Protocol v1.4

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Introduction

This is the protocol for an update of a Cochrane overview of reviews of interventions for improving upper limb function after stroke. The current version of this overview is available here: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD010820.pub2/full

Title

Interventions for improving upper limb function after stroke: a Cochrane overview of reviews

Plain language summary

Title: Treatments to improve arm and hand function after stroke.

Research question: Which treatments help to improve arm and hand recovery after a person has had a stroke?

Background: Problems with arm and hand function are very common after a stroke, affecting up to 80% of all stroke survivors. These upper limb impairments commonly include difficulty moving and co-ordinating the arms, hands and fingers, often resulting in difficulty carrying out daily activities such as eating, dressing and washing. More than half of people with upper limb impairment after stroke will still have problems many months to years after their stroke. Improving arm function is a core element of rehabilitation. Many possible interventions have been developed; these may involve different exercises or training, specialist equipment or techniques, or a drug (pill or injection) given to help arm movement.

Research studies (known as *randomised controlled trials*) have investigated how well these interventions work, and these have been brought together within *systematic reviews* to provide best evidence about each of the different interventions. As there are many possible interventions to help arm movement, there are many systematic reviews. An *overview* of systematic reviews brings together all the systematic reviews about a particular topic with the aim of helping health professionals easily access information about how well interventions work, and helping them compare the effects of different interventions. In 2014 an overview brought together information from 40 systematic reviews of interventions to improve upper limb (arm) function after stroke. This overview has been accessed and used by many people, and has been included in 13 clinical guidelines. However, this overview is now out-of-date and is missing important new information. We will update this overview.

Methods: We will search for all Cochrane reviews about interventions to improve arm function after stroke. Where there are interventions with no up-to-date Cochrane review (published after 2014) we will search for high quality non-Cochrane systematic reviews.

We will bring together the details of the population, interventions and comparisons explored within these reviews. We will report the effects of interventions on outcomes of upper limb function, movement and ability to perform activities of daily living (ADL). We will judge the quality of these findings. If a systematic review is more than 2 years out-of-date we will explore whether there are any important new trials missing from this.

Implications: We will work with key interest-holders (including stroke survivors, caregivers, health professionals and policy makers) to create accessible summaries of the effects of treatments to improve function of the arm and hand after stroke. This will signpost interest-holders toward relevant systematic reviews to support their decisions. This overview will also play a key role in research prioritisation, ensuring effective use of resources, promoting collaborative working toward shared priorities and avoiding duplication of effort.

Interventions for improving upper limb function after stroke: a Cochrane overview of reviews

Background

Stroke is the third most common cause of death and the fourth most common cause of Disability-Adjusted Life Years, with an estimated 12 million new stroke events and 94 million stroke survivors across the globe, with low- and middle-income countries carrying the greatest burden of stroke[1]. Motor impairment, typically affecting movement of the face, arm and leg of one side of the body, affects up to 80% of stroke survivors[2]. Upper limb (UL) (i.e. arm, hand and/or finger) motor impairments are often persistent and disabling[3]; only half of all stroke survivors with an initial plegic (paralysed) UL regain some useful function after six months[4], and, of those with initial UL impairment, 50% have problems with arm function four years post stroke[5]. One year after stroke, UL motor impairment is significantly associated with anxiety and poor quality of life and well-being[6-8]. Therefore, improving UL function is a core element of rehabilitation to maximise recovery after stroke [9]. Therapists use many diverse techniques that aim to rehabilitate arm function after stroke. Evidence on the effects of individual treatment techniques/modalities has been synthesised in a large number of reviews.

Description of the condition

A stroke affects the brain's circulation, which causes damage that can directly affect movement and sensory awareness of the arm and hand. Damage to the sensory motor cortex, subcortical areas and/or cerebellum can result in the following, particularly on the side contralateral to the lesion:

- Loss of motor control, which causes difficulties with, or prevents, the voluntary production of movement, and compromises dexterity and co-ordination of the arm and hand.
- Sensory and proprioceptive deficits, which reduce awareness of limb position and movement.

The reduced level of movement predisposes changes in muscle, connective and neural tissues, resulting in several secondary problems, which may include the following.

- Shortening of muscles and connective tissues ('contracture') and consequent maladaptation of joint ligaments and structures
- Further weakening of muscles due to reduced use.
- Disordered muscle contraction ('spasticity').
- Compromised motor and sensory nerve function, as unused neural pathways lose connectivity and new (sometimes dysfunctional) connections are initiated.
- Shoulder subluxation (partial, temporary dislocation of the shoulder joint), caused by lack of motor control and muscle weakness in the rotator cuff muscles.
- Pain, which is a common complication, often secondary to shoulder subluxation, but also commonly associated with the musculoskeletal changes caused by immobility.

These impairments make many ADLs difficult, especially those activities that depend on co-ordination between both upper limbs or fine finger movements (e.g. self-care, or meal preparation). With time, the tendency is to use the unaffected limb predominantly and to disregard the affected limb, thereby developing learned non-use. Mood and cognitive ability can be adversely affected by

stroke, further diminishing functional abilities, and arm motor impairment itself can impact well-being. The ensuing loss of meaningful activity tends to reduce participation in society (e.g. return to work).

Description of the interventions

A wide range of interventions can be delivered in an attempt to improve the function of upper limbs after stroke. Such interventions may be aimed at particular impairments (e.g. muscle weakness) or functional movements (e.g. grasp and release). Upper limb interventions may be used separately or may be combined so that treatments are designed to meet each stroke survivor's rehabilitation needs, by integrating a number of techniques to address problems and secondary complications. Therefore, upper limb rehabilitation after stroke is likely to involve a combination of complex interventions that require patient, carers and the rehabilitation health professionals to work together.

Upper limb rehabilitation interventions may be delivered at different doses, with 'dose' referring to the intensity (which may relate to a range of parameters, such as force or speed of movement), frequency and duration (time) of an intervention. The dose of an intervention is likely to affect the outcome.

(See 2014 Cochrane overview for references, and for full definitions of doses to be used within this Overview.)

Interventions relevant to this Cochrane overview include, but are not limited to, those listed in Table 1 (in alphabetical order).

Table 1: Interventions relevant to this review (for additional references see 2014 Cochrane review[10])

Intervention	Description of intervention	Notes
Action observation	Action observation involves the person observing the performance of a motor task. This may be a live demonstration or on video. After observation a series of repeated demonstrations, the person attempts to perform the same action. Action observation is thought to work by activating the brain's mirror-neuron system[11].	Not in 2014 overview[10]; identified from Tenberg 2023[12]
Bilateral arm training	Simultaneous bilateral arm training uses activities for which both arms perform identical movements at the same time. Different forms of simultaneous bilateral arm training are available. Some use 'free' arm movements, and others use mechanical or robotic devices to drive active or passive movement of the affected limb through identical movement of the less-affected upper limb. Bilateral training is thought to utilise interlimb coupling, based on the hypothesis that the intact brain hemisphere facilitates activation of the affected hemisphere[13].	Included in 2014 overview[10]
Biofeedback	Proprioceptive and other sensory deficits resulting from the stroke reduce 'normal feedback.' Biofeedback systems utilise signals produced by muscle activity to inform the user	Included in 2014 overview[10]

