Extended Reality Interventions for Chronic Pain

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Appendix

APPENDIX A. SEARCH STRATEGIES

Search Date: 1946 to 05/01/23		Search Statement	Results
MEDLINE	1	exp Chronic pain/ OR Pain.tw.	753765
	2	Intractable pain/ or ((chronic or persistent or intractable or refractory or sustain*) adj3 pain).ti,ab,kf.	100987
	3	exp Back pain/ or exp Neck pain/ or exp Patellofemoral Pain Syndrome/ or exp Mastodynia/ or (carpal tunnel or epicondylitis or Dupuytren's or tenosynovitis or trigger finger or "costovertebral angle pain" or mastalgia).ti,ab,kf.	73784
	4	Mastodynia/ or (mastodynia? or breast pain? or mammalgia?).ti,ab,kf.	1366
	5	exp Musculoskeletal pain/ or exp Arthralgia/ or exp Metatarsalgia/ or (polyarthriti* or monoarthriti* or osteoarthriti* or arthriti*).mp.	361079
	6	(neuralgia or neuropathy or phantom limb or Complex Regional Pain Syndrom* or CRPS).mp. or (morton neuroma or piriformis muscle syndrome or sciatica).ti,ab,kf.	127322
	7	(headache or migrain*).ti,ab,kf.	110726
	8	exp Facial Pain/ or exp Glossalgia/ or ("burning mouth syndrome" or tic douloureaux).tw.	11057
	9	exp Abdominal pain/ or exp Pelvic Pain/ or exp Flank Pain/	44672
	10	Cancer Pain/ or (cancer adj3 pain).ti,ab,kf.	14262
	11	exp Nociceptive pain/ or exp Central Nervous System Sensitization/ or central sensiti#ation.tw.	5757
	12	(somatic pain or tissue pain or nociceptive pain).ti,ab,kf.	2072
	13	exp Myofascial Pain Syndromes/	6827
	14	(myofascial trigger point pain or costen syndrome or temporomandibular joint dysfunction syndrome or tmj syndrome).ti,ab,kf.	273
	15	(fibromyalgia or fibrositides or fibrositis or muscular rheumatism).mp.	13994
	16	exp Muscle Spasticity/ or exp Paresis/ or (spasticity or hemiparesis).ti,ab,kf.	35498
	17	Or/1-16	1304902
	18	((Virtual or augmented or mixed) adj reality*).mp. or (VR or illusion* or ((Virtual or simulat* or immers* or 3D* or 3-D*) adj (environ* or techn*))).tw.	48953
	19	exp Virtual reality exposure therapy/ or (Video gam* or exergam* or artificial intelligence or Wii or Nintendo or Kinect or Xbox or Playstation or Meta Quest or Oculus or HTC-Vive or HTC Vive or HP Reverb or Google Daydream or ((Head-mounted OR headmounted) adj display) or hippotherapy or (horse* adj2 simulat*) or cyberspace).mp.	71578
	20	18 or 19	116722
	21	17 and 20	3612

	22	Limit to English	3505
	23	Limit 22 to (books or chapter or editorial or erratum or letter or note)	67
	24	22 not 23	3458

Search Date: 1947 to 05/01/23		**Search Statement**	**Results**
Embase	1	exp Chronic pain/ OR Pain.tw.	1186047
	2	Intractable pain/ or ((chronic or persistent or intractable or refractory or sustain*) adj3 pain).ti,ab,kf.	150686
	3	exp Back pain/ or exp Neck pain/ or exp Patellofemoral Pain Syndrome/ or exp Mastodynia/ or (carpal tunnel or epicondylitis or Dupuytren's or tenosynovitis or trigger finger or "costovertebral angle pain" or mastalgia).ti,ab,kf.	197177
	4	Mastodynia/ or (mastodynia? or breast pain? or mammalgia?).ti,ab,kf.	5687
	5	exp Musculoskeletal pain/ or exp Arthralgia/ or exp Metatarsalgia/ or (polyarthriti* or monoarthriti* or osteoarthriti* or arthriti*).mp.	813297
	6	(neuralgia or neuropathy or phantom limb or Complex Regional Pain Syndrom* or CRPS).mp. or (morton neuroma or piriformis muscle syndrome or sciatica).ti,ab,kf.	298182
	7	(headache or migrain*).ti,ab,kf.	186866
	8	exp Facial Pain/ or exp Glossalgia/ or ("burning mouth syndrome" or tic douloureaux).tw.	14953
	9	exp Abdominal pain/ or exp Pelvic Pain/ or exp Flank Pain/	247032
	10	Cancer Pain/ or (cancer adj3 pain).ti,ab,kf.	34435
	11	exp Nociceptive pain/ or exp Central Nervous System Sensitization/ or central sensiti#ation.tw.	7995
	12	(somatic pain or tissue pain or nociceptive pain).ti,ab,kf.	3385
	13	exp Myofascial Pain Syndromes/	8889
	14	(myofascial trigger point pain or costen syndrome or temporomandibular joint dysfunction syndrome or tmj syndrome).ti,ab,kf.	347
	15	(fibromyalgia or fibrositides or fibrositis or muscular rheumatism).mp.	27737
	16	exp Muscle Spasticity/ or exp Paresis/ or (spasticity or hemiparesis).ti,ab,kf.	70069
	17	Or/1-16	2320301
	18	((Virtual or augmented or mixed) adj reality*).mp. or (VR or illusion* or ((Virtual or simulat* or immers* or 3D* or 3-D*) adj (environ* or techn*))).tw.	72207
	19	exp Virtual reality exposure therapy/ or (Video gam* or exergam* or artificial intelligence or Wii or Nintendo or Kinect or Xbox or Playstation or Meta Quest or Oculus or HTC-Vive or HTC Vive or HP Reverb or Google Daydream or ((Head-	86157

		mounted OR headmounted) adj display) or hippotherapy or (horse* adj2 simulat*) or cyberspace).mp.	
	20	18 or 19	152523
	21	17 and 20	6428
	22	Limit to English	6209
	23	Limit 22 to (books or chapter or editorial or erratum or letter or note)	259
	24	22 not 23	5950

Search Date: 1987 to 05/30/23		**Search Statement**	**Results**
PsycInfo	1	pain.tw.	99143
	2	chronic pain/ or back pain/ or myofascial pain/ or (patellofemoral syndrome or carpal tunnel or epicondylitis or Dupuytren or tenosynovitis or trigger finger).tw	19010
	3	(mastodynia or mammalgia or mastalgia).tw.	22
	4	Exp Arthritis/ or (arthralgia or metatarsalgia or arthriti* or polyarthriti* or monoarthriti* or osteoarthriti*).tw.	7939
	5	exp Headache/ or headache.tw. or migraine.tw.	21361
	6	exp Neuralgia/ or exp Phantom Limbs/ or exp Neuropathy/ or (neuralgia or neuropathy or phantom limb or complex regional pain syndrom* or CRPS or morton neuroma or piriformis muscle syndrome or sciatica).tw	11356
	7	(Glossalgia or "burning mouth syndrome" or tic douloureaux).tw.	144
	8	“central nervous system sensitization”.tw.	14
	9	exp Somatoform Pain Disorder/ or exp Myofascial Pain/ or tmj syndrome.tw.	1157
	10	exp Fibromyalgia/ or (fibromyalgia or fibrositides or fibrositis or muscular rheumatism).tw.	3799
	11	exp General Paresis/ or exp Hemiparesis/ or (muscle spasticity or hemiparesis).tw	2033
	12	Or/ 1-11	127765
	13	virtual reality/ or virtual environment/ or virtual reality exposure therapy/	11428
	14	computer games/ or (Video gam* or exergam* or artificial intelligence or Wii or Nintendo or Kinect or Xbox or Playstation or Meta Quest or Oculus or HTC-Vive or HTC Vive or HP Reverb or Google Daydream or hippotherapy or ("Head-mounted display" or "headmounted display") or horse* simulat*).tw. or cyberspace.tw.	21693
	15	13 or 14	31648
	16	12 and 15	608
	17	Limit to English	585

Search Date: 1971 to 05/25/23		Search Statement	Results
CINAHL	1	(MH "Chronic pain") OR (TI Pain OR AB Pain)	
	2	(MH "Back pain+") OR (MH "Neck pain") OR (MH "Musculoskeletal pain+") OR (MH “Muscle pain”) OR (MH Arthralgia+) OR (MH Arthritis+) OR (MH “Knee pain”) OR (MH "Patellofemoral Pain Syndrome") OR (MH “Elbow pain”) OR (MH “Heel pain”) OR (MH Metatarsalgia) OR (MH Tendinopathy+)	
	3	TI ("carpal tunnel" OR “tarsal tunnel” OR “Meralgia Paresthetica” OR epicondylitis OR Dupuytr* OR tenosynovitis OR "trigger finger" OR mastalgia# OR mastodynia# OR mammalgia# OR polyarthriti* OR monoarthriti* OR osteoarthriti* OR arthriti*) OR AB ("carpal tunnel" OR “tarsal tunnel” OR “Meralgia Paresthetica” OR epicondylitis OR Dupuytr* OR tenosynovitis OR "trigger finger" OR mastalgia# OR mastodynia# OR mammalgia# OR polyarthriti* OR monoarthriti* OR osteoarthriti* OR arthriti*)	
	4	(MH “Phantom pain”) OR (MH “Neuralgia+”) OR (MH “Referred pain”) OR (MH "Complex Regional Pain Syndromes+”) OR TI (neuralgia OR neuropathy OR "phantom limb" OR "Complex Regional Pain Syndrom*" OR CRPS OR "morton neuroma" OR "piriformis muscle syndrome" OR sciatica) OR AB (neuralgia OR neuropathy OR "phantom limb" OR "Complex Regional Pain Syndrom*" OR CRPS OR "morton neuroma" OR "piriformis muscle syndrome" OR sciatica)	
	5	(MH Headache+) OR TI(headache OR migrain*) OR AB (headache OR migrain*)	
	6	(MH "Facial Pain+") OR TI "burning mouth syndrome" OR AB "burning mouth syndrome" OR TI "tic douloureaux" OR AB "tic douloureaux"	
	7	(MH "Abdominal pain+") OR (MH "Pelvic Pain+") OR (MH "Cancer Pain") OR (MH "Nociceptive pain+") OR TI "central sensiti*" OR AB "central sensiti*"	
	8	(MH "Myofascial Pain Syndromes+") OR TI "myofascial trigger point" OR AB "myofascial trigger point"	
	9	MH “Temporomandibular Joint Syndrome” OR TI ("costen syndrome" OR “temporomandibular joint dysfunction” or TMJ) OR AB ("costen syndrome" OR “temporomandibular joint dysfunction” or TMJ)	
	10	MH fibromyalgia OR TI (fibromyalgia OR fibrositis OR "muscular rheumatism") OR AB (fibromyalgia OR fibrositis OR "muscular rheumatism")	
	11	(MH "Muscle Spasticity") OR TI (spasticity OR hemiparesis) or AB (spasticity OR hemiparesis)	
	12	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11	
	13	(MH “Virtual reality+”) OR (MH “Augmented reality”) OR TI (((Virtual OR augmented OR mixed) W1 reality*) OR VR OR illusion* OR cyberspace) OR AB (((Virtual OR augmented OR mixed) W1 reality*) OR VR OR illusion* OR cyberspace) OR TI ((Virtual OR simulat* OR immers* OR 3D* OR 3-D*) W1	

	(environ* OR techn*)) OR AB ((Virtual OR simulat* OR immers* OR 3D* OR 3-D*) W1 (environ* OR techn*))	
14	(MH "Virtual reality exposure therapy") OR (MH “Video games+”) OR MH “Equine-assisted therapy” OR TI ("Video gam*" OR exergam* OR "artificial intelligence" OR Wii OR Nintendo OR Kinect OR Xbox OR Playstation OR "Meta Quest" OR Oculus OR HTC-Vive OR "HTC Vive" OR "HP Reverb" OR "Google Daydream" OR ((Head-mounted OR headmounted) W1 display) OR hippotherapy OR (horse* N2 simulat*)) OR AB ("Video gam*" OR exergam* OR "artificial intelligence" OR Wii OR Nintendo OR Kinect OR Xbox OR Playstation OR "Meta Quest" OR Oculus OR HTC-Vive OR "HTC Vive" OR "HP Reverb" OR "Google Daydream" OR ((Head-mounted OR headmounted) W1 display) OR hippotherapy OR (horse* N2 simulat*))	
15	S13 OR S14	
16	S12 AND S15	
	Total	20,727
	Total after deduplication	**10,932**

APPENDIX B. STUDIES EXCLUDED DURING FULL-TEXT SCREENING

1. Virtual reality system for the treatment of chronic pain and stroke rehabilitation. Journal of Pain & Palliative Care Pharmacotherapy 2008;**22**(1):83-84 Online First. *Ineligible study design*
2. HELPING VETS DEAL WITH CHRONIC PAIN: Virtual reality program provides real results. InMotion 2021;**31**(2):16-17 Online First. *Ineligible study design*
3. Erratum: Effects of an 8-Week Virtual Reality Training Program on Pain, Fall Risk, and Quality of Life in lderly Women with Chronic Low Back Pain: Double-Blind Randomized Clinical Trial (Games for Health Journal (2022) 11:2 (85-92) DOI: 10.1089/g4h.2021.0175). Games for Health Journal 2022;**11**(4):275 Online First. *Ineligible study design*
4. Adaikkammai S, Singhal M, Smita E, Sreenivas S, Abhishek Appaji M. Virtual Reality in Rehabilitating Amputees Suffering from Phantom Limb Pain. 2019 11th International Conference on Communication Systems and Networks, COMSNETS 2019 2019:801-06 Online First. *Ineligible study design*
5. Aivaliotis VI, Dlamini V, Callahan M, Kelly C, Nguyen LAB. 697 VIRTUAL REALITY MINDFULNESS THERAPY VS. VIRTUAL REALITY DISTRACTIVE THERAPY IN CHRONIC ABDOMINAL PAIN. Gastroenterology 2020;**158**(6 Supplement 1):S-145 Online First. *Ineligible study design*
6. Akbulut A, Aşçi G, Tarakçi E, Aydin MA, Zaim AH. A Wearable Device for Virtual Cyber Therapy of Phantom Limb Pain. 2018 International Conference on Artificial Intelligence and Data Processing, IDAP 2018 2019 Online First. *Ineligible study design*
7. Akbulut A, Gungor F, Tarakci E, Cabuk A, Aydin MA. Immersive virtual reality games for rehabilitation of phantom limb pain. TIPTEKNO 2019 - Tip Teknolojileri Kongresi 2019 Online First. *Ineligible study design*
8. Alazba A, Al-Khalifa H, AlSobayel H. A proposed game for promoting physical activities among people with low back pain using virtual reality. ACM International Conference Proceeding Series 2018:141-44 Online First. *Ineligible study design*
9. Alazba A, Al-Khalifa H, AlSobayel H. RabbitRun: An Immersive Virtual Reality Game for Promoting Physical Activities Among People with Low Back Pain †. Technologies 2019;**7**(1) Online First. *Ineligible population*
10. Alnuman N, Jbara AA. Video Games and the Prevalence of Musculoskeletal Disorders in Young Adults. 2022 IEEE Zooming Innovation in Consumer Technologies Conference, ZINC 2022 2022:34-38 Online First. *Ineligible population*
11. Alphonso AL, Monson BT, Zeher MJ, et al. Use of a virtual integrated environment in prosthetic limb development and phantom limb pain. Annual Review of CyberTherapy and Telemedicine 2012;**10**:305-09 Online First. *Ineligible study design*
12. Alves CM, Rezende AR, Marques IA, Silva DC, Paiva TS, Naves ELM. Serious Games and Virtual Reality in the Treatment of Chronic Stroke: Both Sides Rehabilitation. IFMBE Proceedings 2022;**83**:239-44 Online First. *Ineligible population*
13. Ambron E, Buxbaum L, Kuchenbecker K, Miller A, Coslett B. Virtual reality treatment for phantom limb pain. Neurorehabilitation and Neural Repair 2019;**33**(12):1083 Online First. *Ineligible study design*

14. Ambron E, Buxbaum LJ, Miller A, Stoll H, Kuchenbecker KJ, Coslett HB. Virtual Reality Treatment Displaying the Missing Leg Improves Phantom Limb Pain: A Small Clinical Trial. Neurorehabilitation and neural repair 2021;**35**(12):1100-11 Online First. *Ineligible study design*
15. Amin AM. Effectiveness of mobile virtual reality as a means for pain distraction. 2016 Online First. *Ineligible population*
16. Anam M, Sizemore K, Mansour H, et al. (309) Virtual Reality Walking for Neuropathic Pain in Spinal Cord Injury: Preliminary Efficacy Findings. Journal of Pain 2019;**20**:S51-S51 Online First. *Ineligible study design*
17. Anwar N, Karimi H, Ahmad A, et al. Virtual Reality Training Using Nintendo Wii Games for Patients With Stroke: Randomized Controlled Trial. JMIR serious games 2022;**10**(2):e29830 Online First. *Ineligible population*
18. Arnoni JLB, Kleiner AFR, Lima CRG, De Campos AC, Rocha NACF. Nonimmersive Virtual Reality as Complementary Rehabilitation on Functional Mobility and Gait in Cerebral Palsy: A Randomized Controlled Clinical Trial. Games for Health Journal 2021;**10**(4):254-63 Online First. *Ineligible population*
19. Artifon M, Adachi L, Schestatsky P. Proceedings #39: Effects of tDCS alone and combined with virtual reality in clinical practice. Brain Stimulation 2019;**12**(2):e109-e10 Online First. *Not published in English*
20. Bahirat K, Annaswamy T, Prabhakaran B. Mr.MAPP: Mixed reality for MAnaging phantom pain. MM 2017 - Proceedings of the 2017 ACM Multimedia Conference 2017:1558-66 Online First. *Ineligible study design*
21. Bahirat K, Raval G, Chung YY, et al. Using Mr. MAPp for lower limb phantom pain management. MM 2019 - Proceedings of the 27th ACM International Conference on Multimedia 2019:1071-75 Online First. *Ineligible study design*
22. Baltaci G, Harput G, Haksever B, Ulusoy B, Ozer H. Comparison between Nintendo Wii Fit and conventional rehabilitation on functional performance outcomes after hamstring anterior cruciate ligament reconstruction: prospective, randomized, controlled, double-blind clinical trial. Knee surgery, sports traumatology, arthroscopy 2013;**21**:880-87 Online First. *No eligible outcomes provided*
23. Bani Mohammad E, Ahmad M. Virtual reality as a distraction technique for pain and anxiety among patients with breast cancer: A randomized control trial. Palliative & supportive care 2019;**17**(1):29-34 Online First. *Ineligible setting or follow-up*
24. Baqai A, Memon K, Memon AR, Shah SMZA. Interactive Physiotherapy: An Application Based on Virtual Reality and Bio-feedback. Wireless Personal Communications 2019;**106**(4):1719-41 Online First. *Ineligible study design*
25. Bartlett J, Fisher E, Liikkanen S, Turunen J, Skog M, Eccleston C. The Design and Development of an Embodied Semi-Autonomous Mentoring Intelligence (SAMI) for Use in Virtual Reality Interventions, Operationalized for the Self-Management of Chronic Pain. Frontiers in Virtual Reality 2022;**3** Online First. *Ineligible study design*
26. Basha MA, Aboelnour NH, Alsharidah AS, Kamel FH. Effect of exercise mode on physical function and quality of life in breast cancer-related lymphedema: a randomized trial. Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer 2022;**30**(3):2101-10 Online First. *Ineligible population*
27. Behar C, Lustick M, Foreman MH, Webb J, Engsberg JR. Personalized virtual reality for upper extremity rehabilitation: Moving from the clinic to a home exercise program. Journal of

Intellectual Disability - Diagnosis and Treatment 2016;**4**(3):160-69 Online First. *Ineligible population*

28. Beltran-Alacreu H, Navarro-Fernandez G, Godia-Lledo D, et al. A Serious Game for Performing Task-Oriented Cervical Exercises Among Older Adult Patients With Chronic Neck Pain: Development, Suitability, and Crossover Pilot Study. JMIR serious games 2022;**10**(1):e31404 Online First. *Ineligible study design*
29. Benham S, Kang M, Grampurohit N. Immersive Virtual Reality for the Management of Pain in Community-Dwelling Older Adults. OTJR : occupation, participation and health 2019;**39**(2):90-96 Online First. *Ineligible study design*
30. Ber R, VanOosterhout S, Van Loo L, et al. TCT-261 Impact of Virtual Reality on Pre-Procedural Anxiety Prior to Heart Catheterization: The VR-THEIA Study. Journal of the American College of Cardiology 2022;**80**(12 Supplement):B103-B04 Online First. *Ineligible population*
31. Bogdanovych A, Chuan A. The Island of Pain: A Virtual Reality Experience for Patients with Chronic Pain. SIGGRAPH Asia 2020 XR, SA 2020 2020 Online First. *Ineligible study design*
32. Bolte B, e Lussanet M, Lappe M. Virtual reality system for the enhancement of mobility in patients with chronic back pain. Technology, rehabilitation and empowerment of people with special needs. 2015:47-59 Online First. *Ineligible study design*
33. Botella C, Garcia-Palacios A, Vizcaino Y, Herrero R, Banos RM, Belmonte MA. Virtual reality in the treatment of fibromyalgia: a pilot study. Cyberpsychology, behavior and social networking 2013;**16**(3):215-23 Online First. *Ineligible population*
34. Bottiroli S, Matamala-Gomez M, Allena M, et al. The virtual Enfacement Illusion on pain perception in patients suffering from chronic migraine: Preliminary data from a randomized controlled trial. Cephalalgia 2022;**42**(1 Supplement):47 Online First. *Ineligible study design*
35. Bratosin IA, Pavaloiu IB, Goga N, Luca AI. Virtual Reality Application for Pain Management: User Requirements. International Journal of Advanced Computer Science and Applications 2022;**13**(4):351-56 Online First. *Ineligible population*
36. Bratosin IA, Pavaloiu IB, Vasilateanu A, Gavajiuc D, Dragoi G, Goga N. Pain Relief using Virtual Reality. Proceedings of the 11th International Conference on Electronics, Computers and Artificial Intelligence, ECAI 2019 2019 Online First. *Ineligible study design*
37. Buttress S, Granat M, Barratt A, Roy B. The use of gamified virtual physiotherapy as an effective treatment for patients with shoulder problems. Physiotherapy (United Kingdom) 2019;**105**(Supplement 1):e162-e63 Online First. *Ineligible study design*
38. Cacau LdAP, Oliveira GU, Maynard LG, et al. The use of the virtual reality as intervention tool in the postoperative of cardiac surgery. Revista brasileira de cirurgia cardiovascular : orgao oficial da Sociedade Brasileira de Cirurgia Cardiovascular 2013;**28**(2):281-9 Online First. *Ineligible setting or follow-up*
39. Carrougher GJ, Hoffman HG, Nakamura D, et al. The effect of virtual reality on pain and range of motion in adults with burn injuries. Journal of burn care & research : official publication of the American Burn Association 2009;**30**(5):785-91 Online First. *Ineligible population*
40. Cawthorne D, March L, Parker D, Coolican M, Negus J. TKR-power-patient outcomes using wii enhanced rehabilitation after a total knee replacement. Physiotherapy (United Kingdom) 2015;**101**(SUPPL. 1):eS204-eS05 Online First. *Ineligible study design*
41. Chandler JM, Taylor JS, Portelli KI, et al. Small surgeries, big smiles: Reducing sedation through virtual reality. Journal of Laparoendoscopic and Advanced Surgical Techniques 2019;**29**(6):A64 Online First. *Ineligible population*

42. Chau B, Phelan I, Ta P, et al. Immersive Virtual Reality for Pain Relief in Upper Limb Complex Regional Pain Syndrome: A Pilot Study. Innovations in clinical neuroscience 2020;**17**(4-6):47-52 Online First. *Ineligible population*
43. Chavez T. (410) Therapeutic Virtual Reality in Pain Management. Journal of Pain 2019;**20**:S74-S74 Online First. *Ineligible study design*
44. Chen C-C. Multimedia virtualized environment for shoulder pain rehabilitation. Journal of physical therapy science 2016;**28**(4):1349-54 Online First. *No eligible outcomes provided*
45. Christensen SWM, Almsborg M H, Vain M TS, Vaegter HB. The Effect of Virtual Reality on Cold Pain Sensitivity in Patients with Fibromyalgia and Pain-Free Individuals: A Randomized Crossover Study. Games for health journal 2022 Online First. *No eligible outcomes provided*
46. Christiansen CL, Bade MJ, Davidson BS, Dayton MR, Stevens-Lapsley JE. Effects of weight-bearing biofeedback training on functional movement patterns following total knee arthroplasty: a randomized controlled trial. journal of orthopaedic & sports physical therapy 2015;**45**(9):647-55 Online First. *Ineligible intervention*
47. Chughtai M, Kelly JJ, Newman JM, et al. The Role of Virtual Rehabilitation in Total and Unicompartmental Knee Arthroplasty. The journal of knee surgery 2019;**32**(1):105-10 Online First. *Ineligible study design*
48. Clavelin G, Bouhier M, Tseng WJ, Gugenheimer J. Exploring the Perception of Pain in Virtual Reality through Perceptual Manipulations. Conference on Human Factors in Computing Systems - Proceedings 2023 Online First. *Ineligible population*
49. Cuneo A, Yang R, Wang K, et al. Utility of a Novel, Combined Biofeedback-Virtual Reality Tool as Add-on Treatment for Chronic Migraine. Neurology 2022;**98**(18 SUPPL) Online First. *Ineligible study design*
50. D. M P, L. A M, R. B W, L. J H. Effect of Virtual Reality Immersion on Phantom Limb Pain and Phantom Limb Sensation...45th Academy Annual Meeting and Scientific Symposium, March 6–9, 2019, Orlando, Florida. Journal of Prosthetics & Orthotics (JPO) 2019;**31**:6-6 Online First. *Ineligible study design*
51. Dagenais M, Brun C, Ohayon A, Mercier C. Virtual Reality in Fibromyalgia: Does Altering Visual Feedback Impact on Pain and Movement During Reaching? Frontiers in Virtual Reality 2021;**2** Online First. *Ineligible study design*
52. Dailey F, Tashjian VC, Mosadeghi S, et al. The clinical utility of virtual reality in inpatient pain management among patients with gastrointestinal disorders. American Journal of Gastroenterology 2016;**111**(Supplement 1):S464-S65 Online First. *Ineligible population*
53. Daste C, Foissac F, Abdoul H, Rannou F, Poiraudeau S, Nguyen C. Patient acceptable symptom state for patient-reported outcomes in 2 populations of patients with non-specific chronic low back pain: A secondary analysis of 2 randomized trials. Annals of Physical and Rehabilitation Medicine 2018 Online First. *Ineligible study design*
54. Demeter N, Josman N, Eisenberg E, Pud D. Who can benefit from virtual reality to reduce experimental pain? A crossover study in healthy subjects. European journal of pain (London, England) 2015;**19**(10):1467-75 Online First. *Ineligible population*
55. Depauw L, Bosteels A, Maes S, Sermeus L, Saldien V. Virtual reality hypnosis for postoperative pain after total knee arthroplasty. Acta Anaesthesiologica Belgica 2020;**71**:73-77 Online First. *Ineligible study design*

56. Deshpande AK, Bhatt I, Rojanaworarit C. Virtual reality for tinnitus management: a randomized controlled trial. International journal of audiology 2022;**61**(10):868-75 Online First. *Ineligible population*
57. Diaz-Orueta U, Alvarado S, Gutierrez D, Climent G, Banterla F. "Isla Calma", a Novel Virtual Reality Environment for Pain and Anxiety Distraction: Report on Usability, Acceptability, and Subjective Experience. Games for health journal 2012;**1**(5):353-61 Online First. *Ineligible study design*
58. DiMeola KA, Haynes J, Barone M, et al. A Pilot Investigation of Nonpharmacological Pain Management Intervention Groups in Methadone Maintenance Treatment. Journal of addiction medicine 2022;**16**(2):229-34 Online First. *No eligible outcomes provided*
59. Dingli A, Bondin L. Realtime adaptive virtual reality for pain reduction. IEEE Conference on Computatonal Intelligence and Games, CIG 2019;**2019-August** Online First. *Ineligible study design*
60. Donegan T, Ryan BE, Swidrak J, Sanchez-Vives MV. Immersive Virtual Reality for Clinical Pain: Considerations for Effective Therapy. Frontiers in Virtual Reality 2020;**1** Online First. *Ineligible study design*
61. Dulau E, Botha-Ravyse CR, Luimula M. Virtual reality for physical rehabilitation: A Pilot study How will virtual reality change physical therapy? 10th IEEE International Conference on Cognitive Infocommunications, CogInfoCom 2019 - Proceedings 2019:277-82 Online First. *Ineligible population*
62. e Carvalho MS, Carvalho LC, Alves RdS, et al. Analysis of the Muscular Activity, Peak Torque in the Lower Limbs, and Static Balance after Virtual Rehabilitation in Women with Fibromyalgia: A Randomized Controlled Study. Games for health journal 2021;**10**(3):190-97 Online First. *No eligible outcomes provided*
63. e Oliveira PF, Alves RdS, Iunes DH, et al. Effect of Exergaming on Muscle Strength, Pain, and Functionality of Shoulders in Cancer Patients. Games for health journal 2020;**9**(4):297-303 Online First. *Ineligible study design*
64. e Tommaso M, Ricci K, Laneve L, Savino N, Antonaci V, Livrea P. Virtual visual effect of hospital waiting room on pain modulation in healthy subjects and patients with chronic migraine. Pain research and treatment 2013;**2013**:515730 Online First. *Ineligible setting or follow-up*
65. e Villiers E, Stone T, Wang N-W, Sarangi V, Pelah A, Shenker N. Virtual Environment Rehabilitation for Patients with Motor Neglect Trial (VERMONT): A Single-Center Randomized Controlled Feasibility Trial. Brain sciences 2021;**11**(4) Online First. *Ineligible study design*
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APPENDIX C. ONGOING STUDIES

Trial #	Study Title	Status	Total N*	Location
KQ1 Studies				
NCT04468074	Virtual Reality Treatment for Adults With Chronic Back Pain	Completed (no publication)	72	Boulder, Colorado, USA
NCT05634291	Effects of the Nottingham Augmented Reality (AR) App for Arthritis Hand Joint Pain	Completed (no publication)	36	San Diego, California, USA
NCT05285462	Feasibility of Virtual Reality Delivery of Pain Neuroscience Education	Completed (no publication)	52	Nashville, Tennessee, USA
NCT04849897	Virtual Reality Guided Imagery for Chronic Pain	Completed (no publication)	36	Los Angeles, California, USA
NCT05398549	Effects of Virtual Reality in Adhesive Capsulitis on Pain, Range of Motion and Function	Completed (no publication)	36	Lahore, Punjab, Pakistan
NCT04572074	Virtual Reality for Cancer Pain Management	Completed (only protocol paper)	128	Washington, D.C., USA
NCT05701891	Virtual Reality Integrated Within Physiotherapy for Patients With Complex Chronic Low Back Pain	Recruiting (only protocol paper)	120	Nijmegen, Netherlands
NCT05483816	Multisensory Stimulation to Target Sensory Loss and Chronic Pain in Neuropathic Patients	Recruiting (no publication)	80	Zurich, Switzerland
NCT05172492	Endocare for Pelvic-perineal Pain Related to Endometriosis Used at Home	Recruiting (no publication)	120	Bordeaux, Gironde, France
NCT05085821	Cardio-visual Stimulation in Augmented Reality for Pain Reduction	Recruiting (no publication)	50	Nancy, France
NCT02995434	Immersive Multimedia as an Adjunctive Measure for Pain Control in Cancer Patients	Recruiting (no publication)	100	Surrey and Vancouver, British Columbia, Canada
NCT05859321	Virtual Reality Based Physical Therapy for Patients With Lower Back Pain	Recruiting (no publication)	84	Lahore, Punjab, Pakistan
NCT05838924	Changing Lower Back Pain Through Virtual Reality	Recruiting (no publication)	60	Valencia, Spain
NCT05776992	Effect of Various Virtual Reality Exercise Individuals With Low Back Pain	Recruiting (no publication)	52	Istanbul, Turkey

Trial #	Study Title	Status	Total N*	Location
NCT05546749	Virtual Reality for Chronic Pain and Opioid Use Disorder Pilot	Recruiting (no publication)	40	Bronx, New York, USA
NCT05726123	Therapeutic Intervention With Neuromodulation and Inverse Virtual Reality in Patients With Fibromyalgia	Recruiting (no publication)	60	Madrid, Spain
NCT05595317	The Effects of Non-Immersive Virtual Reality Exercises on Muscle Excitability in Knee Osteoarthritis	Recruiting (no publication)	44	Erzurum, Turkey
NCT04867187	rTMS Efficacy Coupled With Mirror Therapy	Recruiting (no publication)	64	Bron and Saint-Étienne, France
NCT05296265	Efficacy and Mechanisms of Virtual Reality Treatment of Phantom Leg Pain	Recruiting (no publication)	40	Elkins Park and Philadelphia, Pennsylvania, and Seattle, Washington, USA
NCT05254509	Virtual Reality, Debriefing and Chronic Pain	Recruiting (no publication)	50	Pittsburgh, Pennsylvania, USA
NCT04933474	Pragmatic Comparative Effectiveness Trial of Evidence-based, On-demand, Digital Behavioral Treatments for Chronic Pain	Recruiting (no publication)	300	Los Angeles, California, USA
NCT05005026	Virtual Walking Intervention for Neuropathic Pain in Spinal Cord Injury	Recruiting (no publication)	250	Birmingham, Alabama & Richmond, Virginia, USA; Sydney, New South Wales, Australia
NCT04906707	Home-Based Intervention for Chronic Pain in Adults With Sickle Cell Disease (RelieVRx)	Recruiting (no publication)	50	Atlanta, Georgia, USA
NCT05160038	Embodied Virtual Reality for Chronic Pain	Recruiting (no publication)	80	Zurich, Zurich, Switzerland
NCT04907643	Virtual Reality for GI Cancer Pain to Improve Patient Reported Outcomes	Recruiting (no publication)	360	Los Angeles, California, USA
NCT04253691	Sleep and Pain Intervention for Chronic Insomnia Using Virtual Reality Pilot Study	Recruiting (no publication)	60	Columbia, Missouri, USA
NCT05348174	Randomized Controlled Trial of Virtual Reality Assisted Guided Imagery (VRAGI) for Pain in Advanced Cancer Patients.	Not yet recruiting (only protocol paper)	80	Clemson, Columbia, and Greenville, South Carolina, USA

Trial #	Study Title	Status	Total N*	Location
NCT05971966	Effects of Virtual Reality Rehabilitation and Muscle Energy Technique in Patients With Patellofemoral Pain Syndrome.	Not yet recruiting (no publication)	32	Islamabad, Punjab, Pakistan
NCT05933941	Virtual Reality as a Treatment Tool for Chronic Neck Pain in Patients With Fibromyalgia	Not yet recruiting (no publication)	50	Madrid, Spain
NCT05880511	Augmented Reality Sensorimotor Training to Treat Chronic Neck	Not yet recruiting (no publication)	40	Hamilton, Ontario, Canada
NCT05810428	Artificial Intelligence to Predict Surgical Outcomes and Assess Pain Neuromodulation in Trigeminal Neuralgia Subjects	Not yet recruiting (no publication)	50	Milan, Italy
NCT05639764	Immersive Virtual Reality for Pain-related Movement Dysfunctions in Patients With Chronic Shoulder Pain	Not yet recruiting (no publication)	66	Málaga, Spain
NCT05263037	EaseVRx-8w+ for the Treatment of Chronic Lower Back Pain	Active not recruiting (no publication)‡	1093	Van Nuys, California, USA
NCT04241172	TKR Rehabilitation Through the Immersive Virtual Reality in Aquatic Scenarios	Active not recruiting (no publication)	96	Rome, Italy
NCT03592394	Virtual Reality for Chronic Neuropathic Pain	Unknown (no publication)	40	White Plains, New York, USA
NCT04651478	Mental Representation Techniques for the Treatment of Parkinson´s Disease-related Pain	Unknown (only protocol paper)	32	Madrid, Spain
NCT04955613	6Degrees VR System for Treatment of Phantom Limb Pain	Unknown (no publication)	122	Ramat Gan, Israel
NCT04411264	Evaluation of the Effect of Virtual Reality on Pain in the Management of Chronic Wounds.	Unknown (no publication)	124	Limoges and Saint-Pierre, France
NCT04237766	Movement Visualization in Patients With Hemophilic Arthropathy	Unknown (no publication)	140	NR
NCT04966468	Look of Life 2.0. Virtual Reality for Cancer Patients in Home Palliative Care	Unknown (no publication)	60	Bologna, Italy
NCT05088668	Augmented Reality for Shoulder Pain and Scapular Dyskinesis	Suspended	52	Alcala de Henares, Spain
ACTRN12623000745640	Supercharging Chronic Pain Education: Efficacy of Experiential Immersive Education (iED) using Virtual Reality for Pain Beliefs in Adults with Chronic Non-Cancer Pain.	Not yet recruiting	90	Southport, Queensland, Australia
ISRCTN59420095	Trunk Flexion Improvement in People with Low Back Pain Through Visual-Haptic Illusion: A Randomised Controlled Trial	Completed (publication intended 3/31/23)	60	Savona, Italy

Trial #	Study Title	Status	Total N*	Location
ISRCTN12473220	At-Home Virtual Reality as a Therapeutic Approach for Individuals with Chronic Temporomandibular Joint Disorders	Completed (publication intended 12/30/24)	54	Baltimore, Maryland, USA
KQ2 Studies				
NCT04010266	RelieVRx for Total Knee Arthroplasty (TKA) for the Reduction of Acute Postoperative Pain and Opioid Use	Active not recruiting (no publication)	113	Danville and Wilkes-Barre, Pennsylvania, USA
NCT03987334	Virtual Reality Rehabilitation in Neck Pain Subjects	Unknown (no publication)	72	Milan, Italy
NCT03476148	Home Rehabilitation Using Interactive Device Versus Inpatient Rehabilitation in Total Knee Arthroplasty	Unknown (no publication)	60	NR

Notes. *Total participants are actual enrolled for completed studies; all others are estimated totals.

