

Immersive Virtual Reality for Pediatric Procedural Pain: A Randomized Clinical Trial

Søren Walther-Larsen, MD, Trine Petersen, RN, Susanne M. Friis, RN, Gitte Aagaard, RN, Bergitte Drivenes, MD, Pernille Opstrup, MD

ABSTRACT

BACKGROUND AND OBJECTIVES: Pain management in children often is inadequate, and the single most common painful procedure in children who are hospitalized is needle procedures. Virtual reality (VR) is a promising and engaging intervention that may help to decrease anxiety and pain in children undergoing painful procedures. Our aim for this study is to investigate patient satisfaction and pain reduction by using a three-dimensional VR interactive game as a distraction.

METHODS: In this randomized clinical trial, we enrolled 64 children aged 7 to 16 years who were scheduled for venous cannulation. Patients assigned to the control group were adherent to our standard of care, including topical numbing cream, positioning, and distraction by a specialized pain nurse. In the study group, children were adherent to the standard of care and were distracted by an interactive VR game. Primary outcomes were patient satisfaction and the procedural pain assessed by using a visual analog score; secondary outcomes were the procedural time and any adverse events.

RESULTS: We found a high level of patient satisfaction with using the VR custom-made three-dimensional interactive game. All children (28 of 28 [100%]) in the VR group answered that they would prefer VR as a distraction for a later procedure, a borderline significant result compared with that of the control group (26 of 31 [84.9%]). No significant difference was found in pain scores and procedural times between the 2 groups. The number of adverse effects was low, with no significant difference between the 2 groups.

CONCLUSIONS: We found no difference in pain scores but higher satisfaction when using VR versus standard care as part of a multimodal approach for management of procedural pain in children.

www.hospitalpediatrics.org

DOI:<https://doi.org/10.1542/hpeds.2018-0249>

Copyright © 2019 by the American Academy of Pediatrics

Address correspondence to Søren Walther-Larsen, MD, The Pediatric Pain Clinic, Juliane Marie Centre, Rigshospitalet, 9 Blegdamsvej, 2100 Copenhagen, Denmark. E-mail: soeren.walther-larsen@regionh.dk

HOSPITAL PEDIATRICS (ISSN Numbers: Print, 2154-1663; Online, 2154-1671).

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Funded by Khora Virtual Reality Denmark and Kristian Bluff (Motivates) for software development. CGI/Cynergi Danmark A/S donated funds for software development.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

Dr Walther-Larsen conceptualized and designed the study, drafted the initial manuscript, conducted the initial analyses, and reviewed and revised the manuscript; Ms Petersen and Dr Opstrup conceptualized and designed the study, designed the data collection instruments, and coordinated and supervised data collection; Ms Friis, Ms Aagaard, and Dr Drivenes conceptualized and designed the study, designed the data collection instruments, coordinated and supervised data collection, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

*The Pediatric Pain Clinic,
Juliane Marie Centre,
Rigshospitalet,
Copenhagen, Denmark*

Pain management in children who are hospitalized is often inadequate.¹⁻⁴ In a recent Danish study, the single most common painful procedure named by the children was needle procedures, such as blood draws and intravenous (IV) cannulation.⁵ Procedural pain has therefore been an area of focus in our pediatric pain service. Mandatory measures before needle procedures in our department are topical numbing cream, positioning, sucrose feeding or breastfeeding (children age <1 year), and distraction as part of a multimodal approach.⁶⁻¹⁰ Application of these 4 evidence-based measures is considered as standard care during needle procedures in our hospital, for example, during IV induction of anesthesia.¹¹

Distraction is a powerful measure as part of multimodal approach to acute pain management.⁶⁻¹⁰ Distraction can be conducted by any health care worker but can be time and staff consuming. In our experience, it is most effectively conducted by child-life specialists or pediatric pain nurses (playing, singing, storytelling, or guided imagery). When these health care workers are not available, immersive virtual reality (VR) is a promising and engaging intervention that may help to decrease anxiety and pain in children undergoing painful procedures and other types of acute pain.¹²⁻²¹ In the pediatric clinical setting, VR has been used as a tool of distraction for managing pain during repetitive dressing changes in children with burn wounds.¹² In relation to needle procedures, such as IV cannulation, permanent IV device access, and blood sampling, VR has proven successful in decreasing pain and anxiety, although there are few studies in which distraction during venous cannulation is addressed.²¹⁻²³

The immersive VR software in the current study was developed in cooperation with a professional VR company, and it is custom-made for the needle procedure scenario. We randomly assigned all children to a VR group and a control group using mandatory pharmacologic and nonpharmacologic measures.¹¹ Our aim for this randomized study was to investigate the efficacy and safety of VR distraction for decreasing pain

in children aged 7 to 16 years during venous cannulation before induction of anesthesia.

