USE OF VIRTUAL REALITY-BASED TRAINING IN DIFFERENT FIELDS OF REHABILITATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

Sebastian RUTKOWSKI, PhD¹, Pawel KIPER, PhD²*, Luisa CACCIANTE, MSc³, Blażej CIEŚLIK, PhD³, Justyna MAZUREK, PhD³, Andrea TUROLLA, PhD¹ and Joanna SZCZEPANSKA-GIERACHA, PhD²

From the 1Department of Physical Education and Physiotherapy, Opole University of Technology, Opole, Poland, 2Azienda ULSS 3 Serenissima, Physical Medicine and Rehabilitation unit, Venice, Italy, 3Laboratory of Neurorehabilitation Technologies, San Camillo IRCCS s.r.l., Venice, Italy, 4Institute of Physical Education, Tourism and Physiotherapy, Faculty of Pedagogy, Jan Długosz University, Częstochowa, Poland, 5Department and Division of Medical Rehabilitation, Wrocław Medical University, Wrocław, Poland, 6Department of Physiotherapy, University School of Physical Education, Wrocław, Poland

Objectives: To analyse the effectiveness of virtual reality-based interventions within several fields of rehabilitation, and to investigate whether the outcomes of virtual reality-based interventions, in terms of upper or lower limb function, gait and balance, differ with respect to the virtual reality system used.

Methods: A search of PubMed database resulted in an initial total of 481 records. Of these, 27 articles were included in the study. A final total of 20 articles, with neurological, orthopaedic, geriatric or paediatric patients, published between 2012 and 2019, were included in the study. Two independent reviewers selected potentially relevant articles based on the inclusion criteria for full-text reading. They extracted data, and evaluated the methodological quality of each study.

Results: Seventeen studies were included in the meta-analysis. Eight studies analysed upper limb function, with no significant evidence that specialized VR is superior to conventional treatment. Regarding Fugl-Meyer scale results, the effect of specialized virtual reality therapy was found to be significantly better than conventional treatment. No significant differences between specialized VR and conventional treatment were observed in effects on hand dexterity and gait. There was a significant difference in effects on balance in favour of specialized virtual reality as compared to conventional treatment. Gaming virtual reality was significantly better than conventional treatment for upper limb function, but not for hand dexterity, gait and balance.

Conclusion: Use of specialized virtual reality and gaming virtual reality can be advantageous for treatment of the upper extremity, but not for hand dexterity and gait in all pathologies considered. Specialized virtual reality can improve balance in neurological patients.

Key words: virtual reality; rehabilitation; upper limb; hand dexterity; lower limb; gait, balance.

Accepted Oct 6; 2020; Epub ahead of print Oct 19, 2020

V
tual reality (VR) is an innovative technology consisting of a high-end user–computer interface that involves real-time simulation and interactions through visual and auditory sensorial channels (1, 2). Computer-based 3-dimensional (3D) environments provide sensory information in a form similar to that received from real-world objects and events. VR allows individuals to experience and interact with or within environments with enhanced feedback (3, 4). The definition of VR is based on a concept of “presence”, which refers to the sense of being in a surrounding environment. Four branches are currently defined in relation to VR technology, characterized by their different sense of “presence” within virtual worlds, i.e. non-immersive VR, immersive VR, augmented VR, and mixed VR (3). Thus, what determines the sense of “presence” is the level of immersion provided (i.e. VR interaction level), which in turn depends on the system used.

Since VR technology has been introduced into clinical practice, its importance and usefulness have increased significantly. This meaningful progress in the use of VR systems for patient recovery, which has important favourable results, has led to interest in studying the impact of VR on motor recovery. VR technology is widely

doi: 10.2340/16501977-2755
MATERIAL AND METHODS

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for reporting systematic reviews (13).

Search strategy

Studies related to VR training were considered eligible for review. PubMed database was searched for appropriate articles, using the following criteria: ((virtual reality [Title/Abstract] OR virtual environment [Title/Abstract]) OR virtual therapy [Title/Abstract]) AND rehabilitation [Title/Abstract] AND (“loattrfree full text”[sb] AND (“2012/01/01”[PDAT] : “2019/12/31”[PDAT])). Articles were filtered by date of publication, with the aim of including only those published within the last 7 years, due to the large available literature on the topic of VR. Only randomized controlled trials (RCTs) were included. All treatments provided to participants were reported with as much detail as possible. If needed, the trials’ author was contacted for clarification and to obtain missing data.

Eligibility of studies

Rehabilitative interventions for the upper and lower limbs in the virtual environment, in different clinical fields (e.g. neurology, orthopaedics, paediatrics, etc.) were considered for review. Both specialized VR and gaming systems were included.

Data collection

Screening of research records was conducted by 2 independent reviewers, with the intervention of a third researcher in case of disagreement. A data extraction form was created and applied by the reviewers to extract relevant data. All articles included in the review underwent methodological assessment for risk of bias using Review Manager 5.3 (RevMan) (Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) “Risk of bias” (Appendix 1).

RESULTS

Electronic searching of the PubMed database identified 481 records (Fig. 1). After screening the abstracts, 27 papers were selected for full-text reading. Of these, a total of 20 papers were included in the review. Of the 20 included studies, 16 (with 518 participants) related to treatment of neurological disorders, 1 (with 30 participants) related to treatment of orthopaedic impairment, 1 (with 70 participants) related to geriatric patients, and 2 (with 128 participants) related to treatment of paediatric patients. Table I shows the characteristics of the included studies. Fig. 2 shows the risk of bias in the included trials.

Summary of included studies

All studies focused on VR treatment for the upper or lower limb. Within the neurological diseases 14 studies assessed the effects of VR treatment in patients after...
stroke for both upper and lower limb impairment (12, 16–26). The following studies focused on upper limb recovery (12, 17–19, 21, 23, 25–28). Ballester et al. showed between-group significant improvement in upper limb function in chronic stroke patients in the Fugl-Meyer upper extremity (FMUE) test ($p = 0.037$), Chedoke Arm and Hand Activity Inventory ($p < 0.552$), Barthel Index ($p < 0.241$) and Hamilton Scale ($p < 0.05$) (12). Kiper et al. studied kinematics of the upper limb and demonstrated a significant difference between training groups for both kinematic parameters (i.e. time $p = 0.008$; peak $p = 0.018$; except speed $p = 0.140$), and clinical scales (i.e. FMUE $p = 0.030$; FIM $p = 0.021$). The authors showed that patients after ischaemic or haemorrhagic stroke can benefit similarly from VR training (27), whereas Saposnik et al. did not find statistical differences between VR gaming compared with conventional rehabilitation. Authors suggest that the type of task used in motor rehabilitation post-stroke might have no importance, as long as it is sufficiently intensive and task-specific (25). Another study that assessed the effect of VR on upper limb function was by Shin et al. The authors conclude that combining occupational therapy with specific VR training can be beneficial for hand recovery. However, this was not confirmed by between-group analysis for distal upper limb function, i.e. FMUE ($p > 0.05$), Jebsen-Taylor hand
### Table I. Characteristics of included studies

