Is Virtual Reality a Game Changer in Pediatrics' Acute Pain Perception?

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Abstract: *Purpose of review:* Virtual reality (VR) is a promising tool that is becoming increasingly popular for the prevention and treatment of procedural pain in children. This review aims to investigate the current literature on the use and effectiveness of VR in paediatric procedural pain management, focusing on needle-related procedures, burn wound care, dental procedures among others; limitations and future perspectives on the use of VR will also be highlighted.

Recent findings: in addition to the most researched fields of application (*e.g.* needle procedures), VR has also started to be used in new areas, such as nasal and gastrointestinal endoscopies as well as minor surgeries. From the latest evidence, VR seems to be effective in many procedures, especially compared to no distraction; however, there is conflicting data in the literature due to numerous factors such as differences between technologies, degree of VR-immersion, patients coping styles among others.

Summary: there are still no data of absolute certainty on the effectiveness of VR in reducing procedural pain in paediatric patients and data pooling is still difficult. Future research should carry on large randomised-controlled, multicentre studies to better define VR properties and how best to optimise VR software and user experience for maximum pain reduction.

Keywords: Acute pain mitigation, Virtual reality, Children.

INTRODUCTION

Acute paediatric pain is often accompanied by a considerable emotional impact [1] with short- and long-term consequences in the child's subsequent perception and response to pain [2]. Several studies demonstrated that repeated nociceptive stimulation in childhood causes increased pain and stress during further procedures, fear and avoidance of medical care, or sometimes the development of needle phobias that persist into adulthood especially when it is not adequately covered by analgesic therapy [2, 3].

Consequently, procedural pain prophylaxis in the paediatric population is critical as its recognition and prevention can enhance children's development, well-being and future pain response.

Virtual reality (VR) fits into this context, as a key tool for the management of procedural pain in children [4-5]. By providing realistic stimulation to multiple senses (visual, auditory, tactile) simultaneously, through its highly immersive and multi-sensory nature, VR engages the sensorimotor system more extensively than other common distractors, such as watching music or video during the procedure, reading a book or tablet use, among others [6-7]. Several theories have attempted to explain the mechanism by which VR acts as a distractor. Melzack and Wall hypothesised the presence of transmission stations (gates) in the spinal cord influencing the flow of nerve impulses to the brain; according to this *gate theory* nerve transmission could be modulated at these intermediate stations by different factors, such as emotion, attention and past experience [8]. Subsequently, McCaul and Malott stated that a painful stimulus is perceived as such only when the individual pays attention to it [9]. Demonstration of the impact of distraction on pain perception have been provided by Bantick *et al*. using functional magnetic resonance imaging (fMRI); in their study, subjects received a noxious thermal stimulus together with a harmless vibratory counter-stimulus, reporting a reduction in perceived pain when the subjects directed their attention to the vibration (or to a neutral visual stimulus). Imaging data showed reduced activity in the pain processing areas (anterior cingulate, insula, thalamus) when attention was directed away from the painful stimulus, demonstrating the important role that attention plays in pain perception [10]. For these reasons, VR is gaining interest in the healthcare system as a potential adjuvant to pain prophylaxis and treatment.

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VR is currently a very accessible and popular tool due to its low cost, the variety of applications available, its ease of use and the increased commercial availability [11]. In the last decades, VR has been applied in different healthcare settings in children. For the management of acute pain, VR has been used in both healthy and chronically ill children during the placement of venous accesses and other needle-related procedures (*e.g*. venipunctures [12, 13], vaccinations [14], administration of anaesthetics [15] among others), lumbar puncture [16], dressing changes in burn patients [17, 18], dental procedures [19, 20] and in chronic pain for amputations [21]. In recent years, VR has also been used in the orthopaedic field, *e.g*. during cast or pin removal [22, 23], in plastic surgery [24], in minor surgical procedures [24], including circumcision [25], and during nasal [26] and gastrointestinal endoscopies [27], demonstrating that VR is an easy-to-use tool that can be applied in a large number of different hospital settings.

This review discusses the current literature on the use of VR as an acute pain management strategy during different procedures and the future directions of the field.

