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, published in Issue 9, 2011.
Review content assessed as up-to-date: 19 May 2011.

Citation: Laver KE, George S, Thomas S, Deutsch JE, Crotty M. Virtual reality for stroke rehabilitation. *Cochrane Database of Systematic Reviews* 2011, Issue 9. Art. No.: CD008349. DOI: 10.1002/14651858.CD008349.pub2.

ABSTRACT

Background

Virtual reality and interactive video gaming have emerged as new treatment approaches in stroke rehabilitation. In particular, commercial gaming consoles are being rapidly adopted in clinical settings; however, there is currently little information about their effectiveness.

Objectives

To evaluate the effects of virtual reality and interactive video gaming on upper limb, lower limb and global motor function after stroke.

Search methods

We searched the Cochrane Stroke Group Trials Register (March 2010), the Cochrane Central Register of Controlled Trials (*The Cochrane Library* 2010, Issue 1), MEDLINE (1950 to March 2010), EMBASE (1980 to March 2010) and seven additional databases. We also searched trials registries, conference proceedings, reference lists and contacted key researchers in the area and virtual reality equipment manufacturers.

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 outcomes of interest were: upper limb function and activity, 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 all investigators to obtain missing information.

Main results

We included 19 trials which involved 565 participants. Study sample sizes were generally small and interventions and outcome measures varied, limiting the ability to which studies could be compared. 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 outcomes: results were statistically significant for arm function (standardised mean difference (SMD) 0.53, 95% confidence intervals (CI) 0.25 to 0.81 based on seven studies with 205 participants). There were no

statistically significant effects for grip strength or gait speed. We were unable to determine the effect on global motor function due to insufficient numbers of comparable studies. Secondary outcomes: results were statistically significant for activities of daily living (ADL) outcome (SMD 0.81, 95% CI 0.39 to 1.22 based on three studies with 101 participants); however, 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 were relatively mild. Studies that reported on eligibility rates showed that only 34% (standard deviation (SD) 26, range 17 to 80) of participants screened were recruited.

Authors' conclusions

We found limited evidence that the use of virtual reality and interactive video gaming may be beneficial in improving arm function and ADL function 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 or gait speed. 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. Furthermore, there are currently very few studies evaluating the use of commercial gaming consoles (such as the Nintendo Wii).

PLAIN LANGUAGE SUMMARY

Virtual reality for stroke rehabilitation

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 may 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.

This review aimed to determine the evidence for effectiveness of virtual reality and interactive video gaming as a therapy approach. We identified 19 studies involving 565 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 (rather than smaller movements such as moving a joystick). Seven 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. Three trials tested whether the use of virtual reality compared with conventional therapy resulted in improved walking speed. However, there was no evidence that virtual reality was more effective in this case. Three 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. Further trials involving larger numbers of participants and longer-term follow-up are required.

BACKGROUND

Description of the condition

Stroke is one of the leading causes of death and disability and has been described as a worldwide epidemic (Donnan 2008; Feigin 2009). 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 (Mayo 1999). While most recovery is thought to be made in the first few weeks after stroke, patients may make improvements on functional tasks and experience neural reorganisation many months after having a stroke (Teasell 2005). 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 (French 2007). Virtual reality is a relatively recent approach that may enable simulated practice of functional tasks at a higher dosage than traditional therapies (Kwakkel 2004; Merians 2002). 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 (Burdea 2003), the use of virtual reality is not yet commonplace in clinical rehabilitation settings. However, gaming consoles are ubiquitous (Burdea 2003) and so researchers and clinicians are turning to low-cost commercial gaming systems as an alternative way of delivering virtual reality (Deutsch 2008; 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).

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.

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).

Virtual reality has been used in a neurological rehabilitation population to improve upper (Henderson 2007) and lower extremity function and gait (Deutsch 2011), as well as cognition, perception, and functional tasks such as crossing a street, driving, preparing food and shopping (Rose 2005).

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 (Dobkin 2004). 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.

Research with animals and humans has also shown us that intensive task-specific practice is able to induce cortical reorganisation (Nudo 1996; Nudo 2001) and behavioural change (Dean 1997). Virtual reality programs capitalise on this by offering simulated real-life functional activities that may provide enhanced ecological validity when compared with traditional rehabilitation tasks (Rizzo 2005). Virtual tasks have been described as more interesting and enjoyable by both children and adults, thereby encouraging higher numbers of repetitions (Bryanton 2006; Thornton 2005).

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 (Holden 2005).

Why it is important to do this review

As technology becomes more accessible and affordable, virtual reality is likely to become more widely used in clinical rehabilitation settings. It is important to evaluate the effectiveness 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.

A recent systematic review examined the effectiveness of virtual reality for stroke rehabilitation (Crosbie 2007). The authors included 11 studies, of which only three were randomised controlled trials RCTs). These were grouped and presented according to their assessed level of evidence (1 to 5). The authors concluded that

while effects were generally positive, the studies were too limited by design and power issues to decide their value. The review could have been strengthened by a more exhaustive search strategy as well as a more rigorous assessment of methodological quality of the included studies. Since this review was published, several additional RCTs have been published.

A more recent systematic review and meta-analysis aimed to evaluate the evidence for the effectiveness of virtual reality in rehabilitation of the upper limb post stroke (Saposnik 2011). The authors identified 12 studies, comprising five RCTs and seven observational studies. Pooled analysis of the RCTs showed there was a significant positive effect of virtual reality on motor impairment as measured by the Fugl Meyer Upper Extremity Scale. Analyses of the observational studies also suggested beneficial effects of virtual reality on upper limb impairment and function. The authors were limited by the number and quality of studies identified and once again, concluded that there was limited but promising information available. Furthermore, this review was limited to determining the effect of virtual reality on upper limb function without exploring its effect on other important outcomes such as participation and quality of life.

OBJECTIVES

Primary objective

The primary objective of this review was to determine the effectiveness of virtual reality compared with an alternative intervention or no intervention on:

1. upper limb function and activity;
2. gait and balance function and activity;
3. global motor function.

Secondary objective

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

1. cognitive function;
2. activity limitation;
3. participation restriction and quality of life;
4. imaging studies;
5. 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 RCTs and quasi-randomised (e.g. allocation by birth date) controlled trials (QRCTs). However, we did not find any relevant QRCTs and therefore, we only included RCTs. If we had found any relevant QRCTs, we intended to carry 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 as defined by the World Health Organization (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 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 there is a wide range of virtual reality applications, we examined their effects on three primary outcomes as follows.

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.

2. Gait and balance function and activity:

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

ii) standing reach: including assessments such as the Berg Balance Scale and laboratory-based force plate measures.

3. Global motor function: including assessments such as the Motor Assessment Scale.

Secondary outcomes

1. Cognitive function: including assessments such as Trail making test, Useful Field of View Test.
2. Activity limitation: including assessments such as the Functional Independence Measure (FIM), Barthel Index, Activities-specific Balance Confidence Scale, On-road driving test.
3. Participation restriction and quality of life: including assessments such as the SF36, EQ5D, Stroke Impact Scale or other patient-reported outcomes.
4. Imaging studies: including functional magnetic resonance imaging (MRI).
5. Adverse events: including motion sickness, pain, injury, falls and death.

Search methods for identification of studies

Electronic searches

See the 'Specialised register' section in the Cochrane Stroke Group module.

We searched the Cochrane Stroke Group Trials Register, which was searched by the Managing Editor in March 2010 using the intervention codes 'computer-aided therapy' and 'virtual reality therapy'. We identified 36 studies in total.

In addition, we searched the following electronic bibliographic databases: the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2010, Issue 1), MEDLINE (1950 to March Week 3, 2010) (Appendix 1), EMBASE (1980 to Week 11, 2010) (Appendix 2), AMED (1985 to March 2010) (Appendix 3), CINAHL (1982 to April Week 1, 2010) (Appendix 4), PsycINFO (1840 to March Week 4, 2010) (Appendix 5), PsycBITE (Psychological Database for Brain Impairment Treatment Efficacy, http://www.psycbite.com/) (to 26 March 2010), and OTseeker (http://www.otseeker.com/)(to 26 March 2010). We also searched the engineering databases COMPENDEX (1970 to 28 March 2010) and INSPEC (1969 to 28 March 2010) for studies from a non-medical background.

Our search strategy was developed in collaboration with the Cochrane Stroke Group Trials Search Co-ordinator for MEDLINE (Ovid) and we adapted it 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 26 March 2010;
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 and of two systematic reviews (Crosbie 2007; Henderson 2007);
4. searched Dissertation Abstracts (using Proquest to 29 March 2010) and contacted key researchers in the area;
5. scanned the abstracts of non-English language studies if they were available in English;
6. 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);
7. searched the IEEE (Institute of Electrical and Electronic Engineers) electronic library (to 28 March 2010);
8. 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.

We searched for relevant trials in all languages and arranged translation of trial reports published in languages other than English.

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 or MC 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) 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 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 participants, personnel and outcome assessors, and incomplete outcome data. We classified items as 'low risk', 'high risk' or 'unclear risk' of bias. 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.

Measures of treatment effect

Two review authors independently classified outcome measures in terms of the domain assessed (arm function, hand function, lower limb and gait function, standing reach, 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% 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. One study had three arms (Lam 2006) in which virtual reality was compared 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.

Dealing with missing data

We contacted study authors to obtain any missing data and converted available data when possible (for example, gait speed reported as metres per minute was converted to metres per second (Jaffe 2004)). Where possible, we conducted intention-to-treat analyses to include all people randomised 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 2008), 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. We inspected funnel plots for each of the analyses; however, interpretation was limited due to the small number of studies and 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 5.0 (RevMan 2008). 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 using 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, the type and severity of stroke, time since onset of stroke, frequency of intervention (number of sessions per week), intensity 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 small number of trials and 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).

Sensitivity analysis

We were unable to perform the planned sensitivity analyses based on methodological quality of studies (allocation concealment, blinding of outcome assessor, intention-to-treat analysis) or size of the study due to poor reporting, small numbers of trials and homogeneity of study methods and sample sizes. We performed sensitivity analyses to determine whether there was a difference in using a fixed-effect model versus a random-effects model.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of ongoing studies.
See Characteristics of included studies; Characteristics of excluded studies.

