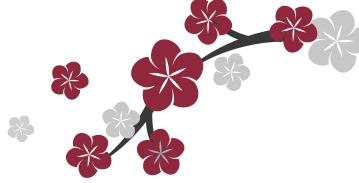




Efficacy of Immersive Virtual Reality in Patients with Cancer Receiving Chemotherapy: A Systematic Review and Meta-Analysis







Made Satya Nugraha Gautama^{1,2}, Tsai-Wei Huang^{1,3,4,5*}, Haryani⁶

¹Master Program in School of Nursing, College of Nursing, Taipei Medical University, Taipei, Taiwan

²Master of Nursing Program, Faculty of Medicine Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia

³Cochrane Taiwan, Taipei Medical University, Taipei, Taiwan

⁴Center of Nursing and Healthcare Research in Clinical Practice Application, Department of Nursing, Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan

⁵Department of Nursing, Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan

⁶Department of Surgical Medical Nursing, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia

*Corresponding author: Tsai-Wei Huang, RN, Ph.D. E-mail: tsaiwei@tmu.edu.tw

Introduction

The use of immersive virtual reality (IVR) in the cancer field is promising, especially for those receiving chemotherapy. Therefore, examining the current evidence on the application of VR in chemotherapy settings and strengthening the evidence are crucial to support standard care for cancer patients. This systematic review and meta – analysis examined the efficacy of IVR in adult and pediatric patients with cancer receiving chemotherapy.

Methods

We searched for relevant studies in PubMed, Cochrane Library, Embase, Scopus, Web of Science, and MEDLINE. The primary outcomes were anxiety, depression, fatigue, heart rate and blood pressure. The secondary outcomes were pain and distress. The study protocol has been registered and approved by PROSPERO (CRD42022359886).

Figure 1. PRISMA Flow Diagram of Study Selection Process

Records identified from Electronic Database (n=993): PubMed (n = 129) Cochrane Library (n = 125) Embase (n=168) Scopus(n=477) Web of Science (n=70) MEDLINE (n=26) Records removed before screening Ooggle Scholar (n=5) Citation searching (n=8) Records screened (n = 701) Reports sought for retrieval (n = 13) Reports assessed for eligibility (n = 25) Reports assessed for eligibility (n = 11) Non-immers/we VR (n = 11) Non-RCT design (n = 4)
Reports sought for retrieval (n = 766) Reports sought for retrieval (n = 13) Reports assessed for eligibility (n = 25) Reports assessed for eligibility (n = 17): Non-immersive VR (n = 1) Non-RCT design (n = 4)
Reports sought for retrieval (n = 766) Reports sought for retrieval (n = 13) Reports assessed for eligibility (n = 25) Reports assessed for eligibility (n = 17): Non-immersive VR (n = 1) Non-RCT design (n = 4)
Reports assessed for eligibility (n = 25) Non-immersive VR (n = 1) Non-CCT design (n= 4) Reports assessed for eligibility (n = 13) Reports assessed for eligibility (n = 13) No
Reports assessed for eligibility (n = 25) Non-immersive VR (n = 1) Non-CT design (n = 4) Reports assessed for eligibility (n = 13) No
Conference Abstract (n = 5) Study protocol (n = 5) Review study (n = 1) Secondary analy sis (= 1)
Studies included in qualitative synthesis (n = 14)

Result

Fourteen trials were enrolled, of which 9 enrolled 547 adult cancer patients and 5 recruited 257 pediatric cancer patients. In adult patients, IVR significantly reduced anxiety (SMD = -1.73, 95% CI = -2.59 to -0.86), depression (SMD = -2.21, 95% CI = -3.97 to -0.45), and fatigue (SMD = -1.81, 95% CI = -2.93 to -0.69) and systolic blood pressure (MD = -3.54, 95% = -6.67 to -0.40). However, IVR did not significantly reduce distress (SMD = -0.63, 95% CI = -1.77 to 0.52), pain (SMD = -0.70, 95% CI = -2.66 to 1.27), and heart rate (MD = -0.13, 95% CI = -0.61 to 0.36). In pediatric patients, IVR significantly reduced pain (SMD = -1.17, 95% CI = -1.84 to -0.50) and anxiety (SMD = -1.18, 95% CI = -1.77 to -0.59) but not

