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## Abstract

**Background:** Stroke inevitably results in a range of disabilities. Both virtual reality (VR) and mirror therapy (MT) have shown efficacy in stroke rehabilitation. In recent years, the combination of these two approaches has emerged as a potential treatment for stroke patients.

**Objective:** This systematic review and meta-analysis aim to assess the efficacy of combination treatment of VR and MT in stroke rehabilitation.

**Methods:** Five electronic databases were systematically searched for relevant articles published up to Jan. 2025. Randomized controlled trials (RCTs) that investigated combination treatment of VR and MT for participants with stroke were included. The risk of bias and the certainty of the evidence were assessed using the Cochrane collaboration’s tool and the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) guideline, respectively.

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# Original Manuscript

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**Trial Registration:** PROSPERO CRD42024572150

**Keywords:** mirror therapy, virtual reality, stroke, upper extremity, hand, systematic review, meta-analysis, rehabilitation

# Introduction

### Background

Stroke is one of the leading cause of disability, significantly impairing an individual's quality of life[1]. It can lead to a range of functional impairments, including motor dysfunction[2], cognitive dysfunction[3] and speech dysfunction[4]. Given the global prevalence and profound impact of stroke[5], there is an urgent need to improve healthcare service and rehabilitation methods.

Mirror therapy (MT) is a rehabilitation method based on the theory of "mirror neurons", which will be activated both when individuals execute a given motor action and when they merely observe others performing the identical action[6]. First demonstrated by Ramachandran in the 1990s, MT is an effective approach for the recovery of phantom limb pain[7] and hemiparesis[8]. Subsequently, MT has become a widely utilized approach in the context of stroke rehabilitation. Several systematic reviews and meta-analyses have demonstrated the efficacy of MT in enhancing upper extremity (UE) and lower extremity (LE) motor function, balance, gait, pain, and activities of daily living (ADL)[9-11]. In addition, MT has been proved to be effective in the recovery of cognitive and speech functions[12, 13]. Consequently, MT can be considered a complementary treatment to conventional therapy for stroke patients.

With advancements in technology, virtual reality (VR) has emerged as a prevalent therapeutic approach in stroke rehabilitation, since its strength in patients' motivation, adaptability and variability based on patient baseline, as well as its potential to reduce medical costs[14]. Similarly to MT, VR therapy has been shown to improve UE gross motor function and independence in daily life[15]. It has also demonstrated benefits for LE motor function, balance, gait, cognition[16] of stroke patients. The mechanisms of VR effects in stroke rehabilitation are related to VR-induced changes in neural plasticity and positive correlations between the neural plasticity changes and functional recovery[17].

Recent research suggests that combining VR and MT may offer additional benefits in stroke rehabilitation. For instance, Okamura et al have demonstrated that this combined therapy can significantly improve UE function following a stroke[18]. Although several reviews have independently confirmed the effectiveness of MT or VR in stroke rehabilitation, fewer have investigated the synergistic effects of their combination. Moreover, many of these reviews have suffered from methodological shortcomings, such as the direct analysis of post-intervention data rather than changes from pre- to post-intervention, which may lead to biased conclusions. In response to these limitations, we undertook this systematic review and meta-analysis.

### Objective

Based on this background, the overall objective of this study was to assess the efficacy of using VR and MT as a rehabilitation therapy for the patients with stroke. We hypothesized that a systematic review and meta-analysis of randomized controlled trials (RCTs) would provide robust and comprehensive evidence for the efficacy of combining VR and MT in stroke rehabilitation.

## Methods

This systematic review adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines[19]. The review protocol has been prospectively registered in the PROSPERO database (ID: CRD42024572150).

### Search Strategy

The literature search was conducted across the scientific databases PubMed, Embase, Web of Science, Cochrane, and Scopus up to Jan. 2025. No language or publication date filters were applied during the search. Keywords and Medical Subject Headings (MeSH) descriptors were utilized, combined using Boolean operators “AND” and “OR”, were employed to structure the search strategy, detailed in Multimedia Appendix 1.

### Inclusion and Exclusion Criteria

The PICOS framework (population, intervention, comparison, outcome, and study design) [20] was employed to delineate the inclusion criteria: (1) patients diagnosed with stroke (population); (2) VR therapy combined with MT (intervention); (3) any other therapy or control group (comparison); (4) stroke-related outcomes, such as motor, cognitive, and speech function (outcome); and (5) randomized controlled trials (RCTs) (study design).

Exclusion criteria for this review included: (1) the presence of comorbidities in patients; (2) they did not report mean and SD values for the changes in outcomes for effect size calculations; (3) the data could not be imputed based on the information available in the publication; (4) the data could not be obtained within 1 month of contacting the corresponding authors; or (5) they were review studies, case reports, or abstracts.

### Study Selection

Two reviewers independently executed the search, adhering to the PRISMA guidelines throughout the entire screening and selection procedure. Discrepancies were resolved through consultation with a third reviewer. The screening and selection process comprised the following stages: (1) removal of duplicate records, (2) screening titles and abstracts for relevance, and (3) a full-text review of the remaining studies to determine their eligibility based on the predetermined inclusion or exclusion criteria.

