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SYSTEMATIC REVIEW

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Effects of virtual reality on stroke rehabilitation: An umbrella review of systematic reviews

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Abstract

Background and Aims: Virtual reality is an emerging technology in rehabilitation. This umbrella review aimed to identify, critically appraise, and summarize current systematic reviews on the effects of virtual reality on stroke rehabilitation.

Methods: Five biomedical databases, PubMed, Embase, CINAHL, PsycINFO, and Scopus were searched from inception to December 30th, 2023, for systematic reviews with or without meta-analyses published in English. Two reviewers independently conducted abstract screening, full-text selection, and quality assessments. The methodological quality of included studies was evaluated by the Assessing the Methodological Quality of Systematic Reviews 2. Results were qualitatively synthesized according to domains of function to ascertain the effects of virtual reality intervention on functional improvement within stroke rehabilitation.

Results: A total of 78 articles were included; 23 were systematic reviews, and 55 were systematic reviews with meta-analyses. Among them, 30 studies were evaluated as critically low quality, 32 as low, 15 as moderate, and one as good. Outcomes regarding upper extremity motor function, upper extremity activity, participation, functional independence, balance, functional mobility, walking speed, and cognitive function were summarized. While positive effects in favor of virtual reality were revealed by a majority of systematic reviews on these outcomes, evidence supporting the significantly different effects of virtual reality compared to conventional rehabilitation on participation and cognitive function was lacking.

Conclusion: The umbrella review demonstrated promising clinical outcomes regarding the use of virtual reality as an advanced therapeutic approach in stroke rehabilitation to optimize patient care. Future systematic reviews and meta-analyses in this field should adhere to established guidelines to enhance the quality of evidence.

KEYWORDS
function, recovery, simulation, stroke, virtual reality

1 | INTRODUCTION

Stroke is one of the leading causes of mortality and morbidity in the world. More than 12 million new strokes occur per year, and one in four people over age 25 will experience a stroke in their lifetime. Likewise, more than 100 million people are currently living with a history of stroke.[1] Stroke imposes an immense burden on patients, families, and society. The global annual total cost of stroke is over $721 billion, accounting for 0.66% of the gross domestic product.[1] Stroke survivors suffer from a variety of neurological deficits and sequelae, including hemiparesis, gait abnormalities, impaired functional mobility, reduced independence in activities of daily living, cognitive deficits, communication dysfunctions, and psychological distress.[2] Stroke-related disabilities impede patients' participation in functional activities and their quality of life.

Stroke rehabilitation plays a critical role to mitigate body impairments, activity limitations, and participation restrictions to facilitate patients' return to their prior level of function. Traditional rehabilitation includes physical, occupational, and speech therapy to restore sensorimotor, neurocognitive, communication, and self-care abilities. Contemporary neuroscience research supports the use of timely and intensive task-specific practices with high repetitions to promote experience-dependent neuroplasticity and functional recovery.[3] However, traditional rehabilitation requires a significant amount of manpower and time, often leading to suboptimal outcomes for patients due to limited resources. Substantial advances in traditional rehabilitation interventions need to be made to improve effectiveness and optimize functional recovery outcomes.

The development of innovative technology (e.g., virtual reality) and its application in rehabilitation is transforming stroke rehabilitation research and practice. Virtual reality (VR) is defined as computer-generated interactive simulations that can engage users in virtual environments that appear similar to real-world events and objects.[4] VR can be present through a computer monitor, TV screen, large screen projector, goggles, head-mounted displays, Cave Automatic Virtual Environment, or other viewing mediums. With the three key features consisting of immersion, imagination, and interaction, VR has the potential to promote neurorehabilitation through its positive impact on prevention, plasticity, and participation.[5] The use of VR in stroke rehabilitation has several potential benefits, including the ability to provide repetitive practice, immediate feedback, and the opportunity to perform tasks in a safe, controlled, and motivating environment.

The number of publications addressing VR and stroke rehabilitation has been growing exponentially in the last two decades (Figure 1). Among those publications, 240 are systematic reviews and meta-analyses, which stand on top of the evidence hierarchy and are critical components of evidence-based practice. Although numerous systematic reviews have been conducted on this topic, inconsistent methods and results prevent from drawing definitive conclusions. A Cochrane systematic review[6] revealed that the effect of VR was not significant for upper extremity function compared to conventional therapy. Conversely, other systematic reviews[7,8] reported that VR was superior to conventional therapy to restore upper extremity function. The similar discordant findings exist in reviews examining the effects of VR on balance[9,10] and mobility.[11,12] The abundance of inconsistent information from systematic reviews hinders rehabilitation professionals in making informed clinical decisions and practicing evidence-based care.

Because the application of VR to stroke rehabilitation is a rapidly developing field of research, there is a need to systematically collect and critically evaluate information from multiple systematic reviews

