



# Virtual reality in pediatrics, effects on pain and anxiety: A systematic review and meta-analysis update

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## Abstract

**Introduction:** Medical procedures are often accompanied by pain and anxiety in pediatric patients. A relatively new technique to reduce pediatric pain and anxiety is virtual reality. Virtual reality is both applied as a distraction tool and as an exposure tool to prepare patients for medical procedures. Research into the application of virtual reality in medical settings is rapidly evolving. This meta-analysis is an update of the meta-analysis of Eijlers et al. investigating the effectiveness of virtual reality as an intervention tool on pain and anxiety in pediatric patients undergoing medical procedures.

**Methods:** We searched the databases Embase, Medline, Web of Science Core Collection, Cochrane Central Register of Controlled Trials and PsycINFO. For each of these databases, different search strategies were developed. The search period from the meta-analysis from Eijlers et al., reaching until April 2018, was extended to December 2020. Pain and anxiety outcomes during medical procedures were compared for virtual reality and standard care conditions for various medical procedures.

**Results:** The search yielded 1824 articles, of which 13 met our inclusion criteria. Combined with 13 articles of Eijlers' review study, this resulted in 26 articles. Virtual reality was applied as distraction ( $n = 23$ ) during medical procedures or as exposure ( $n = 4$ ) before medical procedures. The effect of virtual reality distraction was mostly studied in patients during venous access ( $n = 10$ ). The overall weighted standardized mean difference for virtual reality distraction was  $-0.67$  (95% CI,  $-0.89$  to  $-0.45$ ;  $p < .001$ ) on patient-reported pain (based on 21 studies) and  $-0.74$  (95% CI,  $-1.00$  to  $-0.48$ ;  $p < .001$ ) on patient-reported anxiety (based on 10 studies). The effect of virtual reality as an exposure tool on patient-reported anxiety was significant too (standardized mean difference =  $-0.58$ ; 95% CI,  $-1.15$  to  $-0.01$ ;  $p < .05$ ).

**Discussion:** The current updated systematic review and meta-analysis indicates that virtual reality is a useful tool to reduce pain and anxiety in pediatric patients undergoing a range of medical procedures as it significantly decreases pain and anxiety outcomes when compared to care as usual.

\*The authors contributed equally to this project as co-first authors.

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## KEYWORDS

anesthesia &lt; Audit, child &lt; Age, pain &lt; Complications, research

## 1 | INTRODUCTION

Medical procedures often come with pain, which can result in a lot of distress in children. This may then lead to preprocedural anxiety,<sup>1</sup> affecting 30% to 75% of children undergoing medical procedures.<sup>2,3</sup>

In children, higher anxiety levels before and during medical procedures are associated with more peri- and post-procedural pain, slower and more complicated recovery and lower success of sedation.<sup>4–8</sup> Furthermore, inadequate relief of pain and distress may lead to less pain tolerance and more pain responses in the long-term.<sup>9</sup> Psychological preparation of children for surgery has shown to be related to improved postoperative recovery.<sup>4</sup> Hence, addressing preprocedural anxiety is likely to not only increase patient comfort, but may also improve recovery from medical procedures and lessen pain.

Distraction is a commonly used technique to reduce anxiety and pain during medical procedures.<sup>10–13</sup> Especially listening to music and relaxation-guided imagery seem effective ways of reducing anxiety and pain.<sup>12,13</sup> Another way to deliver distraction is by using Virtual Reality (VR), an advanced technology that allows us to create realistic simulations of the world around us that can be explored and interacted with freely.<sup>14</sup> In medicine, VR has proven to be useful,<sup>15–18</sup> for example, in reducing pain and anxiety,<sup>19,20</sup> especially when VR is interactive compared with passive.<sup>21</sup> More interaction comes with more immersion, which is linked to greater pain tolerance.<sup>22</sup> As children appear more sensitive to anxiety and pain,<sup>4</sup> VR might be more effective in reducing anxiety and pain than in adults. Thus, it is important to study the effects of VR interventions in children independently, as Eijlers et al. did in their review.<sup>23</sup>

Next to distraction, VR offers promise as a tool for exposure.<sup>23</sup> Exposure can be used to calm patients by informing them about the medical procedure in advance.<sup>6</sup> VR as exposure is well-established within general psychology,<sup>15–18,24</sup> and thus, VR may be even more suited as a tool of exposure compared with distraction.

The aim of this paper was to provide an update of the meta-analysis of Eijlers et al., building on the studies that have been published since April 2018. We will further investigate the effectiveness of VR as an intervention tool on pain and anxiety in pediatric patients undergoing medical procedures both as a way of distraction and as a way of exposure. This update is needed, as the number of studies using VR interventions has grown exponentially. VR equipment has become more accessible for day-to-day use in clinical settings. Mainly because nowadays, a lot of cheap VR glasses that can be used with mobile phones are broadly available. Based on the earlier study of Eijlers et al., we expect VR distraction to be a useful technique to reduce pain and anxiety in children during medical procedures. Furthermore, due to the growing interest in the field of VR interventions, we expect an increase in the number of studies targeted towards VR exposure. This would allow the current study to get an

insight into the effects of VR exposure on anxiety and pain in pediatric medical procedures, which was not possible for Eijlers et al. due to the limited amount of exposure studies they found.

## 2 | METHODS

### 2.1 | Selection criteria

Corresponding with Eijlers' meta-analysis,<sup>23</sup> the following inclusion and exclusion criteria were used. Studies investigating the effect of VR on pain and/or anxiety in patients  $\leq 21$  years of age undergoing medical procedures were included. Since various interpretations and definitions of VR exist, we defined VR as a technology that allows for the creation of immersive and interactive environments and is projected in front of the user's eyes via a head-mounted display. Studies were selected for inclusion if they had at least the following data available: a mean/median score for pain or anxiety during the procedure, as well as a measure of dispersion, for both the intervention and standard care groups.

Exclusion criteria consisted of the application of VR in nonsomatic patients, no possibility of interaction between the user and the virtual reality environment, and the absence of distinction between pediatric and adult patients. In contrast to our earlier meta-analysis,<sup>23</sup> studies that consisted of noninteractive movies displayed on VR glasses were excluded. This way, only studies with highest immersion were included, due to the interactive component that makes the entire experience more immersive. Additionally, the following study types were excluded: reviews, meta-analyses, single-case studies, dissertations, conference papers, and abstract only papers.