Results of the search

We identified 36 studies from searching the Cochrane Stroke Group trials register and 4225 references from the database searches totaling 4261 references to studies. A search of the trials registries elicited a further seven potentially relevant studies. From the 4268 titles and abstracts retrieved, we sought 73 of the articles in full text for further review, including four published in languages other than English. 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 19 studies. We have provided details on eight excluded studies (Broeren 2008; Chortis 2008; Der-Yeghiaian 2009; Edmans 2009; Fischer 2007; Gnajaraj 2007; Katz 2005; Krebs 2008) (Characteristics of excluded studies) which were closest to, but did not meet the inclusion criteria.

Included studies

We identified 19 randomised controlled trials which met the inclusion criteria.

Sample characteristics

The included studies were conducted in 11 different countries: four in Korea, three in the US, three in Italy, two in Canada and one each in Belgium, the UK, the Netherlands, Hong Kong, Mexico, Taiwan and Turkey. All trials, which were published in English, took place between 2004 and 2010. Twelve studies involved sample sizes of less than 25 participants (Crosbie 2008, Jaffe 2004; Jang 2005; Jannink 2008; Kang 2009; Kim 2009; Mirelman 2008; Saposnik 2010; Sucar 2009; Yang 2008; Yavuzer 2008; You 2005), five studies involved sample sizes between 26 and 50 participants (Housman 2009; Mazer 2005; Piron 2007; Piron 2009; Piron 2010) and two studies involved more than 50 participants with samples of 58 (Lam 2006) and 83 (Akinwuntan 2005). Therefore, a total of 565 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 51 to 73 years (actual range 30 to 83 years).
Inclusion criteria were specified for 13 studies; two trials recruited participants within three months of stroke (Akinwuntan 2005; Piron 2007); one trial recruited within six months of stroke (Saposnik 2010); six trials recruited participants more than six months post stroke (Housman 2009; Jaffe 2004; Jang 2005; Piron 2010; Sucar 2009; Yang 2008); one trial recruited within 12 months (Yavuzer 2008); two trials recruited participants more than 12 months post stroke (Kim 2009; You 2005); and one study recruited participants within two years (Crosbie 2008). 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. Three trials specified that people with a history of epilepsy would be excluded (Akinwuntan 2005; Mazer 2005; Saposnik 2010). All studies (with the exception of Akinwuntan 2005) 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; Housman 2009; Lam 2006; Mazer 2005; Mirelman 2008; Piron 2007; Piron 2009; Piron 2010; Saposnik 2010; Yang 2008; Yavuzer 2008), apraxia (Housman 2009; Lam 2006; Piron 2007; Piron 2009; Piron 2010) and visual impairment (Housman 2009; Jang 2005; Kang 2009; Kim 2009; Lam 2006; Piron 2007; Piron 2009; Piron 2010; Yang 2008; You 2005) as exclusion criterion. One study excluded people with computer-related phobia (Lam 2006). Studies involving upper limb training only included patients with mild to moderate upper limb impairment. 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 34% (SD 26, range 17 to 80) 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 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)). Eight trials involved upper limb training (Crosbie 2008; Housman 2009; Piron 2007; Piron 2009; Piron 2010; Saposnik 2010; Sucar 2009; Yavuzer 2008). Three trials involved lower limb and gait training (Jaffe 2004; Mirelman 2008; Yang 2008). Three trials used the same virtual reality program to improve global motor function (Jang 2005; Kim 2009; You 2005) and one trial used a visual-perceptual retraining approach (Kang 2009).

Two of the studies used commercially available gaming consoles: one study used the Playstation EyeToy (Yavuzer 2008) and another used the Nintendo Wii (Saposnik 2010). Three studies used GestureTek IREX, which is commercially available but more difficult to obtain and expensive than off-the-shelf consoles (Jang 2005; Kim 2009; You 2005). The remaining studies used customised virtual reality programs.

Setting

The majority of interventions were delivered in an outpatient setting, with only five studies taking place while the participants were inpatients (Kang 2009; Piron 2007; Piron 2010; Saposnik 2010; Yavuzer 2008). One study used a tele-rehabilitation approach to deliver the intervention in the participant's own home (Piron 2009).

Amount of therapy provided

The total dose of therapy provided varied between studies. Two studies provided less than five hours of total therapy (Jannink 2008; Yang 2008). Seven studies provided between six and 10 hours of therapy (Crosbie 2008; Jaffe 2004; Kang 2009; Kim 2009; Lam 2006; Saposnik 2010; Yavuzer 2008). A further eight studies provided between 11 and 20 hours of therapy (Akinwuntan 2005; Jang 2005; Mazer 2005; Mirelman 2008; Piron 2009; Piron 2010; Sucar 2009; You 2005) and the remaining two studies provided more than 21 hours of therapy (Housman 2009; Piron 2007).

Comparison interventions

The majority of trials compared the 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). Three studies compared the virtual reality intervention with no intervention (Jang 2005; Mazer 2005; You 2005) and the three-armed trial (Lam 2006) compared virtual reality intervention with an alternative intervention or no intervention.

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 (Crosbie 2008; Jaffe 2004; Mirelman 2008; Piron 2009; Saposnik 2010; 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). Eight studies reported on the presence or absence of adverse events (Crosbie 2008; Housman 2009; Jaffe 2004; Piron 2007; Piron 2010; Saposnik 2010; Sucar 2009; Yavuzer 2008).

Excluded studies

We excluded eight studies: six were non-randomised trials, one did not meet the definition of virtual reality and the other compared different types of virtual reality interventions rather than comparing virtual reality with an alternative intervention or no intervention (Characteristics of excluded studies)

Risk of bias in included studies

Refer to Figure 1; Figure 2.

Figure 1. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

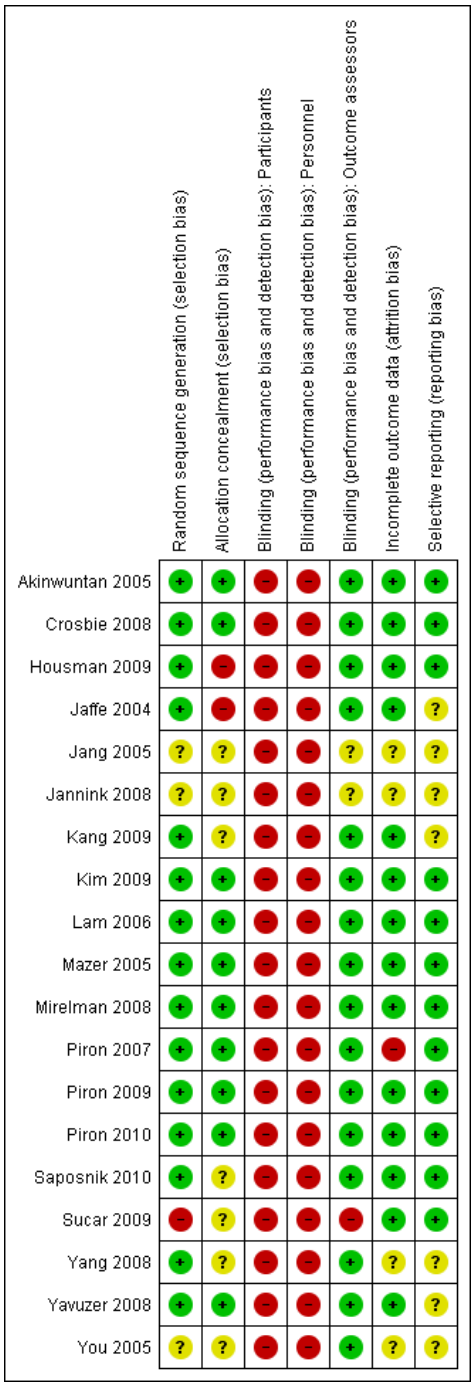
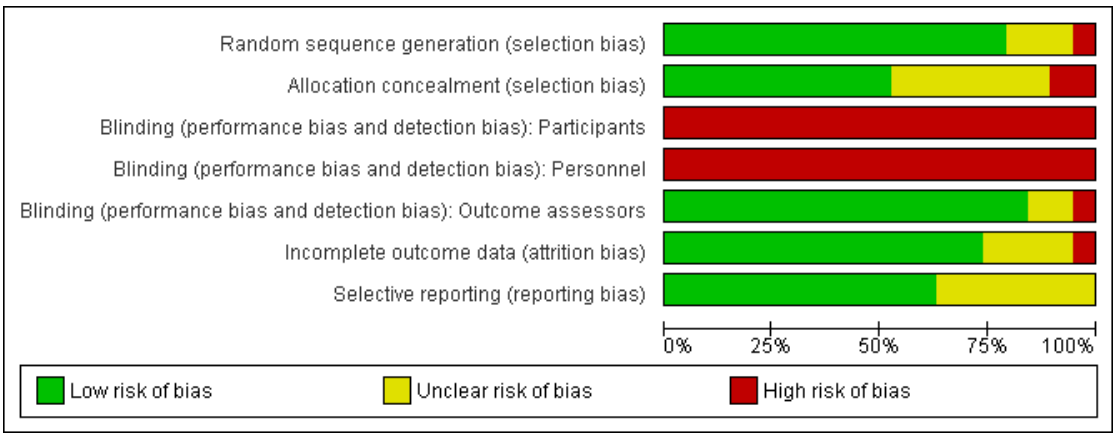


Figure 2. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.



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

Allocation concealment was adequate in nine trials (Akinwuntan 2005; Crosbie 2008; Kim 2009; Lam 2006; Mirelman 2008; Piron 2007; Piron 2009; Piron 2010; Yavuzer 2008).

Blinding

Sixteen trials included blinding of the outcome assessor (Akinwuntan 2005; Crosbie 2008; Housman 2009; Jaffe 2004; Kang 2009; Kim 2009; Lam 2006; Mazer 2005; Mirelman 2008; Piron 2007; Piron 2009; Piron 2010; Saposnik 2010; Yang 2008; Yavuzer 2008; You 2005). No trials were able to blind participants or personnel.

