

Systematic Review

Effects of Virtual Reality-based Interventions on Depression, Anxiety, and Abilities of Daily Living in Stroke Survivors: A Systematic Review and Meta-analysis

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Academic Editor: Bettina Platt

Submitted: 26 October 2024 Revised: 20 December 2024 Accepted: 14 January 2025 Published: 23 May 2025

Abstract

Background: Stroke survivors often experience varying levels of psychological stress, depression, and anxiety, which can exacerbate their physical impairments and adversely affect their recovery process. Virtual reality (VR) technology has been proven to be effective for patients with depression, garnering significant interest from researchers focused on stroke rehabilitation. However, the precise impact of VR on stroke-related psychology remains unclear. This meta-analysis aimed to appraise the effect of VR on depression, anxiety, and the abilities of daily living in stroke survivors. **Methods:** The research involved a search of six electronic databases, including the Cochrane Library, Embase, Web of Science, PubMed, CINAHL, and PsycINFO, from the inception of the databases to June 2, 2024. Two investigators independently screened the databases based on the inclusion and exclusion criteria, extracted data from the included studies, and tested their methodological quality using Cochrane's risk of bias tool. The intervention effect was estimated using Review Manager 5.4 to calculate the standard mean difference (SMD) and 95% confidence interval (CI). **Results:** This review identified 16 studies out of the 4439 records retrieved, consisting of a total of 756 stroke patients. Post-intervention analysis provided low certainty evidence that VR training reduced depression (SMD = -0.47; 95% CI: -0.88, -0.05, $p = 0.03$), but there was no significant effect on anxiety (SMD = -0.25; 95% CI: -0.53, 0.03, $p = 0.08$) and activities of daily living (SMD = 0.34; 95% CI: -0.05, 0.73, $p = 0.09$). Subgroup analysis indicated that participants under 60 years old who received VR intervention had a significant reduction in depression scores (SMD = -1.13; 95% CI: -1.89, -0.37, $p = 0.004$) compared with the control group. Those with moderate depression (SMD = -1.02; 95% CI = -1.96 to -0.07, $p = 0.04$) and intervention that lasted more than 6 weeks (SMD = -1.16; 95% CI: -1.87, -0.44, $p = 0.002$) also showed lower scores. **Conclusions:** Due to heterogeneity concerns and the poor quality of included studies, our meta-analysis that provided evidence with very low certainty indicates that VR technology may be a beneficial approach for improving the psychological health issues faced by stroke survivors, helping to reduce their depression, but has no significant effect on reducing anxiety and improving their activities of daily life. However, additional comprehensive research is required to reinforce these conclusions. Specifically, future research needs to involve larger scale and more rigorous approaches, utilizing tailored VR interventions to further improve patient well-being. **PROSPERO Registration:** CRD42024575981, <https://www.crd.york.ac.uk/PROSPERO/view/CRD42024575981>.

Keywords: virtual reality; stroke; depression; anxiety; abilities of daily life; meta-analysis

1. Introduction

Stroke remains a global challenge. The latest report indicates that stroke is the third primary cause of disability worldwide and the second leading cause of death [1]. It is the foremost cause of mortality and disability in China [2], severely affecting individuals' ability to live independently, and results in considerable physical and mental health issues [3]. The recent Corona Virus Disease 2019 (COVID-19) pandemic has greatly deteriorated the prognosis for stroke patients worldwide. A study suggests that ischemic stroke patients during this pandemic suffer from more severe conditions compared with their non-COVID-19 counterparts. Additionally, they also face worse functional recovery and higher mortality rates [4], leading to a serious disease burden on the global healthcare system. The annual

rise in stroke cases suggests an escalating public health crisis globally [5], frequently resulting in both physical and psychological challenges, such as limb dysfunction, post-stroke depression (PSD), and post-stroke anxiety (PSA) [3,6]. Approximately 39.1% of stroke survivors experience depression, while 34.9% suffer from anxiety. Additionally, 45.3% to 86.1% of stroke survivors may experience varying degrees of physical disability [7]. Current rehabilitation approaches mainly focus on the recovery of limb function to target the recovery of motor skills and postural control on the affected side [8,9]. Nevertheless, the overall ability of stroke survivors to attain independent living and reintegrate into society is dependent not only on motor function restoration but also on emotional well-being, which demands serious attention [10]. Research [3] shows that stroke survivors



have a higher incidence of developing depression and anxiety disorders. These adverse emotional states are linked to increased disability, diminished daily living skills, and elevated mortality rates [6,11]. Expert consensus emphasizes that the presence of post-stroke psychological disorders deserves considerable focus due to their potential to hinder patients' recovery and impair their daily functions [12].

Individuals who experience stroke have a higher likelihood of facing issues related to their mental health [13]. Various factors, including physiological conditions, cognitive function, and social support, often cause stroke patients to experience negative emotions [14]. However, due to the subtlety of negative emotions like anxiety and depression, family members and healthcare professionals may prioritize the assessment of physical health, such as limb recovery and daily living skills, while overlooking the importance of mental health evaluations [15]. Furthermore, many stroke survivors may lack the consciousness or ability to express their emotional needs, which can exacerbate feelings of depression and anxiety, ultimately lowering their quality of life [16]. Depression typically presents as a persistent low mood, diminished interest in activities, and various other symptoms, whereas anxiety is characterized by excessive apprehension, fear, and related manifestations. These psychological distresses can reduce motivation and adherence to rehabilitation efforts [17], delaying recovery from neurological impairments, harming functional recovery [10,15], and exacerbating the decline of health-related quality of life, leading to increased mortality rates [18,19]. Therefore, there is an urgent need to seek effective interventions that provide mental support, alleviate the psychological burden, address psychosocial challenges, and ultimately improve the overall quality of life for these patients.

Virtual reality (VR) training offers numerous benefits for stroke rehabilitation when compared with conventional training techniques. It is reported that VR-based neurorehabilitation interventions can enhance rehabilitation engagement during virtual interactions and training processes [20], thereby boosting motivation and encouraging active participation in diverse rehabilitation activities [8]. Specifically, VR training can markedly enhance the activation of particular cerebral regions, including the frontal cortex and the mirror neuron system. These neural modifications are intricately linked to advancements in behavioral outcomes [21]. Furthermore, the application of VR technology engages patients' sensory modalities, such as visual and auditory stimuli, thereby optimizing the interplay between cerebral and cortical networks and facilitating the reorganization of neuronal structures. This neuroplasticity is instrumental in rehabilitating impaired brain function [22], consequently alleviating the negative psychological symptoms of stroke patients. VR allows for adjusting the difficulty level of training tasks according to individual capabilities and switching between various safe training scenarios [9]. The immersive nature of VR creates a simulated environment that

enhances learning through multi-sensory engagement, interactive feedback, self-reflection, and practice, which can generate thought resonance and promote psychological immersion [23]. Consequently, it establishes a positive feedback loop and enhances their functional capabilities.

