Virtual reality for stroke rehabilitation (Review)

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[Intervention Review]

Virtual reality for stroke rehabilitation

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Editorial group: Cochrane Stroke Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 2, 2015.
Review content assessed as up-to-date: 29 November 2013.

Citation: Laver KE, George S, Thomas S, Deutsch JE, Crotty M. Virtual reality for stroke rehabilitation. *Cochrane Database of Systematic Reviews* 2015, Issue 2. Art. No.: CD008349. DOI: 10.1002/14651858.CD008349.pub3.

ABSTRACT

Background

Virtual reality and interactive video gaming have emerged as recent treatment approaches in stroke rehabilitation. In particular, commercial gaming consoles have been rapidly adopted in clinical settings. This is an update of a Cochrane Review published in 2011.

Objectives

Primary objective: To determine the efficacy of virtual reality compared with an alternative intervention or no intervention on upper limb function and activity.

Secondary objective: To determine the efficacy of virtual reality compared with an alternative intervention or no intervention on: gait and balance activity, global motor function, cognitive function, activity limitation, participation restriction and quality of life, voxels or regions of interest identified via imaging, and adverse events. Additionally, we aimed to comment on the feasibility of virtual reality for use with stroke patients by reporting on patient eligibility criteria and recruitment.

Search methods

We searched the Cochrane Stroke Group Trials Register (October 2013), the Cochrane Central Register of Controlled Trials (*The Cochrane Library* 2013, Issue 11), MEDLINE (1950 to November 2013), EMBASE (1980 to November 2013) and seven additional databases. We also searched trials registries and reference lists.

Selection criteria

Randomised and quasi-randomised trials of virtual reality ("an advanced form of human-computer interface that allows the user to 'interact' with and become 'immersed' in a computer-generated environment in a naturalistic fashion") in adults after stroke. The primary outcome of interest was upper limb function and activity. Secondary outcomes included gait and balance function and activity, and global motor function.

Data collection and analysis

Two review authors independently selected trials based on pre-defined inclusion criteria, extracted data and assessed risk of bias. A third review author moderated disagreements when required. The authors contacted investigators to obtain missing information.

Main results

We included 37 trials that involved 1019 participants. Study sample sizes were generally small and interventions varied. The risk of bias present in many studies was unclear due to poor reporting. Thus, while there are a large number of randomised controlled trials, the evidence remains 'low' or 'very low' quality when rated using the GRADE system. Control groups received no intervention or therapy based on a standard care approach. Intervention approaches in the included studies were predominantly designed to improve motor function rather than cognitive function or activity performance. The majority of participants were relatively young and more than one year post stroke. Primary outcome: results were statistically significant for upper limb function (standardised mean difference (SMD) 0.28, 95% confidence intervals (CI) 0.08 to 0.49 based on 12 studies with 397 participants). Secondary outcomes: there were no statistically significant effects for grip strength, gait speed or global motor function. Results were statistically significant for the activities of daily living (ADL) outcome (SMD 0.43, 95% CI 0.18 to 0.69 based on eight studies with 253 participants); however, we were unable to pool results for cognitive function, participation restriction, quality of life or imaging studies. There were few adverse events reported across studies and those reported were relatively mild. Studies that reported on eligibility rates showed that only 26% of participants screened were recruited.

Authors' conclusions

We found evidence that the use of virtual reality and interactive video gaming may be beneficial in improving upper limb function and ADL function when used as an adjunct to usual care (to increase overall therapy time) or when compared with the same dose of conventional therapy. There was insufficient evidence to reach conclusions about the effect of virtual reality and interactive video gaming on grip strength, gait speed or global motor function. It is unclear at present which characteristics of virtual reality are most important and it is unknown whether effects are sustained in the longer term.

PLAIN LANGUAGE SUMMARY

Virtual reality for stroke rehabilitation

Review question: We wanted to compare the effects of virtual reality on arm function (and other outcomes such as walking speed and independence in managing daily activities) after stroke versus an alternative intervention or no intervention.

Background: Many people after having a stroke have difficulty moving, thinking and sensing. This often results in problems with everyday activities such as writing, walking and driving. Virtual reality and interactive video gaming are new types of therapy being provided to people after having a stroke. The therapy involves using computer-based programs that are designed to simulate real life objects and events. Virtual reality and interactive video gaming may have some advantages over traditional therapy approaches as they can give people an opportunity to practise everyday activities that are not or cannot be practised within the hospital environment. Furthermore, there are several features of virtual reality that might mean that patients spend more time in therapy: for example, the activity might be more motivating.

Study characteristics: We identified 37 studies involving 1019 people after stroke. A wide range of virtual reality programs were used and most of the programs required the person using the program to be relatively active (as opposed to smaller movements associated with simply moving a joystick). The evidence is current to November 2013.

Key results: Twelve trials tested whether the use of virtual reality compared with conventional therapy resulted in improved ability to use one's arm and found that the use of virtual reality resulted in better arm function. Four trials tested whether the use of virtual reality compared with conventional therapy resulted in improved walking speed. There was no evidence that virtual reality was more effective in this case. Eight trials found that there was some evidence that virtual reality resulted in a slightly better ability to manage everyday activities such as showering and dressing. However, these positive effects were found soon after the end of the treatment and it is not clear whether the effects are long lasting. Results should be interpreted with caution as the studies involved small numbers of participants. Very few people using virtual reality reported pain, headaches or dizziness and no serious adverse events were reported.

Quality of the evidence: We classified the quality of the evidence as low for arm function. The quality of the evidence was very low for walking ability, global motor function and independence in performing daily activities. The quality of the evidence for each outcome was limited due to small numbers of study participants, inconsistent results across studies and poor reporting of study details.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Virtual reality for stroke rehabilitation

Patient or population: patients receiving stroke rehabilitation
Settings: hospital, clinic or home
Intervention: virtual reality

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Virtual reality				
Upper limb function	Same dose of conventional therapy	The mean upper limb function in the intervention groups was **0.29 standard deviations higher** (0.09 to 0.49 higher)		397 (12 studies)	⊕⊕◯◯ **low**[1,2,3]	SMD 0.29 (0.09 to 0.49)
Quality of life - not measured						None of the studies reported on outcomes for quality of life
Gait speed	Same dose of conventional therapy	The mean gait speed in the intervention groups was **0.07 metres per second faster** (0.09 lower to 0.23 higher)		58 (3 studies)	⊕◯◯◯ **very low**[1,2,3,4]	MD 0.07 (-0.09 to 0.23)

ADL outcome	Same dose of conventional therapy	The mean ADL outcome in the intervention groups was **0.43 standard deviations higher** (0.18 to 0.69 higher)	253 (8 studies)	⊕○○○ **very low**[1,2,4]	SMD 0.43 (0.18 to 0.69)
Global motor function [6]	Same dose of conventional therapy	The mean global motor function in the intervention groups was **0.14 standard deviations higher** (0.63 lower to 0.9 higher)	27 (2 studies)	⊕○○○ **very low**[3,4,5]	SMD 0.14 (-0.63 to 0.9)

ADL: activities of daily living; **CI:** confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardised mean difference

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Risk of bias was unclear in a number of studies.
[2]Downgraded by 1 due to inconsistency in findings across studies.
[3]Surrogate outcome.
[4]Small total population size (<400).
[5]Serious risk of bias in most studies.
[6]The intervention group in this comparison received additional therapy therefore the dose was not equal between groups.

BACKGROUND

Description of the condition

Stroke is one of the leading causes of death and disability and has been described as a worldwide epidemic (Feigin 2014; Go 2014). The effects of a stroke may include sensory, motor and cognitive impairment as well as a reduced ability to perform self care and participate in social and community activities (Miller 2010). While most recovery is thought to be made in the first few weeks after stroke, patients may make improvements on functional tasks many months after having a stroke (Teasell 2014). Many stroke survivors report long-term disability and reduced quality of life (Patel 2006; Sturm 2004)

Description of the intervention

Repetitive task training has been shown to be effective in some aspects of rehabilitation, such as improving walking distance and speed and improving upper limb function (French 2007; Veerbeek 2014). Virtual reality is a relatively recent approach that may enable simulated practice of functional tasks at a higher dosage than traditional therapies (Demain 2013; Fung 2012; Kwakkel 2004; Merians 2002; National Stroke Foundation 2012). Virtual reality has been defined as the "use of interactive simulations created with computer hardware and software to present users with opportunities to engage in environments that appear and feel similar to real-world objects and events" (Weiss 2006).

Virtual reality has previously been used in a variety of vocational training settings, such as flight simulation training for pilots (Lintern 1990) and procedural training for surgeons (Larsen 2009). Within health care, the intervention has been used to treat phobias, post-traumatic stress disorder and body image disorders (Schultheis 2001). Although its research in rehabilitation is becoming more prevalent as technology becomes more accessible and affordable, the use of virtual reality is not yet commonplace in clinical rehabilitation settings (Burridge 2010). However, gaming consoles are ubiquitous and so researchers and clinicians are turning to low-cost commercial gaming systems as an alternative way of delivering virtual reality (Deutsch 2008; Lange 2012; Rand 2008). These systems, which were originally designed for recreation, are being adapted by clinicians for therapeutic purposes. In addition, interactive video games are specifically being designed for rehabilitation (Lange 2010; Lange 2012).

In virtual rehabilitation, virtual environments and objects provide the user with visual feedback, which may be presented though a head-mounted device, projection system or flat screen. Feedback may also be provided through the senses, for example, hearing, touch, movement, balance and smell (Weiss 2006). The user interacts with the environment by a variety of mechanisms. These may be simple devices, such as a mouse or joystick, or more complex systems using cameras, sensors or haptic (touch) feedback devices (Weiss 2006). Thus, depending on the intervention, the user's level of physical activity may range from relatively inactive (for example, sitting at a computer using a joystick), to highly active (for example, challenging full-body movements). Virtual reality relies on computer hardware and software that mediates the interaction between the user and the virtual environment (Greenleaf 1994).

Key concepts related to virtual reality are immersion and presence. Immersion refers to the extent to which the user perceives that they are in the virtual environment rather than the real world and is related to the design of the software and hardware (Weiss 2006). Virtual environments can range in their degree of immersion of the user. Systems that include projection onto a concave surface, head-mounted display or video capture in which the user is represented within the virtual environment are generally described as immersive, whereas a single screen projection or desktop display are considered low immersion.

Presence is the subjective experience of the user and is dependent on the characteristics of the virtual reality system, the virtual task and the characteristics of the user. People are considered present when they report the feeling of being in the virtual world (Schuemie 2001).

How the intervention might work

Virtual reality may be advantageous as it offers several features, such as goal-oriented tasks and repetition, shown to be important in neurological rehabilitation (Langhorne 2011; Veerbeek 2014). Animal research has shown that training in enriched environments results in better problem solving and performance of functional tasks than training in basic environments (Risedal 2002). Virtual reality may have the potential to provide an enriched environment in which people with stroke can problem solve and master new skills. Virtual tasks have been described as more interesting and enjoyable by both children and adults, thereby encouraging higher numbers of repetitions (Lewis 2012).

Evidence of neuroplasticity as a result of training in virtual reality is modest; however, neuroimaging findings are guiding the development of virtual reality. Two investigators have shown that functional improvements after virtual reality training were paralleled with a lateralisation of neural activation from the contralesional sensorimotor activation prior to training, to an ipsilesional representation after training (Jang 2005; You 2005). A perspective on virtual reality compared with regular exercise was provided by Kim and colleagues (Kim 2014). They reported that for people post stroke virtual reality wrist exercises with transcranial direct current stimulation facilitated a greater post-exercise cortico-spinal excitability than virtual reality or active exercises alone. Tunik and colleagues have shown that when individuals post stroke were presented with discordant feedback, they activated the primary motor region (M1) to a greater extent than when feedback was not discordant (Tunik 2013). Notably, when discordant feedback cor-

responded to the affected and moving hand, the contralateral M1 region was recruited (Bagce 2012; Tunik 2013). Conversely, by having participants move the unaffected hand with virtual mirror feedback, the ipsilateral (affected) M1 region was recruited (despite the affected hand remaining static) (Saleh 2014). Their findings suggest that tailoring manipulation of the visual feedback in virtual reality to the needs of the patient may serve as a tool for rehabilitation.

Grading of tasks and immediate feedback have been shown to optimise motor learning (Sveistrup 2004). Virtual reality offers clinicians the ability to control and grade tasks to challenge the user, and programs often incorporate multimodal feedback provided in real time. Furthermore, clinicians are able to trial tasks that are unsafe to practise in the real world, such as crossing the street. Many programs are designed to be used without supervision, also meaning that increased dosage of therapy can be provided without increased staffing levels.

Why it is important to do this review

As technology becomes more accessible and affordable, virtual reality is likely to become even more widely used in clinical rehabilitation settings (Bohil 2011; Burridge 2010). It is important to evaluate the efficacy of virtual reality in order to guide future design and use. Furthermore, therapeutic interventions that increase the dose of task-specific training without increasing staffing will be sought after as economic pressure and an ageing population impact on health care.

There are now a number of systematic reviews examining the efficacy of virtual reality for stroke rehabilitation (Crosbie 2007; Lohse 2014; Moreira 2013; Saposnik 2011) and more specifically commercial gaming devices for upper limb stroke rehabilitation (Thomson 2014). Our initial review published in 2011 identified 19 studies and a number of ongoing studies. The area is rapidly expanding and therefore an update of our review was warranted.

OBJECTIVES

Primary objective

To determine the efficacy of virtual reality compared with an alternative intervention or no intervention on:

1. upper limb function and activity;

Secondary objective

To determine the efficacy of virtual reality compared with an alternative intervention or no intervention on:

1. gait and balance activity;
2. global motor function;
3. cognitive function;
4. activity limitation;
5. participation restriction and quality of life;
6. voxels or regions of interest identified via imaging; and
7. adverse events.

Additionally, we aimed to comment on the feasibility of virtual reality for use with stroke patients by reporting on patient eligibility criteria and recruitment.

METHODS

Criteria for considering studies for this review

Types of studies

We planned to include randomised controlled trials (RCTs) and quasi-randomised (e.g. allocation by birth date) controlled trials (QRCTs). We included one QRCT and the remaining studies were RCTs. Where the QRCT was included in a meta-analysis we carried out a sensitivity analysis restricting analysis to truly randomised studies. We looked for studies that compared virtual reality with either an alternative intervention or no intervention. We did not include studies that compared two different types of virtual reality without an alternative group. We included trials that evaluated any intensity and duration of virtual reality that exceeded a single treatment session.

Types of participants

The study participants had a diagnosis of stroke, defined by the World Health Organization as "a syndrome of rapidly developing symptoms and signs of focal, and at times global, loss of cerebral function lasting more than 24 hours or leading to death with no apparent cause other than that of vascular origin" (WHO 1989), diagnosed by imaging or neurological examination. We included patients who were 18 years and older with all types of stroke, all levels of severity, and at all stages post stroke, including those patients with subarachnoid haemorrhage. We excluded studies of participants with mixed aetiology (for example, participants with acquired brain injury) unless data were available relating to the people with stroke only.

Types of interventions

We included studies using virtual reality interventions that met the following definition: "an advanced form of human-computer

interface that allows the user to 'interact' with and become 'immersed' in a computer-generated environment in a naturalistic fashion" (Schultheis 2001).

We included studies using any form of non-immersive or immersive virtual reality, and studies that used commercially available gaming consoles.

The comparison group received either an alternative intervention or no intervention. Given the broad range of alternative interventions, we considered these to include any activity designed to be therapeutic at the impairment, activity or participation level that did not include the use of virtual reality.

Types of outcome measures

Primary outcomes

As one of the most common applications of virtual reality in stroke rehabilitation is upper limb rehabilitation we selected the following primary outcome:

1. Upper limb function and activity:

i) arm function and activity: including assessments such as the Motor Assessment Scale (upper limb), Action Research Arm Test, Wolf Motor Function Test;

ii) hand function and activity: including assessments such as the Nine Hole Peg Test, Box and Block Test.

Secondary outcomes

1. Gait and balance activity:

i) lower limb activity: including assessments such as walking distance, walking speed, Community Walk Test, functional ambulation, Timed Up and Go Test;

ii) balance and postural control: including assessments such as the Berg Balance Scale and laboratory-based force plate measures.

2. Global motor function: including assessments such as the Motor Assessment Scale.
3. Cognitive function: including assessments such as Trail Making Test, Useful Field of View Test.
4. Activity limitation: including assessments such as the Functional Independence Measure (FIM), Barthel Index, Activities-specific Balance Confidence Scale, on-road driving test.
5. Participation restriction and quality of life: including assessments such as the SF36, EQ5D, Stroke Impact Scale or other patient-reported outcomes.
6. Voxels or regions of interest identified via imaging.
7. Adverse events: including motion sickness, pain, injury, falls and death.

We included the primary outcome (upper limb function) and gait, global motor function and quality of life in Summary of findings for the main comparison.

Search methods for identification of studies

See the 'Specialised register' section in the Cochrane Stroke Group module. We searched for relevant trials in all languages and arranged translation of trial reports published in languages other than English.

Electronic searches

The search for studies in our previous review was conducted in March 2010; the search for this update was completed in November 2013. We searched the Cochrane Stroke Group Trials Register, which was searched by the Managing Editor in October 2013 using the intervention codes 'computer-aided therapy' and 'virtual reality therapy'. We identified 48 studies in total.

In addition, we searched the following electronic bibliographic databases: the Cochrane Central Register of Controlled Trials (CENTRAL 2013, Issue 11), MEDLINE (1950 to October Week 3, 2013) (Appendix 1), EMBASE (1980 to Week 44, 2013) (Appendix 2), AMED (1985 to October 2013) (Appendix 3), CINAHL (1982 to November Week 3, 2013) (Appendix 4), PsycINFO (1840 to November Week 3, 2013) (Appendix 5), PsycBITE (Psychological Database for Brain Impairment Treatment Efficacy, http://www.psycbite.com/) (to 26 October 2013) and OTseeker (http://www.otseeker.com/) (to 26 October 2013). We also searched the engineering databases COMPENDEX (1970 to 29 November 2013) and INSPEC (1969 to 29 November 2013) for studies from a non-medical background.

Our search strategies were developed by the Cochrane Stroke Group Trials Search Co-ordinator for MEDLINE (Ovid) and we adapted them for other databases with the assistance of an experienced medical librarian.

Searching other resources

In order to identify further published, unpublished and ongoing trials, we:

1. searched the following ongoing trials registers: Current Controlled Trials (www.controlled-trials.com), National Institute of Health Clinical Trials Database (http://www.clinicaltrials.gov) and Stroke Trials Registry (www.strokecenter.org/trials/) to 30 January 2014;
2. used the Cited Reference Search within Science Citation Index (SCI) and Social Science Citation Index (SSCI) to track relevant references for all included studies;
3. scanned the reference lists of all included studies;
4. searched Dissertation Abstracts (15 June 2014);
5. scanned the abstracts of non-English language studies if they were available in English;
6. searched the IEEE (Institute of Electrical and Electronic Engineers) electronic library (to 27 October 2013).

For the previous version of this review we carried out the following searches.

1. We handsearched the proceedings of the International Workshop on Virtual Rehabilitation (2003 to 2005), Virtual Rehabilitation Conference (2007 to 2009), International Conference Series on Disability, Virtual Reality and Associated Technologies (2000 to 2008) and Cybertherapy (2003 to 2007).

2. We contacted 12 manufacturers of virtual reality equipment to ask for details of trials. We contacted the following manufacturers by telephone, email or postal mail: Nintendo, Sony, GestureTek, NeuroVR, Hocoma, Motek, Virtual Realities, Haptic Master, Microsoft Xbox, Essential Reality, SensAble, Novint and Cyberglove. Three of the manufacturers responded (Nintendo, Motek and Novint); however, they were unable to provide details of studies eligible for inclusion in the review.

Data collection and analysis

Selection of studies

One review author (KL) performed the searches. Two of the authors (KL and ST) independently reviewed the titles and abstracts identified from the database searches to assess whether they met the pre-defined inclusion criteria. The review authors obtained potentially relevant articles in full text and KL contacted authors when more information was required. KL and ST then independently reviewed full-text articles and correspondence with investigators to determine studies to be included in the review. JD made the final decision on studies that KL and ST disagreed on. We documented the reasons for the exclusion of studies. Where studies published in non-English languages appeared relevant, we sought the full text of the study. In these cases, the Trials Search Co-ordinator arranged for someone fluent in the non-English language to review the paper to ascertain whether the study met the inclusion criteria.

Data extraction and management

Two review authors (KL and ST, SG or JD) independently extracted data using a pre-designed data extraction form for each selected study. Data extracted included citation details, trial setting, inclusion and exclusion criteria, study population, participant flow, intervention details, outcome measures and results, and methodological quality. We resolved disagreements by discussion or by referral to a third review author (MC) as necessary. The review authors contacted authors by email to gain any missing information necessary for the review.

Assessment of risk of bias in included studies

Two review authors (KL and ST, SG or JD) used The Cochrane Collaboration's 'Risk of bias' tool to independently assess the methodological quality of the included studies (Appendix 6). The tool covers the domains of sequence generation, allocation concealment, blinding of outcome assessors, incomplete outcome data and selective reporting. We classified items as 'low risk', 'high risk' or 'unclear risk' of bias. We omitted the domain that assesses the blinding of participants as we were of the opinion that this domain related to the nature of the intervention and not study quality. We contacted the authors of the included studies for more information where insufficient information was published to assess the risk of bias. We resolved disagreements with help from a third review author (MC).

We employed GRADE to interpret findings and used GRADEpro to create a 'Summary of findings' table (Guyatt 2008). The table provides outcome-specific information concerning the overall quality of evidence from studies included in the comparison, the magnitude of effect of the intervention and the sum of available data on the outcomes considered. When using GRADE, we downgraded the evidence from 'high quality' by one level for serious (or by two for very serious) study limitations (risk of bias), indirectness of evidence, serious inconsistency, imprecision of effect estimates or potential publication bias.

Measures of treatment effect

Two review authors (KL and ST, SG or JD) independently classified outcome measures in terms of the domain assessed (upper limb function, hand function, lower limb and gait activity, balance and postural control, global motor function, cognitive function, activity limitation, participation restriction and quality of life, neuroimaging studies). When a study presented more than one outcome measure for the same domain, we included the measure most frequently used across studies in the analysis. We planned to calculate risk ratios (RR) with 95% confidence intervals (CIs) for any dichotomous outcomes, if recorded. We calculated mean differences (MD) or standardised mean differences (SMD) for continuous outcomes as appropriate.

Unit of analysis issues

The unit of randomisation in these trials was the individual patient. We did not include any cluster-randomised controlled trials. Five of the studies were three-armed trials. Lam 2006 compared virtual reality with an alternative intervention and no intervention. We used the data comparing the virtual reality arm with the alternative intervention arm to avoid double counting. Coupar 2012 compared a usual care group with a group that received additional 'low intensity' virtual reality intervention and a group that received additional 'high intensity' virtual reality intervention. We compared the high intensity virtual reality group with the usual care group. da Silva Cameirao 2011 compared a virtual reality intervention using a specialised program with virtual reality using the Nintendo Wii and conventional therapy. We used the data from the specialised virtual reality group and the conventional therapy group. Byl 2013 compared conventional therapy with unilateral

and bilateral virtual reality intervention. We used the data from the bilateral virtual reality intervention as it was thought to be closest to the type of therapy included in the conventional therapy sessions. Finally, Zucconi 2012 compared a virtual reality intervention with feedback on performance with a virtual reality intervention without feedback and conventional therapy. We included the data from the virtual reality with feedback group and compared it with the conventional therapy group.

Dealing with missing data

We contacted study authors to obtain any missing data and converted available data when possible (for example, we converted gait speed reported as metres per minute to metres per second (Jaffe 2004)). Where possible, we conducted intention-to-treat analyses to include all randomised participants and, where drop outs were clearly identified for an outcome assessment, we used the actual denominator of the participants contributing the data.

Assessment of heterogeneity

We pooled results to present an overall estimate of the treatment effect using a fixed-effect model in the primary analysis. We assessed heterogeneity by visual inspection of the forest plot. We quantified inconsistency amongst studies using the I^2 statistic (Higgins 2011), where we considered levels greater than 50% as substantial heterogeneity. We used a random-effects model as part of a sensitivity analysis.

Assessment of reporting biases

Our search of clinical trial registers assisted in reducing publication bias. We also investigated selective outcome reporting through the comparison of the methods section of papers with the results reported and contacting authors to check whether additional outcomes were collected. We inspected funnel plots for each of the analyses; however, interpretation was limited due to the small sample sizes.

Data synthesis

Where there were acceptable levels of heterogeneity, we pooled results. We used the fixed-effect model with 95% CI using RevMan 5.3 (RevMan 2014). We used a random-effects model as part of a sensitivity analysis. Where meta-analysis was not appropriate due to unacceptable heterogeneity, we have presented a narrative summary of study results. We pooled outcomes measured with different instruments using the SMD.

Subgroup analysis and investigation of heterogeneity

We attempted to perform subgroup analyses to determine whether outcomes varied according to age, severity of stroke, time since onset of stroke, dose of intervention (total hours of intervention) and type of intervention (highly specialised program designed for rehabilitation versus commercial gaming console). However, not all of these analyses were possible due to the homogeneity of trial participants. We were able to undertake subgroup analysis in some cases for:

1. dosage of intervention (for upper limb function we compared less than 15 hours intervention with more than 15 hours intervention and for lower limb function we compared less than 10 hours intervention with more than 10 hours intervention);
2. time since onset of stroke (less than or more than six months);
3. type of intervention (specialised program or commercial gaming console);
4. severity of impairment (upper limb).

Sensitivity analysis

We performed sensitivity analyses to determine whether there was a difference in using a fixed-effect model versus a random-effects model. We conducted sensitivity analyses where possible to explore the effects of the methodological quality of the included studies on overall effect.