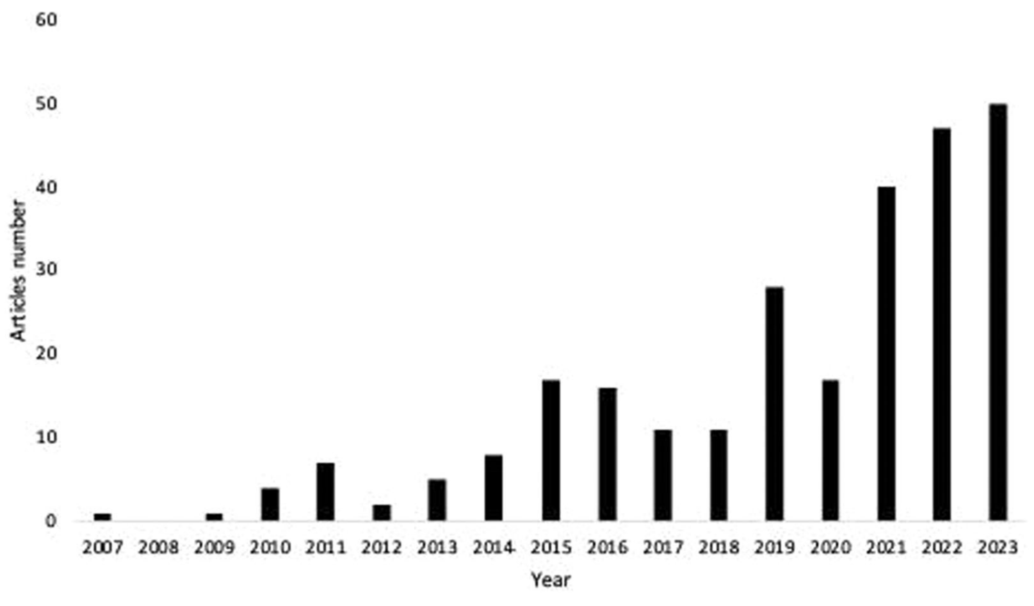

FIGURE 1 The number of systematic reviews in PubMed on virtual reality in stroke rehabilitation. The bar graph shows the number of systematic review articles in each year from 2007 to 2023.

and meta-analyses on all relevant clinical outcomes to navigate the expanding body of research literature for clinicians, researchers, and policymakers. An umbrella review has been considered as a methodological approach to synthesize the accumulating evidence and to facilitate readers to keep pace with the increasing volume of reviews.[13] Therefore, this umbrella review aimed to identify, critically appraise, and summarize current systematic reviews on the effects of VR on stroke rehabilitation.

2 | METHODS

This umbrella review was conducted by following the Preferred Reporting Items for Overviews of Reviews guideline[14] to guarantee high-quality reporting. This review was registered at the International prospective register of systematic reviews (PROSPERO): CRD42022381498.

We searched PubMed, Embase, CINAHL, APA PsycINFO, and Scopus using search strategies designed for each database from inception to December 30th, 2023. The search strategies combined medical subject headings and title/abstract keywords on search themes of VR, stroke, and systematic review or meta-analysis. The full search strategies are described in Appendix. The literature search was limited to human studies reported in English in peer-reviewed journal articles.

Review studies were eligible for this umbrella review if they met all the following criteria:

(1) Participants: participants with a diagnosis of stroke. For systematic reviews encompassing a variety of neurological conditions, they will only be included if outcomes of stroke were reported separately.
(2) Intervention: VR-based rehabilitation, or its combination with conventional therapy or other rehabilitation approaches.
(3) Comparison: conventional rehabilitation or usual care.
(4) Outcome: motor, cognitive, perceptual, psychological, physiological and functional outcomes of stroke rehabilitation.
(5) Study design: systematic review and/or meta-analysis.

Review studies were excluded in this umbrella review if they met any of the following criteria:

(1) For the Cochrane systematic review, only the latest version will be included, all previous versions will be excluded.
(2) Scoping review, narrative literature review, protocol of systematic review, clinical practice guideline, overview of systematic review, meta-meta-analysis, abstract-only, or non-peer-reviewed articles.

Two reviewers independently assessed the titles and abstracts for potential eligibility and then retrieved full-text articles for those that appeared relevant. They assessed full-text articles against the inclusion and exclusion criteria for final eligibility. For each included trial, data were extracted on publication year, publication journal, number of included original studies, type of included original studies, participant characteristics and sample size, intervention, functional domain, and outcome measures. Throughout this process, we resolved discrepancies through group discussion with a third experienced reviewer until reaching a consensus. Any missing or incomplete data was requested from the corresponding authors of included studies.

The methodological quality of included systematic reviews was evaluated by the Assessing the Methodological Quality of Systematic Reviews 2 (AMSTAR-2) assessment tool. This instrument was developed by an expert panel to critically appraise systematic reviews of randomized and non-randomized interventional studies.[15] There are 16 items in this instrument, and seven of them are set as critical domains. Based on the number of critical flaws and noncritical weaknesses, the overall confidence in the results of the systematic review being examined is classified into one of the four levels: high, moderate, low, and critically low. The same two reviewers independently completed the quality assessment, and any discrepancies were identified and solved with the third experienced reviewer.

Results of the included systematic reviews were qualitatively synthesized according to domains of function and types of reported outcome measures to ascertain the effects of VR intervention on functional improvement. Bubble plots were created using Microsoft Excel (Microsoft Corp, Redmond, WA) to present the evidence base regarding the effects of VR on different functional domains, including upper extremity function, upper extremity activity, activities of daily living, participation, balance, functional mobility, walking speed, and cognitive function. Standardized mean differences (SMD) and 95% confidence intervals (CI) were extracted from included meta-analyses as effect size measures. If the meta-analysis only reported the mean difference, the SMD was calculated through the following formulas:

$$\textit{Standard Deviation} = \sqrt{n \times (\textit{upper limit} - \textit{lower limit of } 95\%\ \textit{CI}) \div 3.92}$$

$$\textit{Standardized Mean Diffrence} = \textit{Mean Difference} \div \textit{Standard Deviation}$$

In the bubble plots, the y-axis displays the effect size, the x-axis displays individual studies, the bubble size represents the sample size included in each analysis, and the bubble color represents the quality of evidence (green: high; yellow: moderate; orange: low; red: critically low).

3 | RESULTS

A total of 1084 records were identified from five databases, and 638 duplications were removed. After screening the titles and abstracts of the remaining 446 records, 99 studies were selected for full text retrieval. Finally, 78 articles met the eligibility criteria and were included in this umbrella review; 23 were systematic reviews only, and 55 were systematic reviews with meta-analyses. The study identification process and reasons for excluding papers are illustrated in the PRISMA flow diagram (Figure 2).

