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Effectiveness of Robot-assisted Arm Therapy in Stroke Rehabilitation: an Overview of Systematic Reviews.

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Abstract:

Background

Robot-assisted arm therapy (RAT) has been used mainly in stroke rehabilitation in the last 20 years with rising expectations and growing evidence summarized in systematic reviews (SRs).

Objective

The aim of this study is to provide an overview of SRs about the effectiveness, within the ICF domains, and safety of RAT in the rehabilitation of adult with stroke compared to other treatments.

Methods

The search strategy was conducted using search strings adapted explicitly for each database. A screening base on title and abstract was realized to find all the potentially relevant studies. The methodological quality of the included SRs was assessed using AMSTAR-2. A pre-determined standardized form was used to realize the data extraction.

Results

18 SRs were included in this overview. Generally, positive effects from the RAT were found for motor function and muscle strength, whereas there is no agreement for muscle tone effects. No effect was found for pain, and only a SR reported the positive impact of RAT in daily living activity.

Conclusions

RAT can be considered a valuable option to increase motor function and muscle strength after stroke. However, the poor quality of most of the included SRs could limit the certainty around the results.

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Keywords: Stroke, arm rehabilitation, robot-assisted arm therapy, end-effector devices, exoskeleton devices.

Introduction

Stroke is a leading cause of worldwide mortality and long-term disability; upper limb motor impairment is one of the major causes of reduced daily living activities and quality of life (Nichols-Larsen et al., 2005; Winstein et al., 2016). Recently, intensity and task-specificity of motor training have been recognized as critical factors to foster a functional recovery in stroke patients (Kwakkel, 2006). Within this perspective, robot-assisted arm therapy (RAT) has been proposed to increase the dose of well-defined motor tasks in an engaged environment (Li et al., 2014). Conceptually, these devices can be classified as end-effectors or exoskeletons. The end-effectors train multiplanar reaching movements, controlling only the distal part of the paretic limb. The exoskeletons deliver an increased complexity of movements with actuators handling multiple joints (Molteni et al., 2018). So far, more than 100 arm devices have been developed and proposed for clinical use in the rehabilitation of stroke patients (Maciejasz et al., 2014) with evidence that is rapidly increasing and summarized in several systematic reviews (SRs) (Morone et al., 2020).

Although robots in neurorehabilitation have been steadily growing for the past 20 years with rising expectations, many researchers and clinicians question the efficacy and, in particular, cost-effectiveness. If on one side, the expenses on robotic research in rehabilitation are expected to have a compound annual growth rate (*Rehabilitation Robots Market Size, Share | Global Analysis 2026*, s.d.) of more than 20% by 2026, with several national clinical guidelines that recommend the use of robot therapy during rehabilitation; on the other side, the most important clinical study ever completed on upper limb robotics (RATULS) (Rodgers et al., 2019) recently failed to demonstrate the superiority of robot therapy in subjects affected by stroke, feeding the doubts of those who believe that the contemporary neurological rehabilitation does not pass through robots and technologically assisted treatments.

In this scenario, it is necessary to deeply understand the phenomenon and change the researchers' point of view and aims. It is essential to define which subjects might benefit the most from this treatment, as affirmed by Mehrholz et al. in their Cochrane systematic review (CSR) (Mehrholz et al., 2018), and to know the specific targets (and outcomes measures) for which a robot might be effective, more than looking for a global efficacy (Masiero et al., 2014).

In particular, within the WHO International Classification of Functioning (ICF) framework (McDougall et al., 2010; Stucki et al., 2008), outcomes at different levels should measure RAT's effects. In this line, this overview of reviews aims to appraise and synthesize knowledge (Pieper et al., 2017) on RAT in stroke patients' rehabilitation in a single document that might guide health care professionals on clinical decision-making (Baker et al., 2014; Thomson et al., 2010). This overview of SRs determined the effectiveness, within the ICF domains, and safety of RAT in the rehabilitation of adults with stroke compared to other treatments.

Methods

The overview protocol was registered on PROSPERO (no. CRD42020161191). All analyses were based on previously published studies, so there was no need for ethical approval or patient consent. Given that our overview is based on a systematic review, we consider a systematic review as a review of a formulated question that uses systematic and explicit methods to identify, select and critically appraise relevant research, and collect and analyse data from the studies that are included in the review (Moher et al., 2009).

Search strategy

The search strategy was conducted in May 2020 on the following electronic databases: PubMed (MEDLINE, PMC, NCBI Bookshelf), PEDro, Embase, Epistemonikos, Web of Science, Scopus, Cinahl and Cochrane Library. A methodologist (SL) adapted the search strings explicitly for each database to respect the PICO approach. The Patient, Intervention, Comparison and Outcomes of interest is determined. The Mesh terms used were: stroke, brain ischemia, hemiplegia, paresis, robotics, automation, exoskeleton device, therapy computer-assisted, man-machine systems, orthotic devices, upper extremity, shoulder, arm, elbow, forearm, wrist, hand, rehabilitation, physical therapy modalities, recovery of function, systematic reviews as a topic, meta-analysis as topic, humans. The complete search strategy and the strings are available in Supplementary Table 1 (S1).

Selection criteria

One reviewer (LB) conducted a screening based on title and abstract to find all the potentially relevant studies after removing duplicates. Full-text articles were obtained and assessed for eligibility. We included SRs of randomized-controlled clinical trials (RCTs) and not-RCTs, with or without meta-analysis, in the English language that presented a straightforward research question relevant to our specific aim. A comprehensive search strategy and a defined PICO approach in which the population (P) of interest were adults with stroke (ischemic or haemorrhagic), with arm paresis, the intervention (I) was RAT targeting the paretic upper limb (I), the comparison (C) conventional therapy, other interventions, or no treatment, the outcome (O) relevant for our overview were motor recovery, arm strength, activities of daily living (ADLs), quality of life, independence, and any other outcome measure related to ICF domains, was conducted. We excluded narrative reviews and reviews that included other studies in the analysis. Furthermore, if an SR analysed the efficacy of a different type of interventions or other populations separately, we extracted data that only dealt with the RAT in adults with stroke.