| Author et al., (year) | Groups characteristic | n | Interventions | VR type | VR system | Outcome measures | Training type | Conclusion | Assessed body part |
|-----------------------|-----------------------|---|---------------|---------|-----------|------------------|---------------|------------|-------------------|
| **NEURO-REHABILITATION** | | | | | | | | | |
| Ballester et al. (2016) | 1) Chronic post-stroke VR (CG) 2) Chronic post-stroke Rehabilitation Control group (CC) | 12 | Both groups EG and CC were asked to perform 30 training sessions over the course of six weeks. One session consisted of playing every of three scenarios once for 10 min (30 min in total per training session). Undisclosed to the EG subjects, researchers applied a movement amplification on the virtual representation of the paretic limb that led to a reduced exposure to visuomotor error feedback whereas no such modulation was applied in the CG | Specialized Rehabilitation Gaming System (manufacture not provided) | Fugl-Mayer Motor Assessment for the upper extremities (UE-MA), Cheddoke Arm and Hand Activity Inventory (CAHAI-7), Activity of Daily Living (ADLs), Barthel Index (BI), Hamilton Scale | The three training scenarios used: neglect, Whack-a-mole and Collector. In the Spheroids and Collector scenarios the patients were required to intercept colored or patterned spheres by performing horizontal lateral arm movement. A bar in the middle of the scenery split the virtual workspace in two sides, herewith forcing the patient to perform ipsilateral movements only. In scenario themed Whack-a-mole, patients executed a horizontal reaching movement to eliminate targets that appeared sequentially on a planar surface | Implicity adding arm-assessment by augmenting visuomotor feedback as proposed by RMT seems beneficial for inducing significant improvement in chronic stroke patients | Upper limb |
| Cho et al. (2012) | 1) Chronic post-stroke VR (2) Control group | 24 | Both groups participated in a standard rehabilitation program including physical therapy for 60 min a day, 5 times a week for 6 weeks. In addition, the VRBT group participated in VRBT for 30 min a day, 3 times a week for 6 weeks | Gaming | Nintendo Wii Fit (Nintendo, Kyoto, Japan) | Posturography (dynamic balance), Berg Balance scale (BBS), Timed Up and Go test (TUG) | Virtual reality balance training was performing using the VR system bubble, ski slalom, ski jumping, soccer heading, table tennis and the penguin slide | Virtual reality balance training is feasible for chronic stroke patients with balance deficit in clinical settings | Lower limb |
| Cho et al. (2015) | 1) Chronic post-stroke VR (2) Chronic post-stroke control group | 20 | Both groups participated in a standard rehabilitation program including physical therapy for 60 min a day, 5 times a week for 4 weeks. Subjects participated in the Virtual Reality Training with Cognitive Load (VRTCL) for 4 weeks, while subjects in the control group participated in a VR program for 4 weeks. VRTCL was consisted of 4, one-week cognitive load tasks | Specialized Virtual reality system Toyra (Xerox Inc., Netherlands) | Walking function (spatio-temporal gait parameters) under single and dual task conditions was measured using the GAITRite walkway system | During the 30-min VRTCL, Virtual reality familiar objects such as apple, an umbrella, and be on effective flowers appeared in the virtual method for the environment video (one object achievement per a minute) as subjects were dependent asked to remember the objects from the virtual environment stroke patients video and their recollection was tested after the training session. Simple addition and subtraction problems were provided in the virtual environment video. A verbal task that involved citing words that start with letters presented on the screen. Subjects participated in 20 sessions over 4 weeks, which include a total of 30-min walking during each session. Even though rest breaks were upon request, it was not included in the overall walking time | Virtual reality added to conventional therapy produces similar results in upper limb function compared to only conventional therapy. VR rehabilitation appear to produce high motivation during execution of the assigned tasks | Lower limb (gait) |
| Dimberg et al. (2016) | 1) Tetraplegia x VR 2) Tetraplegia control group | 28 | Experimental group received 15 sessions with Toyra® virtual reality system for 6 weeks, 30 minutes/day, 3 days/week in addition to conventional therapy the control group only received conventional therapy | Specialized Virtual reality System Toyra (Xerox Inc., Netherlands) | Manual Muscle Test (MMT), Functional Independence Measure (FIM), Spinal Cord Injury Independence Measure (SCIM), Barthel Index (BI), Motricity Index (MI), Minimal Clinically Important Difference (MCID), Quebec User Evaluation of Satisfaction (QUEST) | The main objective of game was to achieve the maximum degree of autonomy that is possible in basic ADL. The monitored displayed several daily objects (spoon, fork, comb, or patterned spheres) by asking the patient to reproduce the movements necessary to perform the corresponding activities (eating, combing hair, or washing the face) | Virtual reality to add conventional therapy rehabilitation produces similar results in upper limb function compared to only conventional therapy. VR rehabilitation appear to produce high motivation during execution of the assigned tasks | Virtual reality added to conventional therapy produces similar results in upper limb function compared to only conventional therapy. VR rehabilitation appear to produce high motivation during execution of the assigned tasks | Upper limb |
| In et al. (2016) | 1) Chronic post-stroke VR+rehabilitation 2) Chronic post-stroke placebo | 16 | The conventional rehabilitation program is patient-specific and consists of neurodevelopmental treatment, physical therapy, occupational therapy, and speech therapy. Participants in the VRRT group additionally received VRRT program, 35 minutes a day, five days a week, for four weeks. The control group performed the placebo VRRT program for the same duration. | Specialized Virtual reality reflection therapy (VRRT) (manufacture not provided) | Berg Balance Scale (BBS), Functional Reaching Test (FRT), Timed Up and Go (TUG), 10-meter walking velocity (10 m/s), postural sway (for static balance ability) | Participants in the VRRT group placed their affected lower limbs along with a request of subjects to put their leg into the VRRT box to observe the projected movement of the rehabilitation unaffected lower limb without program for visual asymmetry causing filling patients with the head and trunk. The chronic stroke unaffected lower limb of each might be even participant was placed so that more beneficial the center of the camera was than conventional over the limb. Participants then adjusted the lower extremities program alone in that the image was projected in improving affected the location of the affected/lower limb function extremitites. When the program started, the participants were asked to watch the movement of the lower limbs on the monitor only | Virtual reality training added to conventional therapy rehabilitation produces similar results in upper limb function compared to only conventional therapy. VR rehabilitation appear to produce high motivation during execution of the assigned tasks | Lower limbs |
| Kalen et al. (2016) | 1) Multiple Sclerosis+VR 2) Multiple Sclerosis Control Group | 20 | Each group received balance training sessions for 6 consecutive weeks, two sessions per week, 30 min sessions | Specialized CAREN Integrated Reality System with D-flow software (Hoxton Medical BV, Amsterdam, Netherlands) | Posturography –CoP (ellipse sway area, path length, sway area, position, pressure distribution), Berg Balance Test (BBT), Four Square Step Test (FSST), Fial Efficacy Scale International (FES-I) | The VR training session included a secondary task: intercepting 16 moving targets. In each of the two conventional exercise program sessions, the participants underwent 10 min of stretching exercises and 20 min of intervention. The virtual training protocol included a combination of static postural control, weight shifting and perturbations exercises | The balance training based on CAREN device is an effective method of balance training for MS | Lower limb (balance) |
Use of virtual reality in rehabilitation