### 2.2 | Search strategy

We used the same search terms as Eijlers et al.,<sup>23</sup> namely "VR" and "children" or "adolescents". The databases Embase, Medline, Web of Science Core Collection, Cochrane Central Register of Controlled Trials and PsycINFO were used. For each of these databases, different search strategies were developed. The initial search period from the previous review<sup>23</sup> that reached until April 2018 was extended to December 2020.

### 2.3 | Assessment of study quality

Two authors (F.Q.T. and C.A.M.v.E.) independently examined the quality of the included studies using the Delphi List (see [Table 1](#)). This criteria list consists of nine items which can be scored as "Yes,"

**TABLE 1** Delphi list for quality assessment of randomized controlled trials

Criteria	Evaluation
1 Was a method of randomization performed?	Yes (1)/No (0)/Don't know (0)
2 Was the treatment allocation concealed?	Yes (1)/No (0)/Don't know (0)
3 Were the groups similar at baseline regarding the most important prognostic indicators?	Yes (1)/No (0)/Don't know (0)
4 Were eligibility criteria specified?	Yes (1)/No (0)/Don't know (0)
5 Was the outcome assessor blinded? <sup>a</sup>	Yes (1)/No (0)/Don't know (0)
6 Was the care provider blinded? <sup>a</sup>	Yes (1)/No (0)/Don't know (0)
7 Was the patient blinded? <sup>b</sup>	Yes (1)/No (0)/Don't know (0)
8 Were point estimates and measures of variability presented for the primary outcome measures?	Yes (1)/No (0)/Don't know (0)
9 Did the analysis include an intention-to-treat analysis?	Yes (1)/No (0)/Don't know (0)

<sup>a</sup>Depending on the moment of VR use, the application of criteria 5 and 6 differed. When VR was applied before the medical procedure, the maximum possible score was 8. When VR was applied during the medical procedure, the maximum possible score was 6.

<sup>b</sup>Criteria item 7 was not applicable in this study context.

"No," or "Don't know." Only items valued "yes" were given a score of 1 point.

## 2.4 | Synthesis of results

Mean scores and SDs for pain and anxiety during the procedure in the VR intervention and standard care conditions were either extracted from articles or estimated using median scores and interquartile ranges.<sup>25</sup> These data were analyzed with Comprehensive Meta-analysis software version 2<sup>26</sup> by three authors (F.Q.T., C.A.M.v.E., and B.D.). Self-reported pain and anxiety were considered as primary outcome. Assessment instruments for pain and anxiety were categorized as visual scales or questionnaires. In addition, anxiety and pain scores from children undergoing the medical procedure, as reported by caregivers and/or professionals, were included as a secondary outcome if reported by the study. The nature of the VR intervention was the same for all reporters. Study design was divided in parallel or crossover design. When data on different aspects of pain were available, (e.g., sensory, affective, and cognitive) the sensory component was used in our analysis.

The outcomes of pain and anxiety were analyzed separately. Effect sizes were computed as standardized mean difference (SMD) by calculating the mean difference on pain or anxiety outcomes between VR and standard care conditions during the procedure and

dividing the result by the pooled SD.<sup>25</sup> A generally accepted rule of thumb is that a Cohen's *d* of 0.2 represents a small effect size, 0.5 a medium effect size, and 0.8 a large effect size.

Meta-analyses for both pain and anxiety were conducted to compare overall effect sizes of VR distraction to control conditions. Studies using VR distraction and VR exposure therapy were analyzed separately.

A random-effects model was used, because of the expected heterogeneity of the included studies due to the broad range of medical procedures. Sensitivity analyses were performed by removing studies with low methodological quality (i.e., a quality score of 0–2) from both meta-analyses. Additionally, separate sensitivity analyses were run for type of medical procedure and type of informant on VR distraction effectivity. In these analyses, low-quality studies were excluded as well.

Finally, a meta-regression analysis was performed with mean age of the patients as predictor and a random-effects model (with methods of moments) to investigate if young children respond differently to VR distraction interventions than older children. Heterogeneity was assessed using the  $I^2$  statistic, with values  $\geq 75\%$  indicating substantial heterogeneity.<sup>27</sup> Publication bias was assessed with funnel plot asymmetry and Egger's regression tests.<sup>28</sup>

## 3 | RESULTS

### 3.1 | Data extraction

In Eijlers' search, 17 articles were selected based on full text.<sup>23</sup> We included 13 of these articles, due to the exclusion of studies without interactive VR. The current search resulted in 1824 articles. Two authors (F.T. and C.E.) screened the titles and abstracts of these articles independently, applying the inclusion and exclusion criteria. Discrepancies (1.8%) were discussed until consensus was reached. The authors selected 74 articles based on title and abstract. The full text of these 74 articles was read by the two authors independently. Discrepancies (18%) were discussed until consensus was reached. We excluded 61 of the 74 studies. Most of these studies were excluded because they did not use interactive VR. Another important reason for exclusion was a research population of only adults. The resulting 13 articles together with the 13 previous articles were used for final analysis. One study<sup>29</sup> comprised two RCT's, which are included as separate studies. This resulted in an inclusion of 27 studies. The outcome of our search strategy is summarized in the flow diagram shown in [Figure 1](#).