Data extraction and management

One reviewer (LB) used a pre-determined standardized form to conduct the data extraction that was double-checked by a second reviewer (SL). The information collected in the data extraction included: i) title, authors, and year of publication of the SR; ii) number and type (RCT or non-RCT) of the primary studies included; iii) number of participants of the primary studies; iv) number and characteristics of the participants of the SR; v) characteristics of the rehabilitative interventions in the experimental group; vi) characteristics of interventions in the control group; vii) assessment method of the quality of the primary studies included in each SR; viii) outcome measure examined in each SR; ix) results of SRs and meta-analyses: effect size, heterogeneity and statistical significance of the results. Furthermore, any effect in each rehabilitation phase (subacute and chronic), type of device (end-effector and exoskeleton), part of the upper limb trained (proximal or distal), or level of impairment (moderate/mild or severe paresis) were reported.

Assessment of methodological quality of included reviews

Two reviewers (MB, SS) applied the AMSTAR-2 tool (Shea et al., 2017) independently to assess the methodological quality of the included SRs. A third assessor (CA) solved any disagreement. To ensure a correct methodology, the application of AMSTAR-2 followed what previously described by Shea et al. (2017) to identify the presence of critical items that might influence the overall quality of the SRs. A negative evaluation of a critical item might affect the validity of a review and its conclusion. The specific item that revealed critical weaknesses were: item 2 (protocol registered before the start of the review), item 4 (adequacy of the literature search), item 7 (reason for exclusion of primary studies), item 9 (risk of bias of the primary studies included in the review), item 11 (appropriate methods for meta-analysis), item 13 (consideration of risk of bias when interpreting the results of the review), and item 15 (assessment of presence and likely impact of publication bias). Following the consensus through the reviewers involved in this overview, we divided each SR in high, moderate, low and critically low quality.

Data synthesis

We summarized the main characteristics of the included systematic reviews and synthesized the main findings following the ICF framework (*ICF Browser*, s.d.; Sivan et al., 2011; Stucki et al., 2008).

Results

Search results

We searched for systematic reviews on the effects of RAT in adult stroke patients. After database searching, 578 records were identified, of which 29 were assessed for full-text screening eligibility. Finally, 18 systematic reviews were included in the qualitative analysis (Arya et al., 2018; Da-Silva et al., 2018; Dixit & Tedla, 2019; Ferreira et al., 2018; Hayward et al., 2010; Kim et al., 2017; Kwakkel et al., 2008; Lin et al., 2019; K. Lo et al., 2017; Mehrholz et al., 2018; Mubin et al., 2019; Norouzi-Gheidari et al., 2012; Pelton et al., 2012; Péter et al., 2011; Prange et al., 2006; Veerbeek et al., 2017; Wolf et al., 2014; Zhang et al., 2017). The final agreement for all the included systematic reviews was reached involving all review authors. The PRISMA flow diagram is reported in Figure 1.

INSERT FIGURE 1 ABOUT HERE

Reasons for exclusion of each SR and references are reported in (S2).

Characteristics of included reviews

One hundred and twenty-five primary studies (68 RCTs, 52 non-RCTs, and five studies in which the study design was not available from the SR) were included in the selected SRs (see S3). Among the included SRs, three were the more comprehensive: a CSR including 45 studies and 1619 participants (Mehrholz et al., 2018), and two non-CSRs. The first had 44 studies and 1362 participants (Veerbeek et al., 2017) and the other 38 studies with 1174 participants (Ferreira et al., 2018). Only some of the primary studies in these two SRs (Ferreira et al., 2018; Veerbeek et al., 2017) overlapped with the CSR (Mehrholz et al., 2018), 70.5% for the one from Veerbeek et al.

(2017) and 57.9% for Ferreira et al. (2018), revealing how search strategies and inclusion criteria were partially different. Figure 2 shows the overlap of trials in the included SRs.

A summary of the characteristics of the included SRs is reported in Table 1. In ten of the included SRs, a meta-analysis was conducted (Da-Silva et al., 2018; Ferreira et al., 2018; Kwakkel et al., 2008; Lin et al., 2019; K. Lo et al., 2017; Mehrholz et al., 2018; Norouzi-Gheidari et al., 2012; Prange et al., 2006; Veerbeek et al., 2017; Zhang et al., 2017).

INSERT TABLE 1 ABOUT HERE

INSERT FIGURE 2 ABOUT HERE

Review Quality Assessment

The AMSTAR-2 assessment highlighted an overall low (Ferreira et al., 2018; Kwakkel et al., 2008; Norouzi-Gheidari et al., 2012; Pelton et al., 2012; Veerbeek et al., 2017; Zhang et al., 2017), or critically low (Arya et al., 2018; Da-Silva et al., 2018; Dixit & Tedla, 2019; Hayward et al., 2010; Kim et al., 2017; Lin et al., 2019; Mubin et al., 2019; Péter et al., 2011; Prange et al., 2006; Wolf et al., 2014) quality of the included SRs; only the CSR was rated as high quality (Mehrholz et al., 2018) and another SR as moderate quality (K. Lo et al., 2017). The complete AMSTAR-2 quality assessment is reported in Table 2.