RESULTS

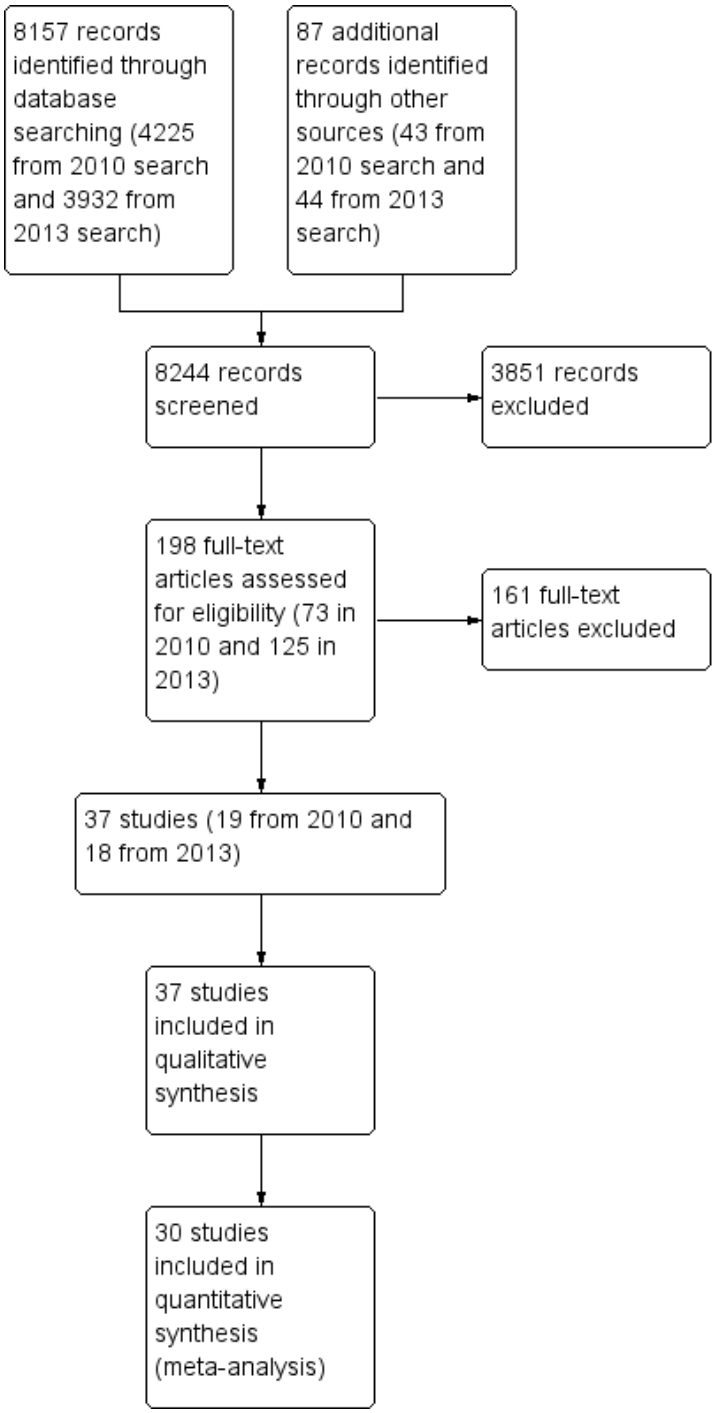
Description of studies

See Characteristics of included studies; Characteristics of excluded studies.

Results of the search

We identified 84 studies from searching the Cochrane Stroke Group trials register and 8109 references from the database searches, totaling 8193 references to studies. A search of the trials registries elicited a further 51 potentially relevant studies. From the 8244 titles and abstracts retrieved, we sought 198 of the articles in full text for further review. We grouped articles reporting the same study. We removed articles that did not meet the inclusion criteria, such as studies that used interventions that were not considered virtual reality and non-randomised controlled trials. We included a total of 37 studies. We have provided details on 17 excluded studies (Broeren 2008; Cameirao 2012; Cho 2013; Chortis 2008; Cikaljo 2012; Der-Yeghiaian 2009; Edmans 2009; Fischer 2007; Fritz 2013; Gnajaraj 2007; In 2012; Katz 2005; Kim 2012a; Krebs 2008; Manlapaz 2010; Shin 2010; Song 2010) in the Characteristics of excluded studies table, which were closest to, but did not meet the inclusion criteria (Figure 1). We identified nine ongoing studies (Characteristics of ongoing studies).

Figure 1. Study flow diagram.



Included studies

We identified 37 randomised controlled trials, with a total of 1019 participants, which met the inclusion criteria. Of the 37 included studies, we included 19 (with 565 participants) in the previous version of this review and we identified 18 (with 454 participants) in the updating process.

Sample characteristics

All trials, which were published in English, took place between 2004 and 2014. Twenty-two (59%) of the studies involved sample sizes of fewer than 25 participants and three studies involved more than 50 participants (Akinwuntan 2005; Kiper 2011; Lam 2006) (Table 1). A total of 1019 participants post stroke were included in the trials.

All studies included both male and female participants. Although not always clearly reported, it appears that participants in the included studies were relatively young, with studies reporting mean ages of 46 to 75 years.

Inclusion criteria were clearly specified for 31 studies; five trials recruited participants within three months of stroke (Akinwuntan 2005; Coupar 2012; da Silva Cameirao 2011; Kwon 2012; Piron 2007); one trial recruited within six months of stroke (Saposnik 2010); two trials recruited within 12 months (Kiper 2011; Yavuzer 2008); 17 trials recruited participants more than six months post stroke (Byl 2013; Crosbie 2008; Housman 2009; Jaffe 2004; Jang 2005; Jung 2012; Kim 2009; Kim 2012; Mirelman 2008; Piron 2010; Sin 2013; Sucar 2009; Subramanian 2013; Yang 2008; Yang 2011; You 2005; Zucconi 2012). Time since onset of stroke was not reported in the inclusion criteria for the remaining studies. The average recruitment time since stroke for each study is reported in the Characteristics of included studies table.

Several trials excluded patients who were deemed medically unstable, though how this was determined was often unclear. Five trials specified that people with a history of epilepsy or seizures would be excluded (Akinwuntan 2005; Kim 2012; Mazer 2005; Saposnik 2010; Sin 2013). Most studies reported that patients with significant cognitive impairment would be excluded; however, this criterion was often poorly defined. Several studies listed the presence of aphasia (Akinwuntan 2005; Coupar 2012; da Silva Cameirao 2011; Housman 2009; Kim 2011a; Kim 2011b; Kiper 2011; Kwon 2012; Lam 2006; Mazer 2005; Mirelman 2008; Piron 2007; Piron 2009; Piron 2010; Saposnik 2010; Shin 2013; Subramanian 2013; Yang 2008; Yavuzer 2008; Zucconi 2012), apraxia (Coupar 2012; Housman 2009; Kiper 2011; Lam 2006; Piron 2007; Piron 2009; Piron 2010; Subramanian 2013) and visual impairment (Barcala 2013; Coupar 2012; Housman 2009; Jang 2005; Kang 2009; Kim 2009; Kim 2011b; Lam 2006; Piron 2007; Piron 2009; Piron 2010; Rajaratnam 2013; Sin 2013; Subramanian 2013; Yang 2008; Yang 2011; You 2005; Zucconi 2012) as exclusion criteria. One study excluded people with computer-related phobias (Lam 2006). Studies involving upper limb training included patients with a range of function including those with severe functional impairment (Byl 2013; Coupar 2012; da Silva Cameirao 2011; Kiper 2011; Shin 2013; Sin 2013). Studies involving lower limb and gait training only involved patients that were able to walk independently.

Although few studies provided clear details on participant recruitment and withdrawal, data from eight studies showed that only 26% of the target population screened were recruited. Table 1 shows further details of recruitment and retention.

Interventions

Intervention approaches

Five intervention approaches were used: activity retraining, upper limb training, lower limb, balance and gait training, global motor function training and cognitive/perceptual training. Four trials involved activity retraining (Akinwuntan 2005; Mazer 2005 (automobile driving retraining); Jannink 2008 (scooter driving retraining); Lam 2006 (retraining skills in using public transport)). Eighteen trials involved upper limb training (Byl 2013; Coupar 2012; Crosbie 2008; da Silva Cameirao 2011; Housman 2009; Kim 2012; Kiper 2011; Piron 2007; Piron 2009; Piron 2010; Saposnik 2010; Shin 2013; Sin 2013; Standen 2011; Subramanian 2013; Sucar 2009; Yavuzer 2008; Zucconi 2012). Eight trials involved lower limb, balance and gait training (Barcala 2013; Jaffe 2004; Jung 2012; Kim 2009; Mirelman 2008; Rajaratnam 2013; Yang 2008; Yang 2011). Seven trials used the same virtual reality program to improve global motor function (Cho 2012; Jang 2005; Kim 2009; Kim 2011a; Kim 2011b; Kwon 2012; You 2005) and one trial used a visual-perceptual retraining approach (Kang 2009).

Six of the studies used commercially available gaming consoles: one study used the Playstation EyeToy (Yavuzer 2008), four studies used the Nintendo Wii (Barcala 2013; Kim 2012; Rajaratnam 2013; Saposnik 2010) and two studies used the Microsoft Kinect (Rajaratnam 2013; Sin 2013). Seven studies used GestureTek IREX, which is commercially available but more difficult to obtain and more expensive than off-the-shelf consoles (Cho 2012; Jang 2005; Kim 2009; Kim 2011a; Kim 2011b; Kwon 2012; You 2005). One study used the Armeo (Coupar 2012) and one used the CAREN system (Subramanian 2013), which are also commercially available. The remaining studies used customised virtual reality programs.

Setting

The majority of interventions were delivered in either an outpatient or inpatient setting, although two of the studies delivered the intervention in the participant's own home (Piron 2009; Standen 2011). One of these studies used a telerehabilitation approach to deliver the intervention (Piron 2009).

Amount of therapy provided

The total dose of therapy provided varied between studies. Six studies provided less than five hours of total therapy (Barcala 2013; Jannink 2008; Kim 2012; Shin 2013; Yang 2008; Yang 2011). Thirteen studies provided between six and 10 hours of therapy (Crosbie 2008; Jaffe 2004; Jung 2012; Kang 2009; Kim 2009; Kim 2011a; Kim 2011b; Kwon 2012; Lam 2006; Saposnik 2010; Sin 2013; Subramanian 2013; Yavuzer 2008). A further 14 studies provided between 11 and 20 hours of therapy (Akinwuntan 2005; Byl 2013; Cho 2012; da Silva Cameirao 2011; Jang 2005; Kiper 2011; Mazer 2005; Mirelman 2008; Piron 2009; Piron 2010; Rajaratnam 2013; Sucar 2009; You 2005; Zucconi 2012) and three studies provided more than 21 hours of therapy (Housman 2009; Piron 2007; Standen 2011). The remaining study, Coupar 2012, had three arms; one of the arms received lower intensity therapy (four hours total) and another received higher intensity therapy (10 hours total).

Comparison interventions

Most of the trials compared virtual reality intervention with a comparable alternative intervention. The alternative intervention was often described as therapy using a conventional approach. One study allocated participants to either actively participating in the virtual reality intervention or watching others participate in the virtual reality intervention (Yavuzer 2008). Eleven of the studies examined the effect of virtual reality when used alone (the control group received no intervention) or as an adjunct (the control group received usual care or rehabilitation) (Barcala 2013; Cho 2012; Jang 2005; Kim 2011a; Kim 2012; Kwon 2012; Mazer 2005; Shin 2013; Sin 2013; Standen 2011; You 2005). There were five three-armed trials with two comparison interventions (Byl 2013; Coupar 2012; da Silva Cameirao 2011; Lam 2006; Zucconi 2012).

Outcomes

As a result of the diverse intervention approaches, a wide range of outcome measures were used. Outcome measures for each of the predefined outcome categories are shown in Table 2. Due to the heterogeneity of outcome measures, we were unable to include all of them in the analyses. With regard to timing of outcome measurements, one study waited until five weeks after the end of the intervention to collect outcome measures (Jannink 2008). All remaining studies measured outcomes soon post-intervention. For studies including further follow-up, the time interval until follow-up was generally at or less than three months (Coupar 2012; Crosbie 2008; da Silva Cameirao 2011; Jaffe 2004; Mirelman 2008; Piron 2009; Saposnik 2010; Subramanian 2013; Yang 2008). Only two studies involved longer-term follow-up: one at six months (Housman 2009) and one at both six months and five years (Akinwuntan 2005). Twelve studies reported on the presence or absence of adverse events (Byl 2013; Coupar 2012; Crosbie 2008; Housman 2009; Jaffe 2004; Kiper 2011; Piron 2007; Piron 2010; Saposnik 2010; Subramanian 2013; Sucar 2009; Yavuzer 2008).

Excluded studies

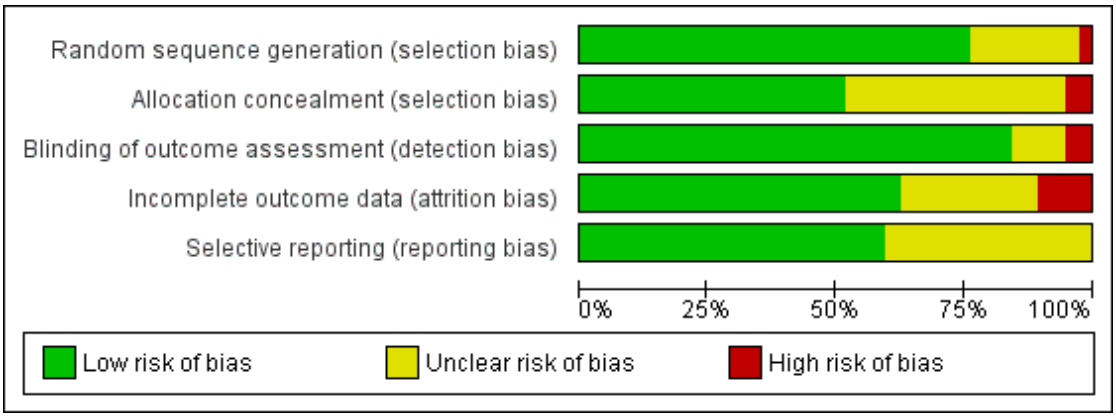
We provided details of the 17 studies that we excluded. We listed studies as excluded if they were obtained in full text and required discussion between authors to confirm exclusion. Of the 17 studies nine were non-randomised trials, four did not meet the definition of virtual reality and two compared different types of virtual reality interventions rather than comparing virtual reality with an alternative intervention or no intervention. We excluded two studies for which we were unable to confirm whether they met the inclusion criteria based on information presented in a conference abstract and the authors did not respond to two emails requesting further information (Characteristics of excluded studies).

Risk of bias in included studies

Refer to Figure 2 and Figure 3.

Figure 2. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

Figure 3. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.



Not all included studies followed the CONSORT guidelines (Schulz 2010), in which case we contacted the corresponding authors for clarification of study methodology. If we did not obtain a response from a corresponding author we recorded the 'Risk of bias' criterion as 'unclear'.

Allocation

Random sequence generation was reported as adequate in 28 trials (76%) (Akinwuntan 2005; Barcala 2013; Byl 2013; Cho 2012; Coupar 2012; Crosbie 2008; da Silva Cameirao 2011; Housman 2009; Jaffe 2004; Jung 2012; Kang 2009; Kim 2009; Kiper 2011; Lam 2006; Mazer 2005; Mirelman 2008; Piron 2007; Piron 2009; Piron 2010; Rajaratnam 2013; Saposnik 2010; Shin 2013; Sin 2013; Standen 2011; Subramanian 2013; Yang 2008; Yavuzer 2008; Zucconi 2012).

Allocation concealment was reported as adequate in 19 trials (51%) (Akinwuntan 2005; Barcala 2013; Byl 2013; Coupar 2012; Crosbie 2008; da Silva Cameirao 2011; Kim 2009; Kiper 2011; Lam 2006; Mazer 2005; Mirelman 2008; Piron 2007; Piron 2009; Piron 2010; Shin 2013; Standen 2011; Subramanian 2013; Yavuzer 2008; Zucconi 2012).

Blinding

Thirty trials (81%) reported blinding of the outcome assessor (Akinwuntan 2005; Barcala 2013; Byl 2013; Coupar 2012; Crosbie 2008; da Silva Cameirao 2011; Housman 2009; Jaffe 2004; Jung 2012; Kang 2009; Kim 2009; Kim 2011b; Kwon 2012; Lam 2006; Mazer 2005; Mirelman 2008; Piron 2007; Piron 2009; Piron 2010; Rajaratnam 2013; Saposnik 2010; Shin 2013; Sin 2013; Standen 2011; Subramanian 2013; Yang 2008; Yang 2011; Yavuzer 2008; You 2005; Zucconi 2012). No trials were able to blind participants or personnel.

Incomplete outcome data

We deemed 22 trials (59%) to be at low risk of bias in relation to incomplete outcome data (Akinwuntan 2005; Barcala 2013; Byl 2013; Coupar 2012; Crosbie 2008; Housman 2009; Jaffe 2004; Kang 2009; Kim 2009; Kim 2011a; Kim 2011b; Lam 2006; Mazer 2005; Mirelman 2008; Piron 2009; Piron 2010; Saposnik 2010; Shin 2013; Subramanian 2013; Sucar 2009; Yavuzer 2008; Zucconi 2012). Drop outs from studies appeared generally balanced across groups.

Selective reporting

Trialists from 21 studies reported that their published data were free of selective reporting (Akinwuntan 2005; Byl 2013; Coupar 2012; Crosbie 2008; da Silva Cameirao 2011; Housman 2009; Kim 2009; Kim 2011a; Kim 2011b; Lam 2006; Mazer 2005; Mirelman 2008; Piron 2007; Piron 2009; Piron 2010; Saposnik 2010; Shin 2013; Standen 2011; Subramanian 2013; Sucar 2009; Zucconi 2012). It was unclear whether selective reporting was present in the other studies.

Effects of interventions

See: **Summary of findings for the main comparison** Virtual reality for stroke rehabilitation

Primary outcomes

We present results for upper limb function and activity.

Virtual reality versus conventional therapy: effect on upper limb function and activity: post-intervention

Results are presented for upper limb function and activity and hand function. All outcomes were taken within days of the end of the intervention program.

Comparisons 1.1 and 1.2: Upper limb function and activity

Twelve studies presented outcomes for upper limb function and activity (375 participants) (Byl 2013; Crosbie 2008; da Silva Cameirao 2011; Housman 2009; Kiper 2011; Piron 2007; Piron 2009; Piron 2010; Saposnik 2010; Subramanian 2013; Sucar 2009; Zucconi 2012). The impact of virtual reality on upper limb function showed a small significant effect: standardised mean difference (SMD) 0.29, 95% confidence interval (CI) 0.09 to 0.49 (Analysis 1.1). Statistical heterogeneity was low (I^2 = 11%).

Sensitivity analysis

Analysis excluding the one trial that was quasi-randomised, Sucar 2009, found that the result on upper limb function remained significant although the effect was slightly smaller (SMD 0.28, 95% CI 0.08 to 0.49). Analysis excluding four studies that we deemed to be at high risk of bias in one or more domains (da Silva Cameirao 2011; Housman 2009; Piron 2007; Sucar 2009) showed a trend towards improved upper limb function in the virtual reality group. However, the result was not statistically significant (SMD 0.18, 95% CI -0.06 to 0.41).

Ten of the trials (with 363 participants) used the Fugl Meyer Upper Extremity (UE) Scale as an outcome measure (368 participants) (Byl 2013; da Silva Cameirao 2011; Housman 2009; Kiper 2011; Piron 2007; Piron 2009; Piron 2010; Subramanian 2013; Sucar 2009; Zucconi 2012). The impact of virtual reality as measured by the Fugl Meyer UE Scale also showed a significant effect: mean difference (MD) 3.30, 95% CI 1.29 to 5.32 (Analysis 1.2). The other two trials used the Action Research Arm Test (Crosbie 2008) and Abbreviated Wolf Motor Function Test (Saposnik 2010) as their measure of upper limb function and activity.

Comparison 1.3: Hand function

Two trials measured the effect of virtual reality versus alternative therapy on grip strength (kg) (44 participants) (Housman 2009; Saposnik 2010). The impact was not significant: MD 3.55, 95% CI -0.20 to 7.30 (Analysis 1.3). No statistical heterogeneity was indicated.

Upper limb function: follow-up

Only Housman 2009 measured the longer-term effects of virtual reality on upper limb function (more than three months after the end of treatment). This study reported that participants in the virtual reality group had improved significantly more on the Fugl Meyer UE Scale at the six-month follow-up assessment than participants in the alternative treatment group (P value = 0.045). Participants in the virtual reality group improved by 3.6 points (standard deviation (SD) 3.9) whereas participants in the alternative treatment group improved by 1.5 points (SD 2.7). However, the trial found no other significant differences between groups at six months on the other outcome measures used (Rancho Functional Test, grip strength and Motor Activity Log).

Upper limb function: subgroup analyses

Comparison 2.1: Dose of treatment

We compared trials providing under 15 hours of intervention with trials providing 15 hours or more of intervention. Trials providing less than 15 hours of intervention had a non-significant effect (SMD 0.24, 95% CI -0.13 to 0.62) whereas trials providing more than 15 hours of intervention showed a small significant effect (SMD 0.31, 95% CI 0.07 to 0.55). However, the difference between groups was not statistically significant (Chi^2 = 0.09, df = 1, P value = 0.84) (Analysis 2.1).

Comparison 2.2: Time since onset of stroke

We classified trials based on whether their participants were recruited within six months of stroke or more than six months post stroke. The group recruited within six months of stroke showed a moderate significant effect (SMD 0.78, 95% CI 0.28 to 1.29) whereas the group recruited more than six months after stroke did not show a significant effect (SMD 0.21, 95% CI -0.04 to 0.46) although there was a trend towards the virtual reality intervention. The difference between groups was significant (Chi^2 = 3.90, df = 1, P value = 0.05) (Analysis 2.2).

Comparison 2.3: Specialised virtual reality system or commercial gaming console

We could include only one trial using a commercial gaming console in this analysis in comparison to six trials using specialised virtual reality programs (Saposnik 2010). Both groups showed a significant effect on upper limb function (commercial gaming consoles: SMD 1.15, 95% CI 0.06 to 2.24 compared with specialised system: SMD: 0.26, 95% CI 0.05 to 0.46) (Analysis 2.3). The test for subgroup differences did not indicate significance (P value = 0.12).

Comparison 2.4: Severity of upper limb impairment

We compared outcomes for people with mild to moderate upper limb impairment and people with moderate to severe impairment. The group with mild to moderate impairment showed a significant positive effect (SMD 0.35, 95% CI 0.10 to 0.59) whereas the group with moderate to severe impairment did not show a significant effect (SMD 0.16, 95% CI -0.19 to 0.52) (Analysis 2.4). However, the difference between groups was not significant (P value = 0.41).

We did not undertake other planned subgroup analyses due to similarities in these studies in regard to the age of participants and frequency of intervention sessions.

Additional virtual reality intervention: effect on upper limb function

We examined the effects of virtual reality intervention when it was compared with no intervention or when it was used to augment standard care (i.e. people in the virtual reality intervention group received additional therapy time relative to the control group).

Comparison 3.1: Upper limb function

Nine studies with a total of 190 participants presented outcomes for upper limb function (Cho 2012; Coupar 2012; Jang 2005; Kim 2011a; Kwon 2012; Shin 2013; Sin 2013; Standen 2011; Yavuzer 2008). There was a small to moderate significant effect that demonstrated that a virtual reality intervention was more effective than no intervention: SMD 0.44, 95% CI 0.15 to 0.73 (Analysis 3.1). There was no statistical heterogeneity.

Sensitivity analysis

We excluded trials that we deemed to be at high risk of bias in one or more categories (Cho 2012; Kim 2011a; Standen 2011). The result was consistent with the original analysis (SMD 0.48, 95% CI 0.11 to 0.86).

Comparison 3.2: Hand function (dexterity)

Three studies with 60 participants reported on the effect of additional virtual reality intervention on hand function (Jang 2005; Sin 2013; Standen 2011). The effect was not significant: SMD 0.25, 95% CI -0.27 to 0.77 (Analysis 3.2). Statistical heterogeneity was present (I^2 = 38%).

Upper limb function: subgroup analyses

Comparison 4.1: Dose of treatment

We compared trials providing less than 15 hours of intervention with trials providing 15 hours or more of intervention. Trials with less than 15 hours of intervention had a significant effect on upper limb function (SMD 0.40, 95% CI 0.05 to 0.75). Trials providing more than 15 hours of intervention did not have a significant effect (SMD 0.54, 95% CI 0.00 to 1.07). The difference between groups was not significant (Chi^2= 0.19, df = 1, P value = 0.67) (Analysis 4.1).

Comparison 4.2 Time since onset of stroke

We compared trials recruiting participants within six months of stroke with trials recruiting participants more than six months post stroke. The difference between groups was not significant (Chi^2= 0.40, df = 1, P value = 0.53) (Analysis 4.2).

Comparison 4.3 Specialised virtual reality system or gaming console

We compared two trials evaluating the efficacy of gaming console use with seven trials evaluating the efficacy of virtual reality systems specifically designed for rehabilitation. Gaming consoles were not found to have a significant effect (SMD 0.50, 95% CI -0.04 to 1.04) whereas specialised systems had a significant effect (SMD 0.42, 95% CI 0.07 to 0.76). The difference between groups was not significant (Chi^2 = 0.06, df = 1, P value = 0.8) (Analysis 4.3).

Secondary outcomes

Virtual reality versus conventional therapy: Effect on gait and balance activity: post-intervention

Results are presented for gait speed. All outcomes are taken within days of the end of the intervention program and measured in metres per second. We were unable to include four relevant studies; one of these studies, Barcala 2013, compared different doses of therapy and three studies did not report data in a format that allowed pooling (Kim 2009; Rajaratnam 2013; Yang 2011).

Comparison 4.1: Gait speed

Three studies provided data on gait speed (58 participants) (Jaffe 2004; Mirelman 2008; Yang 2008). The effect of virtual reality on gait speed was not significant: MD 0.07, 95% CI -0.09 to 0.23 (Analysis 5.1). No statistical heterogeneity was indicated. Jaffe 2004 examined the effect of virtual reality on comfortable walking speed and fast walking speed. We included the data relating to comfortable walking speed in the meta-analysis. The effect on fast walking speed was found to be significantly greater in the virtual reality intervention group than the comparative group.
Jung 2012 reported outcomes as measured by the Timed Up and Go Test. The study found a trend towards improved outcomes in the virtual reality intervention group (Cohen's d = 0.78). However, the difference between groups was not statistically significant.

Sensitivity analysis

We excluded the study that we deemed to be at high risk of bias in one or more categories (Jaffe 2004). The result was non-significant (MD 0.13, 95% CI -0.07 to 0.33).

Gait and balance activity: follow-up

Only Mirelman 2008 measured the longer-term effects (at three months) of virtual reality on gait speed. This study found that the intervention group had significantly improved outcomes at follow-up.

Balance

Rajaratnam 2013 reported the effects of intervention on balance. The study found no significant improvements in balance function within the experimental group.
Yang 2011 reported outcomes for gait and balance that could not be pooled due to the nature of the outcome measures and the way in which data were presented. The results showed no significant differences between groups for quiet stance but significant improvement within the virtual reality group for sit-to-stand and aspects of level walking.

Gait and balance activity: subgroup analyses

Comparison 5.1: Effect of dose of treatment on gait speed

We compared two trials providing less than 10 hours of intervention with one trial providing more than 10 hours of intervention. Neither subgroup showed a significant effect (trials providing less than 10 hours intervention: MD 0.01, 95% CI -0.22 to 0.24, and trial providing more than 10 hours intervention: MD 0.13, 95% CI -0.09 to 0.35). The difference between subgroups was not significant (P value = 0.47) (Analysis 6.1).
We did not undertake other planned subgroup analyses due to homogeneity with regard to the age of participants, severity of stroke, time since onset of stroke, frequency of intervention sessions and type of virtual reality program.

Global motor function

Three studies reported outcomes for global motor function (using the Modified Motor Assessment scale). However, Kim 2009 compared virtual reality with an alternative intervention. We pooled two studies (with 27 participants) that examined the effect of virtual reality on global motor function when used in addition to usual care, thus increasing the therapy dose received by the intervention group (Kim 2012; You 2005). The effect on global motor function was not significant (SMD 0.14, 95% CI -0.63 to 0.90) (Analysis 7.1).