‡ After the database searches were completed, including of registries for clinical trials, a report of this trial was published in December 2023 (Maddox et al 2023, doi: 10.1016/j.mcpdig.2023.09.003).

Abbreviations. NR=not reported; USA=United States of America.

APPENDIX D. RISK OF BIAS ASSESSMENTS

RANDOMIZED CONTROLLED TRIALS (ROB-2)

Trial Name or Author Year	Bias from randomization process	Bias from deviation from intended interventions (Assignment)	Bias from deviation from intended interventions (Adherence)	Bias from missing outcome data	Bias in measurement of outcome	Bias in selection of reported result	Overall risk of bias (Low, Some concerns, High)
Afzal, 2022[38]	Some concerns	Low	Some concerns	Low	Some concerns	Low	Some concerns
Ambrosino, 2020[75]	Some concerns	Low	Low	Low	Some concerns	Some concerns	Some concerns
Bahat, 2020[90]	Low	Low	Some concerns	Low	Some concerns	Low	Some concerns
Carvalho, 2020[58]	Some concerns	Low	High	High	Some concerns	Some concerns	High
Cetin, 2022[51]	Low	High	High	High	Some concerns	Low	High
Chuan, 2023[71]	Some concerns	Low	Some concerns	Low	Low	Low	Some concerns
Collado-Mateo, 2017[60]	Low	Low	Some concerns	High	Some concerns	Low	High
Cuneo, 2023[70]	Some concerns	High	High	High	Some concerns	Low	High
Darnall, 2020[72]	Some concerns	Low	Some concerns	Some concerns	Some concerns	Some concerns	High
Ditchburn, 2020[76]	Some concerns	Low	Some concerns	Low	Some concerns	Some concerns	High
Eccleston, 2022[27]	Low	Low	Some concerns	Low	Low	Low	Some concerns
Eichler, 2019[84]	Some concerns	Low	Low	High	Some concerns	Low	High
Elshazly, 2016[66]	Some concerns	Low	Low	Low	Some concerns	Some concerns	Some concerns
Fatoye, 2022[36]	Some concerns	High	High	High	Some concerns	Some concerns	High
Fuchs, 2022[82]	Some concerns	Low	Some concerns	High	Some concerns	Some concerns	High
Garcia-Palacios, 2015[64]	Some concerns	Low	Some concerns	Low	Some concerns	Some concerns	High
Gouveia, 2020[77]	Low	Low	Some concerns	Some concerns	Some concerns	Low	Some concerns
Groenveld, 2023[28]	Some concerns	Low	Low	Low	Some concerns	Low	Some concerns
Harvie, 2022[24]	Low	Low	Low	Low	Some concerns	Low	Some concerns in Domain 4 only
Janhunen, 2023[85]	Low	Low	Some concerns	Some concerns	Some concerns	Low	Some concerns
Jin, 2018[83]	Some concerns	Low	Some concerns	Low	Some concerns	Some concerns	High

Trial Name or Author Year	Bias from randomization process	Bias from deviation from intended interventions (Assignment)	Bias from deviation from intended interventions (Adherence)	Bias from missing outcome data	Bias in measurement of outcome	Bias in selection of reported result	Overall risk of bias (Low, Some concerns, High)
Kammler-Sucker, 2023[26]	Some concerns	Low	Low	Low	Some concerns	Low	Some concerns
Karahan, 2016[78]	Low	Low	Low	Low	Some concerns	Some concerns	Some concerns
Kim, 2014[48]	Some concerns	Low	Low	Low	Some concerns	Some concerns	High
Kim, 2020[43]	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	Some concerns	High
Lewis, 2021[79]	Low	Low	Some concerns	High	Some concerns	Low	High
Li, 2021[39]	Some concerns	Low	Some concerns	Low	Some concerns	Some concerns	High
Lin, 2020[67]	Some concerns	Low	Low	Low	Some concerns	Low	Some concerns
Maddox, 2022[32]	Low	Low	Low	Low	Some concerns	Low	Some concerns in Domain 4 only
Mbada, 2019[50]	High	Low	High	High	High	Some concerns	High
Mete, 2022[68]	Some concerns	Some concerns	Some concerns	Low	Some concerns	Low	High
Monteiro-Junior, 2015[46]	Some concerns	High	Low	High	Some concerns	Low	High
Nambi, 2020a[37]	Some concerns	Low	Some concerns	Low	Some concerns	Some concerns	Some concerns
Nambi, 2020c[69]	Low	Low	Low	Low	Some concerns	Some concerns	Some concerns
Nambi, 2021[41]	Some concerns	Low	Some concerns	Low	Some concerns	Some concerns	High
Nambi, 2021[42]	Some concerns	Some concerns	Some concerns	Low	Some concerns	Some concerns	High
Nambi, 2022[35]	Low	Low	Low	Low	Some concerns	Low	Some concerns in Domain 4 only
Nusser, 2021[52]	Some concerns	High	Low	High	Some concerns	Some concerns	High
Oh, 2014[49]	Some concerns	Low	Low	High	High	Some concerns	High
Ozlu, 2023[65]	Some concerns	High	High	High	Some concerns	Some concerns	High
Piqueras, 2013[86]	Low	Low	High	High	Some concerns	Low	High
Polat, 2021[57]	Some concerns	Low	Low	Some concerns	Some concerns	Some concerns	High
Prvu Bettger, 2020[87]	Low	Low	Low	Low	Some concerns	Low	Some concerns in Domain 4 only
Reynolds, 2022[73]	Some concerns	High	High	High	Some concerns	Low	High
Rezaei, 2019[56]	Some concerns	Low	Low	High	Some concerns	Low	High
Rodriguez-Hernandez, 2021[92]	Some concerns	Low	Some concerns	High	Some concerns	Low	High

Trial Name or Author Year	Bias from randomization process	Bias from deviation from intended interventions (Assignment)	Bias from deviation from intended interventions (Adherence)	Bias from missing outcome data	Bias in measurement of outcome	Bias in selection of reported result	Overall risk of bias (Low, Some concerns, High)
Rothangel, 2018[80]	Some concerns	Low	Some concerns	Low	Some concerns	Low	Some concerns
Sarig Bahat, 2015[55]	Low	Low	Low	Low	Some concerns	Low	Some concerns in Domain 4 only
Sarig Bahat, 2018[54]	Low	Low	Some concerns	Some concerns	Some concerns	Low	Some concerns
Sato, 2021[40]	Low	Some concerns	Some concerns	Low	Some concerns	Some concerns	High
Shim, 2023[88]	Low	Low	Some concerns	Some concerns	Low	Some concerns	
Taveggia, 2016[94]	Low	Some concerns	Some concerns	Low	Some concerns	Low	Some concerns
Tejara, 2020[53]	Low	Low	Low	Low	Some concerns	Low	Some concerns in Domain 4 only
Thomas, 2016[45]	Low	Low	Low	Low	Some concerns	Low	Some concerns in Domain 4 only
Villafaina, 2019[59]	Low	Low	Low	Some concerns	Some concerns	Low	Some concerns
Wankhade, 2022[74]	Some concerns	Some concerns	High	Low	Some concerns	Some concerns	High
Yilmaz Yelvar, 2017[25]	High	Low	High	Low	Some concerns	Some concerns	High
Yoo, 2014[47]	Some concerns	Low	Low	Low	Some concerns	Some concerns	Some concerns
Zadro, 2019[44]	Low	Low	Some concerns	Low	Some concerns	Low	Some concerns

NONRANDOMIZED COMPARISON STUDIES (ROBINS-I)

Study Name or Author Year	Preliminary considerations	Bias due to confounding	Selection bias	Bias in classification of interventions	Bias due to departures from intended interventions	Bias due to measurement of outcomes	Bias due to missing data	Bias in the selection of reported results	Overall risk of bias (Low, Moderate, Serious, Critical, No Information)
Abd-Elsayed, 2021[91]	Critical	--	--	--	--	--	--	--	Critical

APPENDIX E. CHRONIC BACK PAIN

Appendix Table E1. Detailed Characteristics for Included Trials on Chronic Low Back Pain

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
VR Interventions				
Eccleston, 2022[27] Some concerns 10 Months NR, Finland Orion Corporation; Business Finland	**Inclusion**: Adults with LBP ≥3 months, average pain intensity ≥ 4/10 over past week on NRS, ODI ≥26%, and medium (34-41) or high (42-68) TSKscore; had clear, flat ground surface at home of at least 2 m^2 using the digital intervention for pain; and could bend without severe pain. **Exclusion:** history of epilepsy, migraine, vertigo, or psychosis, a confirmed diagnosis of cancer, susceptibility to motion sickness requiring treatment, pregnancy, current physiotherapy that contraindicated intervention goals, severe or acute structural pathologies that the intervention could make worse, had psychotherapy in the previous 2 years or currently receiving psychotherapy, reported any condition that affected posture or balance, any prior participation in a digital therapeutics intervention for pain study	N=14 Age, mean (SD): 55.1 (10.5) Female: 86% Home 15-60 minute sessions, 5 sessions per week, for 30 unique days designed to last 6-8 weeks DTxP: Mentor guidance and instruction for tasks and building working alliance using an Oculus Quest headset. Participants entered the virtual world from inside cabin then engaged in gamified activities like fruit picking outside. 24 behavior change modules alternated new content and practice.	N=17 Age, mean (SD): 52.8 (11.19) Female: 82% Home 15-60 minute sessions, 5 sessions per week, for 30 unique days designed to last 6-8 weeks Relaxation instructions to enjoy virtual summer cabin and lakeshore environment with ambient wildlife sounds using an Oculus Quest headset. No DTxP content provided. N=11 Age, mean (SD): 57.1 (8.3) Female: 100% Home NA Usual care	**Primary: NR** **Pain-related functioning (8 wk):** • ODI • PROMIS pain interference **Pain intensity (8 wk):** • NRS • PROMIS pain intensity **Adverse events (8 wk):** • Mild, moderate, severe • Treatment-related **Pain catastrophizing (8 wk):** • TSK **Quality of life (8 wk):** • European Quality of Life 5 **Opioid use (5 mo)** **Pain global change (8 wk):** • PGIC

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Groenveld, 2023[28] Some concerns 4 Months Rijnstate Hospital, Netherlands This work was supported by the European Regional Development Fund (ERDF) [PROJ-00840, 2018]	**Inclusion**: 18 years and older with nonspecific chronic lower back pain (lasting at least 3 months) reporting an average pain score of 4 and higher on an 11-point Likert scale in the week preceding enrollment. Additionally, the person has an estimated waiting period of at least 6 weeks on the day of recruitment on the waiting list, is not yet receiving treatment, apart from analgesics or physiotherapy, and did not receive any invasive treatment for his chronic nonspecific low-back pain in the last year. **Exclusion:** People with radicular pain that is worse than the CLBP, participating in another trial to evaluate new ways of treating pain, severe anxiety or depression, unable to handle VR due to delirium, dementia, epilepsy, severe hearing/visual impairment, skin of the head or face not intact, and high risk of Meticillin-resistant Staphylococcus aureus	N=20 Age, mean (SD): 51 (2.9) Female: 85% Home Four weeks of thrice daily sessions lasting between 10 and 30 minutes. Pain education and psychological therapy VR treatment using the Oculus Gof. Patients embark on a 'journey' through the nervous system and can play five games, each rooted in different psychological treatment principles.	N=21 Age, mean (SD): 52 (2.5) Female: 80% NA NA Usual care	**Primary: SF-12** **Pain-related functioning (4 wk, 4 mo):** • BPI • ODI **Pain intensity (30 days):** • VAS **Adverse events (4 mo)** **Pain Catastrophizing (4 wk, 4 mo):** • PCS **Non-eligible outcomes:** • Pain Coping and Cognition List (PCCL) • Nottingham Extended Activities of Daily Living (NEADL) • Positive Health Questionnaire • Hospital Anxiety and Depression Scale (HADS)
Harvie, 2022[24] Some concerns 1 Week Metro South Health Persistent Pain	**Inclusion**: Adults referred to the Metro South Health Persistent Pain Management Service for the management of CLBP (duration at least six months), scored at least 'moderate' on Question 7 ('How much bodily pain have you had during the past 4 weeks?'), and Question 8 ('During the past 4 weeks, how much did pain interfere with your normal work [including	N=20 Age, mean (SD): 51.9 (14.5) Female: 45% Clinic 1 session, three 6 minute long experiences with 5 minute intervals between each.	N=10 Age, mean (SD): 56.9 (14.3) Female: 50% Clinic 1 session, three 6 minute blocks with 5 minute intervals	**Primary: NRS** **Pain global change (1 wk):** • PGIC **Pain catastrophizing (1 wk):** • Photograph Series of Daily Activities **Physical performance (1 wk):** • Maximum grip strength

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Management Service, Australia Seeding grant from The Hopkins Centre; Early Career Research Fellowship from the National Health and Medical Research Council of Australia (GNT1142929)	both work outside the home and housework]?') of the SF-36 **Exclusion:** Diagnosis of, or the presence of red flags, indicating serious spinal pathology (i.e., infection, tumour, recent fracture, significant structural deformity, such as unstable/unstabilized spondylolisthesis or progressive scoliosis, inflammatory disorder, and neuropathic radicular syndrome or cauda equina syndrome). They were also excluded if they had an inability to tolerate visual stimulation (e.g., susceptibility to migraines aggravated by light) or inability to tolerate the head mounted display (e.g., sensitivity to touch around the face and head).	Embodiment experiences and movement (e.g., boxing, creating earthquakes) using the Oculus Rift S head mounted display with touch controllers with three avatar characters: a boxer, superhero, and rock climber using the Oculus Rift S.	VR control condition. Embodiment of cartoon-like virtual hands. Explored 3 scenarios in Vacation Simulator app: built sandcastle, stood in sea at beach, cooked barbecue at beach using the Oculus Rift S.	**Non-eligible:** • Body image • Embodiment

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Kammler-Sücker, 2023[26] Some concerns 117 Days VR Core Facility at the Center for Innovative Psychiatric and Psychotherapeutic Research (CIPP) at Central Institute for Mental Health (Mannheim, Germany), Gernaby Reinhart Koselleck award of the Deutsche Forschungsgemeinschaft to HF (FL 156/41-1)	**Inclusion**: Chronic back pain lasting for more than 6 months and an age of 18–75 years. **Exclusion:** Any acute primary causes for back pain (e.g., injuries or inflammation), acute neurological complications, inability or medical prohibition to lift weights of up to 15 kg, and a history of epileptic seizures triggered by flickering lights.	N=17 Age, mean (SD): 46.1 (17.6) Female: 71% Clinic Three sessions at least 4 and a maximum of 117 days apart. Due to the pandemic situation they had to reschedule the participants when there was a ban on laboratory activity. The mean duration between sessions was 13.65 ± 16.08 days. 3D photos taken for avatar creation in AVA. The avatars were animated with prerecorded movements of a healthy model (motion capture with an infrared 12-camera system, OptiTrack, Corvallis, OR). Participants copied movements from virtual models based on previous kinematic studies.	N=16 Age, mean (SD): 51.9 (17.4) Female: 56% Clinic The subsequent three experimental sessions (sessions 1–3) were at least 4 and a maximum of 117 days apart. Due to the pandemic situation they had to reschedule the participants when there was a ban on laboratory activity. The mean duration between sessions was 13.65 ± 16.08 days. Control group watched a virtual 2D screen inside the virtual environment showing a videotaped movement model (VID).	**Primary: NR** **Pain-related functioning (sessions 1-3):** • NRS **Pain intensity (sessions 1-3)**: • NRS
Maddox, 2022[29-33] Some concerns in domain 4 only 18 Months United States AppliedVR	**Inclusion**: People aged 18-85, with self-reported diagnosis of chronic low back pain without radicular symptoms lasting 6 months or more, an average pain intensity of 4 or more out of 10 for the past month. **Exclusion:** People with gross cognitive impairment, current or prior diagnosis of epilepsy, seizure disorder, dementia, migraines, or other neurological diseases that may prevent the use of virtual reality or	N=94 Age, mean (SD): 51.5 (13.5) Female: 75.3% Home 56 sessions 2-16 minutes in length for 8 weeks EaseVRx (AppliedVR) incorporates evidence-based principles of CBT, mindfulness, and pain neuroscience	N=94 Age, mean (SD): 51.4 (12.9) Female: 78.7% Home Each VR experience is 2-16 minutes in length (average of 6 minutes). Nonimmersive, 2D content within a VR headset as the most rigorous VR placebo. The Sham VR headset	**Primary: DVPRS** **Non-eligible outcomes (8 wk):** • PROMIS physical function • PROMIS sleep disturbance

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
	adverse effects medical condition predisposing to nausea or dizziness, hypersensitivity to flashing light or motion, no stereoscopic vision or severe hearing impairment, injury to eyes, face, or neck that impedes comfortable use of virtual reality, cancer-related pain, moderate depressive symptoms as indicated by the Patient Health Questionnaire-2 (PHQ-2 [44,45]) depression screen score of 2 or more, previous use of EaseVRx for pain, current or recent completion of participation (past 2 months) in any interventional research study, currently pregnant or planning to become pregnant during the study period.	education. Participants complete modules that include pain education, relexation/interoception, mindful escapes, pain distraction games, and dynamic breathing.	displayed 2D nature footage (eg, wildlife in the savannah) with neutral music that was selected to be neither overly relaxing, aversive, nor distracting. The experience of Sham VR is similar to viewing nature scenes on a large-screen television and is not interactive. Twenty videos were rotated over the 56 sessions, with average duration of sessions closely matching those of EaseVRx.	
Yelvar, 2016[25] High 2 Weeks Turgut Ozal University Hospital Department of Physical Therapy and Rehabilitation, Turkey NR	**Inclusion**: Diagnosis of subacute and chronic LBP by a physician, no experience with surgical treatments for disc herniation, spina bifida, or spinal stenosis, no visual problems, no nerve root compression, no neurological problems, and patients who have fear of avoidance. **Exclusion:** None	N=23 Age, mean (SD): 46.3 (3.4) Female: 45.5% Clinic Five times a week for 2 weeks Embodiment using iPod with video glasses where participants passively viewed a virtual walking video clip and were asked to imagine they were walking. They also underwent physical therapy (15 minutes of hotpack therapy, 15 minutes of TENS, and 5 minutes of deep heat with ultrasound, and therapeutic exercises, including extension exercise, posterior pelvic tilt, cat–camel exercise, and stretching of the lumbar extensor muscle).	N=23 Age, mean (SD): 52.8 (11.5) Female: 81.8% Clinic Five times a week for 2 weeks Participants underwent physical therapy (15 minutes of hot pack therapy, 15 minutes of TENS, and 5 minutes of deep heat with ultrasound, and therapeutic exercises, including extension exercise, posterior pelvic tilt, cat–camel exercise, and stretching of the lumbar extensor muscle).	**Primary: NR** **Pain-related functioning (2 wk):** • ODI **Pain intensity (2 wk):** • VAS **Pain catastrophizing (2 wk):** • TSK **Physical performance (2 wk):** • Timed-up and go test (TUG) • 6-minute walk test **Quality of life (2 wk):** • Nottingham Health Profile

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
AR Intervention				
Afzal, 2022[38] Some concerns 4 Weeks Government Services Hospital, Lahore, Pakistan, Pakistan None	**Inclusion**: Adults aged 25-50 with a history of CLBP. **Exclusion:** "Patients with congenital deformity, history of trauma, fracture of the spine, or the lower extremity, any systematic disease, or neurological diseases, those on corticosteroid and pregnant females were excluded."	N=45 Age, mean (SD): 38.2 (11.8) Female: 69.0 % Clinic 3 sessions per week for a total of 12 sessions "kinetic exergames, like the body ball game and reflex ridge, with on-screen display for 5 minutes each, along with RPT... patients were subjected to trunk slide flexion, sitting to avoid obstacles, jumping and combined movement of arms for 5 minutes... After 30 seconds of rest, the body ball game, including moving arm, head pushing and kicking of ball, for 5 minutes was introduced."	N=45 Age, mean (SD): 37.5 (12.5) Female: 64.3% NR 3 sessions per week for a total of 12 sessions "RPT with 10 minutes of heat therapy by a moist hot pack, and hamstring stretching. Back strengthening exercises included 10 repetition of bridging, prone leg raises, trunk extension in prone with arms behind the back, trunk rotation exercises, knee to chest, and prone position with a diagonal elevation of the arm and the leg."	**Primary: VAS** **Pain-related functioning (4 wk)** • MODI
Fatoye, 2022[36] High 8 Weeks Obafemi Awolowo University; Ladoke Akintola University of	**Inclusion**: Patients with LBP of not less than 3 months, as determined by the standard McKenzie Institute Lumbar Spine Assessment Algorithm. Patients who demonstrated Directional Preference (DP) for extension. **Exclusion:** Patients with DP for flexion, positive history of red flags indicative of serious spinal	N=29 Age, mean (SD): 47.6 (11.5) NR NR Three times a week for 8 weeks Microsoft Kinect interactive video game to achieve therapeutic activities comparable	N=28 Age, mean (SD): 48.8 (10.2) NR NR Three times a week for 8 weeks Participants did the McKenzie extension protocol, where they stand	**Primary NR** **Pain-related functioning (8 wk)** • ODI **Non-eligible: Resource use, cost, cost-effectiveness**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Technology Teaching Hospital, Nigeria This research was partially funded by an African Doctoral Dissertation Research Fellowship (ADDRF) re-entry grant awarded by the African Population and Health Research Centre (APHRC) in partnership with the International Development Research Centre (IDRC).	pathology; any obvious spinal deformity or neurological disease; pregnancy; previous spinal surgery; and previous experience of MDT extension protocol, as well as, those with underlying systemic or visceral disease and specific condition such as dementia, cognitive dysfunction, visual impairment and previous history of epilepsy were excluded.	to the McKenzie "extension in standing" protocol. Participants were asked to head virtual balls on the screen as though they were coming towards them, moving only their trunk and head.	upright with feet slightly apart, place their hands on the small of their back, then stretch their trunk backwards as far as they can 10 times.	
Kim, 2014[48] High 4 Weeks A K hospital, Korea NR	**Inclusion**: Suffer from chronic lower back pain **Exclusion:** None listed	N=15 Age, mean (SD): 44.3 (NR) Female: 100% Clinic 12 sessions over the course of four weeks, with each session lasting 30 minutes. "A 30-minute virtual reality-based yoga program using Wii Fit activities such as deep breathing, the half-moon pose, warrior pose, tree pose, chest to knee pose, chair pose, and palm tree pose... There were seven exercise programs. Three minutes of exercise were performed followed by one minute of rest."	N=15 Age, mean (SD): 50.5 (NR) Female: 100% Clinic Each movement was comprised of two sets lasting 30 minutes. One set included 10 repetitions. "Trunk stabilizing exercise was performed with contraction exercise for the transverse abdominis and multifidus followed by curl ups in order to contract the rectus abdominis. The dead bug exercise, quadruped opposite arm and leg reach exercises, bridge, side bridge on knees, middle anterior plank position, and balancing on unstable surfaces were performed."	**Primary: RMDQ, VAS, ODI** **Pain Catastrophizing (4 wk):** • FABQ

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Kim, 2019[43] High 6 Months Korea University, Republic of Korea NR	**Inclusion**: People aged 20–64 years with nonspecific LBP lasting at least 3 months, with an average numeric rating scale (NRS) in the previous 7 days of ≥4 (scale 0–11) **Exclusion:** Presented with specific causes of LBP, had other sensory or motor dysfunctions resulting from neurological disorders, had any cardiovascular or psychological disease, had any other mental or physical limitation, had surgery or trauma within the past 6 months, or were pregnant or planning to become pregnant	N=24 Age, mean (SD): 26 (3.8) Female: 31.8% Clinic 16 46-minute sessions over 8 weeks Equine therapy using the SHR system, that simulates a horse gait. The workout consists of walking, slow trotting, and fast trotting at a real horse gait.	N=24 Age, mean (SD): 28.8 (9.1) Female: 57.7% Clinic 16 46-minute sessions over 8 weeks "The STB exercise with suspension (Redcord AS, Arendal, Norway) consisted of a supine pelvic lift, supine and prone bridging exercise, and side-lying hip abduction… Time required to perform each movement was about 10 seconds."	**Primary: NRS** **Pain-related functioning (8 wk, 6 mo):** • ODI • RMDQ **Pain Catastrophizing (8 wk, 6 mo):** • FABQ physical • FABQ work
Li 2021[39] High 2 Weeks First Affiliated Hospital of Sun Yat-sen University, China "This research project was supported by the National Natural Science Foundation of China (grant numbers	**Inclusion**: People aged between 18 and 40 years with persistent or periodic LBP for longer than 3 months, and no referred symptoms of radiating pain below the knee or paresthesia during the straight-leg raise test. **Exclusion:** People with a history of pelvic or spinal column surgery in the past two years, diagnosis of any specific lumbar pathological condition and/or severe or progressive scoliosis, body mass index (BMI) ≥30kg/m2, history of a treatment program within the past	N=11 Age, mean (SD): 21.91 (2.4) Female: 72.7% Home; Clinic 6 3-minute sessions per day, with a 2 minute break between sessions, 5 days a week for 2 weeks Participants played Fruit Ninja on the Microsoft Kinect, wherein participants waved their hands to crush fruit in the game. Participants were asked to limit	N=12 Age, mean (SD): 23.75 (4.1) Female: 83.3% Home; Clinic Approximately 1 30-minute session, 5 days a week for 2 weeks Participants did Motor Control Exercise (MCE) with ultrasound-guided abdominal drawing-in maneuver (ADIM). 3 sets of 10 repetitions holding for 10 sec, with 2 min breaks between sets. Four-point kneeling lifting each	**Primary NR** **Pain-related functioning (2 wk):** • ODI **Pain intensity (2 wk):** • VAS **Non-eligible: Muscle activation times, electromyography**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
82002375, 81772434, and 32071316); the Guangdong Province Medical Science Technology Research Grant (grant number A2019452) and the Guangdong Basic and Applied Basic Research Foundation (No. 2020A1515011356); the Guang zhou Science and Technology Program key projects (grant numbers 201704020122 and 201907010034); and the Non Profit Central Research Institute Fund of Chinese Academy of Medical Sciences (No. 2020-JKCS-005)."	three months, pregnant, history of severe dysfunction of vital organs (heart, lungs, and kidneys) and/or cognitive deficits, and history of visual or hearing problems.	bending their trunk or turning. They also received 20 minutes of magnetic therapy.	arm/leg for 5 sec, 3 reps each with 15 sec breaks. Raised contralateral arm and leg in bird dog position, held 5 sec, 3 reps with 15 sec breaks. They also received 20 minutes of magnetic therapy. N=11 Age, mean (SD): 25.4(3.7) Female: 63.6% Home; Clinic 20 minute sessions, 5 days a week, two weeks Participants received 20 minutes, medium heat level conventional magnetic therapy	
Mbada, 2019[50] High 8 Weeks Obafemi Awolowo University (OAU) Teaching Hospital, Ile Ife, Nigeria (OAUTHC); Department of Medical Rehabilitation, OAU; and Ladoke Akintola University of Technology Teaching Hospital,	**Inclusion**: Adults with long-term mechanical lower back pain and directional preference for extension. **Exclusion:** Patients who demonstrated directional preference for flexion, lateral, or no directional preference.	N=28 Age, mean (SD): 32.6 (11.5) Female: 45.5% NR Thrice weekly for 8-week[s] Microsoft Kinect interactive video game to achieve therapeutic activities comparable to the McKenzie "extension in standing" protocol. Participants were asked to head virtual balls on the screen as though they were coming towards them, moving only their trunk and head.	N=29 Age, mean (SD): 48.8 (10.2) Female: 79.2% NR Thrice weekly for 8-week[s] Participants did the McKenzie extension protocol, where they stand upright with feet slightly apart, place their hands on the small of their back, then stretch their trunk backwards as far as they can up to 10 times. Participants also received a 9-item	**Primary: ODI, RMDQ, VAS, TSK, FABQ work, FABQ physical, Modified Biering-Sørensen test of Static Muscular Endurance (bSME)** **QoL (8 wk):** • SF-12 mental • SF-12 physical

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Osogbo, Nigeria (LAUTECH), Nigeria This research was partially funded by an African Doctoral Dissertation Research Fellowship re-entry grant awarded by the African Population and Health Research Centre in partnership with the International Development Research Centre (IDRC).			back care education guide on activities of daily living.	
Monteiro-Junior, 2015[46] High 8 Weeks Fisioprime Clinical of Physiotherapy, Brazil NR	**Inclusion**: People with chronic lower back pain, not participating in systematic exercise program **Exclusion:** People without medical recommendation (Physical Activity Readiness Questionnaire (PAR-Q),who underwent spine surgery, with cancer, with acute musculoskeletal injuries in lower limbs, with neurological illnesses; and with vestibular noncontrolled disorders.	N=17 Age, mean (SD): NR (NR) Women: 100% Clinic Eight weeks with three sessions a week The intervention lasted eight weeks and sessions were performed three times a week. In core exercises the postures adopted by subjects lasted 15-30 seconds or in accordance with the capacity of each person. Each exercise (squat, lunge, chair abductor, chair adductor, leg curl, knee extension, unilateral plantar flexion) was performed three times (i.e., sequential method) with 10 repetitions. Participants also did 30 minutes of virtual physical training (eight exercises) using Nintendo Wii-motion and Wii Balance Board.	N=17 Age, mean (SD): NR (NR) Women: 100% Clinic Eight weeks with three sessions a week Control group performed strength training and core exercises. Weight load was moderate and was increased gradually based on pain reduction. Each exercise was performed in 3 sets of 10 repetitions.	**Primary: NRS, Sit-to-stand test** **Non-eligible: Balance, Total Mood**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Nambi 2020a[37] Some concerns 6 Months Prince Sattam bin Abdul Aziz University; University Hospital and King Khalid Hospital, Saudi Arabia Deanship of Scientific Research at Princess Nourah Bint Abdulrahman University through the Fast-track Research Funding Program	**Inclusion**: University male football players aged 18–25 years, with chronic (≥3 months) LBP, and 4 to 8 pain intensity in VAS. **Exclusion:** People with severe musculoskeletal, neural, somatic, and psychiatric conditions, waiting for spine surgery, having alcohol or drug abuse, and involving in other weight and balance training programs were excluded from the study. Participants with other soft tissue injuries, fracture at the lower limbs and pelvic bone, and deformities were also excluded from the study.	N=15 Age, mean (SD): 21.25 (1.2) Male: 100% Home; Clinic 30 minute sessions, 5 days a week for 4 weeks Participants used the ProKin system to play a shooting game. The game was controlled by participants moving their trunk back and forth and left and right. They also performed a home-based exercise protocol and underwent 20 minutes of hot pack therapy and five minutes ultrasound therapy.	N=15 Age, mean (SD): 20.23 (1.6) Male: 100% Home; Clinic 5 days a week for 4 weeks Participants used the Isokinetic Dynamometer to perform extension and flexion exercises consisting of 3 sets of 15 repetitions. They also performed a home-based exercise protocol and underwent 20 minutes of hot pack therapy and five minutes ultrasound therapy. N=15 Age, mean (SD): 20.8 (1.6) Male: 100% Home; clinic 5 days per week for 4 weeks Participants did conventional balance training for core muscles, including active isotonic and isometric exercises for abdominal muscles (ie, internal oblique, external oblique, transverse abdominis, and rectus abdominis) and deep abdominal muscles. They also underwent 20 minutes of hot pack	**Primary: NR** **Pain intensity (4 wk, 8 wk, 6 mo):** • VAS **Physical performance (4 wk, 8 wk, 6 mo):** • 40 m sprint performance • 4x5 sprint • Submaximal shuttle running • Countermovement jump • Squat jump **Non-eligible: Self-reported player wellness (Likert scale)**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
			therapy and 5 minutes ultrasound therapy.	
Nambi, 2020b[42] High 6 Months Prince Sattam Bin Abdulaziz University Hospital, Al-Kharj; King Khalid Hospital, Saudi Arabia self-funded	**Inclusion**: University male students in the age group of 18–25 years with cLBP (3 months) and 4 to 8 pain intensity on the VAS **Exclusion:** Participants with severe musculoskeletal-, neural-, somatic- and psychiatric conditions, who were waiting for spine surgery, with alcohol or drug abuse symptoms, are involved in other weight and balance training programs, have other soft tissue injuries, fracture at the lower limbs and pelvic bone, or deformities.	N=20 Age, mean (SD): 23.2 (1.5) Male: 100% NR 30 minute sessions 5 days a week for 4 weeks Participants used the ProKin system to play a shooting game. The game was controlled by participants moving their trunk back and forth and left and right. They also performed a home-based exercise protocol and underwent 20 minutes of hot pack therapy and five minutes ultrasound therapy. Exercises other than the ones in the protocol were at the decision of the supervising therapist and were documented in the log book.	N=20 Age, mean (SD): 22.8 (1.6) Male: 100% NR 5 days a week for 4 weeks Participants used the Isokinetic Dynamometer to perform extension and flexion exercises consisting of 3 sets of 15 repetitions. They also performed a home-based exercise protocol and underwent 20 minutes of hot pack therapy and five minutes ultrasound therapy. Exercises other than the ones in the protocol were at the decision of the supervising therapist and were documented in the log book.	**Primary: VAS, TSK** **Non-eligible: Stress hormone levels**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
			N=20 Age, mean (SD): 23.3 (1.5) Male: 100% NR 5 days a week for 4 weeks Participants did conventional balance training for core muscles, including active isotonic and isometric exercises for abdominal muscles (i.e., internal oblique, external oblique, transverse abdominis, and rectus abdominis) and deep abdominal muscles. They also underwent 20 minutes of hot pack therapy and 5 minutes ultrasound therapy.	
Nambi, 2021[41] High 6 Months King Khalid University Hospital and Department of Physical Therapy andHealth Rehabilitation, Prince Sattam Bin Abdulaziz University, Saudi Arabia NR	**Inclusion**: Male American university soccer players aged 18–25 years, with chronic (≥3 mo) LBP, and 4 to 8 pain intensity on a VAS **Exclusion:** Participants with severe musculoskeletal, neural, somatic, and psychiatric conditions, as well as those waiting for spine surgery, having alcohol or drug abuse issues, or involved in other weight and balance training programs, with other soft tissue injuries, fracture at the lower limbs and pelvic bone, and deformities.	N=18 Age, mean (SD): 22.3(1.6) Male: 100% Home 30 minutes in each session for 5 days a week for 4 weeks. Participants used the ProKin system to play a shooting game. The game was controlled by participants moving their trunk back and forth and left and right. They also performed a home-based exercise protocol and underwent 20 minutes of hot pack therapy and five minutes ultrasound therapy. Exercises	N=18 Age, mean (SD): 21.9 (1.8) Male: 100% Home 5 days a week for 4 weeks Participants used the Isokinetic Dynamometer to perform extension and flexion exercises consisting of 3 sets of 15 repetitions. They also performed a home-based exercise protocol and underwent 20 minutes of hot pack therapy and five minutes ultrasound therapy. Exercises other than the ones in the protocol were at	**Primary: VAS, TSK** **Non-eligible: Stress hormone levels**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
		other than the ones in the protocol were at the decision of the supervising therapist and were documented in the log book.	the decision of the supervising therapist and were documented in the log book.	
			N=18 Age, mean (SD): 21.4 (1.8) Male: 100% Home 15 times per set for 3 sets, 5 times per week for 4 weeks. Participants did conventional balance training for core muscles, including active isotonic and isometric exercises for abdominal muscles (i.e., internal oblique, external oblique, transverse abdominis, and rectus abdominis) and deep abdominal muscles. They also underwent 20 minutes of hot pack therapy and 5 minutes ultrasound therapy.	