INSERT TABLE 2 ABOUT HERE

Effectiveness on ICF domains

RAT effects on stroke patients were reported according to the ICF domains of body function and activity, as included in the summary of all quantitative results (see Table 3). No evidence was found at the body structure and participation level.

INSERT TABLE 3 ABOUT HERE

A comprehensive report of all outcomes (qualitative and quantitative) is available in S4.

Body functions

Motor functions (b710, b1470, b7651, b760, b7602, b750)

Arm motor functions, which represent the most common primary outcomes measured by the Fugl-Meyer Assessment scale, (Fugl-Meyer et al., 1975) are reported as improved following RAT than other interventions (Ferreira et al., 2018; Lin et al., 2019; Mehrholz et al., 2018; Prange et al., 2006; Veerbeek et al., 2017; Zhang et al., 2017). Specifically, RAT was superior to other interventions (Ferreira et al., 2018) with a SMD 0.3 (95% CI 0.1 to 0.4) or to conventional therapy (Zhang et al., 2017) with a SMD 0.56 (95% CI 0.19 to 0.93). However, two SRs do not support these findings (Kwakkel et al., 2008; K. Lo et al., 2017).

In four SRs (K. Lo et al., 2017; Norouzi-Gheidari et al., 2012; Veerbeek et al., 2017; Zhang et al., 2017), subgroup analysis reported no effect of RAT in the acute/subacute phase. In contrast, in another subgroup analysis of one of the SRs (Norouzi-Gheidari et al., 2012), it was shown that when RAT is applied as additional therapy in the acute/subacute phase, there is a statistically significant improvement in the motor functions with an SMD 0.48 (95% CI 0.09 to 0.87) compared with conventional therapy.

Three SRs reported no effect of RAT in patients in the chronic phase (K. Lo et al., 2017; Norouzi-Gheidari et al., 2012; Veerbeek et al., 2017). In contrast, one SR (Zhang et al., 2017) found that when RAT alone was used in patients in the chronic phase, motor functions were significantly better than in the conventional therapy group, with an SMD of 0.82 (95% CI 0.20 to 1.43).

Subgroups analysis in the CSR (Mehrholz et al., 2018) showed statistically significant improvement in both the experimental groups receiving RAT targeting the proximal upper limb (shoulder elbow joints) and distal arm (wrist, hand) compared with other interventions, without proving any superiority of one over the other. One SR (Veerbeek et al., 2017) reported effects for proximal training (using shoulder/elbow robotics), distal training (using elbow/wrist robotics) and end-effector devices compared with other interventions. One SR reported no effects of RAT in severely impaired patients and moderate/mild impaired patients (K. Lo et al., 2017).

Muscle strength (b730)

It was reported a beneficial effect of RAT compared with other interventions on muscle strength, with an SMD 0.46 (95% CI 0.16 to 0.77) in the CSR (Mehrholz et al., 2018) and SMD 0.5 (95% CI 0.2 to 0.8) in another SR (Ferreira et al., 2018). In another SR (Veerbeek et al., 2017), no effects of RAT compared with other interventions were reported for muscle strength, furthermore authors performed several subgroups analysis and registered no effects of robot-assisted therapy in both acute and chronic phase, proximal training with shoulder/elbow/wrist robotics, distal training with elbow/wrist robotics, end-effector and exoskeleton devices; while reported effects for shoulder/elbow robotics compared with other interventions (Veerbeek et al., 2017).

Muscle tone (b735)

The effects on muscle tone are mixed. One SR (Veerbeek et al., 2017) reported the control group's superiority who received other interventions, whereas another SR (Ferreira et al., 2018) did not affect muscle tone.

Subgroups analysis found no RAT effects in the acute phase, chronic phase, shoulder/elbow robotics, shoulder/elbow/wrist robotics, end-effector and exoskeleton devices (Veerbeek et al., 2017).

Pain (b280)

Only one SR investigated pain as an outcome measure and reported no effect (Ferreira et al., 2018).

Activity

Activities of daily living (d550, d5202, d540, d510, d530, d420)

In the CSR (Mehrholz et al., 2018) was reported that RAT might have positive effects on independence in daily living, measured by FIM or BI, compared to other interventions with an SMD 0.31 (95% CI 0.09 to 0.52). However, other SRs do not sustain these findings (Kwakkel et al., 2008; K. Lo et al., 2017; Veerbeek et al., 2017). Subgroups analysis performed in the CSR (Mehrholz et al., 2018) reported effects of: robot-assisted therapy in acute phase, robot-assisted distal arm training and robot-assisted proximal arm training, compared with other interventions. No effect was found in the chronic phase (Mehrholz et al., 2018). Two SRs (K. Lo et al., 2017; Veerbeek et al., 2017) found no effects of robot-assisted therapy in acute/subacute phase and chronic phase. There is no effect in subgroups analysis for robot-assisted proximal arm training (shoulder/elbow robotics) and end-effector devices (Veerbeek et al., 2017). One SR found no impact in severe and moderate/mild impaired patients (K. Lo et al., 2017).

Arm use (d440, d4401, d4400, d550, d445, d4459, d2101, d540, d2102, d2100, d5202)

No effect on arm use, measured by functional tests (WMFT, ARAT) or patient-reported questionnaires, were found (Da-Silva et al., 2018; Veerbeek et al., 2017). Subgroups analysis shows no results of robot-assisted therapy in the acute phase, chronic phase, proximal training using shoulder/elbow robots, distal training using hand robotics, end-effectors and exoskeleton devices (Veerbeek et al., 2017).