3.1 | Description of reviews

Seventy-eight studies were published between 2007 and 2023. Fifty-one were systematic reviews of randomized controlled trials, and 27 were systematic reviews of randomized and non-randomized trials. The number of included primary studies within these systematic reviews ranged from four to 87, and the total number of included participants ranged from 72 to 3540. Most systematic reviews only included patients with stroke; eight studies[16–23] included patients with a variety of neurological disorders, and among them, only the data from stroke was extracted for this umbrella review. Most systematic reviews did not specify the stage of stroke; six studies[10,24–28] included only chronic stroke (over 6 months post onset), one study[29] included acute and subacute stroke (within 6 months post onset), and one study[11] included only acute stroke (within 1-month post-onset). Four studies investigated the combination of VR and other rehabilitation technology, including noninvasive brain stimulation,[18,30] telerehabilitation,[31] and haptic gloves.[32] Several specific categories of VR based on taxonomy were reported in some reviews, including commercial, immersive, semi-immersive, non-immersive, and augmented VR, as well as VR gaming systems. The characteristics of systematic reviews and meta-analyses are summarized in Supplementary Tables 1 and 2, respectively.

3.2 | Quality assessment

For quality assessment using the AMSTAR-2, 30 studies were evaluated as critically low quality,[8,9,18,20,25,26,28,30,33–54] 32 as low,[6,10–12,16,21,23,24,27,29,31,55–75] 15 as moderate,[7,17,19,22,32,76–85] and

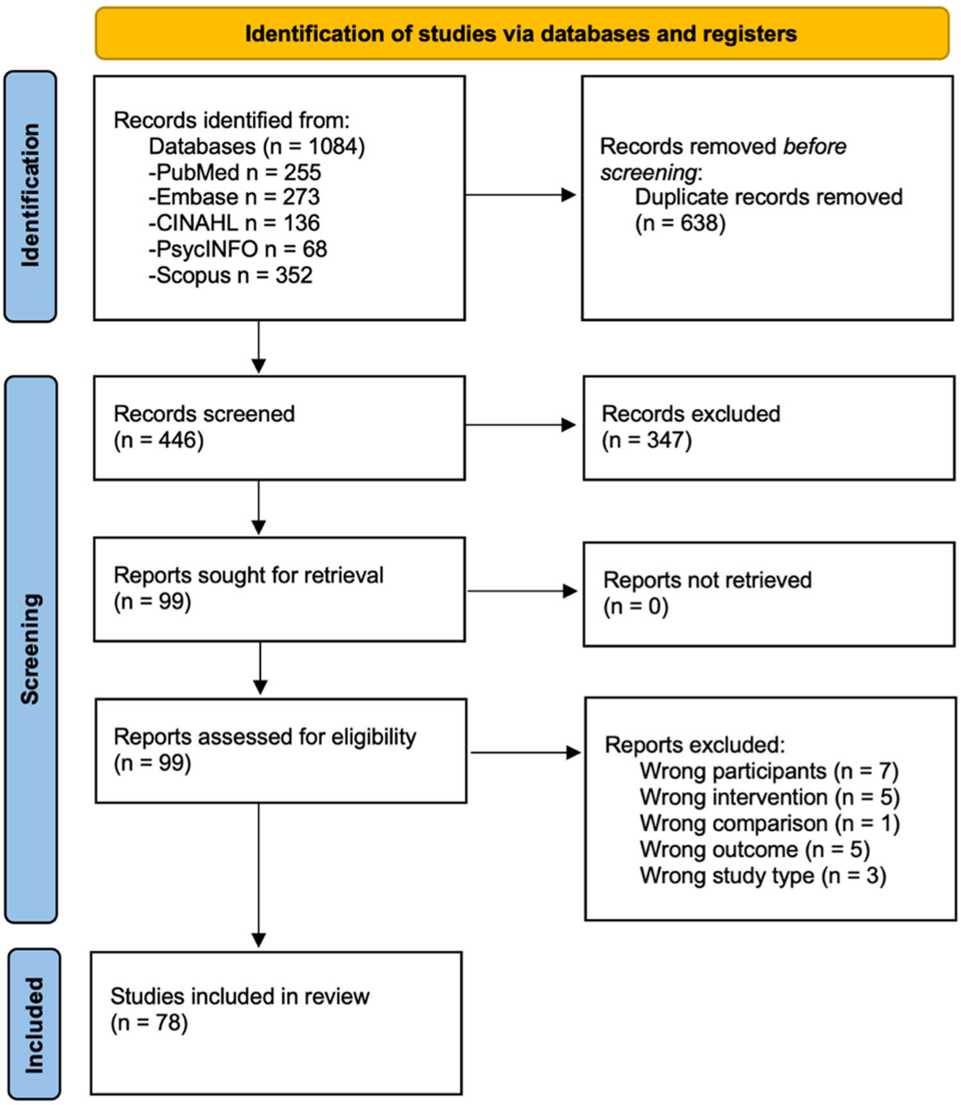

FIGURE 2 PRISMA flow diagram.

only one study was evaluated as good quality.[86] There were only 30 studies (38%) that established a registered protocol before the conduct of the review, and registered at the PROSPERO. Only 11 studies (14%) justified the inclusion of different study designs within the systematic reviews. Most reviews used proper tools to assess the risk of bias in individual studies (74 studies, 95%), and performed study selection (58 studies, 74%) and data extraction (44 studies, 56%) with final consensus achieved from the initial examination of at least two independent reviewers. No reviews report on the sources of funding for the individual studies. Seventy-one studies (91%) account for the risk of bias in individual studies in the interpretation and discussion of the results, and 67 studies (86%) conducted proper explanations of the heterogeneity of the results. Twenty-seven out of 55 systematic reviews with meta-analyses (49%) carried out an investigation of publication bias. The detailed scoring of the AMSTAR-2 of systematic reviews and meta-analyses are summarized in Supplementary Tables 3 and 4, respectively.