Cognitive function

Insufficient trials included assessments of cognition to allow us to perform analysis for this outcome.

Activity limitation

Two studies reported outcomes of a driving evaluation. However, we were unable to pool results as Akinwuntan 2005 compared virtual reality intervention with an alternative intervention and Mazer 2005 compared virtual reality intervention with no alternative intervention. Akinwuntan 2005 reported the results from the follow-up assessments, which were completed at six months and five years post-intervention. Six months post-intervention they found that participants in the virtual reality intervention group had improved significantly more in their on-road performance (measured by the Test Ride for Investigating Practical fitness to drive checklist) than participants in the alternative intervention group (P value = 0.005). Furthermore, 73% of the virtual reality group compared with 42% of the group that participated in driving-related cognitive tasks were classified by driving assessors as 'fit to drive' at six months. At five years, there was no significant difference between the groups in regards to 'fitness to drive' or resumption of driving.
Results are presented for activities of daily living (ADL) function.

Comparison 7.1: Virtual reality versus conventional therapy: effect on ADL function

Although none of the following study interventions targeted ADL retraining specifically, eight studies (with 199 participants) measured the effects of virtual reality versus the same dose of alternative therapy on ADL function (Byl 2013; da Silva Cameirao 2011; Kang 2009; Kim 2011b; Kiper 2011; Piron 2007; Piron 2010; Zucconi 2012). The impact of intervention had a moderate significant effect: SMD 0.43, 95% CI 0.18 to 0.69 (Analysis 8.1). Statistical heterogeneity was negligible (I^2 = 2%).

Sensitivity analysis

We explored the effects of methodological quality on the overall effect by excluding studies deemed to be at high risk of bias in one or more categories from the analysis (da Silva Cameirao 2011; Piron 2007). The results remained similar (SMD 0.39, 95% CI 0.10 to 0.67).

Comparison 8.1: Additional virtual reality intervention: effect on ADL function

Eight studies (with 153 participants) reported outcomes for ADL following virtual reality intervention where the therapy was provided in addition to usual care and thus the dose of therapy was greater in the virtual reality group (Barcala 2013; Coupar 2012; Kim 2011a; Kim 2012; Kwon 2012; Shin 2013; Standen 2011; Yavuzer 2008). There was a small to moderate significant effect: SMD 0.44, 95% CI 0.11 to 0.76 (Analysis 9.1).

Sensitivity analysis

We explored the effects of methodological quality on the effect by excluding studies classified as being at high risk of bias in one or more categories (Kim 2011b; Standen 2011). The result suggested a smaller effect size and wider confidence intervals (SMD 0.39, 95% CI 0.00 to 0.78).

Participation restriction and quality of life

Heterogeneity between trials and outcome measures used meant that we did not perform analysis for this outcome.

Two of the studies assessed whether intervention was associated with changes on the Stroke Impact Scale (Byl 2013; Saposnik 2010). These studies were not pooled as the treatment of the control group differed substantially. Neither of the studies reported between-group differences on the scale.

Four of the studies examined effect of intervention on the 'amount of use' scale within the Motor Activity Log. There were differences in the intervention approaches examined. One of the studies examined whole body physical retraining (Jang 2005), whereas the other studies specifically examined upper limb retraining. In addition, one of the studies used virtual reality in addition to usual care and thus increased the therapy dose in the intervention group (Standen 2011), whereas the other two studies compared training in a virtual environment with an alternative intervention (Housman 2009; Subramanian 2013). While one of the studies reported no significant difference between groups (Housman 2009), three of the studies reported that there were greater improvements in the intervention group than the control group on the 'amount of use' scale (Jang 2005; Standen 2011; Subramanian 2013).

Voxels or regions of interest identified via imaging

We did not perform meta-analysis for this outcome as the two studies including imaging studies as an outcome measure had small sample sizes (total of 20 participants for both studies) and compared virtual reality with no intervention (Jang 2005; You 2005). The variables in these studies were the laterality index and activated voxels. Jang 2005 reported that following intervention all participants in the intervention group showed significantly increased ipsilesional activation (measured by number of voxels activated) at the primary sensorimotor cortex area during affected elbow movement. You 2005 reported that in the primary sensorimotor cortex the laterality index in the virtual reality group showed a significant increase as a function of the intervention and in comparison to the control group who received no intervention.

Adverse events

Twelve studies monitored and reported on adverse events. Ten studies reported no significant adverse events (Byl 2013; Coupar 2012; Housman 2009; Jaffe 2004; Kiper 2011; Piron 2007; Piron 2010; Saposnik 2010; Subramanian 2013; Yavuzer 2008). Crosbie 2008 found that two people in the virtual reality group reported side effects of transient dizziness and headache, and Sucar 2009 found that three participants in the virtual reality group reported pain caused by the treatment in contrast to two participants in the conventional therapy group.

DISCUSSION

Summary of main results

This review included 37 trials with 1019 participants. The main results are presented in the 'Summary of findings' table (Summary of findings for the main comparison).

Upper limb function and activity

Twelve trials with 397 participants compared virtual reality intervention with conventional therapy and measured effects on upper limb function. These trials used 10 different virtual reality programs and all interventions were delivered in a hospital or clinic setting, with the exception of one trial that used a home-based telerehabilitation approach. The majority of trials recruited patients more than six months after stroke, with only three trials recruiting patients within the first six months of stroke. In addition, only one study included in the analysis evaluated the effects of a commercial gaming console.

Two trials compared virtual reality intervention with conventional therapy and measured hand function (using grip strength). However, there was considerable heterogeneity between these studies in regard to the time since onset of stroke in which patients were recruited, the dose of therapy and the type of intervention (specialised program compared with commercial gaming console).

We also examined the effect of a virtual reality intervention on upper limb function when the intervention was provided to augment the usual dose of therapy. Thus, the intervention group received more therapy time than the control group. Nine studies with 190 participants found a moderate significant effect in favour of the intervention. Seven of these studies involved the use of commercially available virtual reality programs and one of the studies provided the intervention in the home setting.

In summary, these studies showed that the addition of a virtual reality intervention to usual care resulted in improvements in upper limb function. Furthermore, a virtual reality intervention was a more effective approach than conventional interventions and achieved more improvement in upper limb function although the effect size was small. Results showed that there were benefits when the intervention was conducted in the first six months of stroke but not when conducted more than six months after stroke, suggesting that a virtual reality intervention is most useful in the subacute phase of rehabilitation. In addition, results suggested that higher doses of therapy (programs involving more than 15 hours of therapy) were more beneficial. We found insufficient evidence to draw conclusions on the effect of a virtual reality approach on grip strength.

Secondary outcomes

Three trials with 58 participants measured gait speed and could be included in the analysis. Two of these trials used treadmill training whereas the other study used a force feedback program designed to elicit improved movement and control at the ankle. Participants in the studies were more than one year post stroke. There was insufficient evidence to draw conclusions on whether a virtual reality approach was more effective in improving gait speed than conventional therapy. Three trials using the same virtual reality program measured global motor function. Two of these studies examined the effect of additional therapy (in the form of virtual reality intervention). However, the effect on global motor function was not significant. There was a small to moderate significant effect on ADL. We were unable to pool results for cognitive function, participation restriction and quality of life or imaging studies. There were few adverse events reported across studies and those reported (transient dizziness, headache, pain) were relatively mild.

Heterogeneity of included studies

There was considerable clinical heterogeneity between the studies included in the review, particularly in regard to the variety of intervention approaches used to address a variety of different patient needs. Some of these interventions were very specific (for example, retraining participants to use the local public transport system) and therefore studies were not comparable in many circumstances. In addition, a wide variety of outcome measures were used; this also limited our ability to pool results. The use of meta-analysis in cases where such heterogeneity is present can be considered controversial (Higgins 2011); however, we felt that meta-analysis in this review was justified and we were careful only to pool studies that were relatively comparable in terms of participants, interventions, comparison and outcome measures. Meta-analysis of the individual studies enabled us to explore the overall treatment effect of the intervention when compared with an alternative more traditional intervention or no intervention. Our sensitivity analyses suggested that there were no notable differences between using random-effects and fixed-effect models.

Overall completeness and applicability of evidence

Although we identified 37 studies, the sample sizes of the included studies were generally small. The studies included in our previous review predominantly recruited patients more than six months after stroke whereas in this review there are a larger number of studies recruiting patients within the first few months. Patients with cognitive impairment or communication or visual deficits were often excluded, thereby raising questions about how applicable this intervention is to a wide range of stroke survivors. Furthermore, the average age of participants in the included studies was relatively low, therefore, it is unclear how acceptable or effective this approach may be with older stroke survivors. Researchers involved in future studies should provide more detail in their reporting, ensuring they clearly describe their eligibility criteria, consent rate and the adherence and satisfaction of participants with the intervention. These details will be of interest to clinicians who will need to weigh up the cost of the virtual reality program with the potential benefits and the number of clients who may benefit from use.

In contrast to our previous review in which most of the virtual reality programs were specifically designed for rehabilitation purposes, this review has found a rise in the number of studies evaluating commercial gaming programs designed for the general population. Yet it remains difficult to examine the effects of game-based interventions as the approach and gaming consoles used vary. It seems that most studies are still at the level of testing feasibility (Thomson 2014).

Several trials reported on the presence or absence of adverse events. There were few events reported; the small number of events were mild and limited to dizziness, headache and pain.

Quality of the evidence

While we were able to include a relatively large number of studies in the review, sample sizes in the included studies were small and larger, adequately powered studies are required to confirm initial findings. The risk of bias present in many studies was unclear due to poor reporting and lack of clarification from study authors.

Approximately half of the studies reported adequate allocation concealment, and in four of the included studies it was unclear as to whether there was blinding of outcome assessors. Thus, while there are a large number of randomised controlled trials, the evidence remains 'low' or 'very low' quality when rated using the GRADE system.

Potential biases in the review process

While our search strategy was comprehensive, it is possible that some studies were not identified in the search process, for example studies where there is no published abstract in English. Whilst in the previous version of this review we contacted manufacturers of virtual reality equipment and searched conference proceedings, we opted not to do so in this update as this method was not previously effective in eliciting original studies. However, this does mean that unpublished data may not have been identified. Furthermore, although we contacted all corresponding authors of included studies, not all authors responded. This resulted in the study methodology of some trials being unclear (Cho 2012; Jang 2005; Jannink 2008; Jung 2012; Kang 2009; Kim 2011a; Kim 2011b; Kim 2012; Rajaratnam 2013; Yang 2008; You 2005), and resulted in us being unable to include some data in the analyses. The process of two review authors independently reviewing abstracts and extracting data (with a third review author to moderate disagreements) enabled us to minimise bias. The search date of this review was October 2013. As this field is rapidly expanding there are likely to be more studies now eligible for inclusion.

Agreements and disagreements with other studies or reviews

Previous systematic reviews have argued that virtual reality appears promising (Crosbie 2007; Lohse 2014; Moreira 2013; Saposnik 2011). This review is consistent with these reviews; however, due to the more recent and comprehensive search strategy we were able to identify a greater number of studies and conduct subgroup analyses. The findings in this update are consistent with the findings of our initial review although the updated effect sizes were smaller for upper limb function and ADL function. In addition, this review provided new information about the effectiveness of virtual reality when used as an adjunct to conventional rehabilitation.

AUTHORS' CONCLUSIONS

Implications for practice

We found low quality evidence that virtual reality is a safe intervention that is effective at improving arm function and activities of daily living (ADL) function following stroke. The evidence, albeit limited, suggests that improvements in function are greatest when a greater dose of therapy is delivered. In addition, it appears that patients with low to moderate upper limb impairment, and who are less than six months post stroke, may have the greatest benefit. Gains made appear to be clinically significant with analyses showing reasonable effect sizes (that is, a small effect on upper limb function (standardised mean difference (SMD) 0.29) and a small to moderate effect on ADL function (SMD 0.43)). However, at present, there is significant heterogeneity between studies. For example, there are only two studies that have examined the use of a virtual reality driving simulation program and thus it is unclear how effective virtual reality may be for driver rehabilitation after stroke. In addition, as virtual reality interventions may vary greatly (from inexpensive commercial gaming consoles to expensive customised programs), it is unclear which characteristics of the intervention are most important. Our analyses did not provide clear direction as to which virtual reality programs are superior to others. Studies that compare different configurations of virtual reality were excluded from this review but are now beginning to provide more information regarding the comparative effectiveness of different programs (Cameirao 2012; Fluet 2013).

Furthermore, the applicability of the intervention to stroke survivors needs further research in terms of which type of approach is best suited to the individual patient and how acceptable the technology may be to stroke survivors. Clinicians who currently have access to virtual reality programs should be reassured that their use as part of a comprehensive rehabilitation program appears reasonable, taking into account the patient's goals, abilities and preferences.

The lack of adverse events, including motion sickness, nausea, headache or pain, suggests that these factors should not be of great concern to clinicians; however, this may vary depending on the characteristics of the person, the virtual reality hardware and software and the task.

Implications for research

This updated version of the review revealed that 18 new randomised controlled trials (RCTs) were published over approximately three years. However, the sample sizes and methodological quality of the new RCTs mirror those included in the previous review. Researchers in this field are strongly encouraged to conduct larger, adequately powered trials that can provide more definitive results.

Researchers and manufacturers designing new virtual reality programs for rehabilitation purposes should include the use of pilot studies assessing usability and validity as part of the development process. This is an important part of the development process and should be conducted with the intended users of the program.

Our review included only RCTs, resulting in the exclusion of ob-

servational studies that showed improvements in real-world tasks based on virtual reality training. It is evident that the field is still developing and many studies are at feasibility and proof-of-concept levels. In addition, it is challenging to design a controlled trial comparing virtual reality to real-world correlates. This is in part because virtual reality systems allow us to train in ways that are not possible in the real world. Future research needs to carefully examine what we control for when comparing real-world with virtual reality-based interventions and overcome, when possible, the challenge of making groups equivalent.

Ideally, studies should use common outcome measures. However, this is likely to be difficult due to the range of virtual reality interventions. Studies should measure whether effects are long lasting with outcome assessment more than three months after the end of the intervention. Researchers should also examine the impact of virtual reality on the person's motivation to participate in rehabilitation, engagement in therapy and level of enjoyment.

Many of the studies included in this review did not report the number of participants screened against eligibility criteria. Future research trials should report these data as they provide useful information regarding the proportion of stroke survivors for whom virtual reality intervention may be appropriate.

The majority of studies to date have evaluated interventions that were designed to address motor impairments. There are few studies that include cognitive rehabilitation or studies that aim to make improvements at the levels of activity or participation. There is also currently insufficient evidence from RCTs to tell whether activity training in a virtual environment translates to activity performance in the real world.

One of the key potential advantages of using virtual reality programs is that they could be used without the need for direct therapist supervision. For example, they could be used alone in the home environment or in a group setting with supervision from therapy aids as a way of increasing therapy dose without increasing staffing. There are few research studies that have examined virtual reality interventions in this way, yet this is one of the most desirable characteristics of this approach.

ACKNOWLEDGEMENTS

We would like to thank Brenda Thomas for her help with the search strategies. We would like to thank Hazel Fraser, Alex Pollock, Gillian Mead and Richard Parker for their editorial review and recommendations.

We would also like to thank Abiodun Akinwuntan, Jacqueline Crosbie, Sarah Housman and David Reikensmeyer, David Jaffe, Sung You, David Man, Barbara Mazer, Anat Mirelman, Andrea Turolla and Lamberto Piron, Gustavo Saposnik, Enrique Sucar, Penny Standen, Min Cheol Chang, Nancy Byl, Paul Vershure, Joon-Ho Shin, Carla Zucconi, Pawel Kiper, Sandeep Subramanian and Mindy Levin who generously provided additional details and analyses from their trials to assist us with the review.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Akinwuntan 2005

Methods	RCT
Participants	Recruited from 1 rehabilitation unit in Belgium 83 participants: 42 intervention, 41 control Inclusion criteria: within 3 months of first stroke, actively driving before stroke, in possession of an active driver's licence Exclusion criteria: ≥ 75 years old, history of epilepsy within previous 6 months, severe motor or sensory aphasia Mean (SD) age: intervention group 54 (12) years, control group 54 (11) years 81% male Stroke details: 77% ischaemic, 44% right hemiparesis Timing post stroke: intervention group mean (SD) 53 (6) days, control group 54 (6) days
Interventions	Virtual reality intervention: driving simulator in full sized automatic gear transmission Ford Fiesta; a variety of 5 km driving scenarios were used including positioning on straight and curvy roads, stopping at crossings and avoiding pedestrians, overtaking and road sign recognition Control intervention: driving-related cognitive tasks: these included route finding on a paper map, recognition of road signs, commercially available games including 'rush hour' and 'tantrix' Sessions were 60 minutes, 3 times a week for 5 weeks (15 hours total)
Outcomes	Outcomes recorded at baseline, post-intervention and at 6 months with some participants followed up at 5 years Cognitive outcome measures: Useful Field of View Test Activity limitation outcome measures: on-road driving test (using Test Ride for Investigating Practical Fitness to Drive checklist), decision of fitness to drive, Barthel Index (assessed at baseline and 5 years only) Other outcome measures: binocular acuity, kinetic vision, components of the Stroke Driver Screening Assessment Other outcome measures assessed at baseline and 5 years only: Hospital Anxiety and Depression Scale, number of kilometres driven per year, number of self reported traffic tickets and accidents and driving status (actively driving or stopped driving)
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computerised number generation

Akinwuntan 2005 (*Continued*)

Allocation concealment (selection bias)	Low risk	Allocation managed by an independent person
Blinding of outcome assessment (detection bias) All outcomes	Low risk	
Incomplete outcome data (attrition bias) All outcomes	Low risk	A large amount of missing data due to the number of participants who withdrew (14% withdrew from their allocated intervention, 29% of participants were lost at 6-month follow-up); however, the authors completed an intention-to-treat analysis and found that drop out was random and balanced evenly across groups
Selective reporting (reporting bias)	Low risk	No other outcomes were collected

Barcala 2013

Methods	RCT
Participants	Recruited from the physical therapy clinic at a University in Brazil 20 participants: 10 intervention, 10 control Inclusion criteria: people after stroke receiving weekly physical therapy sessions at the University; able to sit unsupported; able to understand the visual biofeedback; absence of osteoarticular deformities Exclusion criteria: unspecified comorbidities Mean (SD) age: intervention group 65.2 (12.5), control group 63.5 (14.5) years 45% male Stroke details: 65% right hemiparesis Timing post stroke: intervention group mean (SD) 12.3 (7.1) months, control group 15.2 (6.6 months)
Interventions	Virtual reality intervention: conventional physical therapy plus an additional 30 minutes of balance training with visual feedback using three of the Nintendo Wii Fit program games Control intervention: convention physical therapy (stretching, joint movement, muscle strengthening, balance training, training of functional activities) Sessions were 2 times a week over 5 weeks. Conventional therapy lasted 60 minutes; the intervention sessions were an additional 30 minutes (approximately 5 hours duration of additional training in total)
Outcomes	Outcomes recorded at baseline and post intervention Gait outcomes: Timed Up and Go Test Balance outcomes: Berg Balance Scale, centre of pressure data, body symmetry Activity outcomes: Functional Independence Measure
Notes	-
Risk of bias	

Barcala 2013 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation table at central office
Allocation concealment (selection bias)	Low risk	Sealed, opaque envelopes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop outs
Selective reporting (reporting bias)	Unclear risk	No access to study protocol

Byl 2013

Methods	RCT
Participants	Recruited via the University of California, USA 15 participants completed the study: 5 intervention, 5 intervention, 5 control Inclusion criteria: stroke survivors more than 6 months post stroke between 25 and 75 years of age. Participants were independent in self care and independent in the community with minimal to moderate voluntary function in the upper limb (Upper Limb Fugl Meyer score 16 to 39). Participants needed to speak English or attend with an interpreter Exclusion criteria: people were excluded if they suffered from a neurological disease other than stroke, had co-morbidities that would impact on participation, were in severe pain, were not mentally alert or had a skin condition that would prevent wearing the robotic orthosis Mean (SD) age: intervention group 65.2 (5.4), control group 54.2 (20.5) Stroke details: 70% right hemiparesis Timing post stroke: intervention group 8.4 (4.2), control group 10.2 (5.0) months
Interventions	This trial had 3 arms: 2 of the intervention groups performed virtual reality tasks; 1 of the virtual reality groups performed bilateral tasks and the other group performed unilateral tasks Virtual reality intervention: the participant wore a robotic orthosis. Each session started with a motor control evaluation task and then followed with treatment in which participants performed repetitive movements while playing task-specific games Control intervention: repetitive task practice involved reaching, grasping, object manipulation and self care activities. Dynamic orthoses were not included in training Sessions were 90 minutes for 12 treatment sessions (approximately 18 hours total)
Outcomes	Outcomes recorded at baseline and post-intervention Upper limb function outcomes: Fugl Meyer, Motor Proficiency Speed (abbreviated Wolf Motor Function Test and Digital Reaction Time Test)

Byl 2013 (*Continued*)

	Hand function outcomes: motor skill performance (Box and Block test and Tapper test) Activity limitation outcomes: functional independence (CAFE40) Quality of life outcomes: Stroke Impact Scale
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated
Allocation concealment (selection bias)	Low risk	Allocated prospectively using a computer program
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	
Selective reporting (reporting bias)	Low risk	All outcomes reported

Cho 2012

Methods	RCT
Participants	Recruited from a hospital in Korea 29 participants: 15 intervention, 14 control Inclusion criteria: no virtual reality intervention in the previous 2 years, no surgery in the previous 2 months and no specific medical problems, including psychological problems Exclusion criteria: none described Mean (SD) age: intervention group 64 (7.1), control group 63.7 (8.8) 62% male Stroke details: 41% hemiparesis Timing post stroke: not reported
Interventions	Virtual reality intervention: the Interactive Rehabilitation and Exercise System (IREX) was used for training. The participant performed 6 programs; each program was performed for 5 minutes Control intervention: no intervention Sessions were 60 minutes, 5 times a week for 4 weeks (approximately 20 hours total)
Outcomes	Outcomes recorded at baseline and post-intervention Upper limb function outcomes: Wolf Motor Function Test Other outcomes: Motor Free Visual Perception Test

Cho 2012 (*Continued*)

Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Table of random sampling numbers
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	Withdrawals not clearly explained
Selective reporting (reporting bias)	Unclear risk	Protocol not publicly available

Coupar 2012

Methods	RCT
Participants	Recruited from a stroke unit in Glasgow, UK 12 participants: 4 high intensity intervention, 4 low intensity intervention, 4 control Inclusion criteria: ≥ 18 years with a clinical diagnosis of stroke and grade 1 to 4 on MRC scale of arm impairment. Medically stable and within 10 days post stroke. Able to give informed consent, understand and follow simple instruction and sitting balance sufficient to use the device safely Exclusion criteria: orthosis could not be fitted to the affected limb due to previous stroke or other condition, bone instability of affected upper limb, no functional use of affected upper limb due to previous stroke or other condition. Pronounced fixed contractures of affected upper limb, open skin lesions on affected upper limb; major sensory deficit of affected upper limb; shoulder instability or excessive pain; severe spasticity; severe spontaneous movements; confused or non-co-operative; isolation due to infection; visual, perceptual or cognitive problems precluding participation in study involvement or involvement in any other intervention study Mean (SD) age: high intensity intervention group 65 (14), low intensity 72 (10), control 59 (16) 66% male Stroke details: 42% right hemiparesis Timing post stroke: high intensity intervention 8 (1) days, low intensity 9 (2), control 8 (3)
Interventions	Virtual reality intervention: Low intensity: standard care plus Armeo®Spring arm orthosis and virtual reality games for arm rehabilitation used for 40 minutes per day, 3 days a week

Coupar 2012 (*Continued*)

	High intensity: standard care plus Armeo®Spring arm orthosis and virtual reality games for arm rehabilitation used for 60 minutes per day, 5 days a week Games included catching rain drops, picking apples and cleaning a cooker Control intervention: standard care including standard physiotherapy and occupational therapy targeted at arm recovery Sessions were for 2 weeks or until discharge from the stroke unit (whichever was soonest)
Outcomes	Outcomes recorded at baseline, completion of intervention and 3 months following completion Upper limb function: Action Research Arm Test, Fugl Meyer UE Activity restriction: Barthel Index Other outcomes related to feasibility, acceptability, safety, arm pain, perceived exhaustion and adverse events
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated sequence
Allocation concealment (selection bias)	Low risk	Sealed, numbered, opaque envelopes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded to allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Few withdrawals and balanced across groups for reasons not clearly related to the study
Selective reporting (reporting bias)	Low risk	All outcomes reported in thesis

Crosbie 2008

Methods	RCT
Participants	Recruited from 2 hospital stroke units and members of Stroke Association Clubs in Northern Ireland 18 participants: 9 intervention, 9 control Inclusion criteria: within 2 years of first stroke, medically stable, can follow 2-stage commands, score of $\geq$ 25 on the upper limb Motricity Index Exclusion criteria: mental score < 7/10, neglect (star cancellation < 48/52), comorbid conditions impacting on rehabilitation potential, cardiac pacemaker, severe arm pain reported on visual analogue scale Mean (SD) age: intervention group 56 (15) years, control group 65 (7) years 55% male

Crosbie 2008 (*Continued*)

	Stroke details: 39% right hemiparesis Timing post stroke: intervention group mean (SD) 10 (6) months, control group 12 (8) months
Interventions	Virtual reality intervention: the participant chooses from a variety of activities involving reaching and grasping of virtual objects at a variety of heights, speeds and with varied number of targets; the participant wears a head-mounted device and data glove Control intervention: therapy provided is based on the Bobath approach Sessions were 35 to 45 minutes, 3 times a week over 3 weeks (approximately 6 hours total)
Outcomes	Outcomes recorded at baseline, post-intervention and at 6 weeks Upper limb function and activity outcomes: Action Research Arm Test, Upper Limb Motricity Index Adverse events were reported Other outcome measures: an exit questionnaire including questions about enjoyment and perception of improvement
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	An independent colleague generated the sequence using a computer random number generator
Allocation concealment (selection bias)	Low risk	Group allocation cards were concealed in sealed, opaque envelopes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Masked to allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	An intention-to treat analysis was completed. Missing data points were dealt with using the simple mean imputation method
Selective reporting (reporting bias)	Low risk	No other outcomes were collected

da Silva Cameirao 2011

Methods	RCT
Participants	Recruited from a subacute rehabilitation unit in Spain 19 participants: 13 intervention, 6 control Inclusion criteria: recruited within 3 weeks of first stroke, severe to moderate upper limb impairment, no moderate to severe aphasia, not other cognitive deficits as assessed by the Mini Mental State Examination and aged $\leq$ 80 years