METHODS

General Study Design

This was a randomized and observer-blinded clinical trial in which we enrolled 64 children scheduled for a venous cannulation before a planned IV anesthesia induction at the anesthetic department. The patients were admitted in the morning for elective, mainly urologic-genital surgery at the University Hospital Rigshospitalet in Copenhagen, Denmark. Standard induction of anesthesia for this age group in our department is IV induction after insertion of an IV cannula on the dorsum of the hand. Induction with an inhalational anesthetic is an alternative not offered for otherwise healthy children in our study. Enrollment of patients took place from March 9, 2018, to May 20, 2018. Patients were eligible when between 7 and 16 years of age and Danish speaking.

We adhered to the Consolidated Standards of Reporting Trials statement, and the trial was approved by the Danish Data Protection Agency (2018-41-5332). Data protection rules were complied. Data from the patient record were not collected in this trial. Data were entered into an Excel spreadsheet and stored on a secured hospital server.

Before writing the protocol, we systematically searched PubMed for relevant references.

Exclusion Criteria

Exclusion criteria included an American Society of Anesthesiologists classification score of >2; speaking a language other than Danish; children on analgesia or sedatives; cognitive impairment; psychiatric diagnosis; headache, dizziness, recent head injury, epilepsy, and other conditions in which application of VR goggles was judged to be potentially harmful; and when a topical anesthetic (lidocaine and prilocaine [eutectic mixture of local anesthetics (EMLA)]) or tetracaine (Ametop) was not properly applied before the invasive procedure.

Fifty-nine patients proceeded to data analysis. Five patients dropped out because

of the following reasons: IV cannulation was not possible in 2 patients after a reasonable number of attempts, and 3 patients disliked the VR game and the setup, leading to discontinuation (Fig 1).

Patient Enrollment

Study personnel contacted the child and the child's caregiver in the waiting room in the operation theater to determine eligibility. Preprocedural written and oral information was provided to the parents and the child. Written informed consent was obtained from the caregiver. A pain assessment tool was provided to the child by introducing the visual analog score (VAS) pain assessment.

Randomization (computer-generated) (Research Randomizer 2, www.randomizer.org) was conducted for 2 groups: an intervention group with VR gear and a control group. In the control group, children were distracted with a tablet or a smartphone according to their own choice. The study started with distraction according to randomization, and the invasive procedure started within minutes, maximally after 5 minutes. The procedure time (in minutes from tourniquet to dressing application) was noted in the result sheet by the phlebotomist, an attending pediatric trained anesthesiologist.

Control Group

Patients assigned to the control group were adherent to our mandatory standard of care (SOC): topical numbing cream, positioning, and distraction. The distraction was led by an experienced specialized pediatric pain nurse by use of a smartphone. During the procedure, the child played a two-dimensional game of his or her own choice.

VR Group

Patients assigned to the VR group were also adherent to SOC: topical numbing cream, positioning, and distraction. In this group, distraction was provided by VR. Patients engaged with the VR game *Seagull Splash*, a three-dimensional (3D) interactive game made in cooperation with a professional VR company (Khora Virtual Reality Denmark, Copenhagen, Denmark) and custom-made for the needle procedure scenario. During the needle procedure, it is essential to completely immobilize the extremity. The