Incomplete outcome data

Four trials reported that they performed intention-to-treat analyses (Akinwuntan 2005; Crosbie 2008; Piron 2010; Saposnik 2010). Seven trials reported that they did not have any missing outcome data (Jaffe 2004; Kang 2009; Kim 2009; Lam 2006; Piron 2009; Sucar 2009; Yavuzer 2008). Drop outs from studies appeared generally balanced across groups.

Selective reporting

Trialists from 12 studies reported that their published data were free of selective reporting (Akinwuntan 2005; Crosbie 2008; Housman 2009; Kim 2009; Lam 2006; Mazer 2005; Mirelman 2008; Piron 2007; Piron 2009; Piron 2010; Saposnik 2010; Sucar 2009). It was unclear whether selective reporting was present in the other studies.

Other potential sources of bias

Other potential sources of bias were difficult to determine due to lack of reporting according to CONSORT guidelines (Schulz 2010).

Effects of interventions

Primary outcomes

Results are presented for (1) upper limb function and activity, (2) gait and balance function and activity, and (3) global motor function.

Upper limb function and activity: post-intervention

Results are presented for arm function and activity and hand function. All outcomes are taken post-intervention.

Comparisons 1.1 and 1.2: Arm function and activity

Seven studies (Crosbie 2008; Housman 2009; Piron 2007; Piron 2009; Piron 2010; Saposnik 2010; Sucar 2009) presented outcomes for arm function and activity (205 participants). The impact of virtual reality on arm function showed a moderate significant effect: SMD 0.53, 95% CI 0.25 to 0.81 (Analysis 1.1). No statistical heterogeneity was indicated.

Five of these trials (Housman 2009; Piron 2007; Piron 2009; Piron 2010; Sucar 2009) used the Fugl Meyer UE Scale as an outcome measure (171 participants). The impact of virtual reality as measured by the Fugl Meyer UE Scale also showed a significant effect: MD 4.43, 95% CI 1.98 to 6.88 (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 arm function and activity.

Comparison 1.3: Hand function

Two trials (Housman 2009; Saposnik 2010) measured the effect of virtual reality versus alternative therapy on grip strength (kg) (44 participants). 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 one trial (Housman 2009) measured the longer-term effects of virtual reality on arm 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 = 0.045). Participants in the virtual reality group improved by 3.6 points (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

Trials providing under 15 hours of intervention were compared with trials providing 15 hours or more of intervention. Trials providing less than 15 hours of intervention had a non-significant effect (SMD 0.58, 95% CI -0.12 to 1.29) whereas trials providing more than 15 hours of intervention showed a moderate significant effect (SMD 0.52, 95% CI 0.21 to 0.83); however, the difference between groups was not statistically significant (Chi^2 = 0.03, df = 1, P = 0.87) (Analysis 2.1).

Comparison 2.2: Time since onset of stroke

Trials were classified based on whether their participants were recruited within six months of stroke or more than six months post stroke. Both groups showed a moderate significant effect (trials recruiting within six months: SMD 0.76, 95% CI 0.18 to 1.34 compared with trials recruiting after six months: SMD 0.46, 95% CI 0.13 to 0.78). The difference between groups was not significant (Chi^2 = 0.81, df = 1, P = 0.37) (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. Both groups showed a significant effect on arm function (commercial gaming consoles: SMD 1.15, 95% CI 0.06 to 2.24 compared with specialised system: SMD: 0.48, 95% CI 0.19 to 0.78) (Analysis 2.3).

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

Gait and balance function and activity: post-intervention

Results are presented for gait speed. All outcomes are taken post-intervention and measured in metres per second. We were unable to include one relevant study (Kim 2009) in the analyses as data were not available in this format.

Comparison 3.1: Gait speed

Three studies (Jaffe 2004; Mirelman 2008; Yang 2008) provided data on gait speed measured in metres per second (58 participants). The effect of virtual reality on gait speed was not significant: MD 0.07, 95% CI -0.09 to 0.23 (Analysis 3.1). No statistical heterogeneity was indicated.

Gait and balance function and activity: follow up

Only one study (Mirelman 2008) measured the longer-term effects (at three months) of virtual reality on gait speed, therefore we could not undertake further analysis.

Gait and balance function and activity: subgroup analyses

Comparison 4.1: Effect of dose of treatment on gait speed

Trials providing less than 10 hours of intervention (two trials) were compared with trials providing more than 10 hours of intervention (one trial). Neither subgroup showed a significant effect (trials providing less than 10 hours intervention: MD 0.01, 95% CI -0.22

to 0.24, and trials providing more than 10 hours intervention: MD 0.13, 95% CI -0.09 to 0.35). The difference between subgroups was not significant (Chi^2 = 0.53, df = 1, P = 0.47) (Analysis 4.1). 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

Two studies reported outcomes for global motor function (using the Modified Motor Assessment scale). However, Kim 2009 compared virtual reality with an alternative intervention whereas You 2005 compared virtual reality with no intervention. We therefore decided not to perform further analysis for this outcome.

Secondary outcomes

Cognitive function

Insufficient trials included assessments of cognition in order 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 et al reported the results from their 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 = 0.005). Futhermore, 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 5.1: ADL function

Though none of the following study interventions targeted ADL retraining specifically, three studies (Kang 2009; Piron 2007; Piron 2010) measured the effects of virtual reality versus alternative therapy on ADL function. The impact of intervention had a large significant effect: SMD 0.81, 95% CI 0.39 to 1.22 (Analysis 5.1). No statistical heterogeneity was indicated.

Participation restriction and quality of life

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

Imaging studies

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 number of participants for both studies = 20) and compared virtual reality with no intervention.

Adverse events

Eight studies monitored and reported on adverse events. Six studies reported no significant adverse events (Housman 2009; Jaffe 2004; Piron 2007; Piron 2010; Saposnik 2010; 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

Upper limb function and activity

Seven trials with 205 participants measured arm function and the results could be included in the analysis. These trials used six different virtual reality programs and all interventions were delivered in a hospital or clinic setting with the exception of one trial which used a home-based tele-rehabilitation approach. The majority of trials recruited patients more than six months after stroke, with only two 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 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).
In summary, these studies showed that virtual reality was a more effective approach than conventional interventions and achieved more improvement in arm function with a moderate effect size. We found insufficient evidence to draw conclusions on the effect of a virtual reality approach on grip strength. We also found insufficient evidence to draw conclusions on the most effective dose of therapy,

the time point in which virtual reality programs are best delivered or the most effective type of virtual reality programs.

Lower limb function and activity

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 all three 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.

Global motor function

The two trials measuring global motor function were not comparable therefore we were unable to pool results for this outcome.

Secondary outcomes

There was a large significant effect on activities of daily living. 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 the adverse events 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 2008); 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 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.

Overall completeness and applicability of evidence

Although we identified 19 studies, significant gaps in the evidence were apparent and the sample sizes of the included studies were generally small. Participants in the studies were most commonly more than six months post stroke and there are fewer studies that have evaluated virtual reality within the first few months after stroke. 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 potential benefits and the number of clients who may benefit from use.

The majority of virtual reality programs evaluated were specialised programs designed by the researchers and are not accessible to clinicians at present. In contrast, it appears that commercial gaming consoles are commonly used in clinical practice with a recent audit showing that 61% of urban stroke rehabilitation facilities in Australia had purchased a Nintendo Wii (National Stroke Foundation 2010). At present, however, there are fewer studies evaluating this approach.

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

Lastly, while virtual reality appears to be a promising approach, few of the included studies measured whether the effects were sustained.

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. Less than half of the studies reported adequate allocation concealment, and in five of the included studies it was unclear as to whether there was blinding of outcome assessors.

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. 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 (Jang 2005; Jannink 2008; Kang 2009; 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.

Agreements and disagreements with other studies or reviews

Previous systematic reviews have argued that virtual reality appears promising but were unable to determine an effect. 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 for the first time pool results for some outcomes.

AUTHORS' CONCLUSIONS

Implications for practice

The findings of this review suggest that virtual reality is a promising new rehabilitation approach for stroke recovery, with reasonable effect sizes (that is a moderate effect on arm function (SMD 0.53) and large effect on ADL function (SMD 0.81)). However, at present, the studies are too few and too small to draw conclusions. In addition, as virtual reality interventions may vary greatly (from inexpensive commercial gaming consoles to expensive customised programs), it is unclear what characteristics of the intervention are most important. Furthermore, the applicability of the intervention to stroke survivors needs further research in terms of which type of patient is most likely to benefit, at what point in their rehabilitation it should be used (for example acute, subacute or chronic) and how acceptable the approach 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.

Due to the increasing number of studies in this area and advances in technology, clinicians should monitor developments in this field.

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

More RCTs are required to determine which types of virtual reality programs are most effective: this information will be valuable in guiding future development of the intervention. Researchers should ensure that future RCTs are adequately powered and carried out in a methodologically rigorous way and future studies should attempt to minimise their risk of bias and report their study methodology according to CONSORT guidelines (Schulz 2010). A virtual reality intervention should be compared with an alternative therapy rather than no therapy in order to ensure that results are due to the intervention and not the dose of therapy, and studies are required with different participant groups in order to determine the client group that will benefit most from this intervention. This includes participants with different levels of severity of stroke and at different time points since the onset of stroke.

Researchers and manufacturers designing new virtual reality programs should include the use of pilot studies assessing usability and validity as part of the development process. One of the limitations of this review is that it does not provide information about the characteristics of the virtual reality intervention which are most important. For example, it is unclear whether the effectiveness of the intervention is based on the opportunity for massed practice or on the level of 'presence' experienced by the user which some research has suggested leads to a different type of learning (Sanchez-Vives 2005). Researchers should aim to determine the impact of these variables in exploratory studies.

Our review included only RCTs, resulting in the exclusion of observational 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.

This is a rapidly evolving area of rehabilitation and our understanding of the area is likely to shift over the next few years. As commercial gaming consoles are now frequently used in stroke rehabilitation settings, studies are required to determine the effectiveness of these programs on a range of outcomes. With the introduction of newer and more advanced systems, such as Microsoft Kinect and Sony Playstation 3, it is likely that there will be an explosion of studies in this area. In addition, while most of the studies to date evaluate interventions targeted at the impairment level, evaluation of interventions targeting the activity and

participation level are required.

