Supplementary materials

Table 1. Studies that evaluated VR in ED medical procedures and burn units.

Study	**Sample size (N)**	**Mean Age and Sex prevalence**	**Study design**	**Sample type**	**VR equipment**	**Medical procedure**	**Pain and anxiety scales**	**Outcomes**
Mott et al. (2008)	42 patients	9 years 29 males 13 females	RCT	VR group: 20 patients Control group (basic cognitive techniques): 22 patients	LCD screen operated by inserting plastic figures into a camera unit mounted on the screen.	Burn wound care	FLACC scale FPS-R VAS	The pain in the VR group was significantly less severe (2.81± 0.89) than in the control group (5.38 ±0.58)
Kipping et al. (2012)	41 patients	13.08 years 28 males 13 females	RCT	VR group: 20 patients	VR system included a HMD, joystick hand control, personal computer and off the-	Burn wound care	VAS FLACC scale	Mean pain scores were higher for the control group compared to the VR group in both dressing removal (VAS 4.2 vs 2.9, p = 0.16)

				Control group (TV, stories, music, caregivers): 21 patients	shelf, age appropriate software games			and application (VAS 3.8 vs 2.33, p = 0.40).
Jeffs et al. (2014)	28 patients	13.5 years 19 males 9 females	RCT	VR group: 8 patients SOC group: 10 patients Passive distraction group (watching a movie): 10 patients	SnowWorld, a three-dimensional, computer- generated, interactive VR software program with a HMD	Burn wound care	APPT STAI-CH	VR group reported significantly less procedural pain than the Passive distraction group (difference = 23.7 mm, 95% CI: 2.4–45.0, P = .029) and less procedural pain compared with the SOC group (difference = 9.7 mm, 95% CI: −9.5 to 28.9, P = .32).

Hoffman et al. (2020)	50 patients	6-17 years 42 males 8 females	RCT	VR group: 25 patients Control group (standard burn wound care): 25 patients	Arm goggle suspension system mounted to the cart allowing to position the VR goggles near the patient's head, without wearing a helmet. The goggles used were MX90 VR goggles, from NVISinc.com.	Burn wound care	GRS	Less pain intensity (mean worst pain ratings for the No VR group = 7.46 (SD = 2.93) vs. 5.54 (SD = 3.56) in VR group) and lowest pain (No VR = 4.29 (SD = 3.75) vs. 1.68 (2.04) for the VR group).
Xiang et al. (2021)	90 patients	11.3 years 45 males 45 females	RCT	VR group: 60 patients Control group (standard burn care and distraction tools such as music, books):	VR pain alleviation tool (VR-PAT), a lightweight, low-cost VR paired with an Apple iPhone 6 and detachable earphones (VR game titled Virtual River Cruise)	Burn wound care	VAS FLACC-R scale	Lower overall pain (VAS score, 24.9 [95%CI, 12.2-37.6]) in VR group compared to control group (VAS score, 47.1 [95%CI, 32.1-62.2]; P = .02). Lower worst pain score in VR group (VAS score, 27.4 [95%CI,

				30 patients				14.7-40.1]) than control group (VAS score, 48.8 [95%CI, 31.1-64.4]; P = .03).
Kaya et al. (2023)	65 patients	7-12 years 29 males 36 females	RCT	VR group: 33 patients Control group (standard burn wound care): 32 patients	Two Samsung Gear and Oculus Rift VR headsets	Burn wound care	WBFPRS	Less pain intensity, less fear and anxiety during burn wound care in VR group.

Alrimy et al. (2023)	9 patients	1.5 years 3 males 9 females	RCT	VR or pain medication (paracetamol) in different days	Desktop VR (VR Animal Rescue World)	Burn wound care	FLACC scale	Significant 40% reduction in pain during VR treatment compared to traditional treatment. Pain During Wound care 4.00 (SD = 2.24) with VR vs 6.67 (SD = 2.45) with paracetamol ($p < 0.01$)
Butt et al. (2022)	110 patients	15 years 66 males 44 females	RCT	VR group: 55 patients Control group (traditional distraction technique with an iPad): 55 patients	Take-Pause (Take Pause Inc., released 2017, version 2.0) VR immersion tool	Clinical visit	STAI-CH WBFPRS	The mean anxiety score for the VR group improved by 10 points versus 6 points in the iPad group ($p < 0.001$; 95% confidence interval= 0.44 to 7.6). There was no statistical significance in the reduction of pain scores ($p = 0.953$) and