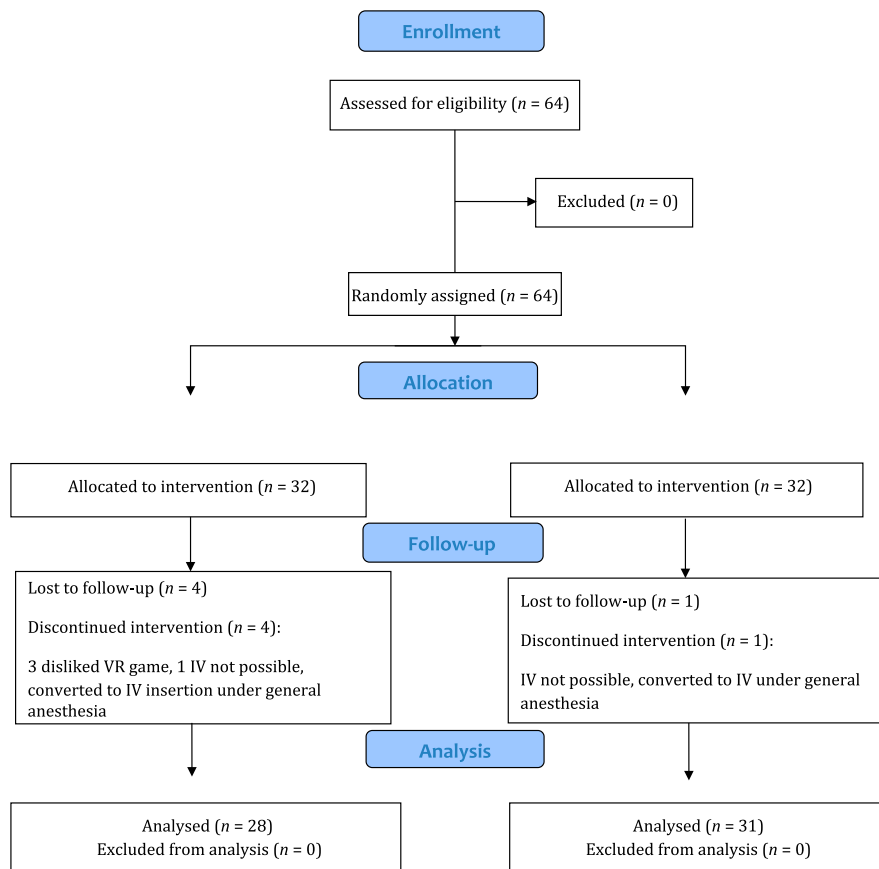


FIGURE 1 Enrollment diagram.

patients used the Samsung Galaxy S6 mobile-based Gear VR goggles and held a controller in the hand not assigned for the procedure. We made a short introduction to the children, after which children were able to start the game without further training. An assistant was present, but no special training in VR was needed for operating our VR gear. In the game scenario, a boat with a bucket of fish is approached by seagulls that aim to eat the fish, and the task for the player is to avoid this by shooting water balloons with a slingshot at the seagulls. After each round of shooting, the player is awarded with a score, and the scenario becomes increasingly difficult: The seagulls approach the boat with increasing speed, demanding the child shooting down the seagulls faster and more accurately. The scenario background is a sea with boats, starfish, birds, mountains, and more. The scenario is kept neutral and becomes uninteresting behind the patient to keep the

patient from turning his or her torso and making venous puncture difficult for the anesthesiologist. After each session, the VR gear was cleaned with alcohol-based sanitary wipes to prevent contamination.

Finally, 15 minutes after the procedure a postanesthesia care unit (PACU) nurse who was blinded to the randomly assigned groups interviewed the child, noting efficacy and any side effects of the intervention. The nurse who was blinded to the randomization (ie, way of distraction) noted the pain score and the satisfaction with the distraction modus using a VAS ruler. Finally, the procedure time and any adverse effects were noted.

Outcomes

The pain experience in children is a complex subjective feeling that consists of nociceptive input modified by anxiety level, former experience, coping skills, caregiver and staff attitude, etc. To evaluate the

efficacy of VR, we chose 2 primary outcomes: patient satisfaction and pain score. Patient satisfaction was assessed by using a 0 to 100 scale and by whether the child would use VR again. Pain was assessed by a VAS. A VAS is validated for self-reporting pain assessment in children in this age group, which is considered superior to observational scoring or parental scoring. Secondary outcomes were the procedural time and any adverse events. Safety issues and serious immediate adverse outcomes (eg, nausea, vomiting, dizziness, or claustrophobia after use of VR) were evaluated during the follow-up period of 15 minutes.

Ethics

The National Committee on Biomedical Research Ethics (H-18000975) waived the need for review of the project. The Danish Medicines Agency was not involved because of the study design (no medicine involved) and because our VR gear was not considered a medical device. Patient anonymity was carefully protected. We received informed consent from the parents after oral and written information was sought and granted.