| Author, year | Groups characteristic | n | Interventions | VR type | VR system | Outcome measures | Training type | Conclusion | Assessed body part |
|-------------|----------------------|---|--------------|--------|-----------|-----------------|--------------|------------|-------------------|
| Karasu et al. (2018) | (1) Post-stroke VR (EG) | (1) 12 | Both groups participated in conventional balance rehabilitation for 2-3 h a day, 5 days a week. In addition, the experimental group received 20 min of balance exercise, 5 days a week, for 4 consecutive weeks, with Wii Fit and Wii Balance Board. | Gaming | Nintendo Wii Fit (Nintendo, Kyoto, Japan) | Berg Balance Scale (BBS), Functional Reach Test (FRT), Postural Assessment Scale for Stroke Patients (PAS) | The Wii Balance Board can serve the transfer of weight in different directions. The balance games included in the Wii Fit package were used during the exercises, selecting those in which the hemiplegic patients included in the study would be able to play. | VR exercises with the Nintendo Wii system could represent a useful adjunctive therapy to conventional treatment to improve static and dynamic balance in stroke patients. | Lower limb (balance) |
| Kiper et al. (2014) | (2) Post-stroke control group (CG) | (2) 11 | The RFVE treatment consisted of multidirectional exercises providing augmented feedback provided by virtual reality, while in the VR treatment the same exercises were provided without augmented feedbacks | Specialized | Virtual Reality Rehabilitation System VRRS (VR Systems, Kyhnalm Group, Ltd., Newtownpon, Canada) | Fugl-Meyer upper extremity scale (FMUES), Functional Independence Measure Scale (FIM), kinematic parameters (time, speed, peak) | The real object, held by the subject, was matched to the virtual object displayed on the wall screen. In the virtual scenario, the therapist determined the location of the starting position, the target to reach for each task, and the path to follow | These results indicated that some post-stroke patients may benefit from reinforced feedback in Virtual Environment program for the recovery of upper limb motor function. | Upper limb |
| Lee et al. (2018) | (1) Subacute post-stroke VR (EG) | (1) 15 | Both the experimental and control groups received a conventional rehabilitation program consisting of physical therapy and occupational therapy. Each type of therapy was performed for 30 minutes per session, twice daily, 5 days a week, for 4 weeks. The patients in the experimental group performed the game-based virtual reality (VR) canoe paddling training for 30 minutes per day, 3 days per week, for 5 weeks. | Gaming | Nintendo Wii Sports Resort game (Nintendo, Kyoto, Japan) | modified Functional Reach Test (mFRT), postural sway, manual function test (MFT) | The study participants operated the paddle in the direction of the virtual character displayed on an LED TV during the intervention sessions. The intervention consisted of three sessions. The first session was carried out in a 'free practice' mode for 5 minutes. The second session was performed in a 'timed run' mode in which each patient established a personal record of paddling distance during 15 minutes. The third session was performed in a 'competition mode' during which the patient was motivated to improve their performance by competing with a caregiver or therapist for 10 minutes. | Game-based VR canoe paddling training is an effective rehabilitation therapy that enhances postural balance and upper extremity function in patients with subacute stroke when combined with conventional physical rehabilitation programs. | Upper limb |
| McEwen et al. (2014) | (2) Post-stroke Control group (CG) | (2) 29 | The treatment group received standard stroke rehabilitation therapy plus a program of VR exercises that challenged balance (eg, soccer goalkeeper, snowboarding) performed while standing. The control group received standard stroke rehabilitation therapy plus exposure to identical VR environments but whose games did not challenge balance (performed in sitting). VR training consisted of 10 to 12 thirty-minute daily sessions for a 3-week period. | Specialized | Interactive Rehabilitation Exercise software (IREX) (Vivid group, Toronto, Canada) | Timed Up and Go Test (TUG), Two-Minute Walk Test (MTWT), Stroke Assessment Scale (CMSA-Leg) | The study participants interacted with the VR games (e.g., soccer goalkeeper, snowboarding) in a standing position, thereby challenging their balance and weight shifting. | This VR exercise intervention for inpatient stroke patients improved mobility-related outcomes. | Lower limb (balance) |
| Sapouni et al. (2016) | (1) Post-stroke VR | (1) 47 | The VR group played games with goals of enhancing flexibility, range of motion, strength, and coordination of the affected arm. The recreational activity in control group was designed as a customary active control with similar intensity and complexity to simulate the skills required in the VR group and favoring motivation | Gaming | Nintendo Wii (Nintendo, Kyoto, Japan) | Wolf Motor Function Test (WMFT), Box and Block Test (BBT), Stroke Impact Scale (SIS), Functional Independence Measure (FIM), Barthel Index (BI) | Participants were randomly Simple, low-cost allocated and received a wide program of structured, available task-oriented, upper extremity recreational sessions (ten sessions, 60 min activities might each) of either non-immersive be as effective as virtual reality using the Nintendo innovative non-VR gaming system (VRWii) or immersive virtual simple recreational activities reality technologies (playing cards, bingo, Jenga, or ball games) as add-on therapies to conventional rehabilitation over a 2-week period. | Upper limb |
| Shin et al. (2014) | (2) Chronic post-stroke control group (CG) | (2) 7 | The OT was delivered for 20 minutes by trained occupational therapists who were blinded to the protocol in order to provide participants the same OT used in the conventional clinical setting. The rehabilitation games were designed to combine a variety of rehabilitation exercises with gaming elements, thus making the otherwise monotonous practice more competitive, motivating, interesting and enjoyable. Four different types of games that address general UE functional deficits in patients were suggested: Underwater Fry, Goalkeeper, Bug hunter, and Rollercoaster | Specialized | Rehabilitation (manufacturer not provided) | Fugl-Meyer Assessment (FMA), Modified Barthel Index (MBI) | Rehabilitation training simulates arm and trunk movements designed to restore specific functional deficits. The participants is able to practice various movements by copying specific motions made by the Rehabilitation avatar. The motions were intended to promote incremental improvement in range of motion and endurance, strength, and deviation from synergic movement patterns. | The Rehabilitation in a feasible and safe VR system for enhancing upper extremity function in patients with stroke. | Upper limb |

Table I. Cont.
### Table I. Cont.