There are certain differences in the application of VR intervention in post-stroke depression and post-stroke anxiety. The VR technology designed for post-stroke depression seeks to facilitate stress relief and the reconstruction of positive emotions by providing pre-set virtual scenes for interaction [20]. For post-stroke anxiety, the simulation of anxiety-inducing triggers within these virtual settings can assist patients in developing strategies to maintain composure and effectively manage their responses. The emphasis of VR may be more on replicating reactions and coping mechanisms in scenarios that provoke anxiety [17]. Simulated environments prove beneficial in addressing psychological disorders by allowing individuals to tailor and rehearse these aspects in diverse manners. VR has gained attention as a novel therapy in stroke rehabilitation [24], with research indicating that VR intervention can significantly reduce the negative emotions experienced by patients with mental health disorders, reduce social and psychological pain, and thus improve their overall quality of life [25].

Systematic reviews evaluating the impact of VR on the mental and physical health outcomes of stroke survivors have produced contradictory results, particularly regarding anxiety, depression, and the abilities of daily life [12,26,27]. These variations could stem from disparities in the age demographics of the participants, differences in how the intervention techniques were applied, and the evaluation tools used [12]. This undermines the reliability of the studies and hinders the further promotion and application of the research results. In addition, prior systematic reviews [27] have faced some issues, such as limited sample sizes and limited outcome measures that only focused on the impact of VR on depression. Systematic reviews based on these studies may introduce biases and disagreements among healthcare providers, ultimately affecting the physical and mental well-being of stroke survivors [12,26,27]. Therefore, this study aims to conduct a systematic review and meta-analysis of randomized controlled trials to assess the effects of virtual reality interventions on anxiety, depression, and daily living activities in stroke patients, providing evidence-based recommendations for clinical practice.

2. Materials and Methods

This systematic review was registered on PROSPERO with registration number CRD42024575981 and was performed following the PRISMA 2020 criterion [28]. The PRISMA checklist is shown in **Supplementary Material 1**.

2.1 Search Strategy

A total of six electronic databases were searched, including PubMed, Embase, Web of Science, Cochrane Library, CINAHL, and PsycINFO. The reason why certain databases were chosen is that PubMed and Embase are widely recognized databases within the medical domain, while Web of Science is an internationally recognized comprehensive academic information resource repository. The Cochrane Library is renowned for its high-quality clinical trials. Additionally, CINAHL is an authoritative literature database focused on nursing and related health fields. Furthermore, the PsycINFO database covers literature in the field of psychology and its applications. The data were comprehensively collected from the establishment of these databases to June 2nd, 2024. To ensure the quality of the analysis, the search strategy was designed according to the principles of PICOS (P: Participants, I: Interventions, C: Comparisons, O: Outcomes, S: Study design). The proposal put forward by the Cochrane Collaboration is to use medical topic headings (MeSH) terminology and free word searches, and connect them using Boolean logical operators such as AND and OR. The specific strategy words were as follows “virtual reality/virtual environment/virtual rehabilitation/virtual game/virtual therapy/educational virtual reality/instructional virtual reality/VR/VRS” AND “stroke/cerebrovascular accident/brain vascular accident/ischemic stroke/hemorrhagic stroke” AND “randomized controlled trial/RCT/randomized”. There were no limitations regarding the language or the publication date. The entire literature screening process used Endnote software to deduplicate, screen, and manage search results. In addition, the reference lists included in the articles were manually reviewed to search for other relevant studies that might have been missed in database searching. **Supplementary Material 2** provides a detailed record of the search strategy used in PubMed.

2.2 Inclusion and Exclusion Criteria

Literature qualified for inclusion in this review if they met the following criteria: the study population (P) was diagnosed with stroke by Computed Tomographic (CT) or Magnetic Resonance Imaging (MRI), and the intervention (I) involved VR (including non-immersive, semi-immersive, and immersive). Specifically, head-mounted 3D displays were coded as fully immersive, while more complex visuals with bigger surface displays were semi-immersive. Interaction with a PC monitor, keyboard, and mouse was considered non-immersive. The control (C) was conventional rehabilitation treatment and the result (O) should include at least one of the following indicators: depression, anxiety state, or ability to engage in activities of daily life. The type of study design (S) was randomized clinical trial (RCT). Literature excluded: (1) qualitative studies, animal experiments, meta-analyses, systematic reviews, reviews, letters, case reports, conference papers, and

pilot studies; and (2) repeated research, inability to obtain the full text, or incomplete relevant data.

2.3 Data Extraction

A table was established to store a large amount of extracted information, including the following specific contents: first author name, year of publication, country of the studies included in the analysis, sample size, participant age, interventions in the intervention group and control group, duration and frequency of interventions, and the measurement tools. Two authors (HHL and GL) independently extracted data from the included studies and inputted it into the data extraction table. Any disputes were resolved by discussion with a third author (ELC) to reach a consensus.

2.4 Risk of Bias

According to the Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB-2) (<https://methods.cochrane.org/risk-bias-2>) [29], two review authors (HHL and GL) independently evaluated the existing bias risk of the seven aspects of the article. If there was any disagreement in the quality evaluation, it was judged by a third author (ELC). The seven specific domains of the bias risk tool include: random process bias, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, and selective reporting; other issues were also evaluated. Using this tool, there are three possible bias risks in each domain, which are “low”, “high”, or “unclear”. The process of evaluating each domain is as follows: in terms of selection bias, it is unclear if only randomness is mentioned without specifying the specific method used for randomization; not mentioning randomness is high risk; detailing random sequence methods (coin toss, random number table, computer randomization) is low risk. Concerning allocation concealment, the mention of allocation concealment strategies is deemed low risk. Implementing blinding for both participants and personnel is also classified as low risk. The blinding method utilized by the evaluator is considered low risk. Follow-up bias refers to incomplete outcome measures and missing data. Intention-to-treat (ITT) analysis for missing data is low risk. The registration number of the research protocol was recorded and all results were reported (positive and negative), indicating a low risk of reporting bias. Additionally, other biases such as conflicts of interest or research design deficiencies were recorded. If none were present, the risk was considered low. The studies were categorized as low risk of bias (all domains assessed as low risk), some concerns (at least one domain with concerns but no high risk), or a high risk of bias (at least one domain assessed as high risk). Higher risk leads to lower research quality, in the form of less accurate or reliable findings, weaker evidence, and limited reproducibility and applicability.