The VR glasses and the VR game were in use for a limited time (10–20 minutes). No harm by VR glasses or the game was expected according to the literature. The VR game (*Seagull Splash*) complies with directives of professional VR films for children age ≥ 7 years. VR gear was removed immediately on request. Hygiene rules were followed according to hospital practice.

Several evidence-based pharmacologic and nonpharmacologic measures are efficient for preventing procedural pain (topical numbing cream, positioning, sucrose feeding or breastfeeding [children age < 1 year], and distraction). Accordingly, we found it ethically correct to adhere to these measures in both groups.

The study results, whether they were positive, negative, or inconclusive, were scheduled for publication in a peer-reviewed medical journal.

Statistical Analysis

Values were reported as medians with interquartile ranges, and differences were

reported as mean differences or relative risks with 95% confidence intervals (CIs). Groups were compared by using the Mann–Whitney *U* Test (continuous data) or Fisher's exact test (categories). $P \leq 0.05$ was considered statistically significant.

We considered a difference of 20 in pain score to be clinically relevant on a scale of 0 to 100. With an estimated SD of 20, this would require a sample size of 42 patients with 90% power at the 5% significance level.²⁴ Therefore, to account for dropout and missing data, we decided to recruit 60 patients.

RESULTS

Characteristics of children allocated to either the VR or the control group are shown in Table 1; the 2 groups were roughly equivalent on relevant variables.

In this randomized study of children obtaining venous cannulation before anesthesia, we focused on distraction for pain reduction. We found a high level of patient satisfaction in using the custom-made 3D VR interactive game. On a 100-point scale, the children scored ~80 for satisfaction with the distraction measures (Table 2). Answering the question of whether they would use the same distraction again for procedural pain, 28 of 28 children (100%) in the VR group versus 26 of 31 (84.9%) in the control group replied positively, which was borderline significantly higher.

No significant difference was found in pain scores between the 2 groups. The VAS scores for the procedural pain between the 2 groups were 27 of 100 vs 15 of 100 (Table 2). We sought to detect a difference of 20 on the VAS pain score, and the 95% CI was rather narrow (–3 to 13), suggesting that a clinically important difference has not been overlooked.

TABLE 1 Characteristics of Children Allocated to Either VR or the Control Group

Variable	VR (<i>n</i> = 28)	Control (<i>n</i> = 31)
Girls	1 (3.6)	6 (19.4)
Boys	27 (96.4)	25 (80.7)
Age, mean (SD), y	10.9 (2.8)	10.1 (2.2)

TABLE 2 Efficacy, Satisfaction, and Adverse Effects of 59 Children Allocated to Either VR or the Control Group

Variable	VR (<i>n</i> = 28)	Control (<i>n</i> = 31)	Difference (95% CI)	<i>P</i>
Pain VAS (0–100), median (IQR)	27 (8 to 33)	15 (5 to 30)	5 (–3 to 13)	.23
Procedural time, min, mean (SD)	1.75 (1.0 to 3.6)	2.0 (1.0 to 2.5)	0.4 (–0.5 to 1.3)	.58
Satisfaction (0–100), median (IQR)	81 (68 to 100)	89 (73 to 100)	0.04 (–11 to 11)	.82
Use again?, <i>n</i> (%)	28 (100)	26 (84.9)	0.48 (0.37 to 0.64)	.05
Adverse effects, <i>n</i> (%)				
Nausea	1 (3.6)	1 (3.2)	0.95 (0.23 to 3.9)	1.0
Dizziness	0 (0)	1 (3.2)	1.9 (1.5 to 2.5)	1.0
Other discomfort	3 (10.7)	2 (6.5)	0.75 (0.25 to 2.2)	.66

Differences are reported as mean differences or relative risks with 95% CIs. Groups were compared by using the Mann–Whitney *U* test (continuous data) or Fisher's exact test (categories). IQR, interquartile range.

The procedural times in the 2 groups were equal, with a mean time of ~2 minutes from tourniquet to dressing application. Adverse effects were few, with no significant differences between the 2 groups.

