

KRAŚNIK, Wojciech, JANKOWSKA, Olga, KURZEJA, Jacek, PIOTROWICZ, Katarzyna, PIOTROWICZ, Hubert, BAJKACZ, Agnieszka, ROGALA, Anna and OSMÓLSKA, Joanna. The benefits and challenges of virtual reality application in rehabilitation for chronic conditions. Journal of Education, Health and Sport. 2024;75:56379 eISSN 2450-3118.

<https://dx.doi.org/10.12775/JEHS.2024.75.56379>

<https://apcz.umk.pl/JEHS/article/view/56379>

The journal has had 20 points in Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.

Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).

Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.

Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

© The Authors 2024;

This article is published with open access at Licensee Open Journal Systems of Nicolaus Copernicus University in Torun, Poland Open Access. This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author (s) and source are credited. This is an open access article licensed under the terms of the Creative Commons Attribution Non commercial license Share alike. (<http://creativecommons.org/licenses/by-nc-sa/4.0/>) which permits unrestricted, non commercial use, distribution and reproduction in any medium, provided the work is properly cited.

The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 23.11.2024. Revised: 14.12.2024. Accepted: 16.12.2024. Published: 18.12.2024.

The benefits and challenges of virtual reality application in rehabilitation for chronic conditions

Wojciech Kraśnik¹, Olga Jankowska¹, Jacek Kurzeja¹, Katarzyna Piotrowicz², Hubert Piotrowicz², Agnieszka Bajkacz³, Anna Rogala⁴, Joanna Osmólska^{4a}

¹ J Strus City Multispecialty Hospital, Szwajcarska 3, 61-285 Poznań, Poland

² University Clinical Hospital in Poznan, Przybyszewskiego 49, 60-355 Poznań, Poland

³ University Hospital (UH) in Wroclaw, Borowska 213, 50-556 Wrocław, Poland

⁴ Poznan University of Medical Sciences, Fredry 10, 61-701 Poznań, Poland

Wojciech Kraśnik; wojkras@op.pl; ORCID: 0009-0003-7754-2174

Olga Jankowska; jankowskaolga.jo@gmail.com; ORCID: 0009-0001-8047-7962

Jacek Kurzeja; jacekkurzeja96@gmail.com; ORCID: 0009-0004-4075-7208

Katarzyna Piotrowicz; katarzyna.piotrowicz@op.pl; ORCID: 0009-0009-3888-3885

Hubert Piotrowicz; hubert1411@poczta.onet.pl; ORCID: 0009-0008-2453-3561

Agnieszka Bajkacz; agnieszkabajkacz99@gmail.com; ORCID: 0000-0002-2027-8216

Anna Rogala; ania.rogala123@gmail.com; ORCID: 0009-0005-5465-6771

Joanna Osmólska; jnn.osmolska@gmail.com; ORCID: 0000-0002-8754-7222

Abstract

The recent era of rapid advancements in information technology has enabled various medical disciplines to tackle longstanding problems in novel ways. Among these, virtual reality (VR) has emerged as a promising alternative or complement to conventional physical therapy (CPT) for managing chronic musculoskeletal, degenerative, neurological, and pulmonary conditions. Increased patient motivation during treatment, low drop-out rates, and instant feedback are among the primary reasons VR is gaining trust among physicians, patients, and caregivers worldwide. Evidence suggests that VR can significantly enhance motor performance, cognitive skills, pulmonary function, activities of daily living (ADLs), quality of life (QoL), and even reduce pain intensity in several chronic diseases. Notably, patients with stroke, Parkinson's disease, multiple sclerosis (MS), and chronic obstructive pulmonary disease (COPD) are poised to be the primary beneficiaries of VR. Thus, it appears that VR-based techniques are set to leave a footprint on clinical practice globally. However, challenges to the clinical adoption of VR remain, including technical limitations, the lack of standardized guidelines, and minor safety concerns that must be addressed. This paper summarizes the background, current developments, and key considerations for future research in this rapidly evolving field.

Keywords: virtual reality, rehabilitation, chronic diseases

Introduction

Chronic neurological, degenerative, musculoskeletal, and cardiopulmonary conditions are among the leading causes of disability among middle-aged and older adults globally (1). Physical rehabilitation is an evidence-based approach critical for addressing a wide range of impairments, including motor control dysfunction, muscle paralysis, weakness, deconditioning, altered sensation, and brain–body–nervous system dysregulation (2). By focusing on progressive strengthening and functional mobility training, intensive skilled rehabilitation not only aids in managing these conditions but also enhances clinical outcomes. Rehabilitation training has been shown to rapidly improve limb function and muscle strength, prevent muscle atrophy and joint stiffness, reduce the disability rate, and significantly enhance patients' quality of life (3, 4). This approach is particularly vital in chronic conditions, where continuous,

professional, and systematic rehabilitation minimizes long-term impairment (5). Thus, integrating comprehensive rehabilitation into treatment plans is essential for optimizing patient recovery and functional independence.