VR AND PAEDIATRIC NEEDLE PROCEDURES

Paediatric needle procedures - primarily venipuncture and IV line placement - are the most common cause of pain in United States children's hospitals [28]. Therefore multiple pharmacological, physical (*e.g*. cooling of the skin) and psychological elements have been incorporated to control needle-related paediatric procedural pain, including VR [29, 30]. This section focuses on the data present on the use of VR as a pain management strategy during needle-procedures.

The first randomized controlled clinical trial (RCT) on the efficacy and suitability of VR as a pain distraction in children was published in 2006. This pilot study included 20 children aged 8 to 12 years, without cognitive impairment, who were randomized to either immersive VR distraction or no distraction during planned paediatric IV placement for MRI/CT imaging; the results were promising as responses from the Faces Pain Scale–Revised (FPS-R) indicated a 4 fold increase in affective pain (before and after the venous placement) within the control condition while no significant differences were detected within the VR group; moreover, children receiving VR distraction throughout IV placement were twice as satisfied with their pain management as compared to children not exposed to VR intervention [31]. However, when this study was analyzed by a 2019 Cochrane review, no evidence of a beneficial effect of immersive VR was identified (mean difference: -0.60, 95% CI -2.47 to 1.27). In addition, multiple factors, including small sample size, lack of blinding for participants, personnel and outcome assessment limit this study [32]. Nevertheless, since 2006 several studies have been carried out to assess the effect of VR on pain perception in children giving rise to a growing body of literature on the topic. These studies have been exploring the effect of VR on pain perception in different needle-related procedures, such as IV cannulation, venipuncture or port access, different type of patients, including healthy children, onco-hematological patients, pediatric and adolescents with kidney disease, and different type of situations such as scheduled or not scheduled interventions

Seven RCTs have evaluated the effect of VR on unscheduled venipunctures or IV cannulations in children in different Emergency Departments (EDs) (Table **1**) [12, 13, 30, 33-36]; EDs are considered a particularly unsettling environment, where children are exposed to an unexpected hospital visit, with consequent child's distress that can be compounded by the fear of a painful procedure to follow, previous conditioning from unexpected "jabs" when receiving immunisations, or previous visits to an ED [37]. The studies included between 59 and 136 subjects aged between 4 and 17 years old; children with developmental delay, psychiatric illnesses, epilepsy, critical medical illnesses or deteriorating clinical status were excluded. Three RCTs evaluated the feasibility and acceptability of the VR implementation during IV insertion in the ED, observing a high rate of recruitment (68 to 78.8%) and game completion (90.3%) [30-35-36]; while tolerance to VR headset was achieved in 79% of the subjects, with older age being the only significant predictor of success [30]. A minimal disruption to clinical workflow was reported; however, this was related to the study procedure rather than the intervention itself [35]. Furthermore, these studies observed no consequences on first attempt IV success rates, number of IV attempts nor time required for successful insertion [13, 30].

The efficacy of immersive VR on pain management during needle-related procedure in the ED, has been compared to either no distraction [13] or non-VR distractions [12, 30, 33-36, 38]; while VR reduces post-procedural self- and observed-reported pain compared to no distraction [13], it is uncertain whether VR is