| Author, year | Group characteristic | n | Interventions | VR type | VR system | Outcome measures | Training type | Conclusion | Assessed body part |
|--------------|----------------------|---|---------------|---------|-----------|------------------|---------------|------------|-------------------|
| **NEURO-REHABILITATION** | | | | | | | | | |
| Shen et al. (2016) | Post-stroke VR group | 19 | (1) EX group | Specialized | The RAPAL (Neofect, Yong-in, Korea) | Fugl-Meyer Assessment (FM), Jøbsen-Taylor hand function test (JTHFT), Upper Extremity Portion of the Fugl-Meyer Motor Assessment (FMUET), Hand subcomponent (FMH), grip strength (GS), lateral pinch strength (LPS), 3-point pinch strength (PPS) | The intervention programs VR-based exclusively focused on rehabilitation of the upper extremity and combined were administered by 3 trained occupational therapists who were exclusively dedicated more effective than to this study. Standard OT amount-matched involved targeted therapy might be and were exclusively dedicated more effective than to this study. Standard OT amount-matched involved targeted therapy might be | Upper limb |
| | | | (2) post-stroke control group | | | | | | |
| Standen et al. (2017) | Post-stroke VR group | 16 | (1) EX group | Specialized | The virtual glove (manufactured not provided) | Wolf Motor Function Test (WMFT), Nine-Hole Peg Test (NHP), Motor Activity Log (MAL), Nottingham Extended Activities of Daily Living (NEADL) | The intervention was developed to achieve the based on motor learning required sample size and aimed to increase size, a definitive number of repetitions of home-based trial functional movements, whilst would require providing games that were additional challenging with feedback on strategies to boosting performance. Three games recruitment rates were produced specifically for adequate for the project. In order to play patient support them, users had to perform the movements of reach to grasp, grasp and release, pronation and supination that are not practical for many activities of daily living | Upper limb |
| | | | (2) post-stroke control group | | | | | | |
| Thiebaut et al. (2014) | Post-stroke VR group | 14 | (1) EX group | Specialized | Actuated virtual keypad system (AVK) with PneuGlove (Dassault Systèmes, France) | Action Research Arm Test (ARAT), Jøbsen-Taylor Hand Function Test (JTHFT), Upper Extremity Portion of the Fugl-Meyer Motor Assessment (FMUET), Hand subcomponent (FMH), grip strength (GS), lateral pinch strength (LPS), 3-point pinch strength (PPS) | The VR group trained exclusively with the AVK system to practice movements of different combinations of digits | Using of VR may prove to be valuable clinical tools for increasing the effectiveness and efficiency of therapy following stroke | Upper limb |
| | | | (2) post-stroke control group | | | | | | |
| Zondervan et al. (2016) | Post-stroke conventional therapy | 16 | (1) EX group | Specialized | The MusicGlove devices used in this study were manufactured by Fire Rehabilitation Devices | Quality of Movement (QOM) and Amount of Use (AOU) subscales of the Motor Activity Log (MAL), the Nine Hole Peg test, Action Research Arm Test (ARAT), Geriatric Depression Scale, the upper-limb section of the Fugl-Meyer score, the National Institute of Health stroke scale, the modified Ashworth spasticity scale for the wrist | Users were visually cued by MusicGlove therapy. Upper limb was not superior specific grip in time with popular to conventional exercises, similar to the video game Guitar Hero. Grips include key for the primary pinch grip, pincer grip, and end point finger-thumb opposition was nevertheless second third, and fourth fingers feasible and led to a significantly greater increase in self-reported functional use and quality of movement of the impaired hand than conventional home exercises | Upper limb |
| | | | (2) non-ex group | | | | | | |

**ORTHOPEDIC REHABILITATION**

| Author, year | Group characteristic | n | Interventions | VR type | VR system | Outcome measures | Training type | Conclusion | Assessed body part |
|--------------|----------------------|---|---------------|---------|-----------|------------------|---------------|------------|-------------------|
| Pekayevs et al. (2017) | Post-stroke conventional therapy | 16 | Home exercise group | Gaming | Nintendo Wii (Nintendo, Kyoto, Japan) | Visual Analogue Scale (VAS) (based on rest, activity and nights pain), Nuer and Hawkins Tests, Scapular Retraction Test (SRT), Scapular Assistance Test (SAT), Lateral Scapular Slide Test (SSST), and shoulder disability (Shoulder Pain and Disability Index (SPADI)) | Exercise training included bilateral shoulder elevation, boxing, bowling and tennis games accompanied by avatar VR exergaming programs with these programs were found more effective than home exercise programs at short term in subjects with SAIS | Upper limb |
| | | | (1) EX group | | | | | | |
| | | | (2) non-ex group | | | | | | |

---

Note: The table continues with additional groups and characteristics not fully visible in the image.
function test \((p < 0.05)\), Purdue Pegboard Test \((p < 0.05)\), or Stroke Impact Scale \((p < 0.05)\) (19), or for whole upper limb assessment, i.e. FMUE \((p < 0.61)\) and Modified Barthel Index \((p < 0.16)\) (23). Home-based VR intervention for the upper limb was studied by Standen et al. The authors analysed the feasibility of this training, showing statistically important changes in comparison between VR and control group \((9\% \text{ WolfGrip test } p < 0.01)\), Motor Activity Log \(p < 0.05)\) (18). Thielbar et al. showed statistically significant improvements for both measures of impairment \((p = 0.048)\) and measures of task performance \((p = 0.021)\). The authors suggest that using VR may increase the effectiveness and efficiency of therapy following stroke (21). Finally, Zondervan et al. showed significantly greater improvements in an experimental group using VR home-based therapy than in conventional exercise in the Motor Activity Log Quality of Movement \((p = 0.007)\) and Amount of Use \((p = 0.04)\) (17). The effects of VR therapy on lower limb recovery in stroke survivors were presented by Cho et al., In et al., Karasu et al. and McEwen et al. Specifi- cally, studies by Cho et al. showed that, after 4 weeks of intervention in dual-task conditions, greater improvement in walking function was observed in the VR group than in a control group \((gaits analysis system p < 0.05)\) (20). The authors concluded that VR therapy is also a feasible treatment for patients with chronic stroke in terms of balance improvement \((p < 0.05)\), Timed Up and Go test \(p < 0.05)\) (24). In et al. assessed the influence of VR environment on gait and balance in people after stroke. The results showed statistically significant improvement between training groups in Berg Balance Scale \(p < 0.05)\), Timed Up and Go test \(p < 0.05)\), Functional Reach Test \(p < 0.05)\, and 10-m walking test \(p < 0.05)\). These results were confirmed by kinematics obtained from the static balance assessment (16). Karasu et al. aimed to evaluate the efficacy of balance gaming system as an adjunctive therapy to conventional rehabilitation in stroke patients (31). The results showed significant improvement in the Berg Balance Scale \(p < 0.001)\) and Functional Reach Test \(p < 0.001)\. Finally, McEwen et al. showed that VR balance and mobility exercise are
positive additions to inpatient stroke rehabilitation (Timed Up and Go test $p<0.05$, Two-Minute Walk test $p<0.05$, Chedoke McMaster Stroke Assessment Scale Leg domain $p<0.04$) (22). Only Lee et al. investigated the effects of game-based VR training in both upper limb and postural balance (26). They concluded that game-based VR canoe paddling training is an effective rehabilitation therapy that enhances postural balance and upper extremity function in patients with subacute stroke when compared with the control group ($p<0.05$).