3.3 | Upper extremity motor function

Seventeen systematic reviews with meta-analyses (total sample size = 9241) reported upper extremity motor function with outcome measures on the Body Function and Structure (impairments) domain of the International Classification of Function, Disability, and Health (ICF) framework.[87] Twelve of them revealed significant improvement in VR compared to conventional rehabilitation; two were considered moderate quality, five were low, and five were critically low. The bubble plot is shown in Figure 3A. Customized VR built specifically for rehabilitation use was significantly more effective than commercial VR.[65,71,73,80] Unibaso-Markaida et al.[51] only included commercial VR systems in their systematic review and found although these systems demonstrated significant effects post-intervention compared to baseline, they did not produce significantly better outcomes than conventional rehabilitation (SMD = 0.3, 95% CI: −0.01 to 0.61; $p = 0.06$).

In addition, Jin et al.[7] demonstrated that immersive VR induced a greater effect than conventional rehabilitation (SMD = 0.42, 95% CI: 0.17 to 0.67; $p < 0.001$). Through sub-group analyses, Chen et al.[80] reported that a higher total dose (>15 h) and a longer training duration (>4 weeks) led to significantly better outcomes. Gao et al.[25] also conducted sub-group analyses and concluded that daily intensity over 60 min, weekly frequency over 4 sessions, and total dose over 20 h of VR led to significantly improved outcomes. Laver et al.[6] revealed a trend in favor of VR intervention for over 15 h, although it did not reach statistical significance. In contrast, Aminov et al.[65] found no additional benefits achieved by VR through higher dosage and massed practice schedules using moderate analysis. Similarly, Lee et al.[27] used meta-regression and found that intervention duration and weekly sessions of VR did not produce significant differences in effects.

3.4 | Upper extremity activity

Ten systematic reviews with meta-analyses (total sample size = 6280) reported upper extremity activity with outcome measures on the Activities (limitations) domain of the ICF framework. Four[7,52,65,73] of them revealed significant improvement in VR compared to conventional rehabilitation; one review[7] was considered as moderate quality, two[65,73] were low, and the other one[52] was critically low. The bubble plot is shown in Figure 3B. These four studies[7,52,65,73] also demonstrated significantly better effects of VR on the upper extremity function of the Body Function and Structure domain of the ICF framework. Four other reviews[41,70,71,80] revealed significant effects of VR in upper extremity function, but not activity measures. Hao et al.[11] and Al-Whaibi et al.[24] reported no significant differences between VR and conventional rehabilitation in both upper extremity function and activity measures.

3.5 | Participation

Seven systematic reviews with meta-analyses (total sample size = 1756) reported outcome measures on the Participation (restrictions) domain of the ICF framework (Figure 3C). Six of them reported nonsignificant differences between VR and conventional rehabilitation; two were considered as moderate quality, three were low, and one was critically low. Only one review[19] with moderate quality reported significant improvement in VR compared to conventional rehabilitation (SMD = 0.22, 95% CI: 0.1 to 0.34; $p = 0.01$).

3.6 | Activities of daily living

Thirteen systematic reviews with meta-analyses (total sample size = 4673) reported on the ability to complete activities of daily living (Figure 3D). Seven of them revealed significant improvement in VR compared to conventional rehabilitation; two were considered moderate quality, three were low, and three were critically low. Ahn et al.[38] reported a moderate effect size in favor of VR (SMD = 0.41, 95% CI: 0.25 to 0.57; $p < 0.001$) with no significant heterogeneity, however, descriptions of the included studies' control groups in this review were not mentioned. Three systematic reviews analyzed game-based VR interventions. Chan et al.[10] included studies in which the control group received equal or less dose intervention time than the VR group and found significantly better effects of VR with no heterogeneity (SMD = 0.41, 95% CI: 0.09 to 0.73; $p = 0.01$). Dominguze-Tellez et al.[41] reported significantly better outcomes of VR in both upper extremity motor function and functional independence (SMD = 0.77, 95% CI: 0.05 to 1.49; $p = 0.04$). By contrast, Wang et al.[52] reported significantly improved upper extremity motor and activity outcomes, but not functional independence (SMD = 0.26, 95% CI: −0.06 to 0.54; $p = 0.12$); there was also no significant difference between commercial and customized VR in terms of the