	Exclusion criteria: none specified Mean (SD) age: intervention group 63.7 (11.83), control group 59.4 (10.62), control group (Wii) 58 (14) 47% male Stroke details: 37% right hemiparesis Timing post stroke: intervention group mean (SD) 11.5 (5.1) days, control group 16.8 (5.0) days, control group (Wii) 13 (4.7) days
Interventions	Virtual reality intervention: Rehabilitation Gaming System (RGS). The main elements of the system are the vision based analysis and tracking system that capture upper limb movements through colour detection, data gloves to capture finger flexion and a virtual environment where an avatar mimics the movements of the user Control intervention (occupational therapy): occupational therapy with emphasis on motor tasks similar to those in the RGS (i.e. object displacement, grasp and release) Control intervention (Wii): used the Wii gaming system. This intervention involved the gaming features but not the neuro-scientific hypothesis regarding recovery Sessions were 20 minutes, 3 times a week for 12 weeks (approximately 12 hours total). This was provided in addition to standard rehabilitation
Outcomes	Outcomes recorded at baseline, weeks 5, 12 and 24 Upper limb outcomes: Fugl Meyer, Chedoke Arm and Hand Activity Inventory Activity outcomes: Barthel Index Other outcomes: participant satisfaction
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated program
Allocation concealment (selection bias)	Low risk	Managed externally
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded to allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	Outliers excluded from the data analysis
Selective reporting (reporting bias)	Low risk	All outcomes reported

Housman 2009

Methods	RCT
Participants	Recruited from 1 rehabilitation institute in Chicago, USA 34 participants: 17 intervention, 17 control Inclusion criteria: single stroke ≥ 6 months ago, Fugl Meyer UE score 10 to 30 Exclusion criteria: significant pain or instability of the shoulder, current participation in upper limb therapy program, severe cognitive dysfunction, aphasia, neglect, apraxia Mean (SD) age: intervention group 54 (12) years, control group 56 (13) years 64% male Stroke details: 61% ischaemic, 29% right hemiparesis Timing post stroke: intervention group mean (SD) 85 (96) months, control group 112 (129) months
Interventions	Virtual reality intervention: a custom-designed software package ('Vu Therapy') provided activities including grocery shopping, cleaning a stove and playing basketball. The participant wore an arm orthosis (T-WREX), which supports the weight of the arm allowing movement in the horizontal and vertical plane. Position sensors at each joint enable interaction with the virtual environment Control intervention: upper extremity exercises including passive and active ranging, stretching, strengthening and using the arm in functional tasks Both groups involved 3 sessions of direct training followed by semi-autonomous practice in the research clinic Sessions were 60 minutes, approximately 3 times per week for 6 weeks (approximately 24 hours total)
Outcomes	Outcomes recorded at baseline, post-intervention and at 6 months Upper limb function and activity outcomes: Fugl Meyer UE Scale, Rancho Functional test UE, Reaching ROM (deficit) Hand function and activity: grip strength (dynamometer) Participation restriction and quality of life: Motor Activity Log (amount of use and quality of movement) Adverse events reported
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants were randomly assigned using a lottery system in which the supervising therapist (with an independent witness) drew a labelled tile from an opaque container. Randomisation occurred in blocks of 4 to ensure equal numbers in each group
Allocation concealment (selection bias)	High risk	Participants were allocated in strict sequential order of enrolment. However, with small blocks of 4 and the use of tiles it might have been possible to predict allocation in advance in some cases

Blinding of outcome assessment (detection bias) All outcomes	Low risk	
Incomplete outcome data (attrition bias) All outcomes	Low risk	Small number of drop outs balanced across groups with similar reasons for drop out
Selective reporting (reporting bias)	Low risk	No other outcomes were collected

Jaffe 2004

Methods	RCT
Participants	Recruited from community stroke association meetings in California, USA 20 participants: 10 intervention, 10 control Inclusion criteria: more than 6 months post stroke with a diagnosis of hemiplegia secondary to single documented lesion, walks independently or with an aid and has an asymmetric gait pattern and short step-length with either step (< 95th percentile of normal step length), scores representing average or minimally impaired in all Cognistat categories unless performance was markedly limited by aphasia making assessment of cognition difficult Exclusion criteria: neurological diagnoses of spinal cord injury, multiple sclerosis or brainstem lesion; any progressive critical or long-term illness or unstable cardiovascular, orthopaedic, musculoskeletal or neurological condition that would preclude exercise or is not controlled by medication or requires oxygen during ambulation Mean (SD) age: intervention group 58 (11) years, control group 63 (8) years 60% male Stroke details: 50% right hemiparesis Timing post stroke: intervention group 4 years (SD 2), control group 4 years (SD 3)
Interventions	Virtual reality intervention: participants walked on a treadmill at a self selected walking speed and were secured by an overhead harness. The participant wore a head-mounted display that showed real-time video images of their feet walking and virtual objects. The participant was asked to step over the virtual objects and visual, vibrotactile and auditory feedback was provided during any collisions Control intervention: participants wore a gait belt and stepped over foam obstacles in a hallway. The sessions were videotaped and reviewed for collisions with the obstacles after the session was completed Sessions were approximately 60 minutes, for 6 sessions over 2 weeks (6 hours total)
Outcomes	Outcomes recorded at baseline, post-intervention and 2 weeks post-intervention Lower limb function and activity outcomes: 6-metre walk test, obstacle test, 6-minute walk test, the researcher's own balance test (adapted from others) that included natural stance, eyes close, on toes, tandem stance, left and right leg stand Adverse events reported
Notes	-

Jaffe 2004 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	An Excel spreadsheet was generated with a pre-determined computerised randomisation sequence
Allocation concealment (selection bias)	High risk	The allocation in the spreadsheet was not visible due to black font and black background shading; however, there is the possibility that staff with access to the spreadsheet could have checked this
Blinding of outcome assessment (detection bias) All outcomes	Low risk	
Incomplete outcome data (attrition bias) All outcomes	Low risk	No outcome data were missing (according to personal correspondence with the researcher)
Selective reporting (reporting bias)	Unclear risk	Unclear - not privy to protocol

Jang 2005

Methods	RCT
Participants	Study took place in Korea 10 participants: 5 intervention, 5 control Inclusion criteria: > 6 months post first stroke, able to move the elbow against gravity Exclusion criteria: severe spasticity (Modified Ashworth Score of > 2) or tremor. Severe visual and cognitive impairments Mean (SD) age: intervention group 60 (8) years, control group 54 (12) years 60% male Stroke details: 60% ischaemic, 50% right hemiparesis Timing post stroke: intervention group 14 months, control group 13 months
Interventions	Virtual reality intervention: IREX virtual reality system using a video capture system to capture the participant's whole body movement. The participant is able to view their body movements in real time on a screen in front of them immersed in a virtual environment. The games included soccer and moving objects from a conveyor belt and focused on reaching, lifting and grasping Control intervention: no intervention provided Sessions for the virtual reality intervention group were 60 minutes, 5 times per week for 4 weeks (20 hours total)
Outcomes	Outcomes recorded at baseline and post-intervention Upper limb (arm) function and activity outcomes: Fugl Meyer UE Scale, Manual Function Test Upper limb (hand) function and activity outcomes: Box and Block Test Participation restriction and quality of life: Motor Activity Log (amount of use and

Jang 2005 (*Continued*)

	quality of movement) Other outcomes: functional MRI (laterality index and activated voxels)
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear
Allocation concealment (selection bias)	Unclear risk	Unclear
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear
Selective reporting (reporting bias)	Unclear risk	Unclear

Jannink 2008

Methods	RCT
Participants	Recruited from a rehabilitation centre in the Netherlands 10 participants: 5 intervention, 5 control Inclusion criteria: not reported Exclusion criteria: not reported Mean (SD) age: intervention group 62 (3) years, control group 58 (13) years Timing post stroke: intervention group mean (SD) 89 days (31), control group 112 days (50)
Interventions	Virtual reality intervention: the participant sat on an electric scooter with customised interface and completed training in a traffic garden, residential area and a grocery store. The virtual environment was displayed using a head-mounted device as well as a computer display. Training included 50% of the time using the virtual reality simulation program and 50% training in the real world Control intervention: real-world scooter training program Sessions were 30 minutes, 2 times per week for 5 weeks (5 hours total)
Outcomes	Outcomes recorded at baseline and 5 weeks after training Other outcome measures: Functional Evaluation Rating Scale, Subjective Experience Questionnaire
Notes	-

Jannink 2008 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Unclear
Allocation concealment (selection bias)	Unclear risk	Unclear
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear
Selective reporting (reporting bias)	Unclear risk	Unclear

Jung 2012

Methods	RCT
Participants	Recruited from outpatient community centre in Korea 21 participants: 11 intervention, 10 control Inclusion criteria: participants within 6 months after first stroke with a history of falling. Able to walk independently for more than 30 minutes with no cognitive impairment, Brunnstrom Stage > 4 and no cardiovascular, orthopaedic or other neurological conditions that may interfere with study procedures Exclusion criteria: not reported Mean (SD) age: intervention group 60.5 (8.6), control group 63.6 (5.1) 62% male Stroke details: 52% right-sided hemiparesis Timing post stroke: intervention group mean (SD) 12.6 (3.3) months, control group 15.4 (4.7) months
Interventions	Virtual reality intervention: treadmill training while viewing a virtual scene through a head mounted device. The virtual reality program simulated a park stroll Control intervention: treadmill training without the virtual reality program Sessions were 30 minutes a day, 5 times a week for 3 weeks (approximately 7.5 hours total)
Outcomes	Outcomes recorded at baseline and post-intervention Gait outcomes: Timed Up and Go Test Other outcomes: Activity Specific Balance Confidence Scale
Notes	-
Risk of bias	

Jung 2012 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Drawing lots
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded assessment
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear
Selective reporting (reporting bias)	Unclear risk	Unclear

Kang 2009

Methods	RCT
Participants	Study took place in Korea 16 participants: 8 intervention, 8 control Inclusion criteria: left hemiplegia after stroke, Mini Mental State Examination score of > 18/30 and Motor Free Visual Perception Test standard score < 109 Exclusion criteria: significant multiple small lacunar infarct, significantly decreased visual acuity or visual impairment from diabetic retinopathy or senile cataract, hearing difficulty or cranial nerve dysfunction Mean (SD) age: intervention group 60 (11) years, control group 63 (10) years Timing post stroke: intervention group mean (SD) 64 (37) days, control group 58 (30) days
Interventions	Virtual reality intervention: participants were seated and participated in visual spatial and motor tasks using their unaffected arm. Software recognised and displayed the movements of the hand through a camera and displayed the images on a computer screen Control intervention: training using the PSS CogRehab program Sessions were 30 minutes, 3 times per week for 4 weeks (6 hours total)
Outcomes	Outcomes recorded at baseline and post-intervention Cognitive outcome measures: Mini Mental State Examination Activity limitation outcomes: Modified Barthel Index Other outcome measures: motor free visual perception test, interest in performing the task
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement

Kang 2009 (*Continued*)

Random sequence generation (selection bias)	Low risk	Random allocation using block randomisation process. Envelopes were shuffled and the participant drew 1 after enrolment
Allocation concealment (selection bias)	Unclear risk	Whether the envelopes were opaque is unclear
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	There does not appear to be any attrition and all outcome measures appear to be reported in full
Selective reporting (reporting bias)	Unclear risk	Unclear - not privy to protocol

Kim 2009

Methods	RCT
Participants	Study took place in Korea 24 participants: 12 intervention, 12 control Inclusion criteria: ≥ 1 year post stroke with plateau in motor recovery after conventional rehabilitation and the ability to stand for 30 minutes and walk indoors independently (approximately 30 metres) Exclusion criteria: severe visual or cognitive impairment or musculoskeletal disorders that could interfere with tests Mean (SD) age: intervention group 52 (10) years, control group 52 (7) years 54% male Timing post stroke: intervention group mean (SD) 26 (10) months, control group 24 (9) months
Interventions	Virtual reality intervention: IREX virtual reality system using a video capture system to capture the participant's whole body movement. The participant is able to view their body movements in real time on a screen in front of them immersed in a virtual environment. Games included stepping up/down, shark bait (capturing stars while avoiding eels and sharks by weight shift) and snowboarding. Participants were challenged by increasing resistance (e.g. adding weights) or increasing the speed Control intervention: conventional physiotherapy designed to facilitate standing balance function during walking. Included practice of weight shift, muscle strengthening, functional reach or picking up objects Sessions for virtual reality group: 30 minutes, 4 times a week for 4 weeks (8 hours) of virtual reality plus conventional physiotherapy 40 minutes, 4 times per week for 4 weeks (approximately 10.5 hours) (approximately 18.5 hours total) Sessions for control group: 40 minutes, 4 times per week for 4 weeks (approximately 10.5 hours total)
Outcomes	Outcomes recorded at baseline and post-intervention Lower limb function and activity outcomes: 10-metre walk test, GAIT-RITE gait analysis system, Berg balance scale, Balance performance monitor

Kim 2009 (*Continued*)

	Global motor function outcomes: modified Motor Assessment Scale	
Notes	-	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	The sequence was generated using a lottery system
Allocation concealment (selection bias)	Low risk	Using sealed, opaque envelopes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	Does not appear to have any missing data
Selective reporting (reporting bias)	Low risk	No other outcomes were collected

Kim 2011a

Methods	RCT
Participants	Recruited from a rehabilitation hospital in Korea 28 participants: 15 intervention, 13 control Inclusion criteria: not stated Exclusion criteria: people with a MMSE-K score of less than 10; people presenting with severe cognitive impairment of aphasia and unable to understand instructions. People with poor sitting balance such that they could not sit on a chair with back and armrests. People with limited range of motion of the neck due to orthopaedic problems, and people with loss of visual acuity such that they could not perceive content on a computer screen Mean (SD) age: intervention group 66.5 (11) years, control group 62 (15.8) years 39% male Stroke details: 39% right hemiparesis Timing post stroke: intervention group mean (SD) 18.2 (11.3) days, control group 24 (31.1) days
Interventions	Virtual reality intervention: IREX system (30 minutes 3 times a week) plus computer-assisted cognitive rehabilitation (30 minutes 2 times a week) Control intervention: computer-assisted rehabilitation (30 minutes 5 times a week) Sessions were 30 minutes, 5 times a week over 4 weeks (approximately 6 hours of virtual reality in total)
Outcomes	Outcomes recorded at baseline and post-intervention Upper limb function outcomes: Motricity index Lower limb function outcomes: Motricity index

Kim 2011a (*Continued*)

	Cognitive function: computerised neuropsychological test and Tower of London test Activity limitation outcome: Korean modified Barthel Index
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No withdrawals
Selective reporting (reporting bias)	Low risk	No other outcome data collected

Kim 2011b

Methods	RCT
Participants	Recruited from a Department of Rehabilitation, Korea 24 participants: 12 intervention, 12 control Inclusion criteria: participants diagnosed with unilateral spatial neglect through the line bisection test or star cancellation test Exclusion criteria: severe cognitive impairment or aphasia. Patients with insufficient sitting balance to sit on a chair with a back and armrests. Patients with restricted neck movement, poor eyesight or unable to recognise objects on a screen Mean (SD) age: intervention group 62.3 (10.2) years, control group 67.2 (13.9) years 58% male Timing post stroke: intervention group 22.8 (7.6) days, control group 25.5 (18.5) days
Interventions	Virtual reality intervention: IREX Control intervention: conventional rehabilitation tasks such as visual tracking, reading and writing, drawing and puzzles Sessions were 30 minutes, 5 days a week for 3 weeks (approximately 7.5 hours total)
Outcomes	Outcomes recorded at baseline and post-intervention Activity limitation outcomes: Korean Modified Barthel Index Other outcomes: Star cancellation test, Line bisection test, Catherine Bergego Scale
Notes	-

Kim 2011b (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded to allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	No withdrawals
Selective reporting (reporting bias)	Low risk	No other outcome data collected

Kim 2012

Methods	RCT
Participants	Recruited from an inpatient setting in Korea 20 participants: 10 intervention, 10 control Inclusion criteria: more than 6 months post diagnosis of stroke. Score of ≥ 19/30 on the Mini Mental State Examination. Able to maintain upright posture without any assistance Exclusion criteria: orthopaedic surgery, history of arthritis, hand or upper limb pain, epilepsy, psychiatric illnesses Mean age: not reported Timing post stroke: intervention group mean (SD) 12.6 (7.12) months, control group 12.85 (6.06) months
Interventions	Virtual reality intervention: Nintendo Wii Sports (boxing and tennis) Control intervention: no intervention Sessions were 30 minutes, 3 times a week for 3 weeks
Outcomes	Outcomes recorded at baseline and post-intervention Gait outcomes: postural assessment scale Global motor function outcomes: modified Motor Assessment Scale Activity limitation outcomes: Functional Independence Measure
Notes	-

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

Kim 2012 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported in adequate detail to make judgement
Selective reporting (reporting bias)	Unclear risk	No access to protocol

Kiper 2011

Methods	RCT
Participants	Recruited from an Institute of Rehabilitation, Italy 80 participants: 40 intervention, 40 control Inclusion criteria: diagnosis of stroke within 1 year of enrolment and score of > 24/30 on the Mini Mental State Examination Exclusion criteria: clinical evidence of cognitive impairment, apraxia, neglect, language disturbance, complete paralysis of the upper extremity, upper limb sensory disorders or post-traumatic injury, which prevented the execution of exercises Mean (SD) age: 64 (16.4) years 58% male Time since onset of stroke: mean (SD) 5.7 (3.5) months
Interventions	Virtual reality intervention: reinforced feedback in virtual environment (RFVE). Participants in the intervention group received 1 hour of traditional rehabilitation and 1 hour of RFVE. The RFVE involved sitting in front of a wall screen grasping a sensorised real object (ball, disc or cube) with the affected hand. The target objects were displayed on the wall screen. The physiotherapist created a sequence of virtual tasks that the participant had to perform on his workstation (e.g. pouring water from a glass, using a hammer) Control intervention: traditional neuromotor rehabilitation including postural control, exercises for hand pre-configuration, manipulative and functional skills, proximal-distal exercises Sessions were 1 hour a day, 5 days a week for 4 weeks (approximately 20 hours total)
Outcomes	Outcomes recorded at baseline and post-intervention Upper limb function outcomes: Fugl Meyer Activity limitation outcomes: Functional Independence Measure Other outcomes: Modified Ashworth Scale (spasticity)
Notes	-
Risk of bias	

Kiper 2011 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated sequence
Allocation concealment (selection bias)	Low risk	Opaque envelopes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Masked to allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop outs
Selective reporting (reporting bias)	Low risk	

Kwon 2012

Methods	RCT
Participants	Recruited from a hospital in Korea 26 participants: 13 intervention, 13 control Inclusion criteria: adults within 3 months of stroke with the capacity to understand and follow simple instructions. Able to grasp and release affected hand, with manual muscle test grade of 3 or more. Able to maintain standing or sitting position independently and no visual deficit Exclusion criteria: failure to meet above criteria Mean (SD) age: intervention group 57.15 (15.42), control group 57.92 (12.32) Timing post stroke: intervention group mean (SD) 24.69 (15.59) days, control group 23.92 (20.70) days
Interventions	Virtual reality intervention: conventional therapy plus additional therapy time using IREX Control intervention: conventional therapy alone Sessions were 30 minutes, 5 days a week for 4 weeks
Outcomes	Outcomes recorded at baseline and post-intervention Upper limb function outcomes: Fugl Meyer, Manual Function Test Activity limitation outcomes: Modified Barthel (Korean)
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported

Kwon 2012 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded to allocation
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported in adequate detail to make judgement
Selective reporting (reporting bias)	Unclear risk	Protocol not available

Lam 2006

Methods	RCT
Participants	Recruited from rehabilitation units in Hong Kong 58 participants: 20 virtual reality, 16 video-based program, 22 no treatment Inclusion criteria: 50 to 85 years old, medically stable with no previous psychiatric history, able to follow simple instructions and write with a pen in Chinese or English, consistent volitional motor response, good visual tracking, discrimination ability and figure ground skills, sustained attention span of at least 10 minutes Exclusion criteria: computer-related phobia or previous training in Mass Transit Railway Skills Mean (SD) age: virtual reality group 71 (16) years, video-based program group 71 (15) years, no treatment group 73 (10) years 31% male Timing post stroke: virtual reality group mean (SD) 4 (4) years, video-based program group 3 (3) years, no treatment group 5 (3) years
Interventions	Virtual reality intervention: a virtual reality program designed to retrain skills using the Mass Transit Railway. Activities included crossing the road and using the facilities at the station Video based program intervention: a video-based program included instruction, modelling, demonstration, role playing, coaching and feedback on using the Mass Transit Railway No treatment group: no treatment 10 sessions of unspecified duration were provided for the participants in the virtual reality and video program group
Outcomes	Outcomes recorded at baseline and post-intervention Other outcomes: behavioural rating scale, Mass Transit Railway Self Efficacy Scale
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Lam 2006 (*Continued*)

Random sequence generation (selection bias)	Low risk	Participants were randomly allocated into 2 groups using a statistical package random number generator tool
Allocation concealment (selection bias)	Low risk	Allocation was computer-generated
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no missing data
Selective reporting (reporting bias)	Low risk	No other outcomes were collected

Mazer 2005

Methods	RCT
Participants	Recruited from a rehabilitation hospital in Quebec, 2 driving evaluation centres in Montreal and from a private driving evaluation clinic 39 participants: 20 intervention, 19 control Inclusion criteria (for stroke participants): people with a diagnosis of stroke that did not pass the driving tests at a recognised driving evaluation service. Had licence to drive and were driving prior to the stroke and desire to return to driving Exclusion criteria: medical condition precluding driving (for example, hemianopia, seizures), received their driving evaluation more than 2 years post diagnosis, unable to communicate in English or French, inadequate communication of basic verbal instructions or judged as dangerous by the therapist in the on-road evaluation Mean (SD) age: intervention group 68 (14) years, control group 69 (9) years Stroke details: 31% right hemiparesis Timing post stroke: intervention group mean (SD) 1.4 (1) years, control group 1.7 (1) years
Interventions	Virtual reality intervention: driving simulator. Simulator is a car frame with 3 large screens providing a large field of view. Participants were progressed through 4 increasingly complex scenarios. In level 1, participants were familiarised with the simulator and controls; level 2 involved a simulated road circuit without traffic; level 3 focused on performing different driving manoeuvres and level 4 involved a variety of traffic conditions (for example, rain, wind, reduced visibility, pedestrians). Instant feedback was provided by the simulator when errors were made Control intervention: no intervention provided Sessions were 60 minutes, 2 times a week for 8 weeks (16 hours total)
Outcomes	Outcomes recorded at baseline and post-intervention (or after 8 weeks for the control group) Activity limitation outcomes: DriveAble Testing Ltd Driver Evaluation

Mazer 2005 (*Continued*)

Notes	Note that this study also recruited 6 participants with traumatic brain injury. However, data for participants with stroke were able to be separated. This review reports on the stroke data only

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Used a computer program to generate
Allocation concealment (selection bias)	Low risk	Opaque, sealed envelopes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	7 participants (5 control group, 2 simulator group) did not complete the outcome evaluation and were therefore considered to have dropped out from the study. Analysis was completed based on the actual number of participants contributing data. Intention-to-treat analyses were conducted
Selective reporting (reporting bias)	Low risk	No other outcomes were collected

Mirelman 2008

Methods	RCT
Participants	Study took place in New Jersey, USA 18 participants: 9 intervention, 9 control Inclusion criteria: chronic hemiparesis after stroke with residual gait deficits, partial antigravity dorsiflexion, able to walk 50 feet without the assistance of another person, sufficient communication and cognitive ability to participate Exclusion criteria: motion sickness and receiving concurrent therapy Mean (SD) age: intervention group 62 (10) years, control group 61 (8) years 83% male Stroke details: 44% right hemiparesis Timing post stroke: intervention group mean (SD) 38 (25) months, control group 58 (26) months
Interventions	Virtual reality intervention: Rutgers ankle rehabilitation system (a 6 degree of freedom platform force-feedback system) that allows participants to exercise the lower extremity by navigating through a virtual environment displayed on a desktop computer. Participants executed the exercises by using the foot movements to navigate a plane or a boat through a virtual environment that consisted of a series of targets Control intervention: Rutgers ankle rehabilitation system without the virtual environment. Participants were instructed by the therapist on which direction to move their

Mirelman 2008 (*Continued*)

	foot and were paced by a metronome cueing them to complete a comparable number of repetitions Sessions were 60 minutes, 3 times a week for 4 weeks (12 hours total)
Outcomes	Outcomes recorded at baseline, post-intervention and at 3 months Lower limb function and activity outcomes: gait speed over 7-metre walkway, 6-minute walk test, Patient Activity Monitor (distance walked, number of steps per day, average speed, step length, top speed)
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomisation was performed based on the table of numbers method (generated by a computer)
Allocation concealment (selection bias)	Low risk	Allocation was done by an external person to the project and held in a database spreadsheet on a computer in his office which was password protected
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 participant in the robotic-virtual reality group was lost to follow-up because of personal reasons. 1 outlier was identified in the robotic-virtual reality group following the descriptive analysis of the endurance test (6MWT), the values presented for this individual were 2 SD from the mean therefore he was excluded from the analysis
Selective reporting (reporting bias)	Low risk	No other outcomes were collected

Piron 2007

Methods	RCT
Participants	Study took place in Italy 38 participants: 25 intervention, 13 control Inclusion criteria: mild-intermediate arm motor impairment due to ischaemic stroke in the MCA territory within the past 3 months Exclusion criteria: cognitive impairment, neglect, apraxia, aphasia interfering with comprehension Mean (SD) age: intervention group 62 (9) years, control group 61 (7) years 66% male Timing post stroke: intervention group mean (SD) 2.5 (1.5) months, control group 2.