One study evaluated upper and lower limb developmental coordination disorder in children (11). The authors showed that the Movement Assessment Battery for Children test ($p<0.0001$), the Bruininks Oseretsky test ($p<0.0001$) and Functional Strength Measure ($p<0.0001$) changed significantly within groups. However, they concluded that skills acquired within VR-game scenarios did not necessarily transfer into the real world (11). One study evaluated VR treatment in relation to cerebral palsy, showing a statistically significant difference between groups in muscular strength flexion and extension ($p<0.05$), in the Pediatric Balance Scale ($p<0.01$), 10-m walking test ($p<0.001$) and 2-min walking test ($p<0.001$). The authors suggest that VR treadmill training is effective for gait and balance improvement (6). One study involved patients affected by multiple sclerosis. Both groups showed a main effect of time on the centre of pressure (CoP) path length with eyes open ($p<0.024$), sway rate with eyes open ($p<0.035$), Functional Reach Test ($p<0.001$), Four Square Step Test ($p<0.031$) and the Fear of Falls self-reported questionnaire ($p<0.023$) (29). One study assessed effects of VR therapy on upper limb impairment in patients with spinal cord injury (SCI). Both groups demonstrated clinical, but no significant, changes related to arm function. Moreover, all patients from the experimental group showed high levels of satisfaction with the VR system (28). Within orthopaedics only one study was included, which assessed the effects of VR therapy in recovery of subacromial impingement syndrome. The authors demonstrated that intensity of pain can be reduced with VR training ($p<0.05$) (8). One study evaluated the effect of VR on lower limb in geriatric patients, showing improvement in balance disorders and fall prevention ($p<0.01$) (30).

The total dose of VR therapy varied between studies. Single sessions lasted from 20 min to 3 h, and a minimum of 10 sessions of training were provided. VR treatments were administered 3–5 times a week. Different types of VR systems were used. Thirteen studies used so-called specialized VR systems (12, 16–23, 27–30), and 7 studies used commercially available gaming consoles (i.e. Nintendo Wii, Nintendo Co., Ltd, Kyoto, Japan) (6, 8, 11, 24–26, 31). Interventions were delivered in inpatient, outpatient, or home settings. Outcome measures were focused on motor skills improvement, and a wide range of clinical scales were used to assess motor and ADL changes (Table 1). All studies measured outcomes at the beginning and soon after the interventions were completed. Twelve studies presented outcomes for upper limb function (8, 11, 12, 17–19, 21, 23, 25–28), and 10 presented outcomes for lower limb function (6, 11, 16, 20, 22, 24, 26, 29–31).

Risk of bias in included studies

Fig. 2 shows the risk of bias in the included trials.

Random sequence generation (selection bias). Thirteen studies were assessed as having a low risk of bias for this domain, as the authors described a random component in the sequence-generation process. Five studies did not report information about the randomization process, resulting in an unclear risk of bias. The remaining studies were assessed as having a high risk of bias, with inappropriate randomization methods used.

Allocation concealment (selection bias). Thirteen studies were assessed as having a low risk of bias in this domain, as the allocation methods used were appropriate. Six studies did not report information about the allocation method used, and one study presented a high risk of bias, as therapists were not blinded to the patients’ assignment.

Blinding of outcome assessment (detection bias). Seventeen studies were at low risk of bias, as outcome measures were assessed by therapists who differed from those who provided treatment sessions. Two studies did not state whether assessors were blinded, hence the risk of bias was unclear. One study was judged to be at high risk of bias, as evaluations and treatment programmes were both carried out by the same therapist.

Incomplete outcome data (attrition bias). Sixteen studies were at low risk of bias, as most of the participants were included in the final analysis. Four studies reported a high risk of bias due to the large number of drop outs.

Selective reporting (reporting bias). All studies reported all the pre-specified outcomes. Only the study of Zondervan et al. (17) did not publish all outcome measures registered in the study protocol, resulting in a high risk of bias for this domain.

Comparison of conventional treatment vs specialized virtual reality

Upper limb function (all measures). A total of 8 studies, with an overall total of 204 participants, who were divided into subgroup analysis with regard to aetiology, were analysed (i.e. 7 studies with post-stroke patients and one study with patients after SCI). The meta-analysis did not provide significant evidence that specialized VR is superior to conventional treatment. However, it should also be noted that the analysis was influenced
Use of virtual reality in rehabilitation

by high heterogeneity. The analyses were performed using standardized mean difference (SMD) with random effects model, since 6 studies used the Fugl-Meyer upper extremity scale, one used the Wolf Motor Function test and one used the Motricity Index. No significant differences were found between specialized VR and conventional treatment in stroke patients (SMD 0.80; 95% CI −0.19 to 1.80, I² = 88%) in SCI patients (SMD −0.13; 95% CI −0.83 to 0.58), or in total comparison (SMD 0.68; 95% CI −0.18 to 1.54, I² = 87%) (Fig. 3).

Upper limb function (Fugl Meyer). A total of 5 studies, with an overall total of 138 stroke survivors, were analysed in relation to upper limb function measured with the Fugl Meyer test. Mean difference (MD) with a fixed effect model was used for analysis. Significant differences (MD 8.41; 95% CI 7.13 to 9.68, I² = 46%) were observed between specialized VR and conventional treatment (Fig. 4).

Upper limb hand dexterity function (all measures). Five studies, with an overall total of 110 post-stroke patients, were analysed in relation to upper limb hand

| Study or Subgroup | Specialized VR Mean | SD | Total | Conventional Treatment Mean | SD | Total | Weight | Std. Mean Difference (IV, Random, 95% CI) | Std. Mean Difference IV, Random, 95% CI |
|-------------------|---------------------|----|-------|-----------------------------|----|-------|--------|-----------------------------------------|----------------------------------------|
| 1.1.1 Stroke      |                     |    |       |                             |    |       |        |                                         |                                        |
| Ballester et al. 2016 (12) | 38.33 | 17.3 | 9      | 43.33                      | 12.62 | 9      | 12.5%  | -0.31 [-1.24, 0.62]                      |                                        |
| Kiper et al. 2014 (27) | 49.8 | 12.5 | 23     | 49.5                      | 16.2 | 21     | 13.6%  | 0.02 [0.07, 0.81]                        |                                        |
| Shin et al. 2014 (23) | 51.1 | 7.8 | 9      | 40.7                      | 9.8  | 7      | 11.8%  | 1.13 [0.04, 2.21]                        |                                        |
| Shin et al. 2016 (19) | 58.3 | 1.7 | 24     | 49.6                      | 2.7  | 22     | 12.2%  | 3.83 [2.83, 4.83]                        |                                        |
| Standen et al. 2017 (18) | 2.19 | 3.1 | 9      | 2.47                      | 4.08 | 9      | 12.5%  | -0.07 [-1.00, 0.85]                      |                                        |
| Thiebar et al. 2014 (21) | 50.4 | 10.4 | 7      | 43.6                      | 8.1  | 7      | 11.8%  | 0.66 [-0.41, 1.77]                       |                                        |
| Zondervan et al. 2016 (17) | 0.7 | 2.3 | 9      | -0.6                      | 2.9  | 8      | 12.3%  | -0.48 [-0.49, 1.44]                      |                                        |
| Subtotal (95% CI) | 83                | 86.7 | 90     |                             |      |        |        |                                         |                                        |
| Test for overall effect: Z = 1.58 (P = 0.11) |

Fig. 3. Upper limb function (all measures): conventional treatment vs specialized virtual reality (VR). SD: standard deviation; 95% CI: 95% confidence interval.