								respiratory rates (p = 0.776) between the group
Goldman et al. (2021)	62 patients	10.1 years 39 males 23 females	RCT	VR group: 32 patients SOC group (distraction tools such as watching TV, listening to music, a tablet or smartphone): 30 patients	VR Headset (ReTrak Utopia 360 VR Headset) and smartphone (Asus Zenfone 2 ZE551ML) pre-loaded with a VR Roller Coaster app (VR Roller Coaster, Frag)	Suturing laceration	FPS-R VAS score	Mean pain post procedure was 1.84 (1.94) in VR group and 1.47 in SOC group (p-value 0.458). Mean anxiety post procedure was 1.50 in VR group and 1.57 in SOC group (p-value 0.890).

Nemetski et al. (2022)	40 patients	9.2 years 21 males 19 females	Observational Study	VR group: 40 patients	VR game using the KindVR (Alameda, CA) consisting of a stereoscopic HMD and headphones	Sutured repair of non-facial lacerations	RCADS VAS	The average change in VAS score from enrollment to first stitch was −39 mm (95% CI −51 mm to −27 mm; $p < 0.001$). Similar results were seen at all secondary time points: −33 mm (95% CI −44 mm to −22 mm; $p < 0.001$) from enrollment to irrigation, −21 mm (95% CI −32 mm to −10mm; $p = 0.001$) from enrollment to local or regional anesthesia with injectable lidocaine, and −42 mm (95% CI −55 mm to −29 mm; p

								< 0.001) from enrollment to procedure completion.
Chan et al. (2019)	123 patients	8.2 years 67 males 56 females	RCT	VR group: 64 patients SOC group (toys, books, and electronic devices): 59 patients	Interactive underwater adventure through Google Pixel XL/Google Daydream (Google, Mountain View, California).	Venous needle procedures (intravenous cannulation or venipuncture)	FPS-R	VR reduced pain by -1.78 units (95% CI, -3.24 to -0.32) in comparison with SOC and post-procedure anxiety (-1.75; 95% CI, 3.09 to -0.40; P = .011). VR group: FPS-R baseline decreased by 31%; SOC group: FPS-R baseline increased by 10%. No change in pain from baseline with SOC, whereas virtual reality produced a significant

								reduction in pain (between-group difference, -1.78; 95% CI, -3.24 to -0.317; P = .018)
Knight et al. (2019)	40 patients	Not mentioned	Observational study	VR group: 20 patients Control group (book, game or tablet computer): 20 patients	VR (Pico Goblin headset, using the 'Happy Place' animated interactive 360° experience),	Venous cannulation, venipuncture, wound closure or foreign body removal	CEMS FLACC scale	Patients using VR were more distracted compared with control group (average CEMS score=5 with VR, 6 in control group, p=0.74). Patients using VR showed fewer reactive pain behaviors than the control group (FLACC score 0 vs 1.5; p=0.004).

Dumoulin et al. (2019)	59 patients	13.37 years 38 males 21 females	RCT	VR group: 20 patients Minimal distraction group (TV): 24 patients SOC group (conversation, I-Spy books, questions ball): 15 patients	Immersive game (two-bedroom apartment) developed by the UQO Cyberpsychology Lab using Virtools4. The game was rendered in real time using a PC, an eMagin z800 HMD and the built-in motion tracker. The VR game was steered by a wireless mouse.	Needle-related procedures (blood work, intravenous placement, or both)	VAS	A larger and statistically significant reduction in fear of pain was observed among children who used VR distraction (from 36.5 to 19.75) compared with the SOC (from 39 to 29.33) and TV conditions (from 33.21 to 35.42).
Özalp Gerçeker et al. (2020)	136 patients	VR Rollercoaster group: 23 males	RCT	VR-Rollercoaster group: 45 patients	Samsung Gear Oculus to watch and listen to VR video and audio	Blood draw	CFS CAM-S	Pain scores were found to be lower in the VR-Rollercoaster group (1.2 ± 2.2) and the VR-Ocean Rift group (1.0