	about the extent and timing of muscle activity by means of a visual or auditory display, or both. Biofeedback provides enhanced awareness of movement or function, with the goal of improving voluntary control of that movement or function. Electromyographic (EMG) biofeedback provides information about muscle activity, which is detected through surface electrodes placed on the skin, or through needle or fine-wire electrodes inserted into the muscle, and is fed back to the patient via electrical activity displayed on a visual display unit or by an auditory signal.	
Bobath therapy	The Bobath approach, which is classed as a 'neurodevelopmental technique,' was originally thought to reduce abnormal tone by positioning, while handling techniques are used to facilitate normal movement. This approach was defined in 2009 as "a problem solving approach to the assessment and treatment of individuals with disturbances of function, movement, and postural control due to a lesion of the central nervous system"[14]. The approach has evolved over time, but content of interventions based on the Bobath approach has been widely debated, and lack of agreement on what constitutes 'Bobath' poses challenges.	Included in 2014 overview[10]
Brain stimulation: Transcranial magnetic stimulation (TMS)	TMS involves stimulation of the brain applied via a wired coil positioned on the head over the sensory motor area. Rapidly changing magnetic fields, initiated by a brief high-intensity electrical current, stimulate the central nervous system. Repetitive pulse TMS (rTMS) is proposed as a treatment for people with stroke, as it can be used to modulate excitability in the cerebral cortex over longer periods of time than are required by other types of TMS.	Included in 2014 overview[10]
Brain stimulation: Transcranial direct current stimulation (tDCS)	This is thought to have an effect similar to that of TMS (above), but it is applied through two surface electrodes placed on the skull.	Included in 2014 overview[10]
Complementary therapies: acupuncture	Complementary therapies that can be used to promote upper limb function after stroke include traditional Chinese therapies, such as acupuncture. With acupuncture, needles are inserted at meridian points or trigger points with the objective of improving neurological function after stroke. Acupuncture is thought to cause biological responses within a person's biochemistry or circulation. Sensory neurons may transmit effects distal to the needle insertion site, thus affecting various physiological systems.	Included in 2014 overview[10]

CIMT	In CIMT, constraint-induced movement therapy or 'forced use therapy,' the less-affected hand is placed in an arm sling or, more commonly, in a mitt that prevents its use during fine movement. With the less-affected hand 'constrained,' operant conditioning (i.e. learning through consequences) is used to increase task difficulty for the affected hand in small amounts, so the stroke survivor can succeed in using the affected limb. Progression is therapeutically directed by using these shaping techniques, thereby reducing learned non-use.	Included in 2014 overview[10]
Electrical stimulation	Electrical stimulation involves stimulation applied to muscles through surface electrodes or percutaneous electrodes (which penetrate the skin). Electrical stimulation is usually delivered with the aim of strengthening a muscle contraction or improving voluntary motor control, or both. Functional electrical stimulation (FES) involves stimulation aimed at replacing or assisting a voluntary muscle contraction during a functional task. Several stimulators are available; these provide single-channel or multi-channel stimulation that can be programmed to an appropriate frequency, bandwidth and strength, to control the duration of stimulation and the duration of intervals between stimulation. Muscles can be stimulated cyclically, triggered by movement or triggered electromyographically (by initiation of muscle activity within the muscle to be stimulated). Electrical stimulation applied to the whole hand through a glove may provide sensory stimulation.	Included in 2014 overview[10]
Gaming (e.g. Wii)	Gaming devices (e.g. Nintendo Wii or Sony Playstation) may be used to encourage repetitive arm movements and skill acquisition, and may motivate people to spend more time using their upper limb[15].	Not in 2014 overview[10]; identified from Saikaley 2022[15]
“Hands-on” therapy (manual therapy techniques)	The arm and hand joints may be moved by a therapist, who may provide partial or full assistance if the patient's active control is inadequate: Such movement may be aimed at maintaining joint and soft tissue mobility. Passive or active joint movements can be used to stretch muscles to their maximum pain-free range. Mobilisation of an accessory movement of a small joint by a therapist may be applied to maintain or increase movement of these joints, or to treat joint pain. Sensory awareness may be increased by tactile stimulation.	Included in 2014 overview[10]

Mental practice	Mental practice, sometimes called mental imagery or motor imagery, is a training method that involves no actual movement. (However, during mental practice training, mental rehearsal is often combined with (or followed by) physical practice when possible). Mental practice may focus on goal attainment or anxiety management, but the type used most often in stroke rehabilitation involves cognitive rehearsal of specific movements or activities by imagining them. Mental practice has been used to enhance elite performance in sports, dance and music, and thus has potential for benefit in the rehabilitation context. A considerable body of evidence from non-impaired people shows that similar areas of the brain are active whether movement is actual, observed or imagined, with the exception of the areas responsible for execution of actual movement.	Included in 2014 overview[10]
Mirror therapy	Exercise-based interventions can use stimulation of other (non-motor) pathways to promote functional movement. Mirror therapy is based on visual stimulation. In mirror therapy, a mirror is placed in the patient's sagittal plane, thus reflecting the non-affected side as if it were the affected side, so that movements of the non-affected limb give the illusion that the affected limb is moving. This visual illusion is then used to stimulate movement of the affected side.	Included in 2014 overview[10]
Music therapy	Music therapy may be used to stimulate movement, cognition and speech, to enhance relaxation or to reduce pain; it is generally delivered by certified/registered music therapists. Music therapy interventions may include listening and moving to music, performing, improvising or composing music, singing or performing vocal activities. Music may be combined with other modalities. Music can be used to cue rhythmical functional movement: This is known as rhythmical auditory stimulation.	Included in 2014 overview[10]
Orthotics	Orthotics are external devices (similar to splints) applied to elbow, wrist and/or finger joints to optimise position, provide stability and prevent, limit or assist movement. These may be used alone or with electrical stimulation in a neuroprosthesis (an orthotic device with prepositioned electrodes that assist function). A wrist orthosis can support the wrist in an extended position; this may facilitate gripping. A	Listed in 2014 overview[10], but no reviews identified

	neuroprosthesis may stimulated muscles to assist grasp and release.	
Pharmacological interventions	A number of systemic drugs may be used to reduce spasticity. Systemic antispasticity medications, such as baclofen and diazepam, act on the nervous system to reduce nerve signals to muscles, thereby reducing spasticity. Dantrolene acts within the muscle by interfering with calcium release from the sarcoplasmic reticulum, weakening muscle contractile function and thus acting as a muscle relaxant. Spasticity can also be treated focally with injections of botulinum neurotoxin. Within muscles, this neurotoxin inhibits the release of acetylcholine, thereby blocking nerve impulses and limiting hyperactivity in treated muscles.	Included in 2014 overview[10]
Repetitive task training	Repetitive task training is an umbrella term for a range of interventions that involve the repeated practice of functional tasks (whole task practice when possible), combining elements of intensity of practice and functional relevance (see also 'Task-specific training,' below). Repetitive task training—when progressed appropriately—is thought to reduce muscle weakness and to form the physiological basis of motor learning. Key components of skill acquisition, such as active cognitive involvement, functional relevance of the task and knowledge of results and performance, are hypothesised to enhance learning during repetitive task training. Repetitive task training may stimulate the activity of neural pathways and muscle that underlie specific functions and promote acquisition of the tasks practised. Findings from animal research have shown that neuroplastic changes emerge only after new skills are learned—not after repetitive movement. Hence, it is important to emphasise that the 'repetition' within repetitive task training refers to repeated practice of new functional skills—not to the reproduction of identical movements per se.	Included in 2014 overview[10]
Robotics	Electromechanical and robotic devices are devices that can move passive limbs, while providing assistance or resistance to movement of a single joint or control of intersegmental co-ordination. Robotic devices may be used to deliver or enhance repetitive task training or task-specific training, and are thought to support	Included in 2014 overview[10] (Robotics included, but not soft robotics, which are an emerging field)