Table 1. Characteristics of the included trials

uthor Year]	Inclusion criteria	Study design	Sample size, N (% of women)	Age (years) (mean ± SD)	Setting	Intervention
oult patient (Dyama et al 2000]	Patients with cancer receiving chemotherapy, aged 18 to 70 years	RCT	EG: 15 (80%) CG: 15 (80%)	18–70 (53.5)	During chemotherapy	EG: D: Three-screen liquid-crystal display (LCD) with a 3D system, headphones, and speakers VE: Three virtual worlds consisting of lake, forest, and country town. T, F: 20 minutes, 1 time CG: Chemotherapy usual care
chneider t al [2004]	Women with breast cancer who were scheduled to receive IV chemotherapy, aged 18-55 years	Crossover RCT	20 (100%)	27-55 (42.6 ± 7.9)	During chemotherapy	EG: D: Sony PC Glasstron PLMS700 (head-mounted display) VE: Deep-sea diving, walking through an art museum, or solving a mystery T, F: 45-90 minutes, once CG: chemotherapy usual care
chneider t al [2007]	First diagnosis of breast, colon or lung cancer, aged ≥18 years, receiving IV chemotherapy	Crossover RCT	123 (77%)	32-78 (53.97 ± 10.89)	During chemotherapy	EG: D: VR HMD; i-Glasses SVGA head-mounted Display, i-C display systems VE: deep-sea diving, walking through an art museum, exploring ancient worlds, and solving a mystery T, F: 45-90 minutes, once CG: chemotherapy usual care
ohammad Ahmad 1018]	Female patients diagnosed as having breast cancer, aged between 18 and 70 years	RCT	EG: 40 (100%) CG: 40 (100%)	30-70 (51.99 ± 10.34)	In chemotherapy phases	EG: D: Head-mounted display with headphones; not specific described VE: deep-sea diving "Ocean Rift" and sitting on the beach with the "Happy Place" track T, F: 15 minutes, once CG: standard care
hirico et al 1020]	Patients with breast cancer aged between 18–70 years, receiving IV chemotherapy	RCT	EGI: 30 (100%) EG2: 30 (100%) CG: 30 (100%)	EGI: 55.18 ± 5.7 EG2: 55.7 ± 5.26 CG: 56.2 ± 6.79	During chemotherapy	ECI: D: Head-mounted glasses (Vuzix Wrap 1200 VR) with a head motion tracking system VE: Relaxing landscapes, participants explored an island, by walking through a forest, observing different animals, climbing a mountain, and swimming in the sea. T, F: 20 minutes, once EC2: Patients listened to 20-min relaxing music pre-taped by an expert music therapist D: Mp3 reader and headphones T, F: 20 minutes, once CG: chemotherapy usual care
erzwyvelt al [2021]	Diagnosed as having stage 0 to IV solid cancer, aged ≥18 years	Crossover RCT	33 (75.8%)	26-84 (59.03 ± 13.2)	During chemotherapy	EG: D: Oculus Quest Head-Mounted Display (HMD). The VR HMD is a stand-alone device with built-in tracking and headphones (to allow audio) and has head tracking and a separate hand-controller VE: The Nature Treks software. Patients can explore tropical beaches, underwater oceans, and even watch the stars. T, F: 53.3 minutes, once CG: standard care
nang et al 022]	Patients with pathologically diagnosed breast cancer, aged between 18 and 70 years	RCT	EG: 38 (100%) CG: 39 (100%)	EG: 52.29 ± 7.68 CG: 51.03 ± 7.97	Post chemotherapy	EG: D: Oculus Go VR headset VE: A stereoscopic visual scene (Tuscany Garden) T, F: 30 minutes, 6 times (3 months) CG: Standard care
annou et [2022]	Patients with histopathological diagnosis of cancer, aged 218 years, and on active chemotherapy treatment	Crossover RCT	50 (42.0%)	57 ± 15.5	During chemotherapy	EC: D: VIVE VR Headset, a head-mounted display (HMD) VE: A sunny environment with a waterfall flowing from snowy mountains into a lake, Sound of falling water and bird sounds were incorporated over a relaxing soundtrack T, F: 20 minutes, once CC: standard care
bi et al 022]	Histological diagnosis of stage I to III breast or ovarian cancer, aged 218 years, ECOC 0 to 2, life expectancy >12 months	RCT	EG: 22 (100%) CG: 22 (100%)	EG: BC 50 (57-71); GC 50 (36-61) CG: BC 50 (39-69); GC 52 (51-62)	During chemotherapy	EC: D: VR headset Oculus Go VE: Relaxing and engaging content, such as concerts, walks in the European capitals, mountain nature trails isolated and fascinating places, pristine, exotic beaches, and yoga sessions T, F: 10 minutes, once CC: Standard care
Pediatric pat	ients (≤18 years)					
ershon et al 2004]	Children with cancer, aged 7-19 years, receiving a port access for chemotherapy	Pilot RCT	EG: 22 (NA) CG1: 22 (NA) CG2: 15 (NA)	12.7 ± NA	Pre chemotherapy	EC: D: A head-mounted display with stereo earphones VE: Virtual Gorilla program, created as an educational tool for children visiting the gorilla habitat at Zoo Atlanta T: S-10 minutes, once CC: standard care
ong et al 021]	Pediatric patients with cancer, aged 6-17 years	RCT	EG: 54 (44.4%) CG: 54 (40.7%)	EG: 10.5 ± 3.8 CG: 10.2 ± 3.5	In chemotherapy phases	EC: D: Google cardboard goggle fitted to Apple and Samsung smartphones VE: VR cartoons over VR museum or VR water worlds and "Minion" movies T: 10 minutes, once CC: standard care
erçeker et [2021]	Children or adolescents with cancer aged 6-17 years undergoing Huber needle insertion for routine chemotherapy	RCT	EG: 21 (38.1%) CG: 21 (38.1%)	NA	Pre chemotherapy	EG: D: Samsung Gear Oculus headset, connected to the Samsung Galaxy S7 Edge VE: Swimming with marine animals underwater (Ocean Rift), riding a rollercoaster (Rilix VR), and exploring the forest through the eyes of woodland species (in the eyes of animal) T: 10 minutes, once CG: standard care
rdős & orváth 022]	Children with cancer aged 10-18 years receiving chemotherapy	Crossover RCT	29 (27.5%)	15.28 ± 2.44	During chemotherapy	EC: D: the Samsung Gear VR (with Samsung Galaxy S7 Edge) and the Oculus Go VE: VR game Night sky (Digital games) T: 30 minutes, once CG: Standard care
Vong et al 2022]	Children with cancer, aged 6 – 12 years, who receiving first chemotherapy	Exploratory – RCT	EG: 9 (44.4%) CG: 10 (30%)	EG: 10.33 ± 1.50 CG: 9.11 ± 1.60	During chemotherapy	EC: D: Google Cardboard goggles VE: Minion mini movies, Doraemon mini movie, and a spider journey 3D cartoon T: 30 minute (1* session), 5 minute (2** dession), 5 minute (3** dession), 5 minute (4** dession), 6 minute (4**