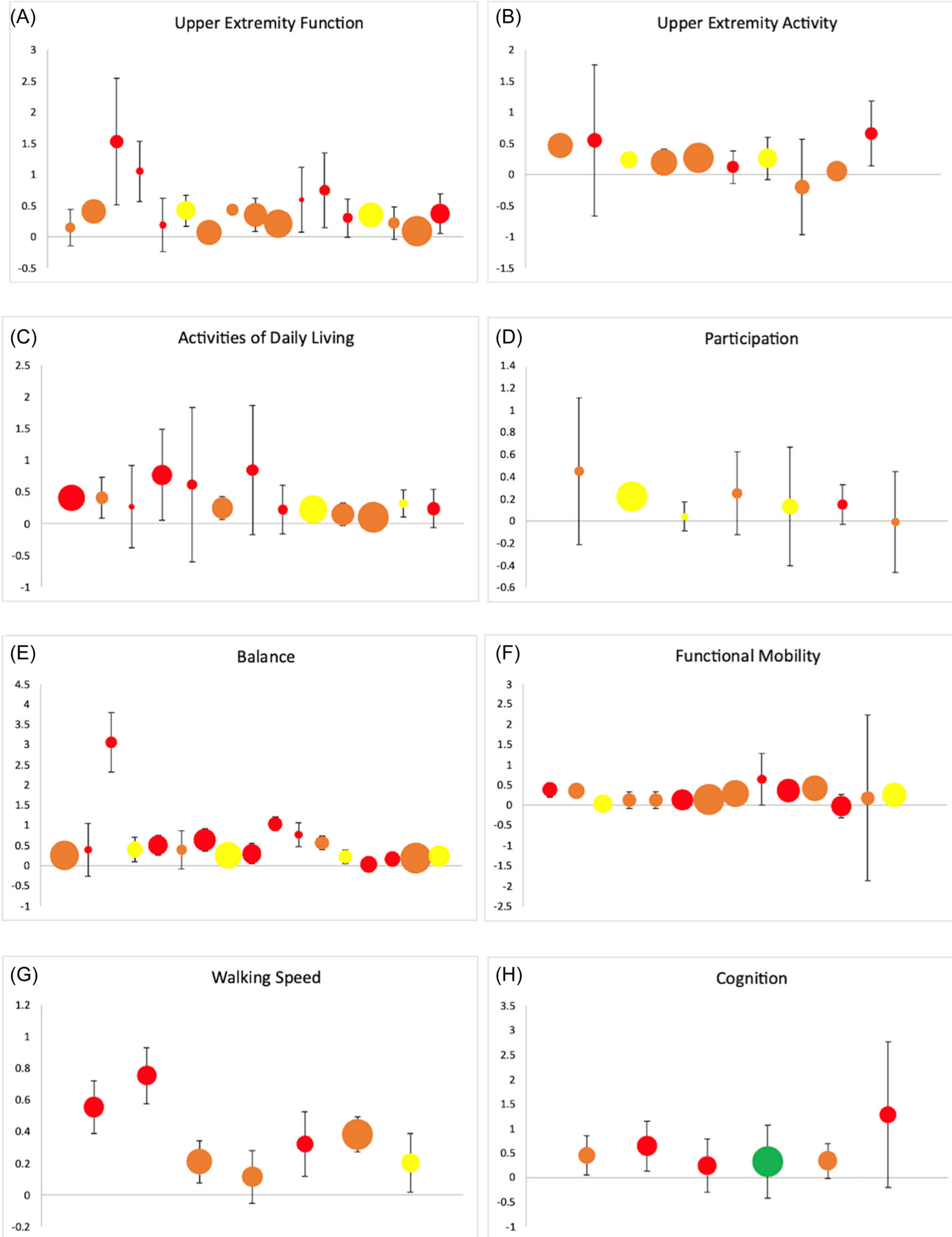

FIGURE 3 Bubble plots depicting the effect sizes of virtual reality in different outcomes. The y-axis displays the effect size, the x-axis displays individual studies, the bubble size represents the sample size included in each analysis, and the bubble color represents the quality of evidence (green: high; yellow: moderate; orange: low; red: critically low). Outcomes: (A) upper extremity function, (B) upper extremity activity, (C) activities of daily living, (D) participation, (E) balance, (F) functional mobility, (G) walking speed, and (H) cognition.

effect on functional independence. In addition, Cheok et al.[39] found the addition of Nintendo Wii intervention to standard rehabilitation did not produce significant differences in functional independence (SMD = 0.27, 95% CI: −0.38 to 0.93; $p = 0.41$), but the meta-analysis was conducted with only two studies with a total sample size of 37.

3.7 | Balance

Seventeen systematic reviews with meta-analyses (total sample size = 3996) reported balance ability (Figure 3E). Fourteen of them revealed significant improvement in VR compared to conventional rehabilitation; four were considered as moderate quality, three were low, and seven were critically low. Corbetta et al.[40] and de Rooij et al.[68] found similar results. VR demonstrated significantly better outcomes when compared with time dose-matched conventional rehabilitation, and there was no heterogeneity; however, insignificant results with high heterogeneity were shown when VR was added to conventional rehabilitation, and the number of included studies in this comparison was limited. Prosperini et al.[22] reported significant effects of game-based VR on balance with a small effect size (SMD = 0.26, 95% CI: 0.02 to 0.51; $p = 0.04$); meta-regression analyses revealed that high-frequency VR interventions were associated with a larger effect size, and the effects on the balance were maintained for at least 4 weeks after intervention. Shen et al.[83] also found that the superior effects of VR on balance were maintained five to 8 weeks after intervention. Two systematic reviews[51,81] included commercial VR gaming systems and both reported significantly improved outcomes of VR compared to conventional rehabilitation on balance.

3.8 | Functional mobility

Fourteen systematic reviews with meta-analyses (total sample size = 2802) reported functional mobility (Figure 3F). Nine of them revealed significant improvement in VR compared to conventional rehabilitation; one review was considered as moderate quality, four were low, and four were critically low. Corbetta et al.[40] (SMD = 0.38, 95% CI: 0.2 to 0.57; $p = 0.04$) and de Rooij et al.[68] (SMD = 0.35, 95% CI: 0.18 to 0.52; $p < 0.001$) reported significantly better outcomes of VR regardless of using add-on or dose-matched intervention compared to conventional rehabilitation. The two reviews[51,81] that included commercial VR gaming systems demonstrated significant effects on balance, but not functional mobility. Khan et al.[9] and Laver et al.[6] reported insignificant between-group differences in both functional mobility and balance outcomes.

3.9 | Walking speed

Seven systematic reviews with meta-analyses (total sample size = 1129) reported walking speed (Figure 3G). Six of them revealed significant improvement in VR compared to conventional rehabilitation; one was considered as moderate quality, two were low, and three were critically low. Four systematic reviews reported the mean differences in walking speed obtained by the VR group to be more than conventional rehabilitation; Keersmaecker et al.[20]: 0.11 m/s (95% CI: 0.02 to 0.20, $p = 0.02$), Corbetta et al.[40]: 0.15 m/s (95% CI: 0.1 to 0.19; $p = 0.04$), Rodrigues-Baroni et al.[28]: 0.15 m/s (95% CI: 0.05 to 0.24; $p = 0.02$), and Zhang et al.[12]: 0.12 m/s (95% CI: 0.08 to 0.15; $p < 0.001$). In addition, Corbetta et al.[40] found the significant superior effect of VR on walking speed was well maintained one to 3 months after the completion of the intervention, with a mean difference of 0.12 m/s compared to conventional rehabilitation.

3.10 | Cognition

Six systematic reviews with meta-analyses (total sample size = 910) reported cognitive function (Figure 3H). Two[25,65] of them revealed significant improvement in VR compared to conventional rehabilitation; one[65] was considered as low quality and the other[25] was critically low. Four systematic reviews[11,52,53,86] reported nonsignificant differences between VR and conventional rehabilitation; one[86] was considered as high quality, one[11] was low, and two[52,53] were critically low.