Globally, healthcare systems face significant challenges related to the availability, insurance coverage, and accessibility of outpatient and home health services, limiting the continuity of care for individuals with chronic conditions (6). These limitations often result in episodic care of short duration or a lack of access to necessary services altogether (7). Effective management of chronic diseases frequently depends on patients' ability to sustain adherence to behavior modifications and movement strategies learned during rehabilitation (3). However, evidence suggests that many individuals are unable to engage in evidence-based movement strategies at the intensity required to achieve clinically meaningful outcomes, and adherence to recommended regimens remains consistently low (2). As a result, the majority of individuals with chronic conditions experience a gradual decline in function over time (6).

Virtual Reality (VR) is a computer-mediated technology that creates a three-dimensional, simulated environment in which users can experience and interact with virtual worlds in real time (8). By leveraging advanced sensory feedback systems—including visual, auditory, haptic, and sometimes cognitive inputs—VR enables users to achieve a heightened sense of immersion, where the virtual environment responds dynamically to their actions and sensory perceptions (9). This immersive interaction is facilitated through consistent and realistic presentation of computer-generated stimuli, fostering a sense of presence within the simulated experience (10). Consequently, there is a wide range of clinical contexts, where VR can be utilized, ranging from neurological and degenerative disorders to pain management (11). Its integration into rehabilitation programs has demonstrated significant improvements in motor and functional skills, such as gait and balance, establishing VR as a viable alternative to conventional physical therapy (CPT) for conditions such as stroke, Parkinson's disease (PD) multiple sclerosis (MS) and chronic obstructive pulmonary disease (COPD) (11). In the realm of neurological rehabilitation, VR has been effectively utilized for the assessment and treatment of physical and cognitive impairments (12). Additionally, evidence supports the positive impact of VR on enhancing rehabilitation outcomes through the incorporation of different breathing patterns, which contributes to improved emotional well-being (13).

However, the adoption of these technologies to augment therapeutic approaches has challenges. Due to the technical limitations derived from providing a user-friendly wearing experience i.e. lightweight and a compact, glasses-like form factor, the design of high-performance VR devices often entails several tradeoff relations (14). Moreover, such technology is often cost-prohibitive and has lower levels of acceptance in the elderly population. The VR still lacks guideline for standardization of the use of these technologies in medicine, thus resulting in the challenging adoption in the clinical setting (15).

Motor performance

VR-based neurorehabilitation for stroke is closely linked to recovery, reorganization, and neuroplasticity (16) From a neurophysiological perspective, VR has been shown to activate the mirror neuron system, enabling a visuo-motor transformation phenomenon through the activation of parietal areas and generating an efferent copy of motor actions, even when the actions are virtual (17). Several meta-analyses (7, 18) have provided evidence for improved upper limb (UL) recovery in stroke patients, with VR groups scoring higher on the Fugl-Meyer Assessment for Upper Extremities (FMA-UE). Upper limb functionality, as measured by range of motion (ROM) and muscle strength in Manual Muscle Testing (MMT), favored VR-supported exercise therapy (7).

However, some researchers reported that statistically significant results for UL function were observed only when compared to no therapy; no significant improvements were seen when compared to CPT (19). Outcomes on the Box and Block Test (BBT) were inconsistent, with some studies showing improvement (7), while others found no statistically significant gains (18). Another study demonstrated statistically significant differences in balance (Berg Balance Scale (BBS)) and risk of falls (Timed Up and Go (TUG)) with VR interventions compared to conventional treatments (17).

In Parkinson's disease (PD) patients, repetitive motor exercises performed in a VR environment induced remodeling of neuronal dendrites, leading to activation of the primary sensorimotor cortex and improved motor abilities (4). VR interventions have shown improvements in step and stride length compared to physiotherapy (4, 20). However, no significant effects were observed in balance (20), walking speed (4) and gait (4, 20, 21). Conversely, the results of other studies demonstrated that VR-based rehabilitation led to a

significant improvement in balance function, as assessed by the BBS and the Activities-Specific Balance Confidence (ABC) scale, along with enhanced motor function measured by the Unified Parkinson's Disease Rating Scale (UPDRS III) (4, 21).