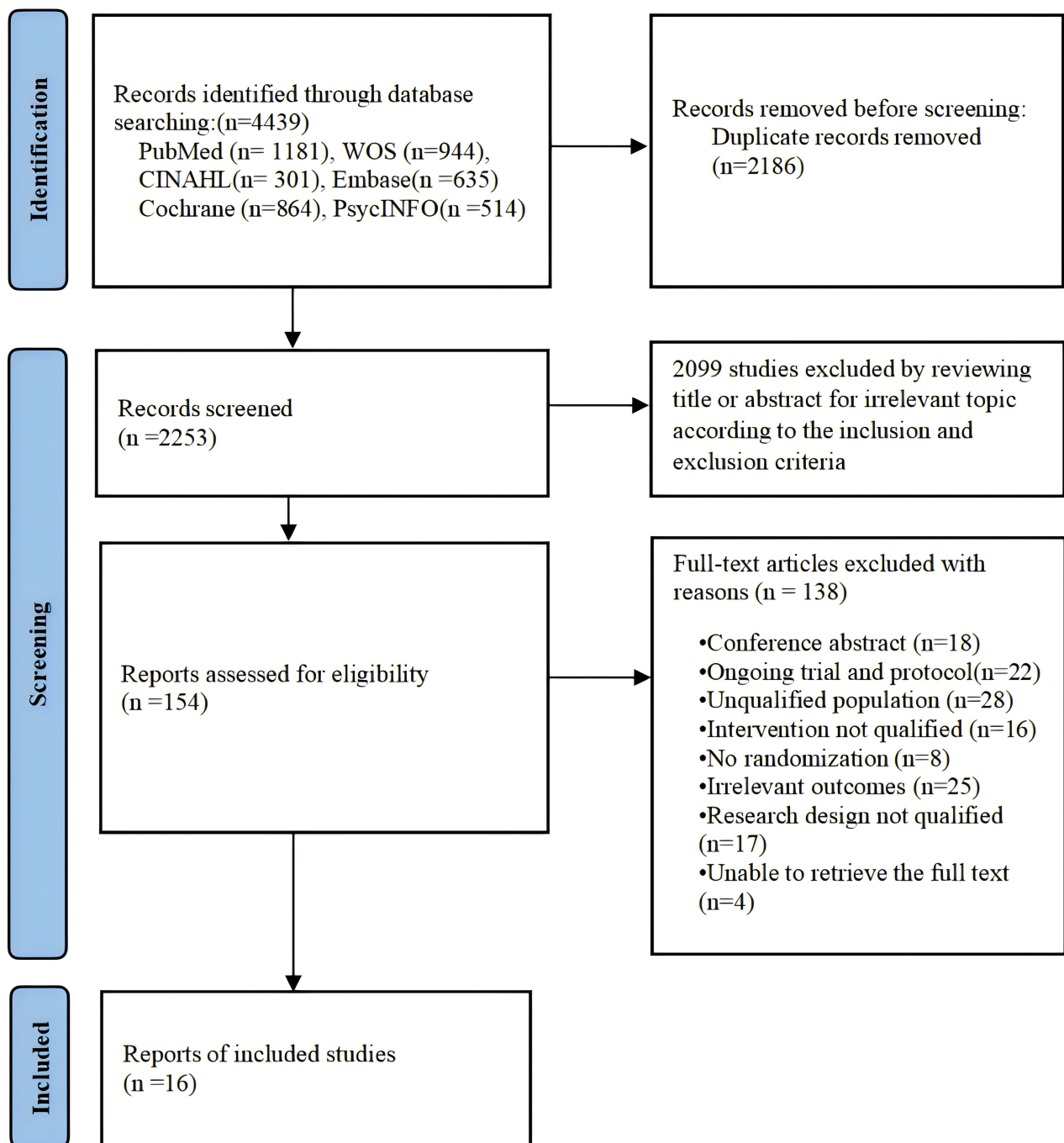


Fig. 1. PRISMA flow diagram.

2.5 Quality Assessment

Using the GRADE system (<https://ebn.bucm.edu.cn/xzffxzy/zjfjxt/54213.htm>) to evaluate the methodological quality of selected researchers, evidence was classified into four possible levels: high, medium, low, and extremely low [30]. **Supplementary Material 3** provides specific details on the evaluation of evidence for each study.

2.6 Data Synthesis and Analysis

Meta-analysis was conducted on each included study using the software Review Manager (RevMan 5.4, Interna-

tional Cochrane Collaboration, London, UK), developed by the International Cochrane Collaboration. For continuous variables, the corresponding 95% confidence interval (95% CI) was calculated based on whether the results were measured using the same scale. The same evaluation tool used mean difference (MD), while different measurement tools used the standard mean difference (SMD). The statistical heterogeneity included in the study was determined through a Q-test. If $p < 0.1$ and $I^2 \geq 50\%$, there was statistical heterogeneity between the studies, and a random effects model was used to merge the effect sizes. Otherwise, a fixed ef-

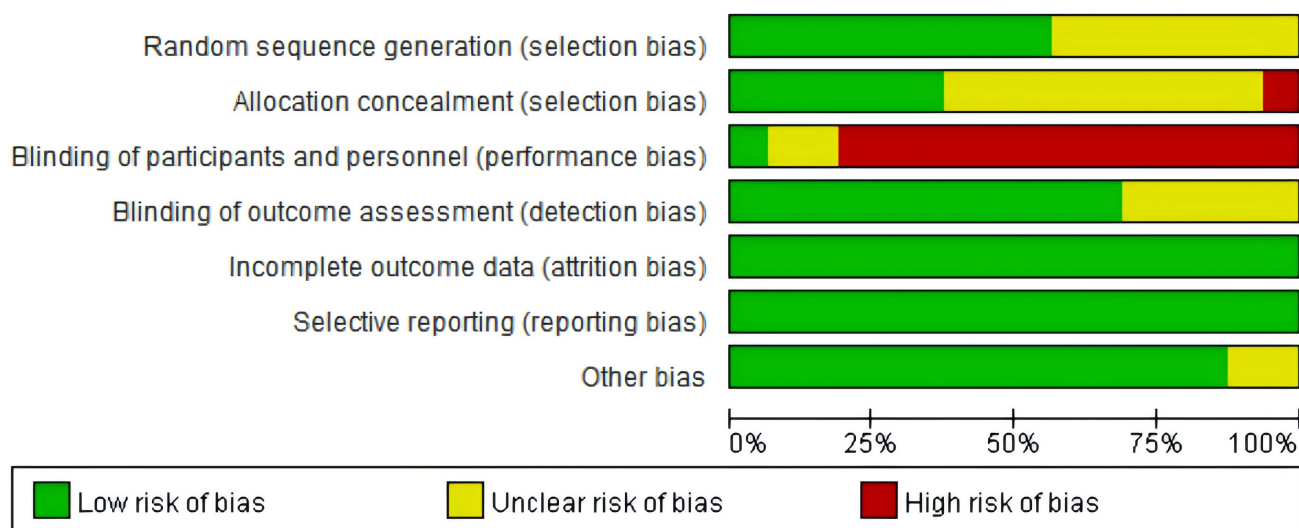


Fig. 2. Risk of bias graph of RCTs. RCTs, randomized controlled trials.

fects model was used. Sensitivity analysis through the elimination of included studies was conducted to examine the robustness and reliability of the results. Subgroup analysis was performed when heterogeneity was vast to identify the source of heterogeneity [31]. Sensitivity analysis was conducted using the software Stata 17, while the Egger test was employed to detect any potential publication bias (when $p < 0.05$, it indicates that publication bias was significant). For meta-analyses of outcomes consisting of ≥ 10 studies, Egger's test was used to generate a funnel plot to evaluate publication bias. When the number of studies reporting the same outcome measures was less than 3, the research results were presented in narrative form. Statistical significance was assumed when $p < 0.05$.