Table 2. Assessment of methodological quality of included trials (RCTs evaluated using RoB 2.0)

Study	Dì	D2	D3	D4	D5	Overall
Oyama et al (2000)	Some concerns	Low	Low	Low	Low	Some concerns
Schneider et al (2004)	Some concerns	Low	Low	Low	Low	Some concerns
Gershon et al (2004)	Some concerns	Low	Low	Low	Low	Some concerns
Schneider et al (2007)	Low	Low	Low	Low	Low	Low
Mohammad & Ahmad (2018)	Low	Low	Low	Low	Low	Low
Chirico et al (2020)	Some concerns	Some concerns	Low	Low	Low	Some concerns
Wong et al (2021)	Low	Low	Low	Low	Low	Low
Verzwyvelt et al (2021)	Some concerns	Low	Low	Low	Low	Some concerns
Gerceker et al (2021)	Low	Low	Low	Low	Low	Low
Zhang et al (2022)	Low	Low	Low	Low	Low	Low
Ioannou et al (2022)	Low	Low	Low	Low	Low	Low

Figure 2. Forest plot comparing immersive virtual reality versus standard care; primary outcomes: anxiety and depression; (A) Anxiety in adult patients; (B) Anxiety in pediatric patients; (C) Depression in adult patients; (D) Distress in adult patients.