Adverse effects

Four of the included systematic reviews (Dixit & Tedla, 2019; Mehrholz et al., 2018; Prange et al., 2006; Veerbeek et al., 2017) investigated the safety of RAT and the eventual presence of adverse effects. The CSR (Mehrholz et al., 2018) reported that two participants in the treatment group from a primary study (Lum et al., 2002) experienced medical complications unrelated to the study. Another SR (Dixit & Tedla, 2019) found a mild form of adverse effects from three primary studies (Hesse et al., 2014; A. C. Lo et al., 2010; Takahashi et al., 2016). In contrast, in another SR (Prange et al., 2006), none of the primary studies reported RAT's negative effects. Moreover, in an SR (Veerbeek et al., 2017), none of the included studies registered severe adverse events. At the same time, one primary study (Klamroth-Marganska et al., 2014) described one mild adverse event of a patient assigned to robot therapy that reported mild shoulder pain.

Discussion

In this overview of SRs, we focused on the effectiveness and safety of robot-assisted arm therapy in the rehabilitation of adults with stroke. Arm robotic devices have been used in clinical settings as motor learning machine to increase motor practice and promote task-oriented training for stroke survivors for the past two decades (Morone et al., 2020). It has been hypothesized that arm training could have positive effects beyond body functions, including activity and functional independence (Mehrholz et al., 2018). In this overview, we included 18 systematic reviews with 125 primary studies (more than 3000 participants). Most of the included reviews (89%) have been assessed as low or critically low quality, with only two reviews (11%) of high or moderate quality. Among the critical items of AMSTAR-2, those that were less frequently met are item 4 (adequacy of the literature search) – which is essential to increase the likelihood of including all relevant primary studies; item 7 (reason for exclusion of primary studies) – which is necessary for the sake of clarity in the screening process and the impact of their exclusion from the review; and item 15 (assessment of presence and likely effect of publication bias) – which is once again crucial for the inclusion of all eligible studies and because it may have an impact on the completeness of results.

There were no significant major adverse effects linked to RAT, showing that this intervention is safe and well-tolerated. The main conclusion of our analysis is that RAT has a beneficial impact on body functions. Specifically, it increases arm motor control, as primarily measured by the Fugl-Meyer Assessment Scale (Ferreira et al., 2018; Lin et al., 2019; Mehrholz et al., 2018; Prange et al., 2006; Veerbeek et al., 2017; Zhang et al., 2017). A smaller set of data supports that this therapy also increases muscle strength (Ferreira et al., 2018; Mehrholz et al., 2018). The outcomes related to activity and participation were reported in a minority of the studies. The assessment of loss of body functions is usually selected as the primary outcomes in robotic stroke trials, whereas measures of limitation of activity and participation were rarely used (Sivan et al., 2011). However, functional ability and participation are of significant interests to stroke survivors (Gadidi et al., 2011). The three domains described in the ICF framework (body functions, activity and participation) are not necessarily linked (Burridge et al., 2009; Lewthwaite et al., 2018). For example, the severity of impairment does not determine the limitation in activities and participation. Such differences can also affect the RAT (Wu et al., 2020). The only CSR (Mehrholz et al., 2018) on the topic reported a potential benefit on functional independence. However, further studies are needed to support this result consistently. While most of the trials so far addressed chronic stroke patients trained with proximal (shoulder-elbow) end-effector devices, more studies are needed that focus on subacute patients or consider hand or exoskeleton robotic devices. Indeed, it can be hypothesized that the current devices tested so far did not sufficiently elicit the sensorimotor integration, the motor cognition or the complexity of movements of the upper limb in an ecological scenario (Gassert & Dietz, 2018; Ingemanson et al., 2019) as the latest generation of robots with many degrees of freedom, a more sophisticated assistance-as-needed system and more refined mechanisms to involve cognitive and perceptual functions during rehabilitation, permits (Klamroth-Marganska et al., 2014; Ranzani et al., 2020). Moreover, increased knowledge of the RAT effectiveness within the different rehabilitation phases, subacute or chronic, might help clinicians define specific aims of neural repair instead of compensation and re-learning. In this scenario, a more detailed analysis of the motor learning processes involved could be beneficial both for developing future devices and driving the clinical decision-making process. It is well established how most spontaneous recovery occurs within 10-12 weeks after stroke, representing the time window when rehabilitation can hopefully harness neuroplasticity (Kwakkel et al., 2006). In administering RAT, current evidence does not inform on the optimum delivery timing (acute, subacute, chronic), or the best type of device (exoskeleton or end-effector), or arm site (proximal or distal).

Our overview presents several limitations. Firstly, we relied on SRs and did not extract data from primary studies. It results in a potential bias toward the choice of information as reported by review authors. For example, three systematic reviews did not address some specific outcomes, preventing us from including them in our analysis (Dixit & Tedla, 2019; Kim et al., 2017; Mubin et al., 2019). Secondly, we included only papers written in English due to limited resources, but this could have prevented us from including additional eligible studies. Thirdly, the GRADE approach has not been applied given the heterogeneity of the studies included (Berkman et al., 2013). Fourthly, the motor learning principles embedded in the control of robotic devices were not considered.

Conclusion

This overview provides up-to-date available evidence for the use of RAT in stroke rehabilitation clinical practice. This intervention can be considered a valuable option to increase arm motor control and muscle strength within the body function ICF domain. Nevertheless, the poor quality of the included studies, as highlighted in this work, should be acknowledged when interpreting the results as it limits the certainty around them. This uncertainty could only be overcome by producing high-quality systematic reviews, which are highly needed in the current low-level available evidence. The production of future reviews on this topic should therefore be guided by the principle of methodological rigour, which encompasses both conducting and reporting, as well as that of clinical meaningfulness.

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Declaration of Interests

The Author(s) declare(s) that there is no conflict of interest.