3. Results

3.1 Literature Search Results

Initially, 4439 records were retrieved across the six electronic databases. From these, 2186 duplicate records were excluded automatically and manually, and 2099 records were further filtered by reading the title and abstract. Among these, 138 studies proceeded to full-text review. Finally, the remaining 16 studies were included in the systematic review. The literature screening flowchart illustrates the selection process (Fig. 1).

3.2 Description of Included Studies

3.2.1 Study Characteristics

Table 1 (Ref. [17,32–46]) shows the features of the included studies in this review, which were published from 2012 to 2024. Among the 16 studies, four [32–34,46] were from China, six [17,35–39] were from Korea, three [40–42] from Italy, and three were from Spain [43], Australia [44], and Europe [45].

3.2.2 Intervention Characteristics

The frequency and duration of VR exposure varied greatly between different studies. According to the analysis, the duration of VR-based intervention ranged from 2 to 8 weeks in this review, with the majority being 4 weeks. The frequency of intervention varied from two to seven times per week and the intervention time ranged from 15 minutes to 90 minutes per session. Among the 16 included trials, the results of interest included depression levels (10 trials), anxiety levels (three trials), and activities of daily living (10 trials). Six studies [33,34,43–46] involved follow-up after the VR intervention, ranging from 1 to 3 months. The types of VR technology varied among these studies. Five studies adopted VR technology with a wireless Kinect sensor (Microsoft Corporation, Redmond, WA, USA) [17,32,34,37,43] and two studies applied immersive VR system head-mounted displays (HMD, VR EYES, SMART PIA, Yongin, Korea) [33,35]. One study used immersive programs with goggles and controllers to manipulate virtual objects in the 3D virtual world (InTheTech Co, Ltd, Daegu, Korea) [38] and another study used 2D displays (YouRehab, Ltd, Schlieren, Switzerland) [40]. One study used the VR TierOne device (Stolgraf®, Stanowice, Poland), which represents a virtual therapeutic garden [42]. One study used the Lokomat device for personalized gait rehabilitation [41], one study used software from the cognitive rehabilitation training system (Moto Cog, Cybermedic, Korea) [36], one study trained on the Gait Real-time Analysis Interactive Lab (GRAIL, Motekforce Link, Amsterdam, the Netherlands) [46], and one study used the Elements VR interactive tabletop system [44]. Among these sixteen studies, nine used immersive VR [17,32,33,37–39,42,43,46], five used semi-immersive VR [34,35,40,41,45], and two used non-immersive VR [36,44].

Table 1. Characteristics of the included studies.

Study	Country	Publication Year	Sample (T/C)	Age, years (T/C)	Intervention (training intensity)	Comparison	Measurement Time Point	Outcomes Used
Chao <i>et al.</i> [32]	China	2024	33 (16/17)	59.9 ± 12.8/ 63.1 ± 9.3	Early rehabilitation and VR training (treated for 60 minutes each time, five times a week)	Early rehabilitation	Baseline, at discharge (7–21 days later)	HADS-D, HADS-A, BI
Huang <i>et al.</i> [33]	China	2024	40 (20/20)	63.3 ± 14.3/ 65.1 ± 6.1	IM-VR and conventional rehabilitation therapy (treated for 60 minutes each time, five times a week, 3 weeks)	Conventional rehabilitation therapy	Baseline, end of treatment (3 weeks), and follow-up (12 weeks)	BI
Park <i>et al.</i> [39]	Korea	2023	40 (20/20)	62.5 ± 4.7/ 62.5 ± 4.8	VR cognitive intervention and conventional treatment (each session: 30 minutes, five times a week, 8 weeks)	Conventional treatment	Baseline, end of treatment (8 weeks)	K-MBI
de Rooij <i>et al.</i> [46]	China	2021	52 (28/24)	65 (57–70)/ 61 (53–71)	Conventional rehabilitation and VR (each session: 30 minutes, twice a week, 6 weeks)	Conventional rehabilitation	Baseline, end of treatment (6 weeks), and follow-up (3 months)	HADS-D, HADS-A
Lin <i>et al.</i> [17]	Korea	2020	145 (38/107)	64.5 ± 13.5/ 66.9 ± 13.3	Conventional rehabilitation and VR training (treated for 15 minutes each time, twice a day)	Conventional rehabilitation training	Baseline (within 4 h following admission) and on the day of discharge (7 to 21 days)	HADS-D, HADS-A, BI
Kim <i>et al.</i> [35]	Korea	2020	24 (12/12)	71.92 ± 3.23/ 71.92 ± 3.23	Core stability training and conventional physical therapy based on VR (4 weeks; each session: 30 minutes, three times a week)	Core stability training and general physical therapy	Baseline, end of treatment (4 weeks)	GDS
Lee <i>et al.</i> [36]	Korea	2020	22 (11/11)	58.18 ± 8.22/ 59.09 ± 11.65	Conventional treatment and VR cognitive training (4 weeks; five times a week, 30 minutes each time)	Conventional cognitive therapy	Baseline, end of treatment (4 weeks)	BDI
Manuli <i>et al.</i> [41]	Italy	2020	60 (30/30)	48.0 ± 12.1/ 40.1 ± 10.7	Lokomat robot training RRG (the Robotic Rehabilitation Group) and VR (8 weeks; five times a week, with approximately 1 h of training per session)	Lokomat robot training RRG	Baseline, end of treatment (8 weeks)	BDI, FIM
Brunner <i>et al.</i> [45]	Europe	2017	120 (62/58)	62 (23–89)/ 62 (41–87)	VR training (4 weeks; 60 minutes each time, four times per week)	Conventional therapy	Baseline, end of treatment (4 weeks), and follow-up (3 months)	FIM
Rogers <i>et al.</i> [44]	Australia	2019	21 (10/11)	64.3 ± 17.4/ 64.6 ± 12.0	Conventional treatment and VR training (4 weeks; 30–40 minutes each time, once a day, three times per week)	Conventional treatment	Baseline, immediately following training (post-test) and follow-up (1 month)	NFI

Table 1. Continued.

Study	Country	Publication Year	Sample (T/C)	Age, years (T/C)	Intervention (training intensity)	Comparison	Measurement Time Point	Outcomes Used
Calabrò <i>et al.</i> [40]	Italy	2017	24 (12/12)	60 ± 4/ 63 ± 6	Robot-assisted gait training (RAGT) and VR (8 weeks; five times a week, 45 minutes each time)	Robot-assisted gait training (RAGT)	Baseline, end of treatment (8 weeks)	HAMD
Lee <i>et al.</i> [34]	China	2017	47 (26/21)	59.35 ± 8.95/ 55.76 ± 9.59	VR plus standard treatment (90 minutes each, twice a week, 6 weeks)	Standard treatment	Baseline, end of treatment (6 weeks) and follow-up (3 months)	MBI
Ballester <i>et al.</i> [43]	Spain	2016	18 (9/9)	63.40 ± 9.40/ 54.80 ± 12.00	Conventional rehabilitation therapy and VR training (6 weeks; seven times a week, 30 minutes each time)	Conventional rehabilitation therapy	Baseline, end of treatment (6 weeks) and follow-up (12 weeks)	HAMD, BI
Song <i>et al.</i> [37]	Korea	2015	40 (20/20)	51.37 ± 40.6/ 50.10 ± 7.83	Conventional rehabilitation therapy and VR training (8 weeks; 30 minutes each time, five times a week)	Conventional rehabilitation therapy	Baseline, end of treatment (8 weeks)	BDI
Kiper <i>et al.</i> [42]	Italy	2022	44 (23/21)	63.1 ± 9.5/ 64.3 ± 12.6	Virtual reality training (4 weeks; 60 minutes each time, five times a week)	Conventional therapy	Baseline, end of treatment (4 weeks)	FIM
Kwon <i>et al.</i> [38]	Korea	2012	26 (13/13)	57.15 ± 15.42/ 57.92 ± 12.32	Conventional therapy and VR training (4 weeks; 30 minutes each time, five times a week)	Conventional therapy	Baseline, end of treatment (4 weeks)	K-MBI