A. Anxiety [adult]

	Favours [immersive	VR]	Favours [standard	care]		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 Baseline to immediate a	fter - VR								
Chirico [2020]	-6.85	1.11	30	-1.47	0.99	30	15.5%	-5.05 [-6.11, -3.99]	
Fabi [2022]	-12.5	7.53	22	-2	5.87	22	16.6%	-1.53 [-2.21, -0.85]	*
Ioannou [2022]	-5.1	3.72	27	-1.7	2.81	23	16.8%	-1.00 [-1.60, -0.41]	*
Mohammad & Ahmad [2018]	-27.3	3.27	40	-13.17	5.6	40	16.7%	-3.05 [-3.71, -2.40]	-
Schneider [2007]	-5.84	9.89	107	-4.25	7.35	107	17.4%	-0.18 [-0.45, 0.09]	•
Zhang [2022] Subtotal (95% CI)	-7.5	7.06	38 264	5.9	4.41	39 261	16.9% 100.0%	-2.26 [-2.84, -1.68] -2.13 [-3.38, -0.89]	•
Test for overall effect: Z = 3.36 1.1.2 Baseline to 48 hours aft		,							
Fabi [2022]	-5	7.51	22	3.4	6.54	22	46.1%	-1.17 [-1.82, -0.53]	-
Schneider [2007] Subtotal (95% CI)	-3.85	7.93	107 129	-3.07	7.5	107 129	53.9% 100.0%	-0.10 [-0.37, 0.17] -0.59 [-1.64, 0.45]	•
Heterogeneity: Tau ² = 0.51; Ch Test for overall effect: Z = 1.11		= 1 (P = 0.	003); I² =	89%					-10 -5 0 5 10

B. Anxiety [pediatric]

	Favours [standard	-		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	I otal	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Gerceker [2021]	-1.7	2	21	-0.3	1.7	21	35.9%	-0.74 [-1.37, -0.11]	
Wong [2020]	-5.56	3.14	54	-2.06	3.01	54	46.8%	-1.13 [-1.54, -0.72]	
Wong [2022]	-6	3.32	9	0.7	2.41	10	17.3%	-2.23 [-3.43, -1.03] •	•
Total (95% CI)			84			85	100.0%	-1.18 [-1.77, -0.59]	•
Heterogeneity: Tau ² =	0.15; Chi ² =	4.66, df = :	2 (P = 0.1	0); I ² = 57%	6			_	-2 -1 0 1 2

C. Depression [adult]

	Favours [i	immersiv	e vrj	Favours [standard	carej		Std. Mean Difference		Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95% CI	
1.4.1 Baseline to imme	ediate after	- VR									
Chirico [2020]	-2.61	0.52	30	1.21	0.47	30	22.3%	-7.61 [-9.10, -6.11]			
Ioannou [2022]	-3.1	3.04	27	-0.7	2.77	23	25.8%	-0.81 [-1.39, -0.23]			
Zhang [2022] Subtotal (95% CI)	-4.69	6.96	38 95	1.57	2.96	39 92	26.1% 74.2%	-1.16 [-1.65, -0.68] -3.04 [-5.46, -0.62]		•	
Test for overall effect: 2	4.34; Chi² = 7 Z = 2.46 (P =		- 0	"							
			- (,,							
	Z = 2.46 (P =	0.01)	22	1.3	2.1	22	25.8%	0.00 [-0.59, 0.59]			
Test for overall effect: 2 1.4.2 Baseline to 48 he	Z = 2.46 (P = ours after - '	0.01) VR			2.1	22 22		0.00 [-0.59, 0.59] 0.00 [-0.59, 0.59]		•	
Test for overall effect: 2 1.4.2 Baseline to 48 he Fabi [2022] Subtotal (95% CI)	Z = 2.46 (P = ours after - 1.3	0.01) VR	22		2.1					*	
Test for overall effect: 2 1.4.2 Baseline to 48 he Fabi [2022] Subtotal (95% CI)	Z = 2.46 (P = ours after - 1.3	0.01) VR 2.34	22		2.1					•	
Test for overall effect: 2 1.4.2 Baseline to 48 hr Fabi [2022] Subtotal (95% CI) Heterogeneity: Not app Test for overall effect: 2	Z = 2.46 (P = ours after - 1.3	0.01) VR 2.34	22		2.1	22				•	
Test for overall effect: 2 1.4.2 Baseline to 48 he Fabi [2022] Subtotal (95% CI) Heterogeneity: Not app	Z = 2.46 (P = ours after - 1.3 licable Z = 0.00 (P =	0.01) VR 2.34 1.00)	22 22 21	1.3		22	25.8%	0.00 [-0.59, 0.59]	-10	•	10