### 3.2 | Study characteristics

Main characteristics and relevant results of all included studies can be found in [Table 2](#). The 27 studies were organized based on the type of medical procedure. VR was used as a way of distraction in 23, and exposure in 4 of the included studies. Types of medical procedures using VR distraction included venous access

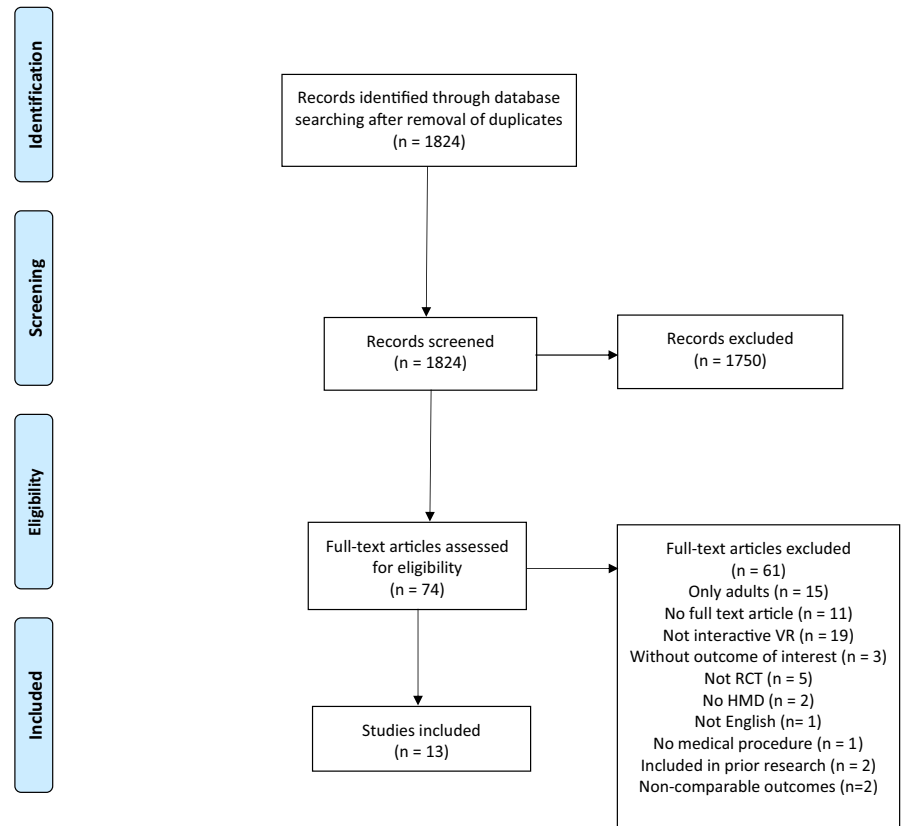


FIGURE 1 Flow diagram showing different stages of study selection

( $n = 10$ ),<sup>29-37</sup> oncological care ( $n = 3$ ),<sup>38-40</sup> burn care ( $n = 7$ ),<sup>41-47</sup> endoscopy ( $n = 1$ ),<sup>48</sup> dental care ( $n = 1$ ),<sup>49</sup> or before surgery ( $n = 1$ ).<sup>50</sup> Types of medical procedures using VR exposure included radiography ( $n = 1$ )<sup>51</sup> or before surgery ( $n = 3$ ).<sup>52</sup> All studies were conducted between 1999 and 2020. The number of participants varied between 5 and 201, with a median of 56. Furthermore, all studies used validated visual scales or questionnaires to measure anxiety or pain. To be able to compare the study results with each other, we calculated effect size scores with corresponding  $p$ -values for all studies by using available mean scores and standard deviations from the groups in each study. As effect sizes were calculated the same way, regardless of the questionnaire or scale used, we could compare these effect sizes directly to each other in the software package that was used.

Most studies were randomized controlled trials (RCT) ( $n = 23$ ), of which 17 used a parallel design and six used a crossover design. The remaining four studies were quasi-experimental, of which three were not randomized and one used an interrupted time series design with removed treatment. All studies compared an intervention group (VR) to care-as-usual (CAU), although care-as-usual was often not well defined. Studies used nonVR distraction like playing games, while other studies did not use any form of distraction. Parental presence was not clear in all studies, as well as if and which pharmacological analgesia was being used. Four RCT's added a nonVR intervention group, such as distraction by a computer game or television.

The ages of participants in the 26 studies varied between 4 and 21 years. One study did not indicate an age range and only provided

a mean age ( $M = 6.54$ ). Studies were heterogeneous regarding VR software and hardware.

### 3.3 | Study quality assessment

Criteria 5 and 6 of the Delphi List, blinding of the outcome assessor and caregiver, were only applicable to four studies.<sup>51-54</sup> These studies used VR as an exposure intervention before the medical procedure. The other studies used VR as distraction during the procedure, and therefore, the outcome assessor and caregiver could not be blinded. This resulted in a maximum possible score of 6 instead of 8 for these studies.

As shown in Table 2, the quality scores (see Table 2) varied between 1 and 8 points, with an average score of 4.5 ( $SD = 1.7$ ). Discrepancies in study quality scores (16%) were discussed until consensus was reached. Most studies had a high quality ( $n = 14$ ) (i.e., a maximum score, or 1 point below the maximum score). Eight studies had moderate quality, and four studies poor quality (i.e., a score of 0–2).

Elaborate explanation of the quality assessment of the studies used by Eijlers et al.<sup>23</sup> are described in their article.

Of the new included studies, three studies performed intention-to-treat analysis (23%). In five studies, there were no dropouts, and therefore, no intention-to-treat analysis was performed (38%). These five studies were scored as 1 on the question if intention-to-treat analysis was performed. A method of randomization was performed in 92% ( $n = 12$ ) studies, 69% ( $n = 9$ ) of the studies guaranteed a concealed treatment allocation. In 85%

TABLE 2 Study characteristics and results of included studies that investigate the effect of virtual reality on pain and anxiety in pediatric patients undergoing medical procedures (n = 27)