### Data Extraction

Data extraction was conducted in accordance with the PRISMA guidelines by two independent reviewers. The following data were extracted from each article: author, publication year, sample size, patient characteristics (sex, age, and disease duration), intervention details (type, duration, and frequency), and outcomes related to upper extremity motor function, spasticity, and hand dexterity. Should conflicts arise, a third reviewer was involved to facilitate resolution. In cases where the required data were insufficient, communication with the corresponding author was initiated via email to request additional information.

### Assessment of Risk of Bias and Certainty of Evidence

The risk of bias in the included trials was assessed following the Cochrane Collaboration tool focusing on the following domains: random sequence generation; allocation concealment; blinding of participants and health care providers; blinding of outcome assessors; incomplete outcome data; selective reporting; and other sources of bias, including significant differences between study groups at baseline and different intervention durations between study groups[21]. The Review Manager software (RevMan, version 5.4), developed by The Cochrane Collaboration, was utilized for this review. The software offers a structured description and assessment for each item, with predefined responses that categorize the risk of bias as low (indicated by “yes”), high (indicated by “no”), or unclear (indicating a lack of information or uncertainty regarding potential bias). The assessment was conducted by two independent authors, and any discrepancies were addressed by a third reviewer to mediate conflicts as they arose.

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) guideline was employed by two independent reviewers to assess the certainty of the evidence. The GRADE guideline stands as the preeminent tool for grading evidence certainty in systematic reviews and clinical practice guidelines. It categorizes evidence certainty into four levels: “very low”, “low”, “moderate” or “high”, each determined by specific criteria[22]. Factors that may diminish evidence certainty (such as risk of bias, inconsistency, indirectness, imprecision, and publication bias) as well as those that may enhance it (including large effect, plausible confounding, and dose-response) were evaluated[23]. In the event of discrepancies in the certainty ratings among the reviewers, a third reviewer was sought for consultation.

**Data Analysis**

Statistical analysis and the generation of forest plots for result visualization were performed using RevMan. Relevant statistical measures, including means, standard deviations (SDs), and sample sizes, were extracted and then imported into RevMan. The effect size of intergroup change differences was quantified using the mean difference (MD), with 95% confidence intervals (CIs) reported. For studies reporting medians and interquartile ranges (IQRs), the data were transformed into means and SDs as follows: (1) mean=median and (2) SD=IQR/1.35[24]. The inverse variance method was applied for continuous variables. Heterogeneity among the trials was evaluated through the chi-square test and $I^2$ statistics, with thresholds of 25%, 50%, and 75% defining low, moderate, and high levels of heterogeneity, respectively[25]. A fixed effects model was adopted to estimate the pooled effect size. In cases of substantial heterogeneity ($I^2$>50%), the random effects model was employed. Subgroup analyses were performed to investigate potential associations between outcomes and disease durations. Publication bias was not assessed due to the small number of studies included.

# Results

**Study Selection Process**

The initial literature search yielded 364 articles, of which 136 (37.4%) were duplicates and excluded. From the remaining 228 articles after excluding duplicates, 205 (89.9%) were removed due to irrelevance to the study objectives. After further exclusion of 12 non-RCTs and 1 duplicate study, a total of 10 RCTs were included in the current systematic review[26-35]. Figure 1 presents the selection process and reasons for study exclusion.

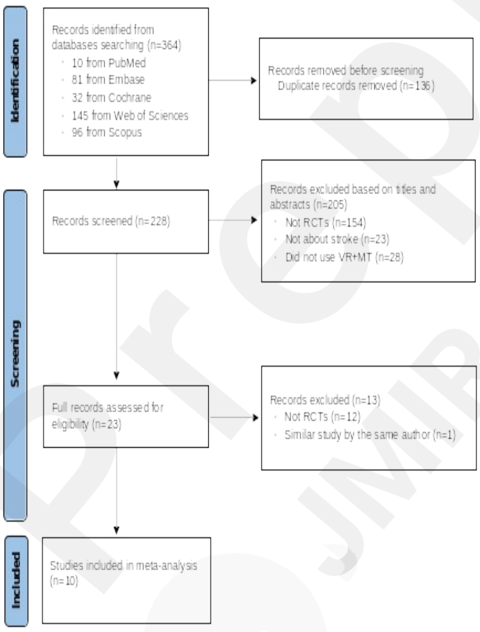


**Figure 1.** Study selection process. RCT: randomized controlled trial, VR: virtual reality, MT: mirror therapy.

**Characteristics of the Included Trials**

The 10 RCTs[26-35] included in the review were all published in English, spanning from 2012[26] to 2024[35],These trials were conducted across Asia (China[29, 30, 33] and Republic of Korea[26, 27, 35]), North America (America[28]) and Europe (Romania[31], The United Kingdom[32], and Poland[34]), involving a total of 293 participants (experimental group: n=129, 44%; control group: n=164, 56%) were involved. Among the included studies, Miclaus et al, 2021[31] reported the highest number of participants (N=59), while Strong et al, 2021[32] had the smallest sample size (N=7). The detailed characteristics of the included trials are presented in Table 1, and the measuring instruments are summarized in Table 2.