ACKNOWLEDGEMENTS

We would like to thank Janet Surma and Jan Badcock for their editorial assistance, as well as Cochrane editors Gillian Mead, Alex Pollock, Ashma Krishan and Brenda Thomas.

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 and Enrique Sucar 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 (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	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

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 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 patient 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 patient 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)

Crosbie 2008 (*Continued*)

Outcomes	Outcomes recorded at baseline, post-intervention and at 6 weeks Arm 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 (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	Low risk	
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

Housman 2009

Methods	RCT
Participants	Recruited from 1 rehabilitation institute in Chicago, USA 34 participants: 17 intervention, 17 control Inclusion criteria: single stroke $\geq$ 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 patient 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 Arm 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	Patients were randomly assigned using a lottery system in which the supervising therapist (with 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	Patients 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 (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	

Housman 2009 (*Continued*)

Blinding (performance bias and detection bias) Outcome assessors	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: patients walked on a treadmill at a self-selected walking speed and were secured by an overhead harness. The patient wore a head-mounted display which showed real-time video images of their feet walking and virtual objects. The patient was asked to step over the virtual objects and visual, vibrotactile and auditory feedback was provided during any collisions Control intervention: patients 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) which 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 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 (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	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 patient's whole body movement. The patient 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

Jang 2005 (*Continued*)

	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 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 (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	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 patient 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	

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 (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	Unclear risk	Unclear
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: patients 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**
Random sequence generation (selection bias)	Low risk	Random allocation using block randomisation process. Envelopes were shuffled and the patient drew 1 after enrolment
Allocation concealment (selection bias)	Unclear risk	Whether the envelopes were opaque is unclear
Blinding (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	Low risk	

Kang 2009 (*Continued*)

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 patient's whole body movement. The patient 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. Patients 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 practise 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 Global motor function outcomes: Modified motor assessment scale
Notes	

Risk of bias

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

Kim 2009 (*Continued*)

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 (performance bias and detection bias) Participants	High risk	States that patients were unaware of allocation however this does not appear possible
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	Low risk	
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

Lam 2006

Methods	RCT (with three arms)
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

Lam 2006 (*Continued*)

	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**
Random sequence generation (selection bias)	Low risk	Participants were randomly allocated into two groups using a statistical package random number generator tool
Allocation concealment (selection bias)	Low risk	Allocation was computer generated
Blinding (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	Low risk	Authors confirmed that outcome assessors were blinded to allocation
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

Mazer 2005 (*Continued*)

	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 three 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
Notes	Note that this study also recruited patients with traumatic brain injury (6 patients). 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 (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	Low risk	
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

Mazer 2005 (*Continued*)

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 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 data base spread sheet on a computer in his office which was password protected

Mirelman 2008 (*Continued*)

Blinding (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	Low risk	
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 patient 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 2.6 (1.6) months
Interventions	Virtual reality intervention: magnetic receivers were positioned on the patient's arm. As the patient 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 patient 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)

Piron 2007 (*Continued*)

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 (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	Low risk	
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)

Piron 2009 (*Continued*)

	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 (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	Low risk	
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 (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	

Piron 2010 (*Continued*)

Blinding (performance bias and detection bias) Outcome assessors	Low risk	
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 reasons for this were reported
Selective reporting (reporting bias)	Low risk	No other outcomes were collected

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 $\geq$ 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	

Saposnik 2010 (*Continued*)

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
Allocation concealment (selection bias)	Unclear risk	Unclear
Blinding (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	Low risk	
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

Sucar 2009

Methods	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)

Sucar 2009 (*Continued*)

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

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 (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	High risk	
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)
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 one of the sealed envelopes before the start of the intervention
Allocation concealment (selection bias)	Unclear risk	Unclear whether envelopes were opaque
Blinding (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	Low risk	

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

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 Eye Toy games involving use of the upper limbs Control intervention: watched the Playstation Eye Toy 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 program 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 (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	Low risk	
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
Interventions	Virtual reality intervention: IREX virtual reality system using a video capture system to capture the patient's whole body movement. The patient 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	

You 2005 (*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 (performance bias and detection bias) Participants	High risk	
Blinding (performance bias and detection bias) Personnel	High risk	
Blinding (performance bias and detection bias) Outcome assessors	Low risk	
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Unclear
Selective reporting (reporting bias)	Unclear risk	Unclear

CT: computerised tomography
MCA: middle cerebral artery
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
Chortis 2008	Study design: not a RCT
Der-Yeghiaian 2009	Study design: not a RCT

(*Continued*)

Edmans 2009	Study design: not a RCT
Fischer 2007	All groups received virtual reality intervention therefore there was no comparison with an alternative intervention or no intervention
Gnajaraj 2007	Intervention did not meet review's definition of virtual reality
Katz 2005	Study design: not all participants were randomised
Krebs 2008	Study design: participants were not randomly allocated to groups

RCT: randomised controlled trial

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

Cameirao 2008

Trial name or title	The effect of the Rehabilitation Gaming System in the acute phase of stroke
Methods	RCT (3 arms)
Participants	Within first 3 weeks of first ever stroke, ≤ 80 years old, mild to severe deficit of the paretic arm, absence of cognitive impairment
Interventions	Intervention group: use of the Rehabilitation Gaming System, a specialised virtual reality program involving a LCD display, motion capture camera and data gloves in which the participant focusses on 3 main activities (hitting, catching and placing) Control group A: similar hitting, catching and placing tasks but without the virtual reality stimulus Control group B: non-specific games using the Nintendo Wii Intervention is performed 3 times weekly, 20 minutes per session for 12 weeks (total = 12 hours) Outcomes will be assessed post-intervention and at 6 months
Outcomes	Functional Independence Measure, the Barthel Index, the Motricity Index, the Fugl-Meyer Assessment Test for the upper extremity and the Chedoke Arm and Hand Activity Inventory
Starting date	Commenced
Contact information	Mónica Cameirão, Institut Universitari de l'Audiovisual (IUA), Universitat Pompeu Fabra, Spain, email: monica.cameirao@upf.edu
Notes	

Chern 2002

Trial name or title	Improving the balance skill of stroke patients by virtual reality treadmill exercise
Methods	RCT
Participants	Patients post stroke with hemiparesis
Interventions	Virtual reality intervention: use of a treadmill with virtual reality program Control: use of treadmill only
Outcomes	Balance tasks, sit-to-stand and walking
Starting date	Commenced
Contact information	Jen-Suh Chern, Chang Gung University Department of Occupational Therapy, Taiwan, email jschern@mail.cgu.edu.tw
Notes	

Coupar 2010

Trial name or title	Arm Intervention after Stroke (AIAS)
Methods	RCT (3 arms)
Participants	Adults with a clinical diagnosis of stroke and arm deficits within the acute stroke unit of Glasgow Royal Infirmary
Interventions	Virtual reality intervention: Group 1**:** Armeo®Spring arm orthosis for arm rehabilitation used for 40 minutes per day, 3 days a week Group 2: Armeo®Spring arm orthosis for arm rehabilitation used for 60 minutes per day, 5 days a week The intervention period will last for 14 days or until the patient is discharged from stroke unit, whichever is sooner Control intervention: standard care is usual stroke unit care including standard physiotherapy and occupational therapy targeted at arm recovery
Outcomes	Primary: feasibility and acceptability of experimental device Secondary: safety: number and nature of adverse events at end of intervention period Arm function: Action Research Arm Test Arm impairment: Fugl-Meyer upper limb section Disability: Barthel Index at end of intervention period and 3-month follow-up Outcomes measured post-intervention and at 3 months
Starting date	August 2009. Due to be completed August 2011
Contact information	Fiona MacVicar, email: fmacvicar@yahoo.com
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 meters, 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	Judith Deutsch, Department of Rehabilitation and Movement Science, University of Medicine and Dentistry New Jersey, email: deutsch@umdnj.edu
Notes	Data collection completed with results to be presented at upcoming conferences

Feintuch 2009

Trial name or title	Virhab - A virtual reality system for treatment of chronic pain and disability
Methods	RCT
Participants	Adults post stroke
Interventions	Virtual reality intervention: motion capture camera captures image and displays onscreen Control intervention: unknown
Outcomes	
Starting date	
Contact information	Uri Feintuch, Hebrew University of Jerusalem, Israel, email: urif@cc.huji.ac.il
Notes	

Standen 2010

Trial name or title	A low cost virtual reality system for home based rehabilitation of the upper limb following stroke
Methods	RCT
Participants	Participants are recruited 6 weeks after stroke

Standen 2010 (*Continued*)

Interventions	Virtual reality intervention: participants wear a glove utilising the infrared tracking capacity of the Nintendo Wii. Participants use the device to play computer games which elicit accurate rehabilitation movements Control intervention: usual care
Outcomes	
Starting date	
Contact information	Professor PJ Standen, University of Nottingham, email: P.Standen@nottingham.ac.uk
Notes	

Tanne 2008

Trial name or title	Virtual reality training program for ambulatory patients with chronic gait deficits after stroke
Methods	RCT
Participants	Patients between 3 to 72 months after stroke with mild to moderate residual gait deficits
Interventions	Virtual reality intervention using the CAREN^{TM} Integrated RealitySystem; MOTEK Control: usual care
Outcomes	Community ambulation using Step Activity Monitor, Gait analysis using GaitRite system, body sway, Timed Up and Go, Functional Reach, Four Stick Stepping Test, 6 minute walk test, self-induced perturbations and reaction to perturbations on platform
Starting date	Commenced
Contact information	David Tanne, Sheba Medical Center, email: tanne@post.tau.ac.il
Notes	

LCD: liquid crystal display
RCT: randomised controlled trial

DATA AND ANALYSES

Comparison 1. Upper limb function: post treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Arm function (composite measure)	7	205	Std. Mean Difference (IV, Fixed, 95% CI)	0.53 [0.25, 0.81]
2 Arm function (measured by Fugl Meyer)	5	171	Mean Difference (IV, Fixed, 95% CI)	4.43 [1.98, 6.88]
3 Hand function	2	44	Mean Difference (IV, Fixed, 95% CI)	3.55 [-0.20, 7.30]