	motor learning and increase motor control and strength. Recent developments are leading to introduction of 'soft robots'. These robots are made of soft, compliant, materials (e.g. silicone rubber) and have been defined as 'systems capable of autonomous behaviour and which are primarily composed of materials with modules in the field of soft biological materials'[17].	
Sensory interventions	Movement and somatosensory awareness can be enhanced in several ways, including techniques such as sensory re-education, tactile kinaesthetic guiding, repetitive sensory practice or desensitisation. Sensory and positional awareness may be stimulated by passive or active-assisted movement, as well as by stimulatory techniques such as stroking and tapping.	Included in 2014 overview[10]
Strength training	Muscle strength training is directed at contracting a specific muscle, or group of muscles, by using voluntary control. Movement may be assisted or resisted by a therapist or by gym equipment. Alternatively, exercises may be done in classes directed by a therapist or exercise professional, may utilise various exercise machines or may involve circuit training. Muscle weakness may be reduced through exercises that activate muscles or by electrical stimulation of muscles. Muscles can be strengthened by progressive resistance exercises. When muscles are unable to move the limb against gravity, manual support provided by the therapist or a weight-relieving system (e.g. robot) allows weakened muscles to produce, assist or resist limb movement. Electrical stimulation can be used to strengthen muscles when the muscle contraction produced by stimulation is of adequate intensity.	Included in 2014 overview[10]
Stretching & positioning	Joint contractures and reduced range of motion at joints can result from various factors, including reduced active movement, which leads to reduced muscle length and increased stiffness of muscle and connective tissue. The tendency toward progressive loss of range may be reduced by moving the joints through a full range of motion with pressure at the end of the range; stiffness may be reduced by repetitive movements. Such motion can be delivered by manual therapy or self-stretching. Several techniques may be used to optimise joint position and to maintain or regain soft tissue length. These techniques often involve the use of assistive devices, such as supportive devices,	Included in 2014 overview[10]

	splints and orthoses. Shoulder subluxation has traditionally been treated with supportive devices. Splints are external devices used to fix a joint in one position, often used to support the hand or fingers in an optimal position. Orthoses are external devices (similar to splints) applied to elbow, wrist and/or finger joints to optimise position, provide stability and prevent, limit or assist movement. These may be used alone or with electrical stimulation in a neuroprosthesis (an orthotic device with prepositioned electrodes that assist function).	
Surgical interventions	Several different surgical interventions could be used to promote upper limb function after stroke. For example, tendon surgery can relieve shoulder pain and reduce spasticity in the upper limb after stroke, but it is not part of routine clinical practice in the UK.	Listed in 2014 overview[10], but no reviews identified
Task-specific training	Task-specific training, also referred to as functional task training, involves practice of tasks relevant to daily life, including part- and whole-task practice. Task-specific training is often supplemented by other modalities, such as assistive technologies. Task-specific training may be carried out as a form of repetitive task training (see above). Reach-to-grasp exercise is a form of task-specific training, as reach-to-grasp is a common functional task involving the upper limb.	Included in 2014 overview[10]
Virtual reality	Virtual reality involves interactive simulations created with computer hardware and software to provide a simulated practice environment, as well as feedback on movement execution or goal attainment, or both. Virtual reality enables people to engage in activities within an environment that may be a gaming environment, or one that appears and feels similar to real-world objects and events, using devices such as a keyboard and a mouse, or through multi-modal devices such as a wired glove. Virtual reality may also be used with robotic devices that assist or resist movement (see above). Virtual reality can enhance motivation for practising specific actions at the intensity required to induce cortical reorganisation. Most systems provide Knowledge of Results (i.e. whether or not the outcome was successful), although there is the potential for Knowledge of Performance (i.e. details of the movement itself, for example, through provision of kinematic feedback). Tasks can be graded by clinicians to provide a progressively challenging	Included in 2014 overview[10]

	practice that can be performed without direct clinical supervision.	

In addition to the interventions listed above, upper limb rehabilitation may be delivered in a range of different settings. For example; in-patient or out-patient rehabilitation, home-based rehabilitation, telerehabilitation or self-management.

Further, any single interventions (such as those in Table 1) may be delivered in combination. For example; biofeedback plus electrostimulation.

The list in Table 1 may not be comprehensive of all interventions, and we will work with interest-holders to identify whether there are any additional interventions to consider (see Interest-holder Involvement). We will also add further interventions to this list if we find published evidence (i.e. reviews) addressing interventions not covered by this list.

How the interventions might work

Rehabilitation of the arm following stroke is a complex intervention that integrates different modalities to address deficits that are often multi-factorial, with clinicians individualising treatment programmes in an attempt to optimise outcomes for patients. Understanding of the precise mechanisms of action for many of the interventions delivered by clinicians is limited. The ways that interventions are thought to work can be described by using several different frameworks. The International Classification of Functioning, Disability and Health, known more commonly as the ICF, can be used to describe whether treatments are aimed at increasing function, activity and/ or participation[18]. Alternatively, treatments can be described as being used to prevent or reduce the development of complications (e.g. shortening of muscles (contractures)); to restore original status or to substitute with compensatory mechanisms (altered neural pathways or movements); or to utilise compensatory devices (e.g. neuroprostheses)[19]. Treatments may also prime (act to prepare the sensory motor system for practice) or augment (enhance sensorimotor function during practice), thereby maximising the benefits derived from task-specific practice[20].

For the purposes of this overview, we will use a taxonomy of rehabilitation interventions based on work arising from a major multi-site stroke rehabilitation study[21]. This taxonomy provides a model that describes key types of rehabilitation interventions and attempts to encapsulate the diversity and complexity of rehabilitation treatments. This taxonomy shows that neuromuscular and musculoskeletal interventions may work by leading to and supporting the practice of functional activities. Additional interventions using cognitive, perceptual and sensory attributes can be used to enhance skill acquisition. Such interventions may be delivered by the therapist with or without devices (e.g. orthoses) or additional modalities (e.g. electrical stimulation). These interventions may be delivered in various settings that may impact the people available to provide the intervention or the setting (e.g. hospital or home) of such work, and may influence motivation and integration with ADLs. Services can be delivered at different locations that may affect treatment through environmental and societal factors. Some stroke survivors may be motivated by group sessions. In early supported discharge, the rehabilitation team may be able to advise on how to integrate rehabilitation activities into home life. Accessibility to some interventions may be restricted within some treatment settings as the result of resource issues such as equipment availability or staff training or skills.

Descriptions of mechanisms of specific interventions are provided in Table 1. References relevant to the intervention mechanisms are cited within the 2014 version of the Cochrane overview[10].

Why it is important to do this overview

Prior to the first version of this overview, identifying the most effective upper limb rehabilitation interventions had been recognised as a priority for stroke research[22, 23]. It was important to do this overview, as evidence of the effectiveness of many of interventions aimed at improving upper limb function after stroke had been synthesised and summarised within several systematic reviews. The rapidly growing body of systematic reviews can be overwhelming for decision makers and healthcare practitioners who do not have time to keep up-to-date with this evidence base[22].

The 2014 Cochrane overview[10] comprehensively compiled information from systematic reviews of interventions to improve UL function after stroke, aiming to help inform decisions of clinicians and policy makers. This overview included 40 reviews, containing 503 unique studies (18,078 participants) addressing 18 interventions, plus also considering dose and setting. We extracted pooled data from 31 reviews related to 127 comparisons and summarised where there was high, moderate or low quality evidence of effectiveness. Multiple metrics demonstrate that this overview is accessed and having impact, for example:

- It was in the top 50 most accessed reviews in the whole Cochrane Library, and in the top 3 most accessed Cochrane Stroke reviews, in 2015, 2016 and 2017.
- It has been cited in at least 13 clinical guidelines from round the world (Cochrane UK data), including 2023 UK national guidelines[25, 26]
- Scopus CiteScore place it in the 93rd percentile for the Medicine(all) category and the 96th percentile for Cardiology and Cardiovascular Medicine Category
- Its Almetric Attention Score is 84, placing it in the top 5% of all research outputs scored by Almetric, and scoring higher than 92% of other outputs from the Cochrane Database of Systematic Reviews

This 2014 overview of reviews[10] is now out-of-date. Updating is important as the review informs clinical decisions that affect the effectiveness of treatments provided to stroke survivors; as it is out-of-date and missing important new information stroke survivors may be receiving sub-optimal treatment and failing to achieve the best possible level of functional recovery. The large volume of systematic review evidence makes it unfeasible for a clinician to easily identify up-to-date evidence. This overview is important as it saves time and resources, providing easy access to best evidence, preventing individual clinicians having to spend time searching for and appraising multiple reviews, and helping ensure that stroke survivors receive optimal treatment.

Objectives

To carry out a Cochrane overview by synthesising systematic reviews of interventions provided to improve upper limb function after stroke.