In MS patients, VR provides multisensory feedback that may induce sensorimotor neuroplasticity in the sensorimotor cortex, potentially contributing to functional motor recovery. MS patients have shown significant improvements in motor functions, particularly in gait and balance (22).

In children with cerebral palsy (CP), VR interventions have demonstrated efficacy in promoting the development of gross motor skills, positioning VR as a promising tool for addressing developmental delays early and preventing lasting impairments. VR training has improved body alignment symmetry in children with CP, resulting in a more balanced distribution of the center of gravity across the lower limbs (23, 24). This enhanced symmetry has contributed to greater postural stability during standing. Additionally, the intervention strengthened lower limb muscles, improved postural control, and enhanced walking abilities (23). Further benefits included improvements in motor ability on the hemiplegic side and better action control (24).

Motor function restoration is a critical rehabilitation goal for spinal cord injury (SCI) patients. A meta-analysis indicated that VR interventions can improve outcomes on the BBT, BBS, Walking Index for Spinal Cord Injury (WISCI), and Limits of Stability (LOS) testing (25). However, another study concluded that there is insufficient evidence to suggest that VR interventions are more effective than CPT for recovering upper limb motor function (ULMF) in SCI patients (12).

Lastly, VR interventions have shown a trend toward positively affecting motor function in patients with back pain (26).

Cognitive skills

It has been demonstrated that VR helps improve neuropsychological deficits by stimulating and enhancing cerebral plasticity in neurological populations (17). People with mild-to-moderate dementia caused by Alzheimer's disease (AD) can benefit from cognitive stimulation using VR. While the results did not indicate improvements in executive functions,

a significant effect was observed in global cognition based on changes between pre- and post-treatment assessments (27).

In stroke patients, VR-based therapies have been shown to significantly improve executive function, visuospatial abilities, and memory compared to control groups. However, there is no evidence to suggest that VR significantly improves global cognitive function, verbal fluency, attention, or depression symptoms (3, 28). Patients with higher baseline severity scores appeared to derive greater benefits (28). Research also highlights the therapeutic potential of game-based digital interventions for depression, as positive gaming experiences stimulate the release of endorphins and striatal dopamine. Additionally, rehabilitation exercises can support brain structure recovery, activate relevant brain regions, foster adaptive behaviors, and enhance emotional regulation. This can promote positive emotions and improve coping mechanisms in individuals with depression in chronic conditions (29).

VR is suggested to enhance functional outcomes in patients by improving cognitive reserve, thereby mitigating the impact of gray matter atrophy and brain lesions on cognitive processing speed and memory in people with MS (30). VR-based rehabilitation has shown promise in MS patients by improving global cognitive function, visuospatial skills, and both immediate and delayed recall, as measured by tools such as the Montreal Cognitive Assessment (MoCA) and the Spatial Recall Test (SPART), while also reducing anxiety compared to controls (31). Another study reported improvements in cognitive function, specifically in executive abilities, attention, and memory skills (22).

In COPD patients, VR-based pulmonary rehabilitation was effective in improving mood by reducing depression and anxiety symptoms (32). However, a separate study found no positive effects on anxiety or depression when compared to standard therapy (33).

Daily participation and quality of life

Daily participation encompasses engaging in activities of daily living (ADLs) and instrumental activities of daily living (IADLs), which are key indicators of individual independence (34). Evidence suggests that VR-based interventions can significantly improve ADL performance (19), as indicated by higher scores on the Functional Independence Measure (FIM) (7, 18) and modified Rankin Scale (mRS) (7) compared to conventional treatments,

particularly for patients recovering from stroke. VR has also been shown to enhance the quality of life (QoL) for stroke patients (3), although its impact on QoL in Parkinson's disease (PD) remains inconclusive (20, 21), with some studies reporting no improvement (4) and others highlighting potential benefits linked to motor function improvements and sensory stimulation. Additionally, VR-based cognitive training has demonstrated significant benefits in ADL and IADL performance for individuals with mild cognitive impairment (MCI) and Alzheimer's disease (AD) (35). Improvements in ADLs have also been reported in conditions such as neck pain (36). Moreover, VR has positively influenced the mental component of QoL in fibromyalgia patients, further underscoring its broad therapeutic potential (37).