Comparison 2. Upper limb function: subgroup analyses

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Dose of intervention	7	205	Std. Mean Difference (IV, Fixed, 95% CI)	0.53 [0.25, 0.81]
1.1 Less than 15 hours intervention	2	34	Std. Mean Difference (IV, Fixed, 95% CI)	0.58 [-0.12, 1.29]
1.2 More than 15 hours intervention	5	171	Std. Mean Difference (IV, Fixed, 95% CI)	0.52 [0.21, 0.83]
2 Time since onset of stroke	7	205	Std. Mean Difference (IV, Fixed, 95% CI)	0.53 [0.25, 0.81]
2.1 Less than 6 months	2	54	Std. Mean Difference (IV, Fixed, 95% CI)	0.76 [0.18, 1.34]
2.2 More than 6 months	5	151	Std. Mean Difference (IV, Fixed, 95% CI)	0.46 [0.13, 0.78]
3 Specialised or gaming	7	205	Std. Mean Difference (IV, Fixed, 95% CI)	0.53 [0.25, 0.81]
3.1 Specialised	6	189	Std. Mean Difference (IV, Fixed, 95% CI)	0.48 [0.19, 0.78]
3.2 Gaming	1	16	Std. Mean Difference (IV, Fixed, 95% CI)	1.15 [0.06, 2.24]

Comparison 3. Lower limb function: 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 4. Lower limb function and activity: 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 5. Secondary outcomes

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 ADL outcome	3	101	Std. Mean Difference (IV, Fixed, 95% CI)	0.81 [0.39, 1.22]

Analysis 1.1. Comparison 1 Upper limb function: post treatment, Outcome 1 Arm function (composite measure).

Review: Virtual reality for stroke rehabilitation

Comparison: 1 Upper limb function: post treatment

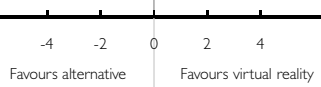
Outcome: 1 Arm function (composite measure)

Study or subgroup	Virtual reality N	Mean(SD)	Comparison intervention N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Crosbie 2008	9	52.8 (6.9)	9	50.2 (18.9)		9.4 %	0.17 [-0.75, 1.10]
Housman 2009	14	24.9 (7.4)	14	19.6 (6.7)		13.6 %	0.73 [-0.04, 1.50]
Piron 2007	25	51.4 (9.8)	13	45.4 (9.3)		17.2 %	0.61 [-0.08, 1.30]
Piron 2009	18	53.6 (7.7)	18	49.5 (4.8)		17.9 %	0.62 [-0.05, 1.30]
Piron 2010 (1)	27	49.7 (10.1)	20	46.5 (9.7)		23.8 %	0.32 [-0.27, 0.90]
Saposnik 2010	9	-19.8 (3.4)	7	-27.4 (8.7)		6.8 %	1.15 [0.06, 2.24]
Sucar 2009	11	30 (12.4)	11	26.36 (2.33)		11.3 %	0.39 [-0.45, 1.24]
Total (95% CI)	**113**		**92**			**100.0 %**	**0.53 [0.25, 0.81]**

Heterogeneity: Chi^2 = 2.81, df = 6 (P = 0.83); I^2 =0.0%

Test for overall effect: Z = 3.66 (P = 0.00025)

Test for subgroup differences: Not applicable



(1) Note that 3 people withdrew from control group therefore analysis done based on actual number contributing to outcome data

Analysis 1.2. Comparison 1 Upper limb function: post treatment, Outcome 2 Arm function (measured by Fugl Meyer).

Review: Virtual reality for stroke rehabilitation

Comparison: 1 Upper limb function: post treatment

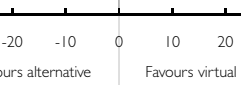
Outcome: 2 Arm function (measured by Fugl Meyer)

Study or subgroup	Virtual reality N	Mean(SD)	Comparison intervention N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Housman 2009	14	24.9 (7.4)	14	19.6 (6.7)		21.9 %	5.30 [0.07, 10.53]
Piron 2007	25	51.4 (9.8)	13	45.4 (9.3)		14.9 %	6.00 [-0.35, 12.35]
Piron 2009	18	53.6 (7.7)	18	49.5 (4.8)		34.1 %	4.10 [-0.09, 8.29]
Piron 2010 (1)	27	49.7 (10.1)	20	46.5 (9.7)		18.4 %	3.20 [-2.51, 8.91]
Sucar 2009	11	30 (12.4)	11	26.36 (2.33)		10.8 %	3.64 [-3.82, 11.10]
Total (95% CI)	**95**		**76**			**100.0 %**	**4.43 [1.98, 6.88]**

Heterogeneity: $Chi^2 = 0.59$, df = 4 (P = 0.96); $I^2 = 0.0\%$

Test for overall effect: Z = 3.55 (P = 0.00039)

Test for subgroup differences: Not applicable



(1) Note that 3 people withdrew from control group therefore analysis done based on actual number contributing to outcome data

Analysis 1.3. Comparison 1 Upper limb function: post treatment, Outcome 3 Hand function.

Review: Virtual reality for stroke rehabilitation

Comparison: 1 Upper limb function: post treatment

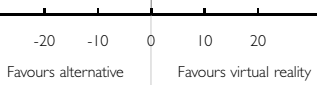
Outcome: 3 Hand function

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



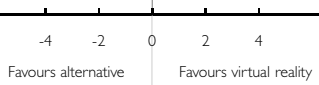
Analysis 2.1. Comparison 2 Upper limb function: subgroup analyses, Outcome 1 Dose of intervention.

Review: Virtual reality for stroke rehabilitation

Comparison: 2 Upper limb function: subgroup analyses

Outcome: 1 Dose of intervention

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 Less than 15 hours intervention							
Crosbie 2008	9	52.8 (6.9)	9	50.2 (18.9)		9.4 %	0.17 [-0.75, 1.10]
Saposnik 2010	9	-19.8 (3.4)	7	-27.4 (8.7)		6.8 %	1.15 [0.06, 2.24]
Subtotal (95% CI)	**18**		**16**			**16.2 %**	**0.58 [-0.12, 1.29]**
Heterogeneity: Chi^2 = 1.79, df = 1 (P = 0.18); I^2 =44%							
Test for overall effect: Z = 1.62 (P = 0.10)							
2 More than 15 hours intervention							
Housman 2009	14	24.9 (7.4)	14	19.6 (6.7)		13.6 %	0.73 [-0.04, 1.50]
Piron 2007	25	51.4 (9.8)	13	45.4 (9.3)		17.2 %	0.61 [-0.08, 1.30]
Piron 2009	18	53.6 (7.7)	18	49.5 (4.8)		17.9 %	0.62 [-0.05, 1.30]
Piron 2010	27	49.7 (10.1)	20	46.5 (9.7)		23.8 %	0.32 [-0.27, 0.90]
Sucar 2009	11	30 (12.4)	11	26.36 (2.33)		11.3 %	0.39 [-0.45, 1.24]
Subtotal (95% CI)	**95**		**76**			**83.8 %**	**0.52 [0.21, 0.83]**
Heterogeneity: Chi^2 = 1.00, df = 4 (P = 0.91); I^2 =0.0%							
Test for overall effect: Z = 3.28 (P = 0.0010)							
Total (95% CI)	**113**		**92**			**100.0 %**	**0.53 [0.25, 0.81]**
Heterogeneity: Chi^2 = 2.81, df = 6 (P = 0.83); I^2 =0.0%							
Test for overall effect: Z = 3.66 (P = 0.00025)							
Test for subgroup differences: Chi^2 = 0.03, df = 1 (P = 0.87), I^2 =0.0%							

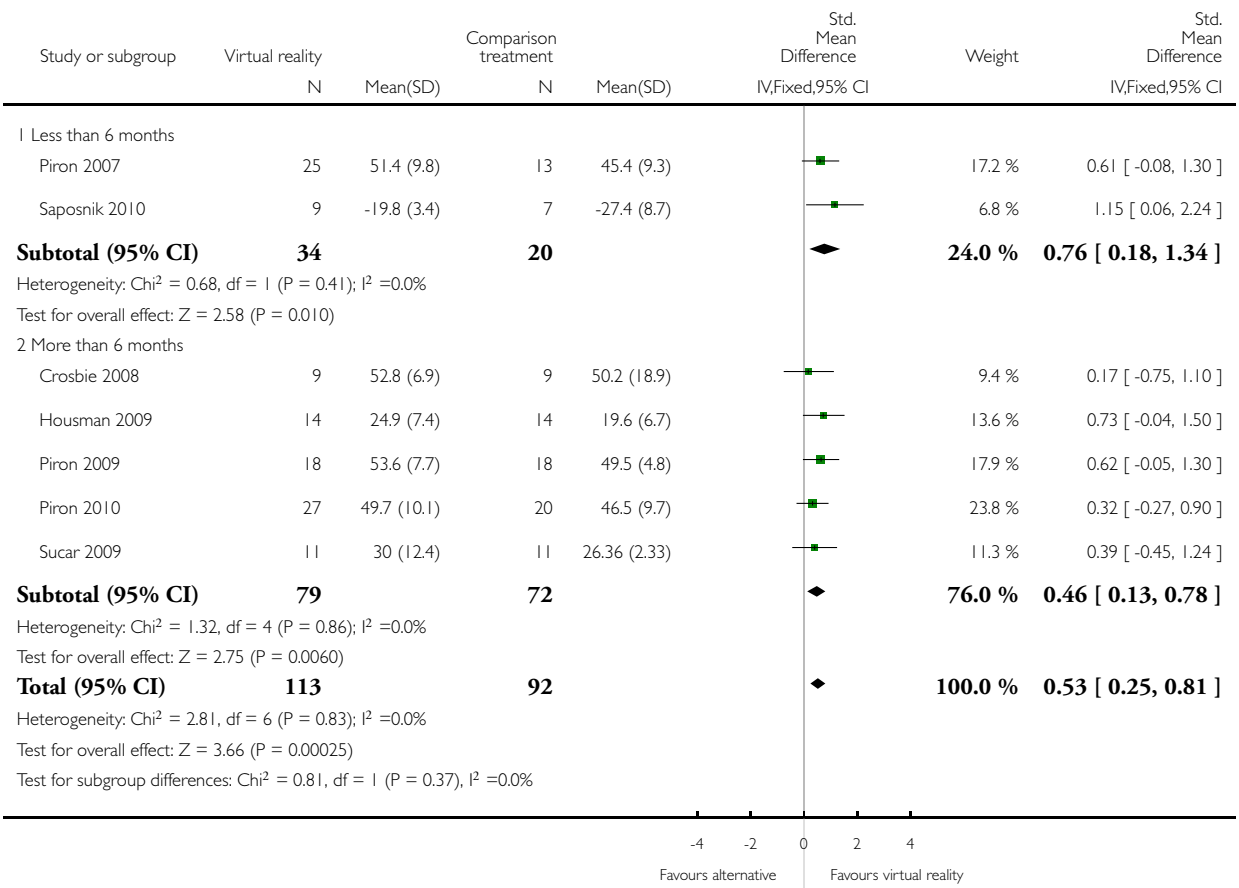


Analysis 2.2. Comparison 2 Upper limb function: subgroup analyses, Outcome 2 Time since onset of stroke.