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Nambi, 2023[35] Some concerns in domain 4 only 4 Weeks Department of Physiotherapy, Prince Sattam bin Abdulaziz University, Saudi Arabia,; University Hospital and King Khalid Hospital, Riyadh, Saudi Arabia, Saudi Arabia Prince Sattam bin Abdulaziz University project number (PSAU/2023/R/1444)	**Inclusion**: Male soccer players aged 18–25 years, chronic non-specific LBP for three or more months, and pain score ranging from 4 to 8 on a 10-centimetre VAS **Exclusion:** People with lumbar stenosis, lumbar radiculopathy, lumbar spondylolisthesis, spinal injuries, associated low back muscle and tendon injuries, fracture of the pelvic bone and lower extremity bones, spine dysfunctions, awaiting spine surgery, participants taking steroids, medications or analgesics, having serious pathologies of the thoracolumbar spine, participating in other resistance training and physical training programs	N=20 Age, mean (SD): 23.2 (1.6) Male: 100% Clinic Thirty minutes per session, five days a week, for 4 weeks Participants used the ProKin system to play a shooting game. The game was controlled by participants moving their trunk back and forth and left and right. They also performed a home-based exercise protocol and underwent 20 minutes of hot pack therapy and five minutes ultrasound therapy.	N=20 Age, mean (SD): 22.9 (1.7) Male: 100% Clinic Thirty minutes per session, five days a week, for 4 weeks Participants used the Isokinetic Dynamometer to perform extension and flexion exercises consisting of 3 sets of 15 repetitions. They also performed a home-based exercise protocol and underwent 20 minutes of hot pack therapy and 5 minutes ultrasound therapy. N=20 Age, mean (SD): 22.8 (1.8) Male: 100% Clinic Thirty minute per session, five days a week, for 4 weeks Participants did conventional balance training for core muscles, including active isotonic and isometric exercises for abdominal muscles (i.e., internal oblique, external oblique, transverse abdominis, and rectus abdominis) and deep abdominal muscles. They also underwent 20 minutes of hot pack	**Primary: VAS** **Non-eligible: Radiological measures, inflammatory biomarkers**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
			therapy and 5 minutes ultrasound therapy.	
Oh, 2014[49] High 8 Weeks Hanseo University, Korea NR	**Inclusion**: Complaining of back pain in everyday life for over 3 months **Exclusion:** Past or present neurological, hypertension, cardiopulmonary diseases, and operation for lower back pain	N=10 Age, mean (SD): 20.6 (0.7) Male: 100% Clinic 10 min (short period) a day for 5 days a week for 8 weeks Equine therapy using a horse simulator machine to perform a 5 minute warm-up, walking for 5 minutes, then 4 maximal warm-up and 4 maximal test repetitions.	N=9 Age, mean (SD): 20.3(0.5) Male: 100% Clinic 20 min (middle period) a day for 5 days a week for 8 weeks Equine therapy using a horse simulator machine to perform a 5 minute warm-up, walking for 5 minutes, then 4 maximal warm-up and 4 maximal test repetitions. N=10 Age, mean (SD): 20.4 (0.3) Male: 100% Clinic 8 weeks Equine therapy using a horse simulator machine to perform a 5 minute warm-up, walking for 5 minutes, then 4 maximal warm-up and 4 maximal test repetitions.	**Primary: VAS**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
			N=9 Age, mean (SD) 20.7 (0.4) Male: 100% NA 8 weeks Usual care	
Sato, 2021[40] High 8 Weeks Chiba University Hospital, Japan No funding for research	**Inclusion**: People with low back pain persisting for more than 3 months and were referred to the hospital without sufficient improvement after receiving conservative treatment at another orthopedic clinic **Exclusion:** People with nerve stenosis whose symptoms could be explained on magnetic resonance imaging (MRI), severe intermittent claudication (100 meters or less), cases where lower limb manual muscle tests were graded 4/5 or less, or patients who were unable to ambulate independently, a history of spinal surgery within 1 year, restricted movement due to heart disease or other diseases, receiving exercise therapy at a health care facility during the study period, and significant cognitive impairment	N=20 Age, mean (SD): 49.3 (12.59) Female: 55% NR One 40 minute session a week for 8 weeks Participants played the Nintendo Ring Fit Adventure game. In Adventure Mode, the player controls the character by jogging or squatting. In a battle scene, in addition to an aerobics menu, intensive resistance training and yoga exercises that exert stress on the muscles of the whole body are aimed at defeating the enemy and clearing the stage. They continued taking already prescribed medication.	N=20 Age, mean (SD): 55.6 (11.0) Female: 40% Clinic Patients came in every 2 weeks to be interviewed for pain. Medication doses, frequency and duration were not reported. New oral treatments were given to each patient in the following order: (1) Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), (2) tramadol, and (3) duloxetine. Each drug was started at the standard dose; if pain relief was not adequate, then the dose was gradually increased to its highest recommended level. If pain relief was still inadequate, the next drug was added.	**Primary: VAS** **Pain catastrophizing (8 wk)** • PCS • TSK **Non-eligible: pain self-efficacy questionnaire (PSEQ)**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Thomas, 2016[45] Some concerns in domain 4 only 12 Days Ohio University, US NR	**Inclusion**: LBP category 1-3 (Classification System of the Quebec Task Force on Spinal Disorders) **Exclusion:** Age <18 or >50; LBP duration < 3 months and has not sought treatment; Tampa Scale for Kinesiophobia score < 35; health conditions that preclude safe participation; personal history of spine surgery or hip arthroplasty; currently taking narcotic pain medication; currently receiving treatments for back pain; personal history of exclusionary neurological, cardiorespiratory, or musculoskeletal disorders; active cancer or reports recent, unexplained weight loss; is blind; reports being pregnant; current or pending litigation related to back pain; clinically significant range for substance abuse (DAST>6), alcohol abuse (AUTID-C>7 for males and > 6 for females) or depression (CES-D >16)	N=27 Age, mean (SD): 23.9 (6.8) Female: 46.2% Clinic 3 sessions, separated by no more than 48 hours The virtual dodgeball intervention was displayed on a 60 inch high definition 3D-TV. The participant played dodgeball against four virtual opponents in a basketball arena. The participant had to attempt to block or duck balls launched by the opponents. The intervention consisted of 3 sessions, separated by no more than 48 hours.	N=26 Age, mean (SD): 26.7 (8.5) Female: 50.0% NA NA Usual care	**Primary: VAS** **Pain-related functioning (4 days):** • RMDQ **Adverse events (4 days)** **Pain catastrophizing (4 days):** • TSK **Non-eligible: Lumbar spine flexion, Game experience survey, Center for Epidemiological Studies - Depression**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Yoo, 2014[47] Some concerns 8 Weeks Hanseo University Hospital, Korea NR	**Inclusion**: Complaining of back pain in everyday life for more than 3 months **Exclusion:** Past or present neurological, hypertension or cardiopulmonary diseases, chronic disease and spine surgery.	N=24 Age, mean (SD): 20.4 (1.3) Male: 100% Clinic 3 days a week for 8 weeks Participants underwent equine therapy using a horse simulator machine. They first completed a 10-minute warm-up, then did the completed the work out phase (including walking, sitting trotting, rising trotting), then completed a 10 minute cool-down.	N=23 Age, mean (SD): 20.7 (1.45) Male: 100% NA None Usual care	**Primary: VAS** **Non-eligible: Night pain, exercise, drug relief, stiffness, walking freedom, walking discomfort, standing still, twisting, hard chair, soft chair, lying down, handicap, work interference, work modification, flexor PT, flexor PTBW, extensor PT, Extensor PTBW, PT ratio, flexor TW, flexor TWBW, extensor TWBW, TW ratio**
Zadro, 2019[44] Some concerns 8 Weeks The University of Sydney (participants from the community)Outpatient Physiotherapy Department of Westmead Hospital (participants on the waiting list), Australia NR	**Inclusion**: Older than 55, nonspecific mechanical LBP for at least 3 months, usual pain intensity of ≥ 3 out of 10 on the numeric rating scale, sufficient English language ability to understand exercise instructions, ability to mobilize independently without the use of walking aids, access to a high-definition multimedia-interface–compatible television at home. **Exclusion:** Diagnosis of serious pathology in the spine (such as fracture, metastatic disease, spinal stenosis, or caudaequina syndrome), evidence of nerve root	N=30 Age, mean (SD): 68.8 (5.5) Women: 30% Home Three 60 minute sessions a week for 8 weeks Wii U console with Wii Fit U software. PT visited home, set up equipment, guided first 1-2 hour session. Preselected flexibility, bodyweight, aerobic exercises in booklet to standardize. Fortnightly calls to encourage progression, monitor adverse events. Used symptoms in 24 hrs	N=30 Age, mean (SD): 67.8 (6) Women: 21.7% Home NA Usual care	**Primary: PSEQ, FEQ-I** **Pain-related functioning (8 wk):** • PSFS • RMDQ **Pain intensity (8 wk):** • NRS **Pain catastrophizing (8 wk):** • TSK

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
	compromise, any medical condition or disability that will prevent participation in the exercise program, including:, cardiovascular risk factors assessed with the PAR-Q, a screening tool recommended for all adults willing to initiate an exercise program, cognitive limitations, as indicated by a score of < 25/30 on the Mini-Mental State Examination, a reliable and valid test of cognitive function, high risk of falls, as indicated by a score of > 15 on the Falls Risk Assessment Tool, a reliable measure of the risk of falls in older adults, physical therapist treatment for LBP in the preceding 6 months.	after to guide increasing/decreasing duration and intensity.		

Abbreviations: BPI=Brief Pain Inventory; DVPRS-II=Defense and Veterans Pain Rating Scale; FABQ=Fear Avoidance Beliefs Questionnaire; MODI=Modified Oswestry Disability Index; NR=not reported; ODI=Oswestry Disability Index; PCS=Pain Catastrophizing Scale; PGIC=Patient Global Impression of Change; PSFS=Patient Specific Functional Scale; QoL=quality of life; RMDQ=Roland-Morris Disability Questionnaire; SF-12=Short Form Health Survey; VAS=Visual Analog Scale.

Appendix Table E2. Detailed Results for Chronic Low Back Pain Studies

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
Pain-Related Functioning or Interference				
Afzal, 2022[38] AR Some concerns	MODI	69.2 (9.1) 4 wk: 16.0 (6.8), -53.1*	65.1 (8.9) 4 wk: 40.6 (8.6), -24.5*	Diff Δ*: 4 wk: -28.6
Eccleston, 2022[27] VR Some concerns	ODI	36.0 (7.6) 8 wk: 28.8 (15.6), -7.2*	VR control 37.2 (9.4) 8 wk: 38.5 (16.2), 1.3*	Diff Δ*: 8 wk: -8.5
			Usual care 36.2 (7.6) 8 wk: 32.8 (8.6), -3.4*	Diff Δ*: 8 wk: -3.8
	PROMIS pain interference	64.5 (3.7) 8 wk: 59.0 (6.6), -5.5*	VR control 63.1 (3.4) 8 wk: 62.6 (5.3), -0.5*	Diff Δ*: 8 wk: -5.0
			Usual care 63.1 (2.5) 8 wk: 60.9 (3.8), -2.2*	Diff Δ*: 8 wk: -3.3
Fatoye, 2022[36] AR High	ODI	14.2 (9.4) 8 wk: 3.5 (3.5), -10.7*	21.1 (10.7) 8 wk: 6.8 (5.1), -14.4*	Diff Δ*: 8 wk: 3.7
Groenveld, 2023[28] VR Some concerns	ODI	40.1 (19.1) 4 wk: 32.4 (15.1), -7.7* 4 mo: 37.3 (14.5), -2.8*	42.8 (18.8) 4 wk: 38.8 (17.7), -4.0* 4 mo: 40.9 (17.6), -1.9*	Diff Δ*: 4 wk: -3.7 4 mo: -0.9
	BPI-Interference	5.9 (1.7) 4 wk: 4.1 (2.4), -1.8* 4 mo: 4.6 (2.1), -1.3*	6.3 (2.0) 4 wk: 4.8 (2.5), -1.5* 4 mo: 5.2 (2.0), -1.1*	Diff Δ*: 4 wk: -0.3 4 mo: -0.2
Kammler-Sücker, 2023[26] VR Some concerns	NRS	2.7 (2.0) Session 2 (~14 days): 2.5 (2.2), -0.2* Session 3 (~27 days): 2.2 (2.2), -0.4*	1.7 (1.8) Session 2 (~14 days): 2.3 (2.4), 0.5* Session 3 (~27 days): 1.7 (2.1), 0.0*	Diff Δ*: Session 2 (~14 days): -0.7 Session 3 (~27 days): -0.4
Kim, 2014[48] AR High	ODI	34.9 (6.2) 4 wk: 13.8 (7.7), -21.1*	36.2 (5.0) 4 wk: 24.6 (10.9), -11.6*	Diff Δ*: 4 wk: -9.5
	RMDQ	18.6 (2.8) 4 wk: 7.5 (4.8), -11.2*	19.1 (2.9) 4 wk: 12.6 (6.5), -6.5*	Diff Δ*: 4 wk: -4.7
Kim, 2019[43] AR High	ODI	20.2 (7.7) 4 wk: 14.7 (8.1), -5.52* 8 wk: 11.6 (9.0), -8.7* 6 mo: 8.3 (6.3), -12.0*	21.8 (7.1) 4 wk: 19.5 (9.3), -2.3* 8 wk: 14.8 (9.4), -7.0* 6 mo: 9.2 (3.3), -12.5*	Diff Δ*: 4 wk: -3.21 8 wk: -1.7 6 mo: 0.6
	RMDQ	7.0 (4.4) 4 wk: 3.3 (3.8), -5.2* 8 wk: 2.9 (4.5), -4.1* 6 mo: 1.9 (1.2), -5.2*	5.1 (2.7) 4 wk: 4.8 (2.5), -3.3* 8 wk: 2.5 (2.3), -2.7* 6 mo: 1.8 (1.1), -3.3*	Diff Δ*: 4 wk: -3.4 8 wk: -1.4 6 mo: -1.8

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
Li 2021[39] AR High	ODI	15.7 (6.4) 2 wk: 12.8 (6.3), -2.9*	MCE 18.4 (9.4) 2 wk: 14.3 (21.3), -4.1*	Diff Δ*: 2 wk: 1.3
			CG 12.7 (4.8) 2 wk: 9.6 (7.2), -3.1*	Diff Δ*: 2 wk: 0.2
Maddox, 2022[32,33] VR Some concerns in Domain 4 only	DVPRS-II overall interference	4.8 (NR) 8 wk: 2.3 (NR), -2.5* 3 mo: 2.7 (NR), -2.1* 4 mo: 2.9 (NR), -1.9* 5 mo: 3.1 (NR), -1.7* 8 mo: 3.0 (2.6), -1.8* 20 mo: 3.3 (2.7), -1.5* 26 mo: 2.8 (2.1), -2.0*	5.1 (NR) 8 wk: 3.3 (NR), -1.8* 3 mo: 3.8 (NR), -1.3* 4 mo: 4.1 (NR), -1.0* 5 mo: 4.1 (NR), -1.0* 8 mo: 4.2 (2.2), -0.9* 20 mo: 4.3 (2.5), -0.8* 26 mo: 3.8 (2.3), -1.3*	Diff Δ*: 8 wk: -0.7 3 mo: -0.8 4 mo: -0.9 5 mo: -0.7 8 mo: -0.9 20 mo: -0.7 26 mo: -0.7
Mbada, 2019[50] AR High	ODI	18.7 (NR) 8 wk: 21.1 (NR), 2.4*	27.8 (NR) 8 wk: 25.7 (NR), -2.1*	Diff Δ*: 8 wk: 4.5
	RMDQ	6.8 (NR) 8 wk: 5.7 (4.7), -1.1*	11.3 (NR) 8 wk: 8.9 (4.1), -2.4*	Diff Δ*: 8 wk: 1.3
Yilmaz Yelvar, 2016[25] VR High	ODI	20.7 (7.2) 2 wk: 16.9 (5.5), -3.8*	26.1 (11.0) 2 wk: 21.1 (9.9), -5.1*	Diff Δ*: 2 wk: 1.2
Zadro, 2019[44] AR Some concerns	RMDQ	6.3 (4.8) 8 wk: 4.9 (4.5), -1.4*	7.4 (5.2) 8 wk: 6.4 (4.4), -1.0*	Diff Δ*: 8 wk: -0.4
	PSFS	5.3 (1.4) 8 wk: 6.5 (2.1), 1.2*	4.3 (2.1) 8 wk: 4.8 (2.5), 0.5*	Diff Δ*: 8 wk: 0.7
Pain Intensity or Severity				
Afzal, 2022[38] AR Some concerns	VAS	6.5 (1.2) 4 wk: 1.0 (0.6), -5.5*	6.6 (1.0) 4 wk: 3.3 (0.8), -3.3*	Diff Δ*: 4 wk: -2.2
Eccleston, 2022[27] VR Some concerns	NRS	6.0 (1.4) 8 wk: 4.1 (1.7), -1.9*	VR control 6.1 (1.4) 8 wk: 4.8 (2.3), -1.3*	Diff Δ*: 8 wk: -0.6
			Usual care 5.7 (1.6) 8 wk: 4.4 (2.4), -1.3*	Diff Δ*: 8 wk: -0.6
	PROMIS pain intensity	66.5 (4.1) 8 wk: 60.0 (7.5), -6.5*	VR control 65.1 (5.4) 8 wk: 61.9 (8.3), -3.2*	Diff Δ*: 8 wk: -3.3
			Usual care 63.0 (5.5) 8 wk: 61.0 (5.9), -2.0*	Diff Δ*: 8 wk: -4.5
Groenveld, 2023[28] VR	VAS – Daily Worst	6.1 (NR) 30 days: 5.3 (NR), -0.8*	7.0 (NR) 30 days: 6.8 (NR), -0.2*	Diff Δ*: 30 days: -0.6
	VAS – Daily Least	3.7 (NR)	4.1 (NR)	Diff Δ*:

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline mean (SD) Follow-Up Mean (SD), M ean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
Some concerns		30 days: 4.1 (NR), 0.4*	30 days: 4.9 (NR), 0.8*	30 days: -0.4
Harvie, 2022[24] VR Some concerns in Domain 4 only	NRS, average pain over past week	6.4 (1.4)† 1 wk: 6.1 (1.3)†, -0.3*	6.6 (2.7)† 1 wk: 5.8 (1.9)†, -0.8*	Diff Δ*: 1 wk: 0.5
Kammler-Sücker, 2023[26] VR Some concerns	NRS	2.6 (1.1) 14 days: 2.4 (1.8), -0.2* 27 days: 2.5 (2.1), -0.1*	1.9 (1.6) 14 days: 2.1 (2.3), 0.2* 27 days: 1.8 (1.7), -0.1*	Diff Δ*: 14 days: -0.4 27 days: 0.02
Kim, 2014[48] AR High	VAS	7.0 (0.9) 4 wk: 2.3 (1.1), -4.7*	7.0 (0.8) 4 wk: 4.6 (1.9), -2.3*	Diff Δ*: 4 wk: -2.4
Kim, 2019[43] AR High	NRS	4.7 (1.0) 4 wk: 2.25 (1.06),-2.45* 8 wk: 1.3 (0.9), -3.4* 6 mo: 1.4 (1.3), -3.3*	4.7 (0.8) 4 wk: 2.09 (1.46), =2.64* 8 wk: 1.6 (1.6), -3.1* 6 mo: 1.2 (1.0), -3.5*	Diff Δ*: 4 wk: 0.19 8 wk: -0.3 6 mo: 0.2
Li 2021[39] AR High	VAS	4.4 (1.4) 2 wk: 3.2 (1.1), -1.2*	MCE 4.6 (1.8) 2 wk: 2.2 (1.9), -2.4*	Diff Δ*: 2 wk: 1.2
			CG 3.6 (1.4) 2 wk: 2.2 (1.2), -1.5*	Diff Δ*: 2 wk: 0.3
Maddox, 2022[32,33] VR Some concerns in Domain 4 only	DVPRS-pain intensity	5.1 (1.2) 8 wk: 3.0 (0.8), -2.2* 3 mo: 3.6 (NR), -1.5* 4 mo: 3.8 (NR), -1.3* 5 mo: 3.7 (NR), -1.4* 8 mo: 3.6 (2.2), -1.5* 20 mo: 4.2 (2.2), -0.9* 26 mo: 3.9 (2.1), -1.2*	5.2 (1.1) 8 wk: 4.0 (0.8), -1.2* 3 mo: 4.4 (NR), -0.8* 4 mo: 4.5 (NR), -0.7* 5 mo: 4.5 (NR), -0.7* 8 mo: 4.6 (1.8), -0.6* 20 mo: 5.3 (1.9), 0.1* 26 mo: 4.5 (2.0), -0.7*	Diff Δ*: 8 wk: -1.0 3 mo: -0.7 4 mo: -0.6 5 mo: -0.7 8 mo: -0.9 20 mo: -1.0 26 mo: -0.5
Mbada, 2019[50] AR High	VAS	4.1 (1.8) 8 wk: 3.5 (1.7), -0.6*	5.0 (1.9) 8 wk: 3.5 (2.3), -1.5*	Diff Δ*: 8 wk: 0.9
Monteiro-Junior, 2015[46] AR High	NRS	6.5 (1.1) 8 wk: 1.7 (1.9), -4.8*	6.6 (1.2) 8 wk: 1.4 (2.9), -5.2*	Diff Δ*: 8 wk: 0.4
Nambi 2020[37] AR Some concerns	VAS	7.1 (0.6) 4 wk: 3.9 (0.5), -3.2* 8 wk: 1.2 (0.4), -5.9* 6 mo: 0.8 (0.4), -6.3*	IKT-G 7.3 (0.5) 4 wk: 4.8 (0.4), -2.5* 8 wk: 2.7 (0.3), -4.6* 6 mo: 1.9 (0.3), -5.4*	Diff Δ*: 4 wk: -0.7 8 wk: -1.3 6 mo: -0.9
			Control-G 7.3 (0.6) 4 wk: 6.2 (0.4), -1.1*	Diff Δ*: 4 wk: -2.1 8 wk: -4.0

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline mean (SD) Follow-Up Mean (SD), M ean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
			8 wk: 5.4 (0.4), -1.9* 6 mo: 4.2 (0.5), -3.1*	6 mo: -3.2
Nambi, 2020b [42] AR High	VAS	7.5 (0.4) 4 wk: 2.4 (0.2), -5.1* 6 mo: 0.6 (0.1), -6.9*	7.3 (0.3) 4 wk: 2.7 (0.3), -4.6* 6 mo: 0.9 (0.2), -6.4*	Diff Δ*: 4 wk: -0.5 6 mo: -0.5
			7.4 (0.4) 4 wk: 4.5 (0.4), -2.9* 6 mo: 3.5 (0.3), -3.9*	Diff Δ*: 4 wk: -2.2 6 mo: -3.0
Nambi, 2021[41] AR High	VAS	7.8 (0.6) 4 wk: 1.8 (0.3), -6.0* 6 mo: 0.5 (0.2), -7.3*	CPR 7.5 (0.5) 4 wk: 3.6 (0.4), -3.9* 6 mo: 2.8 (0.3), -4.7*	Diff Δ*: 4 wk: -2.1 6 mo: -2.6
			Control 7.6 (0.4) 4 wk: 3.8 (0.5), -3.8* 6 mo: 3.2 (0.2), -4.4*\	Diff Δ*: 4 wk: -2.2 6 mo: -2.9
Nambi, 2023[35] AR Some concerns in Domain 4 only	VAS	7.2 (0.4) 4 wk: 1.8 (0.3), -5.4*	Isokinetic 7.3 (0.3) 4 wk: 2.5 (0.5), -4.8*	Diff Δ*: 4 wk: -0.6
			Conventional exercise 7.2 (0.3) 4 wk: 4.8 (0.4), -2.4*	Diff Δ*: 4 wk: -3.0
Oh, 2014[49] AR High	VAS	Horse simulator 30 minutes 5.6 (0.7) 8 wk: 3.4 (1.0), -2.1	Control 3.1 (0.6) 8 wk: 3.8 (0.9), 0.7*	Diff Δ*: 8 wk: -2.8
		Horse simulator 20 minutes 4.9 (0.5) 8 wk: 1.1 (0.1), -3.8*		Diff Δ*: 8 wk: -4.5
		Horse simulator 10 minutes 3.8 (0.5) 8 wk: 1.4 (0.4), -2.3*		Diff Δ*: 8 wk: -3.0
Sato, 2021[40] AR High	VAS	7.4 (2.0) 8 wk: 4.8 (3.0), -2.6*	7.0 (0.9) 8 wk: 6.6 (1.1), -0.4*	Diff Δ*: 8 wk: -2.2
Yilmaz Yelvar, 2016[25] VR High	VAS	6.0 (1.1) 2 wk: 2.5 (1.8), -3.5*	5.6 (2.4) 2 wk: 4.9 (3.4), -0.7*	Diff Δ*: 2 wk: -2.8
Yoo, 2014[47] AR Some concerns	VAS	4.4 (2.1) 8 wk: 2.2 (2.2), -2.1*	1.5 (0.1) 8 wk: 1.0 (0.0), -0.5*	Diff Δ*: 8 wk: -1.6
Zadro, 2019[44] AR Some concerns	NRS	5.2 (1.6) 8 wk: 3.8 (2.4), -1.4*	4.8 (1.7) 8 wk: 4.4 (2.3), -0.4*	Diff Δ*: 8 wk: -1.0

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline mean (SD) Follow-Up Mean (SD), M ean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
Adverse Events				
Eccleston, 2022[27] VR Some concerns	NR	DTxP (n=12) All: 12 (100%) Mild: 4 (33%) Moderate: 10 (83%) Severe: 6 (50%) Treatment-related: 3 (25%) Serious: 0	VR control (n=17) All: 14 (83%) Mild: 6 (35%) Moderate: 11 (65%) Severe: 5 (29%) Treatment-related: 6 (35%) Serious: 0	Diff Δ*: All: 18% Severe: 21%
			Usual care (n=11) All: 7 (64%) Mild: 2 (18%) Moderate: 6 (55%) Severe: 4 (36%) Treatment-related: 2 (18%) Serious: 0	Diff Δ*: All: 36% Severe: 14%
Groenveld, 2023[28] VR Some concerns	NR	3 (20%) reported mild and temporary symptoms of dizziness	No AEs assessed	Diff Δ: NC
Thomas, 2016[45] AR Some concerns in Domain 4 only	NR	No AEs reported	No AEs reported	Diff Δ*: 4 days: 0
Pain Catastrophizing & Kinesiophobia				
Eccleston, 2022[27] VR Some concerns	TSK	41.9 (4.4) 8 wk: 33.7 (7.4), -8.2*	VR control 43.2 (6.0) 8 wk: 43.1 (8.5), -0.1*	Diff Δ*: 8 wk: -8.1
			Usual care 42.5 (5.4) 8 wk: 39.8 (7.1), -2.7*	Diff Δ*: 8 wk: -5.5
Groenveld, 2023[28] VR Some concerns	PCS	21.7 (12.2) 4 wk: 23.4 (13.8), 1.7* 4 mo: 23.9 (12.5), 2.2*	24.7 (7.8) 4 wk: 25.7 (9.5), 1.0* 4 mo: 27.1 (9.7), 2.4*	Diff Δ*: 4 wk: 0.7 4 mo: -0.2
Kim, 2014[48] AR High	FABQ	65.5 (9.6) 4 wk: 17.6 (10.7), -47.9*	70.8 (4.6) 4 wk: 41.6 (18.0), -29.2*	Diff Δ*: 4 wk: -18.7
Kim, 2019[43] AR High	FABQ-physical	15.4 (4.1) 4 wk: 9.0 (3.64), -6.4* 8 wk: 8.8 (5.9), -6.6* 6 mo: 4.1 (4.1), -11.2*	11.9 (5.6) 4 wk: 16.3 (9.55), 4.4* 8 wk: 11.1 (9.1), -0.8* 6 mo: 9.7 (7.1), -2.3*	Diff Δ*: 4 wk: -10.8 8 wk: -5.7 6 mo: -8.9

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline mean (SD) Follow-Up Mean (SD), M ean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
	FABQ-work	17.1 (5.3) 4 wk: 15.2 (7.1), -1.9* 8 wk: 11.4 (7.5), -5.7* 6 mo: 13.9 (7.1), -3.3*	20.5 (7.9) 4 wk: 22.4 (5.62), 1.9* 8 wk: 14.7 (6.5), -5.8* 6 mo: 16.5 (9.0), -4.0*	Diff Δ*: 4 wk: -3.78 8 wk: 0.1 6 mo: 0.7
Mbada, 2019[50] AR High	FABQ-work	21.2 (NR) 8 wk: 24.5 (NR), 3.3*	25.7 (NR) 8 wk: 22.6 (NR), -3.1*	Diff Δ*: 8 wk: 6.4
	TSK	16.5 (NR) 8 wk: 28.8 (NR), 12.3*	29.9 (NR) 8 wk: 18.7 (NR), -11.2*	Diff Δ*: 8 wk: 23.5
Nambi, 2020b[42] AR High	TSK	57.5 (4.8) 4 wk: 26.4 (3.5), -31.1* 6 mo: 20.1 (2.5), -37.4*	IKT 58.1 (4.5) 4 wk: 27.5 (3.8), -30.6* 6 mo: 21.2 (2.4), -36.9*	Diff Δ*: 4 wk: -0.5 6 mo: -0.5
			Control 57.9 (4.3) 4 wk: 46.2 (4.1), -11.7* 6 mo: 38.6 (3.9), -19.3*	Diff Δ*: 4 wk: -19.4 6 mo: -18.1
Nambi, 2021[41] AR High	TSK	56.5 (3.2) 4 wk: 28.3 (3.3), -28.1* 6 mo: 20.1 (2.8), -36.4*	CPR 58.0 (3.8) 4 wk: 38.5 (3.5), -19.5* 6 mo: 29.7 (2.2), -28.4*	Diff Δ*: 4 wk: -8.7 6 mo: -8.0
			Control 57.7 (4.1) 4 wk: 45.4 (3.3), -12.3* 6 mo: 39.1 (2.9), -18.6*	Diff Δ*: 4 wk: -15.9 6 mo: -17.8
Sato, 2021[40] AR High	PCS	43.5 (8.0) 8 wk: 39.9 (7.8), -3.6*	40.8 (0.0) 8 wk: 42.1 (6.9), 1.4*	Diff Δ*: 8 wk: -4.9
	TSK	42.5 (5.9) 8 wk: 39.7 (4.6), -2.8*	38.9 (5.4) 8 wk: 36.2 (3.2), -2.7*	Diff Δ*: 8 wk: -0.1
Yilmaz Yelvar, 2016[25] VR High	Tampa Scale of Kinesiophobia (TSK)	43.7 (4.3) 2 wk: 29.6 (4.0), -14.2*	40.4 (5.6) 2 wk: NR (5.4), NC	Diff Δ: NC
Zadro, 2019[44] AR Some concerns	TSK	33.6 (6.1) 8 wk: 32.3 (7.1), -1.3*	34.7 (5.8) 8 wk: 35.9 (5.8), 1.2*	Diff Δ*: 8 wk: -2.5
Pain Global Change				
Eccleston, 2022[27] VR Some concerns	PGIC (assessed only at follow-up)	8 wk: 2.7 (1.4) 5 mo: 3.0 (1.5)	VR control 8 wk: 3.8 (1.5) 5 mo: 3.0 (1.5)	Diff Δ: 8 wk: -1.1 5 mo: 0.0
			Usual care 8 wk: 3.9 (0.7)	Diff Δ: 8 wk: -1.2
Harvie, 2022[24] VR	PGIC (assessed only at follow-up)	At least minimally improved: 37% No change: 55%	At least minimally improved: 11% No change: 89%	Diff Δ*: 1 wk at least minimally improved): 26%

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline mean (SD) Follow-Up Mean (SD), M ean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
Some concerns in Domain 4 only		Minimally worse: 5%	Minimally worse: 0%	1 wk minimally worse: 5%
Quality of Life				
Eccleston, 2022[27] VR Some concerns	European Quality of Life 5 (EuroQoL-5D-5L) Health State (	47.7 (16.8) 8 wk: 66.1 (22.2), 18.4*	VR control 63.8 (15.1) 8 wk: 58.1 (26.8), -5.7*	Diff Δ*: 8 wk: 24.1
			Usual care 55.7 (19.6) 8 wk: 62.0 (23.9), 6.3*	Diff Δ*: 8 wk: 12.1
Groenveld, 2023[28] VR Some concerns	SF-12-physical	34.9 (7.5) 4 wk: 39.1 (6.3), 4.2* 4 mo: 38.5 (8.7), 3.6*	32.9 (7.7) 4 wk: 34.8 (7.1), 1.9* 4 mo: 36.8 (7.5), 3.9*	Diff Δ*: 4 wk: 2.3 4 mo: -0.3
	SF-12-mental	45.6 (7.2) 4 wk: 48.9 (7.5), 3.3* 4 mo: 46.4 (10.1), 0.8*	43.0 (8.9) 4 wk: 46.0 (10.9), 3.0* 4 mo: 46.2 (11.8), 3.2*	Diff Δ*: 4 wk: 0.3 4 mo: -2.4
Mbada, 2019[50] AR High	SF-12-mental	71.8 (6.0) 8 wk: 19.4 (11.6), -52.4*	70.0 (9.1) 8 wk: 26.6 (13.3), -43.4*	Diff Δ*: 8 wk: -9.0
	SF-12-physical	68.8 (6.1) 8 wk: 11.6 (8.7), -57.2*	64.3 (10.8) 8 wk: 16.3 (13.0), -48.0*	Diff Δ*: 8 wk: -9.2
Yilmaz Yelvar, 2016[25] VR High	Nottingham Health Profile	226.1 (75.9) 2 wk: 196.1 (109.2), -30.0*	158.4 (125.8) 2 wk: 140.9 (117.9), -17.5*	Diff Δ*: 2 wk: -12.5
Physical Performance				
Mbada, 2019[50] AR High	Biering-Sorensen test of Statis Muscular Endurance (BSME)	35.3 (22.5) 8 wk: -21.9 (14.6), -57.2*	20.6 (13.3) 8 wk: -15.1 (7.9), -35.7*	Diff Δ*: 8 wk: -21.5
Monteiro-Junior, 2015[46] AR High	Floor to Sit to Stand-Sit (max 5 pts)	2.3 (1.5) 8 wk: 3.3 (0.9), 1.0*	2.8 (1.0) 8 wk: 3.2 (0.9), 0.4*	Diff Δ*: 8 wk: 0.6
	Floor to Sit to Stand-Stand Up (max 5 pts)	1.7 (1.6) 8 wk: 2.5 (1.0), 0.8*	2.5 (1.2) 8 wk: 2.8 (1.3), 0.3*	Diff Δ*: 8 wk: 0.5
Yilmaz Yelvar, 2016[25] VR High	Timed-up and go test (TUG)	7.7 (1.0) 2 wk: 5.3 (0.9), -2.5*	8.0 (1.7) 2 wk: 7.6 (1.3), -0.4*	Diff Δ*: 2 wk: -3.9
	6-minute walk test	414.3 (120.7) 2 wk: 504.9 (130.8), 90.6*	401.1 (64.0) 2 wk: 400.7 (59.9), -0.4*	Diff Δ*: 2 wk: 91.0
Opioid Use				
Groenveld, 2023[28] VR Some concerns	Used opioids at least once weekly	N (%): 1 wk: 9 (47) 4 wk: 5 (28), -19*	N (%): 1 wk: 7 (37) 4 wk: 7 (37), 0*	Diff Δ*: 4 wk: -19%

Notes. * Calculated by study team.

† Values derived from figures using plotdigitizer.com, SD calculated from 95% CI whenever possible.

Abbreviations. AE=Adverse events; BPI=Brief Pain Inventory; CI=confidence intervals; DVPRS-II= Defense and Veterans Pain Rating Scale; MODI=Modified Oswestry Disability Index; NC=not calculable; NR=not reported; NRS=numeric rating system; ODI=Oswestry Disability Index; PCS=Pain Catrastrophizing Scale; PGIC=Patient Global Impression of Change scale; PSFW=Patient Specific Functional Scale; RMDQ=Roland-Morris Disability Questionnaire; SD=standard deviation; SF-12=Short Form Health Survey; TSK=Tampa Scale of Kinesiophobia; VAS=Visual Analog Scale.