DISCUSSION

Patient Satisfaction and Pain Reduction for Procedural Pain Management

Venous cannulation is still experienced as painful and distressing for children and adolescents. As a consequence, continuous search for measures to improve the pain experience is required. Psychological interventions for pain and distress reduction have been recommended in systematic reviews.^{6–10} This study was focused on distraction for reducing pain and improving satisfaction associated with venous cannulation in children aged 7 to 16 years. By introducing a novel technology, we obtained a high level of patient satisfaction. Apart from case studies, VR distraction in children during invasive procedures has been addressed in only 3 studies. In a study by Gold et al²¹ from 2006, children undergoing venous cannulation without distraction reported a significant increase in affective pain compared with children using VR. In a recent study from the same author, patients in the VR group experienced significantly less pain (pain VAS) and anxiety (anxiety VAS) and had significantly better affect (facial affective scale) during a blood draw procedure compared with patients in the SOC condition.²² To compare our study and

the studies by Gold et al,^{21,22} we find it interesting to focus on the study design. There are significant differences in the study and control group SOC. In 1 of the studies, topical anesthesia spray was applied before venous cannulation apparently as the sole pain reduction measure. In another study, the SOC was “brief interaction with the phlebotomist before the blood draw and a television playing a cartoon movie” as a distraction. These SOC conditions are, in our opinion, insufficient. Contemporary evidence-based measures for pain and anxiety reduction during pediatric procedures are topical numbing cream, positioning, sucrose feeding or breastfeeding (children age <1 year), and distraction as part of a multimodal approach.^{6–11} Therefore, we found it unethical to deprive the children of these measures as part of SOC. In our study, we were not able to detect any difference in VAS pain scores between groups. On the other hand, with the introduction of our VR gear, we were able to achieve VAS scores not significantly different from the VAS scores after a time- and staff-consuming, nurse-led distraction in the control group.

In 1 study, VR was used for distraction during lumbar puncture in patients aged 10 to 19 years.²⁰ The SOC was application of EMLA cream, sedation by using fentanyl and midazolam, full explanation of the procedure, and parental presence. The authors found an insignificant decrease in the VAS score but found satisfaction expressed by the patient concerning

distraction during the procedure and found that the patients wanted to use VR again.²⁰ Nonimmersive VR was found to be a positive experience for children undergoing venous puncture or a subcutaneous venous access port in another study.²³ The SOC was cold-spray or EMLA cream. The Face, Legs, Activity, Cry, and Consolability (FLACC) scale was used to measure observational pain. There were no significant differences of these measures between the intervention group (mean FLACC score 1 of 10) and the control group (mean FLACC score 2 of 10), although children enjoyed the VR game, and the authors found that it did distract children during the procedure.

In conclusion, using evidence-based SOC, we were not able to document the effect of VR in terms of a VAS score reduction; however, on the basis of the reported satisfaction scores, our patients seem to appreciate VR as a distraction measure during procedures. Pain during venous cannulation is well managed with our SOC measures. Still, VR seems to be a promising new technology, increasingly accessible, and appreciated by children and seems to have pain reduction comparable with time- and staff-consuming distractions by specialized pain nurses.

Pain perception is a complex, subjective feeling, and in a biopsychosocial context, pain is subject to numerous factors. The self-reported VAS score should, in that context, be interpreted as a final product of nociceptive, but also emotional and anticipatory, factors. Satisfaction expressed by patients is, as such, a strong indicator of efficient pain and anxiety measures during procedural pain.

Procedural Time

In our study, procedural time from tourniquet to dressing application was ~2 minutes, with no difference between the 2 groups. We had a high success rate of venous cannulation, with only 1 child in each group, whereas venous cannulation was not possible. In the study by Gold and Mahrer²² “phlebotomists reported that they thought that the VR helped and that they wanted to use VR with other patients 98% of the time.” In our study, we were not able to detect any advantages of VR compared with

the control group SOC in terms of the procedure performance.

Adverse Effects

The VR game (*Seagull Splash*) complies with directives of professional VR films for children age ≥ 7 years, and the children were exposed to VR for only 10 to 15 minutes. Only few children in our study experienced symptoms such as nausea, dizziness, or other symptoms of motion sickness, with no statistical difference between the groups. These symptoms are nonspecific symptoms and could be caused by other factors, such as preanesthetic fasting or anxiety. In a study from Gold et al²¹ from 2006, none of the children reported simulator sickness after VR exposure. Further research is needed to study probable short- and long-term side effects of VR, bearing in mind that untreated procedural pain has long-term consequences.