T, intervention group; C, control group; VR, virtual reality; HAMD, Hamilton Depression Scale; BDI, Beck Depression Scale; GDS, Geriatric Depression Scale; HADS-D, Hospital Depression Scale; HADS-A, Hospital Anxiety Scale; NFI, Neurobehavioral Function Index; BI, Barthel Index; MBI, Modified Barthel Index; K-MBI, Korean Version of the Modified Barthel Index; IM, immersive; FIM, Functional Independence Measure.

	Ballesté 2016	Brunner 2018	Calabrò 2017	Chao 2024	Huang 2024	Kim 2020	Kiper 2014	Kwon 2012	Lee 2017	Lee 2020	Lin 2020	Manuli 2020	Park 2023	Rogers 2019	Rooij 2021	Song 2015
Random sequence generation (selection bias)	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	?
Allocation concealment (selection bias)	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	?
Blinding of participants and personnel (performance bias)	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	?
Blinding of outcome assessment (detection bias)	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	?
Incomplete outcome data (attrition bias)	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Selective reporting (reporting bias)	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Other bias	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

Fig. 3. Risk of bias summary.

3.2.3 Measurement Characteristics

Although the tools used for outcome evaluation were different, they are all effective scales, and the data collection process was carried out by experienced staff. The Hamilton Depression Scale (HAMD) [40,43], Beck Depression Scale (BDI) [36,37,41], Geriatric Depression Scale (GDS) [35], Hospital Anxiety and Depression Scale Depression Subscale (HADS-D) [17,32,46], and Neurobehavioral Function Index (NFI) [44] were used to assess depression levels. Tools used to evaluate anxiety levels included the Hospital Anxiety and Depression Scale Anxiety Subscale (HADS-A) [17,32,46]. Activities of daily living were evaluated using the Barthel Index (BI) [17,32,33,43], Modified Barthel index (MBI) [34], Functional Independence Measure (FIM) [41,42,45], and Korean Version of the Modified Barthel Index (K-MBI) [38,39].

3.3 Risk of Bias Assessment Results

The risk of bias graph and summary are shown in Figs. 2,3. Of the 16 included RCTs, one study [36] did not mention randomization and six studies [32,35,37,38,40,43] mentioned randomization but did not describe the specific randomization method. For the implementation of allocation concealment and blinding methods, six [17,32,33,40,44,46] studies described the hidden allocation scheme specifically and only one study [40] conducted blinding on patients, researchers, and measures. Seven studies [17,32,38,41,43,44,46] were blinded by intervention personnel and data collectors but, due to the impact of intervention measures, blinding could not be implemented on the research subjects. The quality assessment of the methods in 16 studies was rated as B-level, while the quality of the literature was deemed acceptable (Supplementary Material 4).

3.4 Description of Included Studies

3.4.1 Depression

Depression was reported in 10 studies, including a total of 439 patients (Fig. 4A). The results suggested that there was high heterogeneity among these studies ($p < 0.0001$, $I^2 = 74\%$). The random effects model was used to merge effect sizes and the results showed that there was a statistically significant difference in depression scores between the VR intervention group and the control group after intervention (SMD = -0.47 , 95% CI: -0.88 , -0.05 , $p = 0.03$). Sensitivity analysis by excluding studies one by one showed that the result was stable.

3.4.2 Anxiety

Three studies included 230 stroke participants who reported changes in anxiety levels. The heterogeneity test showed $I^2 = 0\%$ and $p = 0.66$, which indicated no heterogeneity among the studies. A meta-analysis was conducted using the fixed effects model (Fig. 4B) and the combined SMD = -0.25 (95% CI: -0.53 , 0.03 , $p = 0.08$). Sensitivity analysis was conducted and relevant studies were excluded one by one, indicating the robustness of the results.

3.4.3 Abilities of Daily Living

Data from 10 studies, including 573 patients, were used to assess the effectiveness of VR interventions on activities of daily living. Due to the large level of heterogeneity ($I^2 = 79\%$, $p < 0.00001$) among these studies, a random effects model was used. The meta-analysis showed that VR interventions had no statistical effect on improving activities of daily life compared with the control group (SMD = 0.34 , 95% CI: -0.05 , 0.73 , $p = 0.09$) (Fig. 4C). Sensitivity analysis was carried out and studies were excluded one by one. After excluding the studies of Manuli *et al.* [41], the heterogeneity test indicated that $p = 0.73$ and $I^2 = 0\%$, and a fixed effects model was used for meta-analysis of the