APPENDIX F. CHRONIC NECK PAIN

Appendix Table F1. Detailed Characteristics for Included Trials on Chronic Neck Pain

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
VR Intervention				
Cetin, 2022[51] High 6 weeks Hacettepe University Hospital's Neurosurgery Department, Turkey NR	**Inclusion:** "...aged between 18 and 65 years with a minimum of 6 months of neck pain, a baseline NDI score of at least 20% (10 points), and the neck region as the primary pain area." **Exclusion:** "...having undergone cervical spine surgery; having rheumatologic, vestibular, neurological, or cardiopulmonary diseases; having receiving interventions including exercise or physical therapy in the previous 6 months; and being pregnant."	N=21 Age, mean (SD): 40.0 (11.88) Female: 70.5% Clinic 3 x 40 min (20 min control exercises + 20 min VR) per week; 6 weeks "Two VR applications were installed: “Ocean Rift” and “Gala 360”. “Ocean Rift” provides a VR experience that allows watching sea animals that can be selected with the remote control. “Gala 360” provides views from countries and cities all over the world… The patients were seated in a chair that allowed 360◦ movement and were asked to look in all directions during the VR application…They were encouraged to move their necks by expressions such as “follow that dolphin, the sea turtles you chose will come soon, there may be a starfish below. Now you are in front of the Eiffel Tower, you can look around”.”	N=20 Age, mean (SD): 41.94 (10.76) Female: 64.7% Clinic 3 x 40 min per week; 6 weeks "The MC exercises included strengthening of the deep cervical flexors (DCFs), deep cervical extensors (DCEs), and axioscapular muscles; stretching exercises; and postural correction exercises. The 3-level treatment protocol developed by Jull was used in the training of the cervical muscles in our study (Jull et al., 2004). In the first level, craniocervical flexion (CCF) exercises were used for low-load endurance training of the DCFs and cervical extension exercises were used for endurance training of the DCEs. The exercises were performed slowly to provide MC and increase kinesthetic awareness. The ability to do the CCF exercises for 10 s was used as a	**Primary: ROM, Joint Position Sense Error (JPSE)** **Pain-related functioning (6 wk)** • ProFitMap-Neck **Pain intensity (6 wk)** • VAS **Adverse events (6 wk)** **Quality of life (6 wk)** • SF-36 (domain scores only) **Physical performance (6 wk)** • ROM & JPSE (flexion, extension, right/left lateral flexion, right/left rotation) **Non-eligible: Pain pressure thresholds, HADS**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
			reference to indicate progress in the exercises. In the second level, elastic bands were used to increase the strength and endurance of the DCFs and DCEs. In the third level, the aim was to gain dynamic balance, and this was achieved by the patient holding an exercise ball against a wall with the front/back of the head. All patients were informed about neutral spinal posture from the first session. They were trained to actively correct postures and maintain them for 10 s (in sitting and standing positions)."	
Nusser, 2021[52] High 3 weeks Federseeklinik Bad Buchau, Germany NR	**Inclusion:** "Diagnoses [of non-traumatic chronic neck pain (more than 3 months)] were primarily made by patients' general practitioners and confirmed by the physician in charge at the rehabilitation hospital. Further inclusion criteria were such that the patients must be adults aged 18 years or more and have taken no pain medication or muscle relaxants for 24 hours before the tests." **Exclusion:** "... traumatic neck pain, neck pain originating from whiplash, cervical fracture/dislocation, operations in the cervical spine area, damage to the inner ear, vertebrobasilar insufficiency, basic neurological diseases, range of motion of the cervical spine < 10° in flexion, extension, and/or rotation."	N=17 Mean (SD) age: 51.2 (8.8) 6 20-minute sessions over 3 weeks Clinic "In addition to the "standard rehabilitation programme," patients in the VRG completed a total of 120 min of "neck-specific sensorimotor training" (NSST) using a VR device in individual therapy. Due to the required concentration, the training was divided into 6 20min sessions… A globe was shown, moving in a virtual space on predetermined trajectories, on the monitor... The patient was asked to follow by moving the head the orbital pathways of the globe… A 3Space Fastrak System (Polhemus Inc.,	N=20 Mean (SD) age: 49.8 (8.1) 3 weeks Clinic "The CG underwent a "standard rehabilitation programme", including a combination of individual and group therapies instructed by physiotherapists and certified sports scientists… the programme comprised different forms of general and neck-specific exercise therapy, such as strengthening, mobilization, relaxation, medical training therapy, functional gymnastics, aqua therapy, physical therapy, and traditional "back school"… Patients also received special lectures from orthopaedists	**Primary outcome NR** **Pain-related functioning (3 wk)** • NDI **Pain intensity/severity (3 wk)** • NRS **Adverse events (3 wk)** **Physical performance (3 wk)** • ACROM

Author, Year Risk of Bias Follow-Up Duration Site(s) Funding source	Inclusion/Exclusion Criteria	Intervention: Participants Randomized Demographics Setting Frequency; Duration Detailed Intervention Characteristics	Comparator(s): Participants Randomized Demographics Setting Frequency; Duration Detailed Comparator Characteristics	Primary Outcome Eligible Outcomes & Measures Reported (Time Points) Other Non-Eligible Outcomes Reported
		Colchester, VT, USA) was used for head movement tracking... Before each training session, the current maximum active cervical range of motion (ACROM) of the patient was determined in a total of 8 directions: flexion, extension, right, and left rotation, and the diagonals in between… In every NSST session, the VRG patients underwent each of the following tasks twice: the Head Repositioning Test (HRT) ..., the Head to Target Test (HTT), and a dynamic exercise including 5 different trajectories... Rest breaks of approximately 3 min were given between tasks, and extended if any side effect (*eg*, motion sickness, nausea, or headaches) was reported." N=18 Mean (SD) age: 53.1 (5.7) 4 x 30-minute sessions over 3 weeks Clinic "The SMG received the "standard rehabilitation programme" plus a total of 120 min of "general sensorimotor training". This training... was instructed by a physiotherapist or a certified sports scientist. The objective was training and improvement in patients' coordination through skill exercises (eg, passing an obstacle course,	and psychologists, who provided information about chronic pain, along with therapeutic goals, and an emphasis on the importance of being proactive"	

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
		dribbling, rope skipping, tossing balls through rings), balance exercises (*eg*, standing with eyes closed, single leg stance, slacklining), small game forms (*eg*, juggling, curling, throwing and catching), and partner games, such as badminton or table tennis."		
Tejara, 2020[53] Some concerns 4 months Rey Juan Carlos University; CEU San Pablo University; Community of Madrid, Spain NR	**Inclusion:** "(a) non-specific chronic neck pain; (b) age 18 to 65 years" **Exclusion:** "(a) pregnancy; (b) specific neck pain caused by metastasis, neoplasia, infectious or inflammatory disorders, bone fractures or traumatic precedents with neck injuries; (c) positive neurological signs or evidence of spinal compression (abnormal diuse sensitivity, hyperreflexia, or diuse weakness); (d) cervical osteoarthritis; (e) spondyloarthritis; (f) neck pain associated with vertigo (vestibular involvement); (g) neck pain associated with whiplash injuries; (h) previous cervical surgeries; (i) headaches prior to the onset of neck pain and without cervical origin; and (e) inability to provide informed consent."	N=22 Age, mean (SD): 32.72 (11.63) Female: 50% Clinic 2 sessions/week for 4 weeks "Two VR mobile applications were installed…The subjects started with the free mobile application "Fulldive VR" …. The patient was immersed in an environment that simulated the living room of a house and at the same time they could visualize a gallery of previously selected photos. Then, they had to change the images in the viewfinder by tilting their neck bilaterally, as well as naming the photos that were displayed… Once the patient felt comfortable with the system and adapted to the headset, then after one minute rest, the difficulty of the exercise program was increased with the free mobile application "VR Ocean Aquarium 3D" where flexion, extension and rotation	N=22 Age, mean (SD): 26.68 (9.21) Female: 54.5% Clinic 2 sessions/week for 4 weeks "This group performed three series of 10 repetitions of every exercise, with a 30 s rest between exercises. The researcher provided the necessary verbal corrections for the proper execution of the exercises, using the same verbal commands for all participants. Flexion exercise: in a sitting position, a ball was placed between the wall and the neck of the patient that performed a controlled neck flexion with a previously maintained cranio-cervical flexion. Extension exercise: in a sitting position, the participant was asked to perform a controlled neck extension and a cranio-cervical flexion before returning to the initial position. Rotation and tilt exercises: in a sitting	**Primary: Pain intensity, pain modulation (CPM), temporal summation (TS)** **Pain-related functioning (4 wk, 4 mo)** • NDI **Pain intensity/severity (4 wk, 4 mo)** • VAS **Pain catastrophizing (4 wk, 4 mo)** • Pain Catastrophizing Scale (PCS) • Pain Anxiety Symptom Scale (PASS-20) • Fear Avoidance Beliefs Questionnaire (FABQ) • TSK **Physical performance (4 mo)** • Cervical ROM **Non-eligible: CPM; TS; fear-avoidance beliefs; pain**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
		movements were added. The patient was immersed in a virtual environment that simulated an ocean, moving forward and observing different marine animals by making the neck movements. The patient named the animals they were visualizing…In the first sessions, the patients were instructed to perform a previous cranio-cervical flexion before starting any movement. Then, the therapist controlled the contraction of the superficial musculature with their hands. Gradually, the aid of the physiotherapist was removed so that the participants could integrate deep muscle contraction and the correct cranio-cervical posture innately… For these patients to carry out the same work as the control group, the physiotherapist counted and controlled in each exercise the number of movements the patient performed, in order to not exceed the dose proposed: 3 series of 10 repetitions of each exercise with 30 s rest between exercises."	position, the subject who had previously done a cranio-cervical flexion to activate the deep flexor musculature was asked to perform the movement."	**pressure thresholds; pain-related anxiety**
Bahat, 2017[54,120] Some concerns 4 months[54], 5 months [120] University of Queensland, Australia	**Inclusion:** "Adults aged 18 years or more with neck pain for more than 3 months… NDI score greater than 12%, and VAS during the recent week greater than 20 mm. Lastly, VR assessment indicated a reduction of mean velocity of at least one SD from control values."	N=30 (+18 added in phase 2) Age, median (IQR): 48 (38.5, 57.5) Female: 63% Home	N=30 (+14 added phase 2) Age, median (IQR): 48 (35.5, 59) Female: 70% Home	**Primary: NDI, global perceived effect (GPE), cervical motion velocity (mean & peak)** **Pain-related functioning (4 wks)** • NDI

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Physiotherapy Research Fellowships (HMR); Queensland Government (2013003214)	**Exclusion:** "Existing vestibular pathology; cervical fracture/dislocation; systemic diseases, epilepsy or other neurological condition; cardiovascular, or respiratory disorders affecting physical performance; history of traumatic head injury; inability to provide informed consent; inability to complete the assessment, or pregnancy."	5-minute sessions, 4 times a day (20 mins/day total), 4 days a week, for 4 weeks "Three modules were developed, including range of motion (ROM), velocity and accuracy modules. These modules enable elicitation of cervical motion by the patient's response to the provided visual stimuli. A full kinematic report for each patient was generated after completion of the modules. During the VR session, the virtual pilot flying the red airplane was controlled by the patient's head motion and interacted with targets appearing from four directions (to elicit flexion, extension, right rotation, left rotation). The VR software did not elicit side flexion movement..."	5-minute sessions, 4 times a day (20 mins/day total), 4 days a week, for 4 weeks "Kinematic training with a head-mounted laser beam aimed at a 70 by 70 cm poster. Tasks in the laser group were similar to the VR exercises, such as following the line with the laser, moving quickly from one circle to another, etc. The laser beam provided visual feedback relating to head motion, but unlike the VR, laser training velocity was not controlled." N=30 Age, median (IQR): 48 (35, 59) Female: 77% Home NA (waitlist control)	**Pain intensity/severity (4 wks)** • VAS **Adverse events (4 wks)** • Side effects post-intervention for VR group only, includes both phases 1+2 **Pain catastrophizing (4 wks)** • TSK **Physical performance (4 wks)** • Velocity • # of velocity peaks • Time to peak velocity percentage • Accuracy error • Cervical ROM
Sarig Bahat, 2015[55] Some concerns 4 months Neck Pain and Whiplash Research Unit, University of Queensland, Brisbane, Australia	**Inclusion:** ""age 18 years or more; prolonged neck pain for more than three months; and the… NDI score greater than 10%" **Exclusion:** "existing vestibular pathology; cervical fracture/dislocation; systemic diseases; neurological, cardiovascular, or respiratory disorders affecting physical performance; history of traumatic head injury; inability to provide informed consent; or pregnancy."	N=16 Age, mean (SD): 40.63 (14.18) Female: 68.8% Clinic	N=16 Age, mean (SD): 41.13 (12.59) Female: 68.8% Clinic & Home	**Primary: NDI, cervical ROM, head movement velocity & accuracy** **Pain-related functioning (4 wk, 4 mo)** • NDI **Pain intensity/severity (5 wk, 4 mo)** • VAS

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
University of Haifa		4-6 supervised sessions (30 minutes each) over 5 weeks, 30-minutes at least 3 x per week over 3 months "Three modules were developed, including range of motion (ROM), velocity and accuracy modules. These modules enable elicitation of cervical motion by the patient's response to the provided visual stimuli… During the VR session, the virtual pilot flying the red aeroplane (in the web version) is controlled by the patient's head motion and interacts with targets appearing from four directions (flexion, extension, right rotation, left rotation) ...The VR training program was tailored to each participant and progressed according to the patients' performance... In the VR training system, range of motion was individually challenged by positioning targets further away, velocity by reducing targets lifetime (the shorter time a target appeared it required faster response), and accuracy by increasing velocity of the moving target to pursuit in the accuracy module."	4-6 supervised sessions (30 minutes each) over 5 weeks, KT home sessions x 3 months "The KT group undertook a 30-minute training session using a laser pointer that was mounted on the participant's head and projected onto a poster for feedback. Kinematic training involved active neck movements to increase ROM, quick head movement in between targets to facilitate quick cervical motion control, static head positioning while moving the body was used to advance head stability, and smooth head movement following a target was used to train accurate head neck movement. These exercises were supervised by the physiotherapist and performed in the clinic by the KT group, and then encouraged to be performed at home. The kinematic home exercises were tailored to each individual and their performance re-evaluated and progressed during each supervised session."	**Adverse events (4 mo)** • Motion sickness **Pain catastrophizing (5 wk, 4 mo)** • TSK **Pain global change (4 mo)** • Global Perceived Effect (GPE) on pain **Physical performance (4 mo)** • ROM (flexion, extension, right rotation, left rotation) • Peak Velocity (flexion, extension, right rotation, left rotation), • Mean Velocity (flexion, extension, right rotation, left rotation), • TTP% (flexion, extension, right rotation, left rotation), • Sway SD (pitch, yaw), • Accuracy (pitch, yaw) • Sensorimotor (eyes closed balance, single leg stance, and step test) **Non-eligible: cervical ROM, head movement velocity and accuracy**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
AR Interventions				
Rezaei, 2019[56] High 9 weeks Community health system in Iran Vice Chancellor for Research of Shiraz University of Medical Sciences (grant no. 92-6895)	**Inclusion:** "... history of nontraumatic NP for more than 3 months and age between 20 and 55 years." **Exclusion:** "...a score ≥15 and ≤9 (out of possible 50) on… NDI, history of cervical and thoracic trauma within the 6 months before examination, neurological signs and symptoms in the upper extremities, nerve injury, spinal cord compression, cervical spine pathology or surgery and cancer."	N=22 Age, mean (SD): 36.19 (9.8) Female: 42.9% Clinic 21 min sessions, 2 sessions per week for 4 weeks (8 total) "A new video game (Cervigame® version 1.01) was designed for training... The main visual component of the game is a rabbit attempting to reach carrots. The virtual carrots appear continuously along the line of the movement pattern being trained. This avatar is controlled by the patient's head movements… Stages increase in difficulty as obstacles…appear in predefined positions…The best score in each stage was obtained by capturing all carrots without colliding with any obstacles… Based on the patient's head movement (along a line or in a plane) the stages are divided into two main categories: unidirectional and two-directional...The order of 50 stages progresses from easy to hard, based on the stage category, number and acuity of the angles, shape and variation in the range of trajectories and the arrangement of obstacles. In	N=22 Age, mean (SD): 31.23 (9.49) Female: 52.4% Clinic 21 min sessions, 2 sessions per week for 4 weeks (8 total) "... Exercises consisted of eye-follow, gaze stability, eye-head coordination and position sense and movement sense practice. In the eye-follow exercise, patients moved their eyes to follow the target while seated with their head stationary. The target was a pen held by a physical therapist, who initially moved it slowly in one plane and then increased the speed and changed the direction of movement. For the gaze stability exercise, patients actively moved their head in all directions while visually fixing on the target. The exercise for eye-head coordination began by moving the head and eyes to the same side. Then participants moved their eyes first to keep focused on the target, and then moved their head. Finally, they moved their eyes in one direction while simultaneously rotating their head in the opposite direction. These exercises were initially done slowly in	**Primary: Patient-reported neck pain & disability** **Pain-related functioning (4 wk, 9 wk)** • NDI **Pain intensity (4 wk, 9 wk)** • VAS **Physical performance (4 wk, 9 wk)** • Dynamic balance: Y-balance test

Author, Year Risk of Bias Follow-Up Duration Site(s) Funding source	Inclusion/Exclusion Criteria	Intervention: Participants Randomized Demographics Setting Frequency; Duration Detailed Intervention Characteristics	Comparator(s): Participants Randomized Demographics Setting Frequency; Duration Detailed Comparator Characteristics	Primary Outcome Eligible Outcomes & Measures Reported (Time Points) Other Non-Eligible Outcomes Reported
		the first 3 treatment sessions, the patients play only unidirectional stages. Combinations of unidirectional and two-directional stages are played alternately in the fourth and fifth sessions. In the last 3 sessions, only two-directional stages are played."	a restricted range of movements, then the speed and range of movements gradually increased. Exercises were done in both vertical and horizontal directions. For joint position sense and movement sense exercises, participants wore a laser pointer attached to a headband. The patients sat 1 meter from a point marked on the wall, and were instructed to move their head until the laser beam was aimed on the point, and then to close their eyes and memorize their head-neck position for 5 s. Maximal movement of the head was performed in one direction (flexion, extension, rotation or lateral flexion), after which the patients tried to recover their initial head position as closely as possible, and opened their eyes. The relocation error indicated by the distance of the laser beam from the point marked on the wall was used as feedback. Movement sense was practiced by using the head-mounted laser pointer to trace a moving object held by the physical therapist. The task was progressed by increasing the speed and changing the pattern of movement."	

Abbreviations: ACROM=acute cervical range of motion; AR=augmented reality; CG=control group; CPM=conditioned pain modulation; HADS=Hospital Anxiety-Depression Scale; IQR=interquartile range; JPSE=Joint Position Sense Error; MC=motor control exercises; mo=month; NDI=Neck Disability Index; NR=not reported; NRS=Numeric Rating Scale; ROM=range of motion; SD=standard deviation; SF-36=Short Form-36; SMG=sensorimotor group; TS=temporal summation; TSK=Tampa Scale of Kinesiophobia; TTP=time-to-peak; VAS=Visual Analog Scale; VR=virtual reality.

Appendix Table F2. Detailed Results for Chronic Neck Pain Studies

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
Pain-Related Functioning or Interference				
Cetin, 2022[51] VR High	ProFitMap – Neck	69.3 (11.3) 6 wk: Follow-up NR, 12.97	65.22 (13.49) 6 wk: Follow-up NR, 10.59	Diff Δ: 6 wk: 2.37
Nusser, 2021[52] VR High	NDI	18.7 (5.2) 3 wk: 11.4 (7.5), -7.3*	SMG 21.5 (6.4) 3 wk: 13.7 (7.9), -7.8*	Diff Δ*: 3 wk: 0.5
			Control 18.2 (6.7) 3 wk: 13.7 (7.0), -4.5	Diff Δ*: 3 wk: -2.8
Rezaei, 2019[56] AR High	NDI	13.0 (1.3) 4 wk: 4.57 (2.39), -8.43 9 wk: 4.38 (3.3), -8.62	12.28 (1.38) 4 wk: 8.14 (3.13), -4.14 9 wk: 9.22 (3.66), -3.06	Diff Δ: 4 wk: -4.29 9 wk: -5.56*
Sarig Bahat, 2017[54] VR Some concerns	NDI	32.88 (12.5) 4 wk: 23.75 (15.7), -9.13*	Laser 32.19 (13.3) 4 wk: 26.88 (14.0), -5.31*	Diff Δ*: 4 wk: -3.82
			Control 4.48 (10.7) 4 wk: 23.60 (11.8), -1.12*	Diff Δ*: 4 wk: -8.01
Sarig Bahat, 2015[55] VR Some concerns	NDI	20.38 (7.6) 4 wk: 12.85 (7.5), -7.76 (6.2) 4 mo: 13.57 (7.9), -6.92 (6.0)	20.19 (6.5) 4 wk: 14.0 (15.1), -5.64 (7.0) 4 mo: 14.0 (8.5), -3.42 (14.9)	Diff Δ*: 4 wk: -2.12 4 mo: -3.5
Tejara, 2020[53] VR Some concerns	NDI	13.72 (6.68) 4 wk: 6.9 (6.28), -6.82* 4 mo: 4.95 (6.60), -8.77*	14.09 (9.32) 4 wk: 7.45 (5.36), -6.64* 4 mo: 5.77 (4.67), -8.32*	Diff Δ*: 4 wk: -0.18 4 mo: -0.45
Pain Intensity				
Nusser, 2021[52] VR High	NRS	4.9 (2.1) 3 wk: 2.2 (1.2), -2.7*	SMG: 4.4 (3.1) 3 wk: 2.9 (2.2), -1.5*	Diff Δ*: 3 wk: -1.2
			CG: 4.2 (2.6) 3 wk: 3.2 (3.0), -1.0*	Diff Δ*: 3 wk: -1.7
Rezaei, 2019[56] AR High	VAS	47.11 (10.24) 4 wk: 10.75 (8.43), -36.36 9 wk: 9.75 (11.03), -37.54	38.95 (10.07) 4 wk: 19.63 (9.15), -19.32 9 wk: 20.17 (11.97), -18.78	Diff Δ*: 4 wk: -17.04 9 wk: 18.76
Sarig Bahat, 2015[55] VR Some concerns	VAS	35.72 (17.7) 5 wk: 22.1 (24.1), -13.62* 4 mo: 26.95 (16.5), -8.77	35.17 (16.7) 5 wk: 27.72 (21.9), -7.45* 4 mo: 30.33 (18.5), -4.84	Diff Δ*: 5 wk: -21.07 4 mo: -3.93
Sarig Bahat, 2017[54] VR Some concerns	VAS	47.49 (20.9) 4 wk: 31.1 (23.6), -16.39*	52.47 (19.5) 4 wk.: 35.97 (22.9), -16.5*	Diff Δ*: 4 wk: 0.11
			45.78 (21.5) 4 wk: 39.45 (22.0), -6.33*	Diff Δ*: 4 wk: -10.06
Tejara, 2020[53] VR Some concerns	VAS	4.97 (1.88) 4 wk: 2.67 (1.91), -2.3* 4 mo: 2.17 (1.99), -2.8*	4.27 (1.35) 4 wk: 3.11 (1.47), -1.16* 4 mo: 1.72 (2.09), -2.55*	Diff Δ*: 4 wk: -1.14 4 mo: -0.25

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
Adverse Events				
Cetin, 2022[51] VR High	Count of adverse events	No AE observed	No AE observed	Diff Δ*: 0
Nusser, 2021[52] VR High	Count of adverse events	"Besides the weight of the helmet, which some patients found unpleasant, no other negative side effects were reported regarding the VR device or in general. Therefore, all patients (not including the 4 who discontinued participation) could complete the measurements required for the training, as planned."		Diff Δ: NC
Sarig Bahat, 2017[54] VR Some concerns	Side effects post-intervention, includes phases 1+2	"There were a few cases of side effects from the VR use. Out of 14 dropouts at post-intervention assessment, 5 were due to VR-associated sickness and headache."	AE not assessed	Diff Δ: NC
Sarig Bahat, 2015[55] VR Some concerns	Count of participants who experienced motion sickness	"Four participants experienced motion sickness with the use of the VR device during assessment. Two participants reported motion sickness prior to randomization, and therefore were excluded. Two other participants experienced delayed motion sickness (up to 24 hours after assessment) and after being randomized to the KT[VR] group and hence withdrew from further participation. There were no reports of pain exacerbation."		Diff Δ: NC
Pain Catastrophizing & Kinesiophobia				
Sarig Bahat, 2017[54] VR Some concerns	TSK	35.22 (7.4) 4 wk: 33.26 (7.8), -1.96*	Laser 34.79 (5.9) 4 wk: 34.58 (8.2), -0.21*	Diff Δ*: 4 wk: -1.75
			Control 32.64 (7.2) 4 wk: 33.96 (6.2), 1.32*	Diff Δ*: 4 wk: -3.28
Sarig Bahat, 2015[55] VR Some concerns	TSK	32.75 (6.8) 5 wk: 30.13 (5.7), -2.13 (4.2) 4 mo: 31.23 (6.5), -1.23 (6.8)	30.38 (5.8) 5 wk: 28.64 (9.9), -1.5 (8.3) 4 mo: 30.0 (5.9), -0.92 (4.5)	Diff Δ*: 5 wk: -0.63 4 mo: -0.31
Tejara, 2020[53] VR Some concerns	TSK	22.9 (7.11) 4 wk: 18.9 (10.73), -4.0* 4 mo: 12.09 (7.77), -10.81*	21.4 (6.63) 4 wk: 18.36 (7.48), -3.04 4 mo: 17.5 (6.89), -3.9	Diff Δ*: 4 wk: -0.96 4 mo: -6.91
	PCS	17.36 (11.49) 4 mo: 4.95 (8.08), -12.41*	11.95 (9.39) 4 mo: 4.86 (8.4), -7.09*	Diff Δ*: 4 mo: -5.32
	PASS-20	27.52 (20.52) 4 mo: 12.33 (16.09), -15.19*	26.59 (16.5) 4 mo: 15.9 (11.3), -10.69*	Diff Δ*: 4 mo: -4.5
	FABQ	28.25 (16.43) 4 mo: 12.3 (13.48), -15.95*	25.68 (13.02) 4 mo: 16.59 (14.32), -9.09*	Diff Δ*: 4 mo: -6.86
Quality of Life				
Cetin, 2022[51] VR High	SF-36 – Physical functioning	Median (IQR): 75.0 (60.0-85.0) 6 wk median (IQR): NR, 15.0 (5.0-17.5)	Median (IQR) 75.0 (60.0-90.0) 6 wk median (IQR): NR, 5.0 (0.0-17.5)	Median (95% CI) diff at 6 weeks: 2.94 (-5.17, 11.05)
	SF-36 – Role limitations due to physical health	Median (IQR): 66.7 (33.3-83.3) 6 wk median (IQR): NR, 25.0 (0.0-46.0)	Median (IQR): 33.3 (33.3-66.7) 6 wk median (IQR): NR, 25.0 (10.0-50.0)	Median (95% CI) diff at 6 weeks: -3.62 (27.62, 20.36)

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
	SF-36 – Role limitations due to emotional health	Median (IQR): 55.0 (55.0-60.0) 6 wk median (IQR): NR, 33.3 (0.0-33.5)	Median (IQR): 45.0 (32.6-55.0) 6 wk median (IQR): NR, 33.4 (0.0-66.7)	Median (95% CI) diff at 6 weeks: -5.86 (-18.76, 7.03)
Physical Performance				
Cetin, 2022[51] VR High	Flexion	49.05 (7.89) 6 wk: NR, 10.64 (7.44)	44.64 (9.92) 6 wk: NR, 8.47 (7.21)	Diff Δ: 6 wk: -2.17
	Extension	62.47 (11.88) 6 wk: NR, 10.05 (9.25)	61.23 (9.44) 6 wk: 7.70 (7.05)	Diff Δ: 6 wk: -2.35
	Right lateral flexion	40.23 (8.35) 6 wk: 7.63 (8.84)	39.42 (7.83) 6 wk: 7.30 (5.81)	Diff Δ: 6 wk: -0.33
	Left lateral flexion	42.56 (8.25) 6 wk: 4.96 (7.41)	43.66 (7.23) 6 wk: 4.92 (5.78)	Diff Δ: 6 wk: -0.04
	Right rotation	56.76 (9.83) 6 wk: 6.05 (13.6)	51.47 (8.43) 6 wk: 8.52 (6.06)	Diff Δ: 6 wk: 2.47
	Left rotation	55.0 (9.18) 6 wk: 7.35 (9.0)	49.11 (8.33) 6 wk: 9.41 (9.98)	Diff Δ: 6 wk: 2.05
Nusser, 2021[52] VR High	Flexion	40.9 (14.6) 3 wk: 48.5 (13.3), 7.6*	SMG 38.9 (12.2) 3 wk: 37.9 (14.8), -1.0*	Diff Δ*: 3 wk: 8.6
			CG 45.8 (12.9) 3 wk: 42.9 (12.6), -2.9	Diff Δ*: 3 wk: 10.5
	Extension	35.4 (12.8) 3 wk: 37.7 (15.1), 1.9*	SMG 39.1 (12.7) 3 wk: 44.6 (12.9), 5.5*	Diff Δ*: 3 wk: -3.6
			CG 43.1 (13.3) 3 wk: 39.8 (14.7), -3.3*	Diff D*: 3 wk: 5.2
	Left rotation	57.4 (12.7) 3 wk: 65.2 (16.9), 7.8*	SMG 51.7 (17.9) 3 wk: 55.8 (15.5), 4.1*	Diff Δ*: 3 wk: 3.7
			CG 59.3 (10.1) 3 wk: 59.9 (9.3), 0.6	Diff Δ*: 3 wk: 7.2
	Right rotation	55.6 (10.4) 3 wk: 59.5 (14.0), 3.9*	SMG 54.6 (13.7) 3 wk: 58.6 (13.4), 4.0*	Diff Δ*: 3 wk: -0.1
			CG 61.8 (15.3) 3 wk: 64.0 (0.2), 2.2*	Diff Δ*: 3 wk: 1.7
Rezaei, 2019[56] AR High	Dynamic balance: Y-balance test	78.65 (5.37) 4 wk: 84.67 (7.01), 6.02* 9 wk: 86.24 (8.15), 7.59*	81.55 (8.76) 4 wk: 88.69 (8.92), 7.14* 9 wk: 88.98 (10.7), 7.43*	Diff Δ*: 4 wk: -1.12 9 wk: 0.16
Sarig Bahat, 2015[55] VR Some concerns	Flexion	38.69 (14.6) 5 wk: 57.31 (11.3), 18.62* 4 mo: 55.38 (11.2), 16.69*	43.94 (14.3) 5 wk: 49.87 (17.2), 5.93* 4 mo: 58.4 (11.4), 14.46*	Diff Δ*: 5 wk: 12.69 4 mo: 2.23

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
	Extension	48.72 (15.1) 5 wk: 57.45 (14.1), 8.73* 4 mo: 57.64 (8.8), 8.92*	51.09 (13.2) 5 wk: 54.19 (12.8), 3.1* 4 mo: 54.5 (11.0), 3.41*	Diff Δ*: 5 wk: 5.63 4 mo: 5.51
	Right rotation	62.32 (13.1) 5 wk: 71.84 (14.0), 9.52* 4 mo: 72.04 (16.2), 9.72*	57.06 (16.6) 5 wk: 77.21 (10.6), 20.15* 4 mo: 88.89 (21.4), 31.83	Diff Δ*: 5 wk: 4 mo:
	Left rotation	58.58 (15.3) 5 wk: 77.74 (16.0) 4 mo: 70.38 (20.6)	57.94 (15.3) 5 wk: 72.58 (13.6) 4 mo: 84.26 (23.3)	Diff Δ*: 5 wk: 5.16 4 mo: -13.88
	Eyes closed balance	28.05 (15.3) 5 wk: 26.67 (11.6) 4 mo: 31.73 (19.2)	4.48 (20.1) 5 wk: 25.08 (17.3) 4 mo: 27.87 (32.1)	Diff Δ*: 5 wk: 1.59 4 mo: 3.86
Sarig Bahat, 2017[54] VR Some concerns	Flexion	60.54 (10.1) 4 wk: 61.38 (7.1), 0.84*	Laser 64.7 (7.2) 4 wk: 65.44 (9.0), 0.74*	Diff Δ*: 4 wk: 0.1
			Control 62.98 (7.3) 4 wk: 64.52 (6.0), 1.54*	Diff Δ*: 4 wk: -0.7
	Extension	63.17 (11.9) 4 wk: 64.67 (11.0), 1.5*	Laser 62.91 (14.6) 4 wk: 65.28 (12.8), 2.37*	Diff Δ*: 4 wk: -0.87*.
			Control 65.42 (11.2) 4 wk: 67.11 (7.9), 1.69*	Diff Δ*: 4 wk: -0.19
	Right rotation	73.77 (16.2) 4 wk: 75.28 (13.3), 1.51*	Laser 78.14 (14.7) 4 wk: 80.65 (14.2), 2.51*	Diff Δ*: 4 wk: -1.0
			Control 78.87 (12.2) 4 wk: 79.08 (11.5), 0.21	Diff Δ*: 4 wk: 1.3
	Left rotation	76.86 (14.5) 4 wk: 77.43 (11.9), 0.57*	Laser 77.18 (15.9) 4 wk: 77.45 (15.0), 0.27*	Diff D*: 4 wk: 0.3
			Control 78.93 (16.0) 4 wk: 81.17 (12.3), 2.24*	Diff D*: 4 wk: -1.67

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
Tejara, 2020[53] VR Some concerns	Flexion/ extension	110.22 (19.19) 4 mo: 112.03 (23.99), 1.81*	116.13 (22.34) 4 mo: 117.60 (24.27), 1.47*	Diff Δ*: 4 mo: 0.34
	Lateroflexion	79.54 (20.61) 4 mo: 84.93 (21.47), 5.39*	87.21 (17.96) 4 mo: 86.42 (16.79), -0.79*	Diff Δ*: 4 mo: 6.18
	Rotation	114.1 (18.97) 4 mo: 121.9 (18.49), 7.8*	118.48 (15.19) 4 mo: 124.3 (15.55), 5.82*	Diff Δ*: 4 mo: 1.98

Notes. * Calculated by review team.

Abbreviations. AR=augmented reality; CG=control group; Diff Δ= difference in change scores; FABQ=Fear Avoidance Beliefs Questionnaire; JPSE=Joint Position Sense Error; KT=kinematic therapy; mo=month; NDI=Neck Disability Index; NC=not calculable; NR=not reported; NRS=Numeric Rating Scale; PASS-20=Pain Anxiety Symptom Scale; PCS=Pain Catastrophizing Scale; QoL=quality of life; ROM=range of motion; SD=standard deviation; SF-36=Short Form-36; SMG=sensorimotor group; TSK=Tampa Scale of Kinesiophobia; TTP=time-to-peak; VAS=Visual Analog Scale; VR=virtual reality; wk=week.

APPENDIX G. FIBROMYALGIA

Appendix Table G1. Detailed Characteristics for Included Trials on Fibromyalgia

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding Source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Carvalho, 2019[58] High 7 Weeks Federal University of Alfenas, Alfenas, Mina Gerais Research Support Foundation of Minas Gerais (APQ 02794-11); Tutorial Education Program (PET-MEC-SESU); Coordination for the Improvement of Higher Education Personnel (CAPES)—Finance Code 001.	**Inclusion:** ≥18 years of age Female gender American College of Rheumatology concordant fibromyalgia diagnosis **Exclusion:** Male gender Cardiovascular, pulmonary, orthopedic, neurological, or dermatological conditions, affecting muscle strength and physical capabilities Pregnancy	N=16 Age, mean (SD): 55.64 (9.16) Women: 100% Clinic 1-hour sessions three times weekly; 7 weeks Wii exergames: Participants completed 6 Wii Fit Plus subgames: Jogging Plus which involves stationary running. Activity requires active and constant movement of the lower limb muscles for 15 minutes. 'Bird's-eye Bull's-eye game which requires active movement of the upper limbs in isolation from weight and balance training for 9 minutes. Yoga game which involves control of expiratory and inspiratory movements and active control of the body's center of gravity for 3 minutes.	N=19 Age, mean (SD): 47.70 (15.46) Women: 100% Clinic 1-hour three times weekly; 7 weeks Chain muscle stretching: Positions were held during four deep and prolonged expirations. Stretches were chosen from an existing isometric stretching program to include multiple positions and globally engage muscle groups. Position 1: orthostatic position, feet parallel, semiflexion of the knees, pelvic retroversion, arms outstretched and slightly backward, wrists and fingers flexed in extension, gluteal muscles contracted, scapular adduction, and erect spine . Variation 2 of this position, which is performed with the hands in contact, was also used. Position 15: standing position, anterior trunk inclination, knees	**Primary: FIQ, Exercise capacity** **Pain-related functioning (4, 7 wk)** • FIQ (domain scores for physical function and total) **Physical performance (4, 7 wk)** • Number of steps up/down (25 cm height) **Other non-eligible outcomes reported** • Pain threshold (algometry) • Vitals during exercise (HR, BP, etc.)

		Super Hula Hoop game which involves circular rhythmic movements as well as balance control for 9 minutes. Step game which consists of active and alternating movements of the lower limb muscles, which requires control of balance and unipodal discharge for 9 minutes. Rhythm Parade which consists of stationary walking with active and rhythmic movements of the lower limb muscles for 9 minutes.	flexed, and arms flexed with the hands supported on the back of the head. Position 16: dorsal decubitus position, legs flexed, feet on the floor, and arms crossed. Position 19: dorsal decubitus position, lower limbs in hip flexion at 90 and knees in extension, shoulders and elbows in 90 flexion, foot dorsiflexion, and scapular adduction. Position 21: dorsal decubitus position, knees and hips semiflexed vertically and in external rotation, the soles of the feet in contact, and the arms positioned along the sides of the body. Position 35: dorsal decubitus position, arms in extension and slight abduction, and legs extended at 90. Position 36: seated position, erect spine, lower limbs semiflexed, feet supported on the floor, horizontal abduction and extension of the arms, and wrist extension at 90. Position 38: seated position, erect spine, lower limbs semiflexed, feet supported on the floor, upper limbs in extension behind the body, and hands in contact with one another. Position 40: seated position, shoulder abduction, and hands positioned behind the head."	
Collado-Mateo, 2017a[60]; Collado-Mateo, 2017b[61] Some concerns 8 Weeks Recruitment via 2 local FM associations (per #2284)	**Inclusion:** Female gender Age 30 to 75 years American College of Rheumatology concordant fibromyalgia diagnosis by a rheumatologist	N=42 Age, mean (SD): 52.52 (9.73) Women: 100% Clinic	N=41 Age, mean (SD): 52.47 (8.75) Women: 100% Clinic NR; NR	**Primary: EuroQoL-5D** **Pain-related functioning (8 wk)** • FIQ • FIQ-80 (without work) • FIQ-100 (physical impairment) **Physical performance (8 wk)** • TUG

Spanish National R+D+i plan (no. DEP2012-39828); Government of Extremadura; EU Development Funds (no GR10127); Spanish Ministry of Education, Culture and Sport (no. FPU14/01283)	**Exclusion:** Pregnancy Any change to usual care therapies during 8 weeks of treatment Contraindications for physical exercise.	2 1-hour sessions per week; 8 weeks VirtualEx-FM: Exergame program focused on postural control, coordination of upper and lower limbs, aerobic conditioning, strength and mobility in 3 virtual environments. First, participants complete a warm-up by imitating an expert on video displaying upper and lower limb joint movements. Second, participants complete an aerobic dance routine by following dance steps marked by a kinesiologist and dance teacher. Third, participants train postural control and coordination by following on-screen prompts to reaching for a virtual apple using a specified limb. All activity is completed in groups of three. Training is designed to improve physical conditioning. Fourth, walk training is developed using a circuit comprising a trail of footprints on a virtual floor. Participants must step on the virtual footprints and walk on the circuit. Participants are guided regarding mplitude, cadence, and different types of step.	Comparator group continued usual care without intervention.	• Functional reach
Polat, 2021[57] High 8 Weeks Gazi University Department of Physical Medicine and Rehabilitation NR	**Inclusion:** 2010 American College of Rheumatology concordant diagnosis of fibromyalgia Age 18 to 65 years ≥8 years of formal education Unchanged fibromyalgia medication regimen for ≥3 months. **Exclusion:**	N=20 Age, mean (SD): 47.0 (7.1) Women: 100% Home, Clinic 4 weeks of cycling program for 20-minute sessions, 3 days per week and augmented reality exercise for 15-minute sessions, 3 days per week.	N=20 Age, mean (SD): 42.6 (8.7) Women: 100% Home, Clinic 4 weeks of cycling program for 20-minute sessions, 3 days per week and additional non-aerobic exercise program for 15-minute sessions, 3 days per week	**Primary: FIQ** **Pain intensity (4, 8 wk)** • VAS **Physical performance (4, 8 wk)** • 6-minute walk **Quality of life (4, 8 wk)** • European Quality of Life 5 (EuroQoL-5D-5L) **Other non-eligible outcomes reported (4, 8 wk)**

	Diagnosis of secondary fibromyalgia Presence of intellectual deficits, visual deficits, inflammatory rheumatic disease or orthopedic surgery in preceding 6 months	Home exercises for additional 4 weeks Cycling program: cycling to 60-70% age adjusted maximum heart rate with 5 minutes of stretching prior to and after exercise. Beach Volleyball: Kinect Sports' videogame that involved participant replicating several movements in volleyball including serves, bumps, sets, and spikes. system. Home exercise program: moderate-intensity aerobic physical activity for 30 minutes on 5 days each week, muscle strengthening and balance exercises 2 days a week, and flexibility exercises with stationary stretches every day for 4 weeks.	Home exercises for additional 4 weeks Cycling program: cycling to 60-70% age adjusted maximum heart rate with 5 minutes of stretching prior to and after exercise. Non-aerobic exercises were performed in a single series containing 10 repetitions at an intensity of 40% of the estimated 1 repetitive maximum, including upper and lower extremity large muscle groups in standing and sitting positions, as a standard exercise protocol with moderate intensity. Additional training in balance and flexibility exercises were completed alongside muscle strengthening. Home exercise program: moderate-intensity aerobic physical activity for 30 minutes on 5 days each week, muscle strengthening and balance exercises 2 days a week, and flexibility exercises with stationary stretches every day for 4 weeks.	• Symptom Severity Scale • Fatigue Severity Scale • HADS
Garcia-Palacios, 2015[64] High 6 Weeks Universitat Jaume I and Rheumatology Service of Hospital General de Castellon NR	**Inclusion:** Age 18 to 70 years old American College of Rheumatology concordant diagnosis of fibromyalgia by a rheumatologist **Exclusion:** Severe mental disorders such as schizophrenia, bipolar disorder, mental retardation, substance abuse or dependence, nor a mental disorder in need of immediate treatment Requesting or suing for disability."	N=61 Age, mean (SD): NR Women: 100% Clinic 6 2-hour group sessions twice a week EMMA: Augmented reality display of 5 predefined scenarios aimed at promoting emotions and motivation. Scenarios include projected images, sounds and narratives. Scenarios chosen were beach and the meadow settings. Program structure involved a session with rationale of activity management for fibromyalgia and instructions to	N=30 Age, mean (SD): NR Women: 100% Clinic 1 session in the 4 weeks after the pretreatment assessment Partiipcants continued "usual care in a rheumatology unit in a public setting in Spain that consists of follow-up sessions by a rheumatologist to review the medication treatment."	**Primary: FIQ** **Pain-related functioning (6 wk)** • BPI- interference **Pain intensity (6 wk)** • BPI- intensity **Quality of life (6 wk)** • Quality of Life Index (QLI-Sp) **Other non-eligible outcomes reported** • Chronic Pain Coping Inventory, • Beck Depression Inventory II (BDI-II) • Acceptability and Satisfaction

		enhance motivation to start to perform meaningful activities (VR1). Another session explores overcoming barriers that prevent performance of activities (VR2). Lastly, a third session type provides instructions to acknowledge personal strengths that could motivate participants to get involved in meaningful activities (VR3). VR1 was used in session 2 of the program, VR2 was used in sessions 3 and 5, and VR3 was used in sessions 4 and 6."		
Villafaina, 2019a[59]; Villafaina, 2019b[62]; Viallafaina, 2020[63] Some concerns 24 Weeks NR Spanish National R+D+i Plan, Spanish Ministry of Economy and Competitivenesss (reference no DEP2015-70356); Research Grant for Groups (GR18155) funded by Junta de Extremadura (Regional Government of Extremadura) and European Regional Development Fund (ERDF/FEDER)	**Inclusion:** Female gender Age 30 to 75 years 2010 American College of Rheumatology concordant fibromyalgia diagnosis by rheumatologist **Exclusion:** Any change to usual care therapies during the 24 weeks of the treatment Contraindications for physical exercise programs Pregnancy	N=28 Age, mean (SD): 54.04 (9.56) Female: 100% Clinic 1 hour sessions twice per week; 24 weeks. VirtualEx-FM: Exergame program focused on postural control, coordination of upper and lower limbs, aerobic conditioning, strength and mobility in 3 virtual environments. Activity completed in groups of two participants. First, participants complete a warm-up by imitating an expert on video displaying upper and lower limb joint movements. Second, participants complete an aerobic dance routine by following dance steps marked by a kinesiologist and dance teacher. Third, participants train postural control and coordination by following on-screen prompts to reaching for a virtual apple using a specified limb. All activity is completed in groups of three.	N=27 Age, mean (SD): 53.41 (9.92) Female: 100% Clinic NR; NR Participants continued care as usual, including previous medication use.	**Primary: EuroQoL-5D, VAS** **Pain-related functioning (24, 48 wk)** • FIQ **Physical performance (24, 48 wk)** • 6-minute walk test • Sit-to-stand test • 10 step stair test (seconds) • TUG • Arm curl • back scratch test • sit and reach test (single and dual-task conditions)

		Training is designed to improve physical conditioning. Fourth, walk training is developed using a circuit comprising a trail of footprints on a virtual floor. Participants must step on the virtual footprints and walk on the circuit. Participants are guided regarding mplitude, cadence, and different types of step.		