Methods

Criteria for considering reviews for inclusion

We will include systematic reviews which meet the following criteria:

- Systematic review including RCTs. If a review includes other studies in addition to RCTs (e.g. quasi-RCTs, before-and-after studies), we will include the review, but will not include the

evidence from these other study types. We will exclude reviews of other study designs or of qualitative studies. We will use the definition of systematic review published in the Cochrane Handbook[27], and only include systematic reviews of intervention studies which:

  - Address a pre-stated research question;
  - Clearly define the scope of the review, stating eligibility criteria for inclusion of studies;
  - Have a comprehensive search strategy which aims to find all relevant research (at a minimum; the search strategy must be available, and must include searches of at least two databases; an experienced information specialist will be involved in assessment of the search strategy);
  - Consider the risk of bias in included studies;
  - Analyse/synthesise the results of included studies, using strategies to reduce the introduction of bias into the review process (e.g. use of two independent reviewers during data extraction).
- Included studies in which the participants are adults (aged ≥18 years) with a clinical diagnosis of stroke. We will include reviews that included studies with other participants in addition to people with stroke (e.g. adults with other neurological diseases or traumatic brain injury), when at least 75% of the participants were stroke patients, or when data on stroke patients had been presented and analysed as a separate subgroup; we will highlight when data are reported from a mixed population.
- Investigated an intervention for which the primary aim is to improve functional recovery or to reduce impairment—or both—of the upper limb.
- Investigated the effects of interventions for the upper limb. This may include comparisons of interventions with control, placebo or standard care; comparisons of one active treatment versus another active treatment; and comparisons of different doses, intensities or timing of delivery of the same intervention.

Reasons for exclusion of systematic reviews will be documented and reported.

Managing overlapping systematic reviews

Where SRs overlap we will systematically identify the most up-to-date and methodologically rigorous review (see *selection of reviews*). Older/less methodologically rigorous SRs will be excluded, and listed in Tables of Excluded studies.

We will use a decision tool (Figure V.4.a, in Cochrane Handbook[28]) to inform decisions about inclusion of overlapping reviews (i.e. reviews exploring the same participants, interventions, comparisons and outcomes). This will involve the following steps:

1. Identify whether there is an up-to-date (published 2020 or later) Cochrane systematic review examining an intervention comparison. If so, we will include the Cochrane review for this intervention, and not consider any non-Cochrane reviews.

2. If no up-to-date Cochrane systematic review is identified, we will search for and identify non-Cochrane reviews. Where there are overlapping non-Cochrane reviews we will use a systematic approach to identify and include the most recent review which has adequate methodological quality. Further details of our process are described in 'selection of reviews'.

Outcomes

We will include any review for which the primary aim of the intervention was to improve functional recovery*, or reduce impairment*, of the upper limb, regardless of the outcome measures reported. (*see note on terminology below).

Our selection of outcomes for this update is informed by international consensus recommendations for outcome measurement in post-stroke arm rehabilitation trials[29] and an analysis of the outcome measures included within the trials in the last version of our Cochrane overview[30].

Primary and secondary outcomes of interest to this overview are as follows.

Primary outcome

The primary outcome of interest for the overview is **upper limb function**, including measures that examine capacity, including active function, dexterity, object manipulation and reach-to-grasp, grip or pinch. Many of the outcome measures commonly used to assess upper limb function comprise assessments which combine assessment of arm function and activity/participation[27], this is reflected in our outcomes of interest.

Measures combining assessment of body functions and activities

These include, but are not limited to:

- Action Research Arm Test (ARAT)
- Fugl-Meyer Assessment of Sensorimotor Recovery after Stroke (upper limb section).
- Wolf Motor Function Test (WMFT).
- Motricity Index (upper limb section).
- Motor Assessment Scale—hand movement or advanced hand activities scores.
- Jebsen-Taylor Hand Function Test.

Measures of upper limb activity/participation

These include, but are not limited to:

- Box and Block Test.
- Nine-Hole Peg Test.
- Motor Activity Log
- Stroke Impact Scale (hand function section).

Secondary outcomes

Secondary outcomes of interest include:

Global measures of activities of daily living (ADL). These include assessment of activities of feeding, dressing, bathing, toileting, mobility and transfers. We will include global measures of ADLs, such as Barthel ADL Index, Functional Independence Measure (FIM), Rivermead ADL Assessment, Rankin Scale, and Katz Index of Activities of Daily Living.

Measures of upper limb strength. Muscle strength is a measure of body function. We will include measures of upper limb strength, assessed using dynamometry. International consensus activities recommend dynamometry measures as an important outcome for post-stroke arm rehabilitation[27].

(For references to outcome measures, see 2014 version of overview[10]).

Documentation of outcomes reported in included reviews

We will systematically document other outcomes reported in included reviews, and note where meta-analyses have been conducted. Other outcomes considered will include: other measures of

body function (including kinematic measures of movement, pain, muscle tone/spasticity), measures of extended ADL (e.g. Nottingham Extended ADL scale, Rivermead Extended ADL scale, Frenchay Activities Index), quality of life (e.g. EuroQoL EQ-5D), mood, and adverse events.

*Terminology: During the update we will work in partnership with stroke survivors, carers and health professionals to reflect on the terminology used, with reference to the World Health Organisation International Classification of Functioning, Disability and Health (WHO ICF)[17], and amend or clarify our terminology, when appropriate. (See Interest-holder Involvement).

Search methods for identification of reviews

We will search for up-to-date SRs of UL interventions. We will involve interest-holders (including stroke survivors, caregivers and health professionals) to ensure we address all relevant interventions (see Interest-holder Involvement). We are interested in any intervention which has a primary aim of improving functional recovery, or reducing impairment, of the upper limb. Interventions that we will include are listed in Table 1, but we will also include interventions not listed here if (i) an intervention is identified by an interest-holder, or (ii) we identify a systematic review addressing an intervention not listed here.

We will search the Cochrane Database of Systematic Reviews for new/updated Cochrane reviews (from June 2013) (see Appendix 1). We will search Medline, Embase and CINAHL, using validated filters for SR study type, and Epistemonikos, which is a database of SRs, in order to identify recently published non-Cochrane reviews (this replaces our previous search of the Database of Abstracts of Reviews of Effects (DARE), a comprehensive database of published SRs, as this has not been updated since 2015, and has no direct successor)(see Appendix 2).

In an effort to identify ongoing systematic reviews, we will search for protocols of Cochrane reviews in the CDSR (*The Cochrane Library*) and PROSPERO, an international prospective register of systematic reviews (www.crd.york.ac.uk/prospero/). We will contact authors of protocols meeting our selection criteria and included any reviews that will be completed before the end of December 2024.

To ensure that data included in the overview are as current as possible, we will contact authors of included Cochrane reviews to ascertain details of planned updates.

We will search for relevant reviews in all languages and arrange translation when necessary.

Dealing with multiple related publications

We anticipate that there will be multiple publications relating to some reviews (e.g. a published protocol, conference abstract, full review). We will search for and identify these, merging publications into single 'studies' within Covidence. One reviewer will do this on included full-text publications, prior to conduct of any data extraction. These will be presented as single 'reviews' with multiple publications in Review Manager.

Search methods for identification of new RCTs relevant to included systematic reviews

For all included systematic reviews we will consider any reported "ongoing" RCTs and check whether these are now published. For systematic reviews with a search date >2 years previously, we will search for new RCTs, and use a systematic approach to judge whether inclusion would impact on systematic review results[31] (see 'Assessment of impact of missing/new RCTs', below). Two years is a pragmatic cut-off, selected as we anticipate that any RCTs published within 2 years of a systematic

review will be listed as ongoing studies within the review. We will search for RCTs in Medline, CINAHL and Embase, using validated filters to limit results to RCTs. Depending on the number of searches required, we will either (i) conduct individual searches for each relevant intervention or (ii) conduct one combined search for all interventions relating to upper limb function after stroke, and then use a tagging process (as described for searching for systematic reviews) to identify RCTs relevant to each systematic review. The decision will be made through discussion between overview authors, including our information specialist (CF), and will take into account the number of out of date systematic reviews, dates of last searches of these reviews and the range of interventions addressed and consideration of the resources required for single versus combined searches. Where new RCTs are identified, we will collate these, but do not plan any data extraction, quality assessment, or integration of these into the systematic reviews (see 'Assessment of impact of missing/new RCTs', below).