Medical procedure	Participants			VR equipment	Treatment conditions	Study design	Key findings	Quality score <sup>a</sup>
	Author (Year)	n	Age					
Venous access	Chan et al. (2019) <sup>29</sup>	123	4–11 y	Google Daydream	Emergency department: VR distraction CAU	RCT crossover	VR is effective in decreasing pain and anxiety during intravenous cannulation	6
		129	4–11 y		Outpatient laboratory: VR distraction CAU		VR is effective in decreasing pain and anxiety during venipuncture	
	Dumoulin et al. (2019) <sup>32</sup>	35	8–17 y	eMagin z800 HMD	VR distraction NonVR distraction (television) CAU	RCT parallel	VR is effective in decreasing fear of pain compared to TV and CAU, but this effect was not found for decreasing pain	6
	Atzori, Hoffman et al. (2018) <sup>33</sup>	15	7–17 y	HMZ T-2	VR distraction CAU	Within subjects (not randomized)	During VR, patients reported significant reductions in worst pain compared to CAU	4
	Aydin et al. (2019) <sup>34</sup>	120	9–12 y	Sanal Gözlük VR	VR distraction CAU	RCT parallel	Pain levels reported by children were significantly lower in the VR group compared to control group	5
	Piskorz et al. (2020) <sup>35</sup>	57	7–17 y	Samsung Gear VR	VR distraction (active VR) VR distraction (passive VR) CAU	RCT parallel	Both active and passive VR groups reported less pain and stress than the control group. When comparing active and passive VR, no significant differences were found, although there was a difference in perceived pain and stress	2
	Walther-Larsen et al. (2019) <sup>36</sup>	64	7–16 y	Samsung Gear VR with Samsung Galaxy S6	VR distraction CAU	RCT parallel	There were no significant differences in pain scores between VR distraction and standard care	5
	Gold et al. (2006) <sup>37</sup>	20	8–12 y	5DT HMD 800 with InterSens InertiaCube2 tracker	VR distraction CAU	RCT parallel	Less self-reported pain (FPS-r) in VR than CAU during procedure No differences in self-reported pain measured with faces during procedure No differences in self-reported, parent, or nurse-observed pain (VAS) during procedure	5
	Piskorz and Czub (2018) <sup>55</sup>	38	7–17 y	Oculus Rift DK2	VR distraction CAU	Between subjects design (not randomized)	Less self-reported pain (VAS) and anxiety (VAS) than CAU during procedure	1
	Gold and Mahrer (2018) <sup>30</sup>	143	10–21 y	Samsung Galaxy S6 + 1. Google Pixel Merge VR (10–12) 2. Samsung Gear VR (13–21)	VR distraction CAU (television)	RCT parallel	Less self-reported and parent-observed pain (VAS) and anxiety (VAS) in VR than CAU during procedure	3

(Continued)

TABLE 2 (Continued)

Medical procedure	Participants		Moment of VR	VR equipment	Treatment conditions	Study design	Key findings	Quality score <sup>a</sup>
	Author (Year)	n						
Preoperative	Eijlers et al. (2019) <sup>33</sup>	201	4–12 y	HTC Vive	VR exposure CAU	RCT parallel	VR did not influence self-reported anxiety (VAS) and pain (FPS-r) pre- and postprocedural. Observed preprocedural anxiety (m-YPAS) and observed postprocedural pain (FLACC & PPPM) did not differ between VR and CAU as well	8
	Jung et al. (2020) <sup>30</sup>	71	5–12 y	Samsung Gear VR	VR distraction CAU	RCT parallel	VR led to significant reduction in observed anxiety levels (m-YPAS) compared to standard care	6
	Ryu et al. (2018) <sup>54</sup>	69	4–10 y	Oculus Rift	VR exposure CAU (conventional education)	RCT parallel	Researcher-observed preoperative anxiety (m-YPAS) was significantly lower in the VR group compared to the standard care group	6
	Ryu et al. (2017) <sup>52</sup>	69	4–10 y	Samsung Galaxy S6+ Samsung Gear VR	VR exposure CAU (face-to-face information)	RCT parallel	Less researcher-observed preoperative anxiety (m-YPAS) in VR than in CAU	5
Oncological care	Schneider and Workman (1999) <sup>38</sup>	11	10–17 y	Virtual IO	VR distraction CAU	Interrupted time series with removed treatment	No differences in self-reported state anxiety (state-trait anxiety inventory for children-1) during procedure	2
	Gershon et al. (2004) <sup>39</sup>	59	7–19 y	Unknown	VR distraction NonVR distraction CAU (personal computer game)	RCT parallel	Less nurse-observed pain (VAS) in VR and nonVR distraction than CAU during procedure No differences in researcher-observed pain (CHEOPS), self-reported or parent-observed pain or anxiety (VAS) during procedure	4
	Wolitzky et al. (2005) <sup>40</sup>	20	7–14 y	Unknown	VR distraction CAU	RCT parallel	Less researcher-observed pain (CHEOPS) in VR than CAU during procedure No differences in self-reported, parent-observed, or nurse-observed pain or anxiety (VAS) during procedure	4
Burn care	Das et al. (2005) <sup>41</sup>	11 <sup>b</sup>	5–16 y	IO i-glasses	VR distraction CAU	RCT crossover	Less self-reported pain (faces scale) during procedure in VR than CAU	3
	Chan et al. (2007) <sup>42</sup>	8	M = 6.54	i-glasses	VR distraction CAU	RCT crossover	No differences in self-reported pain (FPS-r) during and after procedure	1
	Schmitt et al. (2011) <sup>43</sup>	54	6–19 y	nVisor SX VR-1280 ProView XL50 ProView SR80	VR distraction CAU	RCT crossover	Less self-reported cognitive, affective, and sensory pain (GRS) in VR than CAU during procedure	3
	Kipping et al. (2012) <sup>44</sup>	41	11–17 y	eMagin, Z800 3Dvisor	VR distraction CAU (television, stories, or music)	RCT parallel	Less observed pain (FLACC) during procedure in VR than CAU. No differences in self-reported or parent-observed pain (VAS) during procedure.	6

TABLE 2 (Continued)

Medical procedure	Participants		Moment of VR	VR equipment	Treatment conditions	Study design	Key findings	Quality score <sup>a</sup>
	Author (Year)	n						
	Jeffs et al. (2014) <sup>45</sup>	28	10–17 y	Kaiser Optical SR80a on tripod	VR distraction NonVR distraction (television) CAU	RCT parallel	Less self-reported pain (APPT-WRGS) during procedure in VR than in nonVR distraction but not less than CAU	5
	Hua et al. (2015) <sup>46</sup>	56	4–16 y	eMagin Z800 3DVisor	VR distraction CAU (toys, television, books)	RCT parallel	Less self-reported pain (faces), during, less parent-observed pain (VAS) before, during and after, and less researcher-observed pain (FLACC) during and after procedure in VR than CAU	5
	Hoffman et al. (2019) <sup>47</sup>	96	6–17 y	MX90 VR Goggle	VR distraction CAU	RCT crossover	VR distraction leads to less self-reported pain (GRS) in children during burn wound care	6
Endoscopy	Liu et al. (2020) <sup>48</sup>	53	7–17 y	Oculus Go	VR distraction CAU	RCT parallel	Self-reported pain (FACES) and self-reported anxiety (SUDS) levels, as well as observed (caregiver) anxiety levels in the VR group, were significantly lower	5
Dental care	Atzori, Lauro et al. (2018) <sup>49</sup>	5	7–17 y	Oculus Rift	VR distraction CAU	Within subjects crossover design (not randomized)	Self-reported (worst) pain (GRS) were significantly lower in the VR intervention group	5
Radiography	Han et al. (2019) <sup>51</sup>	99	4–8 y	Oculus Go	VR exposure CAU	RCT parallel	Observed anxiety levels (OSBD) were significantly lower in the VR intervention group	7

