.org/10.1016/j.burns.2010.07.007 PMID: 20692769

32. van Twillert B, Bremer M, Faber AW. Computer-Generated Virtual Reality to Control Pain and Anxiety in Pediatric and Adult Burn Patients During Wound Dressing Changes: J Burn Care Res. 2007; 28: 694–702. https://doi.org/10.1097/BCR.0b013e318148c96f PMID: 17667488

33. McGrath PJ, Johnson G, Goodman JT, Schillinger J, Dunn J, Chapman J. CHEOPS: A behavioral scale for rating postoperative pain in children. In: Fields H, editor. Advances in Pain Research and Therapy. New York: Raven Press; 1985. pp. 395–402.

34. Hicks CL, von Baeyer CL, Spafford PA, van Korlaar I, Goodenough B. The Faces Pain Scale-Revised: toward a common metric in pediatric pain measurement. Pain. 2001; 93: 173–183. PMID: 11427329

35. Wong DL, Baker CM. Pain in children: comparison of assessment scales. Pediatr Nurs. 1988; 14: 9–17. PMID: 3344163

36. Savedra MC, Holzemer WL, Tesler MD, Wilkie DJ. Assessment of postoperative pain in children and adolescents using the adolescent pediatric pain tool. Nurs Res. 1993; 42: 5–9. PMID: 8424096

37. Choineire M, Auger FA, Latarjet J. Visual analogue thermometer: a valid and useful instrument for measuring pain in burned patients. Burns. 1994; 20: 229–235. PMID: 8054135

38. Schulz KF. CONSORT 2010 Statement: Updated Guidelines for Reporting Parallel Group Randomized Trials. Ann Intern Med. 2010; 152: 726. https://doi.org/10.7326/0003-4819-152-11-20100610-00232 PMID: 20335313

39. Sterne JA., Gavaghan D, Egger M. Publication and related bias in meta-analysis. J Clin Epidemiol. 2000; 53: 1119–1129. https://doi.org/10.1016/S0895-4356(00)00242-0 PMID: 11106885

40. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. Hillsdale, N.J.: L. Erlbaum Associates; 1988.

41. Kenney MP, Milling LS. The effectiveness of virtual reality distraction for reducing pain: A meta-analysis. Psychol Conscious Theory Res Pract. 2016; 3: 199–210. https://doi.org/10.1037/cons0000084

42. Matsangidou M, Ang CS, SakeI M. Clinical utility of virtual reality in pain management: a comprehensive research review. Br J Neurosci Nurs. 2017; 13: 133–143. https://doi.org/10.12968/bjnn.2017.13.3.133
43. Dascal J, Reid M, IsHak WW, Spiegel B, Recacho J, Rosen B, et al. Virtual Reality and Medical Inpatients: A Systematic Review of Randomized, Controlled Trials. Innov Clin Neurosci. 2017; 14: 14–21. PMID: 28386517

44. Won A, Bailey J, Bailenson J, Tataru C, Yoon I, Golianu B. Immersive Virtual Reality for Pediatric Pain. Children. 2017; 4: 52. https://doi.org/10.3390/children4070052 PMID: 28644422