Reference	Type of study	N, age	Comparison (N)	Method of assessment of self-reported or observed pain	Post-procedural self-reported pain	Post-procedural observer-reported pain	Adverse events
[12] Chan 2019	RCT: 2 groups, parallel design	123, aged 4 to 11 years	Child-life therapy, toys, books, and electronic devices (59).	FPS-R	VR reduced pain in comparison with non virtual reality interventions (-1.57 units; P = .016)	Not evaluated	No adverse effects in VR arm (P = .05), while 4 patients in the comparison showed dizziness, nausea, headache, vomiting (P = .05).)
[13] Chen 2020	RCT: 2 groups, parallel design	136, aged 7 to 12 years	No distraction (68)	WBFS	Pain score was significantly lower in the VR group for the children (p =0.031).	Pain score was significantly lower in the VR group for the childrens' caregivers (p = 0.020), and nurses (p = 0.012).	Not evaluated
[33] Dumoulin 2019	RCT: 3 groups, parallel design	59, aged 8 to 17 years	Watching TV (24) child-life program with age selected distractions (15)	VAS	No evidence of a beneficial effect of immersive VR compared with TV (MD -13.68, 95% CI -29.64 to 2.28) and Child Life (MD -3.58, 95% CI -19.31 to 12.15) non-VR distraction	Not evaluated	The change in estimated cyber sickness before and afterer VR immersion was not significant
[34] Goldman 2021	RCT: 2 groups, parallel	66, aged 6 to 16 years	Videos, television, iPad (31) child life specialist	FPS-R	In the VR group, pain after the procedure was reported slightly lower than that before the procedure (− 0.51/10), and in the control group, the pain was slightly higher (+ 0.16/10), but this was not statistically significant (p = 0.64).	Not evaluated	Not evaluated
[35] Litwin 2021	RCT: 2 groups, parallel	60 children aged 8 to 17 years	Video on a tablet (27)	NRS	Non statistically significant but clinically significant reduction in children's self-reported pain during the IV insertion when VR was implemented	No difference in proxy-reported pain from the caregiver, nurse, or research assistant	Dizziness was reported in 12.5% of children in the VR group and 16.7% of children in the control group
[36] Osmanlliu 2021	RCT: 2 groups, parallel	62, aged 7 to 17 years	Distraction by the parent or by the healthcare provider performing the procedure, but variable depending on provider comfort (31).	vNRS	Median level of pain during the procedure was not statistically different between the intervention and control groups, respectively (verbal numerical rating scale: 3 (1, 6)/10 vs 3 (1, 5.5)/10, p = 0.75).	Not evaluated	Five/30 patients (16.7%) who were exposed to VR reported mild side effects (dizziness, n = 3; nausea, n = 1; no serious adverse event were reported
[30] Schlechter 2021	RCT: 2 groups, parallel	115 children aged 4 to 17 years	Reading a book or iPad use (58)	FPS-R	Both VR and control groups having a median change of pain of -2, after IV placement adjustment for adjunctive measures did not change the results.	Both VR and control groups having a median change of pain of -2, after IV placement adjustment for adjunctive measures did not change the results.	Serious adverse events were not witnessed in any member of the trial.

RCT: randomized controlled trial; SOC: standard of care; WBFS: Wong-Baker Faces Pain Rating Scale; VAS: Visual Analogue Scale; FPS-R: Faces Pain Scale-Revised; vNRS: Verbal Numerical Rating Scale; NRS: Numerical Rating Scale; FLACC: Face, Legs, Activity, Cry and Consolability scale; MD: mean deviation; CI: confidence interval.

superior to non-VR distractions (*e.g*. watching favorite video, listening to music, reading a book or playing a game of choice on a tablet) for pain management.

Considering self-reported post-procedural pain, no study highlighted an inferior performance for VR distraction compared to other types of entertainment; one single RCT on 123 subjects, found a beneficial significant effect of immersive VR in younger children aged 4 to 11 years old [12] and another study (60 children involved) reported a clinically, but not statistically, significant reduction in self-reported pain during the IV insertion when comparing VR to watching a video on a tablet in older children (8 to 17 years old) [35]; a third study (66 children aged 6 to 16 years) comparing pain before and after the procedure reported a modest reduction in perceived pain in the VR group after the procedure, and a slightly higher pain score compared to that before the procedure in the control group (videos, television, tablet) [34]. Three studies (237 children, aged 4 to 17 years) did not find evidence of a superior effect of immersive VR compared with other distractions, such as watching TV, reading a book, using tablet, and Child Life program with age-selected entertainments; still the efficacy of both the intervention were comparable [30, 33, 36]. Similarly, no difference in proxy-reported pain from the caregiver, nurse, or research assistant was observed when comparing immersive VR to reading a book or using a tablet [30, 35].