**Table 1.** Characteristics of the RCTs included in the systematic review and meta-analysis.

| Study | Number of participants (male and female) | Sample size and mean age (years) | Disease duration | Intervention of EG | Intervention of CG | Duration and frequency of intervention | Outcome | Measuring instrument |
|---|---|---|---|---|---|---|---|---|
| In et al, 2012[26] | 19 (11 and 8) | EG: 11 (63.45±11.78) CG: 8 (64.50±12.69) | > 6 months | VR+MT | sham therapy | 30min/d5d/week4weeks | UE motor function, hand dexterity | FMA-UE (Total), MAS-UE, BBT, JHFT, MFT |
| Choi et al, 2019[27] | 24(14 and 10) | EG: 12 (58.00±15.15) CG: 12 (59.58±11.87) | > 6 months | VR+MT | MT | 30min/d3d/week5weeks | UE motor function, neck discomfort, life satisfaction | MFT, NDS, SF-8 |
| Choi et al, 2019[27] | 24 (16 and 8) | EG: 12 (58.00±15.15) CG: 12 (59.33±13.63) | > 6 months | VR+MT | sham therapy | 30min/d3d/week5weeks | UE motor function, neck discomfort, life satisfaction | MFT, NDS, SF-8 |
| Bullock et al, 2020[28] | 14 (4 and 10) | EG: 7 (not available) CG: 7 (not available) | Not mentioned | VR+MT | sham therapy | 5–20 min/session 8sessions | Degree of disability | OHS |
| Lin et al, 2021[29] | 18(13 and 5) | EG: 9 (49.7±13.4) CG: 9 (58.8±9.6) | > 6 months | VR+MT | MT | 50min/d2d/week9weeks | UE motor function | FMA-UE (Total, Shoulder/Elbow/Forearm, Wrist, Hand, Coordination) |
| Mekbib et al, 2021[30] | 23(17 and 6) | EG: 12 (52.17 ± 13.26) CG: 11 (61.00±7.69) | < 3 months | VR+MT | OT | 120min/d 4d/week2weeks | UE motor function | FMA-UE (Total), BI, rs-fMRI |
| Miclaus et al, | 59(15 and 44) | EG: 31 (59.03±10.12) | > 6 months | VR+MT | standard physiothe | 70min/d10days | Muscle strength, | ROM, MMT, |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 2021[31] | | CG: 28 (60.67±8.17) | | | rapy | | range of motion, stroke severity, ADL, degree of spasticity, LE motor function, balance, gait | FMA-LE, MRS, FIM, MAS-LE, TUGT, FRT |
| Strong et al, 2021[32] | 7(3 and 4) | EG: 4 (46.0±not available) CG: 3 (53.7±not available) | > 3 months | VR+MT | 9HPT training | 45min/d4d/week4weeks | Finger dexterity | 9HPT |
| Hsu et al, 2022[33] | 35(15 and 20) | EG: 18 (52.9 ± 11.8) CG: 17 (56.7 ± 11.5) | > 6 months | VR+MT | MT | 50min/d2d/week9weeks | UE motor function, hand dexterity, hand touch-pressure threshold, UE spasticity | FMA-UE (Total, Shoulder/Elbow/Forearm, Wrist, Hand, Coordination), MAL, BBT, SWM, MAS-(Wrist, Hand) |
| Hsu et al, 2022[33] | 35(13 and 22) | EG: 18 (52.9 ± 11.8) CG: 17 (56.9 ± 13.0) | > 6 months | VR+MT | OT | 50min/d2d/week9weeks | UE motor function, hand dexterity, hand touch-pressure threshold, UE spasticity | FMA-UE (Total, Shoulder/Elbow/Forearm, Wrist, Hand, Coordination), MAL, BBT, SWM, MAS-(Wrist, Hand) |
| Sip et al, 2023[34] | 20(not available) | EG: 10 (54.9 ± 3.98) CG: 10 (59.2 ± 4.34) | < 12 months | VR+MT | MT | 30min/d18days | UE motor function, ADL, pain | FMA-UE (Total), SF-36, UE pain |
| Jo et al, 2024[35] | 30(15 and 15) | EG: 15 (51.73±13.63) CG: 15 (51±12.97) | < 6 months | VR+MT | MT | 30min/session 3sessions/week 4weeks | UE motor function, hand dexterity | FMA-UE (Total), MFT, BBT |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Jo et al, 2024[35] | 30(15 and 15) | EG: 15 (51.73±13.63) CG: 15 (47.13±13.91) | < 6 months | VR+MT | CPT | 30min/ session 3sessions/week 4weeks | UE motor function, hand dexterity | FMA-UE (Total), MFT, BBT |

Values are presented as number only or mean±SD. EG: experimental group, CG: control group, VR: Virtual Reality, MT: mirror therapy, UE: upper extremity, FMA: Fugl-Meyer assessment, MAS: modified Ashworth scale, BBT: box and block test, JHFT: Jebsen Hand Function Test, MFT: manual function test, NDS: neck discomfort score, SF-8: Short-Form 8, OHS: Oxford handicap scale, OT: occupational therapy, ADL: activities of daily living, ROM: range of motion, MMT: manual muscle testing, LE: lower extremity; MRS: modified rankin scale, FIM: functional independence measure, TUGT: timed Up and Go test, FRT: functional reach test, 9HPT: nine-hole peg test, MAL: motor activity log, SWM: Semmes-Weinstein monofilament test, SF-36: 36-Item Short Form Survey, CPT: conventional physical therapy.