Data collection and analysis

Selection of reviews

Our selection of reviews will involve a hierarchical approach. Our goal is to include (at least) one review for each intervention used to improve UL function after stroke; we aim to include the most up-to-date, highest quality review for each intervention comparison.

Key steps to identify potential reviews for each intervention, conducted by two overview authors and involving a 3rd where there are disagreements, will comprise:

1. Updates of previously included Cochrane reviews. We will search the Cochrane Library for any updates of Cochrane reviews previously included in the overview. Any with search dates of 2020 or later will automatically be included. Those with search dates earlier than 2020 will be tagged according to intervention, using the list of interventions detailed in Table 1, and considered as part of our selection process (see below).

2. New Cochrane reviews (and protocols). We will search the Cochrane Library (see search strategy, above) for any new Cochrane reviews (and protocols). Two reviewers will screen the search results, applying criteria to full texts to assess if these are focussed on (i) people with stroke and (ii) interventions to improve upper limb function. Disagreements will be resolved through consensus, involving a 3rd reviewer if necessary. Any Cochrane reviews which meet these criteria will be tagged by intervention, as described above, and considered as part of our selection process (see below).

3. Non-Cochrane reviews (and protocols). We will conduct a search for non-Cochrane systematic reviews (and protocols), published 2013 onwards (see search strategy, above). We will screen out any Cochrane reviews in Endnote. The search results will be brought into Covidence. Two independent reviewers will screen titles and abstracts, assessing whether these (i) are non-Cochrane systematic reviews, (ii) include participants who have had stroke, (iii) focus on interventions to improve upper limb function. All titles and abstracts judged as "yes", or for which there is insufficient information to judge as "no", move to full text stage. Two reviewers will screen full-texts, applying inclusion criteria. At this stage, each relevant review will be tagged by intervention, as above. Disagreements resolved through consensus.

Selection process

Selection of reviews to include from the screened reviews will be made based on the intervention addressed (according to tagging), with consideration of the date of the search, the comparison and methodological quality of the review, following the steps summarised in Figure 1 and described in

Appendix 3. Two independent reviewers will complete all data extraction and categorisations required for this process, with any disagreements resolved through discussion. Final decisions about inclusion of each review will be reached through discussion between review authors, with all decisions transparently documented.

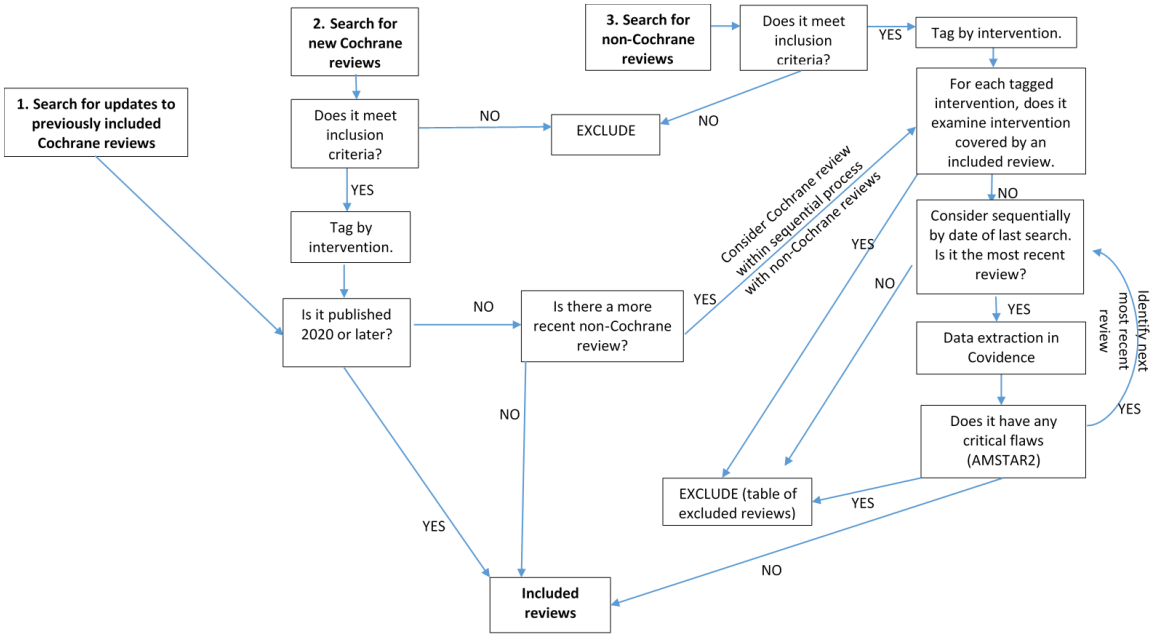

Figure 1: Summary of key steps involved in selection of included reviews

Included reviews will progress to further data extraction. For all remaining reviews addressing the same intervention comparison, no further data extraction or assessment will be conducted. References to these reviews will be listed in a table of excluded reviews. Thus, final included reviews will comprise one review (judged to be the most up-to-date and high quality) for each unique intervention comparison.

Data extraction and management

Key characteristics of included reviews

Two overview authors will independently extract key review features including details of aims and rationale, types of studies, participants, interventions, comparisons, outcomes assessed, date of last search, number of included studies and participants, and meta-analyses conducted, with any disagreements resolved by a 3rd author.

Our previous overview did not extract any data relating to health inequalities. To aid the development and greater understanding of evidence relating to the inclusion of, and reporting of, underrepresented populations in stroke trials, we will use the PROGRESS health-equity criteria[32] to highlight whether the included reviews extract and report data relating to key population characteristics.

Methodological quality of included reviews

Two overview authors will independently assess the methodological quality of included reviews, using the AMSTAR2 measurement tool[33], with consensus reached through discussion. This involves judgements of yes, partial yes or no to the following questions:

1. Did the research questions and inclusion criteria for the review include the components of PICO?
2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
3. Did the review authors explain their selection of the study designs for inclusion in the review?
4. Did the review authors use a comprehensive literature search strategy?
5. Did the review authors perform study selection in duplicate?
6. Did the review authors perform data extraction in duplicate?
7. Did the review authors provide a list of excluded studies and justify the exclusions?
8. Did the review authors describe the included studies in adequate detail?
9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?
10. Did the review authors report on the sources of funding for the studies included in the review?
11. If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results?
12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?
13. Did the review authors account for RoB in primary studies when interpreting/discussing the results of the review?
14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?
15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?
16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

We will follow the guidance of Shea 2017[33]. We will not combine the individual ratings to create an overall score for each review. Instead, we will create a visual representation of the responses to aid comparison between reviews.

Note: Our process for selection of reviews involves exclusion of any reviews judged to have flaws within AMSTAR2[31] critical domains (listed in Appendix 3).

Statistical analyses and quality of evidence within included reviews

Reviews with meta-analyses relevant to this overview

For included reviews reporting relevant meta-analyses (i.e. a pooled analysis comparing effects of intervention compared to no treatment, usual care or other active intervention, for one of our outcomes of interest) we will extract details of the meta-analysis results. This will include intervention, comparison, outcome measure, statistical analysis method, effect size, confidence intervals, and measure of heterogeneity. For any trials included within relevant meta-analyses we will extract risk-of-bias data (from the published review). For any relevant meta-analyses for which data are extracted, we will document the quality of evidence synthesised within the reviews based

on criteria considered within the GRADE approach. We will extract GRADE judgements as reported by review authors or, if this is not available, our overview author team will work in pairs to make considered judgements, involving a third reviewer if there are disagreements. We will apply the objective criteria and algorithm developed to determine GRADE level of evidence for the previous version of this overview[10], and use the results of this to inform our considered judgements. We will make it clear whether GRADE judgements are those of review authors or of our overview team. Reasons for downgrades applied by our overview team will be transparently reported.