When immersive VR was implemented in scheduled venipuncture procedures (phlebotomy and IV insertion) and its efficacy on pain mitigation was compared to no-distraction, the result resembled what happened in the ED; in particular, 8 RCTs focusing on 544 children aged 4 to 12 years old (chronic pathologies excluded) agreed on the superiority of VR over no-distraction regarding both self-reported and observed pain [39, 44]. However, 2 RCTs including 154 children, aged 7 to 12 years compared immersive VR to Buzzy® [39, 41], an easy-to-use, reusable, and fast device that vibrates and apply cold packs at the injection site before the shot, or distraction cards: VR and Buzzy efficacy on pain mitigation was comparable, but superior to distraction cards. Moreover, the VR goggle group had better reported scores (less reported pain) according to children (n=89, 4 to 10 years old), parents and observers reports when compared to distraction from a kaleidoscope [42]. Finally, when immersive VR was compared to tablets, no author observed a lower efficacy for VR entertainment, but a similar capacity in self-reported pain mitigation in youngest children (106 children, aged 4 to 7 years old) with no consequences in procedure's time and adverse reactions, and a better efficacy of VR in older subjects (80 kids aged 7-12 years) during phlebotomy [44, 45].

When children suffering from chronic diseases, who are periodically exposed to venipuncture for checking their medical condition, have been considered, two main categories have been studied: chronic kidney diseases (CKD), and cancer patients [46, 47]. A parallel RCT including 82 subjects among school-aged children, teen and teenagers with CKD aged between 7 to 17 years old, observed that VR was associated with significantly lower reported 'pain intensity' compared to children exposed to standard of care (non-medical conversation by the nurse in charge of the procedure); in particular, younger children reported a 55%

reduction in ‘worst pain’ during VR, and older children a 35% reduction. Conversely, onco-hematological patients undergoing venipuncture, experienced no benefit in self-reported pain when exposed to VR implementation; however their Face, Legs, Activity, Cry, Consolability (FLACC) scale during the procedure did not increase, while it increased in the no-distraction group [46]. Both CKD children and cancer patients had significantly reported to have had an overall more enjoyable experience during the venipuncture procedure if exposed to VR [46, 47].

The effect of VR distraction during port needle insertions has also been tested in 3 RCTs focusing on paediatric hematology-oncology patients, from 6 to 18 years of age. Despite the small sample size, these studies were able to demonstrate VR’s feasibility and acceptability during port needle insertion [48], to highlight VR success in reducing pain when compared to no distraction [39, 49], and to notice a trend in reducing intraprocedural self-reported pain compared with the tablet group, albeit not statistically significant [48].

In conclusion, the effect of VR on pain mitigation in paediatric needle-related procedure have been explored, often providing contrasting results; these might reflect differences in technologies, degree of immersion, patient coping styles, or differences in study design and sample sizes. Nevertheless, the vast majority of the studies demonstrated that VR implementation is feasible and effective compared to no distraction in both scheduled and unscheduled needle-related procedures including IV cannulation, venipuncture and port access; while no study highlighted a poorer performance of VR distraction compared to other types of entertainment.

VR APPLICATION IN BURN WOUND CARE

Burn wound care is a painful procedure which affects up to 2.8 to 13.4 per 100,000 children/ year in the United States; therefore, strategies to help mitigating pain such as VR are currently needed [50]. To address this need, multiple studies have explored the effect of VR in this context. Even if preschool children have been demonstrated to account for up 78.8% of total admitted burn children VR effectiveness in pain management during burn wound care has been explored mainly in older children [51-52]. Just one crossover RCT (38 children aged 6 months to 7 years of age) has analysed procedural pain reduction with VR in younger subjects during hydrotherapy: the hybrid VR intervention significantly reduced observed procedural pain levels evaluated by the FLACC scale, while it increased patients’ comfort, and it did not interfere with the delivery of care, with no side effects encountered [53]. The VR distraction was added to standard pharmacological treatment and sedation [53].

In older children (5 to 17 years old), the efficacy of VR has been studied in both dressing change/debridement or cleaning for burn injuries and physical therapy session after burn [17, 18, 54-56]. When VR was implemented and added to pre-procedure analgesia in physical therapy sessions, a decrease in pain intensity in the VR group was observed, and a significant difference in pain after treatment, favouring the VR distraction compared to no distraction, was noticed; furthermore, VR was associated with a significant increase in the range of motion, with a mean difference of 45.5° of movement [17].

In children undergoing dressing change/-debridement or cleaning for burn injuries, immersive or semi-immersive VR (users interact with a partially virtual environment: for example, a car simulator where the controls are real, but the windows display virtual images) have been tested and added to routine pain medication [18, 54-56] demonstrating the superiority of the immersive artificial environment, but not of the semi-immersive one, on self-reported post-procedural pain over no distraction; however, the included sample size was quite small [18, 54, 55].