**Table 2.** Summary of measuring instrument.

| Measuring instrument | Study |
|---|---|
| FMA-UE (Total) | In et al, 2012[26] Lin et al, 2021[29] Mekbib et al, 2021[30] Hsu et al, 2022[33] Sip et al, 2023[34] Jo et al, 2024[35] |
| FMA-UE (Shoulder/Elbow/Forearm, Wrist, Hand, Coordination) | Lin et al, 2021[29] Hsu et al, 2022[33] |
| BBT | In et al, 2012[26] Hsu et al, 2022[33] Jo et al, 2024[35] |
| MFT | In et al, 2012[26] Choi et al, 2019[27] Jo et al, 2024[35] |

UE: upper extremity, FMA: Fugl-Meyer assessment, BBT: box and block test, MFT: manual function test.

**Risk of Bias and Certainty of Evidence**

Figures 2 and 3 collectively summarize the risk of bias assessment for the included RCTs, providing both global and individual evaluations for each study. Individual assessments (as depicted in Figure 2) revealed that the study by Hsu et al, 2022[33] exhibited the lowest risk of bias, while the study by Lin et al, 2021[29] presented the highest risk of bias. The greatest risk was noted in the "Blinding of participants and personnel" category, which falls under performance bias.

Utilizing the GRADE guideline, moderate-quality evidence was found for improvements in upper extremity motor function (FMA-UE and MFT) and hand dexterity (BBT). These findings suggest that the true effect is probably similar to the estimated effect. Furthermore, the evidence quality for the effects on the FMA-UE (Shoulder/Elbow/Forearm, Wrist, Hand, and Coordination) was deemed very low, suggesting that the true effect could vary significantly from the estimated values. Detailed GRADE assessments are presented in Multimedia Appendix 2. Agreement between the authors was 100% at each stage.