VR as a New Technology

VR equipment is increasingly accessible because of lower costs and straightforward functionality with goggles and a smartphone. Most children are confident with two-dimensional and 3D computer gaming in everyday life. In health care, VR technology has been introduced for various purposes. In pain management, there is, so far, only little evidence of advantage and side effects. VR distraction as a modulator of pain experience was examined in experimental settings by using functional MRI and revealed a neural correlate of pain modulation comparable with other types of distraction.²⁵ Distractions, such as VR, seem to activate pain-modulating areas in the brain, decreasing the nociceptive input. Pain perception is perceived in a biopsychosocial context, and decreasing anxiety has a significant impact on the pediatric pain experience. Although immersed in a 3D video game, children often become deeply absorbed and are therefore able to ignore aversive stimuli (the concept of presence or “being there” as an important factor in immersive mediated environments). It is assumed that greater levels of immersive quality elicit higher levels of presence, enhancing the effectiveness of the mediated experience and therefore the analgesic

efficacy of VR.²⁶ VR software in the current study was developed in cooperation with a professional VR company and was customized for the needle procedure scenario, creating a game with an age-appropriate level of immersion. Also, interactivity seems to enhance the efficacy of distraction and thereby the pain- and anxiety-reducing effects of VR.²⁵ As technology expands, VR gear becomes accessible and cheaper, requiring a VR console, a smartphone, and the software.

Our study did not reveal immediate side effects associated with VR, although we are aware of the potential risk of highly immersive VR. It is beyond the scope of this study to discuss the potential long-term risks. We should be aware of the possible manipulation of the immature brain, bearing in mind how human behavior is influenced by external factors while the person might be totally unaware of this influence. These considerations are discussed in the interesting article by Madary and Metzinger²⁷. Further research, as well as international guidelines for pediatric VR exposure, is needed.

Methodologic Considerations

This is a randomized study of VR distraction versus SOC measures during procedural pain in children. We decided not to design a double-blind study. By randomization, the children were excited about the rather novel VR technology, and treatment bias could favor efficacy in the VR group. Three children allocated to the VR group did not want to use the VR equipment for various reasons. We achieved no data from these children and decided not to include these children in the analysis, although we are aware that it could be perceived as an adverse effect. It could also affect the data dependent on the reason for rejecting VR. Evaluating satisfaction with the VR technology by using the psychometric Likert scale would have revealed more details. In this study, we chose the dichotomous yes/no. A PACU nurse filled out the result sheet 15 minutes after the procedure, noting efficacy and any side effects of the intervention. The PACU nurse was blinded to the randomly assigned group. The groups were also blinded to the data analyst. With

an observational period of only 15 minutes, we were not able to detect any long-term adverse effects of VR. More boys than girls were included in this study. This was because of the surgical population, but future studies need to include more girls. In future studies, an anxiety score would likely be a good complementary measure, especially in adolescents, to assess anxiety influence on pain perception.

CONCLUSIONS

We found a high level of patient acceptability and satisfaction using a VR 3D interactive game distraction as part of a multimodal approach for management of procedural needle pain in children. The development of a 3D interactive game custom-made for needle procedures (procedures feared by most children) may open up clinical applicability for the use of VR for pain and anxiety reduction. All you need is a smartphone, the software, and a VR console.