Pulmonary function

Pulmonary rehabilitation has been shown to help reduce the risk of exacerbations and improve quality of life for patients with COPD (2). One meta-analysis demonstrated that VR-based pulmonary rehabilitation is superior to traditional pulmonary rehabilitation in improving pulmonary function and exercise capacity in COPD patients. Specifically, VR-based rehabilitation was associated with significant improvements in FEV1%pred (forced expiratory volume in 1 second as a percentage of predicted), FEV1/FVC (forced expiratory volume in 1 second/forced vital capacity), dyspnea, and six-minute walking distance (6MWD) (32). Another meta-analysis confirmed findings favoring VR-based training for FEV1%pred with statistical significance (33). However, no significant improvements were observed in exercise capacity (6MWT) or subjective dyspnea when compared to standard therapy (33). Additionally, studies suggest that VR may serve as an effective tool for pulmonary rehabilitation in patients with lung cancer and asthma. Overall, evidence indicates that VR can enhance the functional outcomes of pulmonary rehabilitation by improving breathing awareness, relaxation techniques, and other key therapeutic components (13).

Pain management

VR treatment functions as a pain distraction mechanism by directing attention toward an external stimulus rather than bodily sensations, thereby reducing the focus on pain through divided attention tasks (38). Studies on chronic low back pain (CLBP) patients have shown significant reductions in pain intensity with VR interventions compared to no VR treatment. Subgroup analyses have further demonstrated that VR is significantly more effective than no

intervention, placebo, or oral treatment. However, when VR was combined with physiotherapy, or when VR alone was compared to physiotherapy, no additional benefits were observed (39). Conversely, a separate meta-analysis suggests that VR, particularly VR-based exercises, can provide statistically and clinically significant improvements in pain intensity compared to conventional physiotherapy or usual care without intervention (26). In addition to pain relief, VR has shown significant benefits in reducing kinesiophobia (39). A meta-analysis on VR-assisted active training for chronic musculoskeletal pain indicated that non-immersive VR-assisted training outperforms conventional training in reducing pain, improving disability, and alleviating kinesiophobia in the short term for back pain, with some effects persisting into the intermediate term (40). Similarly, studies on neck pain revealed statistically significant reductions in pain intensity favoring VR interventions over controls (36, 40). VR therapy also led to improvements in disability, kinesiophobia, cervical range of motion (CROM), and mean and peak velocity (36). Furthermore, immersive virtual reality (IVR) combined with exercise significantly reduced pain, kinesiophobia, fatigue, and improved physical activity levels in fibromyalgia patients (37). These findings highlight the potential of VR as a versatile and effective tool for managing pain and associated functional impairments.

Table 1. Positive effects of VR rehabilitation in chosen chronic conditions^(2-4,7,12,13,16-39)

Type	Condition	Positive effects
Motor performance	Stroke	FMA-UE, ROM, MMT, BBT*, BBS, TUG
	PD	step and stride length, BBS*, ABC, UPDRS III
	MS	gait and balance (different scores)
	CP	gross motor skills, lower limb muscle strength, postural control, walking abilities, action control
	SCI	BBT, BBS, WISCI, LOS
	Back pain	motor skills (various scales, questionnaires and physical tests)

Cognitive skills	AD	global cognition
	Stroke	executive function, visuospatial abilities, and memory
	MS	MoCA, SPART
	COPD	mood, depression*, anxiety*
Daily participation and quality of life	Stroke	ADL, FIM, mRS, QoL
	PD	QoL*
	MCI	ADL, IADL
	AD	ADL, IADL
	Neck pain	ADL
	Fibromyalgia	QoL
Pulmonary function	COPD	FEV1%pred, FEV1/FVC, dyspnea*, 6MWD*
Pain management	CLBP	Pain intensity, kinesiophobia
	chronic musculoskeletal pain	Pain intensity, kinesiophobia, disability
	Neck pain	Pain intensity, kinesiophobia, disability, CROM, mean and peak velocity
	Fibromyalgia	Pain intensity, kinesiophobia, fatigue, physical activity levels
*inconclusive		

Benefits of VR

VR-based therapy offers numerous advantages over conventional physical therapy by integrating virtual and real-world elements, enabling experiences and characteristics typically inaccessible in traditional clinical settings. Even when not used as a standalone treatment, VR can provide additional benefits when combined with physical therapy (36). VR-assisted approaches allow for highly intensive, repetitive, and task-oriented training in immersive environments without the need for constant supervision by medical staff (18). These technologies show promise for improving patient care by supporting evidence-based therapeutic activities and enabling their implementation in home settings (2). Customized visual and auditory feedback in VR can continuously improve incorrect postures among participants (36). Depending on the software, the content of VR training may be more targeted than traditional rehabilitation, providing additional benefits to patients (25).