Piron 2007 (*Continued*)

	6 (1.6) months
Interventions	Virtual reality intervention: magnetic receivers were positioned on the participant's arm. As the participant grasped and moved real objects, software created a virtual environment which displayed virtual handling and target objects, for example an envelope and a mailbox, a hammer and a nail, a glass and a carafe. While performing the virtual tasks such as putting the envelope in the mailbox the participant moves the real envelope and sees on screen the trajectory of the corresponding virtual objects toward the virtual mailbox. Participants could see not only their own movement but also the correct trajectory that they had to execute, pre-recorded by the therapist. This allowed participants to easily perceive motion errors and adjust them during the task Control intervention: 'conventional' rehabilitation focused on the upper limb Sessions were 60 minutes, 5 times a week for 5 to 7 weeks (approximately 25 to 35 hours total)
Outcomes	Outcomes recorded at baseline and post-intervention Upper limb function and activity outcomes (arm): Fugl Meyer UE Scale Activity limitation outcomes: Functional Independence Measure Adverse events reported
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Personal correspondence with the author reports the use of a simple computer-generated sequence
Allocation concealment (selection bias)	Low risk	Sealed, opaque envelopes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blind
Incomplete outcome data (attrition bias) All outcomes	High risk	There were 3 drop outs from the control group and the analysis was per-protocol
Selective reporting (reporting bias)	Low risk	No other outcomes were collected

Piron 2009

Methods	RCT
Participants	Study took place in Italy 36 participants: 18 intervention, 18 control Inclusion criteria: single ischaemic stroke in the MCA region with mild to intermediate arm motor impairment (Fugl Meyer UE score 30 to 55)

	Exclusion criteria: clinical evidence of cognitive impairment, apraxia (< 62 points on the 'De Renzi' test), neglect or language disturbance interfering with verbal comprehension (> 40 errors on the Token test) Mean (SD) age: intervention group 66 (8) years, control group 64 (8) years 58% male Stroke details: 44% right hemiparesis Timing post stroke: intervention group mean (SD) 15 (7) months, control group 12 (4) months
Interventions	Virtual reality intervention: the telerehabilitation program used 1 computer workstation at the participant's home and 1 at the rehabilitation hospital. The system used a 3D motion tracking system to record arm movements through a magnetic receiver into a virtual image. The participant moved a real object following the trajectory of a virtual object displayed on the screen in accordance with the requested virtual task. 5 virtual tasks comprising simple arm movements were devised for training Control intervention: specific exercises for the upper limb with progressive complexity. Started with control of isolated movements without postural control, then postural control including touching different targets and manipulating objects Sessions were 60 minutes, 5 times per week for 4 weeks (20 hours total)
Outcomes	Outcomes recorded at baseline, post-intervention and at 1 month Upper limb function and activity outcomes (arm): Fugl Meyer UE Scale Participation restriction and quality of life outcomes: Abilhand scale Other outcome measures: Modified Ashworth Scale
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Personal correspondence with the author reports the use of a simple computer-generated sequence
Allocation concealment (selection bias)	Low risk	Opaque, sequentially numbered envelopes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no missing data
Selective reporting (reporting bias)	Low risk	No other outcomes were collected

Piron 2010

Methods	RCT
Participants	Recruited from a rehabilitation hospital in Rome, Italy 50 participants: 27 intervention, 23 control Inclusion criteria: single ischaemic stroke in the MCA territory > 6 months ago demonstrated by CT or MRI, received conventional physiotherapy early after stroke, mild to intermediate motor impairments of the arm (score of 20 to 60 on the Fugl Meyer UE Scale) Exclusion criteria: clinical history or evidence of cognitive impairments, neglect, apraxia or aphasia interfering with verbal comprehension Mean (SD) age: intervention group 59 (8) years, control group 62 (10) years 58% male Stroke details: 58% right hemiparesis Timing post stroke: intervention group mean 15 (13) months, control group 15 (12) months
Interventions	Virtual reality intervention: participants were asked to perform motor tasks with real objects (for example an envelope or a glass), which were displayed as tasks within the virtual environment (for example putting an envelope in the mailbox, breaking eggs, moving a glass over a table, placing a ball in a basket). A 3D magnetic receiver was used to record the motions. Participants were asked to emulate the tasks as per the therapist's pre-recorded movement Control intervention: participants were asked to perform specific exercises for the arm, for example touching different targets, manipulating objects and following trajectories on a plan Sessions were 60 minutes, 5 times a week for 4 weeks (20 hours total)
Outcomes	Outcomes recorded at baseline and post-intervention Upper limb function and activity outcomes (arm): Fugl Meyer UE Scale Activity limitation outcomes: Functional Independence Measure Adverse events reported
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Personal correspondence with the author reports the use of a simple computer-generated sequence
Allocation concealment (selection bias)	Low risk	Sequentially numbered, opaque, sealed envelopes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	Intention-to-treat analysis was completed. In the case of missing data the authors used a 'best, worst and likely' approach to data imputation. There was a small amount of attrition and the

Piron 2010 (*Continued*)

		reasons for this were reported
Selective reporting (reporting bias)	Low risk	No other outcomes were collected

Rajaratnam 2013

Methods	RCT
Participants	Recruited from a community rehabilitation hospital in Singapore 19 participants: 10 intervention, 9 control Inclusion criteria: recent first stroke with moderate or moderate-severe disability (Modified Rankin Scale Grade 3 or 4) Participants were haemodynamically stable and had a Mini Mental State Examination score of > 23 Exclusion criteria: terminal illness, uncontrolled hypertension and angina and severe spatial neglect or visual impairments Mean (SD) age: intervention group 58.67 (8.62), control group 65.33 (9.59) years 37 % male Stroke details: 42% right hemiparesis Timing post stroke: intervention group mean (SD) 14.7 (7.5) days, control group 15.2 (6.3) days
Interventions	Virtual reality intervention: used either a Nintendo Wii Fit or Microsoft Kinect program during rehabilitation. The Nintendo Wii Fit was performed in standing and the Kinect was performed in sitting and standing. Sessions involved 40 minutes of conventional therapy and 20 minutes of virtual reality Control intervention: conventional therapy (not described). Sessions involved 60 minutes of conventional therapy Sessions were 60 minutes for 15 sessions (approximately 15 hours)
Outcomes	Outcomes recorded at baseline and post-intervention Gait outcomes: Timed Up and Go Test Balance function: Berg Balance Scale, Functional Reach Test, centre of pressure
Notes	Activity limitation outcomes: Modified Barthel Index

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blind

Rajaratnam 2013 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unable to ascertain
Selective reporting (reporting bias)	Unclear risk	Unclear

Saposnik 2010

Methods	RCT
Participants	Recruited from a subacute rehabilitation facility in Toronto, Canada 22 participants: 11 intervention, 11 control Inclusion criteria: 18 to 85 years old with first time ischaemic or haemorrhagic stroke within the last 6 months, Chedoke McMaster scale (UE) score of > 3 in the arm or hand Exclusion criteria: unable to follow instructions, pre-stroke Modified Rankin Score of ≥ 2, medically unstable or with uncontrolled hypertension, severe illness with life expectancy of < 3 months, unstable angina, recent MI (within 3 months), history of seizures or epilepsy, participating in another clinical trial involving an investigational drug or physical therapy, any condition that might put the patient at risk (for example, known shoulder subluxation) Mean age: intervention group 55 years, control group 67 years 64% male Stroke details: 45% right hemiparesis Timing post stroke: intervention group mean (SD) 27 (16) days, control group 23 (9) days
Interventions	Virtual reality intervention: participants used the Nintendo Wii gaming console playing 'Wii sports' and 'Cooking Mama' Control intervention: leisure activities including cards, bingo and jenga Sessions were 60 minutes for 8 sessions (8 hours total)
Outcomes	Outcomes recorded at baseline, post-intervention and at 1 month Upper limb function and activity outcomes (arm): abbreviated version of the Wolf Motor Function Test Upper limb function and activity outcomes (hand): Box and Block test, Grip strength (kg) Participation restriction and quality of life: Stroke Impact Scale (hand function, composite function, perception of recovery) Adverse events reported Other outcomes: therapy time
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants were randomly allocated using a basic computer random number generator

Saposnik 2010 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Unclear
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	Some attrition was reported. Outcomes were calculated based on the number of participants and there was no reporting of imputation of data. Intention-to-treat analysis was completed
Selective reporting (reporting bias)	Low risk	Reports on all measures reported in the study protocol paper

Shin 2013

Methods	RCT
Participants	Recruited from 2 rehabilitation units and the neurorehabilitation ward of a hospital in Korea 16 participants: 9 intervention, 7 control Inclusion criteria: hemiparetic upper limb dysfunction due to first-ever stroke, mild-to-severe deficits of the paretic upper extremity (2 to 4 on the Medical Research Council Scale and 2 to 5 on the Brunnstrom Stage of motor recovery) Exclusion criteria: pre-existing arm impairment, any painful condition affecting the upper limbs, difficulty in sitting for at least 20 minutes, severe cognitive impairment (Mini Mental State Examination score less than 10 points) and severe aphasia Mean (SD) age: intervention group 46.6 (5.8), control group 52.0 (11.9) years 50% male Stroke details: 38% right lesion Timing post stroke: intervention group mean (SD) 76.6 (28.5) days, control group 67.1 (45.3) days
Interventions	Virtual reality intervention: RehabMaster™. The participant sits in a chair in front of a monitor. The therapist can control the program and level of difficulty. Rehabilitation games were designed to combine rehabilitation exercises with gaming elements. The four games suggested were goalkeeper, bug hunter, underwater fire and rollercoaster Control intervention: conventional occupational therapy Sessions were 20 minutes of occupational therapy. The intervention group received an additional 20 minutes of virtual reality. The duration of intervention was 10 sessions over 2 weeks
Outcomes	Outcomes recorded at baseline and post intervention Upper limb function outcomes: Fugl Meyer Activity limitation outcomes; Modified Barthel Index Other outcomes: passive range of motion of the upper limb, Medical Research Council Score
Notes	-

Shin 2013 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated
Allocation concealment (selection bias)	Low risk	Opaque envelopes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded to allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop outs
Selective reporting (reporting bias)	Low risk	All outcomes reported except for the SF36 measure, which will be reported in a subsequent publication

Sin 2013

Methods	RCT
Participants	Recruited from a rehabilitation hospital in Korea 35 participants: 18 intervention, 17 control Inclusion criteria: more than 6 months post stroke, no problems with auditory or visual functioning, active range of motion of the shoulder, elbow, wrist and fingers of more than 10 degrees, ability to walk more than 10 metres independently not taking any medication that could influence balance or gait and no severe cognitive disorders (Mini Mental State Examination score of > 16/30) Exclusion criteria: uncontrolled blood pressure or angina, history of seizure, any intervention other than conventional therapy, or refusal to use a video game Mean (SD) age: intervention group 71.78 (9.42), control group 75.59 (5.55) years 43% male Stroke details: 66% right hemiparesis Timing post stroke: intervention group mean (SD) 7.22 (1.21) months, control group 8.47 (2.98) months
Interventions	Virtual reality intervention: use of Xbox Kinect for 30 minutes followed by conventional occupational therapy for 30 minutes. Kinect programs that required use of the upper extremities were selected Control intervention: conventional occupational therapy, which focused on retraining upper extremity and hand function and activities of daily living Sessions were performed 3 times a week for 6 weeks
Outcomes	Outcomes recorded at baseline and post-intervention Upper limb outcomes: Fugl Meyer UE, Box and Block test Other outcomes: Upper extremity Active Range of Movement

Sin 2013 (*Continued*)

Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number tables
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded to allocation
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	To be determined
Selective reporting (reporting bias)	Unclear risk	To be determined

Standen 2011

Methods	RCT
Participants	Study took place in the UK 27 participants: 17 intervention, 10 control Inclusion criteria: 18 years or over, no longer receiving any other intensive rehabilitation and still had residual upper limb dysfunction Exclusion criteria: failure to meet above criteria Mean (SD) age: intervention group 59 (12.03), control group 63 (14.6) years 59% male Timing post stroke: intervention group mean (SD) 38 (41.28) weeks, control group 24 (36.26) weeks
Interventions	Virtual reality intervention: virtual glove which translates the position of the hand into gameplay. Participants were instructed to use the program at home Control intervention: usual care (no specific intervention) Sessions were 20 minutes, 3 times a day for 8 weeks (approximately 52 hours)
Outcomes	Outcomes recorded at baseline, 4 weeks and post-intervention (8 weeks) Upper limb function outcome: Wolf Motor Function Test, Nine Hole Peg Test Other: Motor Activity Log Activity outcomes: Nottingham Extended Activities of Daily Living Scale (NEADL)
Notes	-

Risk of bias

Standen 2011 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computerised random number generator
Allocation concealment (selection bias)	Low risk	Managed externally
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded to allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	Large number of drop outs in the intervention group
Selective reporting (reporting bias)	Low risk	Unpublished data obtained via personal communication

Subramanian 2013

Methods	RCT
Participants	Study took place in Canada 32 participants: 16 intervention, 16 control Inclusion criteria: between 40 and 80 years, sustained single ischaemic or haemorrhagic stroke 6 to 60 months previously, scored 3 to 6 on the Chedoke McMaster Stroke Assessment arm subscale and had no other neurologic or neuromuscular/orthopaedic problems affecting the upper limb and trunk Exclusion criteria: brainstem or cerebellar lesions, comprehension difficulties and marked apraxia, attention or visual field deficits Mean (SD) age: intervention group 62 (9.7), control group 60 (11) years 72% male Stroke details: 47% right hemiparesis Timing post stroke: intervention group mean (SD) 3.7 (2.2) years, control group 3.0 (1.9) years
Interventions	Virtual reality intervention: a 3D virtual environment (CAREN system) simulated a supermarket scene. Participants had to reach for objects in the virtual environment. Training was high in intensity with 72 trials of reaching in each session Control intervention: pointing at targets in a physical environment Sessions were 45 minutes for 12 days spaced over 4 weeks
Outcomes	Outcomes were recorded at baseline, post-intervention and 3 months following intervention Upper limb outcomes: Fugl Meyer, Reaching Performance Scale for Stroke, Wolf Motor Function Test Other outcomes: Motor Activity Log-AS Other outcomes: Motivation Task Evaluation Questionnaire Other outcomes: kinematic data

Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated
Allocation concealment (selection bias)	Low risk	Managed by external personnel
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded to allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	All completed the assessments. Small number of intervention drop outs and balanced across groups
Selective reporting (reporting bias)	Low risk	All outcomes reported as per entry on clinical trial registry

Sucar 2009

Methods	Quasi RCT
Participants	Recruited from the National Institute of Neurology in Mexico City, Mexico 22 participants: 11 intervention, 11 control Inclusion criteria: $\geq$ 6 months after stroke Exclusion criteria: none reported Mean age: intervention group 51 years, control group 52 years Timing post stroke: intervention group 22 months, control group 26 months
Interventions	Virtual reality intervention: participants used a 'Gesture Therapy' program designed by the researchers. Movements of the participant's upper limbs are tracked by a camera and the person interacts with on-screen games. Games included shopping in the supermarket, making breakfast, playing basketball, cleaning, painting and driving Control intervention: a variety of exercises guided by the therapist using equipment such as cones and balls Sessions were 60 minutes, 3 times a week for 5 weeks (15 hours total)
Outcomes	Outcomes recorded at baseline and post-intervention Upper limb function and activity outcomes (arm): Fugl Meyer UE scale, Motricity Index Adverse events reported Other outcomes: level of interest, competence, effort, pressure and utility of the intervention
Notes	-

Risk of bias

Sucar 2009 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Alternate allocation based on odd or even numbers
Allocation concealment (selection bias)	Unclear risk	Unclear
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	There were no missing data
Selective reporting (reporting bias)	Low risk	No additional outcomes were collected

Yang 2008

Methods	RCT
Participants	Study took place in Taiwan 24 participants: 12 intervention, 12 control Inclusion criteria: hemiparesis resulting from a single stroke occurring > 6 months earlier, limited household walker, unlimited household walker or most-limited community walker by functional walking category, not presently receiving any rehabilitation services, no visual field deficit or hemianopia, stable medical condition to allow participation in the testing protocol and intervention, ability to understand instructions and follow commands Exclusion criteria: any comorbidity or disability other than stroke that would preclude gait training, uncontrolled health condition for which exercise was contraindicated, neurological or orthopaedic disease that might interfere with the study Mean (SD) age: intervention group 55 (12) years, control group 61 (9) years 50% male Stroke details: 45% right hemiparesis Timing post stroke: intervention group mean (SD) 6 (4) years, control group 6 (10) years
Interventions	Virtual reality intervention: the participant walked on a treadmill as virtual environments were displayed on a screen in front of the person with a wide field of view. Speed and incline of the treadmill was able to be varied in conjunction with scenery changes. Leg movements were tracked by an electromagnetic system to detect collisions with virtual objects. The virtual environment was designed to simulate a typical community in Taipei. Scenarios consisted of lane walking, street crossing, negotiating obstacles and strolling through the park Control intervention: treadmill training. While walking on the treadmill the participant was asked to execute different tasks. The tasks included lifting the legs to simulate stepping over obstacles, uphill and downhill walking and fast walking Sessions were 20 minutes, 3 times a week for 3 weeks (3 hours total)

Yang 2008 (*Continued*)

Outcomes	Outcomes recorded at baseline, post-intervention and at 1 month Lower limb function and activity outcomes: walking speed (metres per second), community walk test Participation restriction and quality of life: walking ability questionnaire, Activities Specific Balance Confidence Scale
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	An independent person picked 1 of the sealed envelopes before the start of the intervention
Allocation concealment (selection bias)	Unclear risk	Unclear whether envelopes were opaque
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blind
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear
Selective reporting (reporting bias)	Unclear risk	Unclear

Yang 2011

Methods	RCT
Participants	Recruited from a hospital in Taiwan 14 participants: 7 intervention, 7 control Inclusion criteria: hemiplegia resulting from a stroke more than 6 months ago. Able to understand the treadmill exercises Exclusion criteria: inability to walk independently (without using an assistive device), abnormal neuro-opthalmologic findings after examination and visual acuity problems after correction Mean (SD) age: intervention group 56.3 (10.2), control group 65.7 (5.9) years Stroke details: 36% right hemiparesis Timing post stroke: intervention group mean (SD) 17 (8.6) months, control group 16.3 (10.4) months
Interventions	Virtual reality intervention: standard occupational therapy and physiotherapy program plus virtual reality treadmill training. The treadmill was co-ordinated with the interactive scenes so that a stepping switch turned the scenes left or right as if the person was turning a corner. Participants had to make 16 turns per session Control intervention: treadmill training facing a window Sessions were 20 minutes, 3 times a week for 3 weeks (approximately 3 hours total)

Outcomes	Outcomes recorded at baseline and post-intervention Gait outcomes: bilateral limb loading symmetric index, paretic limb stance time, number of steps of the paretic limb, contact areas of the paretic foot during quiet stance, sit-to-stand transfer and level walking Balance outcomes: centre of pressure
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded to allocation
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient detail reported to tell
Selective reporting (reporting bias)	Unclear risk	Protocol not available

Yavuzer 2008

Methods	RCT
Participants	Recruited from an inpatient rehabilitation centre in Turkey 20 participants: 10 intervention, 10 control Inclusion criteria: first episode of unilateral stroke with hemiparesis during the previous 12 months, score of 1 to 4 on the Brunnstrom stages for the upper extremity, able to understand and follow simple verbal instructions, no severe cognitive disorders that would interfere with the study's purpose (Mini Mental State Examination score of > 16/30) Mean (SD) age: intervention group 58 (10) years, control group 64 (11) years 45% male Stroke details: 45% right hemiparesis Timing post stroke: Intervention group mean (SD) 3 (3) months, control group 5 (1) months
Interventions	Virtual reality intervention: active use of the Playstation EyeToy games involving use of the upper limbs Control intervention: watched the Playstation EyeToy games but did not get physically involved Sessions were 30 minutes, 5 times a week for 4 weeks (10 hours total)

	Sessions were in addition to the conventional rehabilitation programme that both groups were participating in, which involved approximately 60 minutes of therapy for the upper limb
Outcomes	Outcomes recorded at baseline and post-intervention Upper limb function and activity outcome measures (arm function): Brunnstrom UE stages Upper limb function and activity outcome measures (hand function): Brunnstrom hand stages Activity limitation outcome measures: Functional Independence Measure self care component Adverse events reported
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Sequence generated using a computer-generated random number list
Allocation concealment (selection bias)	Low risk	An independent doctor operated the random number program
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	There does not appear to be any attrition and all outcome measures appear to have been reported in full
Selective reporting (reporting bias)	Unclear risk	Unclear

You 2005

Methods	RCT
Participants	Study took place in Korea 10 participants: 5 intervention, 5 control Inclusion criteria: ≥ 1 year after first stroke, plateau in the maximum motor recovery after conventional neurorehabilitation, > 60 degrees extension at the knee Exclusion criteria: severe spasticity (modified Ashworth scale > 2) or tremor, severe visual and cognitive impairment Mean age: intervention group 55 years, control group 55 years 70% male Stroke details: 30% right hemiparesis Timing post stroke: intervention group 18 months, control group 19 months

You 2005 (*Continued*)

Interventions	Virtual reality intervention: IREX virtual reality system using a video capture system to capture the participant's whole body movement. The participant is able to view their body movements in real time on a screen in front of them immersed in a virtual environment. Games included stepping up/down, 'shark bait' and snowboarding Control intervention: no intervention provided Sessions for the virtual reality group were 60 minutes, 5 times a week for 4 weeks (20 hours total)
Outcomes	Outcomes recorded at baseline and post-intervention Lower limb function and activity outcomes: Functional Ambulation Category Global motor function: modified Motor Assessment Scale Imaging studies: functional MRI - laterality index
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Unclear
Allocation concealment (selection bias)	Unclear risk	Unclear
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blind
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear
Selective reporting (reporting bias)	Unclear risk	Unclear

Zucconi 2012

Methods	RCT (3 arms)
Participants	Recruited from a neurorehabilitation ward in Italy 33 participants: 11 intervention, 11 control, 11 control Inclusion criteria: stroke in the MCA territory at least 6 months before enrolment, absence of ideomotor apraxia, neglect and aphasia interfering with verbal comprehension Exclusion criteria: apraxia, neglect and language disturbances Median (IQR) age: intervention group 60 (57.25 to 76) years, control group 60 (49 to 74.25) years, control group 64.5 (54.50 to 69) years 39% male Timing post stroke: intervention group median (IQR) 10.05 (4.05 to 17.90) months, control group 8.75 (2.75 to 24.95) months, control group 5.05 (1.75 to 17.90) months

Interventions	Virtual reality intervention (EVER TEACHER group): Reinforced Feedback in Virtual Environment (RFVE). Participants were asked to manipulate sensorised objects (ball, plastic cup or cylinder). Specific feedback was provided (like a virtual teacher) to encourage the participant to emulate the correct movement Virtual reality intervention (NO TEACHER group): virtual reality intervention but with no feedback Control intervention: conventional rehabilitation programme Sessions were 60 minutes, 5 times a week for 4 weeks
Outcomes	Outcomes recorded at baseline and post-intervention Upper limb outcomes: Fugl Meyer UE, Reaching performance scale Other outcomes: Modified Ashworth Scale, kinematics Activity outcomes: Functional Independence Measure
Notes	-

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated
Allocation concealment (selection bias)	Low risk	Sequentially numbered, opaque, sealed envelopes
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded to allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop outs
Selective reporting (reporting bias)	Low risk	No other outcomes collected

6MWT: 6-minute walk test
CT: computerised tomography
IQR: interquartile range
MCA: middle cerebral artery
MI: myocardial infarction
MMSE-K: Mini Mental State Examination - Korean
MRC: Medical Research Council
MRI: magnetic resonance imaging
RCT: randomised controlled trial
ROM: range of motion
SD: standard deviation
UE: upper extremity

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Broeren 2008	Study design: not a RCT
Cameirao 2012	Compares different types of virtual reality
Cho 2013	Does not meet the definition of virtual reality (no real 'interaction' between the person and the virtual environment)
Chortis 2008	Study design: not a RCT
Cikaljo 2012	Study design: not a RCT
Der-Yeghiaian 2009	Study design: not a RCT
Edmans 2009	Study design: not a RCT
Fischer 2007	Compares different types of virtual reality
Fritz 2013	Not considered to be properly randomised or quasi-randomised
Gnajaraj 2007	Does not meet the definition of a virtual reality intervention
In 2012	Does not meet the definition of a virtual reality intervention
Katz 2005	Study design: not all participants were randomised
Kim 2012a	Does not meet the definition of a virtual reality intervention
Krebs 2008	Study design: participants were not randomly allocated to groups
Manlapaz 2010	Unable to confirm whether this study meets the inclusion criteria. Insufficient information provided in conference abstract and no response received from author upon contact
Shin 2010	Study design: participants were not randomly allocated to groups
Song 2010	Unable to obtain further information to confirm inclusion criteria or obtain basic study data

RCT: randomised controlled trial

Characteristics of ongoing studies *[ordered by study ID]*

Adie 2014

Trial name or title	TWIST - Trial of Wii STroke
Methods	RCT
Participants	Individuals post stroke
Interventions	Virtual reality intervention: Nintendo Wii Sports program used at home for 6 weeks Control intervention: personalised arm exercises at home for 6 weeks
Outcomes	Primary outcome: Action Research Arm Test
Starting date	November 2011
Contact information	Dr Katja Adie: Katja.Adie@rcht.cornwall.nhs.uk
Notes	-

Deutsch 2009

Trial name or title	Interactive video gaming compared with optimal standard of care to improve balance and mobility
Methods	Single-blind pilot RCT
Participants	Individuals post stroke (greater than 6 months), able to up walk 50 metres, follow instructions
Interventions	Virtual reality intervention: Wii-based balance and mobility training Control: optimal standard of care Dosing 3 hours per week for 4 weeks
Outcomes	Gait variables (gait rite), 6-Minute Walk Test, Dynamic Gait Index, Timed Up and Go, Activities Balance Questionnaire, Canadian Occupational Performance Measure, Postural Control
Starting date	Commenced Summer 2008
Contact information	Professor Judith Deutsch: deutsch@umdnj.edu
Notes	Data collection completed with results to be presented at upcoming conferences

Karatas 2014

Trial name or title	Wii-based rehabilitation in stroke
Methods	RCT
Participants	Individuals post stroke

Karatas 2014 (*Continued*)

Interventions	Virtual reality intervention: traditional balance rehabilitation plus Nintendo Wii Fit Control intervention: traditional balance rehabilitation
Outcomes	Berg Balance Scale, Functional Reach Test, postural assessment scale for stroke patients Timed Up and Go Test (TUG) and static balance index
Starting date	Unknown
Contact information	Professor Gülçin Kaymak Karata: gulcink@gazi.edu.tr
Notes	-

Lloréns 2014

Trial name or title	Improvement in balance using a virtual reality-based stepping exercise: a randomised controlled trial involving individuals with chronic stroke
Methods	RCT
Participants	20 people with chronic stroke
Interventions	The experimental group combined 30 minutes with the virtual reality-based intervention with 30 minutes of conventional training
Outcomes	Berg Balance Scale, gait and balance subscales of the Tinetti Performance-Oriented Mobility Assessment, the Brunel Balance Assessment and the 10-metre Walking Test
Starting date	Unknown
Contact information	Email: rllorens@labhuman.com
Notes	-

NCT01304017

Trial name or title	Virtual reality intervention for stroke rehabilitation
Methods	RCT
Participants	Individuals more than 6 months following stroke
Interventions	Virtual reality intervention: group-based intervention Control intervention: conventional group intervention
Outcomes	Primary outcome is physical activity of the lower and upper limb (accelerometer data)
Starting date	February 2011

NCT01304017 (*Continued*)

Contact information	Dr Debbie Rand: drand@post.tau.ac.il
Notes	Date accessed December 2013

NCT01365858

Trial name or title	Virtual action planning in stroke: a control rehabilitation study
Methods	RCT
Participants	Individuals with stroke
Interventions	Virtual reality intervention: rehabilitation using the 'Virtual Action Planning supermarket' Control intervention: conventional rehabilitation
Outcomes	Primary outcome: ability to perform shopping test in real supermarket
Starting date	May 2011
Contact information	Professor Pierre-Alain Joseph: pierre-alain.joseph@chu-bordeaux.fr
Notes	Date accessed December 2013

NCT01406912

Trial name or title	Efficacy of Virtual Reality Exercises in STroke rehabilitation: a multicentre study (EVREST Multicentre)
Methods	RCT
Participants	Individuals within 3 months of stroke
Interventions	Virtual reality intervention: virtual reality Wii games Control intervention: recreational therapy
Outcomes	Primary outcome: Wolf Motor Function Test
Starting date	July 2011
Contact information	Dr Gustavo Saposnik: SaposnikG@smh.ca
Notes	Date accessed December 2013