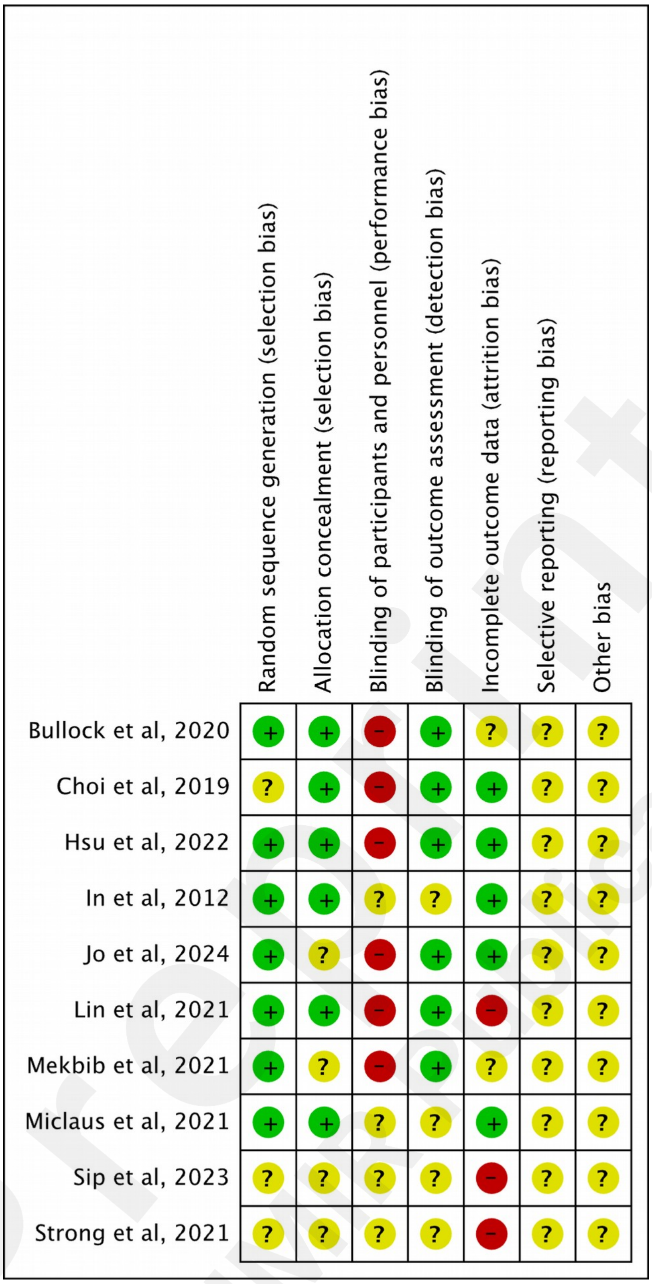


**Figure 2.** Risk of bias of the studies included in the systematic review.

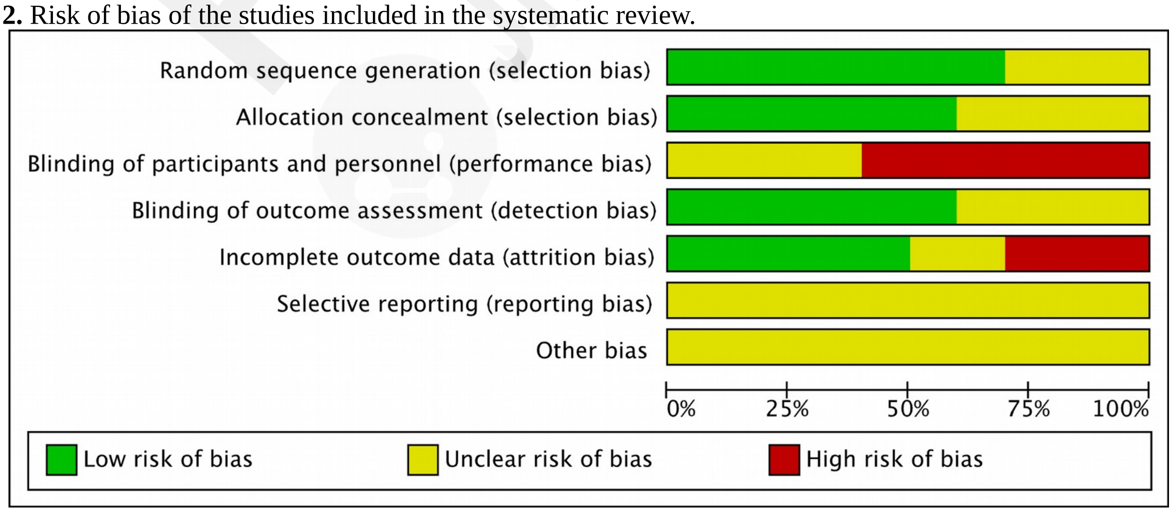


**Figure 3.** Overall risk of bias, with each category presented as percentages.

**Synthesis of Results and Meta-Analysis**

Of the 10 RCTs, 6 (60%) [26, 27, 29, 30, 33, 35] with 193 participants (VR+MT: 77, other treatment: 116) were included in the meta-analysis. Sip et al.'s study was not included due to the incorrect result of the FMA-UE (Total)[34]. A low degree of heterogeneity (I2□50%) was observed across outcomes. The main findings of the meta-analysis are presented in Table 3.

**Effects on Upper Extremity Motor Function (FMA-UE, MFT)**

A total of 5 RCTs (50%)[26, 29, 30, 33, 35] with 157 participants (VR+MT: 65, other treatment: 92) were included in the FMA-UE (Total) analysis. Two RCTs (20%)[29, 33] with 70 participants (VR+MT: 27, other treatment: 43) assessed FMA-UE (Shoulder/Elbow/Forearm, Wrist, Hand, Coordination) outcome, and 3 RCTs (30%)[26, 27, 35] with 100 participants (VR+MT: 38, other treatment: 62) assessed the MFT outcome.

Compared with other treatment, the use of combined therapy was associated with significant improvements in FMA-UE (MD 3.49, 95% CI 1.43 to 5.55; P=0.0009) and MFT (MD 2.64, 95% CI 1.78 to 3.49; P<0.00001).

However, no significant improvements were observed in FMA-UE (Shoulder/Elbow/Forearm; MD 0.22, 95% CI -3.39 to 3.84; P=0.90; Wrist; MD 0.78, 95% CI -0.90 to 2.46; P=0.36; Hand; MD 0.81, 95% CI -1.72 to 3.33; P=0.53; Coordination; MD 0.36, 95% CI -0.09 to 0.80; P=0.12). The forest plots are shown in Figure 4-6.

**Effects on Hand Dexterity (BBT)**

Three RCTs (30%)[26, 33, 35] with 116 participants (VR+MT: 44, other treatment: 72) assessed hand dexterity using the BBT. Compared with other treatment, the use of combined therapy was associated with significant improvements in hand dexterity (BBT; MD 1.02, 95% CI 0.16 to 1.88; P=0.02). The forest plot is shown in Figure 7.

**Subgroup Analyses**

Regarding the FMA-UE (Total) outcome, significant improvements were observed in Disease duration>6 months subgroups (MD 6.29, 95% CI 2.87 to 9.71; P=0.0003). However, no significant improvements were observed in Disease duration<6 months subgroups (MD 1.89, 95% CI -0.69 to 4.48; P=0.15). The forest plot is shown in Figure 4.

Regarding the MFT outcome, significant improvements were observed in Disease duration>6 months subgroups (MD 2.80, 95% CI 1.90 to 3.71; P<0.00001). However, no significant improvements were observed in Disease duration<6 months subgroups (MD 1.26, 95% CI -1.34 to 3.86; P=0.34). The forest plot is shown in Figure 6.

Regarding the BBT outcome, significant improvements were observed in Disease duration<6 months subgroups (MD 1.03, 95% CI 0.06 to 2.00; P=0.04). However, no significant improvements were observed in Disease duration>6 months subgroups (MD 0.98, 95% CI -0.85 to 2.82; P=0.29). The forest plot is shown in Figure 7. The findings of subgroup analyses are presented in Table 4.