Lastly, conflicting results emerge when VR and no VR distraction, such as tablet, music, books, and talking, or watching a movie, are compared [50].

APPLICATION OF VR ON DENTAL PROCEDURES IN CHILDREN

Only a few studies have explored the effectiveness of VR as a pain mitigator during dental treatments, nevertheless, they all unanimously identified VR as an effective distraction tool for easing discomfort [19, 20, 57, 58].

Virtual reality has been studied through parallel RCTs in healthy children between 4 to 12 years (minimum 54, maximum 200 subjects included, total number 428 children) undergoing different type of interventions ranging between short-term and simple dental procedure (*e.g.*, caries treatment, extraction of deciduous teeth, incision of abscess, and root canal therapy), to procedures requiring local anesthesia (*e.g.*, restoration, pulp therapy) or not (*e.g*. fluoride therapy, fissure sealant,) [19, 20, 58]. The VR intervention was compared to traditional behavior guidance procedures or tell-show-do.

Alshatrat *et al*. demonstrated VR's ability to mitigate pain during painful dental procedures requiring local anesthesia. The study observed a significant reduction in both self-reported and observer-reported pain intensity/worst pain when the VR distraction technique was used during painful dental procedures [19]; while, VR did not correlate with any significant reduction in worst pain during dental procedures that did not require local anesthesia [19]. Du *et al*. corroborated Alshtrat's conclusions by confirming VR ability in significantly reducing Wong Baker Scale score during primary teeth extraction under local anesthesia [20].

To explore whether different types of VR could have distinct effect, immersive VR pain management was compared to non-immersive VR [57]; both types of VR were shown effective in mitigating the perceived pain during intraoral injections, with immersive VR having a greater effect.

In all the aforementioned studies no simulator sickness occurred and no consequences on the ability to complete the treatment was encountered [20], if anything VR improved the compliance of children and significantly reduced the duration of the dental procedure [58].

APPLICATION OF VR ON OTHER PROCEDURES

The potential of VR use for pain mitigation during venous access, dental procedures and burn wound care have been the focus of different trials, providing reliable data. VR has been tested in other paediatric procedures, nevertheless, given the small sample sizes analyzed and the paucity of qualitative research, the current data are insufficient to draw any definitive conclusion [22, 27, 59, 60].

No mitigation in the perceived pain has been observed when VR was applied during cast and/or pin removals, acute mild to moderate traumatic/nontraumatic pain or minor plastic surgery procedures [22, 24, 59]. Two studies focusing on orthopedic procedures, such as cast or pin removal in adolescents, provide conflicting results; while Le May *et al*. reported a significant decrease in pain intensity with VR compared to standard of care (20 children included, 16 with orthopedic issues), Rychey *et al*. found no differences in pain scores before, during, or after the procedure, when VR was compared to verbal anxiolysis from the cast technician (130 children included) [22, 23]. Nevertheless, although VR did not correlate with reduced pain in this study, VR was associated with significantly lower average fear scores ($P < 0.001$) and anxiety scores ($P = 0.003$) compared to controls [22].

Likewise, Butt *et al*. demonstrated that a novel VR technology, a mindfulness-based platform, could be more effective than a passive distraction approach (tablet) in lowering anxiety levels in adolescents, but not pain, in acute mild to moderate traumatic/non-traumatic discomfort in adolescents in the EDs [59].

When minor surgical procedures under local anaesthesia (*e.g*., simple excisions, serial excisions, biopsies, scar revisions, among others) were considered, not only mean pain, but also anxiety scores were similar in both semi-immersive VR and standard of care (64 children aged 6 to 16 years) [24]. Conversely, VR has shown not only to be effective in pain mitigation in children undergoing circumcisions, active dressing changes in chronic lower limb wounds, gastrointestinal and nasal endoscopies [25-27, 60], but also to be safe and to increase procedural satisfaction for patients, without disrupting procedural efficiency and workflow [26, 27] (Table **2**). In particular VR technology may be of aid in nasal gastrointestinal endoscopy, as recently the feasibility and tolerance of this last procedure has been tested even in the absence of deep sedation [61, 62].