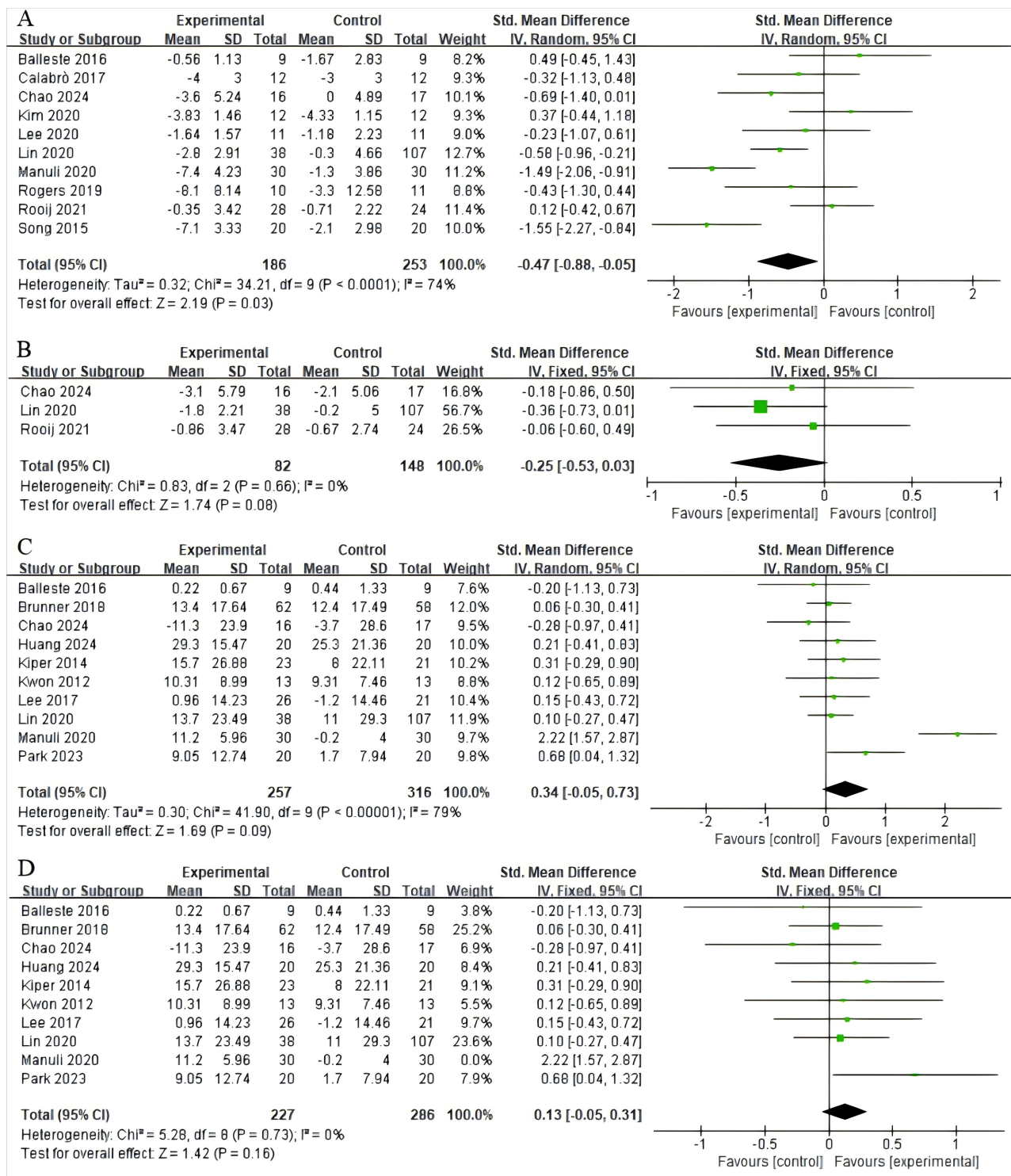


Fig. 4. Forest plots: effect of virtual reality intervention. (A) Comparison of differences in depression between the VR and control groups. (B) Comparison of differences in anxiety between the VR and control groups. (C) Comparison of differences in activities of daily life between the VR and control groups. (D) Comparison of differences in activities of daily life between the VR and control groups (excluding the studies of Manuli). SD, standard deviation; VR, virtual reality; IV, inverse variance.

remaining nine studies. Similarly, the results showed that there was no statistically significant difference in activities of daily life scores between the two groups after VR-based and common interventions (SMD = 0.13, 95% CI: -0.05,

0.31, $p = 0.16$) (Fig. 4D). According to the analysis, the source of heterogeneity may be related to lower study quality and different evaluation scales.

3.5 Subgroup Analysis

The WHO defines elderly individuals as those aged 60 years and above [47]. Therefore, we conducted subgroup analyses based on this age criterion. We also categorized intervention durations into two groups: less than 6 weeks and 6 weeks or more. In light of the participants' depression levels, we further divided the subjects into subgroups with mild and moderate emotional disorders.

3.5.1 Age of the Subjects

The mean age of participants in three studies [36,37,41] was below 60 years and the mean age in six studies [17,35,40,44,46,48] was over 60 years. The age mean $\pm$ standard deviation of the experimental group in one study [43] was 63.40 ± 9.40 years, while that of the control group was 54.80 ± 12.00 years. The two groups in this study are not all elderly and cannot be classified as over 60 years old or under 60 years old, therefore the subgroup analysis did not include this study. As shown in Fig. 5A, the results indicated that, in comparison with the control group, the mean age was more than 60 years ($SMD = -0.29$, 95% CI: -0.62 , 0.05 ; $I^2 = 40\%$, $p = 0.10$) and participants less than 60 years ($SMD = -1.13$, 95% CI: -1.89 , -0.37 ; $I^2 = 71\%$, $p = 0.004$) had lower depression scores in the VR group and more significant improvements for patients less than 60 years of age.

3.5.2 Rating of the Subjects

Seven of the studies [32,35,36,40,41,43,46] involved participants with mild depression and two [17,37] examined individuals with moderate depression. None of the studies involved participants with severe depression. Since Roger's study [44] utilized the NFI subscale without defined grading criteria, a subgroup analysis of grading was not part of this research. As shown in Fig. 5B, the results showed that compared with the control group, mild depression ($SMD = -0.28$, 95% CI: -0.84 , 0.27 ; $I^2 = 76\%$, $p = 0.32$) and moderately depressed participants ($SMD = -1.02$, 95% CI: -1.96 , -0.07 ; $I^2 = 82\%$, $p = 0.04$) had lower depression metrics in the VR group and the improvement was significant in moderately depressed patients.

3.5.3 Intervention Duration of the Study

For the duration of the intervention, three RCTs [37,40,41] lasted longer than 6 weeks, and seven RCTs [17,32,35,36,43,44,46] lasted less than 6 weeks. As shown in Fig. 5C, participants with an intervention period of longer than 6 weeks had lower depression scores in the VR group (combined effect size = -1.16 , 95% CI: -1.87 , -0.44 , $p = 0.002$). There was remarkable heterogeneity among the studies ($I^2 = 69\%$, $p = 0.04$). Moreover, participants with intervention cycles of less than 6 weeks had lower depression scores compared with the control group ($SMD = -0.20$, 95% CI: -0.54 , 0.15 , $p = 0.27$). There was a small amount of heterogeneity among the studies ($I^2 = 46\%$, $p = 0.09$).

3.6 Sensitivity Analysis and Publication Bias

Sensitivity analysis was performed to evaluate depression, anxiety, and activities of daily life. The results indicated that the estimated value closely matched the overall combined value, which implies that the depression meta-analysis findings are trustworthy and consistent (Supplementary Material 5A). Due to the limited number of studies on VR interventions for anxiety, it is not possible to create sensitivity analysis charts. Sensitivity analysis graphs for activities of daily life results are shown in Supplementary Material 5B. Additionally, the Egger test was utilized to evaluate the potential for publication bias, revealing a score indicative of depression, and yielding a score of depression ($Z = 0.519$) and activities of daily living ($Z = 0.544$). This result implies a minimal risk of publication bias in the current study.

4. Discussion

This systematic review, complemented by meta-analyses, demonstrates that virtual reality interventions effectively alleviate depression and anxiety among stroke patients, but do not significantly enhance daily living activities.

4.1 Summary of Main Results

This review describes the current effectiveness of VR in improving the mental health of stroke survivors. A total of 16 studies involving 756 participants evaluated VR intervention availability for post-stroke survivors on depression, anxiety, and the abilities of daily living. This review only included randomized controlled trials. These trials were assessed for methodological quality using Cochrane's risk of bias assessment tool and the "risk of bias" tool in Review Manager 5.4. The absence of clear reports on randomization, blinding, and allocation concealment in the included studies led to some being classified as unclear regarding performance risks and detection biases. Consequently, the overall methodological quality was moderate, indicating a need for more transparent randomized controlled trials in the future.