Abbreviations. 3D=3 dimensional; ACR=American College of Rheumatology; BP=blood pressure; BPI=Beck pain inventory; CG=control group; cm=centimeters; EuroQoL-5D=European Quality of Life 5 dimensions; FIQ=Fibromyalgia Impact Questionnaire; FM=fibromyalgia; FMS=fibromyalgia syndrome; HADS=Hospital Anxiety and Depression Scale; HR=heart rate; NR=not reported; QLI-Sp=Quality of Life Index (Spanish version) SD=standard deviation; TAU=treatment as usual; TUG=timed up and go test; VAS=Visual Analog Scale; VR=virtual reality; wk=weeks.

Appendix Table G2. Detailed Results for Fibromyalgia Studies

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-UpMean (SD), Mean Change	Comparison
Pain-Related Functioning or Interference				
Carvalho, 2019[58] AR High	FIQR	64.6 (16.1) 4 wk: 41.4 (13.6), -23.2* 7 wk: 33.4 (6.3), -31.2*	72.0 (9.1) 4 wk: 63.1 (13.6), -8.9* 7 wk: 46.4 (13.0), -25.6*	Diff Δ*: 4 wk: -14.3 7 wk: -5.6
	FIQR-physical function subscale	7.2 (3.4) 4 wk: 5.1 (3.4), -2.1* 7 wk: 4.6 (1.9), -2.6*	7.5 (5.2) 4 wk: 6.0 (5.3), -1.5* 7 wk: 3.5 (2.6), -4.0*	Diff Δ*: 4 wk: -0.6 7 wk: 1.4
Collado-Mateo, 2017[60] AR Some concerns	FIQ-100 (8 wk)	50.6 (12.9) 44.9 (13.8), -5.7*	49.2 (15.3) 51.8 (16.4), 2.5*	Diff Δ*: -8.3
	FIQ-80 (without work) (8 wk)	42.6 (10.2) 37.3 (10.4), -5.3*	42.4 (12.5) 43.3 (12.9), 0.9*	Diff Δ*: -6.1
	FIQ 100-physical impairment (8 wk)	2.85 (1.73) 2.53 (1.87), -0.32*	2.6 (2.1) 2.5 (2.0), -3.0*	Diff Δ*: -0.3
Garcia-Palacios, 2015[64] AR High	FIQ (6 wk)	61.6 (19.9) 42.4 (15.7), -19.2*	60.6 (21.4) 57.0 (17.5), -3.6*	Diff Δ*: -15.7
	BPI-Interference (6 wk)	32.2 (14.8) 31.2 (17.7), -1.0*	32.3 (16.7) 37.1 (12.9), 4.7*	Diff Δ*: -5.7
Polat, 2021[57] AR High	FIQ-80	54.7 (13.3) 4 wk: 42.7 (11.8), -12* 8 wk: 40.1 (12.8), -14.6*	58.5 (9.2) 4 wk: 51.7 (9.1), -6.8* 8 wk: 50.7 (12.1), -7.8*	Diff Δ*: 4 wk: -5.2 8 wk: -6.8
Villafaina, 2019[59] AR Some concerns	FIQR	53.2 (16.9) 24 wk: 51.6 (18.3), -1.6* 48 wk: 51.1 (19.0), -2.1*	54.2 (20.0) 24 wk: 55.4 (20.1), 1.2* 48 wk: 52.1 (18.4), -2.1*	Diff Δ*: 24 wk: -2.8 48 wk: 0.01
Pain Intensity				
Garcia-Palacios, 2015[64] AR High	BPI-Intensity (6 wk)	23.6 (5.1) 22.6 (6.3), -0.9	22.4 (7.9) 20.7 (8.3), -1.7	Diff Δ*: 0.7
Polat, 2021[57] AR High	VAS	6.40 (1.4) 4 wk: 4.3 (1.3), -2.2* 8 wk: 3.9 (2.1), -2.6*	6.45 (1.3) 4 wk: 4.9 (1.4), -1.6* 8 wk: 4.8 (1.6), -1.7*	Diff Δ*: 4 wk: -0.6 8 wk: -0.9
Villafaina, 2019[59] AR Some concerns	VAS (24 wk)	62.1 (19.3) 58.9 (16.3), -3.26	60.4 (19.3) 68.2 (17.3), 7.8	Diff Δ*: -11.1
Quality of Life				
Collado-Mateo, 2017[60] AR Some concerns	EuroQoL-5D (8 wk)	0.6 (0.2) 0.7 (0.2), 0.1*	0.6 (0.2) 0.6 (0.2), 0.0*	Diff Δ*: 0.1
Garcia-Palacios, 2015[64] AR High	Quality of Life Index (6 wk)	4.5 (1.2) 6.1 (1.4), 1.6*	5.0 (1.2) 5.3 (1.3), 0.2*	Diff Δ*: 1.4
Polat, 2021[57] AR High	EuroQoL-5D (4 wk)	0.5 (0.2) 4 wk: 0.7 (0.2), 0.2* 8 wk: 0.8 (0.2), 0.3*	0.5 (0.1) 4 wk: 0.6 (0.2), 0.1* 8 wk: 0.6 (0.2), 0.1*	Diff Δ*: 4 wk: 0.1 8 wk: 0.2
Villafaina, 2019[59] AR	EuroQoL-5D	0.5 (0.3)	0.57 (0.3)	Diff Δ*: 0.1

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-UpMean (SD), Mean Change	Comparison
Some concerns	(24 wk)	0.6 (0.2), 0.1*	0.52 (0.2), 0.0*	
Physical Performance				
Carvalho, 2019[58] AR High	Number of Steps up/down (25 cm height)	97.6 (16.4) 4 wk: 112.1 (15.0), 14.5* 7 wk: 112.6 (12.1), 15.0*	93.0 (36.1) 4 wk: 95.7 (35.9), 2.7* 7 wk: 103.4 (30.9), 10.4*	Diff Δ*: 4 wk: 11.8 7 wk: 4.6
Collado-Mateo, 2017b[61] AR Some concerns	TUG (8 wk)	6.7 (0.9) 6.2 (0.6), -0.5*	6.7 (0.8) 6.9 (1.1), 0.2*	Diff Δ*: -0.7
	Functional reach (cm) (8 wk)	19.7 (7.5) 23.0 (5.2), 3.3*	19.5 (5.7) 18.4 (6.6), -1.1*	Diff Δ*: 4.4
Polat, 2021[57] AR	6-minute walk test (m)	467.0) 6.7 (1.3), -0.8*	443.2.8), 1.0*	Diff Δ*: -1.8
Villafaina, 2019[59]; Martin-Martinez, 2019[62] AR Some concerns	TUG (24 wk)	7.5 (2.0) 6.7 (1.3), -0.8*	7.7 (1.6) 8.8 (2.8), 1.0*	Diff Δ*: -1.8
	6-minute walk test (m)	491.2 (80.2) 24 wk: 506.5 (70.2), 15.3* 48 wk: 499.7 (80.1), 8.6*	517.5 (58.4) 24 wk: 498.2 (68.5), -19.2* 48 wk: 481.7 (92.3), -35.8*	Diff Δ*: 24 wk: 34.6 48 wk: 44.3
	Sit-to-stand test	10.9 (2.9) 24 wk: 11.8 (2.5), 0.8* 48 wk: 11.1 (2.7), 0.2*	11.67 (2.5) 24 wk: 11.00 (2.4), -0.7* 48 wk: 11.00 (2.9), -0.7*	Diff Δ*: 24 wk: 1.5 48 wk: 0.8
	10 step stair test (s)	5.4 (2.8) 24 wk: 5.2 (2.1), -0.2* 48 wk: 5.3 (1.8), -0.2*	5.5 (1.9) 24 wk: 5.6 (2.3), 0.1* 48 wk: 5.9 (2.3), 0.4*	Diff Δ*: 24 wk: -0.4 48 wk: -0.6

Notes. *Calculated by review team.

Abbreviations. 5D=5 dimension; 5L=5 level; BPI=Beck Pain Inventory; cm=centimeters; Diff Δ= difference in change scores; EuroQoL-5D=European Quality of Life 5 Dimensions; FIQ=Fibromyalgia Impact Questionnaire; FIQR= 2009 Revised Fibromyalgia Impact Questionnaire; SD=standard deviation; TUG=timed up and go test; VAS=Visual Analogue Scale; wk=weeks.

APPENDIX H. CHRONIC KNEE PAIN

Appendix Table H1. Detailed Characteristics for Included Trials on Chronic Knee Pain

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
VR Intervention				
Ozlu, 2023[65] High 7 weeks Kutahya Health Sciences University, Turkey No funding	**Inclusion**: Age between 40 and 64 years American College of Rheumatology concordant diagnosis of stage 2 or 3 knee OA Minimental status test score of ≥22 **Exclusion:** Recent or previous operation on the affected lower extremity History of lower extremity injury including fracture, meniscus and/or ligament tear History of intra-articular injection to the affected knee in preceding 6 months, knee physical therapy in preceding 6 months History of rheumatological disease, septic arthritis, cardiovascular disease or other impairment affecting ability to exercise, balance, hearing or vision	N=41 Age, mean (SD): 53.3(10.4) Female: 48.6% Clinic 15 mins VR (in addition to time for ultrasound and TENS) per day, 5 days a week (total 15 sessions) 3 weeks Fish Game: Participants wear Oculus VR glasses and intercept incoming virtual fish using lateral flexion movement of the trunk. Training focused on weight transfer, balance and proprioception of the patients. Monkey Game: Participants wear Oculus VR glasses and intercept incoming virtual bananas using lateral stepping movements. Training focused on patient depth sense.	N=41 Age, mean (SD): 53.7(9.7) Female: 68.4% Clinic 27 mins per day, 5 days/week (total 15 sessions) 3 weeks Therapeutic ultrasound to affected knee for 7 minutes Transcutaneous electrical nerve stimulation on both knees for 20 minutes	**Primary outcome NR** **Pain-related functioning (3, 7 wk)** • WOMAC **Pain intensity (3, 7 wk)** • VAS **Physical performance (3, 7 wk)** • 6-min walk • Berg Balance Scale

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
AR Interventions				
Elshazly, 2016[66] Some concerns 8 weeks Prince Sattam Bin Abdul Aziz University, Saudi Arabia Grant from deanship of scientific research, Prince Sattam Bin Abdul Aziz University, Saudi Arabia	**Inclusion**: Male and Female Age between 35 and 65 years ≥ 3 months of symptomatic osteoarthrits Ambulate at least 30 feet with or without assistance Not in any sports or physical therapy Able to complete physical therapy three times weekly **Exclusion:** Acute medical illness or knee surgery within 6 months of enrollment History of metal implants, peripheral vascular disease, infection, fever, mental deficit, femur or tibial condyle fracture, joint effusion, laboratory abnormality, systemic or psychiatric illness, corticosteroid use in the preceding 30 days, malignancy, gout or any other disease preventing participation	AR Physical Activity: N=20 Age, mean (SD): 58(6) NR NR 15-30 minute sessions, 3 times weekly 8 weeks Light Race: Participants use Xbox 360 Kinect to step on a virtual platform displayed on a monitor. On-screen commands have participants step forward, backward, right and left in both sitting and standing positions for 10 repetitions with a two-minute rest between exercises. Exercises focused on lower limb strength, flexibility, coordination, and balance. Sessions were held in small groups of three or less subjects	Sensorimotor Training (SMT): N=20 Age, mean (SD): 60(8) NR NR 3 times weekly; 8 weeks Participants were trained through three stages: Static [ie, standing upright position (30 s), single leg stance with closed eyes, half-step position for 10 s, one-leg balance for 10 s] Dynamic [ie, forward stepping thrust, T-band kicks exercise], Functional [ie, 1) walking exercise on a firm surface, then on a foam surface: (a) toe skipping, (b) heel skipping; 2) squatting exercise: (a) against a wall and away from the wall, (b) one leg squats on affected and non-affected limbs; 3) balance exercise on wobble board: (a) multidirectional rolling movement from sitting, (b) multidirectional rolling movement from standing on both legs between parallel bars with eyes open, then eyes	**Primary outcome NR** **Pain-related functioning (4, 8 wk)** • WOMAC **Pain intensity (4, 8 wk)** • VAS **Physical performance (4, 8 wk)** • Position sense **Quality of life (4, 8 wk)** • CDC Health Related Quality of Life

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
			closed, (c) multidirectional rolling movement from standing on one leg between parallel bars with eyes open, then eyes closed]."	
			Conventional Exercise Therapy (CET): N=20 Age, mean (SD): 59(7) NR NR 3 times weekly; 8 weeks 5 minutes warm up followed by 12 minutes of walking at comfortable pace and 5 minutes cool down.	
Lin, 2020[67] Some concerns 3 months Shin Kong Wu Ho-Su Memorial Hospital, Taiwan	**Inclusion**: Age 40 to 85 years American College of Rheumatology concordant diagnosis of knee OA Kellgren and Lawrence score ≥2 Able to walk > 15 m	N=40 Age, mean (SD): 55.9(15.8) Female: 60% Clinic 3 times per week; 4 weeks	N=40 Age, mean (SD): 58.1(16.9) Female: 42.5% Clinic 3 times per week; 4 weeks	**Primary: WOMAC (only separate domain scores for pain, stiffness, & function)** **Pain intensity (2, 4, 8, 16 wk)** • Chronic Pain Grade Questionnaire- overall grade; disability points; disability score; pain intensity **Adverse events (4 wk)**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Grants from Shin Kong Wu Ho-Su Memorial Hospital and Ministry of Science and Technology, Taiwan	Able to undergo 4 weeks of treatment and 3 months of follow-up Not needing non-steroidal anti-inflammatory drugs during the research **Exclusion:** Any infection, inflammation, autoimmune disease, or fracture History or underlying disease affecting posture and balance, such as malignancy, dizziness, vertigo, or stroke History of any knee operation or internal fixation Pregnancy or planning to become pregnant Undergoing any other treatment for knee OA."	Hot packs applied to both knees for 20 min, transcutaneous electric nerve stimulation (TENS) for 20 min, 20 min of active video games or therapeutic exercise Whack-a-mole: Participants use Hot Plus gaming system and a step sensing pad. Participants step on step sensing pad to stamp on-screen moles into holes. Training focused on fast movement and improving lower limb range of motion, strength and coordination. Activity lasts 10 minutes. Archery: Participants use Hot Plus gaming system and a step sensing pad. Participant steps on sensing pad to shoot arrows at on-screen targets. Training focused on fast movement and improving lower limb range of motion, strength, and coordination. Activity last 10 minutes.	Hot packs applied to both knees for 20 min, transcutaneous electric nerve stimulation (TENS) for 20 min, 20 min of active video games or therapeutic exercise Therapeutic exercise includes stretching warm-up, stabilization exercises, weight-shift training for knees and pelvis …, cycling for 10 min with approximately 40% to 60% heart rate reserve, and stretching cool-down. Sandbag and Thera-band were used in strength exercises with a maximum of 10 repetitions and 5 to 10 repetitions per session, for 3 to 5 sets. Activity lasts for a total of 20 min and supervised by physical therapists.	• Non-specific adverse events **Physical performance (2, 4, 8, 16 wk)** • Biodex Stability System, Postural Stability & Limits of Stability, • 10 m walk • Stair ascent, descent times **Quality of life (2, 4, 8, 16 wk)** • WHOQOL-BREF (domain scores for physical, psychological, social, & environmental) **Other non-eligible outcomes reported** • HADS • Multidimensional Fatigue Inventory • Work Ability Index
Mete, 2022[68] High 6 Weeks Physical therapy and rehabilitation clinic of medical center (name NR) in Istanbul, Turkey	**Inclusion**: Aged 40 to 65 years Diagnosis of knee OA Kellgren Lawrence stage 2 or 3 **Exclusion:** History of surgery at knee, hip, ankle, or/and foot, systemic anti-inflammatory joint	N=32 Age, mean (SD): NR Median age: 59.5 (55,64) Female: 80% Clinic 20 games for 5 days per week; 6 weeks	N=32 Age, mean (SD): NR Median age: 57 (51, 65) Female: 76.6% Clinic 5 days per week; 6 weeks	**Primary outcome NR** **Pain related functioning or interference (6 wk)** • WOMAC-stiffness • WOMAC-function **Pain intensity (6 wk)** • WOMAC-pain • VAS **Pain Catastrophizing (6 wk)** • TSK

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Marmara University Scientific Research Projects Committee (Project Number: SAG-C-YLP-070617-0349)	disease, any condition with contraindication for electrical stimulation and/or exercise, previous knee physiotherapy in preceding 6 months and a history of corticosteroid injection in preceding 3 months	Crazy Wings: Participant controls an on-screen bird avatar through obstacles using knee movement. Sensors from the MarVAJED system were placed above and below knee, which evaluate the ROM of the joints, analyze the sensation of joint position, and allow control of on-screen avatars. Knee flexion and extension triggers bird avatar movement up and down, respectively. Training aimed to have participants complete squat exercises. Blasting Ball: Participant controls the size of a virtual ball size on a screen through knee flexion. Sensors from the MarVAJED system were placed above and below knee, which evaluate the ROM of the joints, analyze the sensation of joint position, and allow control of on-screen avatars. The ball would explode when the degree of knee flexion reached a peak value. Training aimed to have participants complete leg press exercises and increase degree of knee flexion.	Electrotherapy, exercise program, hot and cold pack therapy, therapeutic ultrasound, and conventional transcutaneus electrical nerve stimulation were completed. Participants with edema were treated with a cold pack, and participants without edema received hot pack. Exercise program consists of isometric strengthening of the quadriceps muscle, terminal knee extension, leg press exercise with elastic band, and hamstring stretching. Elastic band training involved 3 sets of 10 repetitions.	**Physical performance (6 wk)** • PEDALO Sensamove balance score • Knee flexion/extension ROM • Knee proprioception at 30, 60 degrees • Peak torque of knee flexion/extension (absolute and normalized to body weight) at 120°, 240°
Nambi, 2020c[69] Some concerns 3 months Prince Sattam Bin Abdulaziz University Hospital and King Khalid	**Inclusion:** Male gender Age 18 to 25 years ≥3 months post-traumatic osteoarthritis following ACL injury as diagnosed by an orthopedic surgeon	N=20 Age, mean (SD): 22.8(1.3) NR Clinic 2 20-minute sessions per day, 5 days a week; 4 weeks	SMT: N=20 Age, mean (SD): 22.6(1.4) NR Clinic	**Primary outcome NR** **Pain related functioning or interference (4, 8 wk, 3 mo)** • WOMAC-total **Pain intensity (4, 8 wk, 3 mo)** • VAS

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Hospital, Al-Kharj, Saudi Arabia Deanship of Scientific Research at Princess Nourah bint Abdulrahman University through the Fast-track Research Funding Program	Pain rating 4 to 8 in visual analog scale (VAS) **Exclusion:** Other orthopedic, neural, systemic, psychological diagnosis Any pending surgical procedure Participation in any other treatment and physical training	Participants used the Pro-Kin system PK 252 N Techno body. Training involved standing on the affected limb and following commands on a computer display screen to shoot virtual balls. Interaction with balls was controlled by having the participant follow specified knee movements.	5 days per week; 4 weeks Sensorimotor training exercises in three consecutive stages: Static phase where the participant stands straight for 30 seconds on a hard plate and 30 seconds on a foam plate. Next, the participant was instructed to stand on a single leg (affected side) with closed eyes for 20 seconds on a hard plate and 20 seconds on a foam plate, followed by a semi knee bending position for 10 seconds. Dynamic phase where the participant performs forward kicking for 30 seconds and T-band kicking for 30 seconds. Functional phase where the participant was informed to do toe jumping for 20 meters and heel jumping for 20 meters. Then the participant performs bilateral and unilateral squatting exercises for 10 repetitions with and without the support of a wall. All exercises were continued for 3 sets each with 5 repetitions and 3 minutes rest between the sets. Control, Supervised Exercise: N=20 Age, mean (SD): 21.9(1.3) NR Clinic or health care facility 5 days per week; 4 weeks	**Other non-eligible outcomes reported** • Bone morphogenic protein levels (BMP 2,4,5 and 7) • Inflammatory biomarkers serum levels (CRP, TNF-alpha, IL2, IL4 and IL6)

Author, Year Risk of Bias Follow-Up Duration Site(s) Funding source	Inclusion/Exclusion Criteria	Intervention: Participants Randomized Demographics Setting Frequency; Duration Detailed Intervention Characteristics	Comparator(s): Participants Randomized Demographics Setting Frequency; Duration Detailed Comparator Characteristics	Primary Outcome Eligible Outcomes & Measures Reported (Time Points) Other Non-Eligible Outcomes Reported
			Control group completed supervised conventional exercise programs for the knee muscles. Exercises laid special stress on the quadriceps, hamstrings, glutei, and calf muscles. The participants performed 10–15 repetitions in one set for 3 sets with 1 minute rest between the sets. Then participants completed stretching focused on each muscle group for 3 repetitions for 15 seconds per muscle group"	

Abbreviations. ACL=anterior cruciate ligament; AR=augmented reality; BMP=bone morphogenic protein; CET=conventional exercise therapy; CDC=Centers for Disease Control and Prevention; CRP=C reactive protein; HADS=Hospital Anxiety and Depression Scale; IL=interleukin; m=minutes; MarVAJED=Marmara visual auditory joint education device; Nm=Newton meter; NR=not reported; OA=osteoarthritis; PTOA=post-traumatic osteoarthritis; ROM=range of motion; s=seconds; SD=standard deviation; TENS= transcutaneous electric nerve stimulation; TNF=tumor necrosis factor; US=ultrasound; VAS=visual analogue scale; VRT=virtual reality training; WHO-BREF=World Health Organization Quality of Life-Brief Version; WOMAC=Western Ontario and McMaster Universities Arthritis Index.

Appendix Table H2. Detailed Results for Chronic Knee Pain Studies

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
Pain-Related Functioning or Interference				
Elshazly, 2016[66] AR Some concerns	WOMAC-total	71.6 (3.4) 4 wk: 39.8 (7.8), -31.9* 8 wk: 14.6 (3.1), -57.0*	Sensorimotor training (SMT) 71.7 (2.8) 4 wk: 53.3 (3.8), -18.4* 8 wk: 34.1 (3.9), -37.6*	Diff Δ*: 4 wk: -13.5 8 wk: -19.5
			Conventional exercise training (CET) 71.9 (3.05) 4 wk: 54.1 (6.1), -17.8* 8 wk: 44.8 (4.3), -27.2*	Diff Δ*: 4 wk: -14.05 8 wk: -29.9
Lin, 2020[67] AR Some concerns	WOMAC-function	505.1 (328.4) 2 wk: 520.3 (296.7),15.2* 4 wk: 510.6 (303.5), 5.5* 8 wk: 472.5 (300.1), -32.6* 16 wk: 456.4 (298.2), -48.7*	581.0 (383.8) 2 wk: 557.1 (218.5), -23.9* 4 wk: 526.2 (314.6), -54.8* 8 wk: 458.4 (331.1), -122.6* 16 wk: 449.5 (220.2), -131.5*	Diff Δ*: 2 wk: 39.1 4 wk: 60.3 8 wk: 90.0 16 wk: 82.8
	Graded Chronic Pain Scale, Overall Pain Grade	1.5 (0.4) 2 wk: 1.3 (0.3), -0.2* 4 wk:1.2 (0.3), -0.3* 8 wk:1.2 (0.2), -0.3* 16 wk: 1.0 (0.2), -0.5*	1.4 (0.5) 2 wk: 1.4 (0.4), 0.0* 4 wk: 1.2 (0.1), -0.2* 8 wk: 1.3 (0.3), -0.1* 16 wk: 1.1 (0.2), -0.3*	Diff Δ*: 2 wk: -0.2 4 wk: -0.1 8 wk: -0.2 16 wk: -0.2
	Graded Chronic Pain Scale, disability score	38.6 (20.8) 2 wk: 35.7 (20.3), -2.9* 4 wk: 34.2 (21.2), -4.4* 8 wk: 33.2 (19.3), -5.4* 16 wk: 34.4 (19.2), -4.2*	39.3 (21.5) 2 wk: 38.3 (21.7), -1.0* 4 wk: 37.6 (20.4), -1.7* 8 wk: 36.7 (19.6), -2.6* 16 wk: 35.6 (20.3), -3.7*	Diff Δ*: 2 wk: -1.9 4 wk: -2.7 8 wk: -2.8 16 wk: -0.5
Mete, 2022[68] AR High	WOMAC-total	Means NR Medians (IQR): 19.7 (18.2, 21) 6 wk: 7.59 (4.95, 9.4)	Means NR Medians (IQR): 15.1 (9.3, 18) 6 wk: 9.9 (6.4, 11.5)	Diff Δ: NC
	WOMAC-function	Means NR Medians (IQR): 6.74 (6.4, 7.2) 6 wk: 2.35 (2, 3.38)	Means NR Medians (IQR): 5.2 (5.7, 6.4) 6 wk: 3.23 (2.45, 3.18)	Diff Δ: NC
Nambi, 2020c[69] AR Some concerns	WOMAC-total	72.33 (4.2) 4 wk: 34.1 (3.4), -38.2* 8 wk: 22.4 (2.1), -49.9* 3 mo: 11.2 (2.1), -61.1*	SMT: 72.47 (4.5) 4 wk: 56.3 (3.8), -16.2* 8 wk: 32.4 (2.8), -40.1* 3 mo: 25.3 (2.1), -47.2*	Diff Δ*: 4 wk: -22.1 8 wk: -9.8 3 mo: -13.9
			CET: 71.2 (3.8) 4 wk: 62.3 (3.2), 8 wk: 52.3 (3.2), -18.9* 3 mo: 35.2 (2.8), -36.0*	Diff Δ*: 4 wk: -29.3 8 wk: -30.9 3 mo: -25.1

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
Ozlu, 2023[65] VR High	WOMAC-total	31.66 (6.75) 3 wk: 23.1 (8.7), -8.6* 7 wk: 26.4 (9.4), -5.2*	33.0 (7.86) 3 wk: 33.1 (7.9), 0.1* 7 wk: 32.9 (7.9), -0.2*	Diff Δ*: 3 wk: -8.7 7 wk: -5.0
Pain Intensity or Severity				
Elshazly, 2016[66] VR Some concerns	VAS	6.81 (0.87) 4 wk: 3.7 (1.1), -3.1* 8 wk: 2.9 (0.97), -3.9*	SMT: 6.62 (1.17) 4 wk: 5.4 (0.96), -1.2* 8 wk: 4.5 (0.8), -2.1*	Diff Δ*: 4 wk: -1.9 8 wk: -1.8
			CET: 6.68 (0.84) 4 wk: 5.37 (0.9), -1.3* 8 wk: 4.74 (0.7), -1.9*	Diff Δ*: 4 wk: -1.8 8 wk: -1.97
Lin, 2020[67] AR Some concerns	WOMAC-pain	161.2 (114.7) 2 wk: 160.9(109.4), -0.3* 4 wk: 155.6 (103.1), -5.6* 8 wk: 119.8 (89.5), -41.4* 16 wk: 102.3 (88.9), -58.9*	170.2 (121.3) 2 wk: 169.2 (120.1), -1.0* 4 wk: 160.7 (118.2), -9.5* 8 wk: 148.7 (106.7), -21.5* 16 wk: 106.4 (97.3), -63.8*	Diff Δ*: 2 wk: 0.7 4 wk: 3.9 8 wk: -19.9 16 wk: 4.9
	WOMAC-stiffness	76.9 (60.4) 2 wk: 74.3 (59.1), -2.6* 4 wk: 72.8 (56.7), -4.1* 8 wk: 69.9 (52.2), -7.0* 16 wk: 64.4 (52.1), -12.5*	65.2 (53.7) 2 wk: 66.1 (52.4), 0.9* 4 wk: 67.2 (53.2), 2.0* 8 wk: 61.6 (51.6), -3.6* 16 wk: 63.4 (55.7), -1.8*	Diff Δ*: 2 wk: -3.5 4 wk: -6.1 8 wk: -3.4 16 wk: -10.7
	Graded Chronic Pain Scale, pain intensity	47.8 (20.3) 2 wk: 42.5(19.5), -5.3* 4 wk: 46.2 (19.3), -1.6* 8 wk: 44.6 (20.1), -3.2* 16 wk: 43.3 (19.4), -4.5*	48.4 (20.7) 2 wk: 49.7 (19.5), 1.3* 4 wk: 48.2 (21.2), -0.2* 8 wk: 47.3 (19.1), -1.1* 16 wk: 46.5 (18.2), -1.9*	Diff Δ*: 2 wk: -6.6 4 wk: -1.4 8 wk: -2.1 16 wk: -2.6
Mete, 2022[68] AR High	VAS at rest	Means NR Medians (IQR): 32.2 (20.75, 40 6 wk: 10 (0, 12.5)	Means NR Medians (IQR): 36.6 (30, 40) 6 wk: 20 (10, 20)	Diff Δ: NC
	VAS with activity	Means NR Medians (IQR): 74.2 (60, 80) 6 wk: 30 (30, 40)	Means NR Medians (IQR): 65.2 (50, 70) 6 wk: 40 (30, 40)	Diff Δ: NC
	VAS at night	Means NR Medians (IQR): 43 (27.5, 40) 6 wk: 10 (0, 20)	Means NR Medians (IQR): 44 (20, 50) 6 wk: 20 (10, 30)	Diff Δ: NC
	WOMAC-pain	Means NR Medians (IQR): 6 (5.37, 7.12) 6 wk: 2.25 (1.5, 3)	Means NR Medians (IQR): 4.5 (4.3, 6) 6 wk: 3 (2.5, 4)	Diff Δ: NC
Nambi, 2020c[69] AR Some concerns	VAS	7.2 (0.5) 4 wk: 3.3 (0.4), -3.9* 8 wk: 2.5 (0.4), -4.7*	SMT: 7.4 (0.4) 4 wk: 5.8 (0.5), -1.6* 8 wk: 3.5 (0.5), -3.9*	Diff Δ*: 4 wk: -2.3 8 wk: -0.8

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
		3 mo: 0.5 (0.3), -6.7*	3 mo: 1.5 (0.4), -5.9*	3 mo: -0.8
			Control: 7.3 (0.4) 4 wk: 6.5 (0.5), -0.8* 8 wk: 4.2 (0.5), -3.1* 3 mo: 3.8 (0.4), -3.5*	Diff Δ*: 4 wk: -3.1 8 wk: -1.6 3 mo: -3.2
Ozlu, 2023[65] VR High	Visual analog scale (VAS)	5.57 (0.88) 3 wk: 4.11 (1.34), -1.46* 7 wk: 4.05 (0.72), -1.52*	5.78 (0.74) 3 wk: 5.05 (1.43), -0.73* 7 wk: 5.36 (0.99), -0.42*	Diff Δ*: 3 wk: -0.73 7 wk: -1.1
Adverse Events				
Lin, 2020[67] AR Some concerns	Adverse effects (during 4 wks of intervention)	"No adverse effects were reported during or after treatment in either group."		NR
Pain Catastrophizing & Kinesiophobia				
Mete, 2022[68] AR High	TSK	Means NR Medians (IQR): 46.5 (42.7, 50) 6 wk: 39 (36.7, 40)	Means NR Medians (IQR): 48 (45, 49.25) 6 wk: 45.5 (41, 48)	Diff Δ: NC
Quality of Life				
Elshazly, 2016[66] AR Some concerns	CDC Health Related Quality of Life	1.35 (0.48) 4 wk: 3.1 (0.5), 1.8* 8 wk: 4.5 (0.6), 3.2*	SMT: 1.60 (0.50) 4 wk: 2.5 (0.5), 0.9* 8 wk: 3.3 (0.5), 1.7*	Diff Δ*: 4 wk: 0.9 8 wk: 1.4
			CET: 1.6 (0.51) 4 wk: 2.2 (0.4), 0.7* 8 wk: 2.5 (0.5), 0.95*	Diff Δ*: 4 wk: 1.1 8 wk: 2.2
Lin, 2020[67] AR Some concerns	WHOQOL-BREF Physical	58.1 (10.2) 2 wk: 58.4 (9.1), 0.3* 4 wk: 59.2 (7.4), 1.1* 8 wk: 59.3 (7.5), 1.2* 16 wk: 61.1 (6.6), 3.0*	53.4 (12.1) 2 wk: 53.1 (11.5), -0.3* 4 wk: 53.2 (11.2), -0.2* 8 wk: 54.1 (10.3), 0.7* 16 wk: 54.5 (10.9), 1.1*	Diff Δ*: 2 wk: 0.6 4 wk: 1.3 8 wk: 0.5 16 wk: 1.9
	WHOQOL-BREF Psychological	57.2 (10.4) 2 wk: 57.5 (10.1), 0.3* 4 wk: 58.1 (9.6), 0.9* 8 wk: 58.4 (9.7), 1.2* 16 wk: 60.0 (9.4), 2.8	58.7 (9.8) 2 wk: 58.9 (9.8), 0.2* 4 wk: 59.0 (9.4), 0.3* 8 wk: 59.4 (8.9), 0.7* 16 wk: 60.2 (8.8), 1.5	Diff Δ*: 2 wk: 0.1 4 wk: 0.6 8 wk: 0.5 16 wk: 1.3
	WHOQOLBREF, social	57.3 (12.60) 2 wk: 57.4 (11.2), 0.1* 4 wk: 58.2 (10.8), 0.9* 8 wk: 58.4 (10.1), 1.1* 16 wk: 60.3 (9.9), 3.0*	54.4 (12.60) 2 wk: 55.9 (13.9), 1.5* 4 wk: 55.9 (14.4), 1.5* 8 wk: 57.3 (13.7), 2.9* 16 wk: 57.4 (13.2), 3.0*	Diff Δ*: 2 wk: -1.4 4 wk: -0.6 8 wk: -1.8 16 wk: 0.0