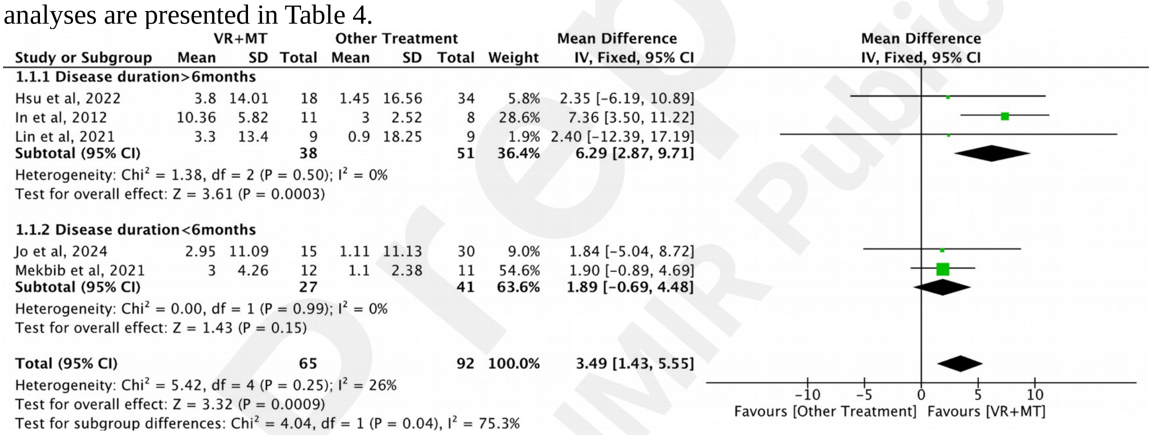


**Figure 4.** Forest plot for FMA-UE (Total). IV: inverse variance, VR: virtual reality, MT: mirror therapy.

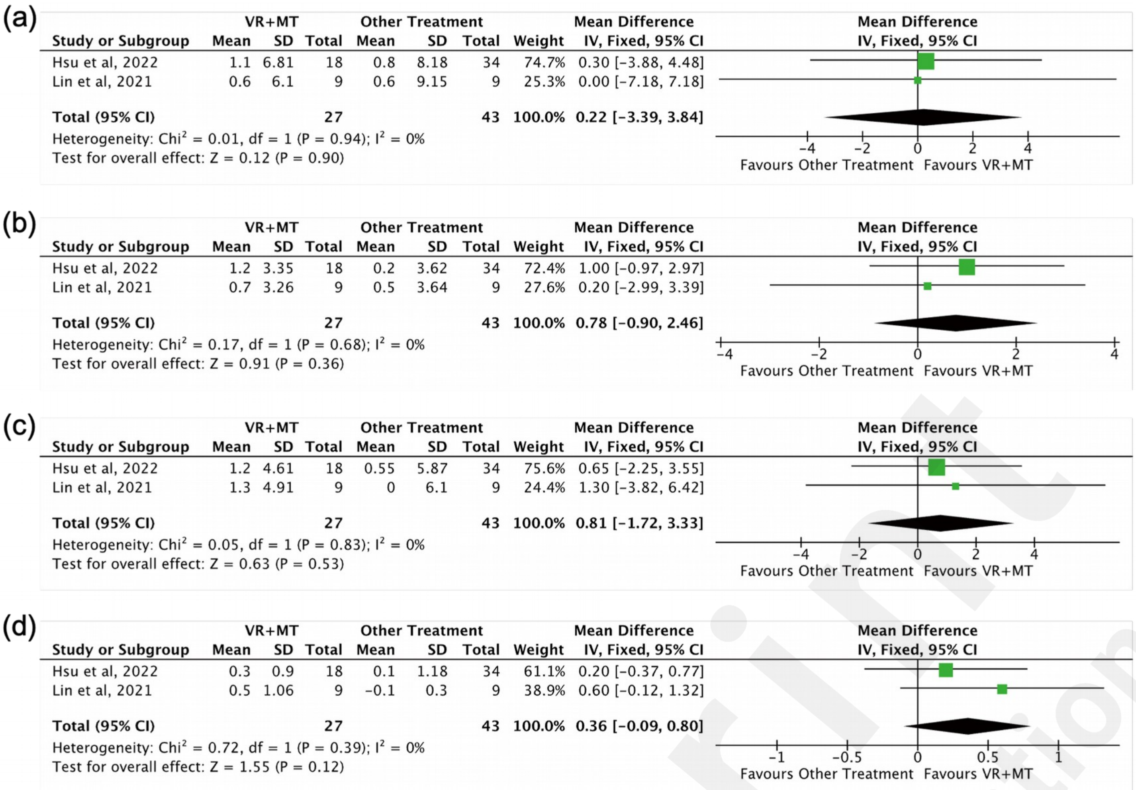


**Figure 5.** Forest plot for FMA-UE. a: FMA-UE (Shoulder/Elbow/Forearm), b: FMA-UE (Wrist), c: FMA-UE (Hand), d: FMA-UE (Coordination), IV: inverse variance, VR: virtual reality, MT: mirror therapy.