Review: Virtual reality for stroke rehabilitation

Comparison: 2 Upper limb function: subgroup analyses

Outcome: 2 Time since onset of stroke



Analysis 2.3. Comparison 2 Upper limb function: subgroup analyses, Outcome 3 Specialised or gaming.

Review: Virtual reality for stroke rehabilitation

Comparison: 2 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							
Crosbie 2008	9	52.8 (6.9)	9	50.2 (18.9)		9.4 %	0.17 [-0.75, 1.10]
Housman 2009	14	24.9 (7.4)	14	19.6 (6.7)		13.6 %	0.73 [-0.04, 1.50]
Piron 2007	25	51.4 (9.8)	13	45.4 (9.3)		17.2 %	0.61 [-0.08, 1.30]
Piron 2009	18	53.6 (7.7)	18	49.5 (4.8)		17.9 %	0.62 [-0.05, 1.30]
Piron 2010	27	49.7 (10.1)	20	46.5 (9.7)		23.8 %	0.32 [-0.27, 0.90]
Sucar 2009	11	30 (12.4)	11	26.36 (2.33)		11.3 %	0.39 [-0.45, 1.24]
Subtotal (95% CI)	**104**		**85**			**93.2 %**	**0.48 [0.19, 0.78]**
Heterogeneity: Chi^2 = 1.48, df = 5 (P = 0.92); I^2 =0.0%							
Test for overall effect: Z = 3.23 (P = 0.0012)							
2 Gaming							
Saposnik 2010	9	-19.8 (3.4)	7	-27.4 (8.7)		6.8 %	1.15 [0.06, 2.24]
Subtotal (95% CI)	**9**		**7**			**6.8 %**	**1.15 [0.06, 2.24]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.07 (P = 0.039)							
Total (95% CI)	**113**		**92**			**100.0 %**	**0.53 [0.25, 0.81]**
Heterogeneity: Chi^2 = 2.81, df = 6 (P = 0.83); I^2 =0.0%							
Test for overall effect: Z = 3.66 (P = 0.00025)							
Test for subgroup differences: Chi^2 = 1.33, df = 1 (P = 0.25), I^2 =25%							

Analysis 3.1. Comparison 3 Lower limb function: post treatment, Outcome 1 Gait speed.

Review: Virtual reality for stroke rehabilitation

Comparison: 3 Lower limb function: 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)

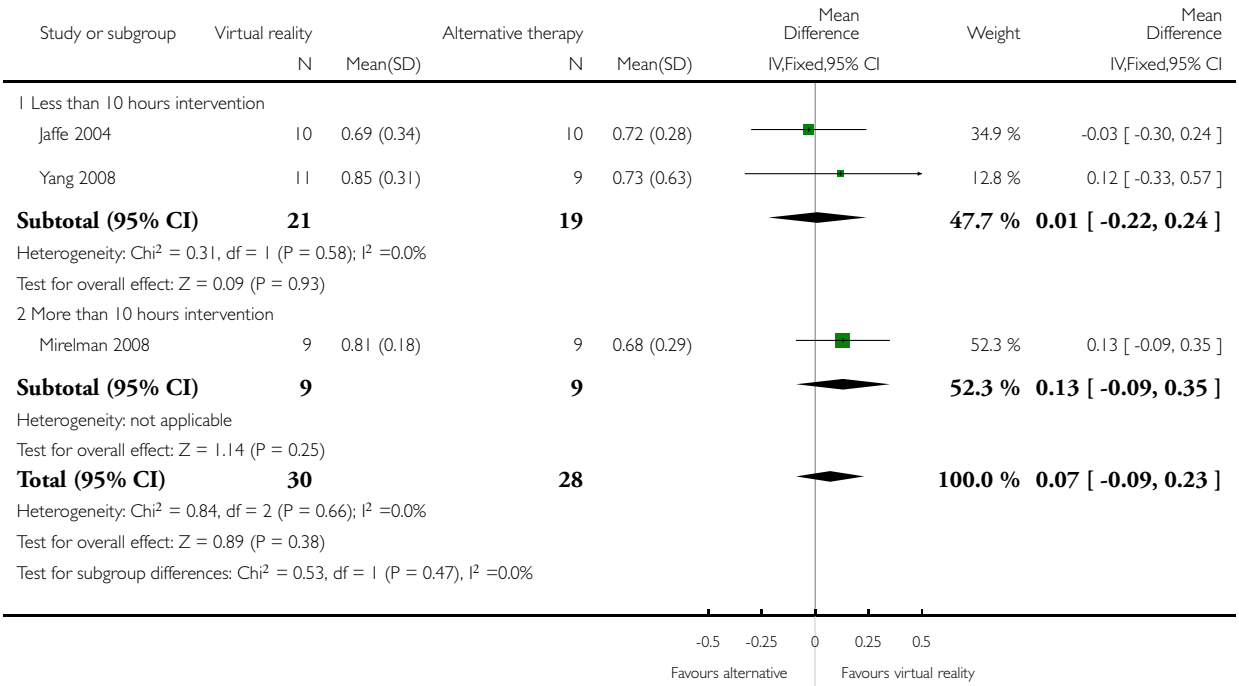
Test for subgroup differences: Not applicable

Analysis 4.1. Comparison 4 Lower limb function and activity: subgroup analyses, Outcome 1 Dose of intervention: effect on gait speed.

Review: Virtual reality for stroke rehabilitation

Comparison: 4 Lower limb function and activity: subgroup analyses

Outcome: 1 Dose of intervention: effect on gait speed

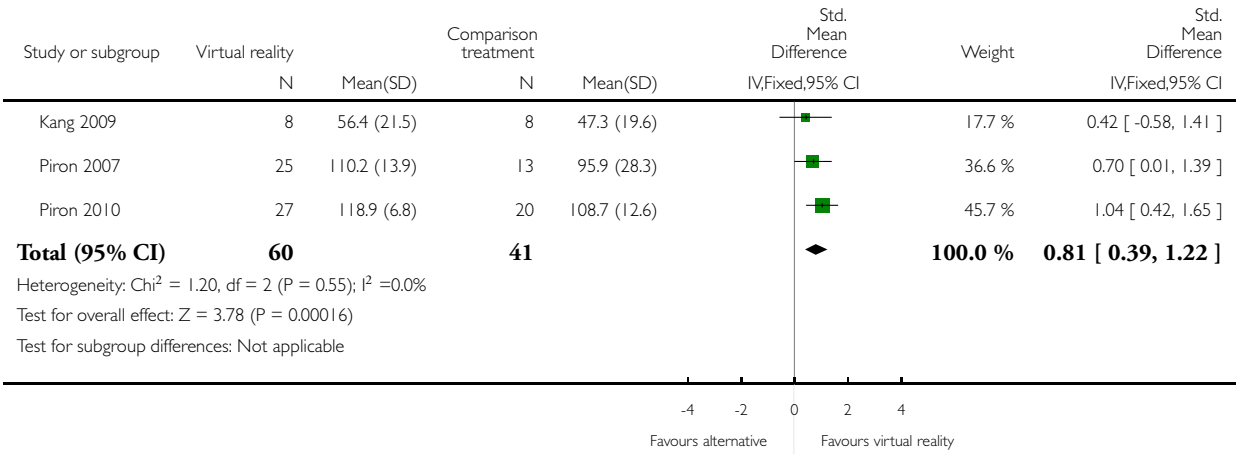


Analysis 5.1. Comparison 5 Secondary outcomes, Outcome 1 ADL outcome.

Review: Virtual reality for stroke rehabilitation

Comparison: 5 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
Crosbie 2008	74	18	9	17	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
Kang 2009	45	16	8	16	8

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

Kim 2009	Not reported	24	12	Not reported	Not reported
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
Saposnik 2010	110	22	11	16	9
Sucar 2009	Not reported	22	11	Not reported	Not reported
Yang 2008	34	24	12	20	9
Yavuzer 2008	25	20	10	20	10
You 2005	Not reported	10	5	10	Not reported

Table 2. Outcome measures used from the included trials

Author and year	Arm function	Hand function	Lower limb function	Standing reach	Global motor function	Cognitive function	Activity limitation	Participation restriction and QOL	Imaging studies
Akinwuntan 2005						Useful Field of View test	On-road driving test score, Decision of fitness to drive		
Crosbie 2008	Action Research Arm Test, Upper Limb Motricity Index								
Housman 2009	Fugl Meyer UE	Grip strength						Motor Activity Log	

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

	Scale, Rancho Functional Test	(kg)						(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)	fMRI (laterality index and activated voxels)
Jannink 2008									
Kang 2009						Minimental 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				
Lam 2006									
Mazer 2005							DriveAble Testing Ltd Driver Evaluation		
Mirelman 2008			Gait speed over 7-metre walkway, 6-minute walk test, Patient Ac-						

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

			tivity 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		
Saposnik 2010	Abbreviated Wolf Motor Function Test	Box and Block Test, Grip strength (kg)						Stroke Impact Scale (hand function, composite function, perception of recovery)	
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	
Yavuzer 2008	Brunnstrom Upper Extremity Stages	Brunnstrom Hand Stages					Functional Independence Measure		