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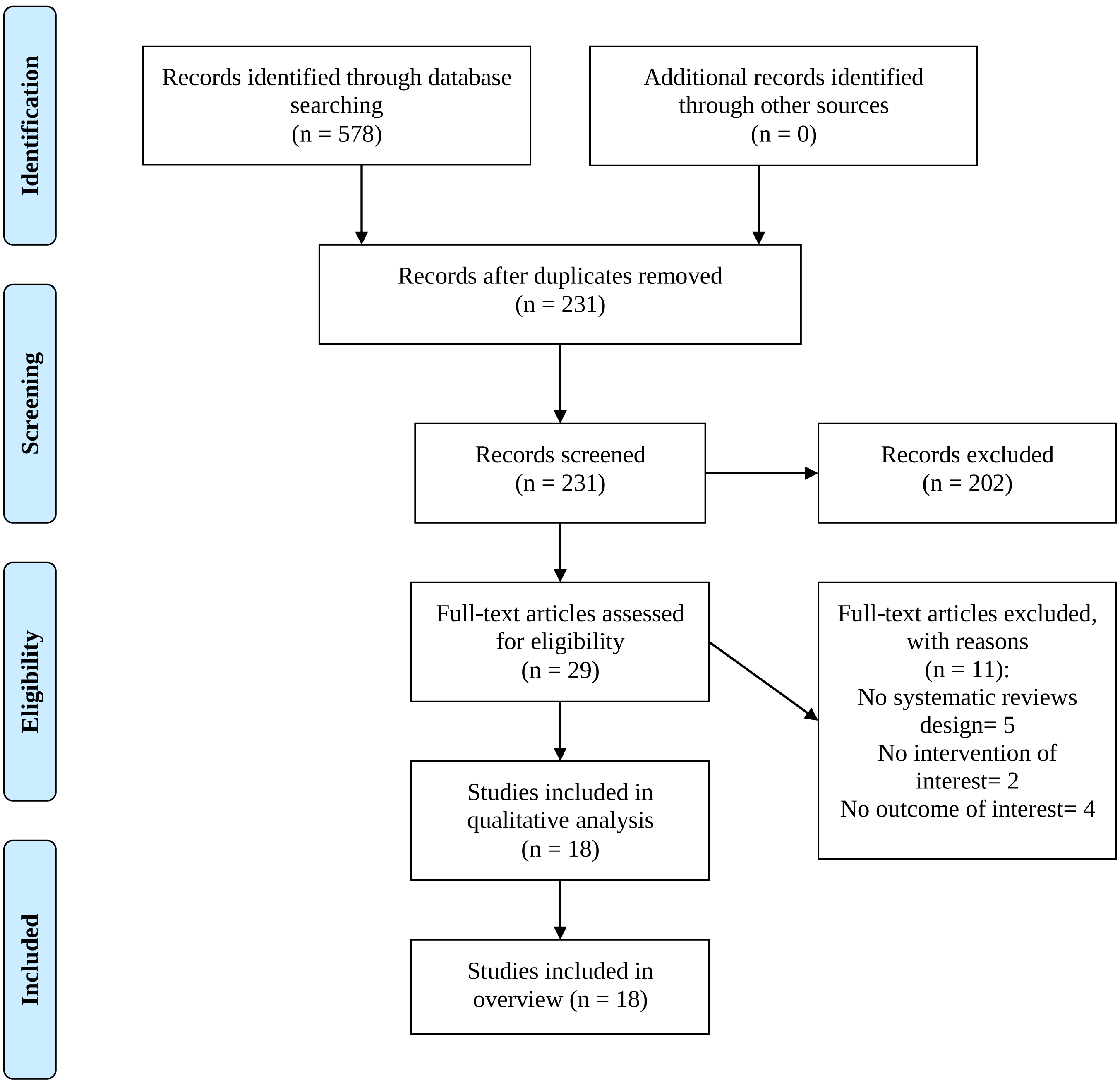
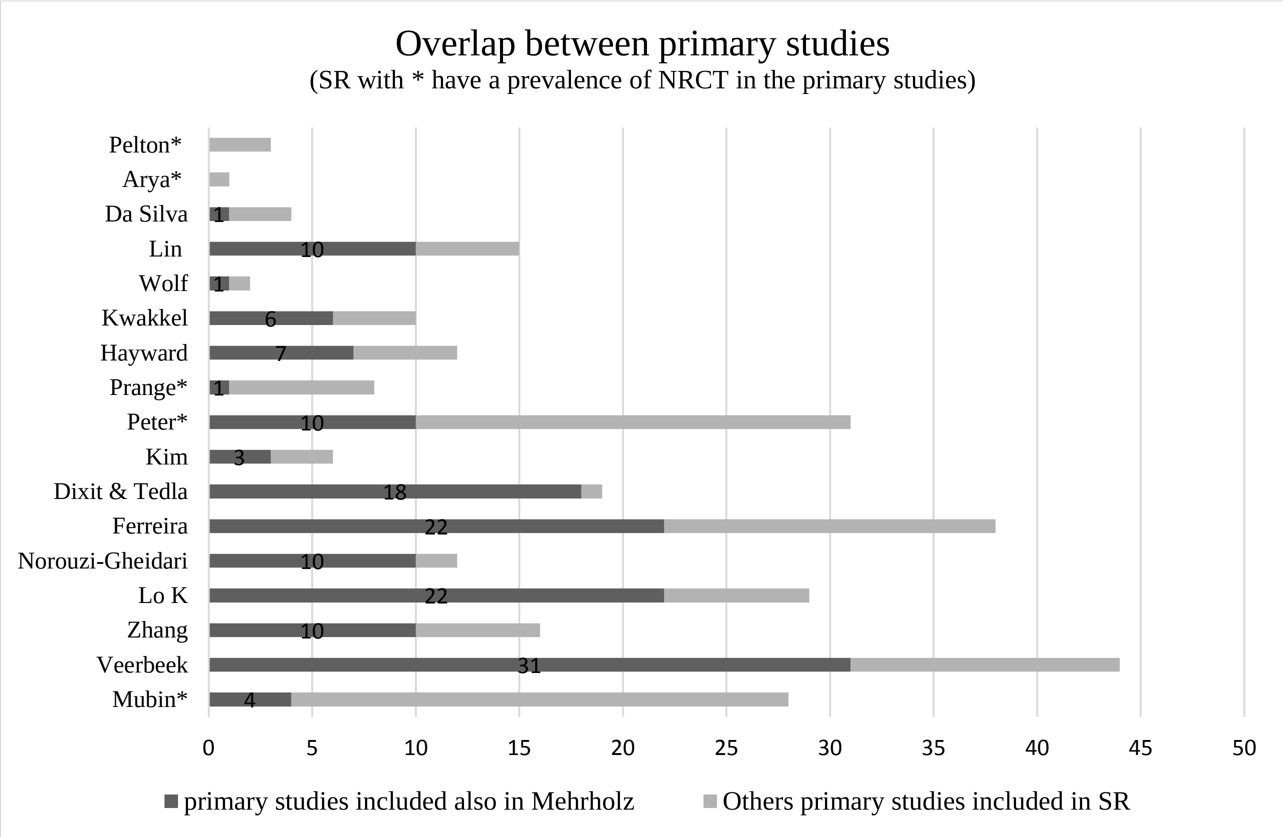
Figure Legend:

Figure 1. The PRISMA 2009 flow diagram for Overview of Systematic Reviews of Robot-assisted arm Rehabilitation in adult stroke patients.

Figure 2. The overlapping of primary studies in the included systematic reviews.


Identification
Screening
Eligibility
Included
Records identified through database searching (n = 578)
Additional records identified through other sources (n = 0)
Records after duplicates removed (n = 231)
Records screened (n = 231)
Records excluded (n = 202)
Full-text articles assessed for eligibility (n = 29)
Full-text articles excluded, with reasons (n = 11):
No systematic reviews design= 5
No intervention of interest= 2
No outcome of interest= 4
Studies included in qualitative analysis (n = 18)
Studies included in overview (n = 18)


Overlap between primary studies
(SR with * have a prevalence of NRCT in the primary studies)
Pelton*
Arya*
Da Silva
Lin
Wolf
Kwakkel
Hayward
Prange*
Peter*
Kim
Dixit & Tedla
Ferreira
Norouzi-Gheidari
Lo K
Zhang
Veerbeek
Mubin*
1
10
1
6
7
1
10
3
18
22
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10
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4
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35
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45
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primary studies included also in Mehrholz
Others primary studies included in SR

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Table 1. Characteristics of the included systematic reviews (PICO).

Review author	Publication year	Primary studies included (n)	Type of studies included	Population	Interventions	Comparison	Methodology quality assessment	Outcomes	Meta-Analysis	AMSTAR-2 judgement of review quality
Cochrane Reviews (CSR)										
Mehrholz et al	2018	45 (1619)	43 RCT 2 NRCT	Adult stroke patients in acute/subacute phase (within three months) and chronic phase (more than three months)	Robot-assisted therapy for the paretic upper limb or RT+CT	Other interventions or placebo interventions, or no treatment	Cochrane Risk of bias tool, GRADE	Primary outcome: activities of daily living. Secondary outcomes: motor function and muscle strength	yes	High
Non-Cochrane Reviews (non-CSRs)										
Mubin et al	2019	28 (656)	7 RCT 18 NRCT 3 N/A	Adult stroke patients in sub-acute phase (less than 3 months poststroke) or chronic phase (more than 3 months poststroke)	robot-assisted therapy combined with virtual reality, augmented reality, or gamification	not mentioned	N/A	Motor function	no	Critically Low
Veerbeek et al	2017	44 (1362)	37 RCT 6 NRCT 1 N/A	Adult stroke patients (ischemic and hemorrhagic) within or beyond 3 months poststroke	Robot-assisted therapy for the paretic upper limb	Non-robotic treatment	PEDro scale	Primary outcome: Motor control, Upper limb capacity, defined as fine hand use, ADL. Secondary outcome: muscle strength and muscle tone	yes	Low
Zhang et al	2017	16 (496)	14 RCT 2 NRCT	Adult stroke patients in acute/subacute phase (7 studies) and chronic phase (6 studies)	Robot-assisted therapy for the paretic upper limb. In 4 studies RT+CT vs CT. In 9 studies RT vs CT	conventional therapy	PEDro scale	Motor function	yes	Low
Lo K et al	2017	29 (860)	29 RCT	Adult stroke patients, 11 studies in acute/subacute phase (within 6 months), 18 studies in chronic phase (more than 6 months)	Robot-assisted therapy for the paretic upper limb. In 13 studies RT+CT vs CT. In 16 studies RT vs CT	conventional therapy	JBI SUMARI, GRADE	Motor movement of upper limb, ADL. Secondary outcome: sustainability of the robot treatment	yes	Moderate
Norouzi-Gheidari et al	2012	12 (425)	10 RCT 1 NRCT 1 N/A	Adult stroke patients, 5 studies in acute/subacute phase and 5 in chronic phase	Robot-assisted therapy for the paretic upper limb. In 6 studies duration/intensity of RT vs CT is the same	conventional therapy	PEDro scale	Motor recovery, functional abilities of the paretic upper limb	yes	Low