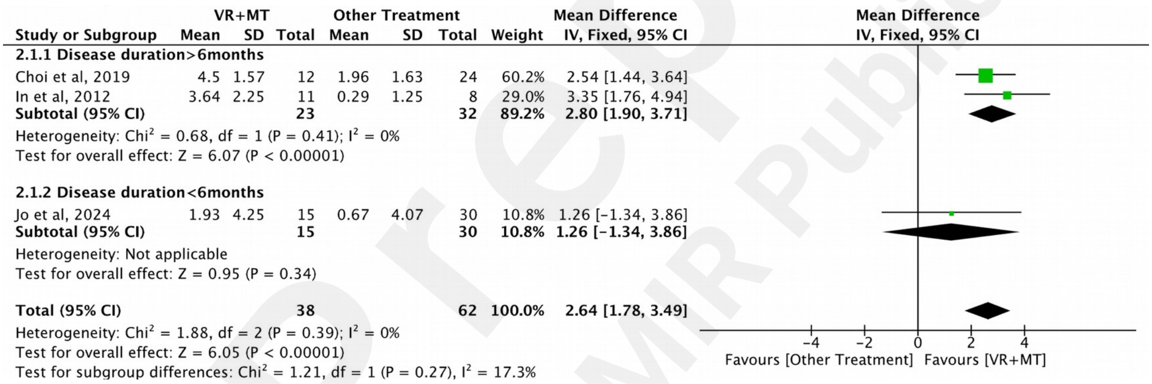


**Figure 6.** Forest plot for MFT. IV: inverse variance, VR: virtual reality, MT: mirror therapy.

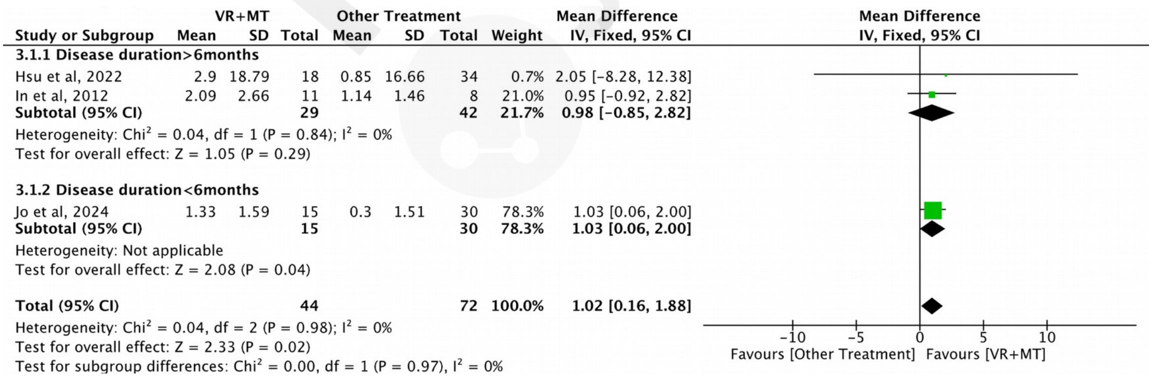


**Figure 7.** Forest plot for BBT. IV: inverse variance, VR: virtual reality, MT: mirror therapy.

**Table 3.** Main meta-analysis findings.

| Outcome | Number of included studies | Heterogeneity test | Statistical model | **MD (95% CI)** | Overall effect |
|---|---|---|---|---|---|

| | | | | | z score | P value |
|---|---|---|---|---|---|---|
| FMA-UE (Total) | 5 | Low | Fixed effects | 3.49(1.43 to 5.55) | 3.32 | 0.0009 |
| FMA-UE (Shoulder/ Elbow/Forearm) | 2 | Low | Fixed effects | 0.22(-3.39 to 3.84) | 0.12 | 0.90 |
| FMA-UE (Wrist) | 2 | Low | Fixed effects | 0.78(-0.90 to 2.46) | 0.91 | 0.36 |
| FMA-UE (Hand) | 2 | Low | Fixed effects | 0.81(-1.72 to 3.33) | 0.63 | 0.53 |
| FMA-UE (Coordination) | 2 | Low | Fixed effects | 0.36(-0.09 to 0.80) | 1.55 | 0.12 |
| MFT | 3 | Low | Fixed effects | 2.64(1.78 to 3.49) | 6.05 | <0.00001 |
| BBT | 3 | Low | Fixed effects | 1.02(0.16 to 1.88) | 2.33 | 0.02 |

MD: mean difference, UE: upper extremity, FMA: Fugl-Meyer assessment, MFT: manual function test, MAS: modified Ashworth scale, BBT: box and block test.

**Table 4.** Findings of subgroup analyses according to different disease duration.

| Outcome | Number of included studies | Heterogeneity test | Statistical model | **MD (95% CI)** | Overall effect | |
|---|---|---|---|---|---|---|
| | | | | | z score | P value |
| **FMA-UE (Total)** | | | | | | |
| >6months | 3 | Low | Fixed effects | 6.29(2.87 to 9.71) | 3.61 | 0.0003 |
| <6months | 2 | Low | Fixed effects | 1.89 (-0.69 to 4.48) | 1.43 | 0.15 |
| **MFT** | | | | | | |
| >6months | 2 | Low | Fixed effects | 2.80 (1.90 to 3.71) | 6.07 | <0.00001 |
| <6months | 1 | Not applicable | Fixed effects | 1.26 (-1.34 to 3.86) | 0.95 | 0.34 |
| **BBT** | | | | | | |
| >6months | 2 | Low | Fixed effects | 0.98 (-0.85 to 2.82) | 1.05 | 0.29 |
| <6months | 1 | Not applicable | Fixed effects | 1.03 (0.06 to 2.00) | 2.08 | 0.04 |

MD: mean difference, UE: upper extremity, FMA: Fugl-Meyer assessment, MFT: manual function test, BBT: box and block test.