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

							self care section		
You 2005			Functional ambulation category		Modified motor assessment scale				fMRI (laterality index)

fMRI: functional magnetic resonance imaging

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).tw.
4. (cerebrovasc$ or cerebral vascular).tw.
5. (cerebral or cerebellar or brain$ or vertebrobasilar).tw.
6. (infarct$ or isch?emi$ or thrombo$ or emboli$ or apoplexy).tw.
7. 5 and 6
8. (cerebral or brain or subarachnoid).tw.
9. (haemorrhage or hemorrhage or haematoma or hematoma or bleed$).tw.
10. 8 and 9
11. exp hemiplegia/ or exp paresis/
12. (hempar$ or hemipleg$ or paresis or paretic or brain injur$).tw.
13. Gait Disorders, Neurologic/
14. 1 or 2 or 3 or 4 or 7 or 10 or 11 or 12 or 13
15. user-computer interface/
16. computers/ or exp microcomputers/ or computer systems/ or software/
17. computer simulation/ or computer-assisted instruction/ or therapy, computer-assisted/
18. computer graphics/ or video games/ or *touch/
19. (virtual reality$ or virtual-reality$ or VR).tw.
20. (virtual adj3 (environment$ or world$ or object$ or treatment$ or system$ or program$ or rehabilitation$ or therap$ or driving or drive$ or car or tunnel or vehicle)).tw.
21. (computer adj3 (simulat$ or graphic$ or game$ or interact$)).tw.
22. (computer adj1 assist$ adj1 (therap$ or treat$)).tw.
23. (computer adj1 generat$ adj1 (environment$ or object$)).tw.
24. video game$.tw.
25. (haptics or haptic device$).tw.
26. (simulat$ adj3 (environment$ or object$ or driving or drive$ or car or tunnel or vehicle or event$)).)).tw.
27. (user adj1 computer adj1 interface).tw.

28. or/15-27
29. 14 and 28
30. Randomized Controlled Trials as Topic/
31. random allocation/
32. Controlled Clinical Trials as Topic/
33. control groups/
34. clinical trials as topic/
35. double-blind method/
36. single-blind method/
37. Placebos/
38. placebo effect/
39. cross-over studies/
40. Multicenter Studies as Topic/
41. Therapies, Investigational/
42. Research Design/
43. Program Evaluation/
44. evaluation studies as topic/
45. randomized controlled trial.pt.
46. controlled clinical trial.pt.
47. clinical trial.pt.
48. multicenter study.pt.
49. (evaluation studies or comparative study).pt.
50. random$.tw.
51. (controlled adj5 (trial$ or stud$)).tw.
52. (clinical$ adj5 trial$).tw.
53. ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw.
54. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw.
55. ((multicenter or multicentre or therapeutic) adj5 (trial$ or stud$)).tw.
56. ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw.
57. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
58. (coin adj5 (flip or flipped or toss$)).tw.
59. latin square.tw.
60. versus.tw.
61. (cross-over or cross over or crossover).tw.
62. placebo$.tw.
63. sham.tw.
64. (assign$ or alternate or allocat$ or counterbalance$ or multiple baseline).tw.
65. controls.tw.
66. (treatment$ adj6 order).tw.
67. or/30-66
68. 67 and 29
69. limit 68 to humans

Appendix 2. EMBASE search strategy

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).tw.
4. (cerebrovasc$ or cerebral vascular).tw.
5. (cerebral or cerebellar or brain$ or vertebrobasilar).tw.
6. (infarct$ or isch?emi$ or thrombo$ or emboli$ or apoplexy).tw.
7. 5 and 6
8. (cerebral or brain or subarachnoid).tw.
9. (haemorrhage or hemorrhage or haematoma or hematoma or bleed$).tw.
10. 8 and 9
11. exp hemiplegia/ or exp paresis/
12. (hempar$ or hemipleg$ or paresis or paretic or brain injur$).tw.
13. Gait Disorders, Neurologic/
14. 1 or 2 or 3 or 4 or 7 or 10 or 11 or 12 or 13
15. user-computer interface/
16. computers/ or exp microcomputers/ or computer systems/ or software/
17. computer simulation/ or computer-assisted instruction/ or therapy, computer-assisted/
18. computer graphics/ or video games/ or *touch/
19. (virtual reality$ or virtual-reality$ or VR).tw.
20. (virtual adj3 (environment$ or world$ or object$ or treatment$ or system$ or program$ or rehabilitation$ or therap$ or driving or drive$ or car or tunnel or vehicle)).tw.
21. (computer adj3 (simulat$ or graphic$ or game$ or interact$)).tw.
22. (computer adj1 assist$ adj1 (therap$ or treat$)).tw.
23. (computer adj1 generat$ adj1 (environment$ or object$)).tw.
24. video game$.tw.
25. (haptics or haptic device$).tw.
26. (simulat$ adj3 (environment$ or object$ or driving or drive$ or car or tunnel or vehicle or event$)).tw.
27. (user adj1 computer adj1 interface).tw.
28. or/15-27
29. 14 and 28
30. Randomized Controlled Trials.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
31. random allocation/
32. Controlled Clinical Trials.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
33. control groups/
34. clinical trials.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
35. double-blind method/
36. single-blind method/
37. Placebos/
38. placebo effect/
39. cross-over studies/
40. Multicenter Studies.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
41. Therapies, Investigational/
42. Research Design/
43. Program Evaluation/
44. evaluation studies as topic/

45. randomized controlled trial.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
46. controlled clinical trial.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
47. clinical trial.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
48. multicenter study.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
49. (evaluation studies or comparative study).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name]
50. random$.tw.
51. (controlled adj5 (trial$ or stud$)).tw.
52. (clinical$ adj5 trial$).tw.
53. ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw.
54. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw.
55. ((multicenter or multicentre or therapeutic) adj5 (trial$ or stud$)).tw.
56. ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw.
57. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
58. (coin adj5 (flip or flipped or toss$)).tw.
59. latin square.tw.
60. versus.tw.
61. (cross-over or cross over or crossover).tw.
62. placebo$.tw.
63. sham.tw.
64. (assign$ or alternate or allocat$ or counterbalance$ or multiple baseline).tw.
65. controls.tw.
66. (treatment$ adj6 order).tw.
67. or/30-66
68. 67 and 29
69. limit 68 to humans
70. from 69 keep 1-905

Appendix 3. AMED search strategy

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).tw.
4. (cerebrovasc$ or cerebral vascular).tw.
5. (cerebral or cerebellar or brain$ or vertebrobasilar).tw.
6. (infarct$ or isch?emi$ or thrombo$ or emboli$ or apoplexy).tw.
7. 5 and 6
8. (cerebral or brain or subarachnoid).tw.
9. (haemorrhage or hemorrhage or haematoma or hematoma or bleed$).tw.
10. 8 and 9
11. exp hemiplegia/ or exp paresis/
12. (hempar$ or hemipleg$ or paresis or paretic or brain injur$).tw.
13. Gait disorders {No Related Terms}
14. 1 or 2 or 3 or 4 or 7 or 10 or 11 or 12 or 13
15. computer interface {No Related Terms}
16. computers/ or exp microcomputers/ or computer systems/ or software/

17. computer simulation/ or computer-assisted instruction/ or therapy, computer-assisted/
18. computer graphics/ or video games/ or *touch/
19. (virtual reality$ or virtual-reality$ or VR).tw.
20. (virtual adj3 (environment$ or world$ or object$ or treatment$ or system$ or program$ or rehabilitation$ or therap$ or driving or drive$ or car or tunnel or vehicle)).tw.
21. (computer adj3 (simulat$ or graphic$ or game$ or interact$)).tw.
22. (computer adj1 assist$ adj1 (therap$ or treat$)).tw.
23. (computer adj1 generat$ adj1 (environment$ or object$)).tw.
24. video game$.tw.
25. (haptics or haptic device$).tw.
26. (simulat$ adj3 (environment$ or object$ or driving or drive$ or car or tunnel or vehicle or event$)).tw.
27. (user adj1 computer adj1 interface).tw.
28. or/15-27
29. 14 and 28
30. Randomized Controlled Trials {No Related Terms}
31. random allocation/
32. Controlled Clinical Trials {No Related Terms}
33. control groups/
34. clinical trials {No Related Terms}
35. double-blind method/
36. single-blind method/
37. Placebos/
38. placebo effect/
39. cross-over studies/
40. Multicenter Studies {No Related Terms}
41. Therapies, Investigational/
42. Research Design/
43. Program Evaluation/
44. evaluation studies {No Related Terms}
45. randomized controlled trial.pt.
46. controlled clinical trial.pt.
47. clinical trial.pt.
48. multicenter study.pt.
49. (evaluation studies or comparative study).pt.
50. random$.tw.
51. (controlled adj5 (trial$ or stud$)).tw.
52. (clinical$ adj5 trial$).tw.
53. ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw.
54. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw.
55. ((multicenter or multicentre or therapeutic) adj5 (trial$ or stud$)).tw.
56. ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw.
57. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
58. (coin adj5 (flip or flipped or toss$)).tw.
59. latin square.tw.
60. versus.tw.
61. (cross-over or cross over or crossover).tw.
62. placebo$.tw.
63. sham.tw.
64. (assign$ or alternate or allocat$ or counterbalance$ or multiple baseline).tw.
65. controls.tw.
66. (treatment$ adj6 order).tw.
67. or/30-66
68. 67 and 29