NCT02013999

Trial name or title	The development of upper extremity rehabilitation program using virtual reality for the stroke patients
Methods	RCT
Participants	Individuals with stroke
Interventions	Virtual reality intervention Control intervention: standard occupational therapy
Outcomes	Primary outcome: Fugl Meyer Upper Extremity Scale
Starting date	October 2013
Contact information	Professor Nam-Jong Paik, Department of Rehabilitation Medicine, Seoul National University Email: njpaik@snu.ac.kr
Notes	Date accessed December 2013

NTR2247

Trial name or title	Effect of virtual reality training on reach after stroke
Methods	RCT
Participants	Individuals in the chronic phase post stroke
Interventions	Virtual reality intervention: reach training using a virtual reality program Control intervention: reach training in a traditional therapy setting
Outcomes	Primary outcomes: Action Research Arm test, Fugl-Meyer assessment, Intrinsic Motivation Inventory
Starting date	April 2010
Contact information	Dr Kottink: a.hutten@rrd.nl
Notes	Date accessed December 2013

Piemonte 2014

Trial name or title	Effects of training in a virtual environment in chronic stroke patients
Methods	RCT
Participants	People in the chronic phase after stroke
Interventions	Virtual reality intervention: Nintendo Wii Fit Plus balance and mobility games Control intervention: conventional balance and mobility training

Piemonte 2014 (*Continued*)

Outcomes	Balance, cognition and functional assessments
Starting date	Unknown
Contact information	Dr Maria Piemonte: elisapp@usp.br
Notes	-

RCT: randomised controlled trial

DATA AND ANALYSES

Comparison 1. Virtual reality versus conventional therapy: effect on upper limb function post-treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Upper limb function (composite measure)	12	397	Std. Mean Difference (IV, Fixed, 95% CI)	0.29 [0.09, 0.49]
2 Upper limb function (Fugl Meyer)	10	363	Mean Difference (IV, Fixed, 95% CI)	3.30 [1.29, 5.32]
3 Hand function (grip strength)	2	44	Mean Difference (IV, Fixed, 95% CI)	3.55 [-0.20, 7.30]

Comparison 2. Virtual reality versus conventional therapy: upper limb function: subgroup analyses

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dose of intervention	12	397	Std. Mean Difference (IV, Fixed, 95% CI)	0.29 [0.09, 0.49]
1.1 Less than 15 hours intervention	4	114	Std. Mean Difference (IV, Fixed, 95% CI)	0.24 [-0.13, 0.62]
1.2 More than 15 hours intervention	8	283	Std. Mean Difference (IV, Fixed, 95% CI)	0.31 [0.07, 0.55]
2 Time since onset of stroke	11	317	Std. Mean Difference (IV, Fixed, 95% CI)	0.33 [0.10, 0.55]
2.1 Less than 6 months	3	70	Std. Mean Difference (IV, Fixed, 95% CI)	0.78 [0.28, 1.29]
2.2 More than 6 months	8	247	Std. Mean Difference (IV, Fixed, 95% CI)	0.21 [-0.04, 0.46]
3 Specialised or gaming	12	397	Std. Mean Difference (IV, Fixed, 95% CI)	0.29 [0.09, 0.49]
3.1 Specialised	11	381	Std. Mean Difference (IV, Fixed, 95% CI)	0.26 [0.05, 0.46]
3.2 Gaming	1	16	Std. Mean Difference (IV, Fixed, 95% CI)	1.15 [0.06, 2.24]
4 Severity of impairment	12	398	Std. Mean Difference (IV, Fixed, 95% CI)	0.29 [0.09, 0.49]
4.1 Mild to moderate impairment	8	274	Std. Mean Difference (IV, Fixed, 95% CI)	0.35 [0.10, 0.59]
4.2 Moderate to severe impairment	4	124	Std. Mean Difference (IV, Fixed, 95% CI)	0.16 [-0.19, 0.52]

Comparison 3. Additional virtual reality intervention: effect on upper limb function post-treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Upper limb function (composite measure)	9	190	Std. Mean Difference (IV, Fixed, 95% CI)	0.44 [0.15, 0.73]
2 Hand function (dexterity)	3	60	Std. Mean Difference (IV, Fixed, 95% CI)	0.25 [-0.27, 0.77]

Comparison 4. Additional virtual reality intervention: effect on upper limb function post-treatment: subgroup analyses

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dose of intervention	9	190	Std. Mean Difference (IV, Fixed, 95% CI)	0.44 [0.15, 0.73]
1.1 Less than 15 hours intervention	6	133	Std. Mean Difference (IV, Fixed, 95% CI)	0.40 [0.05, 0.75]
1.2 More than 15 hours intervention	3	57	Std. Mean Difference (IV, Fixed, 95% CI)	0.54 [0.00, 1.07]
2 Time since onset of stroke	8	161	Std. Mean Difference (IV, Fixed, 95% CI)	0.37 [0.06, 0.69]
2.1 Less than 6 months	5	98	Std. Mean Difference (IV, Fixed, 95% CI)	0.29 [-0.11, 0.70]
2.2 More than 6 months	3	63	Std. Mean Difference (IV, Fixed, 95% CI)	0.50 [-0.00, 1.01]
3 Specialised or gaming	9	190	Std. Mean Difference (IV, Fixed, 95% CI)	0.44 [0.15, 0.73]
3.1 Specialised	7	135	Std. Mean Difference (IV, Fixed, 95% CI)	0.42 [0.07, 0.76]
3.2 Gaming	2	55	Std. Mean Difference (IV, Fixed, 95% CI)	0.50 [-0.04, 1.04]

Comparison 5. Virtual reality versus conventional therapy: effect on lower limb activity post-treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Gait speed	3	58	Mean Difference (IV, Fixed, 95% CI)	0.07 [-0.09, 0.23]

Comparison 6. Virtual reality versus conventional therapy: effect on lower limb activity post-treatment: subgroup analyses

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dose of intervention: effect on gait speed	3	58	Mean Difference (IV, Fixed, 95% CI)	0.07 [-0.09, 0.23]
1.1 Less than 10 hours intervention	2	40	Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.22, 0.24]
1.2 More than 10 hours intervention	1	18	Mean Difference (IV, Fixed, 95% CI)	0.13 [-0.09, 0.35]

Comparison 7. Additional virtual reality intervention: effect on global motor function post-treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Global motor function	2	27	Std. Mean Difference (IV, Fixed, 95% CI)	0.14 [-0.63, 0.90]

Comparison 8. Virtual reality versus conventional therapy: effect on secondary outcomes

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 ADL outcome	8	253	Std. Mean Difference (IV, Fixed, 95% CI)	0.43 [0.18, 0.69]

Comparison 9. Additional virtual reality intervention: effect on secondary outcomes

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 ADL outcome	8	153	Std. Mean Difference (IV, Fixed, 95% CI)	0.44 [0.11, 0.76]

Analysis 1.1. Comparison 1 Virtual reality versus conventional therapy: effect on upper limb function post-treatment, Outcome 1 Upper limb function (composite measure).

Review: Virtual reality for stroke rehabilitation

Comparison: 1 Virtual reality versus conventional therapy: effect on upper limb function post-treatment

Outcome: 1 Upper limb function (composite measure)

Study or subgroup	Virtual reality		Conventional therapy		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
Byl 2013	5	28.2 (4.6)	5	30.6 (6.92)		2.6 %	-0.37 [-1.63, 0.89]
Crosbie 2008	9	52.8 (6.9)	9	50.2 (18.9)		4.7 %	0.17 [-0.75, 1.10]
da Silva Cameirao 2011	8	60.375 (7.614)	8	53.38 (8.087)		3.8 %	0.84 [-0.19, 1.88]
Housman 2009	14	24.9 (7.4)	14	19.6 (6.7)		6.8 %	0.73 [-0.04, 1.50]
Kiper 2011	40	48.9 (15.2)	40	46.4 (17.1)		21.0 %	0.15 [-0.29, 0.59]
Piron 2007	25	51.4 (9.8)	13	45.4 (9.3)		8.6 %	0.61 [-0.08, 1.30]
Piron 2009	18	53.6 (7.7)	18	49.5 (4.8)		9.0 %	0.62 [-0.05, 1.30]
Piron 2010	27	49.7 (10.1)	20	46.5 (9.7)		11.9 %	0.32 [-0.27, 0.90]
Saposnik 2010	9	-19.8 (3.4)	7	-27.4 (8.7)		3.4 %	1.15 [0.06, 2.24]
Subramanian 2013	32	43 (15.2)	32	43.9 (14.7)		16.8 %	-0.06 [-0.55, 0.43]
Sucar 2009	11	30 (12.4)	11	26.36 (2.33)		5.7 %	0.39 [-0.45, 1.24]
Zucconi 2012	11	45.2 (20.3)	11	51.8 (13.1)		5.7 %	-0.37 [-1.22, 0.47]
Total (95% CI)	**209**		**188**			**100.0 %**	**0.29 [0.09, 0.49]**

Heterogeneity: Chi^2 = 12.40, df = 11 (P = 0.33); I^2 =11%

Test for overall effect: Z = 2.82 (P = 0.0048)

Test for subgroup differences: Not applicable

Analysis 1.2. Comparison 1 Virtual reality versus conventional therapy: effect on upper limb function post-treatment, Outcome 2 Upper limb function (Fugl Meyer).

Review: Virtual reality for stroke rehabilitation

Comparison: 1 Virtual reality versus conventional therapy: effect on upper limb function post-treatment

Outcome: 2 Upper limb function (Fugl Meyer)

Study or subgroup	Virtual reality N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Byl 2013	5	28.2 (4.6)	5	30.6 (6.92)		7.7 %	-2.40 [-9.68, 4.88]
da Silva Cameirao 2011	8	60.375 (7.614)	8	53.38 (8.087)		6.9 %	7.00 [-0.70, 14.70]
Housman 2009	14	24.9 (7.4)	14	19.6 (6.7)		14.9 %	5.30 [0.07, 10.53]
Kiper 2011	40	48.9 (15.2)	40	46.4 (17.1)		8.1 %	2.50 [-4.59, 9.59]
Piron 2007	25	51.4 (9.8)	13	45.4 (9.3)		10.1 %	6.00 [-0.35, 12.35]
Piron 2009	18	53.6 (7.7)	18	49.5 (4.8)		23.1 %	4.10 [-0.09, 8.29]
Piron 2010	27	49.7 (10.1)	20	46.5 (9.7)		12.5 %	3.20 [-2.51, 8.91]
Subramanian 2013	32	43 (15.2)	32	43.9 (14.7)		7.6 %	-0.90 [-8.23, 6.43]
Sucar 2009	11	30 (12.4)	11	26.36 (2.33)		7.3 %	3.64 [-3.82, 11.10]
Zucconi 2012	11	45.2 (20.3)	11	51.8 (13.1)		2.0 %	-6.60 [-20.88, 7.68]
Total (95% CI)	**191**		**172**			**100.0 %**	**3.30 [1.29, 5.32]**

Heterogeneity: Chi^2 = 7.80, df = 9 (P = 0.55); I^2 =0.0%

Test for overall effect: Z = 3.21 (P = 0.0013)

Test for subgroup differences: Not applicable

Analysis 1.3. Comparison 1 Virtual reality versus conventional therapy: effect on upper limb function post-treatment, Outcome 3 Hand function (grip strength).

Review: Virtual reality for stroke rehabilitation

Comparison: 1 Virtual reality versus conventional therapy: effect on upper limb function post-treatment

Outcome: 3 Hand function (grip strength)

Study or subgroup	Virtual reality		Comparison intervention		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
Housman 2009	14	9.2 (7)	14	5.6 (2.8)		90.1 %	3.60 [-0.35, 7.55]
Saposnik 2010	9	24.6 (9.67)	7	21.5 (13.6)		9.9 %	3.10 [-8.79, 14.99]
Total (95% CI)	**23**		**21**			**100.0 %**	**3.55 [-0.20, 7.30]**

Heterogeneity: $Chi^2 = 0.01$, df = 1 (P = 0.94); $I^2 = 0.0\%$

Test for overall effect: Z = 1.86 (P = 0.063)

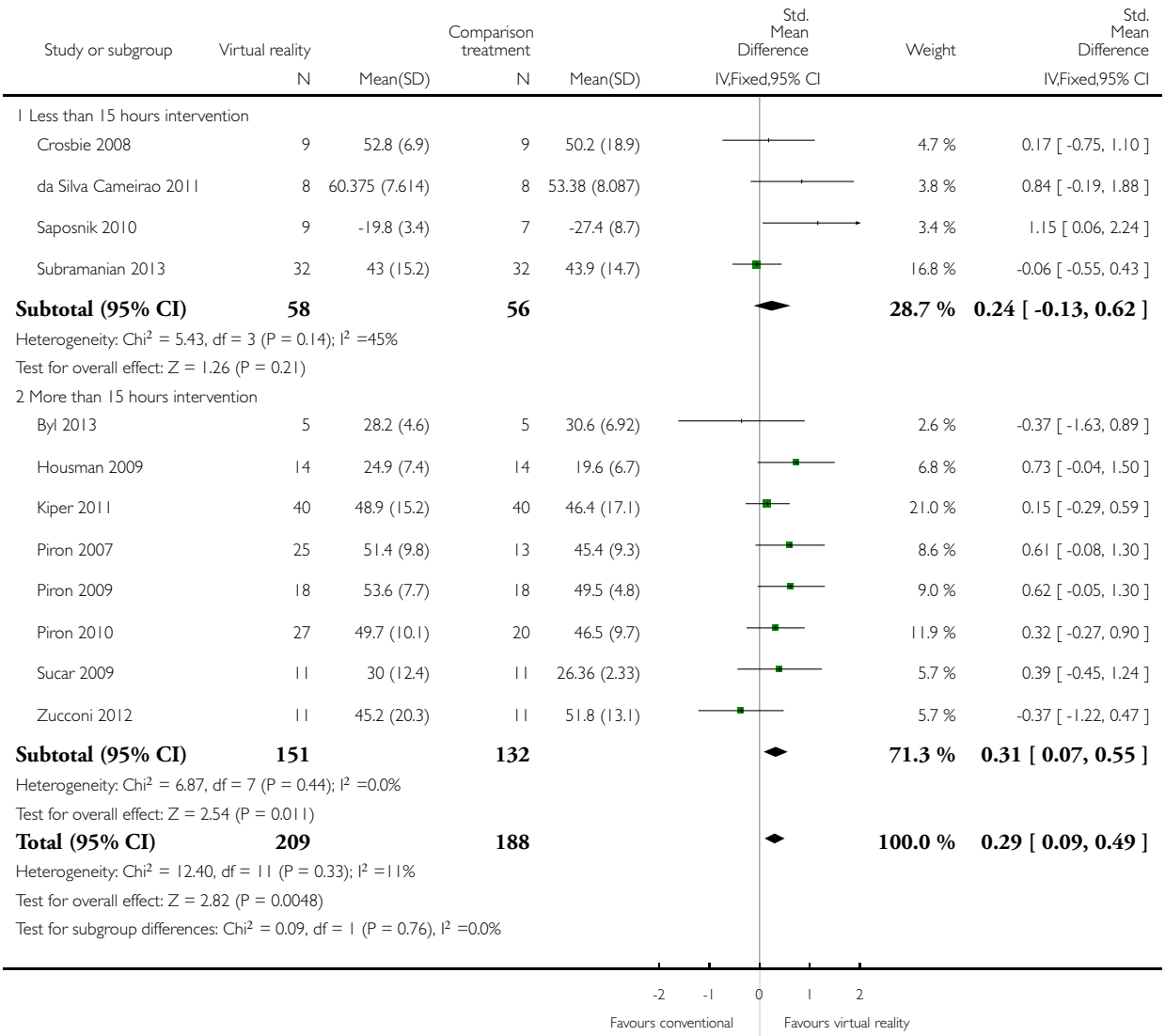
Test for subgroup differences: Not applicable

Analysis 2.1. Comparison 2 Virtual reality versus conventional therapy: upper limb function: subgroup analyses, Outcome 1 Dose of intervention.

Review: Virtual reality for stroke rehabilitation

Comparison: 2 Virtual reality versus conventional therapy: upper limb function: subgroup analyses

Outcome: 1 Dose of intervention

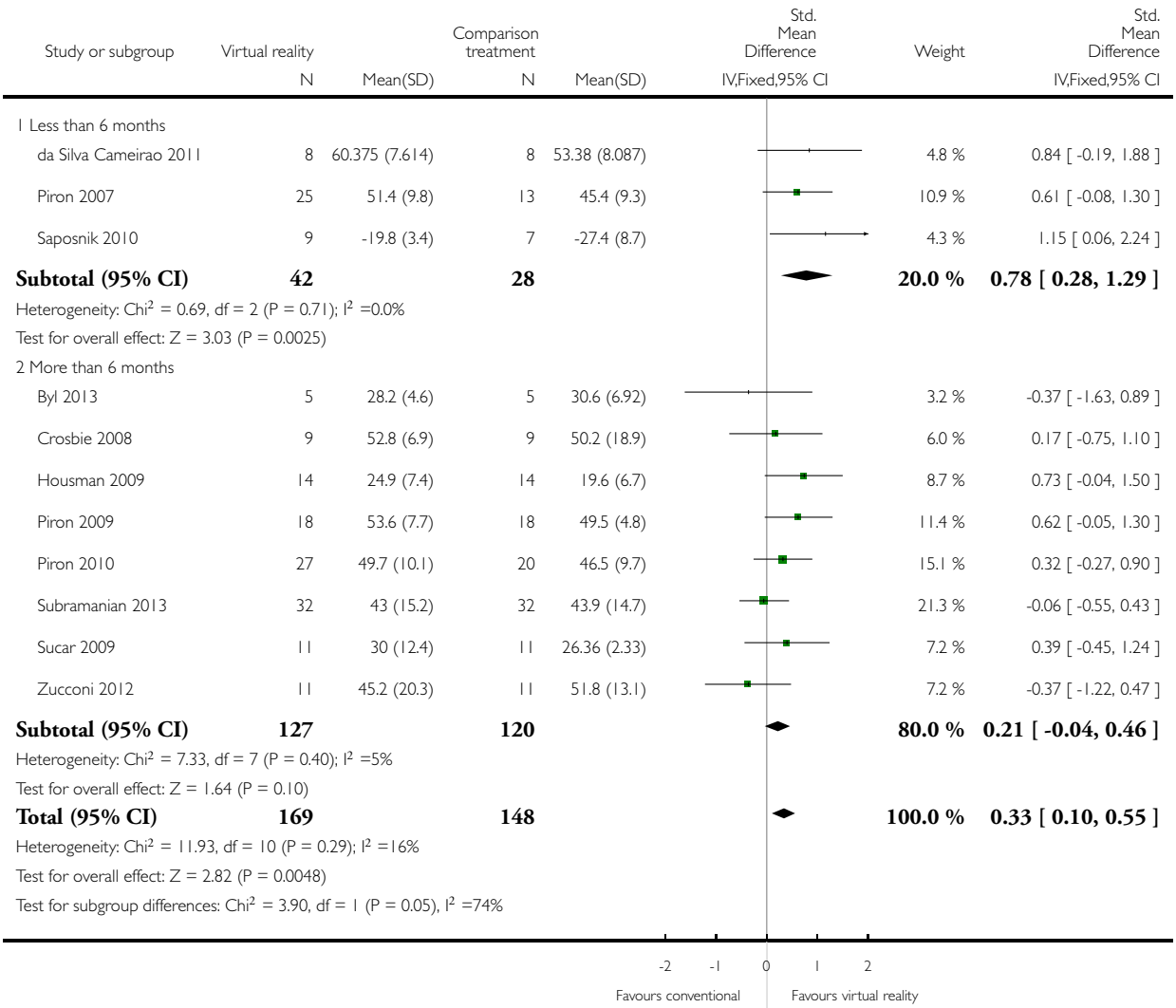


Analysis 2.2. Comparison 2 Virtual reality versus conventional therapy: upper limb function: subgroup analyses, Outcome 2 Time since onset of stroke.

Review: Virtual reality for stroke rehabilitation

Comparison: 2 Virtual reality versus conventional therapy: upper limb function: subgroup analyses

Outcome: 2 Time since onset of stroke



Analysis 2.3. Comparison 2 Virtual reality versus conventional therapy: upper limb function: subgroup analyses, Outcome 3 Specialised or gaming.

Review: Virtual reality for stroke rehabilitation

Comparison: 2 Virtual reality versus conventional therapy: upper limb function: subgroup analyses

Outcome: 3 Specialised or gaming

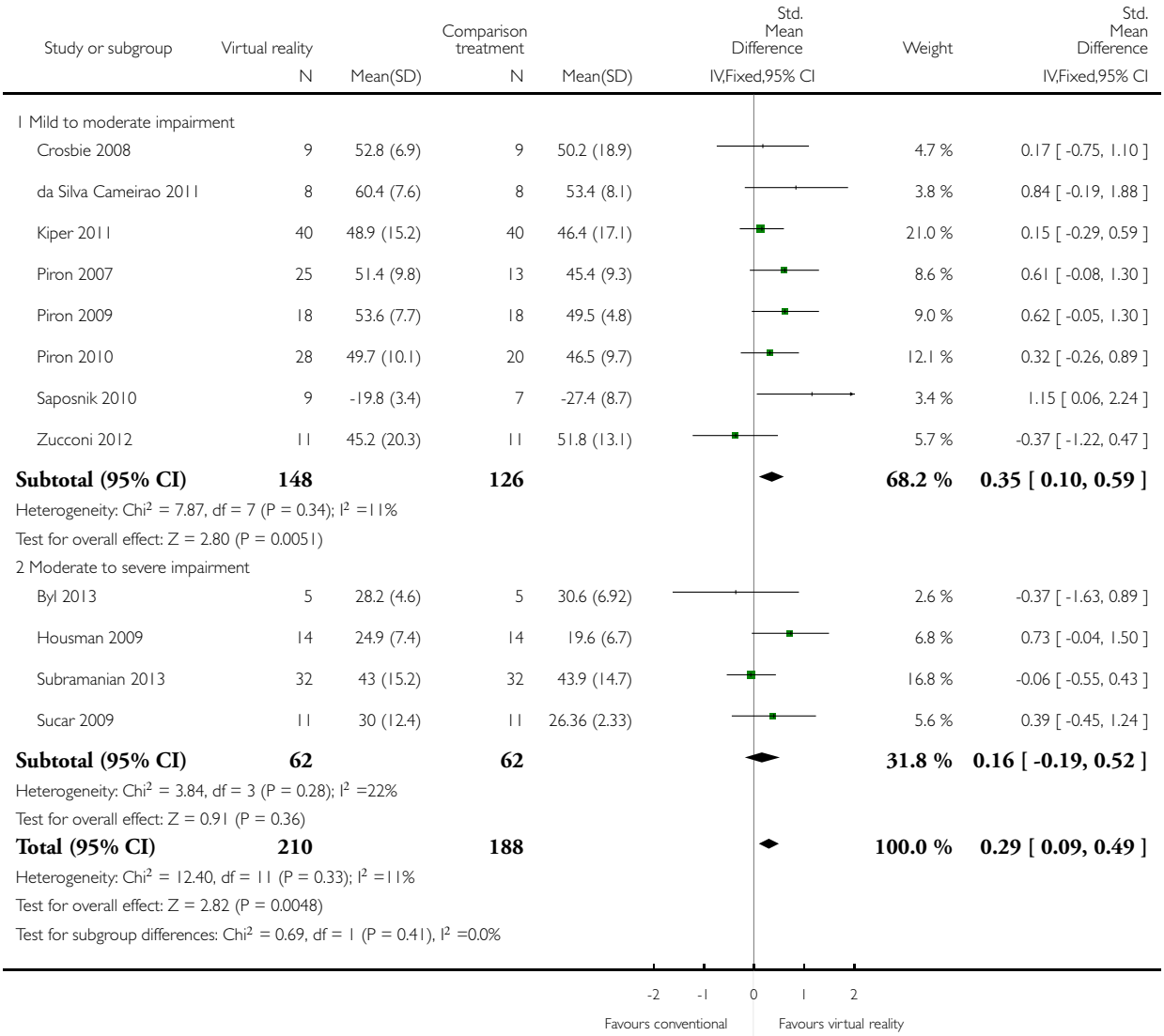
Study or subgroup	Virtual reality N	Mean(SD)	Comparison treatment N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
1 Specialised							
Byl 2013	5	28.2 (4.6)	5	30.6 (6.92)		2.6 %	-0.37 [-1.63, 0.89]
Crosbie 2008	9	52.8 (6.9)	9	50.2 (18.9)		4.7 %	0.17 [-0.75, 1.10]
da Silva Cameirao 2011	8	60.375 (7.614)	8	53.38 (8.087)		3.8 %	0.84 [-0.19, 1.88]
Housman 2009	14	24.9 (7.4)	14	19.6 (6.7)		6.8 %	0.73 [-0.04, 1.50]
Kiper 2011	40	48.9 (15.2)	40	46.4 (17.1)		21.0 %	0.15 [-0.29, 0.59]
Piron 2007	25	51.4 (9.8)	13	45.4 (9.3)		8.6 %	0.61 [-0.08, 1.30]
Piron 2009	18	53.6 (7.7)	18	49.5 (4.8)		9.0 %	0.62 [-0.05, 1.30]
Piron 2010	27	49.7 (10.1)	20	46.5 (9.7)		11.9 %	0.32 [-0.27, 0.90]
Subramanian 2013	32	43 (15.2)	32	43.9 (14.7)		16.8 %	-0.06 [-0.55, 0.43]
Sucar 2009	11	30 (12.4)	11	26.36 (2.33)		5.7 %	0.39 [-0.45, 1.24]
Zucconi 2012	11	45.2 (20.3)	11	51.8 (13.1)		5.7 %	-0.37 [-1.22, 0.47]
Subtotal (95% CI)	**200**		**181**			**96.6 %**	**0.26 [0.05, 0.46]**
Heterogeneity: Chi^2 = 9.91, df = 10 (P = 0.45); I^2 =0.0%							
Test for overall effect: Z = 2.48 (P = 0.013)							
2 Gaming							
Saposnik 2010	9	-19.8 (3.4)	7	-27.4 (8.7)		3.4 %	1.15 [0.06, 2.24]
Subtotal (95% CI)	**9**		**7**			**3.4 %**	**1.15 [0.06, 2.24]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.07 (P = 0.039)							
Total (95% CI)	**209**		**188**			**100.0 %**	**0.29 [0.09, 0.49]**
Heterogeneity: Chi^2 = 12.40, df = 11 (P = 0.33); I^2 =11%							
Test for overall effect: Z = 2.82 (P = 0.0048)							
Test for subgroup differences: Chi^2 = 2.48, df = 1 (P = 0.12), I^2 =60%							

Analysis 2.4. Comparison 2 Virtual reality versus conventional therapy: upper limb function: subgroup analyses, Outcome 4 Severity of impairment.