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
	WHOQOL-BREF, environmental	60.4 (9.8) 2 wk: 60.8 (9.9), 0.4* 4 wk: 61.1 (10.1), 0.7* 8 wk: 61.3 (9.2), 0.9* 16 wk: 61.9 (9.3), 1.5*	58.9 (10.6) 2 wk: 59.2 (10.2), 0.3* 4 wk: 59.3 (9.8), 0.4* 8 wk: 59.7 (10.1), 0.8* 16 wk: 60.2 (9.6), 1.3*	Diff Δ*: 2 wk: 0.1 4 wk: 0.3 8 wk: 0.1 16 wk: 0.2
Physical Performance				
Elshazly, 2016[66] VR Some concerns	Position sense	118.9 (4.60) 4 wk: 127.6 (2.06), 8.7* 8 wk: 134.0 (1.16), 15.1*	SMT: 120.5 (4.16) 4 wk: 123.5 (2.28), 3.0* 8 wk: 127.0 (1.93), 6.5*	Diff Δ*: 4 wk: 5.7 8 wk: 8.6
			CET: 120.95 (3.79) 4 wk: 123.1 (3.29), 2.15* 8 wk: 124.45 (2.96), 3.5*	Diff Δ*: 4 wk: 6.6 8 wk: 11.6
Lin, 2020[67] AR Some concerns	Biodex Stability System, Postural Stability	0.7 (0.5) 2 wk: 0.6 (0.4), -0.1* 4 wk: 0.6 (0.5), -0.1* 8 wk: 0.5 (0.3), -0.2* 16 wk: 0.5 (0.2), -0.2*	0.8 (0.4) 2 wk: 0.7 (0.5), -0.1* 4 wk: 0.6 (0.4), -0.2* 8 wk: 0.5 (0.3), -0.3* 16 wk: 0.5 (0.4), -0.3*	Diff Δ*: 2 wk: 0.0 4 wk: 0.1 8 wk: 0.1 16 wk: 0.1
	Biodex Stability System, Limits of Stability	40.2 (12.9) 2 wk: 41.0 (12.6), 0.8* 4 wk: 42.1 (12.1), 1.9* 8 wk: 43.4 (11.5), 3.2* 16 wk: 45.5 (10.7), 5.3*	41.5 (12.7) 2 wk: 42.1 (14.8), 0.6* 4 wk: 41.9 (14.1), 0.4* 8 wk: 42.6 (13.2), 1.1* 16 wk: 44.3 (12.4), 2.8*	Diff Δ*: 2 wk: 0.2 4 wk: 1.5 8 wk: 2.1 16 wk: 2.5
	10 meter walking time (s)	14.1 (7.6) 2 wk: 14.7 (6.7), 0.6* 4 wk: 12.6 (5.2), -1.5* 8 wk: 12.1 (4.9), -2.0* 16 wk: 11.2 (4.1), -2.9*	15.8 (7.3) 2 wk: 15.3 (6.4), -0.5* 4 wk:14.4 (5.9), -1.4* 8 wk: 13.9 (5.6), -1.9* 16 wk: 13.8 (4.7), -2.0*	Diff Δ*: 2 wk: 1.1 4 wk: -0.1 8 wk: -0.1 16 wk: -0.9
	Stair ascent time (s)	18.8 (10.3) 2 wk: 17.9 (10.2), -0.9* 4 wk: 17.3 (11.8), -1.5* 8 wk: 14.9 (12.7), -3.9* 16 wk: 14.8 (11.9), -4.0*	17.5 (12.3) 2 wk: 16.8 (12.7), -0.7* 4 wk: 15.9 (12.4), -1.6* 8 wk:15.5 (13.2), -2.0* 16 wk: 14.9 (10.8), -2.6*	Diff Δ*: 2 wk: -0.2 4 wk: 0.1 8 wk: -1.9 16 wk: -1.4
	Stair descent time (s)	17.9 (10.8) 2 wk: 17.8 (10.7), -0.1* 4 wk: 16.3 (10.5), -1.6* 8 wk: 15.9 (12.7), -2.0* 16 wk: 14.6 (11.9), -3.3*	15.5 (11.3) 2 wk: 15.8 (11.2), 0.3* 4 wk: 14.5 (10.4), -1.0* 8 wk: 14.3 (10.2), -1.2* 16 wk: 14.1 (9.8), -1.4*	Diff Δ*: 2 wk: -0.4 4 wk: -0.6 8 wk: -0.8 16 wk: -1.9
	Pedalo Balance Score (percentage)	Means NR Medians (IQR): 57 (50.2, 62.2) 6 wk: 75 (65, 80)	Means NR Medians (IQR): 70 (60, 78.5) 6 wk: 72.5 (63.7, 80)	Diff Δ: NC
Mete, 2022[68] AR High	Knee Flexion ROM (°) (6 wk)	Means NR Medians (IQR): 100 (95, 110.5) 6 wk: 115.5 (110 and 120)	Means NR Medians (IQR): 110 (100, 120) 6 wk: 111.5 (104.7 and 120)	Diff Δ: NC

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
	Knee proprioception at 30° (6 wk)	Means NR Medians (IQR) 6.25 (5.75, 8) 6 wk: 3.5 (3, 4)	Means NR Medians (IQR): 7 (6, 8) 6 wk: 6 (5, 7)	Diff Δ: NC
	Knee proprioception at 60° (6 wk)	Means NR Medians (IQR): 8 (6, 10) 6 wk: 4 (3, 5)	Means NR Medians (IQR): 9 (7.3, 10) 6 wk: 8 (6, 9)	Diff Δ: NC
	Peak Torque of knee flexion at 120° (normalized, Nm/kg) (6 wk)	Means NR Medians (IQR): 23.5 (14, 30) 6 wk: 36.9 (26.4, 47)	Means NR Medians (IQR): 20 (12, 26) 6 wk: 30.8 (24.3, 40.5)	Diff Δ: NC
	Peak Torque of knee extension at 120° (normalized, Nm/kg) (6 wk)	Means NR Medians (IQR): 27.9 (21.6, 39.2) 6 wk: 52.5 (43.7, 66.2)	Means NR Medians (IQR): 25.6 (17.7, 35.8) 6 wk: 40.2 (30.6, 60)	Diff Δ: NC
	Peak Torque of knee flexion at 240° (normalized, Nm/kg) (6 wk)	Means NR Medians (IQR): 16.4 (12.4, 23.5) 6 wk: 26 (21.3, 31.4)	Means NR Medians (IQR): 15.8 (10, 21.4) 6 wk: 22.12 (19, 28)	Diff Δ: NC
	Peak Torque of knee extension at 240° (normalized, Nm/kg) (6 wk)	Means NR Medians (IQR): 16.4 (13, 24.8) 6 wk: 36.8 (26.3, 44.2)	Means NR Medians (IQR): 20.3 (13.4, 26.4) 6 wk:31.7 (22.5, 39)	Diff Δ: NC
Ozlu, 2023[65] VR High	6-minute walk test (m)	525.1 (70.5) 3 wk: 525.1 (70.5), 0.0* 7 wk: 526.3 (68.5), 1.1*	530.4 (54.6) 3 wk: 531.3 (54.6), 0.9* 7 wk: 532.5 (67.3), 2.1*	Diff Δ*: 3 wk: -0.9 7 wk: -0.9
	Berg Balance Scale	42.8 (4.8) 3 wk: 45.3 (4.2), 2.5* 7 wk: 46.0 (4.0), 3.6*	42.9 (5.9) 3 wk: 43.5 (6.07), 0.6* 7 wk: 43.2 (6.0), 0.3*	Diff Δ*: 3 wk: 1.9 7 wk: 2.9

Notes. * Calculated by review team.

Abbreviations. AR=augmented reality; CET=conventional exercise training; Diff Δ= difference in change scores; IQR=interquartile range; NC=not calculable; Nm=Newton meter; NR=not reported; PT=physical therapy; ROM=range of motion; SD=standard deviation; SMT=sensorimotor training; VAS=visual analogue scale; VR=virtual reality; WHOQOL-BREF=World Health Organization Quality of Life-Brief Version; wk=weeks; WOMAC=Western Ontario and McMaster Universities Arthritis Index.

APPENDIX I. KQ1 OTHER CONDITIONS

Appendix Table I1. Detailed Characteristics for Included Trials on KQ1 Other Conditions

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding Source**	**Inclusion/Exclusion Criteria**	**Intervention: Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s): Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
VR Intervention				
Cuneo, 2023[70] High 12 weeks University of Washington headache clinic, USA Osher Center for Integrative Medicine Small Research Project Grant	**Inclusion:** "All participants met the International Classification of Headache Disorders (ICHD-3 beta) criteria for chronic migraine, as diagnosed by UW neurologists specializing in headache disorders. All subjects had experienced at least 15 headache days (including at least 8 migraine days) per month in the preceding 3 months. Additional inclusion criteria were 18 to 85 years and the ability to speak English or Spanish." **Exclusion:** "Excluded participants were those with cognitive impairment, severe psychiatric comorbidities (including active suicidal or homicidal ideation and/or psychosis), hearing/seeing difficulties, epileptic or non-epileptic seizures, and prisoners."	N=25 Age, mean (SD): 42.71 (16.07) Female: 78.6% Home 10 minutes/day, at least 3 days/week "Respiratory rate associated with the lowest LF/HF ratio was chosen as the participant's optimal respiratory rate. Then calming music with ascending tones (to cue inhalation) and descending tones (to cue exhalation) at the participant specific optimal respiratory rate was uploaded into the participant's biofeedback-VR device. The Oculus Go headset was placed on the participant's head…with the option to choose between 2 VR environments, a beach or hilltop setting…The participant was then guided through a trial biofeedback-VR session… During the 10-minute session, participants were asked to "try to improve" the appearance of their feedbacked HRV tracing so	N=25 Age, mean (SD): 42.05 (14.65) Female: 86.4% Home 10 minutes/day, at least 3 days/week Waitlist control group	**Primary: mean monthly headache days** **Pain-related functioning (12 wk)** • Migraine Disability Assessment (MIDAS) **Pain intensity/severity (12 wk)** • Monthly headache days **Pain catastrophizing (12 wk)** • Concerns About Pain (CAP) scale **Adverse events (12 wk)** • % of participants with nausea or dizziness **Non-eligible: PHQ-8; Perceived Stress Scale; Insomnia (PROMIS); total acute medication use per month (prescription and over-the-counter)**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding Source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
		that it resembled a sine wave-like curve, the “reward” reflecting synchronous entrainment of respiration and HRV.”		
Chuan, 2023[71] Some concerns 3 months Cancer Therapy Centre, Liverpool Hospital, Sydney, Australia Tour de Cure Cancer Foundation, HCF Health Foundation, and the NSW Health Department Agency for Clinical Innovation	**Inclusion:** "...treating oncologist or palliative care physician diagnosed symptoms of neuropathic pain caused by cancer or interventions for their cancer, ...aged ≥ 18 years; were functionally independent in most activities of daily living with an Eastern Cooperative Oncology Group Performance Status score ≤ 2” **Exclusion:** "Patients with psychological or psychiatric illness not stabilised with therapy or medications were excluded."	N=19 Age, mean (SD): 56 (8) Female: 58% Clinic 3 x 30-min sessions within a 4-week period "We created a bespoke virtual reality-delivered software programme that taught pain self-efficacy to patients using progressive muscle relaxation and guided pain visualisation techniques…For example, a computer-generated, anatomically correct human body highlighted the deltoid and biceps muscles of the proximal arm, asking the patient to localise tension before guiding the patient in a scripted relaxation exercise. In the pain visualisation therapy, an angry, fiery ball symbolised the patient’s neuropathic pain, evoking imagery of burning and shooting.”	N=20 Age, mean (SD): 63 (11) Female: 70% Clinic 3 x 30-min sessions within a 4-week period "Patients in the control arm were instead asked to view a selection of short documentaries and videos specifically filmed in a virtual reality format for viewing through a virtual reality headset. These publicly available videos were selected from the dedicated virtual reality channel on YouTube. In their 30-minute session, patients could choose from any of the following: a documentary on jaguars in Brazil, a documentary on the Apollo 11 moon landing, an animated cartoon in a snow environment and a car review..."	**Primary: feasibility, acceptability, recruitment rates, and risk of cybersickness** **Pain-related functioning (1 mo, 3 mo)** • BPI-Interference **Pain intensity/severity (1 mo, 3 mo)** • BPI-Intensity **Adverse events (1 mo)** • Counts of participants with dizziness, nausea, and eyestrain during any session **Quality of life (1 mo, 3 mo)** • QLQ-C30 (only global quality subscale) **Opioid use (1 mo, 3 mo)** • Average MME in the previous week **Non-eligible: feasibility, acceptability, recruitment rates, tolerability**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding Source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Darnall, 2020[72] High 22 days Community health system, United States AppliedVR Inc.	**Inclusion:** " …aged 18-75 years with self-reported chronic nonmalignant low back pain or fibromyalgia, with an average pain intensity >4 over the past month and chronic pain duration >6 months." **Exclusion:** NR	N=35 NR Female: 26% Home 21-day program with 4-8 treatment sessions from 1-15 minutes. “Treatment consisted of a variety of sessions to support participants in learning self-management skills based on evidence-based CBT principles as well as biofeedback and mindfulness strategies used in pain management. The program was designed to improve self-regulation of cognitive, emotional, and physiological responses to stress and pain and comprised 3 main content categories: skills rooted in pain CBT… relaxation training…[and] mindfulness”	N=39 NR Female: 13% Home 21-day program with 4-8 treatment sessions from 1-15 minutes. "The audio program consisted of the majority of the same narrative content contained in the VR program, with changes made to the descriptive titles for each session…. approximately one-third of the VR program could not be included verbatim in the audio. Rather, the audio session topical content was closely matched to the corresponding VR session for that day and adapted to eliminate any references to visual content that would be confusing to the listener..."	**Primary: Defense and Veterans Pain Rating Scale (DVPRS)** **Pain-related functioning (21 days)** • DVPRS-Stress, Mood, Sleep, & Activity domains **Pain intensity/severity (21 days)** • DVPRS-Pain Rating Scale **Pain catastrophizing (21 days)** • PCS (no follow-up data, only model statistics) **Adverse events (22 days)** **Pain global change (22 days)** • PGIC **Non-eligible: Pain Self-Efficacy Questionnaire, Patient satisfaction with VR**
Reynolds, 2022[73,121] Some concerns 4 weeks Community health system, New Zealand	**Inclusion:** "...required to have a diagnosis of MBC, be over 18 years, be able to physically wear and tolerate the VR headset, and have experienced symptoms of fatigue, pain, or anxiety in the week prior to enrolment..." **Exclusion**: "...any visual, hearing, or cognitive impairments that would limit their ability to take part in the study, or if	N=20 Age, mean (SD): 52.7 (13.2) Women: 100% Home	N=18 Age, mean (SD): 51.28 (9.32) Women: 100% Home	**Primary: EQ-5D-5L** **Pain-related functioning (7 days, 9 days)** • BPI-short form (11 items) **Adverse events (9 days)** **Quality of life (7 days)**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding Source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Breast Cancer Foundation New Zealand (Grant #3719356)	they could not read, speak, or write in English."	>10 minutes/day, 1 week Ripple, 1 week washout, 1 week Happy Place Randomization was to order of VR interventions.: "Group 1 used Ripple, then Happy Place (R:HP), and Group 2 experienced Happy Place before Ripple (HP:R). "Happy Place…is a commercially available VR application in which participants experience a tranquil, animated camping scene. Participants experience changes to the weather and time of day and can interact with optional tasks, guided relaxation, and soothing music. Ripple is a collection of three short 360° [and] are as follows: 1) a beach where the participant can write words in the sand or the sky; 2) a waterfall where the participant can stack stones; and 3) a mountain range where the participant can jump between different locations amongst mountaintops and lakes."	>10 minutes/day, 1 week Happy Place, 1 week washout, 1 week Ripple Happy Place, then Ripple (HP:R). There was a one-week washout period to minimise carryover effects between the two interventions..."	• EuroQoL-5D (only transformed scores) **Non-eligible: FACIT-Fatigue, DASS (Depression, Anxiety and Stress Scales), Acceptability & satisfaction questions/rating**
Wankhade, 2022[74] High 2 weeks Data Meghe Institute of Medical Sciences, Musculoskeletal OPD of Acharya, Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha, India NR	**Inclusion:** "Patients between the age group of 40-60 years…and having stage 2 or stage 3 primary or idiopathic frozen shoulder." **Exclusion:** "Patients with any post-operative history of shoulder joint, fractures, subluxations or dislocations, diabetes, rheumatoid arthritis etc."	N=25 NR NR Clinic 15-20 minute daily sessions for 2 weeks "...patients were treated with Oculus-guided physical therapy in	N=25 NR NR Clinic 15-20 minute daily sessions for 2 weeks	**Primary: not specified** **Pain-related functioning (2 wk)** • NRS **Pain intensity/severity (2 wk)** • Shoulder Pain and Disability Index (SPADI) Scale **Physical performance (2 wk)** • Shoulder flexion

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding Source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
		addition to Maitland's mobilization…Hand Physics Lab on Oculus Quest is a program that allows participants to use their hands and fingers to interact with a virtual environment as well as other goods and experiences. Various shoulder movements such as shoulder internal and external rotations can be performed with the help of this games. Shoulder extensions flexion activities can also be carried out with the help of virtual reality games. This various gaming on virtual reality is useful for improving range of motion of joint."	"...conventional therapy which included Maitland's mobilization..."	• Shoulder extension • Shoulder abduction • Shoulder adduction • Shoulder internal • Shoulder external
AR Interventions				
Ambrosino, 2020[75] Some concerns 12 weeks Intensive Orthopedic and Rheumatologic Rehabilitation Unit at an unspecified university, Italy "No funding was received"	**Inclusion:** "...40 consecutive inpatients 18–35 years of age, diagnosed with RA according to the 1987 American College of Rheumatology revised criteria 21 referring to our Intensive Orthopedic and Rheumatologic Rehabilitation Unit were enrolled. All subjects had been treated with a ''biologic'' agent (22 adalimumab, 10 golimumab, 8 etanercept) for at least 12 months before admission." **Exclusion:** "… malignancy, intolerance to exercise, unstable medical conditions, pregnancy, any condition that could compromise the patient's ability to comply with and/or perform study-related activities."	N= 20 Age, mean (SD): 27.05 (5.71) Female: 65% Home, Clinic 50 mins (10 minutes per game) once daily during acute rehab (4 weeks), then at home x 8 weeks "Participants were asked to play the five preselected Wii-Fit games (running, skiing, balloons shooting, bike slalom, balls moving through labyrinth) for 10 minutes per game, once/daily, throughout the period of hospitalization (Group A and B) and at home (Group A only). Videogames required to perform a	N=20 Age, mean (SD): 27.85 (3.41) Female: 60% Clinic Same as intervention group for 4 weeks, then "habitual activity" for 8 weeks 5 games during acute rehab (4 wk only)	**Primary: "Our study is aimed to assess the effectiveness of home exergaming with a commercially available nonimmersive videogame system as an additional rehabilitative tool in young RA patients, following a 4-week program of in hospital multidisciplinary rehabilitation."** **Pain-related functioning (12 wk)** • Health Assessment Questionnaire (HAQ) measures function & fatigue **Non-eligible: Disease Activity Score (DAS-28); Global Health**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding Source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
		wide range of exercises for upper and lower arms, including shoulder flexion/extension, abduction/adduction, internal/external rotation, circumduction, elbow flexion/extension, forearm pronation/supination, hand digit motion, weight shift back and from side-to-side, and knee and ankle flexion/extension."		**VAS; ESR; swollen & tender joint counts; FACIT-fatigue**
Ditchburn, 2020[76] High 6 weeks Teesside University's physiotherapy laboratory, United Kingdom Teesside University doctoral scholarship	**Inclusion:** "...aged 65 years or over, able to walk unassisted (*ie*, did not use, or require, any walking aids) for at least 0.5 of a mile and having musculoskeletal pain in two or more joints of more than 12 weeks duration." **Exclusion:** "...diagnosis (or suspicion) of any systemic conditions that may cause pain in two or more joints, of more than 12 weeks duration (such as cancer, rheumatic or neurological disease, or condition), self-report of current condition or self-report of history of any condition or injury which would contra-indicate participation in the exercises under study"	N=27 Age, mean (SD): 71.78 (6.1) Female: 81.5% Clinic 40 min sessions twice weekly for 6 weeks. 5 games from the IREX® system: volleyball, sharkbait, formula racing, snowboard, and birds & balls. "Each IREX® exergame was played for 2 minutes and was repeated three times within a session...In both groups participants were given rest periods of 10 to 30 s, or longer, if required, between exergames, or [traditional] exercise sets."	N=27 Age, mean (SD): 69.78 (4.48) Female: 65% Clinic 40 min sessions twice weekly, for 6 weeks. "All exercises were completed on a one-to-one basis, with the first author supervising the sessions (and exercising with the [traditional exercise group])...Those in [this] group performed exercises that were matched to the IREX® exergames for movement patterns required, physiological demands, sequence, duration and mode of exercise, by adopting open and closed kinetic chain movements, in the same range and loading, across both groups…exercise was conducted in sets of 2 minutes	**Primary: Pain & postural control/sway** **Pain intensity/severity (6 wk)** • NRS **Adverse events (6 wk)** **Physical performance (6 wk)** • Postural sway with eyes open & closed **Non-eligible: Multi Affect and Pain Survey (MAPS); acceptability measure (UTAUT); Flow State Scale; Rating of Perceived Exertion; Subjective Mental Effort Questionnaire; HR**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding Source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
			duration and was repeated three times within a session. In both groups participants were given rest periods of 10 to 30 s, or longer, if required, between exergames, or [traditional] exercise sets."	
Gouveia e Silva, 2020[77] Some concerns 11 weeks Instituto Giorgio Nicoli, Sao Paulo, Brazil Coordination for Improvement of Higher Education Personnel—Brazil (CAPES)	**Inclusion:** "...individuals with a diagnosis of [post-polio syndrome] established by the consensus of Halstead and Rossi; 40–75 years of age, muscle strength degree >=3 in shoulders and elbows; motor function impairment (Motor Function Measure (MFM)-32 <=81), and who were not performing rehabilitation or physical exercise during intervention." **Exclusion:** "Individuals with clinically assessed shoulder subluxation by palpation (>=2 fingers), upper limb deformities that made it difficult to perform the interventions, and people who were not available to perform the 14 intervention sessions..."	N=19 Age, mean (SD): 54.94 (9.34) Female: 52.5% Clinic 50 min sessions twice weekly x 7 weeks, totaling 14 sessions "[Interactive video game group] participants were positioned in front of a 32" TV placed 1.2m away and attached to the wall, 1.5m from the ground…Participants were then provided with two opportunities to practice for each game. Each game was performed with the help of the researcher who corrected the movements and posture of participants through guidance and verbal commands, instructing them to carry out each movement correctly, to reach the goal of the game. Each game was played for*10 minutes. Players reproduced the movements of each sport."	N=20 Age, mean (SD): 55.58 (8.08) Female: 55% Clinic 50 min sessions twice weekly x 7 weeks, totaling 14 sessions "[Active Exercises Group] performed similar movements required for playing the four videogames of the IVG... The AEG intervention included upper limb active exercises involving shoulder, elbow, and trunk, in blocks of 8 minutes with a 2-minute rest interval between the exercises (to avoid muscle fatigue)."	**Primary: Motor Function Measure-32 (MFM-32)** **Pain intensity (7 wk, 11 wk)** • VAS **Adverse events (11 wk)** • Count of events such as upper limb pain, dizziness, nausea, and vomiting **Physical performance (7 wk, 11 wk)** • Box and Block • Functional Reach Assessment **Non-eligible: MFM-32; Functional Independence Measure (FIM); Fatigue Severity Scale; acceptability questions**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding Source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Karahan, 2016[78] Some concerns 8 weeks Physical Medicine and Rehabilitation Outpatient Clinic of Beyhekim State Hospital, Turkey NR	**Inclusion:** "aged 18–65, lack of regular exercise habits during the previous six months." **Exclusion:** "the presence of cardiopulmonary dysfunction that hinders aerobic exercise, such as acute congestive heart failure, unstable angina pectoris, third-stage cardiac block, etc.; regular exercise habits during the previous six months; the presence of central or peripheral neurological disease; the presence of issues hindering standing, such as previous surgery on the lower extremities; the presence of a diagnosed serious psychiatric disorder; the presence of a serious visual disorder; the presence of a serious hearing disorder."	N=28 Age, mean (SD): 36.1 (12.4) Female: 14% Clinic 30 minutes/day, 5 days a week for 8 weeks (40 sessions in total) ""Kinect Adventures," "Kinect Sports" and "Kinect Sports Season Two" video game programs, which include soccer, table tennis, skiing, tennis, golfing, volleyball, and bowling simulations...."	N=29 Age, mean (SD): 36.6 (11.3) Female: 21% Clinic N/A\ No exercises or other treatments	**Primary: Not clearly specified but pain at rest and during activity via VAS, change in BASFI score were listed first** **Pain-related functioning (8 wk)** • Bath Ankylosing Spondylitis Functional Index (BASFI) **Pain intensity/severity (8 wk)** • VAS **Quality of life (8 wk)** • Ankylosing Spondylitis Quality of Life (ASQOL) questionnaire **Non-eligible: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)**
Lewis, 2021[79] High 6 weeks Clinics at The Royal National Hospital for Rheumatic Disease, Royal United Hospitals Bath NHS Foundation Trust, Bath and Walton Center NHS Foundation Trust, CRPS UK network registry, United Kingdom	**Inclusion:** "Met the Budapest clinical diagnostic criteria for CRPS affecting one upper limb; aged 18 or over" **Exclusion:** "…had no co-morbidity that might influence CRPS symptoms, *ie*, stroke, diabetes, and fibromyalgia."	N=23 Age, mean (SD): 52 (11) Female: 65% Clinic 5 sessions comprising 4 weekly intervention sessions and a final follow-up session 2 weeks later "...participants sat with each arm placed into one of the two apertures	N=22 Age, mean (SD): 52 (14.5) Female: 64% Clinic 5 sessions comprising 4 weekly intervention sessions and a final follow-up session 2 weeks later "The procedure and duration (approx. 1 min) for non-	**Primary: body perception disturbance, pain intensity rating scale, and perceptual statement ratings** **Pain intensity/severity (1 wk, 6 wk)** • NRS **Non-eligible: Body perception disturbance, perceptual statement ratings**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding Source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
National Institute for Health Research		of the MIRAGE system so that both hands rested palm down on a flat surface within the system... In response to the specific description given by each participant, changes were made in real time to aspects of shape, size and/or colour of the hand, based on how they wished their hand to look, i.e., their desired hand appearance. Participants rated their satisfaction of hand appearance whilst looking at the hand image...the image was further altered to...better match the participant's desired hand appearance. Once they were satisfied, participants viewed the resultant image for 1 min. No visual changes were made to the unaffected hand..."	manipulation was exactly the same as that described in i) manipulated condition by the operator appearing to click the computer keys with the exception that the image was not actually visually altered, although the participant believed it to have been.... The hand image was viewed for 1 min and followed by post-intervention data collection."	
Rothangel, 2018[80] Some concerns 6 months Cologne University; 6 rehabilitation clinics, 2 private practices and 1 hospital, Germany "State of North Rhine-Westphalia (NRW, Germany) and the European Union through the NRW Ziel2 Programme as a part of the European Regional Development Fund (grant no. 005-GW02-035)"	**Inclusion:** "...adult patients who had a unilateral lower limb amputation and reported an average intensity of PLP of 3 or more on the 11-point NRS and minimally one episode of PLP per week...No restrictions were made regarding gender, age, type of pain sensation or the time since amputation...eligible patients needed to have sufficient cognitive and communicative skills and motor functions in order to use the teletreatment, follow instructions and understand and fill out questionnaires." **Exclusion:** "...comorbidity such as stroke, pain or limited range of motion in the intact limb, severe mental disorders (*eg*, PTSD), living >50 km away from a	N=26 Age, mean (SD): 59.7 (16.1) Clinic, home 10 sessions (each 30-minutes) during first 4-weeks delivered by therapist, self-delivered exercises using iPad at home for 6 weeks "During the first four weeks, [participants] performed exercises from the following categories with the intact limb in front of the mirror: observation of different positions, basic motor exercises, exercises using sensory stimuli, motor	Mirror Therapy N=25 Age, mean (SD): 62.5 (11.4) Clinic, home 10 sessions (30-minute each) during first 4-weeks, delivered by therapist, self-delivered MT at home afterwards First 4-weeks same as iPad group, then "patients were encourages to perform self-delivered MT as much as they wished at home. No training materials were provided."	**Primary: Average pain intensity during preceding week on 11-pt NRS** **Pain-related functioning (10 wk, 6 mo)** • PDI **Pain intensity/severity (10 wk, 6 mo)** • NRS **Quality of life (10 wk, 6 mo)** • EuroQoL-5D **Pain global change (10 wk, 6 mo)**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding Source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
	participating center and having received more than 6 sessions of mirror therapy during the previous 3 months."	exercises using various objects and mental practice of phantom limb exercises). Patients were instructed to also perform the exercises with the phantom limb as soon as they perceived voluntary, pain-free movements of the phantom limb. During the last session, patients were given a tablet and a set of training materials. They received detailed verbal and written instructions on how to use the teletreatment... Patients were encouraged to use the teletreatment as often as they wished."	Sensomotor exercises N=24 Age, mean (SD): 61 (15.2) Clinic, home 10 sessions (30-minute each) during first 4-weeks, delivered by therapist. Self-delivered exercise as often as they wished. "Patients received the same amount and frequency of sensomotor exercises performed with the intact limb as those in [other] groups during the first four weeks but without using a mirror. Instead, patients were instructed to look at their intact limb only during all exercises and not to perform exercises with their phantom limb. After these four weeks, patients were encouraged to perform self-delivered sensomotor exercises with the intact limb at home, without handing out training materials."	• Global Perceived Effect (GPE) on pain **Non-eligible: Frequency and duration of phantom limb pain, neuropathic pain symptom inventory (NPSI), patient-specific functional scale (1-3), disturbance in sleep, disturbance in mood, pain-specific self-efficacy**

Abbreviations. AR=augmented reality; BPI=Brief Pain Inventory; CBT=cognitive behavioral therapy; CRPS=Chronic Regional Pain Syndrome; DVPRS=Defense and Veterans Pain Rating Scale; EQ-5D-5L=European Quality of Life scale; ESR=erythrocyte sedimentation rate; FACIT=Functional Assessment of Chronic Illness Therapy scale; HR=heart rate; HRV=heart rate variability; LF/HF=low frequency to high frequency; MFM-32=Motor Function Measure-32; MME=morphine milligram equivalent; mo=month; MT=mirror therapy; NR=not reported; NRS=Numeric Rating Scale; PCS=Pain Catastrophizing Scale; PDI=Pain Disability Index; PHQ-8=Patient Health Questionnaire-8; QLQ-C30=EORTC Core Quality of Life questionnaire; RA=rheumatoid arthritis; S=seconds; SD=standard deviation; USA=United States of America; VR=virtual reality; wk=week.

Appendix Table I2. Detailed Results for KQ1 Other Conditions Studies

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
Pain-Related Functioning or Interference				
Ambrosino, 2020[75] AR Some concerns	HAQ-function & fatigue	1.8 (0.21) 12 wk: 1.1 (NR), -0.7*	1.75 (0.25) 12 wk: 1.6 (NR), -0.15*	Diff Δ*: 12 wk: -0.55
Cuneo, 2023[70] VR High	MIDAS	100.36 (72.76) 12 wk: 72.64 (46.91), -27.72	77.55 (64.7) 12 wk: 59.5 (46.4), -18.05	Diff Δ*: 12 wk:-9.67
Chuan, 2023[71] VR Some concerns	BPI-Interference	4.7 (2.4) 1 mo: 3.7 (2.4), -1.0* 3 mo: 2.8 (2.7), -1.9*	4.1 (2.7) 1 mo: 4.1 (2.9), 0.0* 3 mo: 3.8 (3.7), -0.3*	Diff Δ*: 1 mo: -1.0 3 mo: -1.6
Darnall, 2020[72] VR High	DVPRS - Stress	5.6 (2.8) 21 days: 2.8 (NR), -2.67 (3.02)	5.1 (2.6) 21 days: 3.4 (NR), -1.67 (1.92)	Diff Δ*: 21 days: -1.0
	DVPRS - Mood	5.5 (2.7) 21 days: 2.8 (NR), -2.61 (2.79)	4.8 (2.4) 21 days: 3.6 (NR), -1.58 (2.08)	Diff Δ*: 21 days: -1.03
	DVPRS - Sleep	5.5 (2.6) 21 days: 3.2 (NR), -2.25 (2.58)	5.2 (2.4) 21 days: 3.8 (NR), -1.33 (2.09)	Diff Δ*: 21 days: -0.92
	DVPRS - Activity	4.9 (2.1) 21 days: 3.1 (NR), -1.95 (2.35)	4.8 (2.2) 21 days: 4.2 (NR), -0.62 (2.33)	Diff Δ*: 21 days: -1.33
Karahan, 2016[78] AR Some concerns	BASFI	3.7 (1.5) 8 wk: 2.9 (1.3), -0.8*	3.9 (1.6) 8 wk: 3.9 (1.7), 0.0*	Diff Δ*: 8 wk: -0.8
Reynolds, 2022[73] VR Some concerns	BPI-short form (11 items)	37.7 (95% CI 31.2, 44.2) 7 days: 35.2 (28.7, 42.0), -2.5* 9 days: 33.8 (27.3, 40.3), -3.9*	42.1 (95% CI 35.5, 48.6) 7 days: 40.1 (33.4, 46.6), -2.0* 9 days: 33.9 (27.3, 40.5), -8.2*	Diff Δ*: 7 days: -0.5 9 days: 4.3
Rothgangel, 2018[80] AR Some concerns	PDI	30.5 (16.5) 10 wk:21.5 (13.9), -9.0* 6 mo: 20.6 (14.4), -9.9*	23.6 (18.2) 10 wk: 9.5 (10.9), -14.1* 6 mo: 10.1 (16.9), -13.5	Diff Δ: 10 wk: 5.1 6 mo: 3.6
			32.0 (20.1) 10 wk: 19.1 (16.9), -12.9 6 mo: 21.2 (20.0), -10.8	Diff Δ: 10 wk: 3.6 6 mo: 0.9
Wankhade, 2022[74] VR High	SPADI	NR 2 wk: NR, 30.68 (15.07)	NR 2 wk: NR, 14.4 (2.93)	Diff Δ*: 2 wk:16.28
Pain Intensity or Severity				
Cuneo, 2023[70] VR High	Headache days/month	23.71 (5.58) 12 wk: 15.64 (7.91), -8.07	25.41 12 wk:17.77 (9.45), -7.64	Diff Δ*: 12 wk: -0.43

Author, Year **VR or AR** **Risk of Bias**	**Effect Measure**	**Intervention** **Baseline Mean (SD)** **Follow-Up Mean (SD), Mean Change**	**Comparator** **Baseline Mean (SD)** **Follow-Up Mean (SD), Mean Change**	**Comparison**
Chuan, 2023[71] VR Some concerns	BPI-Intensity	4.9 (1.1) 1 mo: 4.5 (1.6), -0.4* 3 mo: 4.1 (2.1), -0.8*	4.4 (1.9) 1 mo: 4.5 (2.2), 0.1* 3 mo: 3.8 (2.7), -0.6*	Diff Δ*: 1 mo: -0.5 3 mo: -0.2
Ditchburn, 2020[76] AR High	NRS (current)	2.96 (1.87) 6 wk: 2.07 (2.11), -0.89*	3.33 (2.82) 6 wk: 3.48 (3.03), 0.15*	Diff Δ*: 6 wk: 1.04
	NRS (past 30 days)	5.52 (2.24) 6 wk: 5.04 (2.21), -0.48*	6.0 (2.34) 6 wk: 5.85 (2.43), -0.15*	Diff Δ*: 6 wk: -0.33
Darnall, 2020[72] VR High	DVPRS	4.7 (1.7) 21 days: 3.2 (NR), -1.5*	4.5 (1.8) 21 days: 3.8 (NR), -0.7	Diff Δ*: 21 days: -0.8
Gouveia e Silva, 2020[77] AR Some concerns	VAS	6.22 (2.98) 7 wk: 2.0 (2.47), -4.22 (2.82) 11 wk: 2.33 (2.22), -3.89, (2.93)	6.89 (1.59) 7 wk: 2.68 (1.53), -4.21 (1.87) 11 wk: 3.05 (1.47), -3.84 (1.83)	Diff Δ: 7 wk: -0.01 11 wk: -0.05
Karahan, 2016[78] AR Some concerns	VAS	4.9 (2.0) 8 wk: 3.6 (1.7), -1.3*	5.1 (2.2) 8 wk: 5 (2.4), -0.1*	Diff Δ*: 8 wk: -1.2
Lewis, 2021[79] AR High	NRS	5.7 (3.3) 6 wk: 5.15 (3.1), -0.55*	5.45 (3.4) 6 wk: 5.33 (3.4), -0.12*	Diff Δ*: 6 wk: -0.43
Rothgangel, 2018[80] AR Some concerns	NRS	5.9 (1.9) 10 wk: 4.6 (1.9), -1.3* 6 mo: 4.1 (2.6), -1.8*	Non-AR mirror therapy: 5.4 (2.4) 10 wk: 3.6 (3.1), -1.8* 6 mo: 2.7 (2.8), -2.7*	Diff Δ: 10 wk: 0.5 6 mo: 0.9
			Control: 5.8 (2.1) 10 wk: 4.1 (2.6), -1.7* 6 mo: 4.5 (2.8), -1.3*	Diff Δ: 10 wk: 0.4 6 mo: -0.5
Wankhade, 2022[74] VR High	NRS	NR 2 wk: NR, 3.56 (0.5)	NR 2 wk: NR, 2.52 (0.5)	Diff Δ*: 2 wk: 1.04
Adverse Events				
Cuneo, 2023[70] VR High	% with nausea, dizziness (VR only)	Nausea: 28.6% Dizziness: 21.4%	AE not assessed	Diff Δ: NC
Chuan, 2023[71] VR Some concerns	% with nausea, dizziness, eyestrain during any VR session	Nausea: 4/19 (21%) Dizziness: 4/19 (21%) Eyestrain: 4/19 (21%)	Nausea: 5/20 (25%) Dizziness: 4/20 (20%) Eyestrain: 8/20 (40%)	Diff Δ*: Nausea: 4% Dizziness: 1% Eyestrain: -19%
	Free text response on tolerability survey	NR	"For one control patient, the side-effect (severe headache) was severe enough to withdraw…and two control patients were unable to tolerate the headset and did not	Diff Δ: NC