D. Distrest [adult]

	-	immersiv		Favours [-			n. n
y or Subgroup	Mean	SD	Total	Mean	SD	Lotal	Weight	IV, Random, 95% CI	IV, Random, 95% CI
eider [2007]	-3.78	8.06	107	-2.96	7.35	107	34.5%	-0.11 [-0.37, 0.16]	•
vyvelt [2021]	-0.5	1.68	33	-0.8	1.26	33	33.1%	0.20 [-0.28, 0.68]	
g [2022]	-2.76	1.13	38	-0.64	0.94	39	32.5%	-2.02 [-2.58, -1.47]	-
(95% CI)			178			179	100.0%	-0.63 [-1.77, 0.52]	•
ogeneity: Tau² = 0.9	97; Chi² = 4	43.09, df =	2 (P < 0	.00001); I² =	= 95%			-	-10 -5 0 5
,				.00001); I² =	= 95%	179	100.0%	-0.63 [-1.77, 0.52]	-10 -5 0 5

Figure 3. Forest plot comparing immersive virtual reality versus standard care; primary outcome: fatique in adult patients.

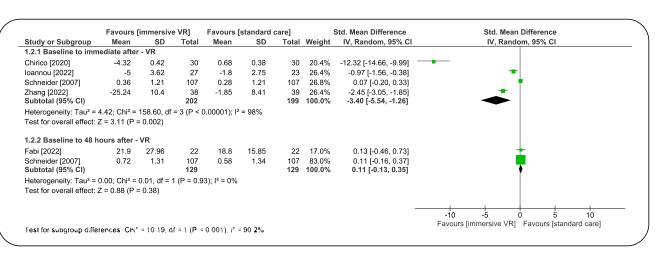
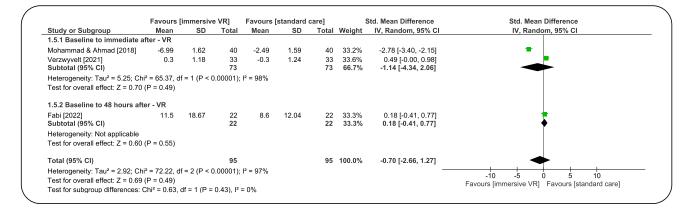


Figure 4. Forest plot comparing immersive virtual reality versus standard care; secondary outcome: pain; (A) pain in adult patients; (B) pain in pediatric patients

A. Pain [adult]



B. Pain [pediatric]

Study or Subgroup	Favours [i	SD	Total	Favours [s Mean	SD	•	Weight	Std. Mean Difference IV, Random, 95% CI	Std. Mean Difference IV, Random, 95% CI
Gerceker [2021]	2.4	1.8	21	5.3	1.8	21	40.9%	-1.58 [-2.28, -0.88]	
Wong [2020]	1.2	1.18	54	2.89	2.4	54	59.1%	-0.89 [-1.28, -0.49]	=
Total (95% CI)			75			75	100.0%	-1.17 [-1.84, -0.50]	•
Heterogeneity: Tau ² =	0.16; Chi ² = 2	2.85, df =	1 (P = 0.0	9); I ² = 65%				_	-

Conclusions

IVR effectively reduced anxiety, depression, fatigue, and blood pressure in adult cancer patients and reduced pain and anxiety in pediatric patients. IVR is possible to distract patient discomfort while receiving chemotherapy. However, more robust RCTs are still needed to strengthen future studies on IVR.

Keywords: immersive virtual reality; chemotherapy; meta-analysis