Reviews with meta-analyses not relevant to this overview
For included reviews reporting meta-analyses exploring:

- effect of an intervention compared to another form of the same intervention (e.g. different dose, intensity, mode of delivery)
- effect of an intervention when delivered in combination with another intervention
- effects of different types of 'service delivery' interventions
- effects on outcomes which are not one of our primary or secondary outcomes of interest

We will not extract any data relating to details of the statistical analyses or quality of evidence. Instead, we will tabulate the meta-analyses conducted, and signpost readers to the relevant reviews for further information.

Assessment of impact of missing/new RCTs

For SRs with a search date >2 years previously, we will search for new RCTs, and use a systematic approach to judge whether inclusion would impact on SR results, based on the workflow decision-tree for updating living systematic reviews[31]. This will involve, for each out-of-date SR:

- Running an update of the review search and two independent reviewers applying inclusion criteria to identify potential new trials
- Creating a list of potential new trials
- At least two overview authors considering the new trials, with particular attention to whether, for the primary outcomes of relevance to this overview, the new trial has data which could be incorporated into review meta-analyses. If yes, the volume of data, and direction of findings, as compared to the volume of data, effect size, heterogeneity and GRADE judgement of the analyses within the (out of date) review. The overview authors will make a judgement of "No important impact on review (or overview) findings" or "Important impact on review (and overview) findings".
- Where it is judged that there may be an important impact on the review findings, details of the relevant new trial data will be summarised within a brief narrative which will detail the participant numbers, and reported effect sizes for our primary outcomes of interest.
- Where the out of date review is a Cochrane review, we will also contact the review authors, providing details of the new trials that we have identified.

Note; updating the results of any analyses within (out of date) reviews is beyond the scope of this overview update, and will not be conducted.

Data synthesis

We will synthesise findings within tables, documenting outcomes, number of studies and participants included in the comparison, and (when available) the statistical data from meta-analyses. Our synthesis will include:

- Overview of intervention comparisons addressed by included reviews (see template Table A, Appendix 2)
- Characteristics of included reviews (see template Table B, Appendix 2)
- Details of ongoing reviews (see template Table C, Appendix 2)
- Table of excluded reviews (see template Table D, Appendix 2)
- Summary of effects of interventions on immediate and follow-up outcomes, where there is high or moderate GRADE evidence (see template tables E:J, Appendix 2)
- Summary of effects of interventions on immediate and follow-up outcomes, where there is low or very low GRADE evidence (see template tables K:P, Appendix 2)

Summary of findings

We will produce a key summary of findings table and figure (see templates in Appendix 1, and Table 2 and Figure 2 in previous version of Cochrane overview[10]).

We will work in partnership with key interest-holders to agree further innovative and impactful methods of data presentation (see Interest-holder Involvement). For example, this might include infographics or visual abstracts.

Interest-holder involvement

We will have two members of the overview team who have lived experience as a stroke survivor or carer of a stroke survivor. Several members of the overview team have previous experience working as health professionals and/or in education.

We will hold a series of meetings with external interest-holders in order to gain a wide range of views about optimal approaches to bringing together and presenting the results of this overview, and to inform a number of decisions relating to the overview.

Who will be involved?

We will involve people with experience of upper limb impairment after stroke, including people who have had a stroke, caregivers and health professionals.

How will we recruit people?

We will recruit people to be involved via existing networks with stroke survivors, caregivers and health professionals. This will include (but not be limited to) university public involvement groups, stroke support groups, and health professional forums (e.g. Scottish Stroke AHP Forum, ACPIN). We will advertise opportunities to take part in a series of individual events, including details of the date and time, meeting format, and the aims/content of the meeting. The meetings will all be 'open', meaning that anyone with appropriate lived experience will be able to attend.

When will we involve people and what will we do?

We will hold events to gain views and inform decisions about the following:

- Interventions. At the start of the overview process we hold an open online event focussed on interventions used in the rehabilitation or treatment of upper limb impairment after stroke. Before and during this event we will share our current list of interventions (Table 1) with interest-holders. We will ask if there are any interventions missing from this list. We will also ask about the best way to group interventions together, and how we should bring together evidence relating to interventions delivered in combination. We will collect details of any new interventions and add them to the current list, ensuring that they are addressed within the overview.

- Outcome terminology. During the overview process we will hold an open online event to reflect on the terminology used within the overview, and to reach agreement on terms to be used in the final overview. Before and during the event we will share definitions of terms, particularly focussing on outcomes, and reflecting on terminology used nationally and internationally, including as part of the WHO ICF[18]. We will aim for interest-holders to reach agreement on suitable terms to be used within the overview.
- Presentation of findings. When we have draft overview results, we will hold an open online event to present the findings, and to share views and ideas about optimal methods of presentation and summary. We will also gather ideas relating to dissemination activities.

For each of the topics above we will hold at least one open online event. We will widely advertise the event through our networks and provide information about the meeting in advance. For each topic, we will hold additional meetings if further input is required to inform decisions, or if it is felt that some interest-holder voices were not represented within the first meeting. If there are timely opportunities for a member of our overview team to attend an existing meeting of a group of key interest-holders (e.g. a planned meeting of a stroke support group, or an AHP forum meeting), then we may do this in addition to the open online event. We will use a recording template (developed by the NIHR ESG PPI community of practice) to collect and summarise information about each event or meeting attended, and the subsequent impact on the overview. We will collate ideas, views and opinions from each event or meeting and use these to inform author decisions; we will report views and subsequent decisions transparently, using the ACTIVE Framework[34] and GRIPP2 guidance[35].

Differences between published overview and update

Criteria for considering reviews for inclusion

In the published (2014) version we included data from quasi-randomised trials (QRCTs) if they had been pooled with data from RCTs. However, if it was possible to extract data pertaining only to the RCTs, we did this in preference to including data from QRCTs. In the event that we included evidence from QRCTs, we planned to highlight and discuss the implications of including this evidence.

For this update we will not include data relating to QRCTs.

Managing overlapping systematic reviews

In the 2014 overview[10] we did make a judgement on the most up-to-date and methodologically rigorous reviews. However, we did not have a clear and explicit process for this, and we did not exclude the older/less methodologically rigorous reviews. For this update we will introduce a clear process, using the decision tool from the Cochrane Handbook. In the 2014 overview[10] we extracted details of references to trials included in reviews to support our judgements. For this update, we will not use details of trials included in reviews as part of this decision making, and we will therefore not extract details of these.

Selection of reviews

For this update, we have introduced a clearly defined hierarchical approach for selection of reviews. This uses pre-stated objective criteria (e.g. year of publication, AMSTAR2[33] critical domains) to improve rigour and reproducibility in the selection of reviews for inclusion. For this update, we have the explicit goal of including "the most up-to-date, highest quality review for each intervention comparison" and our selection process clarifies that other reviews will be excluded, and listed in a table of excluded studies. This differs from the previous version of this review, where all relevant reviews were "included" but different levels of data extraction conducted, according to judgements about date, quality and comparisons addressed.

Outcomes

In the 2014 overview we listed large numbers of potentially relevant outcome measures. These were not listed or grouped with reference to the ICF. Subsequent work, conducted based on our 2014 overview dataset, identified 243 outcome measures reported in the RCTs included in the 2014 overview[30]. For this update, we have refined and reduced our list of relevant outcome measures, building on consensus recommendations for outcome measures for studies of arm rehabilitation after stroke[29], and grouped outcomes of interest according to the ICF[18].

Methodological quality of included reviews

In 2014[10] we used the AMSTAR tool. In this update we will use the updated AMSTAR2 tool[33].

Quality of evidence within included reviews.

In 2014[10] we developed and used an algorithm to support GRADE judgements, and we assigned GRADE judgements to all included meta-analysis results. For this update we will extract GRADE judgements as reported by review authors or, if this is not available, our overview author team will work in pairs to make considered judgements. We will apply the objective criteria and algorithm developed to determine GRADE level of evidence for the previous version of this overview [10], and use the results of this to inform our considered judgements.