Note: Manufacturer information for the equipment noted in the table: i-glasses 920HR (Ilixco, Inc, Menlo Park, CA); i-glasses (i-O Display Systems, LLC, Sacramento, CA); nVisor SX (NVIS, Inc, Reston, VA); VR-1280 (Virtual Research Systems, Inc, Aptos, CA); ProView XL50 (Kaiser Electro-Optics, Inc, Carlsbad, CA); ProView SR80 (Kaiser Electro-Optics, Inc, Carlsbad, CA); eMagin Z800 3DVisor (eMagin Corporation, Hopewell Junction, NY); Kaiser Optical SR80a (on tripod); Kaiser Optical Systems, Inc, Ann Arbor, MI); 5DT HMD 800 (5DT, Inc, Irvine, CA); Oculus Rift DK2 (Facebook Technologies, LLC, Menlo Park, CA); Samsung Galaxy S5 (Samsung Electronics Co, Ltd, Suwon, South Korea); Samsung Gear VR (Facebook Technologies, LLC, Menlo Park, CA); Google Pixel (HTC Corporation, New Taipei City, Taiwan); Merge VR (Merge Labs, Inc, San Antonio, TX); Samsung Galaxy S6 (Samsung Electronics Co, Ltd, Suwon, South Korea).

Abbreviations: APPT-WRGS, adolescent pediatric pain tool - word graphic rating scale; CAU, care as usual; CHEOPS, Children's Hospital of Eastern Ontario pain scale; FLACC, face, legs, activity, cry, consolability; FPS-r, faces pain scale-revised; GRS, graphic rating scale; IV, intravenous; M, mean; m-YPAS, modified Yale preoperative anxiety scale; OSBD, observational scale of behavioral distress; RCT, randomized controlled trial; VAS, visual analog scale; VR, virtual reality.

<sup>a</sup>Maximum possible score for four studies is 8. <sup>51-54</sup> Maximum possible score for all other studies is 6.

<sup>b</sup>Seven subjects were unique and could participate more than once.

( $n = 11$ ) of the studies, groups were similar at baseline regarding the most important prognostic indicators. For the remaining two studies, the article did not provide enough information about baseline characteristics to determine whether the groups were similar at baseline. For only one study (8%), inclusion and exclusion criteria were not described precisely enough.

### 3.4 | Virtual reality distraction and pain management

Figure 2 shows the effect sizes of VR distraction for patient-reported pain (21 studies). Negative effect sizes represent less pain in the VR distraction group. Across all studies, using a random-effects model, the weighted effect size of VR distraction on pediatric self-reported pain during a medical procedure was statistically significant (SMD =  $-0.67$ ; 95% CI,  $-0.89$  to  $-0.446$ ;  $p < .001$ ). A SMD of 0.67 represents a medium effect size. Heterogeneity of study effects was considerable ( $I^2 = 67.9\%$ ). A sensitivity analysis was performed by excluding studies with low methodological quality. This resulted in exclusion of three studies.<sup>35,42,55</sup> This analysis also indicated a statistically significant effect with a medium effect size (SMD =  $-0.60$ ; 95% CI,  $-0.82$  to  $-0.37$ ;  $p < .001$ ). Heterogeneity did not substantially differ compared with the main analysis ( $I^2 = 68.4\%$ ). In addition, the current dataset and the adapted (i.e., studies that were removed in the current study, but included in the original study) dataset from Eijlers et al.<sup>23</sup> was analyzed separately. This analysis indicated a significant effect for both the current dataset (SMD =  $-0.78$ ; 95%

CI,  $-1.12$  to  $-0.44$ ;  $p < .001$ ), as well as the adapted dataset from the earlier review (SMD =  $-0.55$ ; 95% CI,  $-0.84$  to  $-0.28$ ;  $p < .001$ ), suggesting a greater effect size in the current dataset.

Sensitivity analyses were carried out on pain for each type of medical procedure when data from more than 1 study were available. Statistically significant effects were found for burn care (SMD =  $-0.85$ ; 95% CI,  $-1.15$  to  $-0.56$ ;  $p < .001$ ;  $I^2 = 39.2\%$ ) and venous access (SMD =  $-0.521$ ; 95% CI,  $-0.84$  to  $-0.20$ ;  $p < .01$ ;  $I^2 = 75.7\%$ ).

A random-effects model (with methods of moments) was used for the meta-regression analysis with age as a predictor. The results did not suggest that VR distraction interventions for pain reduction were more efficacious for younger than for older children ( $p = .25$ ).

Finally, analyses were carried out for caregivers and professionals as observers of pediatric pain. Statistically significant results were found based on both types of informants (caregivers: SMD =  $-0.47$ ; 95% CI  $-0.72$  to  $-0.22$ ;  $p < .001$ ;  $I^2 = 0.00\%$ , professionals: SMD =  $-0.93$ ; 95% CI,  $-1.31$  to  $-4.78$ ;  $p < .001$ ).