REFERENCES

- Friedrichsdorf SJ, Postier A, Eull D, et al. Pain outcomes in a US children's hospital: a prospective cross-sectional survey. *Hosp Pediatr*. 2015;5(1):18–26
- Kozlowski LJ, Kost-Byerly S, Colantuoni E, et al. Pain prevalence, intensity, assessment and management in a hospitalized pediatric population. *Pain Manag Nurs*. 2014;15(1):22–35
- Stevens BJ, Harrison D, Rashotte J, et al; CIHR Team in Children's Pain. Pain assessment and intensity in hospitalized children in Canada. *J Pain*. 2012;13(9):857–865
- Taylor EM, Boyer K, Campbell FA. Pain in hospitalized children: a prospective cross-sectional survey of pain prevalence, intensity, assessment and management in a Canadian pediatric teaching hospital. *Pain Res Manag*. 2008;13(1):25–32
- Walther-Larsen S, Pedersen MT, Friis SM, et al. Pain prevalence in hospitalized children: a prospective cross-sectional survey in four Danish university hospitals. *Acta Anaesthesiol Scand*. 2017;61(3):328–337
- Uman LS, Birnie KA, Noel M, et al. Psychological interventions for needle-related procedural pain and distress in children and adolescents. *Cochrane Database Syst Rev*. 2013;(10):CD005179
- Taddio A, McMurtry CM. Psychological interventions for needle-related procedural pain and distress in children and adolescents [published correction appears in *Paediatr Child Health*. 2015;20(8):466–467]. *Paediatr Child Health*. 2015;20(4):195–196
- Birnie KA, Noel M, Parker JA, et al. Systematic review and meta-analysis of distraction and hypnosis for needle-related pain and distress in children and adolescents. *J Pediatr Psychol*. 2014;39(8):783–808
- Taddio A, McMurtry CM, Shah V, et al; HELPinKids&Adults. Reducing pain during vaccine injections: clinical practice guideline. *CMAJ*. 2015;187(13):975–982
- Leroy PL, Costa LR, Emmanouil D, van Beukering A, Franck LS. Beyond the drugs: nonpharmacologic strategies to optimize procedural care in children. *Curr Opin Anaesthesiol*. 2016;29(suppl 1):S1–S13
- Postier AC, Eull D, Schulz C, et al. Pain experience in a US children's hospital: a point prevalence survey undertaken after the implementation of a system-wide protocol to eliminate or decrease pain caused by needles. *Hosp Pediatr*. 2018;8(9):515–523
- Won AS, Bailey J, Bailenson J, Tataru C, Yoon IA, Golanu B. Immersive virtual reality for pediatric pain. *Children (Basel)*. 2017;4(7):E52
- Chan E, Foster S, Sambell R, Leong P. Clinical efficacy of virtual reality for acute procedural pain management: a systematic review and meta-analysis. *PLoS One*. 2018;13(7):e0200987
- Malloy KM, Milling LS. The effectiveness of virtual reality distraction for pain reduction: a systematic review. *Clin Psychol Rev*. 2010;30(8):1011–1018
- Morris LD, Louw QA, Grimmer-Somers K. The effectiveness of virtual reality on reducing pain and anxiety in burn injury patients: a systematic review. *Clin J Pain*. 2009;25(9):815–826
- Jeffer D, Dorman D, Brown S, et al. Effect of virtual reality on adolescent pain during burn wound care. *J Burn Care Res*. 2014;35(5):395–408
- Brown NJ, Kimble RM, Rodger S, Ware RS, Cuttle L. Play and heal: randomized controlled trial of Ditto™ intervention efficacy on improving re-epithelialization in pediatric burns. *Burns*. 2014;40(2):204–213
- 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(10):1243–1249
- Gershon J, Zimand E, Lemos R, Rothbaum BO, Hodges L. Use of virtual reality as a distractor for painful procedures in a patient with pediatric cancer: a case study. *Cyberpsychol Behav*. 2003;6(6):657–661
- 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(1):E8–E15
- Gold JI, Kim SH, Kant AJ, Joseph MH, Rizzo AS. Effectiveness of virtual reality for pediatric pain distraction during i.v. placement. *Cyberpsychol Behav*. 2006;9(2):207–212
- Gold JI, Mahrer NE. Is virtual reality ready for prime time in the medical space? A randomized control trial of pediatric virtual reality for acute procedural pain management. *J Pediatr Psychol*. 2018;43(3):266–275
- Nilsson S, Finnström B, Kokinsky E, Enskär K. The use of Virtual Reality for needle-related procedural pain and distress in children and adolescents in a paediatric oncology unit. *Eur J Oncol Nurs*. 2009;13(2):102–109
- ClinCalc LLC. Sample size calculator. Available at: <https://clincalc.com/stats/samplesize.aspx>. Accessed May 2, 2019

25. Hoffman HG, Richards TL, Bills AR, et al. Using fMRI to study the neural correlates of virtual reality analgesia. *CNS Spectr*. 2006;11(1):45–51
26. Cummings JJ, Bailenson JN. How immersive is enough? A meta-analysis of the effect of immersive technology on user presence. *Media Psychol*. 2016;19(2):272–309
27. Madary M, Metzinger TK. Real virtuality: a code of ethical conduct. Recommendations for good scientific practice and the consumers of VR-technology. *Front. Robot*. 2016;3:3