					whether in 4 studies the RT group recived additional therapy					
Ferreira et al	2018	38 (1174)	33 RCT 4 NRCT 1 N/A	Adult stroke patients in acute/subacute phase (within six months) and chronic phase (more than six months)	Robot-assisted therapy for the paretic upper limb or RT+CT	minimal intervention (no intervention, sham, or placebo), or other intervention (conventional therapy, physical therapy)	PEDro scale	Motor control, strength, spasticity, range of motion, pain	yes	Low
Dixit & Tedla	2019	19 (707)	19 RCT	Adult stroke patients in acute/subacute phase (8 studies) and chronic phase (7 studies). In one study the stroke recovery stage was not clear.	Robot-assisted therapy for the paretic upper limb	standard care	PEDro scale (≥ 4)	Functional independence, motor control and Quality of life scores.	no	Critically Low
Kim et al	2017	6 (278)	6 RCT	Adult stroke patients in acute and subacute patients (within three months)	Robot- assisted therapy for the paretic upper limb (1 study) or RT+CT (5 studies)	conventional therapy	PEDro scale (7-9)	Motor function, activities of daily living.	no	Critically Low
Peter et al	2011	30 (493)	12 RCT 19 NRCT	Adult stroke patients 7 trial performed in the acute phase, whereas 20 were in chronic phase	Robot-mediated physiotherapy among patients with hemiparesis	conventional therapy (in two trial control group recived FES)	N/A	Motor control, spasticity, function	no	Critically Low
Prange et al	2006	8 (247)	1 RCT 7 NRCT	Adult stroke patients in subacute phase (2-4 weeks poststroke) and 7 studies in chronic phase (more than 6 months)	Robot-assisted therapy for the paretic upper limb	conventional therapy with additional noncontact or non-operational exposure to the robot	Kottink et al.'s adapted list of methodological items based on the Maastricht-Amsterdam criteria for RCTs	Motor control, functional abilities	yes	Critically Low
Hayward et al	2011	12 (380)	9 RCT 2 NRCT 1 N/A	Adult stroke patients in acute/subacute phase or chronic phase	Robot-assisted therapy for shoulder and elbow in 9 studies and RT for forearm and wrist in 2 study	conventional therapy or sham or robot exposure or occupational therapy or electrical stimulation	PEDro scale	identify interventions which enable stroke survivors to participate in task-oriented training. Improvement in impairment, activity and participation	no	Critically Low
Kwakkel et al	2008	10 (218)	7 RCT 2 NRCT	Adult stroke patients in subacute or chronic stage	Robot-assisted therapy	conventional therapy	PEDro scale	Motor recovery, ADL	yes	Low

			1 N/A							
Wolf et al	2014	2 (50)	1 RCT 1 NRCT	Adult stroke patients in subacute phase (1 week to 3-4 months) and chronic phase (> 6 months)	Bilateral Robot-assisted therapy	conventional therapy	GRADE	Motor recovery, ADL, spasticity	no	Critically Low
Lin et al	2018	15 (621)	13 RCT 2 NRCT	Adult stroke patients with a poststroke time of < 6 months	Robot-assisted training for the paretic upper limb	conventional therapy or no treatment or placebo	PEDro scale	Motor recovery	yes	Critically Low
Da Silva et al	2018	4 (171)	4 RCT	Adult stroke patients in subacute or chronic phase	Self-directed Robot assisted therapy	dose-matched control intervention	Cochrane Risk of bias tool	Arm function, ADL	yes	Critically Low
Arya et al	2017	1 (18)	1 NRCT	Adult stroke patients in chronic phase	Linear robotic movement of the affected side with visual feedback on a screen	N/A	PEDro scale	Reduction of subluxed shoulder	no	Critically Low
Pelton et al	2012	3 (63)	3 NRCT	Adult stroke patients in chronic phase	functional-based robot training or computerised virtual reality exercise system with instrumented gloves	impairment-based robot training or no control group	standardised critical appraisal assessment forms from the Joanna Briggs Institute	Improving coordination of reach to grasp after stroke	no	Low

Abbreviations: ADL= activities of daily living; CT= conventional therapy; FES= functional electrical stimulation; N/A= not available; NRCT= non-randomized controlled trial; RCT= randomized controlled trial; RT= robot-assisted therapy; JBI SUMARI= Joanna Briggs Institute System for the Unified Management, Assessment and Review of Information.

Table 2. Systematic reviews quality assessments (AMSTAR-2).