3.11 | Visual perception

Two systematic reviews examined the application of VR to post-stroke unilateral spatial neglect, with moderate[76] and low[59] quality respectively. Both reviews included a variety of observational and interventional studies. Ogourtsova et al.[59] included 23 studies in total, with VR being used for assessment in 17 studies and treatment in 6 studies. Ogourtsova et al.[59] concluded while VR paradigms augmented the conventional assessment approaches for unilateral neglect, there was limited evidence that it was more effective than conventional therapy. Cinnera et al.[76] focused on the use of immersive VR as a treatment tool and included a total of 10 studies with a heterogeneous study design; three included studies demonstrated significant effects of VR on visual perception outcomes.

3.12 | Neurophysiological outcomes

Three systematic reviews investigated the neurophysiological mechanisms of VR on stroke rehabilitation and focused on the effects of VR on not only functional recovery but also the central nervous system level. Functional magnetic resonance imaging, transcranial magnetic stimulation, and electroencephalography were used to determine neurophysiological outcomes. Ellis et al.[58] included four studies with high potential risk of bias, and found insufficient evidence to identify the neurophysiological changes associated with upper extremity functional recovery. Feitosa et al.[21] included

18 studies that used functional magnetic resonance imaging to examine the effects of VR-based motor rehabilitation and found VR demonstrated evidence of efficacy to facilitate the restoration of normalized cortical activation patterns. Furthermore, Hao et al.[77] included 27 studies with a total of 232 patients and identified VR-induced neural plasticity as well as its positive correlations to functional recovery outcomes.

4 | DISCUSSION

The present umbrella review included 23 systematic reviews and 55 systematic reviews with meta-analyses to collect and evaluate the empirical evidence regarding the effects of VR-based rehabilitation for stroke survivors. Outcomes regarding upper extremity motor function, upper extremity activity, participation, functional independence, balance, functional mobility, walking speed, and cognitive function were summarized. While positive effects in favor of VR were revealed by most systematic reviews on these outcomes, there is a dearth of evidence supporting the significantly different effects of VR compared to conventional rehabilitation on participation and cognitive function domains. In addition, it should be taken into consideration that nearly 80% of the included systematic reviews were evaluated as low or critically low quality according to the AMSTAR-2 assessment tool.

VR as an emerging technology is well positioned to apply neuroscience principles[88] to patient care and clinical research. Results of this umbrella review demonstrate that over two-thirds of included systematic reviews and meta-analyses have shown significant effects of VR on upper extremity motor function and balance compared to conventional rehabilitation. However, several factors related to stroke should be taken into consideration to clarify their influence on the effects of VR. None of the included reviews investigated the impact of stroke type and locality, although it was commonly acknowledged as a limitation. The lack of patient stratification and reporting in the primary clinical studies precluded evidence synthesis within the systematic reviews. Kiper et al.[89] conducted a randomized controlled trial to assess the effect of VR for upper extremity rehabilitation in subacute and chronic stroke survivors, and patients were stratified based on stroke type. They found that VR demonstrated significantly better results in upper extremity motor function and kinematic parameters, and patients with ischemic or hemorrhagic stroke obtained similar outcomes. Further clinical trials should include analysis of stroke type and locality to provide more information on this issue. In addition, the impact of stroke severity and stage remains unclear. Conflicting results exist regarding stroke severity; while Jin et al.[7] found patients with moderate to severe upper extremity impairment improved more through VR, two other systematic reviews[6,69] did not find significant modulation effect of baseline impairment level.

The optimal time window to apply VR in stroke rehabilitation is also inconclusive. Current literature reports distribute unevenly across the stroke rehabilitation continuum; more published studies focus on the chronic stage and studies on the early stage were relatively rare. Hao et al.[11] specifically included randomized controlled trials that recruited stroke survivors within 1-month post-stroke and found VR is feasible and as effective as conventional rehabilitation on upper extremity function, activities of daily living, balance, and cognition. Both Mekbib et al.[8] and Chen et al.[80] found patients in the subacute stage benefited more than the chronic stage, but these effects were not revealed consistently on all outcome measures. In addition, three systematic reviews[6,29,65] reported no significant impact of stroke chronicity on the effectiveness of VR. More studies conducted in the early stage of stroke are warranted to complement current evidence and provide insight into whether and how VR can augment spontaneous recovery and conventional therapy approaches.

There are also a few variables related to VR intervention that can affect the effectiveness of VR. First, different types of VR, commercial or customized, can yield different functional recovery outcomes. Commercial VR is originally built for mainly entertainment purposes of the general population, for example, Nintendo Wii, Microsoft Kinect, and other exergames. On the contrary, customized VR in rehabilitation is specially designed and developed for people with disability and impairments and should be used for therapeutic purposes. Lohse et al.[48] explored the effects of commercial and customized VR in an earlier systematic review and found the limited number of studies regarding commercial VR precluded the assessment of its benefits and the comparison to customized VR. Since then, research on commercial VR in stroke rehabilitation was burgeoning, and three recent systematic reviews[71,73,80] revealed the superior effects of customized VR to commercial VR.

The refined embodiment of neurorehabilitation principles,[73] especially task-specific practice, augmented feedback, and appropriate challenge level, may underpin the improved effects of customized VR. This finding also suggests further research should determine the active ingredients[90] of effective VR paradigms and unravel their contributions to clinical benefits. Notwithstanding, while commercial VR systems are typically available off-the-shelf at a relatively affordable cost, customized VR paradigms can be in different stages of prototype design, clinical validation, and dissemination, and the expenses of them may vary in a wide range. Commercial VR is still a valid and low-cost tool to be incorporated into stroke rehabilitation with appropriate clinical judgements of clinicians. The cost-effectiveness aspect of VR should be further investigated, which is an issue not covered in the included systematic reviews of this umbrella review.