		22 females VR-Ocean Rift group: 24 males 21 females Control group: 26 males 20 females		VR-Ocean Rift group: 45 patients Control group: 46 patients				± 1.5) than control group (4.1 ± 3.5). A statistical difference was found between groups according to self-, parent- and researcher-reported fear and anxiety scores after blood draw. While being in VR-Rollercoaster and VR-Ocean Rift group reduced children's fear and anxiety, being in the control group increased fear levels by 20% and anxiety levels by 34.1%.
Chen et al. (2020)	136 patients	9.13 years 77 males	RCT	VR group: 68 patients	A Xiaozhai V4 HMD for four virtual	Intravenous injection	WBFPRS	Pain score lower in the VR group (3.35 ± 2.38 vs 4.35 ± 2.95, p =

		59 females		Control group: 68 patients	environments (roller coasters, space exploration, a wildlife park and travel destinations)		CFS	.031). Fear score lower in the VR group (1.32 ± 1.19 vs 1.78 ± 1.40, p = .0.43). Shorter times required for intravenous injections in the VR group: (53.5 ± 19.0 seconds vs 61.3 ± 25.8)
Goldman et al. (2021)	66 patients	9.5 years 36 males 30 females	RCT	VR group: 35 patients SOC group (parental comfort, books, videos, television, iPad): 31 patients	VOX+ Z3 3D Virtual Reality Headset with VR Roller Coaster app.	Intravenous catheterization procedure	FPS-R VSA score	Lower median pain score in VR group prior to procedure (2/10 in VR and 4/10 in SOC, p-value 0.02). Lower median pain score in VR group after procedure (−0.51/10 in VR and + 0.16/10 in SOC, p-value 0.64). Satisfaction from anxiety management

								better in the VR group (median score 9 and 7 in VR and control groups, respectively, p < 0.007).
Litwin et al. (2021)	58 patients	VR group: 12.50 years 16 males 15 females Control group: 12.46 years 17 males	RCT	VR group: 31 patients Attention control group (tablet playing a video of fish and sea turtles swimming in the ocean):	Stereoscopic display mounted on a lightweight wireless HMD and noise-canceling headphones. A lightweight, wireless handheld controller was used to interact	Venipuncture	VNRS CFS	VR group had a 10.6% lower mean pain score during the IV insertion compared with the AC group, which is a clinically significant difference based on reduction by 1/10 or a difference between 10% and 20% on pain scales

		10 females		27 patients				
Lee et al. (2021)	19 patients	4.5 years 4 males 15 females	RCT	VR group: 9 patients Control group: 10 patients	Dome screen developed by Dome & Dome Co. and a projector linked to a personal computer that played the animated show 'Pororo the Little Penguin'.	Intravenous placement	FLACC scale	The median FLACC scale at the time of venipuncture was 3.0 (IQR: 3.0–5.0) in the VR group and 4.0 (IQR: 3.0–8.0) in the control group (p = 0.545). Although the average FLACC score at the 3 time points (preparation, tourniquet, venipuncture) in the VR group was lower than the control group, the difference was not statistically significant (median 2.3 (IQR: 2.0–3.0) vs. 3.0 (IQR: 3.0

								(IQR 2.7–6.7)), p = 0.255).
Canares et al. (2021)	55 patients	14.1 years 20 males 35 females	RCT	VR group: 15 patients Child life specialist group: 20 patients Reference group: 20 patients	VR headset (Oculus Go) with passive VR experiences and active game play	Venipuncture	CAMPIS-SF	Patient coping higher in VR group and child life specialist group than in the reference group (Patient coping score 0.70 in reference group vs 0.90 in child life specialist group and 0.88 in VR group (P-value=.05).