VR can simulate real-life environments, enabling real-time interactions and allowing patients to practice therapeutic tasks that might otherwise be impractical due to resource limitations or safety concerns (19). Moreover, VR-based therapy can energize patients, reducing the risk of demotivation from standard therapy by offering enjoyable and engaging experiences that balance task challenges with participant skill levels (21, 33, 41). This minimizes the monotony often associated with conventional rehabilitation (7). Unlike traditional therapy, VR stimulates brain metabolism, enhances cerebral blood flow, and promotes neurotransmitter release, leading to improved therapeutic outcomes (3). Another aspect of VR assisted therapy is the enhancement of observational learning, contributing to the rehabilitation by preferentially activating parts of brain that are involved with the physical performance itself (16).

Studies have highlighted VR's immersive and multi-sensory effects, which provide sufficient distraction to reduce pain sensation and improve physical performance (40). Immersive therapeutic software designed for presence, learning, and habit-building further enhances VR's utility by addressing pain interference with activities, mood, and stress (40). Additionally, VR can improve coordination, better supporting muscles, alleviating postural stress, and relaxing specific muscle groups to relieve pain (36). Personalized VR-based rehabilitation programs offer patients greater autonomy, enhancing daily activity performance

and slowing disease progression (32). Furthermore, immersive VR has been shown to reduce the need for analgesics, decreasing dependence on pharmacotherapy (42).

Adherence is a critical factor in the success of therapeutic interventions, and conventional rehabilitation, often marked by high dropout rates, tends to yield only moderate results at best (3). Factors affecting adherence to exercise include timing, transportation, access to exercise equipment and cost of physiotherapy session (43). Despite VR's ability to address many of those barriers, studies couldn't determine whether it surpassed conventional therapy. Some stated that exercise adherence did not differ between VR and other intervention arms (20), whereas other research indicated better adherence in VR-based therapy groups (17, 44).

Limitations of VR application

One potential limitation of VR treatment systems is the diversity of available platforms, which complicates standardization. Greater attention should be given to developing concrete recommendations regarding therapy duration, session frequency, and training length, as longer durations are generally associated with greater improvements (3, 7, 18, 20). While VR alone provides substantial benefits, combining VR-supported exercise therapy with conventional therapy has been shown to yield even greater improvements (7, 19).

VR-assisted training typically employs two main forms: commercially available games and customized systems designed for upper extremity rehabilitation. Customized systems offer greater flexibility to adapt to recovery progress and have demonstrated higher efficacy in rehabilitation (7, 20). It seems that the use of an avatar and a more realistic scenarios could strengthen the neuroplastic changes within higher sensory and motor areas belonging to the mirror neuron system (17). Another downside, derived from technical limitations, is use handheld controllers that rely on gross motor skills in current VR-supported exercise, which reduces capacity to train fine motor movements. Consequently, significant improvements in fine motor function have not been observed (7).

Effective training for ADLs requires specifically designed rehabilitation programs. Currently, most VR training programs focus on isolated functionalities rather than comprehensive ADL training, limiting their applicability to real-world tasks (25). Additionally, the benefits of VR-supported exercise therapy may not persist after discontinuing its use (7).

Older individuals may face challenges in engaging with VR technologies due to age-related visual and auditory changes, which can hinder their ability to fully benefit from such interventions (28). Furthermore, the realistic environments simulated by VR can introduce sensory complexities, making it difficult for patients to perceive and achieve therapy goals accurately (31).

Barriers to the widespread adoption of VR include issues with user-friendliness, performance reliability, and technical errors (2). Patients with cognitive impairments may experience frustration during VR therapy, leading to negative emotional responses and reduced engagement. Therefore, the degree of motivation and engagement achieved during VR therapy often depends on individual characteristics and the design of the intervention content (3). These limitations underscore the importance of addressing usability, accessibility, and customization to maximize the potential of VR in rehabilitation.

Safety

Regarding the safety of VR-based rehabilitation, the literature indicates that adverse events associated with VR are generally rare and mild (17). Reported issues include transient dizziness, headaches, and pain (19, 26, 36). Additionally, some studies highlight potential risks such as cyber-sickness (20, 21), cognitive overload, head and neck strain and privacy risks (20).