Second, immersion is an essential property of VR; the immersive level varies among different VR systems and may have implications on rehabilitation outcomes. The immersive level is a spectrum and ranges from a 2D laptop display where users can still partially visualize the physical environment to a head-mounted device where users are fully immersed in the simulated environment.[91] Subgroup analyses of Fang et al.[43] and Jin et al.[7] indicated the superior effects of immersive VR on upper extremity function to non-immersive VR. VR with a higher immersive level may induce a higher sense of presence, which refers to the perceptual illusion of being in the virtual world without being aware of the technological mediation.[88] Also, a higher amount of sensory substation in immersive VR may facilitate interactions between people and the task by creating higher embodiment, promoting optimized performance through intrinsic motivation and attention.[92] However, it should be noted that there was no evidence coming from clinical trials that directly compare immersive and non-immersive VR paradigms, and the number of studies utilizing immersive VR was much smaller than non-immersive VR in the above two subgroup analyses.

Third, the effects of VR in systematic reviews were also influenced by the intervention schedule and the research design of control groups. Chen et al.[80] and Mekbib et al.[8] corroborated the tendency which Laver et al.[6] suggested that VR with a dose higher than of 15 h is preferable for significantly better upper extremity outcomes than a lower dose. Similarly, over 18 sessions[43] and total duration over 20 h[25] were also found to induce significantly better outcomes in two subgroup analyses. Whereas two other systematic reviews[27,69] did not find significant effects associated with longer VR total intervention time. In addition, the optimal daily intensity and weekly frequency of VR intervention are also inconclusive. Overall, while ongoing studies and reviews continue to clarify the specifics of the dose effect of VR intervention, the positive relationship between the time scheduled for therapy and therapy outcomes has been revealed in stroke rehabilitation.[93] Considering the limitations placed on rehabilitation sessions by payor sources, it is indispensable to extend the application of VR rehabilitation from clinical facilities to home settings, to attain adequate dosage and favorable outcomes. With regard to the research design of control groups, while some systematic reviews[8,71,82] strictly matched the total dose of treatment in VR and control groups, and some systematic reviews[39,40,68] conducted separate analyses based on whether VR substituted a portion of conventional rehabilitation (active control) or VR was added to conventional rehabilitation (passive control), there were a few systematic reviews[10,38,81] that did not report the details of the control group or included studies with a mix of active and passive control. Therefore, caution should be exercised in interpreting the results from these reviews as the effects of VR could be exaggerated due to the confounding factor of intervention time.

While most systematic reviews focused on the effects of VR on behavioral and functional outcomes, three systematic reviews[21,58,77] were dedicated to summarizing current evidence regarding the effects of VR on the neural substrates to gauge changes in the central nervous system. The included primary studies of these three systematic reviews employed a series of neuroimaging and electrophysiological instruments to measure outcomes. Overall, these findings provide references for future studies to elucidate the underlying mechanism of VR intervention. Further research could consider exploring other relevant biomarkers of neuroplasticity and physiological changes and investigate their potential correlations with outcomes of VR and other rehabilitative interventions. For instance, a recent systematic review and meta-analysis by Ashcroft et al.[94] included 17 studies with a total of 687 stroke survivors and found that high-intensity aerobic exercise can increase circulating brain-derived neurotrophic factor concentrations and may contribute to heightened neuroplasticity. Huang et al.[95] incorporated serum biomarkers to outcome measures in a randomized controlled study of stroke rehabilitation; they found significant changes in biomarkers of inflammation, oxidative stress, and neuroplasticity following intervention, but these changes did not differ between VR and dose-matched conventional rehabilitation groups.

While most systematic reviews treated VR as a standalone intervention and compared it with conventional rehabilitation, the combination of VR and other innovative technologies in stroke rehabilitation is an emerging trend. Some included systematic reviews of this umbrella review discussed the combination of VR with non-invasive brain stimulation,[18,30] haptic glove,[32] and robot-assisted training.[45] Further, the combination of VR and telerehabilitation makes the remote delivery of VR possible, and paves the way for the application of VR in the home- and community-based settings.[96] The synchronized or unsynchronized instructions from clinicians through digital platforms can ensure the proper use of VR by patients at home or in rural area, and clinicians can also gather VR training-related data through telerehabilitation to inform decision-making and plan of care.

The findings from this umbrella review have significant clinical implications for stroke rehabilitation. By leveraging VR technology, clinicians can provide engaging, motivating, and repetitive practice in a controlled environment, potentially leading to more effective and efficient rehabilitation. VR can offer more intensive and varied therapeutic exercises, potentially reducing the burden on both patients and therapists. Furthermore, VR can facilitate remote rehabilitation, which is particularly beneficial for patients with limited access to in-person therapy due to geographic or mobility constraints. On the other hand, although the positive effects of VR to address motor impairments and activity limitations have been supported substantially in the literature, the evidence of VR on cognitive impairments and participation restrictions is limited, pinpointing an area for future research endeavors. Overall, this umbrella review provides a comprehensive overview of the current evidence from selected systematic reviews on the use of VR in stroke rehabilitation. Our review highlights the potential benefits of VR, identifies methodological limitations in the literature, and underscores the need for more rigorous research. It offers practical insights for clinicians and researchers regarding the factors that may likely impact the effectiveness of VR on the stroke population, guiding the implementation of VR interventions in clinical practice and informing the design of future studies. By addressing the gaps in the literature and proposing directions for future research, this review contributes to advancing the field of stroke rehabilitation and improving patient care.

This umbrella review has several limitations. First, the majority of included systematic reviews were graded as low or critically low quality based on the AMSTAR-2 assessment tool. Common methodological deficits included the lack of registration of established review protocols, lack of justification of study designs for inclusion, lack of investigation of publication bias, and overall small sample sizes. As low-quality research can significantly impact the validity of the overall findings, the synthesized results should be interpreted with caution. Adequate sample sizes and rigorous methodology are warranted for future studies to improve research quality of this topic. Second, only publications in English was searched and included in this umbrella review. Finally, there was considerable heterogeneity among included reviews, which limited the ability to draw definite conclusions based on the qualitative syntheses performed.