Recently, VR has been used also in other contexts, such as during the delivery of vaccines with promising results [63]. This cross-sectional study on VR technology intervention during immunization in children involved 104 children and demonstrated that participants who used VR technology experienced significantly less pain and fear compared with the no VR group [63].

CERTAINTY OF THE EVIDENCE

Even if the volume and complexity of data on VR implementation in various procedures in healthcare settings in children is increasing, the heterogeneity in the sampled population (diverse ages and developmental stages of children and their different perceptions), the variations in procedural conditions (*e.g*. phlebotomy, burn wound dressings, physical therapy sessions), and consequent level of pain

Reference	Procedure	N, age	type of study	Type of VR (immersive or not)	comparison	method of assessment of pain	post-procedural self-reported pain	post-procedural observer-reported pain	child/clinician/parent satisfaction with VR	adverse events	time of the procedure
[58] Butt 2022	acute mild to moderate traumatic/nontraumatic pain	118 children,13 to 17 years	RCT: 2 groups, parallel design	immersive	Passive distraction intervention: Ipad	WBFS	There were no statistically significant differences in the reduction of pain scores (p = 0.953)	not evaluated	not evaluated	none	not evaluated
[25] Buyuk 2021	circumcision	78 children, 5-10 years	RCT: 2 groups, parallel design	immersive	SOC: verbal anxiolysis from the cast technician	WBFS	not evaluated	A statistically significant difference favouring VR was observed in the mean pain mean measured by the parents and the nurse (p < .001)	not evaluated	not evaluated	not evaluated
[24] Clerc 2021	minor plastic surgery procedures	64 children, 6 to 16 years	RCT: 2 groups, parallel design	semi-immersive	SOC: tablet or smartphone,DVD movie, music, jokes, discussion, or handholding	FPS-R	A slightly lower mean increase in pain was recorded in the VR group, but not statistically significant	not evaluated	median pain management satisfaction was similar (virtual reality, 9 of 10; SOC, 9 of 10;p = 0.41).	2 children with dizziness; 1 child with mild nausea	Procedure time for participants in the virtual reality arm was 6.6 minutes less than standard of care (p = 0.01).
[59] Hua 2015	active dressing changes in chronic lower limb wounds	65 children aged 4 to 16 years	RCT: 2 groups, parallel design	Immersive	SOC: toys, television, books, parental comforting	WBFS (self-report) VAS (caregivers) FLACC (nurses)	beneficial effect favouring immersive VR (MD -0.90, 95% CI -1.70 to -0.10)	evidence of a beneficial effect favouring immersive VR (BAS: MD -3.27, 95% CI -4.12 to -2.42; FLACC MD -2.11, 95% CI -3.73 to -0.49).).	not evaluated	not evaluated	Time length of dressing changes was significantly reduced in the VR distraction group as compared to the control group (27.9 6.83 minutes vs. 22.3 7.85 minutes, p . .003)
[23] Le May 2021	wound dressing change/ debridement or orthopedic bone pin removal procedure;	20 children aged 7 to 17 years	RCT: within-subject desing	Immersive	SOC: music, comforting or other	NRS (pain) and pain-related fear (CFS)	Children reported significantly less procedural pain (p . .023)	not evaluated	36.4%, of nurses: VR device delayed their process of delivering care; 100.0%: VR increased patient collaboration, VR is an idea that is worth developing	none	not evaluated
[26] Liu 2021	nasal endoscopies	53 childre aged 7 to 17 years	RCT: 2 groups, parallel design	Immersive	SOC: no distraction	WBFS	Patients in the VR group reported experiencing significantly less pain during the procedure compared to patients in the control group	not evaluated	VR users: significantly greater procedural satisfaction compared to control group.	none	No significant "difference in mean procedural time was seen between groups (79.82 seconds 23.36 in VR group vs. 81.60 26.24 in control group, U = 282, P = .934, r = 0.01)
[27] Mantegazza 2021	gastrointestinal endoscopy	72 children, 4 and 18 years	RCT: 3 groups, parallel design	immersive	intranasal midazolam SOC: verbal anxiolysis	VAS/FLACC/NRS	The VR group reported significantly lower pain than IV and IN groups (median VAS VR:0, IV:2, IN:5, p=0.0045	median FLACC VR:2, IV:4, IN:3.5, p=0.0204;median	parent's satisfaction was significantly higher in the VR group, compared to the IN and the IV groups. No differences in the clinicians satisfactions	Adverse events were encountered in 83.5%, 33.3% and 56.7% of children in the IN, IV and VR group respectively (p=0.0115).	no difference in time of discharge
[22] Richey 2022	cast and/or pin removals	129 children,7 to 18 years	RCT: 3 groups, parallel design	Immersive	passive VR SOC: verbal anxiolysis	NRS	no differences in pain between the Active and Passive VR groups; no s differences in average pain scores between VR (Active Passive VR combined) and control during, or after the procedure	not evaluated	Patients and caregivers in the VR group reported high satisfaction scores, with 97% of patients and 95% of caregivers recommending this intervention to others	no side effects in the VR group	not evaluated