Osmanlliu et al. (2021)	62 patients	VR group: 11.1 years 11 males 20 females Control group: 12.3 years 13 males 18 females	RCT	VR group: 31 patients Control group (local standard of care including parental presence, topical anesthetic): 31 patients	Videogame Dreamland, developed by Oniric Interactive, a classic "point & shoot" game that uses head movements for aiming and a hand trigger for shooting balloons. Oculus Rift (high resolution display, integrated 3D audio and motion detection) was provided.	Intravenous insertion or venipuncture	VNRS CFS	VNRS during procedure not statistically different: 3 (1, 6)/10 in VR group vs 3 (1, 5.5)/10 in control group (p = 0.75). Child fear scale was 1 (0, 2)/4 in the VR group vs 2 (0, 3)/4 in the control group. Memory of pain at 24 h: VNRS was 2 (1, 3)/10 in VR group vs 4 (2, 6.5)/10 in control group.

Schlechter et al. (2021)	116 patients	VR group: 11.3 years 28 males 30 females SOC group: 10.7 years 27 males 31 females	RCT	VR group: 58 patients SOC group (distraction techniques such as reading a book or iPad use): 58 patients	The virtual reality headsets, eyemask, iPhone with VR software, and optional headphones, to play a game wherein a narwhal swims through the ocean, and subtle movements of the head can direct the narwhal through hoops, up above the ocean, or down to the base of the ocean.	Intravenous line placement	FPS-R Likert-type anxiety scales	The median time to successful IV placement was shorter in the VR group (78 s vs 104 s), but this difference was not statistically significant ($p = .209$). Changes in pain as scored by FPS-R and Likert-based anxiety scores were also similar between the groups, with both VR and SOC groups having a median change of pain of −2, and a change of anxiety of −1 after IV placement

Wong et al. (2023)	149 patients	7.21 years 63 males 86 females	RCT	VR group: 75 patients Control group: 74 patients	VR HMD	Venipuncture	FPS-R VAS CSAS-C	VR group reported significantly less pain (β = −0.78; 95%CI, −1.21 to −0.35; P < .001) and anxiety (β = −0.41; 95%CI, −0.76 to −0.05; P = .03) immediately after the intervention. Health care professional satisfaction in the VR group (mean [SD] score, 34.5 [4.5]) was significantly higher than that in the control group (mean [SD] score, 32.9 [4.0]; P = .03). Length of venipuncture

								procedure in the VR group (mean [SD] duration, 4.43 [3.47] minutes) was significantly shorter than that in the control group (mean [SD] duration, 6.56 [7.39] minutes; P = .03).
Yıldırım et al. (2023)	150 patients	VR group: 6.4 years 27 males 24 females Buzzy group: 6.7 years 27 males	RCT	VR group: 51 patients Cold vibration device application (Buzzy) group: 50 patients	Oculus Rift VR with headset display to provide 3 virtual environments (ie, roller coaster, mine craft, ocean rift)	Peripheral intravenous catheterization insertion	CEMS WBFPRS CAS CFS	No significant differences in first-attempt intravenous insertion success rates (virtual reality = 47.2%, Buzzy® = 50%, control = 46.9%), preprocedural emotional appearance scores, and procedure-

		23 females Control group: 6.4 years 25 males 24 females		Control group (attention distracted by asking questions): 49 patients			CAM-S	related pain and anxiety scores. Preprocedural emotional appearance scores were 18.8 in VR group, 18.3 in Buzzy group, and 20.1 in control group. Postprocedure WBS pain scores were similar (VR ¼ 5.6 (1.9), Buzzy ¼ 5.8 (1.5), control ¼ 6.0 (1.1). Postprocedure-related anxiety scores were 5.2 in the VR group, 5.1 in the Buzzy group, and 5.5 in the control group. . Postprocedure fear scores were 3.0 in the

								VR group, 2.9 in the Buzzy group, and 3.2 in the control group.
Goktas et al. (2023)	144 patients	7-12 years 72 males 72 females	RCT	VR group: 36 patients Kaleidoscope group: 36 patients Music group: 36 patients	Virtual reality as a 360-degree audio-visual simulation, "Zore G07E VR Shinecon 3D Virtual Reality Glasses", which include a 4.7–6.3 in. headset	Venipuncture	WBFPRS CAM-S CFS	The pain level of the children in the control group was higher (2.72 ± 1.32) than the levels of the children in the kaleidoscope (0.67 ± 0.93), music (0.64 ± 0.96) and VR group (0.42 ± 0.65). The anxiety level was higher (3.00 ± 2.77) in the control group than