Table 2. Advantages and disadvantages of VR-based rehabilitation^(2,3,7,16,18-21,25,28,31-33,36,40-44)

Advantages	Disadvantages
No need of constant supervision	Lack of standardized guidelines
Possible implementation in home setting	Limited availability of specialized equipment and software
Constant feedback	Training limited only to particular skills
Targeted training	Reluctancy in older generations
Safe environment	Technical limitations of the device
Higher patients' motivation	Adverse effects
Lower pain sensation and analgesics use	
Adjustment to individual skills	
Fulfilling unmet medical needs	
Cost-effectiveness	

Conclusions

VR-supported exercise therapy can improve the rehabilitation process at least as effectively as conventional methods. However, several critical considerations must be addressed when implementing VR-based therapies. First, VR interventions should be tailored to the specific needs and characteristics of patients, ensuring that activities, tasks, and assessments are appropriately designed. Second, safety concerns must be prioritized, particularly for older adults with diminished vision or sensory impairments, necessitating careful selection of interaction techniques and methodologies to ensure safe application for individuals with sensory and cognitive limitations. As VR technologies continue to evolve, future research should emphasize longer follow-up periods to evaluate the sustained efficacy and safety of these interventions. Further investigation is also needed to facilitate the development of high-quality, relevant, and accessible VR-based treatments that address a broader spectrum of clinical applications.

Disclosure

Author contribution

Conceptualization, W.K., O.J. and J.K.; methodology: A.R. and J.O.; formal analysis: K.P. and H.P.; investigation: A.B., A.R. and J.O.; resources: A.R. and J.O.; writing: W.K., O.J., J.K., K.P., H.P. and A.B.; supervision: W.K. and O.J.

All authors have read and agreed with the published version of the manuscript.

Funding statement

No financial support was received by any of authors for the manuscript preparation

Conflict of interest

The authors declare no conflict of interest

Institutional Review Board Statement

Not applicable

Statement of Informed Consent

Not applicable

References

1. Hacker K. The Burden of Chronic Disease. *Mayo Clin Proc Innov Qual Outcomes*. 2024;8(1):112-9.
2. LaMarca A, Tse I, Keysor J. Rehabilitation Technologies for Chronic Conditions: Will We Sink or Swim? *Healthcare (Basel)*. 2023;11(20).
3. Zhang Q, Fu Y, Lu Y, Zhang Y, Huang Q, Yang Y, et al. Impact of Virtual Reality-Based Therapies on Cognition and Mental Health of Stroke Patients: Systematic Review and Meta-analysis. *J Med Internet Res*. 2021;23(11):e31007.
4. Yu J, Wu J, Lu J, Wei X, Zheng K, Liu B, et al. Efficacy of virtual reality training on motor performance, activity of daily living, and quality of life in patients with Parkinson's disease: an umbrella review comprising meta-analyses of randomized controlled trials. *J Neuroeng Rehabil*. 2023;20(1):133.
5. Huang J, Ji JR, Liang C, Zhang YZ, Sun HC, Yan YH, et al. Effects of physical therapy-based rehabilitation on recovery of upper limb motor function after stroke in adults: a systematic review and meta-analysis of randomized controlled trials. *Ann Palliat Med*. 2022;11(2):521-31.