5 | CONCLUSIONS

The umbrella review demonstrated promising clinical outcomes regarding the use of VR as an advanced therapeutic approach in stroke rehabilitation to optimize patient care. Outcomes regarding upper extremity motor function, upper extremity activity, participation, functional independence, balance, functional mobility, walking speed, and cognitive function were summarized. While positive effects in favor of VR were revealed by most systematic reviews on these outcomes, there is a dearth of evidence supporting the significantly different effects of VR compared to conventional rehabilitation on participation and cognitive function domains. Randomized controlled trials with large sample sizes and rigorous methodology are warranted to strengthen the empirical evidence of VR. Future systematic reviews and meta-analyses in this field should adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to enhance the quality of evidence.

AUTHOR CONTRIBUTIONS

Jie Hao: Conceptualization; Data curation; Formal analysis; Investigation; Project administration; Software; Visualization; Writing—original draft; Writing—review and editing. Gretchen Crum: Data curation; Investigation; Validation; Visualization; Writing—original draft. Ka-Chun Siu: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Supervision; Validation; Visualization; Writing—original draft; Writing—review and editing.

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All authors have read and approved the final version of the manuscript. Dr. Ka-Chun Siu had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

The author confirms that all data generated or analyzed during this study are included in this article.

STUDY REGISTRATION

International prospective register of systematic reviews (PROSPERO): CRD42022381498

TRANSPARENCY STATEMENT

The lead author Ka-Chun Siu affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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APPENDIX

Search strategy

PubMed

("Virtual Reality"[Mesh] OR "Exergaming"[Mesh] OR "virtual reality" OR "virtual environment" OR "augmented reality" OR "mixed reality" OR "video game*" OR "exergam*" OR "serious gam*" OR "smart glass*" OR "head mounted devic*" OR "head mounted displa*" OR "Kinect" OR "Wii" OR VR) AND ("stroke"[Mesh] OR "stroke" OR "cva" OR "cerebral vascular accident*" OR "cerebrovascular accident*" OR "post-stroke" OR "poststroke" OR "hemiplegi*" OR "hemiparesis") AND ("systematic review*" OR meta-analysis OR "meta analys*" OR "meta-analys*" OR "Meta-Analysis as Topic"[Mesh] OR "Meta-Analysis"[Publication Type] OR "Systematic Reviews as Topic"[Mesh] OR "Systematic Review"[Publication Type])

Scopus

(TITLE-ABS-KEY ("virtual reality" OR "virtual environment" OR "augmented reality" OR "mixed reality" OR "video game*" OR "exergam*" OR "serious gam*" OR "smart glass*" OR "head mounted devic*" OR "head mounted displa*" OR "Kinect" OR "Wii" OR vr) AND TITLE-ABS-KEY ("stroke" OR "cva" OR "cerebral vascular accident*" OR "cerebrovascular accident*" OR "post-stroke" OR "poststroke" OR "hemiplegi*" OR "hemiparesis") AND TITLE-ABS-KEY ("systematic review*" OR meta-analysis OR "meta analys*" OR "meta-analys*")) AND (LIMIT-TO (LANGUAGE, "English"))

CINAHL

("virtual reality" OR "virtual environment" OR "augmented reality" OR "mixed reality" OR "video game*" OR "exergam*" OR "serious gam*" OR "smart glass*" OR "head mounted devic*" OR "head mounted displa*" OR "Kinect" OR "Wii" OR vr) AND ("stroke" OR "cva" OR "cerebral vascular accident*" OR "cerebrovascular accident*" OR "post-stroke" OR "poststroke" OR "hemiplegi*" OR "hemiparesis") AND ("systematic review*" OR meta-analysis OR "meta analys*" OR "meta-analys*") Limiters - English Language; Peer Reviewed; Human

PsycINFO

("virtual reality" OR "virtual environment" OR "augmented reality" OR "mixed reality" OR "video game*" OR "exergam*" OR "serious gam*" OR "smart glass*" OR "head mounted devic*" OR "head mounted displa*" OR "Kinect" OR "Wii" OR vr) AND ("stroke" OR "cva" OR "cerebral vascular accident*" OR "cerebrovascular accident*" OR "post-stroke" OR "poststroke" OR "hemiplegi*" OR "hemiparesis") AND ("systematic review*" OR meta-analysis OR "meta analys*" OR "meta-analys*") Limiters - English; Peer Reviewed

Embase

('virtual reality'/exp/mj OR 'virtual reality head mounted display'/exp/mj OR 'virtual reality':ti, ab OR vr:ti, ab OR 'augmented reality':ti, ab OR 'mixed reality':ti, ab OR 'virtual environment':ti, ab OR 'video game*':ti,ab OR 'exergam*':ti,ab OR 'serious gam*':ti,ab OR 'smart glass*':ti,ab OR 'head mounted devic*':ti,ab OR 'head mounted displa*':ti,ab OR 'kinect':ti, ab OR 'wii':ti, ab OR 'vr':ti, ab) AND ('brain ischemia'/exp/mj OR 'cerebrovascular accident'/exp/mj OR stroke*:ti, ab OR 'hemorrhagic stroke':ti, ab OR 'transient ischemic attack':ti, ab OR 'acute ischemic stroke':ti, ab OR cva*:ti, ab OR 'cerebral vascular accident':ti, ab OR 'cerebrovascular accident':ti, ab OR 'cerebral vascular accidents':ti, ab OR 'cerebrovascular accidents':ti, ab OR 'poststroke':ti, ab OR 'post-stroke':ti, ab OR 'hemiplegi*':ti,ab OR 'hemiparesis':ti, ab)

AND ('systematic reivew'/exp/mj OR 'meta analysis'/exp/mj OR 'systematic review':ti, ab OR 'meta-analysis':ti, ab OR 'meta analys*':ti,ab OR 'meta-analys*':ti,ab) AND [english]/lim AND [humans]/lim