4.2 Principle Findings

4.2.1 Depression

The review results suggest that VR interventions have potential benefits for depression in stroke survivors. This is consistent with previous research findings [12,26,27]. Stroke results in physical and motor impairment. Rehabilitation often spans an extended duration, which can be challenging and burdensome for individuals and families, leading to adverse psychological states and increasing the risk of depression among patients [10]. Emerging sports rehabilitation can improve patient compliance and participation rates based on gaming VR technologies, which significantly boosts interest and immersion in therapeutic activities [23].

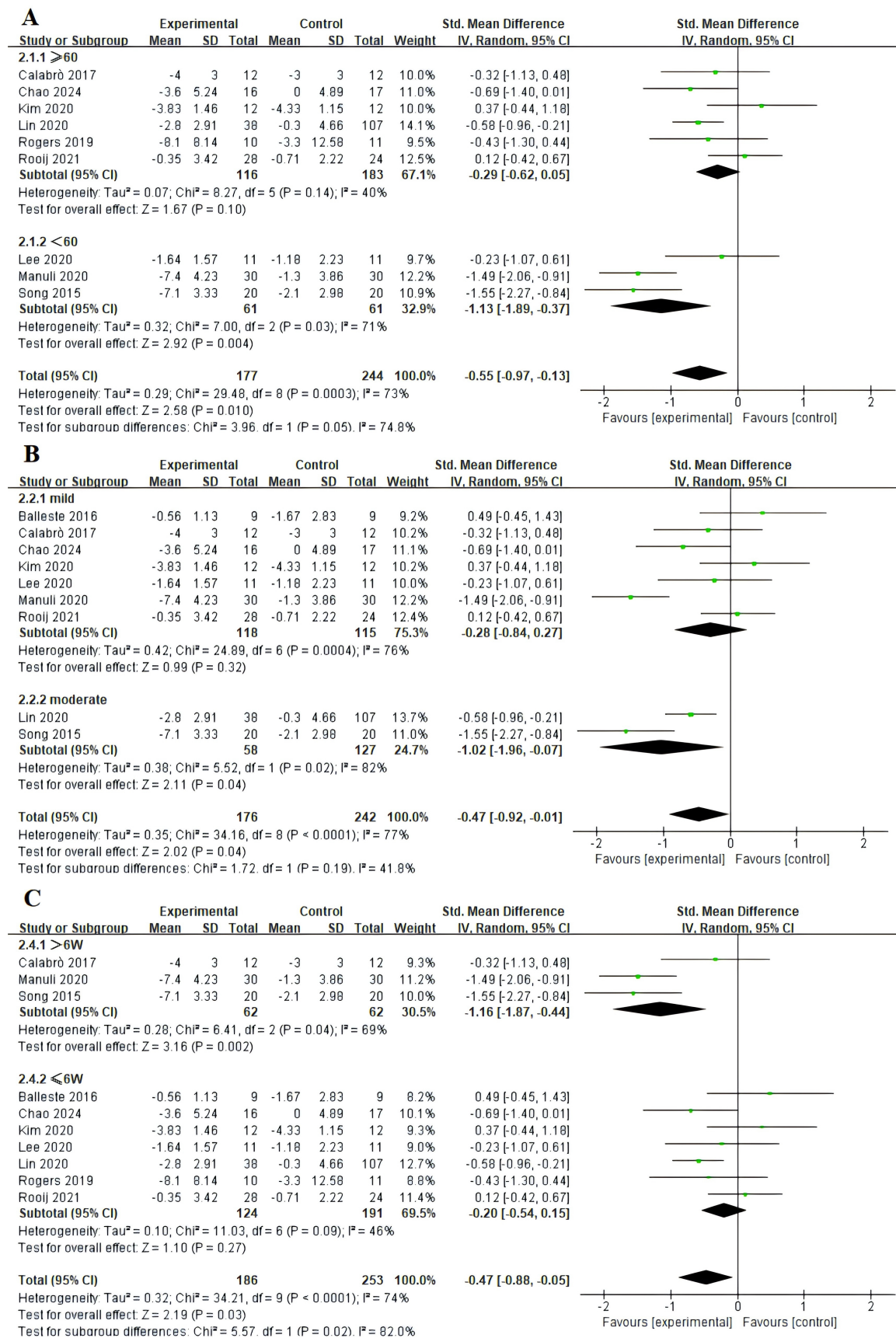


Fig. 5. Forest plots of subgroup analysis. (A) Age of the stroke survivors (≥ 60 years or < 60 years). (B) Degree of depression in stroke survivors (mild depression or moderate depression). (C) Intervention duration of VR (≥ 6 weeks or < 6 weeks).

It aids individuals in facing the illness while actively participating in rehabilitation programs. In addition, VR technology promotes neuronal plasticity and mitigates neuroinflammatory reactions through movement [49], thereby enhancing the neural tissue structure in stroke patients' brains and reducing negative emotional states.

This meta-analysis shows that VR is effective in intervening PSD but with high heterogeneity. Subgroup analysis was conducted based on the age of stroke patients and the results for depression were consistent with previous reviews [27]. VR intervention has a better effect on post-stroke depression in individuals under 60 years old and is effective in improving daily living abilities for stroke patients under 60 years old. The reason may be due to changes in their visual and auditory abilities as they age, which makes it difficult for some elderly people to adapt to new treatment methods [50]. Thus, the benefits of VR interventions for elderly stroke patients may be limited. Younger stroke patients usually have stronger physical functions and greater recovery potential than elderly patients. Their motivation to engage in VR training for the restoration of physical function and enhancement of quality of life is notably higher [51]. Additionally, younger individuals tend to demonstrate greater acceptance and adaptability to new technologies, making it easier for them to understand and operate VR devices, thus enabling them to more effectively utilize VR for rehabilitation training. Therefore, VR is more effective in younger patients. Given the limited research available for each subgroup, further investigation is necessary to comprehensively understand the impacts of VR interventions on the emotions of stroke survivors across various age groups.

VR intervention for stroke patients with a duration greater than 6 weeks is more effective in reducing depression, which is consistent with previous review results [27]. Stroke rehabilitation is a long-term physiological and psychological adaptation process; participants not only need time to familiarize themselves with their physical condition after stroke but also to accept the impact of daily life and real-life help [52]. A continuous accumulation of psychological problems caused by a series of functional problems in patients due to stroke, and improving these problems requires a certain intervention time. Therefore, extending the intervention time can improve patients' depressive moods. Subgroup analysis based on the severity of depression showed that VR has a good effect on moderate levels, but no significant difference in mild levels. The findings align with existing literature indicating that patients with elevated baseline severity scores derive greater advantages from active interventions compared with control conditions [53]. Given the limited quality and constrained sample size of the studies included in this systematic evaluation, it is necessary to further validate the reliability of this evidence-based study using larger sample sizes and rigorously designed multicenter RCTs.