### 3.5 | Virtual reality distraction and anxiety management

Figure 3 shows the effect sizes of VR distraction for patient-reported anxiety (10 studies). Negative effect sizes represent less anxiety in the VR distraction group. Using the random-effects model, a statistically significant effect with a medium effect size was found for VR distraction on patient-reported anxiety (SMD =  $-0.74$ ; 95% CI,  $-1.00$  to  $-0.48$ ;  $p < .001$ ). Heterogeneity of the study effects was moderate ( $I^2 = 59.3\%$ ). A sensitivity analysis was performed by excluding studies

Study	Medical procedure	Effect Size	Lower Limit	Upper Limit	p-value
Walther-Larsen, 2019	Venous access	0,315	-0,199	0,829	0,230
Aydin, 2019	Venous access	-0,054	-0,412	0,304	0,767
Gershon, 2004	Oncological	-0,086	-0,677	0,506	0,776
Dumoulin, 2019	Venous access	-0,157	-0,827	0,514	0,647
Gold, 2006	Venous access	-0,281	-1,161	0,600	0,532
Gold, 2018	Venous access	-0,320	-0,650	0,010	0,057
Kipping, 2012	Burn care	-0,465	-1,085	0,156	0,142
Schmitt, 2011	Burn care	-0,524	-0,908	-0,140	0,007
Jeffer, 2014	Burn care	-0,558	-1,505	0,390	0,249
Atzori, Hoffman, 2018	Venous access	-0,700	-1,438	0,037	0,063
Atzori, Lauro, 2018	Dental care	-0,719	-1,998	0,560	0,271
Chan ED, 2019	Venous access	-0,803	-1,170	-0,435	0,000
Liu, 2020	Endoscopy	-0,832	-1,397	-0,266	0,004
Piskorz, 2017	Venous access	-0,839	-1,503	-0,176	0,013
Hua, 2015	Burn care	-0,891	-1,400	-0,381	0,001
Chan Pathology, 2019	Venous access	-1,008	-1,374	-0,641	0,000
Das, 2005	Burn care	-1,160	-2,063	-0,257	0,012
Hoffman, 2019	Burn care	-1,304	-1,745	-0,864	0,000
Chan, 2007	Burn care	-1,311	-2,392	-0,231	0,017
Piskorz, 2020	Venous access	-1,496	-2,198	-0,794	0,000
Wolitzky, 2005	Oncological	-1,846	-2,892	-0,799	0,001
Total		-0,666	-0,885	-0,446	0,000

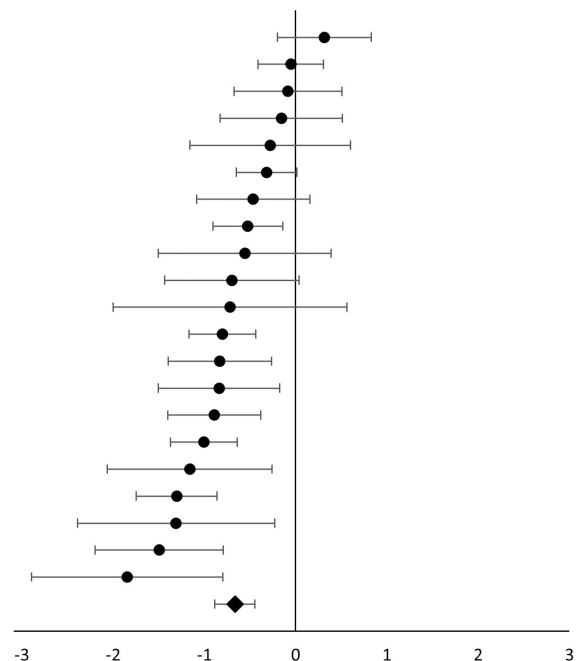


FIGURE 2 Random-effects meta-analysis for the effect of VR on patient-reported pain during a medical procedure compared with CAU



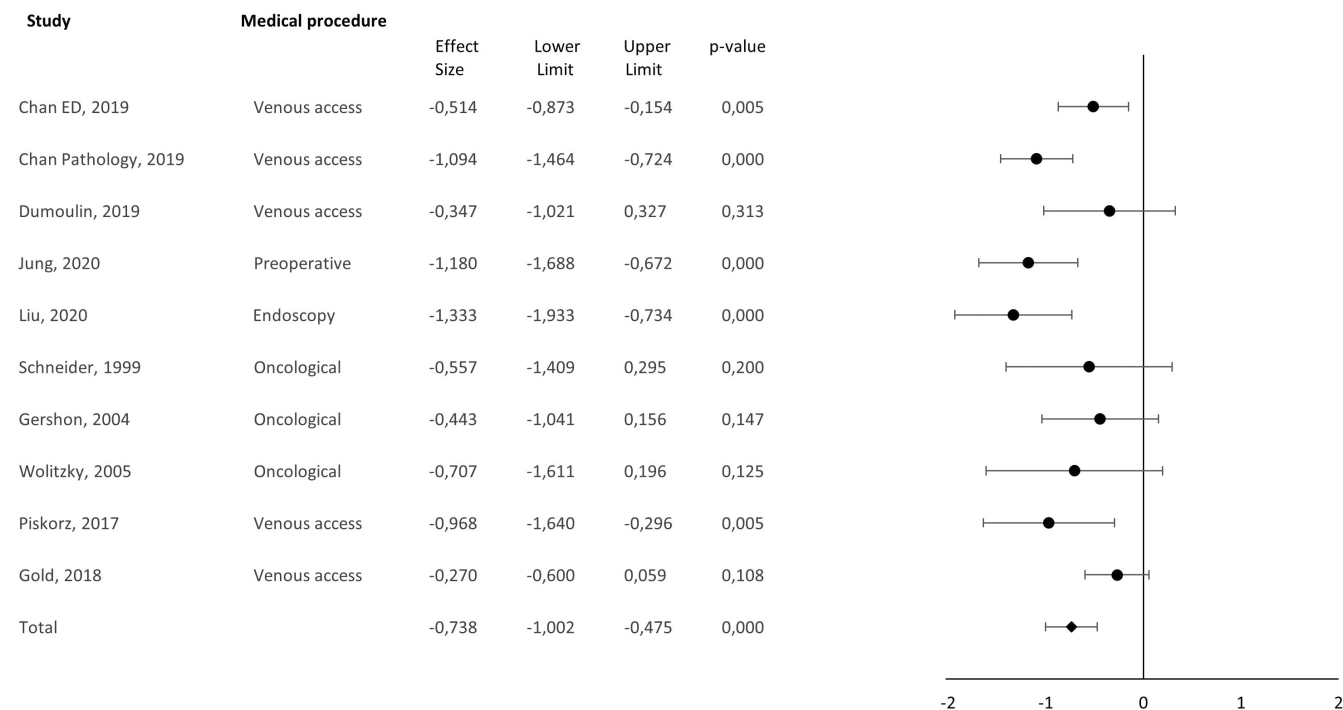


FIGURE 3 Random-effects meta-analysis for the effect of VR on patient-reported anxiety during a medical procedure compared with CAU

with low methodological quality. This resulted in exclusion of two studies.<sup>38,55</sup> This analysis also indicated a statistically significant effect of VR distraction on self-reported anxiety, with a medium effect size (SMD =  $-0.72$ ; 95% CI,  $-1.00$  to  $-0.43$ ;  $p < .001$ ). Heterogeneity did not substantially differ compared with the main analysis ( $I^2 = 62.7\%$ ).