				Control group: 36 patients				kaleidoscope (0.64 ± 1.07), music (0.36 ± 0.76) and VR (0.06 ± 0.33) group.
Akarsu et al. (2023)	153 patients	VR group: 9.53 years Control group: 9.71 years 83 males 70 females	RCT	VR Water skiing group: 51 patients VR Walking in Nature group: 51 patients Control group:	VR goggles and the 3D video called “360 VR Water skiing” and "VR-Walking in Nature".	Blood draw procedures	WBFPRS CFS CAM-S	The children’s mean pain scale score during the venous blood sampling was 1.29±1.11 with the VR-Water skiing; 1.28±1.16 with the VR-Walking in nature; and 4.34±1.41 ($p<0.001$) in the control group. The children’s mean anxiety

				51 patients				scale score during the procedure was 0.82±1.01 with the VRWater skiing; 0.79±1.26 with the VR-Walking in nature; and 6.57±2.08 (p<0.001) in the control group. The children's mean fear scale score during the procedure was 0.58±0.77 with the VR-Water skiing, 0.53±0.78 with the VR-Walking in nature; and 3.17±0.92 (p<0.001) in the control group.

RCT, Randomized Controlled Trial; VR, virtual reality; LCD, Liquid Crystal Display; FLACC, Face, Legs, Activity, Cry, and Consolability Scale; FPS-R, Faces Pain Scale-Revised; VAS, Visual Analog Scale; HMD, Head-Mounted Display; APPT, Adolescent Pediatric Pain Tool STAI-CH, Spielberger State-Trait Anxiety Inventory for Children; GRS, Graphic Rating Scale; WBFPRS, Wong-

Baker FACES Pain Rating Scale; SOC, Standard of Care; RCADS, Revised Children's Anxiety and Depression Scale; CEMS, Children's Emotional Manifestation Scale; CFS, Child Fear Scale; CAM-S, Child Anxiety Meter-State; VSA, Venham Situational Anxiety score; VNRS, Verbal Numerical Rating Scale; CAMPIS-SF, Child–Adult Medical Procedure Interaction Scale-Short Form; CSAS-C, Chinese version of the State Anxiety Scale for Children; CAS, Color Analog Scale.

Table 2. Studies of VR and functional neuroimaging.

Study	**Sample (N)**	**Study design**	**Neuroimaging used**	**Outcome**
Lewis et al. (2016)	4 patients with burn injury	Wound care on two consecutive days - once with standard analgesia and adjunctive VR, and once with standard analgesia alone.	Brain perfusion SPECT	For the VR and non-VR conditions, the average group scores for pain intensity (9.0, 8.8), time spent focusing on pain (5.2, 10.0), pain unpleasantness (5.2, 6.2), enjoyment (6.0, 2.5), and opioid equivalents (7.4, 11.5) were recorded. In VR group SPECT documented increased activation in the right medial frontal lobe, the anterior insula and right caudate, the right occipital lobe,

				bilateral heteromodal auditory cortex, and periaqueductal gray matter. In contrast, there was a suppression of activity in the cerebellum (which activation has been demonstrated in acute and chronic pain).
Hoffman et al. (2004)	14 healthy subjects	Thermal stimuli were applied alternating every 30 seconds between non-painful warmth (36°C) and painful heat (median painful temperature 47.6°C).	Functional Magnetic Resonance	Non-VR group: brain activation in anterior cingulate cortex (ACC), primary (SS1) and secondary (SS2) somatosensory cortices, insula, and thalamus. VR group: reductions in pain-related brain activity in all five regions
Hoffman et al. (2007)	9 healthy subjects	Thermal pain stimulation in four intervention conditions: (a) control (no analgesia),	Functional Magnetic Resonance	Virtual reality alone significantly decreased pain-related brain activity in the insula, secondary (SS2)

		(b) opioid treatment, (c) immersive VR distraction, (d) a combination of opioid and VR.		somatosensory cortices, and thalamus. Similarly, opioid treatment without VR led to significant reductions in pain-related brain activity in the insula and thalamus.