Assessment of impact of missing/new RCTs

This is a new addition to this overview, and was not part of the methods of the 2014 version[10].

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NESSIE Team

Alex Todhunter-Brown, Jackie Price, Sheila Cameron, Pauline Campbell, Emma France, Rosie Hill, Catriona Keerie, Sarah Markham, Peter Matthews, Gillian Mead, Aileen Neilson, Gerry Stansby, Marlene Stewart, Evropi Theodoratou, Cathryn Broderick, Julie Cowie, Bridget Davis, Candida Fenton, Ceri Sellers, Katie Thomson.

Contributions of Authors

Please see Appendix 6 for the CRediT author statement.

Reporting checklist

PRISMA (Preferred Reporting of Systematic Review and Meta-Analysis) for protocols (PRISMA-P) checklist is in Appendix 7.

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APPENDIX 1: Cochrane Library search strategy

#1 (Arm* OR axilla OR elbow OR Finger* OR forearm OR Hand* OR rotator cuff* OR Shoulder* OR Upper limb* OR upper extremit* OR wrist*):ti,ab,kw

#2 (Contracture* OR co ordination OR dexterity OR immobility OR Loss of motor control OR movement OR nerve function OR paresis OR spasticity OR subluxation OR stroke OR acquired brain injury):ti,ab,kw

#3 #1 AND #2 with Cochrane Library publication date Between Jan 2013 and Oct 2024

APPENDIX 2: Medline search strategy

1	exp Stroke Rehabilitation/
2	contracture*.ti,ab.
3	co-ordination.ti,ab.
4	dexterity.ti,ab.
5	immobility.ti,ab.
6	"loss of motor control".ti,ab.
7	movement.ti,ab.
8	"nerve function*".ti,ab.
9	paresis.ti,ab.
10	spasticity.ti,ab.
11	subluxation.ti,ab.
12	stroke.ti,ab.
13	weakness.ti,ab.
14	hemipleg*.ti,ab.
15	"acquired brain injury".ti,ab.
16	or/1-15
17	exp Upper Extremity/
18	(arm adj2 (function or strength or muscle or function or training)).ti,ab.
19	axilla.ti,ab.
20	elbow.ti,ab.
21	finger*.ti,ab.
22	forearm.ti,ab.
23	hand*.ti,ab.
24	"rotator cuff*".ti,ab.
25	shoulder*.ti,ab.
26	"upper limb*".ti,ab.
27	"upper extremit*".ti,ab.
28	wrist*.ti,ab.
29	or/17-28

30 16 and 29

31 "systematic review".pt. or "Systematic Reviews as Topic"/ or ("Cochrane Database of Systematic Reviews" or evidence report technology assessment or evidence report technology assessment summary).jn. or (((((comprehensive or comprehensively) adj (analysis or review or reviewed)) or ((literature or scoping) adj (search or searches))).ti,ab,kf,kw. not "narrative review".ti.) and (database or databases or cinahl or cochrane or embase or psycinfo or pubmed or medline or scopus or (web adj1 science) or ((bibliographic or literature) adj (review or reviews)) or (((electronic adj (database or databases)) or (databases adj3 searched)) and (eligibility or excluded or exclusion or included or inclusion))).ti,ab,kf,kw.) or (((comparative adj effectiveness) and (effectiveness adj review)) or ((critical adj interpretive) and ((interpretive adj review) or (interpretive adj synthesis)))).ti,ab,kf,kw. or ((diagnostic adj test) and ((accuracy adj review) or (accuracy adj reviews) or (accuracy adj studies) or (accuracy adj study)) and (meta-analysis or scoping or systematic)).ti,ab,kf,kw. or ((evidence adj assessment) and GRADE).ti,ab,kf,kw. or ((evidence adj2 gap) and (gap adj map)).ti,ab,kf,kw. or ((evidence adj mapping) or (evidence adj review) or (exploratory adj review) or (framework adj synthesis) or (mapping adj review)).ti,ab,kf,kw. or ((meta adj (epidemiological or ethnographic or ethnography or interpretation or narrative or review or study or synthesis or summary or theory)) or metaethnographic or metaethnography or metasynthesis).ti,ab,kf,kw. or ((methodological or methodology) adj1 review).ti,ab,kf,kw. or ((mixed adj methods) and (methods adj1 (review or synthesis))).ti,ab,kf,kw. or ((narrative adj1 synthesis) or (overview adj4 reviews) or ("PRISMA" adj4 (guideline or guidelines or preferred or reporting or requirements)) or (PRISMA adj "P")).ti,ab,kf,kw. or (((prognostic or psychometric) adj1 review) or ((qualitative adj (evidence or research)) and ((evidence or research) adj synthesis))).ti,ab,kf,kw. or (((rapid adj evidence) and (evidence adj assessment)) or (rapid adj realist) or (rapid adj2 (review or reviews)) or (realist adj2 (review or reviews or syntheses or synthesis))).ti,ab,kf,kw. or (((review adj economic) and (economic adj1 (evaluation or evaluations))) or ((scoping or systematic) adj2 (review or reviews or studies or study))).ti,ab,kf,kw. or ((review adj1 reviews) or ((systematic adj evidence) and (evidence adj map)) or (systematic adj2 mapping) or (systematic adj2 literature) or (systematic adj2 (Embase or Medline or PsycInfo or PubMed)) or (systematic adj2 (review or reviews)) or ((systematical or systematically) adj2 (review or reviewed reviews)) or (systematically adj identified) or (systematized adj review) or (umbrella adj (review or reviews))).ti,ab,kf,kw. or "Meta-Analysis".pt. or "meta-analysis as topic"/ or (meta adj2 (analyse or analyser or analyses or analysis or analytic or analytical or analytics or analyze or analyzed or analyzes)).ti,ab,kf,kw. or (metaanalyse or Metaanalysen or metaanalyser or metaanalyses or metaanalysis* or metaanalytic or metaanalytical or metaanalytics or metaanalyze or metaanalyzed or metaanalyzes).ti,ab,kf,kw. or "network meta-analysis"/ or (network adj1 (meta or metaanalyses or metaanalysis or metaregression)).ti,ab,kf,kw. or (systematic and ((meta adj regression) or metaregression)).ti,ab,kf,kw.

32 30 and 31

33 (2013* or 2014* or 2015* or 2016* or 2017* or 2018* or 2019* or 2020* or 2021* or 2022* or 2023* or 2024*).ed.

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APPENDIX 3: Process for selection of included reviews

As summarised in Figure 1:

- For non-Cochrane reviews of interventions for which there is an up-to-date Cochrane review (published in 2020 or later), no further data extraction or assessment will be conducted. References to these reviews will be listed in a table of excluded reviews.
- For non-Cochrane reviews of interventions for which there is no up-to-date Cochrane review, data extraction and categorisation will be conducted (in Covidence), working in publication date order (most recent first). Data extracted/categorised, conducted by two independent reviewers, with a 3rd reviewer checking consensus, will include:
    - Year of publication
    - Date of search
    - Types of studies included (RCTs only; RCTs + non-randomised intervention studies; RCTs + other designs (including non-intervention studies)
    - Population (stroke only; stroke + other non-progressive neurological disorder; other, but data for stroke participants available separately; none of these)
    - Intervention (see list of interventions in Table 1)
    - Comparator (no treatment; usual care; other active intervention; different dose of same intervention; other)
    - Outcomes (see list of outcomes, above)
    - Number of included studies
    - Number of (stroke) participants within included studies
    - Summary of meta-analyses relevant to this overview (see
    - Judgements for AMSTAR2[31] 'critical' domains:
        - Protocol registered before commencement of the review (item 2)
        - Adequacy of the literature search (item 4)
        - Justification for excluding individual studies (item 7)
        - Risk of bias from individual studies being included in the review (item 9)
        - Appropriateness of meta-analytical methods (item 11)
        - Consideration of risk of bias when interpreting the results of the review (item 13)
        - Assessment of presence and likely impact of publication bias (item 15)

The most recent (by search date) review with no flaws in the AMSTAR2[31] critical domains addressing each intervention comparison will be identified. This will be done through discussion between review authors, with all decisions transparently documented.