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
			complete one of their virtual reality sessions."	
Ditchburn, 2020[76] AR High	AE, motion sickness	No events	No events	Diff Δ*: 0
Darnall, 2020[72] VR High	Frequency of motion sickness or nausea while using VR (only for VR group	Never: 19/25 (76%) Sometimes: 5/25 (20%) Often: 1 (4%)	AE not assessed	Diff Δ: NC
Reynolds, 2022[73] VR Some concerns	Free-text questions on acceptability, suggestions for change	"...some participants reported adverse effects in using the VR headsets including feeling 'claustrophobic' and '…I got a bit dizzy/nauseous'."	AE not assessed	Diff Δ: NC
Gouveia e Silva, 2020[77] AR Some concerns	% with late upper limb pain after first session	15%	10%	Diff Δ*: 5%
Pain Catastrophizing				
Cuneo, 2023[70] VR High	CAP	16.07 (5.36) 12 wk: 13.21 (5.67), -2.86	11.86 (3.55) 12 wk: 11.36 (4.64), -0.5	Diff Δ*: 12 wk: -2.36
Pain Global Change				
Darnall, 2020[72] VR High	PGIC	21/25 (84%) pain improved, 4/25 (16%) no change, 0/25 worsening pain	18/29 (62%) pain improved, 10/29 (34%) no change, 1/29 (3%) worsening pain	Diff Δ*: Improved: 24% Worsened: -3%
Rothgangel, 2018[80] AR Some concerns	GPE on pain	10 wk: 1.1 (1.0) 6 mo: 1.4 (1.1)	non-AR mirror therapy 10 wk: 1.4 (1.5) 6 mo: 1.2 (1.8)	Diff Δ*: 10 wk: -0.3 6 mo: 0.2
			Control 10 wk: 1.0 (1.2) 6 mo: 0.8 (1.3)	Diff Δ*: 10 wk: 0.1 6 mo: 0.6
Quality of Life				
Chuan, 2023[71] VR Some concerns	QLQ-C30 global quality subscale	62 (25) 1 mo: 57 (18), -5* 3 mo: 54 (25), -8*	55 (20) 1 mo: 57 (18), 2* 3 mo: 56 (24), 1*	Diff Δ*: 1 mo: -7 3 mo: -9
Karahan, 2016[78] AR Some concerns	ASQOL (0-18)	9.5 (6.1) 8 wk: 6.8 (4.3), -2.7*	10.2 (6.0) 8 wk: 10.3 (6.4), 0.1	Diff Δ*: 8 wk: -2.8
Rothgangel, 2018[80] AR Some concerns	EuroQoL-5D	0.6 (0.3) 10 wk: 0.7 (0.2), 0.1* 6 mo: 0.8 (0.2), 0.2*	Traditional mirror therapy 0.6 (0.3) 10 wk: 0.8 (0.3), 0.2*	Diff Δ*: 10 wk: -0.1 6 mo: 0.1

Author, Year **VR or AR** **Risk of Bias**	**Effect Measure**	**Intervention** **Baseline Mean (SD)** **Follow-Up Mean (SD), Mean Change**	**Comparator** **Baseline Mean (SD)** **Follow-Up Mean (SD), Mean Change**	**Comparison**
			6 mo: 0.7 (0.3), 0.1*	
			Control 0.4 (0.3) 10 wk: 0.7 (0.3), 0.3* 6 mo: 0.7 (0.3), 0.3*	Diff Δ*: 10 wk: -0.2 6 mo: -0.1
Opioid Use				
Chuan, 2023[71] VR Some concerns	Average MME in the previous week	Means NR Median (IQR baseline 0 (0-23 1 mo0 (0-19 3 mo0 (0-15	Means NR Median (IQR Baseline 0 (0-24 1 mo0 (0-38 3 mo0 (0-51	Diff Δ: NC
Physical Performance				
Ditchburn, 2020[76] AR High	Postural sway with eyes open – AP SD	5.45 (2.06) 6 wk: 4.64 (2.03), -0.81*	4.44 (1.4) 6 wk: 3.92 (1.66), -0.52*	Diff Δ*: 6 wk: -0.29
	Postural sway with eyes open – AP range	25.92 (6.25) 6 wk: 21.25 (6.79), -4.67*	21.42 (5.89) 6 wk: 18.02 (7.54), -3.4*	Diff Δ*: 6 wk: -1.27
	Postural sway with eyes open – ML SD	3.15 (1.89) 6 wk: 2.56 (1.52), -0.59*	2.13 (0.83) 6 wk: 1.84 (0.59), -0.29*	Diff Δ*: 6 wk: -0.3
	Postural sway with eyes open – ML range	17.82 (10.24) 6 wk: 13.97 (7.72), -3.85*	12.42 (4.46) 6 wk: 10.17 (3.78), -2.25*	Diff Δ*: 6 wk: -1.6
	Postural sway with eyes open – Center of pressure velocity	32.69 (10.73) 6 wk: 32.38 (9.58), -0.31	29.47 (6.72) 6 wk: 31.48 (10.43), 2.01	Diff Δ*: 6 wk: -2.32
Gouveia e Silva, 2020[77] AR Some concerns	Functional Reach Assessment	31.1 (3.38) 7 wk: 34.4 (3.45), 2.28 (2.08) 11 wk: 34.1 (3.23), 1.94 (2.04)	30.8 (3.10) 7 wk: 32.1 (3.47), 1.26 (1.10) 11 wk: 31.9 (3.57), 1.11 (1.15)	Diff Δ: 7 wk: 1.02 11 wk: 0.83
	Box and Block test	101 (10.9) 7 wk: 111 (15.7), 9.89 (8.96) 11 wk: 109 (13.95), 8.11 (7.51)	88.2 (13.2) 7 wk: 92.7 (11.9), 4.58 (4.09) 11 wk: 91.4 (11.7), 3.21 (3.51)	Diff Δ: 7 wk: 5.31 11 wk: 4.90

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparison
Wankhade, 2022[74] VR High	Shoulder flexion ROM	NR 2 wk: NR, 29.6 (8.88)	NR 2 wk: NR, 23.4 (8.0)	Diff Δ*: 2 wk: 6.2
	Shoulder extension	NR 2 wk: NR, 9.92 (3.12)	NR 2 wk: NR, 6.8 (3.78)	Diff Δ*: 2 wk: 3.12
	Shoulder abduction	NR 2 wk: NR, 34.0 (10.1)	NR 2 wk: NR, 20.2 (10.04)	Diff Δ*: 2 wk: 13.8
	Shoulder adduction	NR 2 wk: NR, 9.48 (1.89)	NR 2 wk: NR, 6.4 (3.06)	Diff Δ*: 2 wk: 3.08
	Shoulder internal	NR 2 wk: NR, 11.8 (2.84)	NR 2 wk: NR, 7.4 (2.92)	Diff Δ*: 2 wk: 4.4
	Shoulder external	NR 2 wk: NR, 12.84 (2.86)	NR 2 wk: NR, 11.0 (3.22)	Diff Δ*: 2 wk: 1.84

Notes. * Calculated by review team.

Abbreviations. AR=augmented reality; ASQOL=Ankylosing Spondylitis Quality of Life; BASFI=Bath Ankylosing Spondylitis Functional Index; BPI=Brief Pain Inventory; CAP=Concerns About Pain; CI=confidence interval; Diff Δ= difference in change scores; DVPRS=Defense and Veteran Pain Rating Scale; EuroQoL-5D= European Quality of Life 5 Dimensions; GPE=Global Perceived Effect; HAQ=Health Assessment Questionnaire; IQR=interquartile range; MIDAS=Migraine Disability Assessment; MME=morphine milligram equivalents; mo=month; NR=not reported; NRS=Numeric Rating Scale; oMEDD=oral morphine equivalent daily dose; PCS=Pain Catastrophizing Scale; PDI=Pain Disability Index; PGIC=Patient Global Impression of Change; QLQ-C30=Quality of Life Questionnaire-C30; ROM=range of motion; SD=standard deviation; SPADI=Shoulder Pain and Disability Index; VAS=Visual Analog Scale; VR=virtual reality; wk=week.

APPENDIX J. POST-SURGICAL PAIN

Appendix Table J1. Detailed Characteristics for Included Trials on Post-Operative Studies

Author, Year **Risk of Bias** **Follow-Up Duration** **Country** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
Eichler, 2019[84] High 3 months 3 Sites (unspecified) German Pension Insurance Berlin-Brandenburg (grant number 10-40.07.05.07.007); Deutsche Forschungsgemeinschaft; and Open Access Publishing Fund of University of Potsdam	**Inclusion**: "[T]otal hip or knee replacement was performed following idiopathic, posttraumatic, or congenital osteoarthritis, between 18-65 years, and... additional criteria (eg, High Definition Multimedia Interface [HDMI]-compatible screen, minimum 2.5-meter space in front of the screen, and internet access) …" **Exclusion**: "Patients not expected to achieve functional safety in walking with full load by the end of the rehabilitation were excluded. For those patients, it was assumed that they would not be able to perform exercises with adequate load or the assessments at the study site. Insufficient verbal and written German-language skills also led to exclusion."	N=56 Age, mean (SD): 53.5 (7.0) Female: 54.2% Home 3 x per week; 3 months (following 3 weeks of inpatient rehabilitation) "... home-based telerehabilitation program based on the MeineReha system, which consisted of a home component as well as a working portal for the therapist in the clinic...The exercises to build up strength and improve postural control were chosen by the supervising therapist …The training intensity was individualized in terms of the choice of exercises, the number of sets and repetitions, and the duration of the breaks, which could all be adjusted by the therapist... options for the patient and the therapist to communicate …: (1) the patient could record and send audio messages to their therapist...and the therapist was able to listen to it	N=55 Age, mean (SD): 56.8 (5.7) Female: 48.7% Home NR; 3 weeks inpatient followed by no specific therapy "Patients in the control group did not receive any study-specific therapy after their inpatient rehabilitation. The follow-up was carried out identically to the [intervention group] three months after randomization. The patients of both groups were also offered the usual aftercare..."	**Primary: 6-minute walk test** **Pain related functioning or interference (3 mo)** • WOMAC • Five Times Chair Rise Test **Physical performance (3 mo)** • TUG • Stair Ascend Test **Quality of life (3 mo)** • SF-36-physical • SF-36-mental

Author, Year **Risk of Bias** **Follow-Up Duration** **Country** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
		whenever their schedule gave them time to do it; (2) the therapist could respond or start a conversation...with individualized text messages, which the patient was shown whenever they started the system...; and (3) the patient and the therapist were able to make appointments for live video conferences, which they were supposed to conduct on a weekly basis... During the training, the exercises were demonstrated on screen by an avatar... The patient performed the exercises simultaneously and was detected by means of a Kinect sensor…The system…sent them real-time visual feedback in which their relevant body segments were colored green for correct movements and red in the case of incorrect movements … For training supervision, the therapist was given access to the frequency of the training as well as the exercise evaluations."		
Fuchs, 2022[82] High 6 months Kaplan Medical Center, Rehovot "This research did not receive any specific grant from funding agencies in the public,	**Inclusion**: "(1) Patients diagnosed with osteoarthritis, either uni/double/triple compartmental osteoarthritis, and found suitable for surgery. All grades of osteoarthritis were included in the study; (2) Patients undergoing unilateral TKA."	N=30 Age, mean (SD): 70 (7) Female: 63.3% Clinic/facility 1 session per day; 1-2 days post-operatively	N=25 Age, mean (SD): 70 (7) Female: 52.0% Clinic/facility 1 session per day; 1-2 days post-operatively	**Primary: VAS** **Pain related functioning or interference (6 mo)** • WOMAC

Author, Year **Risk of Bias** **Follow-Up Duration** **Country** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
commercial or not-for-profit sectors."	**Exclusion**: "(1) Patients undergoing revision of TKA; (2) Ligament injury or periprosthetic fracture occurring during TKA; (3) Unstable vital signs; (4) Vision loss, hearing loss, or functional illiteracy."	"The VR intervention included a movie that was picked by the patient from several options, either a nature film or a music film. The patient watched the VR film during the CPM physiotherapy."	"The CPM was used as a tool to match the physiotherapy conditions for all patients and to measure a possible change in the range of motion."	
Janhunen, 2023[85] Some Concerns 4 months Turku University of Applied Sciences, University of Jyväskylä Päivikki and Sakari Sohlberg Foundation; the Business Finland (grant numbers: 5794/31/2016, 5941/31/2016, 6057/31/2016); Finnish partner companies (SE Innovations Oy [Senior Some Oy], Suunto Oy, Physiotools Oy, GoodLife Technology Oy, Lingsoft Oy, eSeteli Palveluverkko Oy, PN Turku Oy, Ade Animations Design & Effects Oy, Adesante Oy, 4FeetUnder, Intechso and Realmax Oy)	**Inclusion**: "(1) first primary unilateral TKR, (2) mechanical axis of the limb in varus, (3) posterior stabilising or cruciate-retaining prosthesis and (4) normal vision with or without eyeglasses" **Exclusion**: "[F]ractures, rheumatoid arthritis or other biomechanical disruptions in the affected lower limb within 1 year before surgery, a diagnosed memory disorder, cognitive impairment or a neurological condition."	N=25 Age, mean (SD): 66.9 (3.1) Women: 64.0% Home 4-5 exergames (variable duration and sets) played several times a day; 16 wks "…[P]rotocol included 11 games…The player controls the games using movements similar to the standard postoperative home exercise program…Exergames were categorized according to exercise target: knee extension and flexion, knee flexion or squatting, weight shifting from side to side, stretching, and functional exergames…The knee extension-flexion games (the Cave Game and Intruders) and stretching game (the Cannon) were played in a sitting position, whereas the other games (the Rowing Game, Pick Up,	N=27 Age, mean (SD): 66.4 (4.5) Women: 63.0% Home Multiple exercises 2-5 times a day; 16 wks "[P]rotocol included 11–12 exercises…The control group underwent a standard postoperative home exercise program…The research physiotherapist instructed the control group participants to follow this standard program several times a day for 16 weeks starting after discharge from the hospital. Similar to the exergame group, guidance was provided at the exercise laboratory baseline visit immediately after randomization. Face-to-face individual guidance was provided for 5 to 10 minutes by the same research	**Primary: Oxford knee score 12-item questionnaire, TUG** **Pain intensity (2, 4 mo)** • VAS **Physical performance (4 mo)** • SPPB • Active and passive knee flexion and extension, using universal goniometer • Muscle force flexion and extension, assessed with Metitur Good Strength dynamometer in Jyväskylä (Newton [N]) and a Con-Trex Multijoint dynamometer (Newton-meter [Nm]) in Turku from the operated

Author, Year **Risk of Bias** **Follow-Up Duration** **Country** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
		Squat Pong, Bubble Runner, Hat Trick, Brick Breaker, Hiking, and Toy Golf) were played in a standing position."	physiotherapist who had conducted the baseline assessment."	
Jin, 2018[83] High 6 months Cangzhou Central Hospital NR	**Inclusion**: "1) Patients diagnosed as OA according to The Guidelines for Diagnosis and Treatment of Osteoarthritis issued by the Chinese Rheumatology Association in 2010; 2) Patients undergoing unilateral TKA for the first time..." **Exclusion**: "1) Overweight (BMI ≥ 30 kg/m^2); 2) Severe osteoporosis; 3) Ligament injury or periprosthetic fracture occurring during TKA; 3) Unstable vital signs, complications of incision healing, or clot formation in leg veins; 4) Vision loss, hearing loss, or functional illiteracy.	N=33 Age, mean (SD): 66.45 (3.49) Female: 54.55% Clinic/facility 30 minutes, 3 times per day; NR "… patients exercised by performing foot dorsiflexion and plantar flexion beginning the first day after TKA. Exercises targeting quadriceps muscle strength occurred from the second day after TKA. Passive exercises on knee flexion began after the drainage tube was removed. Exercises were assisted with psychological intervention and pain management education... In addition, VR (Mide Technology Inc., Cangzhou, China) intervention was applied in the experimental group beginning the second day after TKA. Patients were asked to row a boat using knee flexion (interaction of VR) in an immersive virtual environment…"	N=33 Age, mean (SD): 66.30 (4.41) Female: 60.61% Clinic/facility 30 repetitions, 3 times per day; NR "…patients exercised by performing foot dorsiflexion and plantar flexion beginning the first day after TKA. Exercises targeting quadriceps muscle strength occurred from the second day after TKA. Passive exercises on knee flexion began after the drainage tube was removed. Exercises were assisted with psychological intervention and pain management education...Patients in the control group were asked to flex their knees passively using their arms until pain tolerance was reached. They held that position for 20 seconds followed by relaxing for 40 seconds."	**Primary: WOMAC, VAS, ROM** **Other non-eligible outcomes reported (1, 3, 6 mo)** • HSS
Piqueras, 2013[86] High	**Inclusion**: "[S]uccessful primary TKA surgery; post-TKA active range of motion: flexion 80º and	N=90 Age, mean (SD):	N= N=91 Age, mean (SD):	**Primary outcome NR** **Pain intensity (2 wk, 3 mo)**

Author, Year **Risk of Bias** **Follow-Up Duration** **Country** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
3 months An acute-care university general hospital, Barcelona Partially financed by Telefónica Research and Development.	extension –10º, without signs of stiffness; ability to walk with the use of a walking aid; ability to read and understand Spanish; ability to understand and accept the trial procedures and to sign an informed consent form in accordance with national legislation." **Exclusion**: "…[S]ensory, cognitive and/or praxic impairment; concomitant medical conditions that may influence the rehabilitation process; discharge to destination other than home; patients with any local or systemic complication (e.g. surgical wound infection, suspicion of deep vein thrombosis) in the 3-month follow-up period were also excluded."	NR Women: 83% Home/Clinic or health care facility 1 hour sessions; 10 days "The IVT is an interactive virtual software-hardware platform that facilitates the development of remote rehabilitation therapy for multiple diseases...[The] patient receives the information needed to perform the exercises and the therapist can remotely monitor the patient's performance. For the purpose of this trial, the IVT system was designed for lower limb motor recovery in patients undergoing TKA[...]Wireless sensors (WAGYRO) including a 3-axis accelerometer and two self-powered gyroscopes [...] connected to the patient and allow calculation of their movement trajectories. [I]nteractive software with a 3D avatar that demonstrates the exercises to be undertaken, while patients reproduce the movements[...]Web portal for the therapist: receives data and records them for evaluation, with the option to modify the therapy as the rehabilitation evolves[...]The therapist supervised patients remotely on a daily basis from the hospital to check that they were performing the therapy, adjusted the prescribed therapy as appropriate, and	NR Women: 62.5% Home/Clinic or health care facility 1 hour sessions; 10 days "In all cases, functional rehabilitation started the day after TKA. All participants were instructed by a physical therapist in weight bearing to tolerance with an assistive device and underwent inpatient care. (mean length of stay 6.2 days) and outpatient intervention (outpatient physical therapy or IVT) for the first 3 weeks after surgery. Inpatient care consisted of assisted walking within 24 h, knee range of motion exercises and preparing for the return home. After hospital discharge, conventional physical therapy consisted of a 2-week face-to-face rehabilitation programme (progressive exercise and instruction including knee range of motion, gait training, and instructions in negotiating stairs and community-related obstacles). Any signs of adverse knee joint responses (*eg*, increased swelling or pain) resulted in a lowering of the intensity, frequency and duration of the exercises or elimination of a rehabilitation component."	• VAS **Physical performance (2 wk, 3 mo)** • TUG • Quadriceps muscle strength, measured in kg (NMMT dynamometer) • Hamstring muscle strength, measured in kilograms (NMMT dynamometer) • Active Knee extension, measured in degrees with a goniometer • Active Knee flexion, measured in degrees with a goniometer

Author, Year **Risk of Bias** **Follow-Up Duration** **Country** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
		contacted the patient via telephone as necessary."		
Prvu Bettger, 2020[87] Some concerns 12 weeks Two academic medical centers and 2 independent private practices Reflexion Health, “the manufacturer of the VERA system”	**Inclusion**: "Patients who had an in-person clinic visit at least 10 days prior to TKA. Patients who were ≥18 years of age, who were scheduled for TKA for the treatment of nontraumatic conditions, and who had a Risk Assessment and Prediction Tool (RAPT) score of ≥ 6 (indicating expected discharge to home after surgical hospitalization) were eligible." **Exclusion**: "[P]atients who were scheduled to undergo bilateral or staged bilateral TKA, who were in a nursing home prior to surgery, or who were unable or unwilling to provide informed consent."	N=153 Age, mean (SD): 65.4 (7.7) Female: 59.6% Home/Clinic or health care facility NR; NR "VERA is a cloud-based virtual telehealth system that functions with use of 3-dimensional (3D) tracking technology to quantify pose and motion, an avatar (digitally simulated coach) to demonstrate and guide activity, visual and audible instructions and immediate feedback on exercise quality, and a virtual video connection for synchronous telehealth visits with an assigned intervention telehealth physical therapist. Individualized prescribed therapy regimens were electronically programmed for patients through the clinician interface prior to surgery... The VERA system tracked activity, performance, exercise quality, and adherence; the telehealth therapist monitored the patient’s progress asynchronously. Patients had a video visit with their telehealth therapist in	N=153 Age, mean (SD): 65.1 (9.2) Female: 65.4% Home/Clinic or health care facility NR; NR "Patients in the usual care group followed their care team’s recommendations for all preoperative and postoperative medical and rehabilitative care."	**Primary outcome: Total healthcare costs 12 weeks after discharge** **Pain related functioning or interference (6, 12 wk)** • KOOS **Pain intensity (12 wk)** • NRS **Adverse events (12 wk)** • Number of falls, patient-reported **Physical performance (6 wk)** • Knee Extension (degrees) • Knee Flexion (degrees) • 10-meter gait speed **Quality of life (12 wk)** • PROMIS physical function • PROMIS mental health **Other non-eligible outcomes reported** • Healthcare costs, total and by different services • Hospital readmissions, patient-reported

Author, Year **Risk of Bias** **Follow-Up Duration** **Country** **Site(s)** **Funding source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
		the week after hospital discharge and weekly thereafter to review progress and to revise the therapy regimen accordingly. The telehealth therapist provided remote clinician oversight to the patients for the duration of the intervention and communicated progress to each clinical site ahead of the patients' 2 and 6-week postoperative visits. Patients and the telehealth therapist mutually agreed when therapy goals were met for discharge from virtual PT."		
Shim, 2023[88] Some concerns 24 weeks Two academic medical centers, Seoul Korea Health Technology R&D Project through the Korea Health Industry Development Institute; Ministry of Health Welfare, Republic of Korea (grant no.: HR19C0781).	**Inclusion**: "Participants aged ≥ 50 years who underwent TKA and were discharged home." **Exclusion**: "[P]articipants with a history of osteotomy, severe neurological deficits, infection in the affected knee, inability to perform exercises due to severe comorbidities, or inability to participate in the rehabilitation program for other reasons."	N=28 Age, mean (SD): 68.6 (5.8) Women: 82.1% Home 30 min, daily; 12 wks "[AR] group performed brochure-based exercises in the early phase... In the advanced phase, exercise was performed using an AR-based digital healthcare system... At levels 1–4, participants performed range of motion and isometric strengthening of lower extremities while lying down or sitting in a chair. At levels 5–9, participants performed a program designed to train stretching and isotonic strengthening of lower extremities while standing with support. At levels 10–12, participants	N=28 Age, mean (SD): 73.0 (4.6) Women: 75.0% Home 3-5 sets of exercises (10 repetitions each); 12 wks "Both groups performed the same exercises for the same duration, but the types of instructions provided at home differed...Participants in the [conventional rehab] group performed brochure-based home exercises, according to the standard rehabilitation protocol for patients after TKA... In the early phase, an exercise program consisting of ankle pumping, ROM, and isometric/isotonic exercise was	**Primary: 4-m gait speed** **Pain related functioning or interference (3, 12, 24 wk)** • WOMAC **Pain intensity (3, 12, 24 wk)** • NRS **Physical performance (3, 12, 24 wk)** • Berg balance scale • ROM • Quadriceps strength • Hamstring strength **Quality of life (3, 12, 24 wk)** • EuroQoL-5D-5L

Author, Year Risk of Bias Follow-Up Duration Country Site(s) Funding source	Inclusion/Exclusion Criteria	Intervention: Participants Randomized Demographics Setting Frequency; Duration Detailed Intervention Characteristics	Comparator: Participants Randomized Demographics Setting Frequency; Duration Detailed Comparator Characteristics	Primary Outcome Eligible Outcomes & Measures Reported (Time Points) Other Non-Eligible Outcomes Reported
		performed a program designed to train stretching and isotonic strengthening, including lunges and squats, while standing without support… The exercises were displayed on the screen (avatar plus written summaries). Participants…were provided with real-time feedback on the screen... The exercise performance and motion accuracy were recorded online and reviewed by a physician. Participants were provided detailed feedback on their performance at the outpatient clinic visits."	performed in a sitting or lying position. In addition, gait training using a walker and stair up-and-down training were performed. In the advanced phase, participants performed cane/self-gait training and strengthening exercise, such as squats and lunges."	

Abbreviations. AR=augmented reality; BMI=body mass index; CPM=continuous passive motion; h=hour; HSS=hospital for special surgery knee score; IRENA=multimodal intensified aftercare; IVT=interactive virtual telerehabilitation; NMMT=Nicholas manual muscle tester; KOOS=knee injury and osteoarthritis outcome score; NR=not reported; NRS=numerical rating scale; PROMIS=patient-reported outcomes measurement information system; PT=physical therapy; RAPT=risk assessment and prediction tool; ROM=range of motion; SPPB=short physical performance battery; SD=standard deviation; SF-36=short form health survey-36; TKA=total knee arthroplasty; TKR=total knee replacement; TUG=timed up and go test; VAS=visual analogue scale; VERA=virtual exercise rehabilitation assistant; VR=virtual reality; WOMAC=Western Ontario and McMaster Universities Arthritis Index.

Appendix Table J2. Detailed Results for Post-Operative Studies

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change (SD)	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change (SD)	Comparison
Pain-Related Functioning or Interference				
Eichler, 2019[84] AR High	WOMAC (3 mo)	26.4 (18.5) 11.5 (12.7), -14.9 (13.6)	24.8 (16.4) 13.9 (14.3), -10.9 (13.5)	Diff Δ*: -4.0 Stand. Diff Δ: -0.3*
Fuchs, 2022[82] VR High	WOMAC (6 mo)	36.4 (15.1) 57.2 (27.3), 20.8	34.5 (17.0) 54.2 (25.4), 19.7	Diff Δ : 1.1*
Janhunen, 2023[85] AR Some concerns	OKS	26.7 (6.7) 2 mo: 33.4 (6.3), 6.7 4 mo: 38.6 (6.1), 12.1 (7.0*)	26.9 (6.5) 2 mo: 30.3 (5.5), 3.4 4 mo: 36.7 (6.7), 9.8 (7.0*)	Diff Δ*: 2 mo: 3.3 4 mo: 2.3 Stand. Diff Δ*: 4 mo: 0.33, p=0.27
Jin, 2018[83] VR High	WOMAC	45.03 (5.1) 1 mo: 32.0 (5.2), -13.0 3 mo: 25.8 (4.2), -19.2 6 mo: 21.6 (4.2), -23.5	44.18 (5.73) 1 mo: 35.1 (5.2), -9.1 3 mo: 29.7 (5.6), -14.5 6 mo: 26.3 (3.9), -17.9	Diff Δ*: 1 mo: -3.9 3 mo: -4.7 6 mo: -5.6
Prvu Bettger, 2020[87] AR Some concerns	KOOS	37.0 (12.0) 6 wk: 61.0 (11.5), 24.0 12 wk: 69.6 (12.1), 32.6	36.0 (13.0) 6 wk: 61.8 (13.5), 25.8 12 wk: 67.2 (14.3), 31.2	Diff Δ*: 6 wk: -1.8 12 wk: 1.4
Shim, 2023[88] AR Some concerns	WOMAC	83.1 (13.0) 3 wk: 66.1 (12.5), -17 12 wk: 46.5 (9.1), -36.6 24 wk: 40.1 (7.0), -43.0	81.1 (14.4) 3 wk: 62.2 (15.0), -18.9 12 wk: 45.3 (15.0), -35.8 24 wk: 40.9 (16.0), -40.2	Diff Δ*: 3 wk: 1.9 12 wk: -0.8 24 wk: -2.8
Pain Intensity				
Fuchs, 20 VR High	VAS (2 days)	Means NR Median (IQR): Before treatment: 6 (5-8), NC After treatment: 4 (1-7), NC	Means NR Median (IQR): Before treatment: 6 (6-8), NC After treatment: 5 (2-7), NC	Diff Δ: NC
Janhunen, 2023[85] AR Some concerns	VAS	57.1 (18.3) 2 mo: 30.5 (21.0), -26.6 4 mo: 20.8 (20.3), -36.3 (24.4*)	54.2 (21.6) 2 mo: 28.7 (20.0), -25.5 4 mo: 27.0 (27.5), -26.7 (24.7*)	Diff Δ*: 2 mo: -1.1 4 mo: -9.1 Stand. Diff Δ*: 4 mo: -0.39, p=0.18
Jin, 2018[83] VR High	VAS	7.4 (1.14) 3 days: 6.5 (0.9), -0.9 5 days: 5.4 (0.8), -2.0 7 days: 3.9 (0.6), -3.5	7.4 (1.3) 3 days: 6.8 (1.1), -0.6 5 days: 6.0 (0.9), -1.5 7 days: 4.4 (0.8), -3.0	Diff Δ*: 1 mo: -0.3 3 mo: -0.5 6 mo: -0.5

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change (SD)	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change (SD)	Comparison
Piqueras, 2013[86] AR High	VAS	3.8 (2.0) 2 wk: 3.1*, -0.7 (1.4) 3 mo: 2.0*, -1.8 (2.5)	4.3 (1.9) 2 wk: 3.7*, -0.6 (1.9) 3 mo: 2.0*, -2.3 (2.0)	Diff Δ*: 2 wk: -0.1 3 mo: 0.5 Stand. Diff Δ*: 2 wk: -0.1, p=0.80 3-mo: 0.2, p=0.28
Prvu Bettger, 2020[87] AR Some concerns	NRS (12 wk)	5.2 (2.1) 2.7 (2.0), -2.5	5.7 (2.0) 3.0 (2.6), -2.7	Diff Δ: 0.2*
Shim, 2023[88] AR Some concerns	NRS	5.7 (2.1) 3 wk: 5.1 (2.0), -0.6 12 wk: 2.8 (1.5), -2.9 24 wk: 2.5 (1.6), -3.2	5.5 (2.2) 3 wk: 4.7 (2.0), -0.8 12 wk: 3.3 (2.1), -2.2 24 wk: 2.3 (2.1), -3.2	Diff Δ*: 3 wk: 0.2 12 wk: -0.7 24 wk: 0
Adverse Events				
Prvu Bettger, 2020[87] AR Some concerns	Number of falls, patient-reported (12 wk)	19.4%	14.6%	Diff Δ: 4.8%*
Physical Performance				
Eichler, 2019[84] AR High	6-minute walk test (m) (3 mo)	440.6 (78.2) 530.4 (79), 88.3 (57.7)	433.3 (80.2) 513 (70.6), 79.6 (48.7)	Diff Δ: 8.7*
	TUG (s) (3 mo)	9.3 (1.8) 7.5 (1.2), –1.9 (1.5)	9.0 (2.4) 7.5 (1.6), –1.5 (2.2)	Diff Δ: -0.4*
	Stair Ascend Test (3 mo)	8.7 (2.7) 6.2 (1.2), –2.5 (2.4)	8.6 (4) 6.1 (1.5), –2.5 (3.0)	Diff Δ: 0*
Janhunen, 2023[85] AR Some concerns	TUG (s)	9.4 (3.6) 2 mo: 8.2 (1.5), -1.2 4 mo: 7.6 (1.5), -1.8	8.3 (1.7) 2 mo: 8.7 (1.6), 0.4 4 mo: 7.7 (1.2), -0.6	Diff Δ*: 2 mo: -1.6 4 mo: -1.2, p=0.04
	Active and passive knee flexion (4 mo)	107 (18) 106*, -1.0 (15.2*)	107 (13) 100*, −7.0 (14.0*)	Diff Δ*: 6.0, p=0.17
	Active and passive knee extension (4 mo)	7.3 (7.7) 6.8*, -0.5 (7.0*)	6.6 (4.1) 6.7*, 0.1 (7.1*)	Diff Δ*: -0.6, p=0.76
	Muscle force flexion (4 mo)	0.6 (0.3) 0.7*, 0.1 (0.4*)	0.6 (0.2) 0.7*, 0.1 (0.1*)	Diff Δ*: 0.0, p=0.88
	Muscle force extension (4 mo)	1.2 (0.5) 1.1*, -0.1 (0.2*)	1.1 (0.4) 1.0*, −0.1 (0.3*)	Diff Δ*: 0.0, p=0.85
	SPPB (4 mo)	9.5 (1.5) 10.6*, 1.1 (1.5*)	9.6 (1.5) 10.4*, 0.8 (1.6*)	Diff Δ*: 0.3, p=0.51
Jin, 2018[83] VR High	ROM (°) (14 days)	43.6 (3.4) 93.7 (6.6), 50.2	42.9 (3.6) 86.4 (5.0), 43.5	Diff Δ*: 6.7, p=0.0

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change (SD)	Comparator Baseline Mean (SD) Follow-Up Mean (SD), Mean Change (SD)	Comparison
Prvu Bettger, 2020[87] AR Some concerns	10-m gait speed (s) (6 wk)	1 (0.3) 1 (0.3), 0	1 (0.3) 1 (0.3), 0	Diff Δ: 0*
Shim, 2023[88] AR Some concerns	4-m gait speed	0.4 (0.2) 3 wk: 0.5 (0.2), 0.1 12 wk:0.8 (0.2), 0.4 24 wk: 0.9 (0.2),0.5	0.5 (0.3) 3 wk: 0.6 (0.3), 0.1 12 wk: 0.9 (0.1), 0.4 24 wk: 1.0 (0.3), 0.4	Diff Δ*: 3 wk: 0 12 wk: -0.1 24 wk: 0.1
	Berg balance scale	29.8 (11.9) 3 wk: 34.7 (15.3), 4.9 12 wk: 45.8 (11.9), 16.0 24 wk: 49.3 (8.5), 19.5	29.7 (10.3) 3 wk: 37.6 (14.2), 7.9 12 wk: 48.8 (11.3), 19.1 24 wk: 47.9 (11.5), 18.2	Diff Δ*: 3 wk: -3 12 wk: -3.1 24 wk: 1.3
	ROM	79.0 (22.6) 3 wk: 96.6 (21.1), 17.6 12 wk: 117.9 (11.8), 38.9 24 wk: 120.6 (12.9), 41.6	82.0 (12.6) 3 wk: 106.0 (13.6), 24.0 12 wk: 118.8 (12.8), 36.8 24 wk: 122.3 (12.0), 40.3	Diff Δ*: 3 wk: -6.4 12 wk: 2.1 24 wk: 1.3
	Quadriceps strength	NR 3 wk: 107.1 (35.2), NR 12 wk: 138.4 (29.7), NR 24 wk: 149.2 (37.6), NR	NR 3 wk: 98.1 (43.8), NR 12 wk: 131.1 (39.7), NR 24 wk: 146.5 (41.1), NR	Diff Δ: 3 wk: NR 12 wk: NR 24 wk: NR
	Hamstring strength	NR 3 wk: 91.0 (34.1), NR 12 wk: 153.1 (34.2), NR 24 wk: 174.1 (42.0), NR	NR 3 wk: 103.2 (45.3), NR 12 wk: 146.9 (55.1), NR 24 wk: 157.7 (45.1), NR	Diff Δ: 3 wk: NR 12 wk: NR 24 wk: NR
Quality of Life				
Eichler, 2019[84] AR High	SF-36 physical component score (3 mo)	33.8 (7.6) 44.6 (9.9), 10.7 (10.4)	33.3 (7.9) 44.4 (8.3), 11.1 (7.2)	Diff Δ: -0.4*
	SF-36 mental component score (3 mo)	54.8 (10.6) 52.4 (10.6), –2.5 (12.4)	53.9 (11.8) 54.1 (9.8), 0.1 (8.5)	Diff Δ: -2.6*
Prvu Bettger, 2020[87] AR Some concerns	PROMIS physical function (12 wk)	12.5 (2.4) 15.3 (2.4), 2.8	12.3 (2.5) 14.8 (2.8), 2.5	Diff Δ: 0.3*
	PROMIS mental health (12 wk)	15 (2.8) 16.6 (2.5), 1.6	14.9 (3.2) 16.1 (3.2), 1.2	Diff Δ: 0.4*
Shim, 2023[88] AR Some concerns	EuroQoL-5D-5L	0.4 (0.2) 3 wk: 0.6 (0.1), 0.2 12 wk: 0.8 (0.1), 0.3 24 wk: 0.8 (0.1), 0.4	0.5 (0.2) 3 wk: 0.6 (0.1), 0.1 12 wk: 0.7 (0.1), 0.3 24 wk: 0.8 (0.1), 0.3	Diff Δ*: 3 wk: 0.02 12 wk: 0.1 24 wk: 0.1

Notes. * Calculated by review team.

Abbreviations. AR=augmented reality; Diff Δ=between group difference (Intervention-Comparator) in mean change; KOOS=knee injury and osteoarthritis outcome score; NC=not calculable; NR=not reported; NRS=numerical rating scale; OKS=Oxford Knee Score; PROMIS=patient-reported outcomes measurement information system; ROM=range of motion; SD=standard deviation; SF36=36-item Short-Form Health Survey; SPPB=short physical performance battery; Stand Diff Δ=standardized between group differences over SD; TUG=timed up and go test; VAS=visual analogue scale; VR=virtual reality; WOMAC=Western Ontario and McMaster Universities Arthritis Index.