| Study or Subgroup | Specialized VR Mean | SD | Total | Conventional Treatment Mean | SD | Total | Weight | Mean Difference (IV, Fixed, 95% CI) |
|-------------------|---------------------|----|-------|-----------------------------|----|-------|--------|-----------------------------------|
| 1.2 Tetraplegia   |                     |    |       |                             |    |       |        |                                    |
| Dimbaywo-Terr et al. 2016 (28) | 76.56 | 13.28 | 16     | 78.8                      | 20.27 | 15     | 13.3%  | -0.13 [-0.83, 0.58]                |
| Subtotal (95% CI) | 106                | 100.0 | 98     |                             |      |        |        |                                    |
| Test for overall effect: Z = 0.36 (P = 0.72) |

Fig. 4. Upper limb function (Fugl Meyer): conventional treatment vs specialized virtual reality (VR). SD: standard deviation; 95% CI: 95% confidence interval.

| Study or Subgroup | Specialized VR Mean | SD | Total | Conventional Treatment Mean | SD | Total | Weight | Mean Difference (IV, Fixed, 95% CI) |
|-------------------|---------------------|----|-------|-----------------------------|----|-------|--------|-----------------------------------|
| Total (95% CI)    | 72                  | 100.0 | 66     |                             |      |        |        |                                    |
| Test for overall effect: Z = 12.95 (P < 0.00001) |

Fig. 5. Upper limb hand dexterity function (all measures): conventional treatment vs specialized virtual reality (VR). SD: standard deviation; 95% CI: 95% confidence interval.
dexterity. SMD with random effects model was used for analyses, since 1 study used the Chedoke Arm and Hand Activity Inventory, 2 used the Fugl Meyer upper extremity hand section, and 2 used the Nine Hole Peg Test. No significant differences were found between specialized VR and conventional treatment (SMD 0.98; 95% CI –0.51 to 2.47, I² = 91%) (Fig. 5).

Lower limb function (gait). For gait, 3 studies, with an overall total of 106 post-stroke patients, were analysed. SMD with a fixed effect model was used for analyses, since 2 studies used a Timed Up and Go test, and one used temporal gait speed parameter. No significant differences were found between specialized VR and conventional treatment (SMD –0.36; 95% CI –0.74 to 0.03, I² = 0%) (Fig. 6).

Comparison of conventional treatment vs gaming virtual reality

Upper limb function (all measures). For upper limb function, 2 studies, with an overall total of 171 participants, were analysed. The analysis was performed using SMD with random effects model, one study used Manual Function test and one used Wolf Motor Function. Significant differences (SMD 0.34; 95% CI

Lower limb function (balance). For balance, 2 studies, with an overall total of 55 patients, were analysed. Mean difference (MD) with a fixed effect model was used for analyses. Significant differences (MD 3.07; 95% CI 1.11–5.03, I² = 0%) were observed between specialized VR and conventional treatment (Fig. 7).
Use of virtual reality in rehabilitation

0.04–0.64, I² = 0%) were observed between gaming VR and conventional treatment (Fig. 8).

Upper limb hand dexterity function (all measures). For upper limb dexterity function, 2 studies, with an overall total of 171 participants, were analysed. For hand dexterity function, SMD with a fixed effect model was used for analyses, since one study used Manual Function test hand section and one used Box and Block Test. No significant differences were observed between gaming VR and conventional treatment (SMD –0.12; 95% CI –0.42 to 0.18, I² = 74%) (Fig. 9).

Lower limb function (gait). For lower limb function, 8 studies, with an overall total of 63 participants, were analysed, with subgroup analysis in relation to aetiology (i.e. one study with post-stroke patients and one study with cerebral palsy (CP) patients). SMD with a fixed effect model was used for analyses, since 2 studies used the Timed Up and Go test and one used a 10-m walk test. No significant differences were noted between gaming VR and conventional treatment in post-stroke patients (SMD –0.03; 95% CI –0.62 to 0.56, I² = 25%), CP patients (SMD 0.60; 95% CI –0.35 to 1.55) or in total comparison (SMD 0.15; 95% CI –0.36 to 0.65, I² = 22%) (Fig. 10).

Lower limb function (balance). For balance, SMD with random effects model was used for analyses, since 2 studies used the Berg Balance Scale and one used the Pediatric Balance Scale. No significant differences were noted between gaming VR and conventional treatment in post-stroke patients (SMD 0.41; 95% CI –0.75 to 1.57, I² = 73%), CP patients (SMD 0.29; 95% CI –0.64 to 1.22) or in total comparison (SMD 0.37; 95% CI –0.32 to 1.06, I² = 46%) (Fig. 11).
VR therapy has been shown to result in improvements in analysed parameters, but not with statistical significance for all conditions in comparison with conventional treatment. Significant differences were observed between specialized VR and conventional treatment for upper limb function (Fugl Meyer) and lower limb function (balance). Comparative analysis of conventional treatment vs gaming VR, found significant differences only within upper limb function (all measures).

This review shows that most recipients of VR therapy are patients with neurological disorders, mainly stroke. All studies of patients after stroke showed improvement after VR therapy in comparison with conventional therapy in both upper and lower limbs (11, 14–26). The results of the studies included in this review reveal that stroke patients benefit from this innovative treatment, probably through enhanced stimulation provided by an artificially generated environment leading to the activation of motor learning processes. According to the motor learning paradigms, the efficient movement should be repeated, emulating a reference model as exactly as possible, with the aim of achieving the best motor performance (32). Thus, motor learning paradigms can be seen as a basis for movement re-learning and, according to the results of analysed studies, the VR environment has the potential to stimulate both supervised and reinforcement learning, based on augmented visual, acoustic and sensitive feedback.

VR therapy was also used to treat people with developmental coordination disorder and cerebral palsy, showing improvement in learning new movements from VR environments. VR therapy was also shown to be effective for treating people with multiple sclerosis and SCI. These findings demonstrate a wide range of applications for VR in rehabilitation interventions, and its possible advantage in different clinical settings. In addition, studies included in this review did not find any contraindications to the use of this form of therapy. Only one study was published within the orthopaedic field, in which authors evaluated the effect of a VR programme for recovery of subacromial impingement syndrome (SAIS), showing that the VR training was more effective than home exercise programmes in the short-term in subjects with SAIS (8).

Most of the included studies focused on upper limb treatment, whereas training for the lower limb concentrated mostly on balance. This difference may be due to the complexity of treating upper limb function after stroke, relying on changes in muscle synergies of the upper extremity leading to stereotyped voluntary movements. This change is related to both disrupted motor pathways and altered neural reorganization especially following a stroke. Importantly, approximately 60% of stroke survivors do not recover their upper limb function, conversely less than 25% are unable to walk without full physical assistance (33, 34). Another reason can be related to patient safety during gait or balance treatment, which requires specialized VR systems.

It was observed that the specialized VR systems were used both for treatment and assessment of patients. This was especially common in the neurological field, probably due to the fact that neurological patients require specific and individual training programmes, and only a directed in clinical settings system can be beneficial for these kind of patients. On the other hand, gaming systems were used with children, which can be advantageous because some boring or repetitive exercises can be substituted by more interactive activities. This may help both clinicians and parents to motivate children effectively to comply with their daily therapy.