69. from 68 keep 1-66

Appendix 4. CINAHL search strategy

1. (MH "Cerebrovascular Disorders+")
2. (MH "Basal Ganglia Cerebrovascular Disease+")
3. (MH "Cerebral Ischemia+")
4. (MH "Carotid Artery Diseases+")
5. (MH "Intracranial Arterial Diseases+")
6. (MH "Arteriovenous Malformations+")
7. (MH "Intracranial Embolism and Thrombosis+")
8. (MH "Intracranial Hemorrhage+")
9. (MH "Stroke")
10. "brain infarction"
11. (MH "Brain Injuries+")
12. (MH "Brain Damage, Chronic+")
13. TX stroke$ or TX cva or TX poststroke or TX post-stroke
14. TX cerebrovasc$ or TX cerebral vascular
15. TX cerebral or TX cerebellar or TX brain$ or TX vertebrobasilar
16. TX infarct$ or TX isch?emi$ or TX thrombo$ or TX edmboli$ or TX apoplexy
17. S15 and S16
18. TX cerebral or TX brain or TX subarachnoid
19. TX haemorrhage or TX hemorrhage or TX haematoma or TX hematoma or TX bleed
20. S18 and S19
21. (MH "Hemiplegia")
22. MW paresis
23. TX paresis
24. S21 or S23
25. TX hempar$ or TX hemipleg$ or TX paresis or TX paretic and TX brain injur$
26. (MH "Gait Disorders, Neurologic+")
27. S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S17 or S20 or S21 or S23 or S24 or S25 or S26
28. (MH "User-Computer Interface+")
29. (MH "Computers and Computerization+")
30. (MH "Microcomputers+")
31. (MH "Computer Systems+")
32. (MH "Software+")
33. S29 or S30 or S31 or S32
34. (MH "Computer Simulation+")
35. (MH "Computer Assisted Instruction")
36. (MH "Therapy, Computer Assisted+")
37. S34 or S35 or S36
38. (MH "Computer Graphics")
39. (MH "Video Games")
40. (MH "Touch") or (MH "Touch (Iowa NIC)")
41. S38 or S39 or S40
42. (MH "Virtual Reality")
43. TX virtual realit$ or TX virtual-realit$ or TX VR
44. S42 or S43
45. TX (virtual N3 environment$) or TX (virtual N3 world$) or TX (virtual N3 object$) or TX (virtual N3 treatment$) or TX (virtual N3 system$) or TX (virtual N3 program$) or TX (virtual N3 rehabilitation$) or TX (virtual N3 therap$) or TX (virtual N3 driving) or TX (virtual N3 drive$) or TX (virtual N3 car) or TX (virtual N3 tunnel) or TX (virtual N3 vehicle$)

46. TX (computer N3 simulat$) or TX (computer N3 graphic$) or TX (computer N3 game$) or TX (computer N3 interact$)
47. TX (computer N1 assist$) or TX (computer N1 therap$) or TX (computer N1 treat$)
48. TX (computer N1 generat$) or TX (computer N1 environment$) or TX (computer N1 object$)
49. (MH "Video Games")
50. TX video game$
51. S49 or S50
52. TX haptics or TX haptic devices
53. TX (simulat$ N3 environment$) or TX (simulat$ N3 object$) or TX (simulat$ N3 driving) or TX (simulat$ N3 drive$) or TX (simulat$ N3 car$) and TX (simulat$ N3 tunnel$) or TX (simulat$ N3 vehicle$) or TX (simulat$ N3 event$) (SmartText Searching)
54. TX (user N1 computer N1 interface)
55. S28 or S29 or S30 or S31 or S32 or S34 or S35 or S36 or S38 or S39 or S40 or S42 or S43 or S45 or S46 or S47 or S48 or S49 or S50 or S52 or S53 or S54
56. S27 and S55
57. "randomized controlled trials"
58. MH random allocation
59. MH controlled clinical trials
60. MW control groups
61. MH clinical trials
62. MH double-blind method
63. MH single-blind method
64. MH placebos
65. MH placebo effect
66. MW cross-over studies
67. MH multicenter studies
68. MH Therapies, Investigational
69. MH Research Design
70. MH Program evaluation
71. MH evaluation studies
72. PT randomized controlled trial
73. PT controlled clinical trial
74. PT clinical trial
75. PT multicenter study
76. PT evaluation studies or comparative study
77. TX random
78. TX (controlled N5 trial$) or TX (controlled N5 stud$)
79. TX (clinical$ N5 trial$)
80. TX control or treatment or experiment$ or intervention N5 group$ or control or treatment or experiment$ or intervention N5 subject$ or control or treatment or experiment$ or intervention N5 patient$
81. TX quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$
82. TX multicenter or multicentre or therapeutic N5 trial$ or multicenter or multicentre or therapeutic N5 stud$
83. TX control or experiment$ or conservative N5 treatment or control or experiment$ or conservative N5 therapy or control or experiment$ or conservative N5 procedure or control or experiment$ or conservative N5 manage$
84. TX singl$ or doubl$ or tripl$ or trebl$ N5 blind$ or singl$ or doubl$ or tripl$ or trebl$ N5 mask$
85. TX coin N5 flip or TX coin N5 flipped or TX coin N5 toss$
86. TX latin square
87. TX versus
88. TX cross-over or TX cross over or TX crossover
89. TX placebo$
90. TX sham
91. TX assign$ or TX alternate or TX allocat$ or TX counterbalance$ or TX multiple baseline
92. TX controls
93. TX treatment$ N6 order

94. S57 or S58 or S59 or S60 or S61 or S62 or S63 or S64 or S65 or S66 or S67 or S68 or S69 or S70 or S71 or S72 or S73 or S74 or S75 or S76 or S77 or S78 or S79 or S80 or S81 or S82 or S83 or S84 or S85 or S86 or S87 or S88 or S89 or S90 or S91 or S92 or S93
95. S94 and S56
96. S94 and S56
97. S94 and S56 (Limiters - Publication Type: Clinical Trial)
98. S94 and S56 (Limiters - Publication Type: Research)
99. S74 or S82
100. S96 and S99

Appendix 5. PsycINFO search strategy

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 injur*.mp. [mp=title, abstract, heading word, table of contents, key concepts]
3. (stroke$ or cva or poststroke or post-stroke).tw.
4. (cerebrovasc$ or cerebral vascular).tw.
5. (cerebral or cerebellar or brain$ or vertebrobasilar).tw.
6. (infarct$ or isch?emi$ or thrombo$ or emboli$ or apoplexy).tw.
7. 5 and 6
8. (cerebral or brain or subarachnoid).tw.
9. (haemorrhage or hemorrhage or haematoma or hematoma or bleed$).tw.
10. 8 and 9
11. exp hemiplegia/ or exp paresis/
12. (hempar$ or hemipleg$ or paresis or paretic or brain injur$).tw.
13. Gait disorders.mp. [mp=title, abstract, heading word, table of contents, key concepts]
14. 1 or 2 or 3 or 4 or 7 or 10 or 11 or 12 or 13
15. user-computer interface/
16. computers/ or exp microcomputers/ or computer systems/ or software/
17. computer simulation/ or computer-assisted instruction/ or therapy, computer-assisted/
18. computer graphics/ or video games/ or *touch/
19. (virtual reality$ or virtual-reality$ or VR).tw.
20. (virtual adj3 (environment$ or world$ or object$ or treatment$ or system$ or program$ or rehabilitation$ or therap$ or driving or drive$ or car or tunnel or vehicle)).tw.
21. (computer adj3 (simulat$ or graphic$ or game$ or interact$)).tw.
22. (computer adj1 assist$ adj1 (therap$ or treat$)).tw.
23. (computer adj1 generat$ adj1 (environment$ or object$)).tw.
24. video game$.tw.
25. (haptics or haptic device$).tw.
26. (simulat$ adj3 (environment$ or object$ or driving or drive$ or car or tunnel or vehicle or event$)).tw.
27. (user adj1 computer adj1 interface).tw.
28. or/15-27
29. 14 and 28
30. randomized controlled trials.mp. [mp=title, abstract, heading word, table of contents, key concepts]
31. random allocation.mp. [mp=title, abstract, heading word, table of contents, key concepts]
32. controlled clinical trials.mp. [mp=title, abstract, heading word, table of contents, key concepts]
33. control groups.mp. [mp=title, abstract, heading word, table of contents, key concepts]
34. clinical trials.mp. [mp=title, abstract, heading word, table of contents, key concepts]
35. double-blind method.mp. [mp=title, abstract, heading word, table of contents, key concepts]
36. single-blind method.mp. [mp=title, abstract, heading word, table of contents, key concepts]
37. Placebos.mp. [mp=title, abstract, heading word, table of contents, key concepts]
38. Placebo effect.mp. [mp=title, abstract, heading word, table of contents, key concepts]

39. cross-over studies.mp. [mp=title, abstract, heading word, table of contents, key concepts]
40. multicenter studies.mp. [mp=title, abstract, heading word, table of contents, key concepts]
41. therapies, investigational.mp. [mp=title, abstract, heading word, table of contents, key concepts]
42. Research design.mp. [mp=title, abstract, heading word, table of contents, key concepts]
43. program evaluation/
44. evaluation studies.mp. [mp=title, abstract, heading word, table of contents, key concepts]
45. random$.tw.
46. (controlled adj5 (trial$ or stud$)).tw.
47. (clinical$ adj5 trial$).tw.
48. ((control or treatment or experiment$ or intervention) adj5 (group$ or subject$ or patient$)).tw.
49. (quasi-random$ or quasi random$ or pseudo-random$ or pseudo random$).tw.
50. ((multicenter or multicentre or therapeutic) adj5 (trial$ or stud$)).tw.
51. ((control or experiment$ or conservative) adj5 (treatment or therapy or procedure or manage$)).tw.
52. ((singl$ or doubl$ or tripl$ or trebl$) adj5 (blind$ or mask$)).tw.
53. (coin adj5 (flip or flipped or toss$)).tw.
54. latin square.tw.
55. versus.tw.
56. (cross-over or cross over or crossover).tw.
57. placebo$.tw.
58. sham.tw.
59. (assign$ or alternate or allocat$ or counterbalance$ or multiple baseline).tw.
60. controls.tw.
61. (treatment$ adj6 order).tw.
62. or/30-61
63. 62 and 29
64. from 63 keep 1-88

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	Was allocation adequately concealed? Yes No Unsure

(*Continued*)

	during, enrolment	
Blinding of participants, personnel and outcome assessors *Assessments should be made for each main outcome (or class of outcomes)*	Describe all measures used, if any, to blind study participants and 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? Participants ▫ Yes ▫ No ▫ Unsure Personnel ▫ Yes ▫ No ▫ Unsure 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 randomized 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
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

(*Continued*)

HISTORY

Protocol first published: Issue 2, 2010

Review first published: Issue 9, 2011

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; 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; 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

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.

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