6. Rochmah TN, Rahmawati IT, Dahlui M, Budiarto W, Bilqis N. Economic Burden of Stroke Disease: A Systematic Review. *International Journal of Environmental Research and Public Health*. 2021;18(14):7552.
7. Chen J, Or CK, Chen T. Effectiveness of Using Virtual Reality-Supported Exercise Therapy for Upper Extremity Motor Rehabilitation in Patients With Stroke: Systematic Review and Meta-analysis of Randomized Controlled Trials. *J Med Internet Res*. 2022;24(6):e24111.
8. Bruno RR, Wolff G, Wernly B, Masyuk M, Piayda K, Leaver S, et al. Virtual and augmented reality in critical care medicine: the patient's, clinician's, and researcher's perspective. *Crit Care*. 2022;26(1):326.
9. Ali SG, Wang X, Li P, Jung Y, Bi L, Kim J, et al. A systematic review: Virtual-reality-based techniques for human exercises and health improvement. *Front Public Health*. 2023;11:1143947.
10. El Beheiry M, Doutreligne S, Caporal C, Ostertag C, Dahan M, Masson JB. Virtual Reality: Beyond Visualization. *J Mol Biol*. 2019;431(7):1315-21.
11. Afridi A, Malik AN, Tariq H, Rathore FA. The emerging role of virtual reality training in rehabilitation. *J Pak Med Assoc*. 2022;72(1):188-91.
12. De Miguel-Rubio A, Rubio MD, Alba-Rueda A, Salazar A, Moral-Munoz JA, Lucena-Anton D. Virtual Reality Systems for Upper Limb Motor Function Recovery in Patients With Spinal Cord Injury: Systematic Review and Meta-Analysis. *JMIR Mhealth Uhealth*. 2020;8(12):e22537.
13. Pittara M, Matsangidou M, Pattichis CS. Virtual Reality for Pulmonary Rehabilitation: Comprehensive Review. *JMIR Rehabil Assist Technol*. 2023;10:e47114.
14. Nagpal S, Bansal S, Kumar M, Mittal A, Saluja K. Augmented Reality: A Comprehensive Review. *Archives of Computational Methods in Engineering*. 2022;30.
15. Yeung AWK, Tosevska A, Klager E, Eibensteiner F, Laxar D, Stoyanov J, et al. Virtual and Augmented Reality Applications in Medicine: Analysis of the Scientific Literature. *J Med Internet Res*. 2021;23(2):e25499.
16. Teo WP, Muthalib M, Yamin S, Hendy AM, Bramstedt K, Kotsopoulos E, et al. Does a Combination of Virtual Reality, Neuromodulation and Neuroimaging Provide a Comprehensive Platform for Neurorehabilitation? - A Narrative Review of the Literature. *Front Hum Neurosci*. 2016;10:284.
17. Castellano-Aguilera A, Biviá-Roig G, Cuenca-Martínez F, Suso-Martí L, Calatayud J, Blanco-Díaz M, et al. Effectiveness of Virtual Reality on Balance and Risk of Falls in People

with Multiple Sclerosis: A Systematic Review and Meta-Analysis. *Int J Environ Res Public Health*. 2022;19(21).

18. Leong SC, Tang YM, Toh FM, Fong KNK. Examining the effectiveness of virtual, augmented, and mixed reality (VAMR) therapy for upper limb recovery and activities of daily living in stroke patients: a systematic review and meta-analysis. *J Neuroeng Rehabil*. 2022;19(1):93.

19. Laver KE, Lange B, George S, Deutsch JE, Saposnik G, Crotty M. Virtual reality for stroke rehabilitation. *Cochrane Database Syst Rev*. 2017;11(11):Cd008349.

20. Dockx K, Bekkers EM, Van den Bergh V, Ginis P, Rochester L, Hausdorff JM, et al. Virtual reality for rehabilitation in Parkinson's disease. *Cochrane Database Syst Rev*. 2016;12(12):Cd010760.

21. Kwon SH, Park JK, Koh YH. A systematic review and meta-analysis on the effect of virtual reality-based rehabilitation for people with Parkinson's disease. *J Neuroeng Rehabil*. 2023;20(1):94.

22. Maggio MG, Russo M, Cuzzola MF, Destro M, La Rosa G, Molonia F, et al. Virtual reality in multiple sclerosis rehabilitation: A review on cognitive and motor outcomes. *J Clin Neurosci*. 2019;65:106-11.

23. Cho C, Hwang W, Hwang S, Chung Y. Treadmill Training with Virtual Reality Improves Gait, Balance, and Muscle Strength in Children with Cerebral Palsy. *Tohoku J Exp Med*. 2016;238(3):213-8.

24. Ren Z, Wu J. The Effect of Virtual Reality Games on the Gross Motor Skills of Children with Cerebral Palsy: A Meta-Analysis of Randomized Controlled Trials. *Int J Environ Res Public Health*. 2019;16(20).

25. Wang L, Zhang H, Ai H, Liu Y. Effects of virtual reality rehabilitation after spinal cord injury: a systematic review and meta-analysis. *J Neuroeng Rehabil*. 2024;21(1):191.

26. Bordeleau M, Stamenkovic A, Tardif PA, Thomas J. The Use of Virtual Reality in Back Pain Rehabilitation: A Systematic Review and Meta-Analysis. *J Pain*. 2022;23(2):175-95.

27. Oliveira J, Gamito P, Souto T, Conde R, Ferreira M, Corotnean T, et al. Virtual Reality-Based Cognitive Stimulation on People with Mild to Moderate Dementia due to Alzheimer's Disease: A Pilot Randomized Controlled Trial. *Int J Environ Res Public Health*. 2021;18(10).

28. Liu H, Cheng Z, Wang S, Jia Y. Effects of virtual reality-based intervention on depression in stroke patients: a meta-analysis. *Sci Rep*. 2023;13(1):4381.