VR is a growing technology that can provide an important addition to traditional rehabilitation modalities. Research shows that most disabled patients experience not only physical disorders, but also mental health problems (e.g. depression or cognitive impairment) (35, 36). Thus, it could be interesting to combine different motor training aspects with psychological and cognitive ones (e.g. mood improvement, strengthened motivation to active engagement in rehabilitation process, visual-spatial orientation and cognitive stimulation). Future studies should consider this translational aspect for VR therapy.

Study limitations
This study has some limitations that need to be addressed. Firstly, only one database was searched for studies, due to the wide number of publications related to the rehabilitation field. Secondly, only full free-text articles were included, providing an overview of accessible clinical outcomes for a wide audience. In addition, no information was obtained from authors related to p-values for the results of included studies.

Conclusion
Implications for clinical practice
Rehabilitation based on VR therapy is emerging as an effective modality for the treatment of balance as well as the upper extremity. VR-based therapy is widely used in the neurological field, especially for rehabilitation after stroke. To date, studies have shown some efficacy of VR-based approach with both specialized and gaming VR systems for gait and hand dexterity; however, this was not significant. Future research into the use of VR in neurological patients should utilize larger samples assessed over time, in order to investigate long-term effects and psychological aspects of the therapeutic intervention. Specialized VR and gaming VR can be advantageous for...
the upper extremity, but not for balance treatment. There is insufficient evidence across free available articles to reach conclusions about the effects of specialized VR and gaming VR on hand dexterity and gait speed.

Implications for further research
This systematic review highlights the need for further research into VR-based approaches for rehabilitation interventions for gait and hand dexterity. Furthermore, due to the differences in outcome measures, in order to better compare data from different trials specific protocols with equal outcome measures should be developed. Finally, improvements in the methodological quality of evidence are needed, by increasing the number of participants in trials, and correctly randomizing them, in order to minimize the possible effects of confounding factors.

ACKNOWLEDGEMENTS
The authors thank Dr Katie Palmer for language revision.

The authors have no conflicts of interest to declare.

REFERENCES
1. Mazurek J, Kiper P, Cieslik B, Rutkowski S, Mehlich K, Turolla A, et al. Virtual reality in medicine: a brief overview and future research directions. Hum Mov 2019; 20: 16–22.
2. Rutkowski S, Rutkowska A, Jastrzebski D, Rachenius H, Pawelczyk W, Szczegielniak J. Effect of virtual reality-based rehabilitation on physical fitness in patients with chronic obstructive pulmonary disease. J Hum Kinet 2019; 69: 149–157.
3. Kiper P, Szcztudlik A, Mirek E, Nowobilski R, Opara J, Agostini M, et al. The application of virtual reality in neurorehabilitation: motor re-learning supported by innovative technologies. Med Rehabil 2013; 17: 29–36.
4. Rutkowski S, Rutkowska A, Kiper P, Jastrzebski D, Rachenius H, Turolla A, et al. Virtual reality rehabilitation in patients with chronic obstructive pulmonary disease: a randomized controlled trial. Int J Chronic Obstruct Pulmon Dis 2020; 2020: 117–124.
5. Laver K, George S, Thomas S, Deutsch JE, Crotty M. Virtual reality for stroke rehabilitation: an abridged version of a Cochrane review. Eur J Phys Rehabil Med 2015; 51: 497–506.
6. 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: 213–218.
7. Johansen T, Strom V, Simic J, Rike PO. Effectiveness of training with motion-controlled commercial virtual reality systems on hand and arm function in young people with cerebral palsy: a systematic review and meta-analysis. J Rehabil Med. 2019; 52: jrm00012.
8. Pekyavas NO, Ergun N. Comparison of virtual reality exergaming and home exercise programs in patients with subcortical impingement syndrome and scapular dyskinesis: short term effect. Acta Orthop Traumatol Turc 2017; 51: 238–242.
9. Botella C, Fernandez-Alvarez J, Guillem V, Garcia-Palacios A, Banos R. Recent progress in virtual reality exposure therapy for phobias: a systematic review. Curr Psychiatri Rep. 2017; 19: 42.
10. Agostini M, Moja L, Banzì R, Pistotti V, Tonin P, Venneri A, et al. Telerehabilitation and recovery of motor function: a systematic review and meta-analysis. J Telemed Telecare 2015; 21: 202–213.
11. Bonney E, Jelsma LD, Ferguson GD, Smits-Engelsman BC. Learning better by repetition or variation? Is transfer at odds with task specific training? PLoS One 2017; 12: e0174214.
12. Ballester BR, Maier M, San Segundo Moz RM, Castaneda V, Duff A, PF MJV. Counteracting learned non-use in chronic stroke patients with reinforcement-induced movement therapy. J Neuroeng Rehabil 2016; 13: 74.
13. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. J Clin Epidemiol 2009; 62: e1–e34.
14. Cumpston M, Li T, Page MJ, Chandler J, Welch VA, Higgins JP, et al. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. Cochrane Database Syst Rev 2019; 10: ED000142.
15. Laver KE, Lange B, George S, Deutsch JE, Saposnik G, Crotty M. Virtual reality for stroke rehabilitation. Cochrane Database Syst Rev 2017; 11: CD008349.
16. In T, Lee K, Song C. Virtual reality reflection therapy improves balance and gait in patients with chronic stroke: randomized controlled trials. Med Sci Monit. 2016; 22: 4046–4053.
17. Zondervan DK, Friedman N, Chang E, Zhao X, Augsburger R, Reinkensmeyer DJ, et al. Home-based hand rehabilitation after chronic stroke: randomized, controlled single-blind trial comparing the MusicGlove with a conventional exercise program. J Rehabil Res Dev 2016; 53: 457–472.
18. Standen PJ, Thrapleton K, Richardson A, Connell L, Brown DJ, Battersby S, et al. A low cost virtual reality system for home based rehabilitation of the arm following stroke: a randomised controlled feasibility trial. Clin Rehabil 2017; 31: 340–350.
19. Shin JH, Kim MY, Lee JY, Jeon YJ, Kim S, Lee S, et al. Effects of virtual reality-based rehabilitation on distal upper extremity function and health-related quality of life: a single-blinded, randomized controlled trial. J Neuroeng Rehabil 2016; 13: 17.
20. Cho KH, Kim MK, Lee HJ, Lee WH. Virtual reality training with cognitive load improves walking function in chronic stroke patients. Tohoku J Exp Med 2015; 236: 273–280.
21. Thielbar KO, Lord TJ, Fischer HC, Lazzaro EC, Barth KC, Stoykov ME, et al. Training finger individuation with a mechatronic-virtual reality system leads to improved fine motor control post-stroke. J Neuroeng Rehabil 2014; 11: 171.
22. McEwen D, Tailhon-Hoissen A, Bildeau M, Sveistrup H, Finestone H. Virtual reality exercise improves mobility after stroke: an inpatient randomized controlled trial. Stroke 2014; 45: 1853–1855.
23. 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.
24. Cho KH, Lee KJ, Song CH. Virtual-reality balance training with a video-game system improves dynamic balance in chronic stroke patients. Tohoku J Exp Med 2012; 228: 69–74.
25. Saposnik G, Cohen LG, Mardani M, Pouyoul P, Sloum M, Cheung D, et al. Efficacy and safety of non-immersive virtual reality exercising in stroke rehabilitation (EVRест): a randomised, multicentre, single-blind, controlled trial. Lancet Neurol 2016; 15: 1019–1027.
26. Lee MM, Lee KJ, Song CH. Game-based virtual reality canoe paddling training to improve postural balance and upper extremity function: a preliminary randomised controlled study of 30 patients with subacute stroke. Med Sci Monit 2018; 24: 2590–2598.
27. Kiper P, Agostini M, Luque-Moreno C, Tonin P, Turolla A. Reinforced feedback in virtual environment for rehabilitation of upper extremity dysfunction after stroke: preliminary data from a randomized controlled trial. Biomed Res Int 2014; 2014: 8.
28. Dimbwayo-Terrer I, Gil-Aguado A, Segura-Fragoso A, de