Review: Virtual reality for stroke rehabilitation

Comparison: 2 Virtual reality versus conventional therapy: upper limb function: subgroup analyses

Outcome: 4 Severity of impairment



Analysis 3.1. Comparison 3 Additional virtual reality intervention: effect on upper limb function post-treatment, Outcome 1 Upper limb function (composite measure).

Review: Virtual reality for stroke rehabilitation

Comparison: 3 Additional virtual reality intervention: effect on upper limb function post-treatment

Outcome: 1 Upper limb function (composite measure)

Study or subgroup	Virtual reality		No intervention		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
Cho 2012	15	21.6 (5.4)	14	17.7 (3.4)		14.5 %	0.83 [0.07, 1.60]
Coupar 2012	4	44 (15.98)	4	44.25 (24.96)		4.4 %	-0.01 [-1.40, 1.38]
Jang 2005	5	58 (6.24)	5	55 (3.74)		5.2 %	0.53 [-0.75, 1.80]
Kim 2011a	15	64 (26.7)	13	61.2 (18.2)		15.4 %	0.12 [-0.63, 0.86]
Kwon 2012	13	62.92 (3.45)	13	61.85 (4.54)		14.2 %	0.26 [-0.52, 1.03]
Shin 2013	9	51.1 (7.8)	7	40.7 (9.8)		7.2 %	1.13 [0.04, 2.21]
Sin 2013	18	47.72 (15.34)	17	34.59 (20.72)		18.1 %	0.71 [0.02, 1.39]
Standen 2011	9	-2.68 (1.6)	9	-2.86 (1.4)		9.9 %	0.11 [-0.81, 1.04]
Yavuzer 2008	10	3 (1.5)	10	2.8 (0.9)		11.0 %	0.15 [-0.72, 1.03]
Total (95% CI)	**98**		**92**			**100.0 %**	**0.44 [0.15, 0.73]**

Heterogeneity: $Chi^2 = 5.39$, df = 8 (P = 0.72); $I^2 = 0.0\%$

Test for overall effect: Z = 2.96 (P = 0.0031)

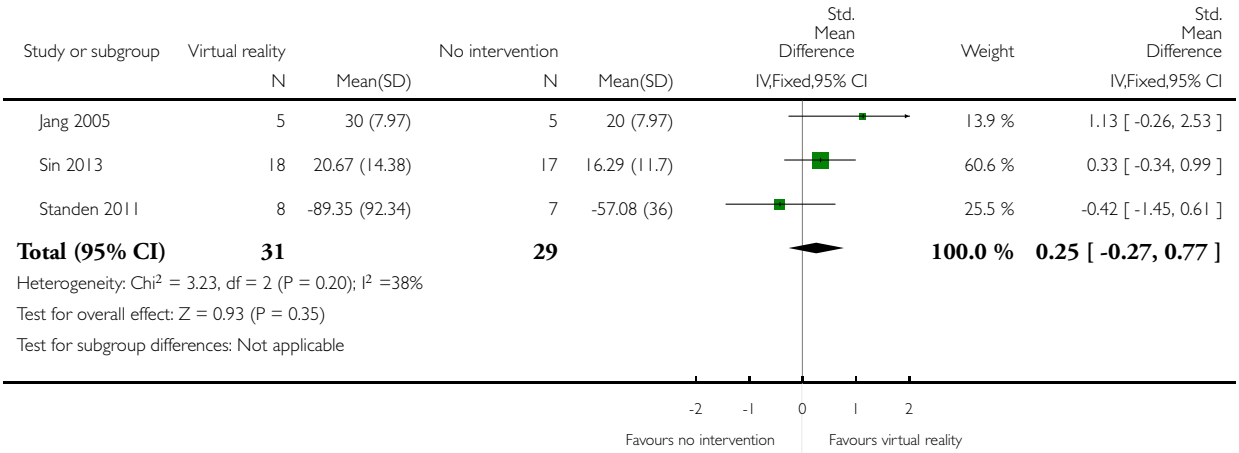
Test for subgroup differences: Not applicable

Analysis 3.2. Comparison 3 Additional virtual reality intervention: effect on upper limb function post-treatment, Outcome 2 Hand function (dexterity).

Review: Virtual reality for stroke rehabilitation

Comparison: 3 Additional virtual reality intervention: effect on upper limb function post-treatment

Outcome: 2 Hand function (dexterity)

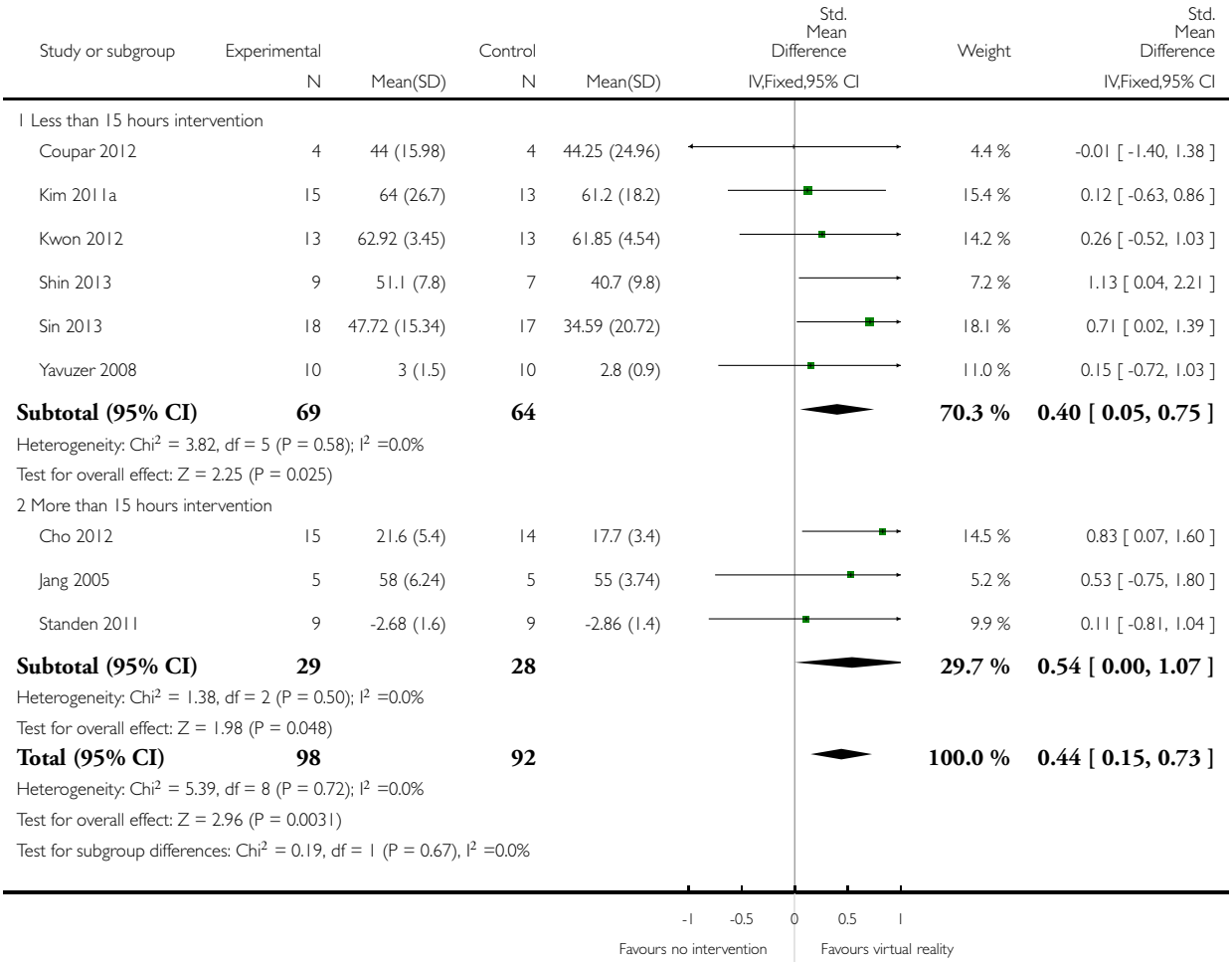


Analysis 4.1. Comparison 4 Additional virtual reality intervention: effect on upper limb function post-treatment: subgroup analyses, Outcome 1 Dose of intervention.

Review: Virtual reality for stroke rehabilitation

Comparison: 4 Additional virtual reality intervention: effect on upper limb function post-treatment: subgroup analyses

Outcome: 1 Dose of intervention

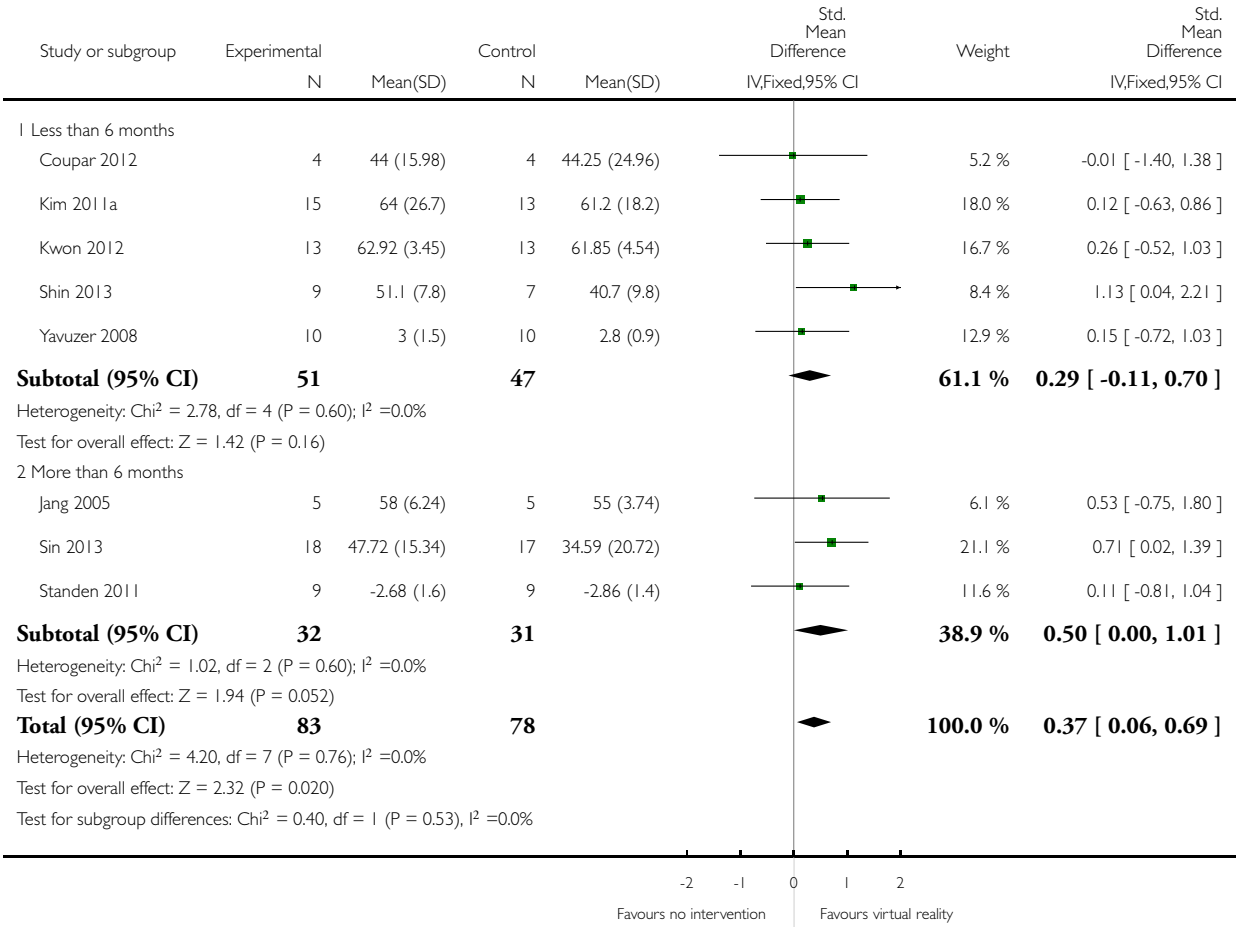


Analysis 4.2. Comparison 4 Additional virtual reality intervention: effect on upper limb function post-treatment: subgroup analyses, Outcome 2 Time since onset of stroke.

Review: Virtual reality for stroke rehabilitation

Comparison: 4 Additional virtual reality intervention: effect on upper limb function post-treatment: subgroup analyses

Outcome: 2 Time since onset of stroke

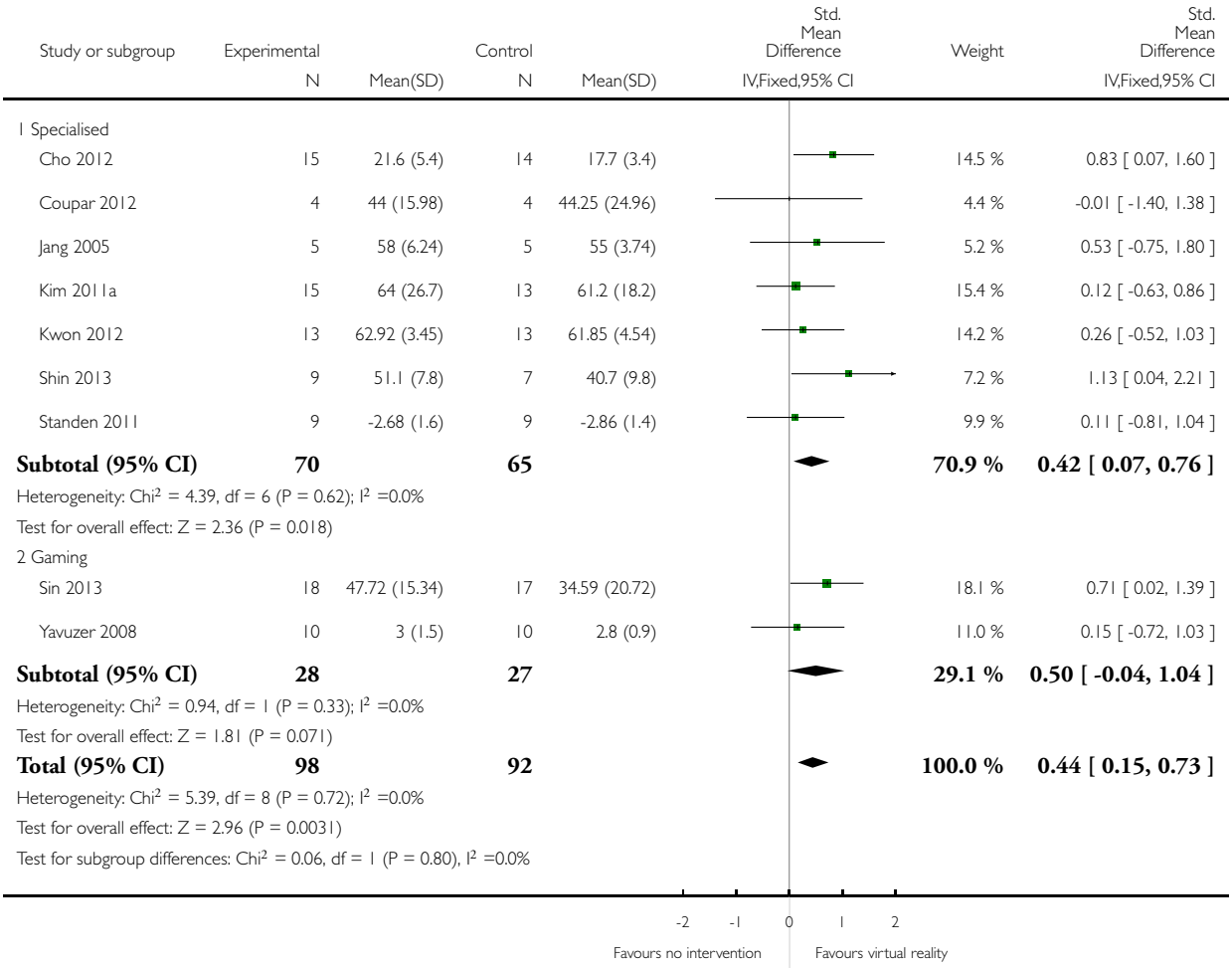


Analysis 4.3. Comparison 4 Additional virtual reality intervention: effect on upper limb function post-treatment: subgroup analyses, Outcome 3 Specialised or gaming.

Review: Virtual reality for stroke rehabilitation

Comparison: 4 Additional virtual reality intervention: effect on upper limb function post-treatment: subgroup analyses

Outcome: 3 Specialised or gaming



Analysis 5.1. Comparison 5 Virtual reality versus conventional therapy: effect on lower limb activity post-treatment, Outcome 1 Gait speed.

Review: Virtual reality for stroke rehabilitation

Comparison: 5 Virtual reality versus conventional therapy: effect on lower limb activity post-treatment

Outcome: 1 Gait speed

Study or subgroup	Virtual reality		Comparison intervention		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
Jaffe 2004	10	0.69 (0.34)	10	0.72 (0.28)		34.9 %	-0.03 [-0.30, 0.24]
Mirelman 2008	9	0.81 (0.18)	9	0.68 (0.29)		52.3 %	0.13 [-0.09, 0.35]
Yang 2008	11	0.85 (0.31)	9	0.73 (0.63)		12.8 %	0.12 [-0.33, 0.57]
Total (95% CI)	**30**		**28**			**100.0 %**	**0.07 [-0.09, 0.23]**

Heterogeneity: Chi^2 = 0.84, df = 2 (P = 0.66); I^2 =0.0%

Test for overall effect: Z = 0.89 (P = 0.38)

Test for subgroup differences: Not applicable

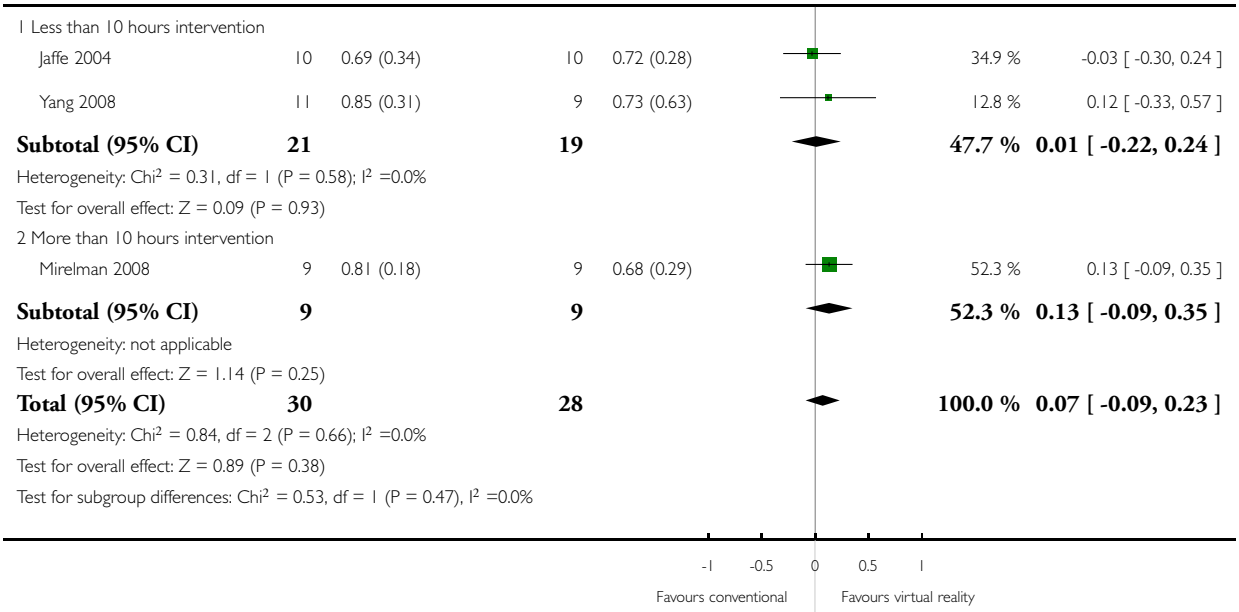
Analysis 6.1. Comparison 6 Virtual reality versus conventional therapy: effect on lower limb activity post-treatment: subgroup analyses, Outcome 1 Dose of intervention: effect on gait speed.

Review: Virtual reality for stroke rehabilitation

Comparison: 6 Virtual reality versus conventional therapy: effect on lower limb activity post-treatment: subgroup analyses

Outcome: 1 Dose of intervention: effect on gait speed

Study or subgroup	Virtual reality N	Mean(SD)	Alternative therapy N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Less than 10 hours intervention							
Jaffe 2004	10	0.69 (0.34)	10	0.72 (0.28)		34.9 %	-0.03 [-0.30, 0.24]
Yang 2008	11	0.85 (0.31)	9	0.73 (0.63)		12.8 %	0.12 [-0.33, 0.57]
Subtotal (95% CI)	**21**		**19**			**47.7 %**	**0.01 [-0.22, 0.24]**
Heterogeneity: Chi^2 = 0.31, df = 1 (P = 0.58); I^2 =0.0%							
Test for overall effect: Z = 0.09 (P = 0.93)							
2 More than 10 hours intervention							
Mirelman 2008	9	0.81 (0.18)	9	0.68 (0.29)		52.3 %	0.13 [-0.09, 0.35]
Subtotal (95% CI)	**9**		**9**			**52.3 %**	**0.13 [-0.09, 0.35]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.14 (P = 0.25)							
Total (95% CI)	**30**		**28**			**100.0 %**	**0.07 [-0.09, 0.23]**
Heterogeneity: Chi^2 = 0.84, df = 2 (P = 0.66); I^2 =0.0%							
Test for overall effect: Z = 0.89 (P = 0.38)							
Test for subgroup differences: Chi^2 = 0.53, df = 1 (P = 0.47), I^2 =0.0%							



Analysis 7.1. Comparison 7 Additional virtual reality intervention: effect on global motor function post-treatment, Outcome 1 Global motor function.

Review: Virtual reality for stroke rehabilitation

Comparison: 7 Additional virtual reality intervention: effect on global motor function post-treatment

Outcome: 1 Global motor function

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Kim 2012	10	34.7 (6.2)	7	33.57 (1.51)		62.0 %	0.22 [-0.75, 1.19]
You 2005	5	38 (4.6)	5	38 (4.4)		38.0 %	0.0 [-1.24, 1.24]
Total (95% CI)	**15**		**12**			**100.0 %**	**0.14 [-0.63, 0.90]**

Heterogeneity: $Chi^2 = 0.07$, df = 1 (P = 0.79); $I^2 = 0.0\%$

Test for overall effect: Z = 0.35 (P = 0.73)

Test for subgroup differences: Not applicable

Analysis 8.1. Comparison 8 Virtual reality versus conventional therapy: effect on secondary outcomes, Outcome 1 ADL outcome.

Review: Virtual reality for stroke rehabilitation

Comparison: 8 Virtual reality versus conventional therapy: effect on secondary outcomes

Outcome: 1 ADL outcome

Study or subgroup	Experimental		Control		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	IV,Fixed,95% CI		IV,Fixed,95% CI
Byl 2013	5	141.7 (14.42)	5	122.8 (26.69)		3.7 %	0.80 [-0.52, 2.11]
da Silva Cameirao 2011	8	96.875 (5.514)	8	93.88 (7.772)		6.5 %	0.42 [-0.57, 1.42]
Kang 2009	8	56.4 (21.5)	8	47.3 (19.6)		6.5 %	0.42 [-0.58, 1.41]
Kim 2011b	12	47.9 (15.1)	12	44.9 (21.8)		10.0 %	0.15 [-0.65, 0.96]
Kiper 2011	40	106 (19.8)	40	102.9 (18.2)		33.5 %	0.16 [-0.28, 0.60]
Piron 2007	25	110.2 (13.9)	13	95.9 (28.3)		13.5 %	0.70 [0.01, 1.39]
Piron 2010	27	118.9 (6.8)	20	108.7 (12.6)		16.9 %	1.04 [0.42, 1.65]
Zucconi 2012	11	113.9 (12.7)	11	112.4 (20.8)		9.2 %	0.08 [-0.75, 0.92]
Total (95% CI)	**136**		**117**			**100.0 %**	**0.43 [0.18, 0.69]**

Heterogeneity: Chi^2 = 7.14, df = 7 (P = 0.41); I^2 =2%

Test for overall effect: Z = 3.33 (P = 0.00086)

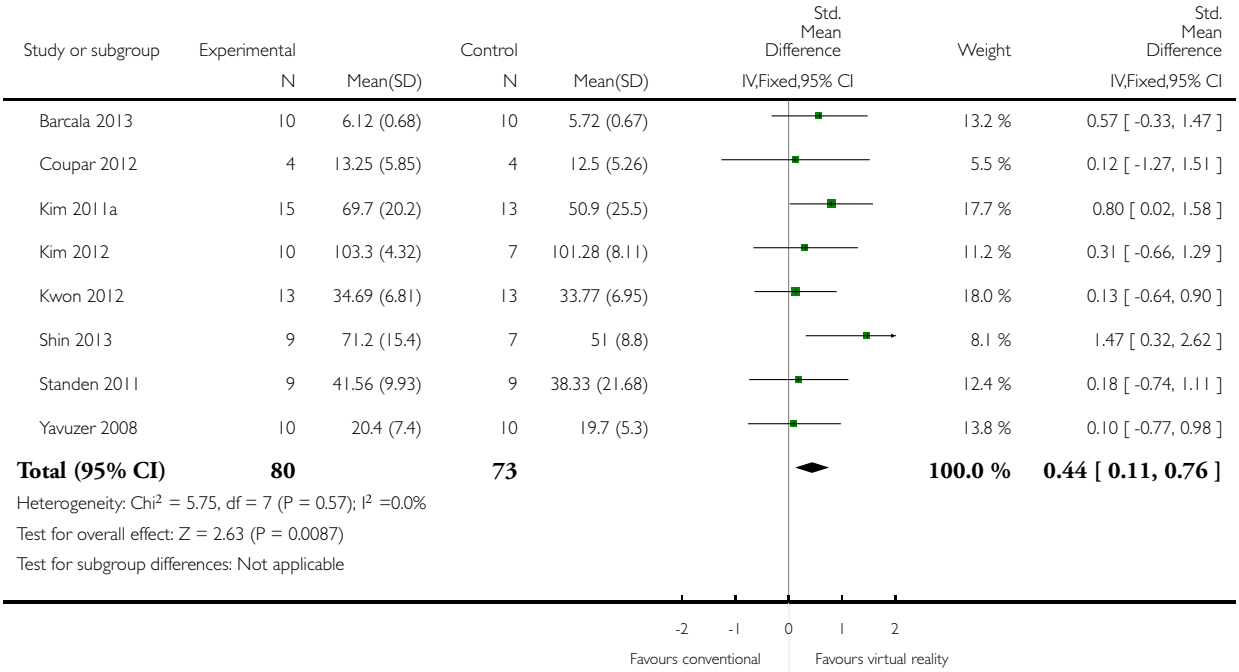
Test for subgroup differences: Not applicable

Analysis 9.1. Comparison 9 Additional virtual reality intervention: effect on secondary outcomes, Outcome 1 ADL outcome.