Sensitivity analyses were carried out on patient-reported anxiety for each type of medical procedure, when data from  $>1$  study were available. Statistically significant effects were found for venous access (SMD =  $-0.63$ ; 95% CI,  $-0.98$  to  $-0.28$ ;  $p < .001$ ;  $I^2 = 68.2\%$ ) and oncological procedures (SMD =  $-0.53$ ; 95% CI,  $-0.96$  to  $-0.101$ ;  $p < .05$ ,  $I^2 = 0.0\%$ ).

A random-effects model (with methods of moments) was used for the meta-regression analysis with age as a predictor. The results did not suggest that VR interventions for patient-reported anxiety reduction were more efficacious for younger than for older children ( $p = .18$ ).

Analyses were also carried out for caregivers as observers of pediatric anxiety. Statistically significant results were found (SMD =  $-0.59$ ; 95% CI  $-1.02$  to  $-0.15$ ;  $p < .01$ ;  $I^2 = 0.00\%$ ).

Finally, the current dataset and the adapted dataset from Eijlers et al.<sup>23</sup> were analyzed separately. This analysis indicated a significant effect for both the current dataset (SMD =  $-0.90$ ; 95% CI  $-1.26$  to  $-0.54$ ;  $p < .001$ ) as well as the adapted dataset from the earlier review (SMD =  $-0.45$ ; 95% CI  $-0.69$  to  $-0.20$ ;  $p < .001$ ), suggesting a greater effect size in the current dataset.

### 3.6 | VR exposure

Figure 4 shows the effect sizes of VR exposure for patient-reported anxiety. Using the random-effects model, a statistically

significant effect size was found for VR exposure on anxiety (SMD =  $-0.58$ ; 95% CI,  $-1.15$  to  $-0.01$ ;  $p < .05$ ). A SMD of 0.58 represents a medium effect size. Heterogeneity of the study effects was high ( $I^2 = 87.1\%$ ).

Only one VR exposure study investigated the outcome "pain." Therefore, we could not perform meta-regression analysis on this outcome.

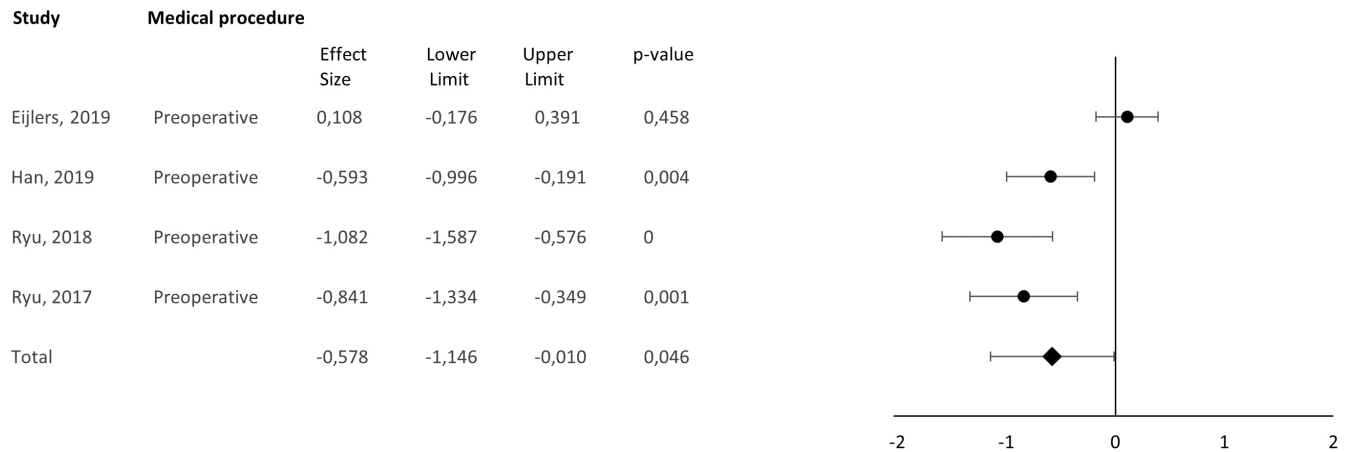
### 3.7 | Publication bias and heterogeneity

Egger regression asymmetry tests did not indicate the presence of a statistically significant publication bias for pain ( $p = .300$ ) or anxiety ( $p = .555$ ) in the VR distraction studies. We did not perform Egger regression asymmetry analysis on the exposure studies, because of the small number of studies.

## 4 | DISCUSSION

As the scientific field of VR research to diminish pain and anxiety during pediatric medical procedures is rapidly evolving, the current paper provides an update of the first systematic review and meta-analysis from Eijlers et al.<sup>23</sup> The current meta-analysis showed that VR is a useful distraction tool for significantly reducing self-reported pain and anxiety, as well as a useful exposure tool during various medical procedures.

Meta-regression analyses showed that VR interventions were not more efficacious for younger than for older children, contradictory to the findings by Eijlers et al.<sup>23</sup> However, as Eijlers et al. already



**FIGURE 4** Random-effects meta-analysis for the effect of VR exposure on patient-reported anxiety during a medical procedure compared with CAU

noted, these results might not represent true relations due to ecological fallacy.<sup>56</sup>

Regarding VR as a distraction technique, VR was found to significantly reduce pain and anxiety more compared with CAU. It should however be noted, that comparing VR to other distraction techniques is difficult due to CAU not always being (clearly) defined. Compared to Eijlers' weighted effect sizes for anxiety (SMD = 1.32) and pain (SMD = 1.30), our weighted effect sizes are lower for both anxiety (SMD = -0.74) and pain (SMD = -0.67). This could be the result of the additional studies the current meta-analysis included, but this could also be due to two studies that the current meta-analysis excluded that were both included in the original meta-analysis. Our effect sizes are closer to the weighted effect size of 0.61 from another meta-analysis that looked at other distraction techniques like games and music<sup>57</sup> and -0.64 found by a more recent meta-analysis into the effect of distraction on self-reported pain.<sup>58</sup>