Use of virtual reality in rehabilitation p. 13 of 16
Effectiveness of the virtual reality system Toyra on upper limb function in people with tetraplegia: a pilot randomized clinical trial. Biomed Res Int 2016; 2016: 6397828.

Kailon A, Fonkatz J, Frid L, Baransi H, Achiron A. The effect of balance training on postural control in people with multiple sclerosis using the CAREN virtual reality system: a pilot randomized controlled trial. J Neuromuscl Disord 2016; 13: 13.

Duque G, Boersma D, Loza-Diaz G, Hassan S, Suarez H, Geisinger D, et al. Effects of balance training using a virtual-reality system in older fallers. Clin Interv Aging 2013; 8: 257–263.

Karasu AU, Batur EB, Karatas GK. Effectiveness of Wii-based rehabilitation in stroke: a randomized controlled study. J Rehabil Med 2018; 50: 406–412.

Kiper P, Szczudlik A, Venneri A, Stocek J, Luque-Moreno C, Opara J, et al. Computational models and motor learning paradigms: could they provide insights for neuroplasticity after stroke? An overview. J Neurol Sci 2016; 369: 141–148.

Wade DT, Langton-Hewer R, Wood VA, Skilbeck CE, Ismail HM. The hemiplegic arm after stroke: measurement and recovery. J Neurol Neurosurg Psychiatry 1983; 46: 521–524.

Lawrence ES, Coshall C, Dundas R, Stewart J, Rudd AG, Howard R, et al. Estimates of the prevalence of acute stroke impairments and disability in a multiethnic population. Stroke 2001; 32: 1279–1284.

Kowalska J, Rymaszewska J, Szczepanska-Gierach J. Occurrence of cognitive impairment and depressive symptoms among the elderly in a nursing home facility. Adv Clin Exp Med 2013; 22: 111–117.

Kowalska J, Bojko E, Szczepanska-Gierach J, Rymaszewska J, Rozek-Piechura K. Occurrence of depressive symptoms among older adults after a stroke in the nursing home facility. Rehabil Nurs 2016; 41: 112–119.
### Use of virtual reality in rehabilitation

| Study (Year) | Authors’ Judgement | Support for Judgement |
|--------------|-------------------|-----------------------|
| Duque et al., 2013 (30) | Random sequence generation (selection bias) | Low risk |
| | Allocation concealment (selection bias) | Low risk |
| | Binding of outcome assessment (detection bias) | Low risk |
| | Incomplete outcome data (attrition bias) | Low risk |
| | Selective reporting (reporting bias) | Low risk |
| In et al., 2016 (16) | Random sequence generation (selection bias) | Low risk |
| | Allocation concealment (selection bias) | Low risk |
| | Binding of outcome assessment (detection bias) | Low risk |
| | Incomplete outcome data (attrition bias) | Low risk |
| | Selective reporting (reporting bias) | Low risk |
| Kalron et al., 2016 (29) | Random sequence generation (selection bias) | Low risk |
| | Allocation concealment (selection bias) | Low risk |
| | Binding of outcome assessment (detection bias) | Low risk |
| | Incomplete outcome data (attrition bias) | Low risk |
| | Selective reporting (reporting bias) | Low risk |
| Karasu et al., 2018 (31) | Random sequence generation (selection bias) | Low risk |
| | Allocation concealment (selection bias) | Low risk |
| | Binding of outcome assessment (detection bias) | Low risk |
| | Incomplete outcome data (attrition bias) | Low risk |
| | Selective reporting (reporting bias) | Low risk |
| Kiper et al., 2014 (27) | Random sequence generation (selection bias) | Low risk |
| | Allocation concealment (selection bias) | Low risk |
| | Binding of outcome assessment (detection bias) | Low risk |
| | Incomplete outcome data (attrition bias) | Low risk |
| | Selective reporting (reporting bias) | Low risk |
| Lee et al., 2018 (26) | Random sequence generation (selection bias) | Low risk |
| | Allocation concealment (selection bias) | Low risk |
| | Binding of outcome assessment (detection bias) | Low risk |
| | Incomplete outcome data (attrition bias) | Low risk |
| | Selective reporting (reporting bias) | Low risk |
| McEwen et al., 2014 (22) | Random sequence generation (selection bias) | Low risk |
| | Allocation concealment (selection bias) | Unclear risk |
| | Binding of outcome assessment (detection bias) | Low risk |
| | Incomplete outcome data (attrition bias) | High risk |
| | Selective reporting (reporting bias) | Low risk |
| Pekyavas et al., 2017 (8) | Random sequence generation (selection bias) | Low risk |
| | Allocation concealment (selection bias) | Unclear risk |
| | Binding of outcome assessment (detection bias) | High risk |
| | Incomplete outcome data (attrition bias) | High risk |
| | Selective reporting (reporting bias) | Low risk |

Note: The table summarizes the bias assessments for each study, with the risk of bias ranging from High risk to Unclear risk, and the support for judgement ranging from No information to All expected and pre-specified outcomes reported.
Low risk

Blinding of outcome assessment (detection bias)

Incomplete outcome data (attrition bias)

High risk

Authors' judgement

Support for judgement

Subjects were randomly assigned to groups using an online random allocation software

Participants were randomly allocated by a computer-generated assignment

Computer-generated assignment used

All investigators assessing outcomes were masked to treatment assignment

40 participants out of 141 did not complete treatment protocol, but analysis were performed in the intention-to-treat population

All pre-specified outcomes reported

All expected and pre-specified outcomes were reported

All expected and pre-specified outcomes were reported

Ten participants lost to follow-up, reasons for losses were disclosed. Losses likely to influence final results

All primary and most of secondary outcome has been reported. Although, in ClinicalTrials.gov authors’ stated Modified Ashworth scale as a secondary outcome measure, which was not reported in the article

The researcher who had collected baseline data phoned the administrator to discover the next unallocated number on the list to determine whether the patient would be allocated to the intervention or control group

not always possible to ensure the researcher was blind to the allocation of the patient

9 participants out of 27 not included in final analysis

All pre-specified outcomes reported

All pre-specified outcomes reported

Not all outcome measures registered in study protocol were published