Review: Virtual reality for stroke rehabilitation

Comparison: 9 Additional virtual reality intervention: effect on secondary outcomes

Outcome: 1 ADL outcome



ADDITIONAL TABLES

Table 1. Number screened, number still in trial and virtual reality intervention at end of trial

Author and year	Screened	Randomised	Allocated virtual reality	Completed trial/analysed at final follow-up	Completed virtual reality
Akinwuntan 2005	126	83	42	73 post training 52 at 6 months 61 at 5 years	37
Barcala 2013	43	20	10	20	10
Byl 2013	Not reported	18	Unclear	15	Unclear

Table 1. Number screened, number still in trial and virtual reality intervention at end of trial (*Continued*)

Cho 2012	Not reported	31	16	29	15
Coupar 2012	393	12	4	4	4
Crosbie 2008	74	18	9	17	8
da Silva Cameirao 2011	142	25	13	Unclear	8
Housman 2009	Not reported	34	17	28	15
Jaffe 2004	Not reported	20	10	20	10
Jang 2005	Not reported	10	5	10	5
Jannink 2008	Not reported	10	5	Not reported	Not reported
Jung 2012	25	21	11	21	11
Kang 2009	45	16	8	16	8
Kim 2009	Not reported	24	12	Not reported	Not reported
Kim 2011a	Not reported	28	15	28	15
Kim 2011b	Not reported	24	23	Not reported	Not reported
Kim 2012	Not reported	20	10	17	10
Kiper 2011	Not reported	80	40	Not reported	Not reported
Kwon 2012	Not reported	26	13	26	13
Lam 2006	Not reported	58	20	Not reported	Not reported
Mazer 2005	Not reported	46	22	39	20
Mirelman 2008	27	18	9	17	8
Piron 2007	Not reported	38	25	Not reported	Not reported
Piron 2009	Not reported	36	18	36	18
Piron 2010	292	50	27	47	27
Rajaratnam 2013	19	19	10	19	10

Table 1. Number screened, number still in trial and virtual reality intervention at end of trial (*Continued*)

Saposnik 2010	110	22	11	16	9
Shin 2013	73	16	9	16	9
Sin 2013	Not reported	14	7	14	7
Standen 2011	47	27	17	18	9
Subramanian 2013	Not reported	32	16	12	16
Sucar 2009	Not reported	22	11	Not reported	Not reported
Yang 2008	34	24	12	20	9
Yang 2011	Not reported	14	7	14	7
Yavuzer 2008	25	20	10	20	10
You 2005	Not reported	10	5	10	Not reported
Zucconi 2012	Not reported	33	11	33	11

Table 2. Outcome measures used from the included trials

Author and year	Upper limb function	Hand function	Lower limb activity	Balance and postural control	Global motor function	Cognitive function	Activity limitation	Participation restriction and QOL
Akinwuntan 2005	-	-	-	-	-	Useful Field of View test	On-road driving test score, decision of fitness to drive	-
Barcala 2013	-	-	Timed Up and Go	Berg Balance Scale, centre of pressure data, body symmetry data	-	-	Functional Independence Measure	-
Byl 2013	Fugl Meyer UE Scale, Motor Proficiency Speed	Motor skill performance (Box and Block	-	-	-	-	Functional Independence (CAFE40)	Stroke Impact Scale

Table 2. Outcome measures used from the included trials (*Continued*)

	(abbreviated Wolf Motor Function test + Digital reaction time test)	and tapper test)						
Cho 2012	Wolf Motor Function Test	-	-	-	-	Motor Free Visual Perception Test	-	-
Crosbie 2008	Action Research Arm Test, Upper Limb Motricity Index	-	-	-	-	-	-	-
da Silva Cameirao 2011	Fugl Meyer UE, Chedoke Arm and Hand Inventory	-	-	-	-	-	Barthel Index	-
Housman 2009	Fugl Meyer UE Scale, Rancho Functional Test	Grip strength (kg)	-	-	-	-	-	Motor Activity Log (amount of use and quality of movement)
Jaffe 2004	-	-	6-metre walk test, Obstacle Test, 6-minute walk test	Customised balance test designed by the researchers	-	-	-	-
Jang 2005	Fugl Meyer UE Scale, Manual Function Test	Box and Block Test	-	-	-	-	-	Motor Activity Log (amount of use and quality of movement)
Jannink 2008	-	-	-	-	-	-	-	-

Table 2. Outcome measures used from the included trials (*Continued*)

Jung 2012	-	-	Timed Up and Go	-	-	-	-	-
Kang 2009	-	-	-	-	-	Mini Mental State Examination	Modified Barthel Index	-
Kim 2009	-	-	10-metre walk test, GAITRITE gait analysis system	Berg Balance Scale, balance performance monitor	Modified Motor Assessment Scale	-	-	-
Kim 2011a	Motricity Index	-	Motricity Index	-	-	Computerised neuropsychological test and Tower of London test	Korean Modified Barthel Index	-
Kim 2011b	-	-	-	-	-	Measures of spatial neglect (star cancellation, line bisection test, Catherine Bergego Scale)	Korean Modified Barthel Index	-
Kim 2012	-	-	-	Postural assessment scale	Modified Motor Assessment Scale	-	Functional Independence Measure	-
Kiper 2011	Fugl Meyer UE	-	-	-	-	-	Functional Independence Measure	-
Kwon 2012	Fugl Meyer UE, Manual Function Test	-	-	-	-	-	Korean Modified Barthel Index	-
Lam 2006	-	-	-	-	-	-	-	-

Table 2. Outcome measures used from the included trials (*Continued*)

Mazer 2005	-	-	-	-	-	-	DriveAble Testing Ltd Driver Evaluation	-
Mirelman 2008	-	-	Gait speed over 7-metre walkway, 6-minute walk test, Patient Activity Monitor	-	-	-	-	-
Piron 2007	Fugl Meyer UE Scale	-	-	-	-	-	Functional Independence Measure	-
Piron 2009	Fugl Meyer UE Scale	-	-	-	-	-	-	Abilhand Scale
Piron 2010	Fugl Meyer UE Scale	-	-	-	-	-	Functional Independence Measure	-
Rajaratnam 2013	-	-	Timed Up and Go	Berg Balance Scale, functional reach, centre of pressure	-	-	-	-
Saposnik 2010	Abbreviated Wolf Motor Function Test	Box and Block Test, grip strength (kg)	-	-	-	-	-	Stroke Impact Scale (hand function, composite function, perception of recovery)
Shin 2013	Fugl Meyer UE	-	-	-	-	-	Modified Barthel Index	-
Sin 2013	Fugl Meyer UE	Box and Block Test	-	-	-	-	-	-

Table 2. Outcome measures used from the included trials (*Continued*)

Standen 2011	Wolf Motor Function Test	Nine Hole Peg Test	-	-	-	-	Nottingham Extended Activities of Daily Living Scale	Motor Activity Log
Subramanian 2013	Fugl Meyer UE, Wolf Motor Function test, Reaching performance scale for stroke	-	-	-	-	-	-	Motor Activity Log
Sucar 2009	Fugl Meyer UE Scale, Upper Limb Motricity Index	-	-	-	-	-	-	-
Yang 2008	-	-	Walking speed, Community Walk Test	-	-	-	-	Walking Ability Questionnaire, Activities Specific Balance Confidence Scale
Yang 2011	-	-	Gait analysis data	Balance analysis data	-	-	-	-
Yavuzer 2008	Brunnstrom Upper Extremity Stages	Brunnstrom Hand Stages	-	-	-	-	Functional Independence Measure self care section	-
You 2005	-	-	Functional ambulation category	-	Modified Motor Assessment Scale	-	-	-
Zucconi 2012	Fugl Meyer UE, Reaching performance scale	-	-	-	-	-	Functional Independence Measure	-

fMRI: functional magnetic resonance imaging

QOL: quality of life
UE: upper extremity

APPENDICES

Appendix 1. MEDLINE search strategy

We used the following search strategy for MEDLINE (Ovid) and adapted it to search the other databases.
1. cerebrovascular disorders/ or exp basal ganglia cerebrovascular disease/ or exp brain ischemia/ or exp carotid artery diseases/ or exp intracranial arterial diseases/ or exp intracranial arteriovenous malformations/ or exp "intracranial embolism and thrombosis"/ or exp intracranial hemorrhages/ or stroke/ or exp brain infarction/
2. brain injuries/ or brain injury, chronic/
3. (stroke$ or cva or poststroke or post-stroke or cerebrovasc$ or cerebral vascular).tw.
4. ((cerebral or cerebellar or brain$ or vertebrobasilar) adj5 (infarct$ or isch?emi$ or thrombo$ or emboli$ or apoplexy)).tw.
5. ((cerebral or brain or subarachnoid) adj5 (haemorrhage or hemorrhage or haematoma or hematoma or bleed$)).tw.
6. exp hemiplegia/ or exp paresis/
7. (hempar$ or hemipleg$ or paresis or paretic or brain injur$).tw.
8. Gait Disorders, Neurologic/
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10. user-computer interface/
11. computers/ or exp microcomputers/ or computer systems/ or software/
12. computer simulation/ or computer-assisted instruction/ or therapy, computer-assisted/
13. computer graphics/ or video games/ or *touch/
14. (virtual reality$ or virtual-reality$ or VR).tw.
15. (virtual adj3 (environment$ or object$ or world$ or treatment$ or system$ or program$ or rehabilitation$ or therap$ or driving or drive$ or car or tunnel or vehicle)).tw.
16. (computer adj3 (simulat$ or graphic$ or game$ or interact$)).tw.
17. (computer adj1 assist$ adj1 (therap$ or treat$)).tw.
18. (computer adj1 generat$ adj1 (environment$ or object$)).tw.
19. (video game$ or video gaming or gaming console$ or interactive game or interactive gaming or Nintendo Wii or gaming program$).tw.
20. (haptics or haptic device$).tw.
21. (simulat$ adj3 (environment$ or object$ or event$1 or driving or drive$ or car or tunnel or vehicle)).tw.
22. (user adj1 computer adj1 interface).tw.
23. or/10-22
24. Randomized Controlled Trials as Topic/
25. random allocation/
26. Controlled Clinical Trials as Topic/
27. control groups/
28. clinical trials as topic/
29. double-blind method/
30. single-blind method/
31. Placebos/
32. placebo effect/
33. cross-over studies/
34. Research Design/
35. randomized controlled trial.pt.

36. controlled clinical trial.pt.
37. clinical trial.pt.
38. (random$ or RCT or RCTs).tw.
39. (controlled adj5 (trial$ or stud$)).tw.
40. (clinical$ adj5 trial$).tw.
41. ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw.
42. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw.
43. ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw.
44. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
45. (cross-over or cross over or crossover).tw.
46. (placebo$ or sham).tw.
47. trial.ti.
48. (assign$ or allocat$).tw.
49. or/24-48
50. 9 and 23 and 49
51. limit 50 to ed=20100301-20131026

Appendix 2. EMBASE search strategy

1. cerebrovascular disease/ or exp basal ganglion hemorrhage/ or exp brain hematoma/ or exp brain hemorrhage/ or exp brain infarction/ or exp brain ischemia/ or exp carotid artery disease/ or cerebral artery disease/ or exp cerebrovascular accident/ or exp cerebrovascular malformation/ or exp intracranial aneurysm/ or exp occlusive cerebrovascular disease/ or stroke/ or stroke unit/ or stroke patient/
2. brain injury/ or acquired brain injury/
3. (stroke$ or cva or poststroke or post-stroke or cerebrovasc$ or cerebral vascular).tw.
4. ((cerebral or cerebellar or brain$ or vertebrobasilar) adj5 (infarct$ or isch?emi$ or thrombo$ or emboli$ or apoplexy)).tw.
5. ((cerebral or brain or subarachnoid) adj5 (haemorrhage or hemorrhage or haematoma or hematoma or bleed$)).tw.
6. hemiparesis/ or hemiplegia/ or paresis/
7. (hempar$ or hemipleg$ or paresis or paretic or brain injur$).tw.
8. exp neurologic gait disorder/
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10. virtual reality/ or computer interface/ or exp computer/ or computer program/ or computer simulation/ or computer assisted therapy/ or computer graphics/ or *touch/
11. (virtual reality$ or virtual-reality$ or VR).tw.
12. (virtual adj3 (environment$ or object$ or world$ or treatment$ or system$ or program$ or rehabilitation$ or therap$ or driving or drive$ or car or tunnel or vehicle)).tw.
13. (computer adj3 (simulat$ or graphic$ or game$ or interact$)).tw.
14. (computer adj1 assist$ adj1 (therap$ or treat$)).tw.
15. (computer adj1 generat$ adj1 (environment$ or object$)).tw.
16. (video game$ or video gaming or gaming console$ or interactive game or interactive gaming or Nintendo Wii or gaming program$).tw.
17. (haptics or haptic device$).tw.
18. (simulat$ adj3 (environment$ or object$ or event$1 or driving or drive$ or car or tunnel or vehicle)).tw.
19. (user adj1 computer adj1 interface).tw.
20. or/10-19
21. Randomized Controlled Trial/
22. Randomization/
23. Controlled Study/
24. control group/
25. clinical trial/
26. Crossover Procedure/
27. Double Blind Procedure/
28. Single Blind Procedure/ or triple blind procedure/

29. placebo/
30. "types of study"/
31. (random$ or RCT or RCTs).tw.
32. (controlled adj5 (trial$ or stud$)).tw.
33. (clinical$ adj5 trial$).tw.
34. ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw.
35. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw.
36. ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw.
37. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
38. (cross-over or cross over or crossover).tw.
39. placebo$ or sham).tw.
40. trial.ti.
41. (assign$ or allocat$).tw.
42. or/21-41
43. 9 and 20 and 42
44. limit 43 to DD=20100301-20131026

Appendix 3. AMED search strategy

1. cerebrovascular disorders/ or cerebral hemorrhage/ or cerebral infarction/ or cerebral ischemia/ or cerebrovascular accident/ or stroke/ or brain injuries/
2. (stroke$ or cva or poststroke or post-stroke or cerebrovasc$ or cerebral vascular).tw.
3. ((cerebral or cerebellar or brain$ or vertebrobasilar) adj5 (infarct$ or isch?emi$ or thrombo$ or emboli$ or apoplexy)).tw.
4. ((cerebral or brain or subarachnoid) adj5 (haemorrhage or hemorrhage or haematoma or hematoma or bleed$)).tw.
5. hemiplegia/ or gait disorders/
6. (hempar$ or hemipleg$ or paresis or paretic or brain injur$).tw.
7. 1 or 2 or 3 or 4 or 5 or 6
8. virtual reality/ or computer systems/ or exp computers/ or internet/ or software/ or computer graphics/ or computer assisted instruction/ or computer simulation/ or therapy computer assisted/ or "play and playthings"/
9. (virtual reality$ or virtual-reality$ or VR).tw.
10. (virtual adj3 (environment$ or object$ or world$ or treatment$ or system$ or program$ or rehabilitation$ or therap$ or driving or drive$ or car or tunnel or vehicle)).tw.
11. (computer adj3 (simulat$ or graphic$ or game$ or interact$)).tw.
12. (computer adj1 assist$ adj1 (therap$ or treat$)).tw.
13. (computer adj1 generat$ adj1 (environment$ or object$)).tw.
14. (video game$ or video gaming or gaming console$ or interactive game or interactive gaming or Nintendo Wii or gaming program$).tw.
15. (haptics or haptic device$).tw.
16. (simulat$ adj3 (environment$ or object$ or event$1 or driving or drive$ or car or tunnel or vehicle)).tw.
17. (user adj1 computer adj1 interface).tw.
18. or/8-17
19. 7 and 18
20. limit 19 to UP=201003-201310

Appendix 4. CINAHL search strategy

S55 S54 and EM 201003-
S54 -S34 AND S53
S53 -S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S46 OR S47 OR S50 OR S51 OR S52
S52 -TI trial OR (TI (RCT or RCTs) OR AB (RCT or RCTs))
S51 -TI (counterbalance* or multiple baseline* or ABAB design) or AB (counterbalance* or multiple baseline* or ABAB design)
S50 -S48 and S49
S49 -TI trial* or AB trial*
S48 -TI (clin* or intervention* or compar* or experiment* or preventive or therapeutic) or AB (clin* or intervention* or compar* or experiment* or preventive or therapeutic)
S47 -TI (crossover or cross-over or placebo* or control* or factorial or sham) or AB (crossover or cross-over or placebo* or control* or factorial or sham)
S46 -S44 and S45
S45 -TI (blind* or mask*) or AB (blind* or mask*)
S44 -TI (singl* or doubl* or tripl* or trebl*) or AB (singl* or doubl* or tripl* or trebl*)
S43 -TI random* or AB random*
S42 -(MH "Community Trials") or (MH "Experimental Studies") or (MH "One-Shot Case Study") or (MH "Pretest-Posttest Design+") or (MH "Solomon Four-Group Design") or (MH "Static Group Comparison") or (MH "Study Design")
S41 -(MH "Clinical Research") or (MH "Clinical Nursing Research")
S40 -(MH "Placebo Effect") or (MH "Placebos") or (MH "Meta Analysis")
S39 -(MH "Factorial Design") or (MH "Quasi-Experimental Studies") or (MH "Nonrandomized Trials")
S38 -(MH "Control (Research)") or (MH "Control Group")
S37 -(MH "Crossover Design") or (MH "Clinical Trials+") or (MH "Comparative Studies")
S36 -(MH "Random Assignment") or (MH "Random Sample+")
S35 -PT randomized controlled trial or clinical trial
S34 -S15 AND S33
S33 -S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32
S32 -TI (user N2 computer N2 interface) or AB (user N2 computer N2 interface)
S31 -TI (simulat* N3 (environment* or object* or event or events or driving or drive* or car or tunnel or vehicle)) or AB (simulat* N3 (environment* or object* or event or events or driving or drive* or car or tunnel or vehicle))
S30 -TI (haptics or haptic device*) or AB (haptics or haptic device*)
S29 -TI (video game* or video gaming or gaming console* or interactive game or interactive gaming or Nintendo Wii or gaming program*) or AB (video game* or video gaming or gaming console* or interactive game or interactive gaming or Nintendo Wii or gaming program*)
S28 -TI (computer generat* N3 (environment* or object*)) or AB (computer generat* N3 (environment* or object*))
S27 -TI (computer assist* N3 (therap* or treat*)) or AB (computer assist* N3 (therap* or treat*))
S26 -TI (computer N3 (simulat* or graphic* or game* or interact*)) or AB (computer N3 (simulat* or graphic* or game* or interact*))
S25 -TI (virtual N3 (environment* or object* or world* or treatment* or system* or program* or rehabilitation* or therap* or driving or drive* or car or tunnel or vehicle)) or AB (virtual N3 (environment* or object* or world* or treatment* or system* or program* or rehabilitation* or therap* or driving or drive* or car or tunnel or vehicle))
S24 -TI (virtual reality* or virtual-reality* or VR) OR AB (virtual reality* or virtual-reality* or VR)
S23 -(MM "Touch")
S22 -(MH "Video Games")
S21 -(MH "Computer Graphics")
S20 -(MH "Microcomputers+")
S19 -(MH "Computer Systems") OR (MH "User-Computer Interface+") OR (MH "Software+")
S18 -(MH "Computer Assisted Instruction")
S17 -(MH "Therapy, Computer Assisted")
S16 -(MH "Computer Simulation") OR (MH "Virtual Reality") OR (MH "Computing Methodologies") OR (MH "Computers and Computerization")
S15 -S1 OR S2 OR S3 OR S6 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14

S14 -TI brain injur* OR AB brain inju*
S13 -(MH “Brain Injuries”)
S12 -(MH “Gait Disorders, Neurologic+”)
S11 -TI (hemipleg* or hemipar* or paresis or paretic) or AB (hemipleg* or hemipar* or paresis or paretic)
S10 -(MH “Hemiplegia”)
S9 -S7 and S8
S8 -TI (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*) or AB (haemorrhage* or hemorrhage* or haematoma* or hematoma* or bleed*)
S7 -TI (brain* or cerebr* or cerebell* or intracerebral or intracranial or subarachnoid) or AB (brain* or cerebr* or cerebell* or intracerebral or intracranial or subarachnoid)
S6 -S4 and S5
S5 -TI (ischemi* or ischaemi* or infarct* or thrombo* or emboli* or occlus*) or AB (ischemi* or ischaemi* or infarct* or thrombo* or emboli* or occlus*)
S4 -TI (brain* or cerebr* or cerebell* or intracran* or intracerebral) or AB (brain* or cerebr* or cerebell* or intracran* or intracerebral)
S3 -TI (stroke or poststroke or post-stroke or cerebrovasc* or brain vasc* or cerebral vasc or cva or apoplex or SAH) or AB (stroke or poststroke or post-stroke or cerebrovasc* or brain vasc* or cerebral vasc or cva or apoplex or SAH)
S2 -(MH “Stroke Patients”) OR (MH “Stroke Units”)
S1 -(MH “Cerebrovascular Disorders”) OR (MH “Basal Ganglia Cerebrovascular Disease+”) OR (MH “Carotid Artery Diseases+”) OR (MH “Cerebral Ischemia+”) OR (MH “Cerebral Vasospasm”) OR (MH “Intracranial Arterial Diseases+”) OR (MH “Intracranial Embolism and Thrombosis”) OR (MH “Intracranial Hemorrhage+”) OR (MH “Stroke”) OR (MH “Vertebral Artery Dissections”)

Appendix 5. PsycINFO search strategy

1. cerebrovascular disorders/ or cerebral hemorrhage/ or exp cerebral ischemia/ or cerebrovascular accidents/ or subarachnoid hemorrhage/ or brain damage/
2. (stroke$ or cva or poststroke or post-stroke or cerebrovasc$ or cerebral vascular).tw.
3. ((cerebral or cerebellar or brain$ or vertebrobasilar) adj5 (infarct$ or isch?emi$ or thrombo$ or emboli$ or apoplexy)).tw.
4. ((cerebral or brain or subarachnoid) adj5 (haemorrhage or hemorrhage or haematoma or hematoma or bleed$)).tw.
5. hemiparesis/ or hemiplegia/
6. (hempar$ or hemipleg$ or paresis or paretic or brain injur$).tw.
7. 1 or 2 or 3 or 4 or 5 or 6
8. virtual reality/ or role playing games/ or exp computer assisted instruction/ or computer assisted therapy/ or computer simulation/ or computer games/ or simulation games/ or computers/ or microcomputers/ or internet/ or computer applications/ or computer software/
9. (virtual reality$ or virtual-reality$ or VR).tw.
10. (virtual adj3 (environment$ or object$ or world$ or treatment$ or system$ or program$ or rehabilitation$ or therap$ or driving or drive$ or car or tunnel or vehicle)).tw.
11. (computer adj3 (simulat$ or graphic$ or game$ or interact$)).tw.
12. (computer adj1 assist$ adj1 (therap$ or treat$)).tw.
13. (computer adj1 generat$ adj1 (environment$ or object$)).tw.
14. (video game$ or video gaming or gaming console$ or interactive game or interactive gaming or Nintendo Wii or gaming program$).tw.
15. (haptics or haptic device$).tw.
16. (simulat$ adj3 (environment$ or object$ or event$1 or driving or drive$ or car or tunnel or vehicle)).tw.
17. (user adj1 computer adj1 interface).tw.
18. or/8-17
19. 7 and 18
20. limit 19 to yr=2010-Current

Appendix 6. Cochrane 'Risk of bias' table

The Cochrane Collaboration's tool for assessing risk of bias

Domain	Description	Review authors' judgement
Sequence generation	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups	Was the allocation sequence adequately generated? ▫ Yes ▫ No ▫ Unsure
Allocation concealment	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment	Was allocation adequately concealed? ▫ Yes ▫ No ▫ Unsure
Blinding of outcome assessors *Assessments should be made for each main outcome (or class of outcomes)*	Describe all measures used, if any, to blind personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective	Was knowledge of the allocated intervention adequately prevented during the study? Outcome assessors ▫ Yes ▫ No ▫ Unsure
Incomplete outcome data *Assessments should be made for each main outcome (or class of outcomes).*	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomised participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors	Were incomplete outcome data adequately addressed? ▫ Yes ▫ No ▫ Unsure

(*Continued*)

Selective outcome reporting	State how the possibility of selective outcome reporting was examined by the review authors, and what was found	Are reports of the study free of suggestion of selective outcome reporting? □ Yes □ No □ Unsure

WHAT'S NEW

Last assessed as up-to-date: 29 November 2013.

Date	Event	Description
27 August 2014	New citation required but conclusions have not changed	The conclusions of the review have not changed.
27 August 2014	New search has been performed	We updated the searches to November 2013. We have added 18 new studies, bringing the total number of included studies to 37, involving a total of 1019 participants. We have revised the review throughout

CONTRIBUTIONS OF AUTHORS

Kate Laver is the guarantor of the review. She was involved in conceiving, designing and co-ordinating the review; designing the search strategies; undertaking the searches; screening the search results; organising retrieval of papers; screening retrieved papers against the inclusion criteria; appraising the quality of the papers; extracting data from the papers; writing to authors for additional information; managing and entering data into RevMan; analysing and interpreting the data and writing the review.

Stacey George was involved in conceiving and designing the review; extracting data, analysing and interpreting the data and writing the review.

Susie Thomas was involved in screening the search results; organising retrieval of papers; screening retrieved papers against the inclusion criteria; appraising the quality of the papers; extracting data from the papers; analysing and interpreting the data and writing the review.

Judith Deutsch was involved in designing the review; screening retrieved papers against inclusion criteria; writing to authors of papers for additional information; extracting data, analysing and interpreting the data and writing the review.

Maria Crotty was involved in conceiving and designing the review; appraising the quality of papers; writing to authors of papers for additional information; analysing and interpreting the data and writing the review.

DECLARATIONS OF INTEREST

Kate Laver: none known.

Stacey George: none known.

Susie Thomas: none known.

Judith Deutsch conducts research on virtual reality for stroke rehabilitation. This research is funded by various sources and presented at scientific and professional meetings. She is co-owner of a company that develops virtual reality for rehabilitation.

Maria Crotty: none known.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The protocol stated that we would handsearch conference proceedings and contact manufacturers of virtual reality equipment. We conducted these searches for the 2010 review. However, they were not successful in identifying additional studies for inclusion and therefore were not repeated in the 2013 review.

The protocol stated that we would assess trials for risk of bias related to blinding of participants and personnel. We assessed blinding of participants and personnel in the 2010 review. As expected, we deemed all the studies included in the 2010 review to be at high risk of bias. As blinding is not possible in most cases we decided to omit this domain of the 'Risk of bias' assessment tool in this update of the review.

The protocol listed three primary outcomes. This review identified upper limb function and activity as being the primary outcome and considered all other outcomes as secondary outcomes. We selected upper limb function and activity as the primary outcome as one of the most common applications of virtual reality in stroke rehabilitation is upper limb rehabilitation.

INDEX TERMS

Medical Subject Headings (MeSH)

*Video Games; Activities of Daily Living; Psychomotor Performance; Randomized Controlled Trials as Topic; Stroke [psychology; *rehabilitation]; Therapy, Computer-Assisted [*methods]; User-Computer Interface

MeSH check words

Humans