# Discussion

### Principal Findings

The results of the 10 RCTs included in this systematic review indicate that combination treatment of VR and MT in patients with stroke is more effective than other therapy. Various VR technologies were employed, including Leap motion technology [27, 29, 30, 33], etee (Tg0 company)[32], MIRA (a software for virtual reality therapy) with a Kinect sensor (Microsoft Corporation, Redmond, WA, USA)[31] and Virtual Mirror Hand 1.0[34]. Most studies[26-30, 32-35] integrated VR with MT into a single intervention system, while only one study[31] applied them separately.

Among the studies reviewed, the study by Hsu et al[33] exhibited the lowest risk of bias, while the study by Lin et al[29] had the highest risk of bias. Performance bias, particularly in participant and personnel blinding, was the most common issue. This highlights a challenge in rehabilitation research where double-blinding is not feasible due to the nature of interventions [36]. In this sense, some studies suggest that double blinding may not be necessary for trials in real-life settings[37].

Moderate-quality evidence was identified for UE motor function (measured by FMA-UE and MFT) and hand dexterity (measured by BBT). In the subsequent sections, we explored potential explanations for these findings, drawing upon the moderate-quality evidence at hand. Regarding findings based on low or very low quality of evidence, further research is necessary to support any broad conclusions.

**Effects on Upper Extremity Motor Function (FMA-UE, MFT)**

Our study revealed significant improvements in UE motor function, as measured by both the FMA-UE and the MFT. The FMA is a clinically validated, feasible, and effective method for evaluating motor function within the stroke population[38]. The MFT comprises four items each for the shoulder and hand, thereby reflecting UE function post-stroke[39], and there is evidence of strong correlations between MFT and FMA-UE[40, 41]. One plausible explanation for these findings is that both VR and MT facilitate motor learning. Firstly, virtual and mirror environments provide visual feedback, which aids in motor skill acquisition and informs individuals of their successes or failures while performing therapeutic tasks[42, 43]. Furthermore, VR can augment perceived movement and body position, enabling individuals to execute minimal movements while perceiving them as more substantial[44]. This capability can enhance individuals' confidence and initiative. Additionally, while MT has been validated as a beneficial rehabilitation strategy through mechanisms related to brain plasticity and mirror neurons[45], it confines patients to a limited exercise area. Conversely, VR offers a significantly larger space[46], allowing us to conceptualize their combined use as a more comprehensive and effective "mirror" for rehabilitation.

**Effects on Hand Dexterity (BBT)**

Our study findings suggest that combined therapy can lead to enhancements in hand dexterity (measured by BBT). The BBT is a standardized assessment tool that measures unilateral gross manual dexterity and is extensively utilized in clinical settings across diverse populations, including the elderly and individuals with neurological disorders[47]. Beyond the explanations previously provided, additional factors contribute to this outcome. In VR-supported MT, the interaction with virtual objects typically necessitates the application of gross manual motor skills to manipulate and move these objects, thereby engaging individuals in dexterity exercises.

**Subgroup Analysis of the Effects of Combined Therapy**

Our research revealed significant improvements in UE motor function, as measured by the FMA-UE and MFT, among individuals with disease duration of over six months, rather than in those with duration of less than six months. This suggests that patients in later stages of recovery may benefit more from combined therapy, potentially because they can engage with a larger motor area. In contrast, patients with less than six months of disease duration may not fully exploit the expanded motor area provided by combined therapy.

Interestingly, the opposite trend was observed in hand dexterity, where improvements were more significant in those with disease duration less than six months rather than those with disease duration more than six months. This discrepancy might be attributed to the rapid recovery at the initial recovery stage (disease duration of less than six months) followed by a slower recovery in the aftermath stage (disease duration of more than six months).

**Limitations**

Several limitations should be acknowledged. The small sample sizes of individual studies may limit the generalizability of the findings. Moreover, long-term effects were not assessed, and the lack of blinded assessments might introduce bias. Furthermore, dose-response relationships were not explored, leaving uncertainty about whether higher doses of combined therapy could lead to better outcomes. The International Classification of Functioning, Disability, and Health (ICF) framework was not integrated, which could provide a more comprehensive understanding of patient outcomes. Lastly, although the search for RCTs did not specifically restrict the type of outcomes, the majority of studies meeting the search criteria focused on upper extremity motor functions. Consequently, there was insufficient investigation into the combined therapy's impact on other domains, such as LE motor function, speech, and cognitive abilities. These limitations should be considered when interpreting the results of this systematic review and meta-analysis.

**Conclusions**

This systematic review and meta-analysis offer moderate evidence supporting the efficacy of combining virtual reality and mirror therapy in stroke patients, particularly in improving upper extremity motor function and hand dexterity. Future research should aim to explore a broader range of outcomes related to this combined treatment. Moreover, associating therapy dosage with observed effects would provide valuable insights.

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**Conflicts of Interest**

None.

**Multimedia Appendix 1**

Details of the search.

**Multimedia Appendix 2**

Results of Grading of Recommendations Assessment, Development, and Evaluation (GRADE).

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# Supplementary Files

# Multimedia Appendixes

Details of the search.
URL: http://asset.jmir.pub/assets/8ae64b5e7ac4f7525a8342ee045ffa6d.docx

Assessment of Certainty of Evidence.
URL: http://asset.jmir.pub/assets/d267cc10c391208016763325 39f375c2.docx