APPENDIX 4: Template summary of findings table/figure

Summary of findings table:

Intervention	**Comparison**	**Included reviews**	**Moderate-quality evidence of effect on upper limb function**	**Moderate-quality evidence of effect on upper limb impairment**	**Moderate-quality evidence of effect on ADL outcomes**	**Low- or very low-quality evidence**	**Implications for clinical practice**	**Recommendations for research**
Bilateral arm training								
Biofeedback								
etc								

Summary of findings figure:

Intervention	**Comparison**	**UL Function**	**UL Impairment**	**ADL**	**Notes**
Bilateral arm training		*	*	*	
Biofeedback					
etc					

* cells will be colour-coded to indicate strength of evidence, with symbols to indicate direction of evidence for those with moderate or high level evidence.

APPENDIX 5: Template tables for overview

Table A: Overview of intervention comparisons addressed by included reviews

	Includes comparison with no treatment					Includes comparison with usual care					Includes comparison with other active intervention					Includes comparison with the same intervention (e.g. at different doses)				
Intervention	**Arm / hand function**	**Motor impairment**	**ADL**	**EADL**	**Other outcomes**	**Arm / hand function**	**Motor impairment**	**ADL**	**EADL**	**Other outcomes**	**Arm / hand function**	**Motor impairment**	**ADL**	**EADL**	**Other outcomes**	**Arm / hand function**	**Motor impairment**	**ADL**	**EADL**	**Other outcomes**
Action observation	*																			
Bilateral arm training																				
Biofeedback																				
Bobath therapy																				
Brain stimulation: Transcranial direct current stimulation (tDCS)																				
Brain stimulation: Transcranial magnetic stimulation (TMS)																				
Complementary therapies: acupuncture																				
CIMT																				
Electrical stimulation																				
Gaming (e.g. Wii)																				
“Hands-on” therapy (manual therapy techniques)																				
Mental practice																				

Mirror therapy																				
Music therapy																				
Orthoses																				
Pharmacological interventions																				
Repetitive task training																				
Robotics																				
Sensory interventions																				
Strength training																				
Stretching & positioning																				
Surgical interventions																				
Task-specific training																				
Virtual reality																				
Combined interventions**																				

*cells will contain names of included reviews. In most cases this will be one review, but there may be occasions where there are two or more reviews listed in a single cell. For example, if there are separate reviews which explore the same intervention comparison, but for different populations (e.g. young stroke survivors and older stroke survivors) or including different outcomes. One review may be included in multiple cells; for example, where a review explores the effect of an intervention compared with no treatment, usual care and other active interventions.
**Details of how best to present and incorporate data from reviews investigating the effect of interventions delivered in combination will be discussed and agreed with key interest-holders (see Interest-holder Involvement section).

Table B: Characteristics of included reviews

Review (source)	Intervention*	Date of search	Objective (as stated within review)	Types of studies included	Participants included	Interventions included	Comparisons included	Outcomes (as defined within review)	Number of studies included (number of participants included)	PROGRESS equity characteristics addressed by review?
Review 1										
Review 2										
etc										

NB. The table will focus on reviews of single interventions. Reviews focussed on the effects of delivering interventions in combinations will be summarised in a separate table. This will have the same headings as within this template, but with the addition of an extra row for "intervention 2".

Table C: Details of ongoing reviews

Reference	Brief description of review/review aim	Dates/Notes
Protocol 1		
Protocol 2		
etc		

Table D: Table of excluded reviews

Reference	Intervention explored	Reason for exclusion

Table E: Summary of effects of interventions on upper limb function: immediate outcomes. High or Moderate-level GRADE evidence
Table F: Summary of effects of interventions on upper limb function: follow-up data. Moderate-level GRADE evidence
Table G: Summary of effects of interventions on upper limb impairment: immediate outcomes. High or Moderate-level GRADE evidence
Table H: Summary of effects of interventions on upper limb impairment: follow-up data. High or Moderate-level GRADE evidence
Table I: Summary of effects of interventions on ADL outcomes: immediate outcomes. High or Moderate-level GRADE evidence
Table J: Summary of effects of interventions on ADL outcomes: follow-up data. High or Moderate-level GRADE evidence

Intervention	Comparison	Review	Outcome category	Outcome measures	Number of trials	Number of participants	Effect size	95% CI	Evidence of effect?	GRADE level of evidence	Reasons for downgrades

Table K: Summary of effects of interventions on upper limb function: immediate outcomes. Further research required (low- and very low-level GRADE evidence)
Table L: Summary of effects of interventions on upper limb function: follow-up outcomes. Further research required (low- and very low-level GRADE evidence)
Table M: Summary of effects of interventions on upper limb impairment: immediate outcomes. Further research required (low- and very low-level GRADE evidence)
Table N: Summary of effects of interventions on upper limb impairment: follow-up outcomes. Further research required (low- and very low-level GRADE evidence)
Table O: Summary of effects of interventions on ADL outcomes: immediate outcomes. Further research required (low- and very low-level GRADE evidence)
Table P: Summary of effects of interventions on ADL outcomes: follow-up outcomes. Further research required (low- and very low-level GRADE evidence)

Intervention	Comparison	Review	Outcome category	Outcome measure	Studies	Participants	Effect size	95% confidence interval	GRADE level of evidence	Reasons for downgrades

APPENDIX 6: CRediT author statement

Term	Definition	Contributors
Conceptualization	Ideas; formulation or evolution of overarching research goals and aims	A Todhunter-Brown* P Langhorne S Farmer F van Wijck B Davis *(* guarantor of the review)*
Methodology	Development or design of methodology; creation of models	A Todhunter-Brown P Langhorne S Farmer F van Wijck B Davis C Fenton
Software	Programming, software development; designing computer programs; implementation of the computer code and supporting algorithms; testing of existing code components; designing of search strategies	C Fenton
Validation	Verification, whether as a part of the activity or separate, of the overall replication/ reproducibility of results/experiments and other research outputs	n/a
Formal analysis	Application of statistical, mathematical, computational, or other formal techniques to analyse or synthesize study data	n/a
Investigation	Conducting a research and investigation process, specifically performing the experiments, or data/evidence collection	n/a
Resources	Provision of study materials, reagents, materials, patients, laboratory samples, animals, instrumentation, computing resources, or other analysis tools	n/a
Data Curation	Management activities to annotate (produce metadata), scrub data and maintain research data (including software code, where it is necessary for interpreting the data itself) for initial use and later reuse	A Todhunter-Brown M Stewart C Fenton

Writing - Original Draft	Preparation, creation and/or presentation of the published work, specifically writing the initial draft (including substantive translation)	A Todhunter-Brown
Writing - Review & Editing	Preparation, creation and/or presentation of the published work by those from the original research group, specifically critical review, commentary or revision – including pre-or postpublication stages	P Langhorne S Farmer F van Wijck NESSIE team
Visualization	Preparation, creation and/or presentation of the published work, specifically visualization/ data presentation	n/a
Supervision	Oversight and leadership responsibility for the research activity planning and execution, including mentorship external to the core team	A Todhunter-Brown J Price M Stewart
Project administration	Management and coordination responsibility for the research activity planning and execution	A Todhunter-Brown J Price M Stewart
Funding acquisition	Acquisition of the financial support for the project leading to this publication	n/a

Appendix 7: PRISMA-P checklist

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Reported on page #
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1a. p1, p12
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	1b. p1, p12
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	Link to published Cochrane review provided (p1)
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	3a. p1 3b. Appendix 6 (p38)
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	4. p21
Support:			
Sources	5a	Indicate sources of financial or other support for the review	P23
Sponsor	5b	Provide name for the review funder and/or sponsor	
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	P3-12
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	P12
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	P12-13
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	P15
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Appendix 1, p28 Appendix 2, p29

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	11a. p16
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	11b. p16
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	11c. p17
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	12. p18
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	P13-14
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	P17-18
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	P19; Appendix 2
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	n/a
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	P18

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.