APPENDIX K. KQ2 OTHER CONDITIONS

Appendix Table K1. Detailed Characteristics for Included Trials on KQ2 Other Conditions

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding Source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
VR Intervention				
Abd-Elsayed, 2021[91] Critical 12 weeks Harvard MedTech Vx Pain Relief Program N/A	**Inclusion:** "All adult patients aged 18 to 65 treated from April 2019 to April 2020 for acute or chronic workplace injuries and were on workers' compensation were retrospectively identified for inclusion. All patients were referred to and overseen by a prescribing physician and referred to the Harvard MedTech Vx Pain Relief Program by orthopedic specialists, pain specialists, primary care physicians, and occupational health providers. All types of workplace injuries were considered..." **Exclusion:** "...patients were excluded if their attorney required them to discontinue therapy. Patients were also excluded if they attended less than five in-person behavioral therapy sessions with their behavioral health clinician, as this would indicate possible poor compliance with the Harvard MedTech Vx Pain Relief Program."	N=36 Age, mean (range): 45 (20-65) Female: 56% Home At least 1 to 2 times daily for 45 min each, over 90 days (~12 weeks) "During headset use, patients selected specialized categories, or experiences, pre-loaded onto the headset to target either the knowledge of pain, meditation techniques, escape from pain, or distraction from pain. The choice to view a specific category of VRT was based on weekly phone calls between the physician and patient. For the tailored behavioral therapy component of the program, patients and clinicians discussed their progress with headset use (all outcomes re-reassessed) and the goals of therapy for 30–60 min each week and set three specific goals for the patients care. The goals could be	--	**Primary: Average pain relief, measured through the VAS (0-10)** **Pain intensity/severity** • VAS **Opioid use** • Self-reported opioid use **Non-eligible: Anxiety awareness and level of immersion in therapy, patients' perception of set goals being achieved, sleep improvement, average time thinking about pain**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding Source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
		related to pain reduction, sleep improvement, behavioral health, or social well-being. Any adjustments in therapy were also made at this meeting (as previously discussed). The patient's clinician directed the program, ensured compliance, and also provided further education on how to generalize the skills acquired by the virtual reality headset."		
Bahat, 2020[90] Some concerns 7 months Israeli Air Force IDF-Medical Corps' research grant	**Inclusion:** "…fighter and helicopter pilots from the Israeli Air Force with acute, subacute, or chronic neck pain; with or without referral to the upper limbs; and with an average neck pain intensity (during the past week) of at least 20% [on a Visual Analog Scale (VAS)/100 mm]." **Exclusion:** "Participants were excluded if they reported suffering from neurological disorders, systemic disease, history of spinal surgery, or any disorders that may have limited the ability to complete the study's procedure."	N=22 Age, mean (SD): 30 (5.8) Female: 5% Home 5 min/session (1 exercise each for 1-2 mins, 1 min break between modules), 4 sessions per week (total 20 min/wk) for 4 weeks "The individualized VR training software programs were installed on personal laptops for independent use by the subjects… During the interactive VR sessions, the subject's head was visualized as an animated image of a pilot flying a small airplane…The subject's head movements controlled interactions within the virtual environment and the various tasks stimulated different therapeutic aims. The VR software	N=23 Age, mean (SD): 28 (5.1) Female: 13% Usual care NR "...both groups (control and intervention) continued physical therapy, if receiving any, and this was the control intervention."	**Primary: NDI, mean velocity** **Pain-related functioning (4 wk, 7 mo)** • NDI **Pain intensity (4 wk, 7 mo)** • VAS **Quality of life (7 mo)** • EQ5D-VAS general health **Physical performance (7 mo)** • Isometric strength flexion/extension • Global peak velocity • Global mean velocity • Global time to peak velocity • Global accuracy • Global # of velocity peaks

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding Source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
		included three modules aimed at stimulating: 1) increased ROM, 2) faster motion with a quick response, and 3) increased neck motion accuracy..."		
AR Interventions				
Rodriguez-Hernandez, 2021[92,96,122] High 15 weeks University General Hospital of Talavera de la Reina, Spain University of Castilla La Mancha (grant # 2020-GRIN-29192)	**Inclusion:** "...attended the hospital rehabilitation unit.... who had been diagnosed with stroke...age: 18 to 85 years... maximum evolution time of six months...upper limb motor involvement...dependence in activities of daily living (Stroke Impact Scale; version 3.0)... life expectancy greater than six months (absence of life-threatening diagnoses such as end-stage cancer)...absence of other serious and disabling pathologies." **Exclusion:** "...presence of other neurological diagnoses, severe hemineglect, psychiatric pathologies"	N=23 Age, mean (SD): 62.6 (13.5) Female: 21.7% Clinic 150 mins per daily session, 5 consecutive days per week x 3 weeks " …conventional upper and lower limb strength and motor training (100 min; guided by the hospital's physiotherapy and occupational therapy team with the use of virtual reality devices (50 min) ...Motor training with virtual reality devices consisted of several systems: First, the Hand-Tutor© glove (Figure 1a) for hand rehabilitation and 3DTutor© for upper extremities. Both systems are based on intensive and repetitive practice through movement and feedback instructions provided by the software with virtual environments and task that stimulate movements	N=23 Age, mean (SD): 63.6 (12.2) Female: 15% Clinic 150 min per daily session, 5 consecutive days per week x 3 weeks "The conventional intervention protocol consisted of receiving manual therapy techniques (massage); passive and active assisted mobilization of the upper and lower limbs; walking in parallel, on slope and stairs; exercises with and without resistance with balls, elastic bands, and dumbbells in therapeutic cage and trellises; active-assisted mobility exercises of the upper limb and fingers in a sitting position; moving objects horizontally on a table; elevation and superposition of objects in vertical plane; biomechanical tasks that simulate flexion–extension and	**Primary: EQ-5D-5L** **Quality of life (15 wk)** • EQ-5D-5L **Physical performance (3 wk, 15 wk)** • Fugl-Meyer Assessment – Upper Extremity • Action Research Arm Test (ARAT) **Non-eligible: Modified Ashworth Scale; Stroke Impact Scale**

Author, Year **Risk of Bias** **Follow-Up Duration** **Site(s)** **Funding Source**	**Inclusion/Exclusion Criteria**	**Intervention:** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Intervention Characteristics**	**Comparator(s):** **Participants Randomized** **Demographics** **Setting** **Frequency; Duration** **Detailed Comparator Characteristics**	**Primary Outcome** **Eligible Outcomes & Measures Reported (Time Points)** **Other Non-Eligible Outcomes Reported**
		that stroke survivors require for daily life."	abduction–adduction of the shoulder and flexion–extension of the wrist and fingers."	
Taveggia, 2016[94] Some concerns 12 weeks 3 hospitals (2 owned by Habilita), Italy NR	**Inclusion:** "... aged 18 to 80 years old...patients in the acute phase of stroke (between 0.5 and 12 months post-onset)...self-reported functional impairments of their upper extremities after stroke... first stroke episode; no history of peripheral nerve injury or musculoskeletal disease (e.g., arthritis, musculotendinous injury or bone fracture) in the affected upper extremity; no contracture of the affected wrist or fingers (Modified Ashworth <3); and no history of any invasive procedure (botulinum toxin type A) for the treatment of spasticity for at least 6 months prior to the start of this study." **Exclusion:** "...unstable medical disorders, aphasia, or cognitive problems (MMSE≤21)."	N=27 Age, mean (SD): 73 (10) Female: 66.7% Clinic 1 hr/day, 5 days per week, for 6 weeks Armeo Spring device "allows the reinforcement and facilitation of movement by means of a visual feed-back with a three-dimensional virtual environment in which the patient is asked to perform various tasks...In the first session the device was adjusted for patient's arms. The physiotherapist controlled functional space of upper limb movement and correct position of working station. Each training session consisted of two parts with 30 minutes per session with Armeo Spring and 30 minutes per session with conventional treatment..."	N=27 Age, mean (SD): 68 (13) Female: 48.1% Clinic 1 hr/day, 5 days per week, for 6 weeks "...traditional rehabilitation...such as passive and active assisted mobilization of the upper limbs traditional training based on the Bobath concept (neuromuscular facilitation, postural control and proprioception exercises, verticalization and gait training)."	**Primary: Functional Independence Measure (FIM), clinician-reported measure of functional ability; Motricity Index (MI) for motor strength** **Pain intensity/severity (6 wk, 12 wk)** • VAS **Adverse events (6 wk)** **Physical performance (6 wk, 12 wk)** • Motricity Index (MI) **Non-eligible: FIM; Modified Ashworth Scale for Grading Spasticity (MAS)**

Abbreviations. AR=augmented reality; EQ-5D-5L=European Quality of Life scale; EQ5D-VAS=European Quality of Life-Visual Analog Scale; mm=millimeters; MMSE=Mini Mental State Examination; NDI=Neck Disability Index; NR=not reported; SD=standard deviation; VAS=Visual Analog Scale; VR=virtual reality.

Appendix Table K2. Detailed Results for KQ2 Other Conditions Studies

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Man (SD) Follow-Up Mean (SD), Mean Change	Comparison
Pain-Related Functioning or Interference				
Bahat, 2020[90] VR Some concerns	NDI	17.6 (8.9) 4 wk median (IQR): 10 (6, 26) 7 mo median (IQR): 9 (6, 18)	17.9 (10.4) 4 wk median (IQR): 16 (8, 20) 7 mo median (IQR): 18 (6, 26)	Diff Δ: NC
Pain Intensity				
Abd-Elsayed, 2021[91] VR Critical	VAS	Baseline pre: 6.0 (NR) Baseline post: 5.4 (NR) 12 wk pre: 3.8 (NR) 12 wk post: 3.1 (NR)	NR	NA
Bahat, 2020[90] VR Some concerns	VAS	36.4 (22.9) 4 wk: 25.7 (24.0), -10.7* 7 mo: 23.0 (22.2), -13.4*	49.5 (21.1) 4 wk: 26.9 (22.3), -22.6* 7 mo: 24.5 (22.3), -25.0	Diff Δ*: 4 wk: 11.9 7 mo: 11.6
Taveggia, 2016[94] AR Some concerns	VAS	4.5 (1.5) 6 wk:1.7 (1.2), -2.8 (1.4) 12 wk: 1.0 (1.1), -3.5 (1.3)	4.2 (2.0) 6 wk: 2.5 (1.6), -1.7 (1.8) 12 wk: 2.6 (1.6), -1.6 (1.8)	Diff Δ∗: 6 wk: -1.1 12 wk: -1.9
Adverse Events				
Taveggia, 2016[94] AR Some concerns	Participants who experienced an AE	No AE	No AE	Diff Δ∗: 0
Quality of Life				
Rodriguez-Hernandez, 2021[92] AR High	EuroQoL -5DL - Mobility	n (%) No problems: 0 Mild/moderate problems: 5 (22) Severe/extreme problems: 18 (78) 15 wk: No problems: 9 (39) Mild/moderate problems: 14 (61) Severe/extreme problems: 2 (10)	n (%) No problems: 0 Mild/moderate problems: 12 (60) Severe/extreme problems: 8 (40) 15 wk: No problems: 0 Mild/moderate problems: 18 (90) Severe/extreme problems: 2 (10)	--
	EuroQoL -5DL - Selfcare	n (%) No problems: 0 Mild/moderate problems: 5 (22) Severe/extreme problems: 18 (78) 15 wk: No problems: 15 (65) Mild/moderate problems: 8 (35) Severe/extreme problems: 0	n (%) No problems: 0 Mild/moderate problems: 12 (60) Severe/extreme problems: 8 (40) 15 wk: No problems: 5 (25) Mild/moderate problems: 15 (75) Severe/extreme problems: 0	--
	EuroQoL -5DL – Daily activities	n (%) No problems: 0 Mild/moderate problems: 5 (22) Severe/extreme problems: 18 (78) 15 wk:	n (%) No problems: 0 Mild/moderate problems: 4 (20) Severe/extreme problems: 16 (80) 15 wk:	--

Author, Year VR or AR Risk of Bias	Effect Measure	Intervention Baseline Mean (SD) Follow-Up Mean (SD), Mean Change	Comparator Baseline Man (SD) Follow-Up Mean (SD), Mean Change	Comparison
		No problems: 8 (35) Mild/moderate problems: 15 (65) Severe/extreme problems: 0	No problems: 0 Mild/moderate problems: 20 (100) Severe/extreme problems: 0	
	EuroQoL -5DL – Pain/ discomfort	n (%) No problems: 13 (56) Mild/moderate problems: 6 (26) Severe/extreme problems: 4 (17) 15 wk: No problems: 4 (17) Mild/moderate problems: 19 (83) Severe/extreme problems: 0	n (%) No problems: 10 (50) Mild/moderate problems: 9 (45) Severe/extreme problems: 1 (5) 15 wk: No problems: 0 Mild/moderate problems: 19 (95) Severe/extreme problems: 1 (5)	--
	EuroQoL -5DL – Anxiety/ depression	n (%) No problems: 0 (0) Mild/moderate problems: 18 (78.3) Severe/extreme problems: 5 (22) 15 wk: No problems: 7 (30) Mild/moderate problems: 15 (65) Severe/extreme problems: 1 (4)	n (%) No problems: 0 Mild/moderate problems: 17 (85) Severe/extreme problems: 3 (15) 15 wk: No problems: 0 Mild/moderate problems: 13 (65) Severe/extreme problems: 7 (35)	--
Opioid Use				
Abd-Elsayed, 2021[91] VR Critical	Self-reported opioid use	Cessation: 38% Decrease: 31% Increase: 6% No Change: 25%	NR	NA
Physical Performance				
Rodriguez-Hernandez, 2021[93,96] AR High	Fugl-Meyer Assessment Upper Extremity	23.3 (6.9) 3 wk: 57.7 (4.7), 34.4* 15 wk: 58.8 (5.9), 35.5	22.7 (5.4) 3 wk: 47.0 (6.1), 24.3* 15 wk: 49.3 (6.3), 26.6	Diff Δ*: 3 wk: 10.1 15 wk: 8.9
	Action Research Arm Test	13.2 (11.7) 3 wk: 46.0 (9.0), 32.8* 15 wk: 46.0 (9.0), 32.8	11.5 (10.6) 3 wk: 29.3 (10.5), 17.8* 15 wk: 29.7 (10.6) 17.4	Diff Δ*: 3 wk: 15.0 15 wk: 15.4
Taveggia, 2016[94] AR Some concerns	Motricity Index (MI)	37.0 (19.3) 6 wk: 54.7 (22.2), 17.7 (20.8) 12 wk: 80.5 (24.1): 43.5 (21.7)	39.2 (15.6) 6 wk: 50.6 (16.4), 11.4 (16.0) 12 wk: 50.3 (16.6), 5.6 (16.1)	Diff Δ*: 6 wk: 6.3 12 wk: 17.9
Sarig Bahat, 2020[90] VR Some concerns	Flexion	137 (32.2) 7 mo: 152.5 (41.9), 15.5*	128.5 (43.7) 7 mo: 140.9 (38.8), 12.4*	Diff Δ*: 7 mo: 3.1
	Extension	190.1 (51.3) 7 mo: 209.6 (68.5), 19.5*	157.6 (50.9) 7 mo: 177.6 (59.1), 20*	Diff Δ*: 7 mo: -0.5

Notes. *Calculated by review team.

Abbreviations. AR=augmented reality; Diff Δ=difference in change scores; EuroQoL-5D=European Quality of Life 5 Dimensions; IQR=interquartile range; mo=month; NC=not calculable; NDI=Neck Disability Index; NR=not reported; ROM=range of motion; SD=standard deviation; VAS=Visual Analog Scale; VR=virtual reality; wk=week.

APPENDIX L. PEER REVIEW COMMENTS AND RESPONSES

Comment #	Reviewer #	Comment	Author Response
Are the objectives, scope, and methods for this review clearly described?			
1	2	Yes	Thank you.
2	3	Yes	Thank you.
3	4	Yes	Thank you.
4	6	Yes	Thank you.
5	7	Yes	Thank you.
6	13	Yes	Thank you.
Is there any indication of bias in our synthesis of the evidence?			
7	2	No	Thank you.
8	3	No	Thank you.
9	4	No	Thank you.
10	6	No	Thank you.
11	7	No	Thank you.
12	13	No	Thank you.
Are there any published or unpublished studies that we may have overlooked?			
13	2	No	Thank you.
14	3	Yes - Garcia et al., 2021 (doi:10.2196/26292); Garcia et al., 2022a (doi: 10.1016/j.jpain.2021.12.002); Garcia et al., 2022b (doi:10.2196/37480); Maddox et al., 2023 (doi: 10.1016/j.mcpdig.2023.09.003 Perhaps outside of the scope of the review, but interesting study on VR Cybersickness: https://doi.org/10.3389/frobt.2020.00004	The 3 articles by Garcia et al. report results of the RelieVRx trial for low back pain and are already included in the report (see Results on Chronic Low Back Pain, *eg*, Table 2). The fourth article by Maddox et al. was published in December 2023, about 6 months after our search date. We added a reference to this newly published study in Appendix C (Ongoing Studies) and also refer to it in the Discussion (Evidence Gaps & Future Research). We appreciate reviewer's suggestion of the article on etiology of gender differences in VR Cybersickness. Although it is not eligible (as it is not evaluating effects of XR interventions for an eligible pain condition), it provides important information about evaluation of VR side effects

Comment #	Reviewer #	Comment	Author Response
			and potentially how to mitigate some of these in future interventions. We have added the results from this reference to the Discussion (Evidence Gaps & Future Research).
15	4	No	Thank you.
16	6	No	Thank you.
17	7	No	Thank you.
18	13	No	Thank you.
Additional suggestions or comments can be provided below.			
19	2	Overall this is every good and I'm sure a reflection of what is available given the rigor of the review. A couple of comments for consideration. I would ensure that citations are used in the intro to support claims made (think I only saw 1 in the exec summary and number of statements made that should have been cited). I would also consider not making a positive statement about possible benefit and then in the same sentence seemingly de-qualifying it with "but there was limited info on adverse events." I understand this was a significant miss across studies, but it would also be helpful to be clear about the potential good that was seen.	The Executive Summary usually does not contain citations, to help keep the content concise and to avoid complications with reference management (*eg*, references in the Discussion may then precede those for the eligible studies, which may not be individually named in the Summary). The Executive Summary content is a high-level summary of statements and findings in the full report, where all appropriate citations are included. We have also carefully reviewed the Introduction and Discussion sections of the main report for adequate citation of references. We organized the Key Findings using the same structure as the Results sections in the main report. Thus, we briefly summarize the evidence addressing various XR interventions and the findings for different outcomes for each pain condition. Within this structure, the findings for adverse events are generally in close proximity to the benefits of each intervention type (per pain condition). Additionally, we emphasize the lack of evidence on adverse events across all the pain conditions and interventions in the Key Findings because this is an important consideration for clinicians and patients when selecting treatments: side effects are often the reason that treatments are declined or stopped. In the rest of the Executive Summary, as well as in the main report, the findings for each outcome (per intervention and comparator pairing for each pain condition) are laid out in greater detail, and these sections are much more focused on the benefits. This was largely due to eligible studies infrequently reporting adverse events.

Comment #	Reviewer #	Comment	Author Response
20	3	Page IX, Lines 15-16 • How were the prioritized primary outcomes of interest determined (e.g., a priori, ad hoc)?	Prioritization of the primary outcomes for GRADE assessments was discussed with Operational Partners and Technical Expert Panel members, and additional information was collected via an online ranking exercise. We clarified in the Executive Summary the stage at which this prioritization occurred (p. viii) and have added more information about this process to the Methods section in the main report (p.11).
21	3	Page X, Lines 35-37, 42-44 • In lines 35-36, when discussing the direction of the effects the authors state "AR physical activity v. any active comparator". ○ To me, this could leave the reader to assume the standardized mean difference (SMD) = MAR – MControl / SD of change. ○ Thus, SMD = -.7 (-1.2, -.2) indicated that mean reduction in pain intensity is larger in comparator groups is than AR (before accounting for uncertainty). • Then in lines 42-44, the authors state that "AR physical activity may result in better pain-related functioning (eg, Diff Δ -0.4 on Roland-Morris Disability Questionnaire), when compared with usual care…" ○ To me, this now indicates that the standardized mean difference (SMD) = MControl – MAR / SD of change. ○ To orient the reader, I think that the general equation posted in page 6 (line 12 = Diff Δ /standard deviation [SD] of change) should be expanded upon to orient the reader whether positive/negative effects size point estimates and confidence intervals reflect the AR/VR or control conditions.	We have clarified the calculation of the Diff Δ (and standardized Diff Δ) in both the Executive Summary (p. viii) and the main report Methods (p.11). The reviewer is correct in the direction of the comparison; however, improvement is reflected by lower scores for most of the outcome measures (including NRS, VAS, and Roland-Morris Disability). For outcome measures where lower scores reflect an improvement (*eg*, less pain or less disability), the negative value for Diff Δ indicates a greater improvement in the XR intervention group. The reverse would be true for measures where higher scores are better but this was uncommon; we have described in greater detail when there are such findings in the main report. Additionally, the direction of comparison in pooled analyses are also indicated on the forest plots in the main report (when meta-analyses were conducted for that outcome).
22	3	Page XI, Lines 19-26 "Five trials evaluated XR interventions for chronic knee pain due to osteoarthritis, and all compared XR physical activity programs (1 VR, 4 AR) with conventional exercises and rehabilitation. The single trial on VR physical activity showed greater improvement in pain-related functioning and pain intensity in the VR group (eg, Diff Δ -5.1 on the Western Ontario and McMaster Universities Arthritis Index [WOMAC] and -1.1 on VAS 0-10 at 7 weeks). This trial did not address adverse events. The evidence is very uncertain on the effects	We have added a summary of AR study results to the Executive Summary (p. x).

Comment #	Reviewer #	Comment	Author Response
		of AR physical activity on pain-related functioning, pain intensity, and adverse events." • No mention of the AR studies or aggregate XR effects?	
23	3	Page 9, Lines 33-37 • Were studies inly specified if they had a specified population (e.g., chronic low back pain, fibromyalgia) versus chronic pain in general regardless of type? If studies were chosen with non-specific chronic pain populations, how please describe how the data from participants were handled in the study.	For KQ1 eligible studies, the included population could comprise individuals with an eligible condition with pain as a primary symptom (*eg*, fibromyalgia), individuals with a mixture of these eligible conditions, and/or individuals with chronic pain symptoms directly assessed in the study (*eg*, pain in 2 or more joints for at least 3 months). In the KQ1 Other Conditions subsection, we report results for those pain conditions (or other chronic pain) with only 1 identified eligible study (pp. 54-62). For example, this subsection includes 1 study evaluating AR intervention for participants with chronic pain in multiple joints, as well as 1 study examining VR intervention for individuals with either chronic low back pain or fibromyalgia. Since this latter study did not provide results broken down by each condition, we were not able to include its findings under the sections for low back pain and fibromyalgia, respectively. We clarified these groupings in the Results Overview (p. 2).
24	3	Page 11, Lines 17-19 • Please provide additional detail KQ1 to describe imputation methodology used to estimate missing standard deviations of change scores.	We added to the Methods a description of the imputation method we used, which was recommended by the Cochrane Handbook for Systematic Reviews (p. 11).
25	3	Page 12, Lines 11-52 • Why are n's in the flow diagram blank?	The literature flow diagram was not produced for the draft report. It has been completed for the final report.
26	3	Page 13, Lines 5-8 • It was stated that 70 eligible articles reported 59 primary studies. Given the very specific methodology (e.g., RCTs for KQ1), please explain how there more eligible articles than primary studies?	Eligible studies could have multiple articles reporting the findings and this is described in greater detail within each Results subsection. For example, the 5 articles reporting results for RelieVRx for chronic low back pain are described in the Results subsection on chronic low back pain (pp. 21-23) and also cited in Table 2 (pp. 17-19).
27	3	Page 16, Lines 17-18 • Table 2 is repeated twice: "Study characteristics and findings for VR interventions are summarized in Table 2Table 2."	This has been fixed.
28	3	Page 16, Lines 33-35	We rated RoB using the Cochrane RoB2 (for RCTs) or ROBINS-I (for observational studies). In the text and

Comment #	Reviewer #	Comment	Author Response
		• This may be beyond the scope of the review, but in the description of single studies comments such as below read as very vague without further details which were also not provided in the cited appendix (E): • "The study was rated as high RoB due to concerns about randomization, adherence to the intervention, measurement of outcomes, and the selection of reported results".	Appendix E, we summarize and provide detailed ratings for each domain addressed by these standardized assessments. Each domain is evaluated through several items, and the number of items may vary depending on the response to preceding items. As the RoB assessment involves answering a potentially large number of questions, we do not customarily report all the response to these items for each study rating. For example, the study cited here (Yilmaz Yelvar 2017) was rated high risk of bias for the domain of randomization because neither the randomization nor the allocation procedures were described, and there were substantial differences between intervention and control groups in baseline characteristics. Overall, the RoB assessment for Yilmaz Yelvar, 2017 involved 20 items.
29	3	Page 20, Lines 33-36 • Error with referencing software? "The evidence is also very uncertain on the effect of VR embodiment on pain-related functioning and pain intensity, compared with other VR experiences (very low COE; Error! Not a valid bookmark self-reference.)"	This has been fixed.
30	3	Page 22, Lines 30-33 • The statement below reads as if many severe events were reported across conditions, and that no serious adverse events were reported across conditions. Please clarify. "Eccleston, 202225 reported a range of adverse events, finding for example that severe adverse events (symptoms leading to inability to perform daily or work activities) were relatively common: 50% of participants experiencing any severe events in the VR psychological skills group, 29% in VR control, and 36% in usual care. No serious adverse event was reported in any group."	We have added the definition of "serious adverse events" (any event leading to death or serious deterioration in health) to clarify that these are actually more severe than the AE described as "severe" in these studies (p. 22).
31	3	Page 23, Lines 8-10 • The AR for back pain section begins by introducing a comparison to active physical activity interventions then a comparison to usual care. Why is the VR for back pain not aligned with similar comparisons (in the previous section)?	For eligible studies examining the same pain condition (*eg*, for chronic low back pain or fibromyalgia), we grouped VR and AR interventions first by intervention type, and then within each intervention type, by comparators, when these were thought to be substantially different. Studies of VR interventions for low back pain evaluated different intervention types (embodiment and psychological skills).

Comment #	Reviewer #	Comment	Author Response
			Within each of these 2 intervention types, there were a range of comparators, which are described in greater detail in the VR results subsection. Similarly, the AR section is broken down first by intervention type (in this case, all AR studies evaluated physical activity interventions) and then by comparators. The VR and AR subsections are different because the studies evaluated different interventions and comparators.
32	3	Page 41, Lines 23-26; Page 52, Lines 46-47 • When discussing the effects of VR v. non-VR physical activity on pain catastrophizing the authors state that all 3 studies used the Tampa Scale of Kinesiophobia. This is puzzling given the noted distinction between these construction in the empirical literature. o Sullivan et al. (2001) often cited definition describes pain catastrophizing as an 'exaggerated negative mental set brought to bear during actual or anticipated experience of pain'. o Influential papers by Kori et al. (1990) and Vlaeyen et al. (1995) define kinesiophobia (or fear of movement) as "an excessive, irrational, and debilitating fear of physical movement and activity resulting from a feeling of vulnerability to painful injury or re-injury". • The influential Fear-Avoidance Model for Chronic Pain identifies pain catastrophizing as an important predictor of pre-cursor factor in pain-related fear and avoidance. Studies often report a fair to moderate correlation between these two constructs. I am curious to the rationale of the authors decisions.	We agree that kinesiophobia and pain catastrophizing are distinct, though related, concepts that are variably correlated. Our goal was to evaluate the impact of XR interventions on negative perceptions (of potential pain triggers) that contribute to poor outcomes -- particularly fear of movement, pain catastrophizing, or both. To ensure we accurately represent the full scope of XR effects on pain-related outcomes, we intended to be inclusive in selecting eligible outcomes. We have revised the description of this outcome to "pain catastrophizing and kinesiophobia" and have clarified the naming of specific findings regarding these concepts throughout the Results.
33	I 3	Page 44, Lines 43-44 • Typo: "Villafaina, 201957) used 0-100 scale and showed greater improvement in the AR group immediately post-intervention at 6 months (Diff Δ -11.1)."	This has been fixed.
34	3	Page 55, Lines 26-28 • Typo: "Pain-related functioning was assessed with BPI-Interference at baseline, 1 month and 3 months, showing slightly greater reduction in the VR psychological skills group (Diff Δ -1.0 at 1 month and -1.6 at 3 monhts).	This has been fixed.

Comment #	Reviewer #	Comment	Author Response
35	3	Page 66, Lines 25-27 • Formatting error: "Prvu-Bettger, 202085 found very similar improvements in both groups at 3 months, using NRS (Diff Δ 0.2). and using the VAS assessed at baseline, 2 and 4 months."	This has been fixed.
36	3	Page 72, Lines 32-33; Page 73, Lines 24-26 • The authors state that "VR psychological skills may have some benefit for chronic low back pain, but this was not compared with an active treatment." I found this to be an inaccurate statement. Specifically, in the Darnall et al. (2020) paper the authors cite, they comparison group is an audio only version of the same psychological skills intervention. To me, this can be interpreted as an active control group, albeit non-XR (as noted on page 73, lines 21-24). Furthermore, in a follow-up RCT by the same group (see Appendix L for recommendation), they compared 3D VR to sham VR (2D) versions of the same program. o The authors claim "For XR physical activity and psychological skills interventions, a proposed mechanism for enhanced benefits is increased patient engagement, so it would be important to compare to the non-XR versions, and also directly compare measures of engagement and adherence." Again, in the Darnall trial, the authors report the number of VR sessions completed by the intervention group compared to the audio-only (non-XR) control group. This can be taken as a measure of adherence in interpreting these findings.	The Darnall 2020 study included individuals with self-reported low back pain or fibromyalgia, but did not provide results separately for each condition. This study also did not report the number of individuals with each condition by treatment arm. We were thus unable to include this study's results in either the low back pain or fibromyalgia section. Of the 7 studies evaluating an XR psychological skill intervention (for any condition), the Darnall 2020 study was also the only one to use an active comparator. We have revised the Discussion paragraph describing the importance of comparing XR interventions with analogous non-XR treatments, to highlight that this is a particular gap for XR psychological skills interventions (XR physical activity interventions typically were compared with non-XR physical activity). In this paragraph, we also added a sentence highlighting there was 1 study (*ie*, Darnall 2020) that did this for VR psychological skills (p. 74).
37	3	Page 74, Lines 34-35 • Given the limited reporting of adverse events noted by the authors, any specific recommendations for reporting adverse events, measuring, or comparing adverse effect across interventions in VR trials?	We have added recommendations for evaluation and reporting of adverse events to the Discussion (pp. 74-75).
38	4	First and foremost, the report is very exhaustive and comprehensive. It takes a lot of effort to put this kind of analyses together and present them in a meaningful and compelling manner. The report is both educative and forward looking, addressing the research and evidence gap and future directions for research. The structure of the report is another aspect to be appreciated: providing an overview, detailed	Thank you. We agree that technology literacy and acceptance are distinct, and it is likely that both are key components of patients' experience (and uptake) of XR interventions. These factors also likely impact commonly proposed XR mechanisms of action, such as increased patient

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		analyses, and following it up with the Appendices that provide the information for the curious ones. With that being said loud and clear, I have to raise an important aspect. While XR in its different avatars as VR and AR has been around for a while, but the wide spread adoption is not really at the same level as a cell phone or laptop. This (the lack of widespread adoption) could lead to a "digital divide" in the population experiencing pain, not necessarily due to economic background, but due to technology acceptance. In this context, I should say I am disappointed about Appendix D on Risk of Bias Assessments in the sense that the biases listed are mostly on the processes used for study design and outcome ana analyses. There is no report (in Appendix D) that can throw light whether the conducted studies have identified the technology literacy level nor the technology acceptance level. Did the studies collect data and report for: 1. What was the level of the participants' knowledge and comfort in using XR: high/medium/low/poor? 2. What was the level of technology acceptance in using XR: high/medium/low/poor? 3. Do the studies attempt to correlate the outcomes with respect to the answers for (1) and (2)? To me, the answers to the above questions are really important, perhaps even more important than the outcome of XR interventions for chronic pain. Simply because, the outcomes *might* heavily depend on answers for (1) and (2). Unlike other psychotherapy interventions where the level of technology might be less intrusive or "low". The only factor in the report that I could see closely related is the tracking of "adverse events" pertaining to motion / VR sickness - which in my opinion is not really the same as (1) and (2). Another disappointment was that these factors (1) and (2) are NOT highlighted in the "EVIDENCE GAPS & FUTURE RESEARCH" section (Page 72, from Line 53). Of course, there is a passing mention of "barriers to technology adoption" in	engagement with exercise. As with other proposed XR mechanisms of action, however, the relationship of XR to patient engagement appears understudied, and evaluation of relevant mechanistic indicators was beyond the scope of this review. We also agree that a systematic review of technology acceptance and its influence on XR outcomes would be useful – although our experience with the current review suggests that there are likely few studies that have rigorously addressed technology literacy and acceptance using a randomized design. We have revised the Discussion to highlight the need for improved understanding of these factors (p. 74).

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		Page 74, Line 27. But this is mentioned only with respect to older adults - for future research. To make my view clear, the point I want to convey is that reluctance to "accept" a technology - as a means for intervention - can *potentially* have a significant impact on the outcomes - and this needs to be studied along with other factors. The acceptance - or lack of it - of technology need not be due to economic or literacy factors alone, in my view. Another important thing is that this "acceptance" could change during the study period: one could be highly enthusiastic initially and might get bored quickly, and vice versa. A systematic study on technology acceptance and its impact on the outcomes is therefore needed.	
39	6	The draft review is a very nicely organized review that follows a clear and standard method to describe the current state of the evidence base. It provides a rationale for not including case studies and similar types of reports that are of the type that are commonly found in a relatively new intervention. It points out the VHA XR Network which is an important resource for readers of this review. It notes the important limitations in research quality that limits the ability to determine the effectiveness of these novel interventions. It describes possible mechanisms and gives guidance for improved research methods to help determine if these mechanism are present and to what degree XR could be a useful adjunct or alternative to more standard treatments. This is careful and helpful review. Its primary benefit is noting current limitation and providing guidance on what will improve the evidence base. Also appreciate the authors wish to be inclusive and the acknowledgement that it can be difficult to categorize XR, i.e., AR vs VR. These issues and the rationale were stated nicely. The appendices are also excellent resources for understanding the reviewed studies.	Thank you.
40	6	The authors are encouraged to be cautious in statements like "XR has great potential as part of a comprehensive plan for pain treatment." page 74, line 18. I share this enthusiasm but am also informed by the draft review which indicates that the current research does not provide reliable guidance on the	We have changed this sentence to state “considerable potential”. Regarding the statements in the Conclusion, the use of “may” is consistent with the low CoE assessments for XR physical activity interventions for neck pain, which takes into consideration the methodological concerns noted in the

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		potential for XR. It may have great potential but the limitations in CoE that are the primary theme of this review do not support the word great. Similarly, stating that XR may be helpful for some conditions but not others, page 74, lines 36-38, should be restated with more care since the problems noted in Page 74, lines 34-35 suggest that such comparisons probably should not be made at this point.	beginning of the Conclusion. However, we have corrected the statement for low back pain to "the evidence is very uncertain," which is more consistent for the very low COE for low back pain (p. 76).
41	6	Pain Catastrophizing: For the most part, in the draft manuscript Pain Catastrophizing is used to refer to both catastrophizing and kinesiophobia. Table 2 Page 17 lines 22-24 has Outcomes column label Pain Catastrophizing & Kinesiophobia (both the TSK and FABQ can be considered measures of kinesiophobia. This table label is correct in that the two are related but not perfectly correlated and can have independent predictions and treatment indications. It would be helpful to note early in the main text that Pain Catastrophizing is being used as a general term to cover both related concepts as indicated in the Table 2.	We have further clarified the inclusion of these 2 related concepts and revised the report accordingly, as noted above in our response to comment #32.
42	6	The reviewed copy is a draft. Recommend further proofing to correct some typos, grammar and similar issues.	We have carefully copyedited the final draft.
43	13	This is an interesting and well-conducted review on an important topic. The limited evidence and paucity of robust studies on XR interventions for chronic pain is for me admittedly rather surprising and somewhat disappointing. Given what appear to be fundamental gaps related to the efficacy, effectiveness and adverse events associated with XR, I was also a bit surprised by some of the discussion about implementation as part of future research. Nonetheless, while some aspects related to implementation may be premature, I don't disagree that it is important to consider implementation, including user-centered design approaches and implementation context, while establishing the efficacy/effectiveness of XR interventions for chronic pain.	We agree that implementation of XR interventions for several pain conditions may be premature given the state of the evidence. However, implementation science frameworks may still be helpful by clarifying the role of XR as core intervention component vs. means of intervention delivery and engagement. Additionally, implementation science can help with evaluating real-world effectiveness and costs of XR interventions, when health systems (such as the VA) have begun to offer these interventions. We have revised the Discussion to reflect these points (pp.75-76).
44	13	Minor issues, mostly typos that may have already been identified Page vii, Key Findings section. Use of the phrase "effects on adverse events" is a bit awkward and potentially confusing. While perhaps technically correct, the issue is whether these interventions might cause or lead to adverse events, which	We have revised this phrase in the first Key Finding to "the evidence for adverse effects is very uncertain" (p. vi).

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		based on the findings of this review appear to be very uncertain or in many cases unreported and it would be helpful if this were more clearly stated, at least in presenting the key findings.	
45	13	Page x, line 49 would suggest rephrasing “but the evidence about adverse events is very uncertain . . .”	We have revised this phrase to “the evidence for adverse effects is very uncertain” (p. x).
46	13	Page 16, line 18, Table 2 is repeated	This has been fixed.
47	13	Page 17, Table 2, line 49, for Kammler-Sucker outcomes it would be helpful to the reader if the two NRS measures had more distinct labels, e.g., pain-interference NRS and pain intensity NRS	We have clarified the labeling of NRS for these 2 outcomes in Table 2.
48	13	Page 20, line 35, flagging error and line 41 I believe the word environment is missing after immersive	This has been added.
49	13	Page 22, line 34, should be assessed rather than assess and lines 55-56 quality of life is repeated	These have been updated.
50	13	Page 24, line 32, word activity is missing after physical	This has been added.
51	13	Page 26, Table 6, line 61 typo for percentage in the second column (496%), perhaps 46% or 49%	This typo has been corrected.
52	13	Page 28, Table 6, line 33, word aged in second column (describing male university student sample) should be deleted	This has been fixed.
53	13	Page 34, several minor typos, line 18 missing period, line 23 missing word to after due and line 30 the word these can be deleted and the sentence start with “All showed . . .”	These have been updated.
54	13	Page 53, line 28, capitalize VAS	This has been fixed.
55	13	Page 66, line 26 there appears to be in advertent period and extra space	This has been fixed.
56	13	Page 67, section on KQ2 Other Conditions, the citations are not suprascript	This has been fixed.