Anxiety levels reported by professionals show a larger effect size than patient-reported anxiety and anxiety reported by parents resulted in a smaller effect size than patient-reported anxiety. A possible explanation for this finding could be the difficulty of estimating children's emotions while they are wearing VR glasses. The lack of visibility of facial expression could make it harder to correctly score patients pain or anxiety, and therefore, not correspond with patients' self-reported pain or anxiety. In future research, this problem could be addressed by using different measurements to score patients pain or anxiety. Possible parameters could be heart rate, temperature or EDA (electrodermal activity). Next to that, professionals reporting the patients' anxiety see both children with and without VR intervention by which they could subconsciously be influenced in their observations. Interestingly, the current dataset without the data from Eijlers et al.<sup>23</sup> showed a greater effect size compared with the data from Eijlers et al.<sup>23</sup> This could be the result of huge advancements within VR which has made VR more accessible to all kinds of users. Simulations are more lifelike, and VR can be used with simple, cheap glasses nowadays. Furthermore, quality scores of studies that were published after the review from Eijlers

et al.<sup>23</sup> are higher (see Table 2), suggesting that the quality of studies has been improved much in the recent years.

Regarding VR as an exposure technique, analysis of four studies showed VR to significantly reduce anxiety more compared with CAU, although it should be noted that the number of studies investigating exposure is rather small. The effect of VR exposure on pain in children during procedures could not be analyzed, as there were too few studies to include in analysis. Hence, more studies investigating exposure are needed.

As pointed out by Eijlers et al., immersion is an important area of focus.<sup>23</sup> Regarding immersion, heterogeneity of studies in the current review was lower than in Eijlers et al., since we were stricter in excluding studies without active VR. By doing this, we ensured that only studies were included where immersion was highest, due to the interactive component that makes the entire experience more immersive. As shown by Gutierrez-Maldonado et al., interactive VR is more effective in reducing pain than passive VR.<sup>21</sup> Nevertheless, immersion is a complex construct and the amount of immersion might vary greatly between studies, as some studies allowed full interaction, while other studies only allowed partial interaction like moving the head. Of course, not all medical procedures allow for an interactive component, as you cannot always move your body. Hence, future research could focus more on the exact role of immersion and how immersion can be improved—perhaps even when movement is not possible.

#### 4.1 | Implications

VR distraction has a statistically significant effect on pediatric pain and anxiety during medical procedures. As it is easy-to-use in clinical practice, provides endless opportunities and can be personalized in almost every way to comfort the patient as much as possible, VR can be used as a way of distraction. In addition, VR exposure has a significant effect on pediatric anxiety during medical procedures, and thus, it seems that exposure also is a useful technique to

reduce anxiety. This is an important finding, because preprocedural anxiety occurs frequently<sup>2</sup> and is linked to postprocedural pain.<sup>4,6</sup> Furthermore, patients are often unable to move during medical procedures, and cannot use electronic devices during MRI scanning, which highlights the importance of a VR intervention that can be applied before the procedure (i.e., exposure procedures) and perhaps even be used at home.

## 4.2 | Limitations

The current review has several limitations that should be considered when interpreting the results. First, the number of studies using VR as a way of exposure are still low, and thus, more research into exposure is needed before accurate conclusions can be drawn from the results. Second, quality assessment scores of the included studies varied. While randomization and concealed treatment allocation were applied in most studies, intention-to-treat analyses were missing in most studies. Additionally, barely any of the studies included possible moderating factors of VR effectivity. Third, heterogeneity was mostly between 60% and 70%, which can be seen as substantial heterogeneity. Excluding low quality studies did not appear to be responsible for these values. The difference between medical procedures seems to be more important. Heterogeneity values for medical procedures that are more specific for one type of care, as is the case with oncological care and burn care, were low. On the contrary, more general procedures that can differ a lot in circumstances, such as venous access, showed substantial heterogeneity. Due to this difference in effect sizes, generalizing the effects of VR should be done carefully, because what appears to work in one procedure, might have different results in another procedure. Of special interest is the high heterogeneity that was found for VR exposure studies on anxiety ( $I^2 = 87.1\%$ ). Three of the four included exposure studies used VR as a preoperative exposure technique. High heterogeneity is understandable as "preoperative" does not imply which type of surgery a patient has to undergo. For example, VR exposure could have less impact in case of major surgeries (or the other way around). Differences in the "care as usual" preoperative preparation could also influence the effect of VR interventions. In case of a very thorough standard preparation, the effect of VR could be limited. Fourth, VR software and hardware differed between the studies and this might influence the amount of immersion and effectivity as well. Some studies used advanced, expensive headsets like Oculus Rift, while others used simple, inexpensive headsets. On the contrary, as Eijlers et al.<sup>23</sup> pointed out, it is possible that VR hardware only plays a small role.<sup>59</sup>

## 5 | CONCLUSIONS

The current systematic review and meta-analysis indicates that VR may be a useful tool to reduce pain and anxiety in pediatric patients undergoing a range of medical procedures, especially when used in a

way of distraction. This was also found when caregivers and/or professionals reported pain and anxiety levels of the child. Regarding exposure, results from a small number of studies suggest that VR may also be useful as a way of exposure. Thus far, VR seems to be an innovative, easy-to-use, and accessible tool to reduce anxiety and pain in children before and during medical procedures, but further research into using VR as an exposure tool is still needed.

## AUTHOR CONTRIBUTIONS

Floris Q. Tas helped perform the literature searches, study selection, and statistical analyses, as well as extracting the data and writing the final article. Cynthia A.M. van Eijk helped perform the literature searches, study selection, and statistical analyses, as well as extracting the data and writing the final article. Lonneke M. Staals helped provide important intellectual content and approve the final version of the manuscript. Jeroen S. Legerstee helped interpret the results of statistical analyses, provide important intellectual content, and approve the final version of the manuscript. Bram Diercxk helped extract the data, perform statistical analyses, provide important intellectual content, and approve the final version of the manuscript.

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## CONFLICT OF INTEREST

The authors have declared no conflicts of interest for this article.

## DATA AVAILABILITY STATEMENT

There is no data availability statement.

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