4.2.2 Anxiety

The results indicate that VR interventions do not have a significant impact on anxiety in stroke patients. Research by Chirico *et al.* [54] indicated that VR environments can activate the parasympathetic nervous system, which can induce strong emotional responses and effectively alleviate patients' mental stress. VR technology benefits patients by creating a lifelike, multi-sensory environment, enhancing motor recovery, improving daily activities, and thus promoting mental health [55]. Nevertheless, a meta-analysis regarding anxiety indicated that VR intervention is not effective. Analyzing possible causes for the results, anxiety may stem from a range of specific triggering factors, including challenges in psychological adaptation, diminished social engagement, and a decline in life skills [6]. While VR technology can replicate various scenarios, it may struggle to authentically reproduce the genuine anxiety-inducing factors experienced by patients, thereby limiting its effectiveness in alleviating anxiety. Moreover, this study included only three investigations regarding post-stroke anxiety and the inadequate sample size may have introduced bias or uncertainty in the findings, complicating the accurate assessment of VR technology's efficacy. Further research involving high-quality trials is warranted to arrive at a more conclusive conclusion. Furthermore, fostering interdisciplinary collaboration including psychology, neuroscience, and computer science, alongside personalized interventions, is crucial for advancing the application and development of virtual reality in stroke rehabilitation.

4.2.3 Activities of Daily Life

The analysis of nine studies did not reveal any notable effects of VR on symptoms related to activities of daily life, which is in agreement with previous studies [12]. VR technology offers stroke patients undergoing physical rehabilitation enjoyable tasks [56], providing instant performance feedback and incorporating playful elements that boost participant engagement, ultimately enhancing physical fitness and exercise capacity [57,58]. Perhaps due to inconsistent intervention times, activities of daily life (ADL) improvements may require a longer intervention time. Additionally, it was found that there is a high degree of heterogeneity, which may be due to the different research subjects and the different cycles of VR interventions implemented. The studies consider activities of daily life as a secondary rather than primary observation indicator, potentially impacting the outcomes. Additionally, variations in VR hardware types led to inconsistent interactivity, and the lack of standardization in the age of participants and stroke duration could introduce biases. This research lacks sufficient evidence of VR's substantial impact on daily activities for stroke patients. Findings are preliminary and may change with future evaluations providing stronger evidence. Therefore, future research should consider specific interventions like immersive VR for analyzing similar measures, while

taking into full account the rehabilitation needs and individual differences of patients, and optimizing the design and implementation of VR-based rehabilitation systems.

4.3 Implications

Prior studies have mostly addressed limb function disorders in stroke patients [59,60] and VR is widely used to improve mobility, balance, or walking speed [61,62]. Our review distinguishes itself by concentrating on stroke patients and incorporating a broader array of comprehensive and experimental studies. A systematic review has been conducted on the impact of VR on psychological distress in stroke patients [63], but its coverage is restricted as it only encompasses English-language publications from 2015 to 2021. Kiper *et al.*'s review [42] involved VR training for stroke patients but primarily examined depression as the sole outcome. Other systematic reviews have explored VR effectiveness in various patient populations [64,65], whereas our review focuses specifically on anxiety and depression in stroke patients.

Psychological distress often arises following a stroke [13]. VR technology offers multi-sensory engagement and interactivity, which can foster thought resonance and promote psychological immersion. Previous research has shown that virtual reality can be effective in boosting an individual's mental health. Research has indicated that virtual reality can be beneficial in alleviating symptoms of prevalent psychological problems like depression and anxiety, while also enhancing overall mental health [26,64]. The results of this review will help to shape future studies by emphasizing the importance of the intensity, duration, and type of VR interventions for individuals who have had a stroke. Given that existing evidence lacks detailed information about the contents and components of these interventions, future RCTs should utilize the Template for Intervention Description and Replication (TIDieR) checklist to provide a thorough description of the interventions [66], and the Consolidated Standards of Reporting Trials (CONSORT) checklist to enhance the quality of reported RCTs [67]. Moreover, individuals who have survived a stroke frequently face psychological issues stemming from the impact of the stroke on brain function and the stress that comes with significant life changes following the event. Virtual reality interventions have many benefits for individuals, including alleviating adverse psychological depression disorders, which can promote an individual's mental health [68]. Therefore, it is crucial for future research to assess the effectiveness of VR interventions on psychological outcomes for stroke survivors.

5. Limitations

This meta-analysis has certain limitations, including variations in the types of VR interventions, the duration and frequency of these interventions, and the outcome evaluation scales used in the studies. The specific aspects of VR

intervention, including hardware configuration, user experience, type of headphones, level of interactivity, the use of commercial gaming systems versus specialized rehabilitation platforms, and so forth, all contribute to the variability in its effectiveness in stroke rehabilitation. Furthermore, differences in outcome measurement scales, such as variations among different versions of depression scales, diverse evaluation methods, and differing standards of assessment, also significantly impact the accurate assessment of VR intervention's efficacy. Moreover, each study exhibited variations in the VR technology devices utilized and the traditional physical rehabilitation methods employed by the control group. The above differences may be the reason for the significant heterogeneity of research results. Furthermore, there may be potential biases in the selection process, as the inclusion was limited solely to pertinent studies sourced from six databases, potentially overlooking studies from other sources. While the review included a wide range of eligible trials, the overall quality of the data was limited. It cannot be denied that the possibility of incomplete data and biases in these studies, with some lacking mean and/or standard deviation values, leading to their exclusion. Consequently, the evidence presented may have inherent limitations. Furthermore, the search was restricted to publicly available literature in Chinese and English, which may have introduced publication bias by omitting pertinent studies published in other languages. Therefore, readers should be cautious when interpreting the findings of this review.

6. Conclusions

With the rapid development of computing and the advent of the big data era, many new technologies are gradually being applied to the medical industry and VR intervention as a feasible option to assist stroke survivors is being increasingly explored. In summary, this systematic review and meta-analysis indicate that VR-based interventions can effectively alleviate depression in stroke patients, but do not significantly enhance activities of daily life. However, the quality of the original studies included is not high, highlighting the need for more rigorous research to determine the most effective intervention components, utilizing larger sample sizes, longer follow-up periods, and varied study designs. In addition, future research should involve larger studies utilizing tailored VR interventions to further enhance patients' well-being. To support the physical and mental well-being of stroke patients and enhance their daily living skills and psychological health, healthcare providers should consider implementing regular VR interventions. This can not only increase their enthusiasm for actively participating in rehabilitation activities but also promote their overall health.

Abbreviations

VR, virtual reality; RCT, randomized controlled trial.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

Author Contributions

HHL, LZ, and ELC conceived and designed the study. HHL, GL, and LW were responsible for conducting the search, acquiring and interpreting the data, and evaluating quality. QWZ and SHX performed the meta-analysis, generated the figures, and drafted the manuscript. ELC reviewed and revised the manuscript, as well as provided funding for the study. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Appreciating the research librarian for reviewing the search strategies.

Funding

2023 Joint General Project of TCM Basic Research of Yunnan Department of Science and Technology (202101AZ070001-221), Yunnan Province TCM Basic Research Joint Special Project (202201AH070163).

Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.31083/JIN27142>.

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