RCT: randomized controlled trial; SOC: standard of care; WBFS: Wong-Baker Faces Pain Rating Scale; VAS: Visual Analogue Scale; FPS-R: Faces Pain Scale-Revised; NRS: Numerical Rating Scale; FLACC: Face, Legs, Activity, Cry and Consolability scale; CFS: Children's Fear Scale; MD: mean deviation; CI: confidence interval.

experienced, make data pooling impossible. Therefore, data can only be described narratively.

Moreover, the use of different types of scales, ranging from the FPS-R, to the Wong Baker faces rating scale, the visual analogue scale or numerical rating scale, prevent direct comparison between the results of those studies [30, 33-36].

In addition, most studies included in this review may be at unclear risk of selection bias, high risk of performance and detection bias, and high risk of bias for small sample sizes, therefore the certainty of evidence is quite low.

FUTURE PERSPECTIVES

This review illustrates the heterogeneity of data among different studies on the use of VR in paediatric age to reduce procedural pain in different hospital settings. To overcome this limitation, future studies should sample a larger population, possibly including several centres using the same assessment tools, focusing on the same age group and procedure, in order to unambiguously define the effectiveness of this promising tool.

This would provide more reliable data and avoid bias due to too small samples.

Furthermore, VR research should focus on understanding how to best optimise VR software and user experience for maximising pain reduction. In these regards, some studies have already correlated higher levels of pain reduction with both a higher degree of immersion in VR and higher quality VR technology [64]. Immersive VR has also been shown to reduce pain more than non-immersive VR. However, to date, there is no evidence to suggest that a single immersive VR scenario is superior to another [65].

It would therefore be interesting for research to focus on finding the best VR scenario in a specific procedure and for a specific age group, analysing the environmental factors influencing pain perception. Studies should also focus on the correct timing of VR use, in order to make the tool even more acceptable. By studying and implementing these aspects the VR experience could be optimised and customised and thus could become even more effective as a pain mitigation strategy in the paediatric population.

CONCLUSIONS

In conclusion, the current literature on the use of VR is increasing but, due to the heterogeneity of the population and variability in procedural conditions, data pooling is difficult and current results do not allow us to draw reliable conclusions as the evidence of certainty is rather low. However VR seems effective in reducing pain compared to no distraction in paediatric needle procedures and in children undergoing change/debridement or cleaning for burn injuries [13, 18, 39, 49, 54-56], while mixed results emerged when comparing VR with other distractions (such as tablets, music or books) [12, 30, 33-35, 36, 38, 50]. Moreover immersive VR proved to be a tool capable of reducing the intensity of perceived pain in dental procedures requiring local anaesthesia, leading to an improvement in children's compliance and a significantly reduced duration of the dental procedure [57, 58]. Finally, while in the cast and/or pin removal, mild to moderate traumatic/non-traumatic pain or minor plastic surgery procedures, VR had no effect in alleviating pain

[22, 24], it was effective in relieving pain in children undergoing circumcision, active dressing changing in chronic lower limb wounds, nasal and gastrointestinal endoscopies [25-27, 60].

Nevertheless, results remain conflicting, probably due to differences in technologies, degree of immersion, patients' coping styles or differences in study design and sample size.

Future large randomised controlled multicentre studies employing standardised procedures and more homogeneous patient population could address this limitation and shed light on the actual role of VR in acute pain management in the paediatric population.

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