29. Koeppe MJ, Gunn RN, Lawrence AD, Cunningham VJ, Dagher A, Jones T, et al. Evidence for striatal dopamine release during a video game. *Nature*. 1998;393(6682):266-8.

30. Modica CM, Bergsland N, Dwyer MG, Ramasamy DP, Carl E, Zivadinov R, et al. Cognitive reserve moderates the impact of subcortical gray matter atrophy on neuropsychological status in multiple sclerosis. *Mult Scler*. 2016;22(1):36-42.
31. Zhang J, Wu M, Li J, Song W, Lin X, Zhu L. Effects of virtual reality-based rehabilitation on cognitive function and mood in multiple sclerosis: A systematic review and meta-analysis of randomized controlled trials. *Mult Scler Relat Disord*. 2024;87:105643.
32. Chai X, Wu L, He Z. Effects of virtual reality-based pulmonary rehabilitation in patients with chronic obstructive pulmonary disease: A meta-analysis. *Medicine (Baltimore)*. 2023;102(52):e36702.
33. Patsaki I, Avgeri V, Rigoulia T, Zekis T, Koumantakis GA, Grammatopoulou E. Benefits from Incorporating Virtual Reality in Pulmonary Rehabilitation of COPD Patients: A Systematic Review and Meta-Analysis. *Adv Respir Med*. 2023;91(4):324-36.
34. Buele J, Varela-Aldás JL, Palacios-Navarro G. Virtual reality applications based on instrumental activities of daily living (iADLs) for cognitive intervention in older adults: a systematic review. *J Neuroeng Rehabil*. 2023;20(1):168.
35. Son C, Park JH. Ecological Effects of VR-Based Cognitive Training on ADL and IADL in MCI and AD patients: A Systematic Review and Meta-Analysis. *Int J Environ Res Public Health*. 2022;19(23).
36. Guo Q, Zhang L, Gui C, Chen G, Chen Y, Tan H, et al. Virtual Reality Intervention for Patients With Neck Pain: Systematic Review and Meta-analysis of Randomized Controlled Trials. *J Med Internet Res*. 2023;25:e38256.
37. Gulsen C Pt M, Soke F Pt P, Eldemir K Pt M, Apaydin Y Pt M, Ozkul C Pt P, Guclu-Gunduz A Pt P, et al. Effect of fully immersive virtual reality treatment combined with exercise in fibromyalgia patients: a randomized controlled trial. *Assist Technol*. 2022;34(3):256-63.
38. Goudman L, Jansen J, Billot M, Vets N, De Smedt A, Roulaud M, et al. Virtual Reality Applications in Chronic Pain Management: Systematic Review and Meta-analysis. *JMIR Serious Games*. 2022;10(2):e34402.
39. Brea-Gómez B, Torres-Sánchez I, Ortiz-Rubio A, Calvache-Mateo A, Cabrera-Martos I, López-López L, et al. Virtual Reality in the Treatment of Adults with Chronic Low Back Pain: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. *Int J Environ Res Public Health*. 2021;18(22).
40. Lo HHM, Zhu M, Zou Z, Wong CL, Lo SHS, Chung VC, et al. Immersive and Nonimmersive Virtual Reality-Assisted Active Training in Chronic Musculoskeletal Pain: Systematic Review and Meta-Analysis. *J Med Internet Res*. 2024;26:e48787.

41. Shin JH, Ryu H, Jang SH. A task-specific interactive game-based virtual reality rehabilitation system for patients with stroke: a usability test and two clinical experiments. *J Neuroeng Rehabil.* 2014;11:32.
42. McSherry T, Atterbury M, Gartner S, Helmold E, Searles DM, Schulman C. Randomized, Crossover Study of Immersive Virtual Reality to Decrease Opioid Use During Painful Wound Care Procedures in Adults. *J Burn Care Res.* 2018;39(2):278-85.
43. Gazendam A, Zhu M, Chang Y, Phillips S, Bhandari M. Virtual reality rehabilitation following total knee arthroplasty: a systematic review and meta-analysis of randomized controlled trials. *Knee Surg Sports Traumatol Arthrosc.* 2022;30(8):2548-55.
44. Prvu Bettger J, Green CL, Holmes DN, Chokshi A, Mather RC, 3rd, Hoch BT, et al. Effects of Virtual Exercise Rehabilitation In-Home Therapy Compared with Traditional Care After Total Knee Arthroplasty: VERITAS, a Randomized Controlled Trial. *J Bone Joint Surg Am.* 2020;102(2):101-9.