Reference	AMSTAR-2 Domains																Overall quality
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
Cochrane Review (CSR)																	
Mehrholz J. et al. (2018)	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	High
Non-Cochrane Reviews (non-CSRs)																	
Mubin O. et al. (2019)	Y	N	N	PY	N	N	N	N	N	N	NMA	NMA	N	N	NMA	Y	Critically Low
Veerbeek JM. et al. (2017)	Y	N	N	Y	N	N	N	Y	Y	N	Y	Y	N	Y	N	Y	Low
Zhang C. et al (2017)	Y	N	N	PY	N	N	N	PY	PY	N	Y	Y	Y	Y	N	Y	Low
Lo K. et al. (2017)	Y	PY	N	PY	N	N	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Moderate
Norouzi-Gheidari N. et al (2012)	Y	N	N	PY	Y	N	Y	PY	PY	N	Y	Y	Y	Y	N	Y	Low
Ferreira M. et al. (2018)	Y	Y	N	PY	N	N	N	PY	PY	N	Y	Y	Y	Y	Y	Y	Low
Dixit & Tedla (2019)	Y	PY	N	PY	N	Y	N	PY	PY	N	NMA	NMA	Y	N	NMA	Y	Critically Low
Kim G. et al. (2017)	N	N	N	PY	N	N	N	PY	PY	N	NMA	NMA	Y	N	NMA	Y	Critically Low
Peter O. et al. (2011)	Y	N	Y	PY	Y	N	N	PY	N	N	NMA	NMA	N	Y	NMA	Y	Critically Low
Prange G. et al. (2006)	Y	N	N	PY	Y	Y	N	N	PY	N	N	N	Y	Y	N	Y	Critically Low
Hayward K. et al. (2011)	Y	N	Y	PY	N	Y	N	PY	PY	N	NMA	NMA	Y	Y	NMA	N	Critically Low
Kwakkel G. et al. (2008)	Y	N	N	PY	N	N	N	PY	PY	N	Y	N	Y	Y	N	N	Low
Wolf A. et al. (2014)	Y	N	N	PY	Y	N	N	PY	PY	N	NMA	NMA	N	N	NMA	N	Critically Low
Lin IH. et al. (2018)	Y	Y	N	N	N	N	N	N	PY	N	Y	N	N	Y	N	Y	Critically Low
Da Silva RH. et al. (2018)	Y	Y	N	PY	Y	N	N	PY	Y	N	N	Y	N	Y	N	Y	Critically Low
Arya KN. et al. (2017)	Y	Y	N	PY	Y	N	N	PY	PY	N	NMA	NMA	N	Y	NMA	N	Critically Low
Pelton T. et al. (2012)	Y	N	Y	Y	Y	Y	N	PY	Y	N	NMA	NMA	Y	Y	NMA	N	Low

Abbreviations: Y= Yes; PY= Partial Yes; N= No; NMA= No meta-analysis conducted.

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Table 3. Robot-assisted arm rehabilitation efficacy on ICF framework.

Table 3a. Body Function.

ICF code	Contributing reviews	Intervention and comparison	Relative effect	Effect size 95% CI	I²	N. of studies (participants)	AMSTAR-2 assessment
Motor function (FMA, MI, CMSA)							
b710, b1470, b7651, b760 b7602, b750	Mehrholz 2018	electromechanical and RT vs OI	Statistically significant improvement in experimental group**	SMD 0.32 (0.18 to 0.46)	36%	41 (1452)	High
	Veerbeek 2017	RT vs any type of control	Statistically significant improvement in experimental group**	MD 2.23 (0.87 to 3.59)	30%	28 (884)	Low
	Zhang 2017	RT vs CT	Statistically significant improvement in experimental group**	SMD 0.56 (0.19 to 0.93)	68%	13 (426)	Low
	Lo K 2017	RT vs CT	no statistically significant difference between groups	SMD 0.07 (-0.11 to 0.26)	41%	29 (860)	Moderate
	Prange 2006	RT vs CT in chronic stroke	Statistically significant improvement in experimental group*	MD 3.7 (2.8 to 4.7)	N/A	2 (70)	Critically Low
	Kwakkel 2008	RT vs CT	no statistically significant difference between groups	SES 0.65 (-0.02 to 1.33)	N/A	9 (218)	Low
	Lin 2018	RT vs CT	Statistically significant improvement in experimental group**	SMD 0.51 (0.22 to 0.80)	0%	5 (187)	Critically Low
	Ferreira 2018	RT vs OI short term	Statistically significant improvement in experimental group**	SMD 0.3 (0.1 to 0.4)	45,68%	17 (595)	Low
Muscle strength (MRC, MI, MPS, MMT)							
b730	Mehrholz 2018	electromechanical and RT vs OI	Statistically significant improvement in experimental group**	SMD 0.46 (0.16 to 0.77)	76%	23 (826)	High

	Veerbeek 2017	RT vs any type of control	no statistically significant difference between groups	SMD 0.19 (-0.12 to 0.50)	56%	15 (494)	Low
	Ferreira 2018	RT vs OI short term	Statistically significant improvement in experimental group**	SMD 0.5 (0.2 to 0.8)	32,08%	6 (203)	Low
Muscle tone (MAS)							
b735	Veerbeek 2017	RT vs any type of control	Statistically significant improvement in control group*	SMD 0.24 (0.04 to 0.44)	25%	13 (429)	Low
	Ferreira 2018	RT vs OI short term	no statistically significant difference between groups	SMD -0.5 (-1.4 to 0.4)	6,96%	6 (281)	Low
Pain (VAS, pain scale of FMA, pain scale of CMSA)							
b280	Ferreira 2018	RT vs OI short term	no statistically significant difference between groups	SMD -0.1 (-0.5 to 0.2)	0%	5 (132)	Low

Abbreviations: b710 = shoulder, elbow, wrist, pronation/supination, finger movements; b1470 = psychomotor control; b7651= tremor; b760= control of voluntary movement functions; b7602= coordination; b750= reflexes; b730 = power; b735 = tone, spasticity; b280= pain; CI= confidence interval; CMSA= Chedoke-McMaster Stroke Assessment; CT= conventional therapy; FMA= Fugl-Meyer Assessment; ICF= International Classification of Functioning, Disability and Health; MAS= Modified Ashworth scale; MD= mean difference; MI= Motricity Index; MMT= Manual Muscle Testing; MPS= Motor Power Scale; MRC= Medical Research Council; N/A= not available; OI= other intervention; RT= robot-assisted therapy; SES= summary effect size; SMD= standardized mean difference; VAS= Visual Analogue Scale; * p<0.05; ** p<0.01

Table 3.b Activity.

ICF code	Contributing reviews	Intervention and comparison	Relative effect	Effect size 95% CI	I²	N. of studies (participants)	AMSTAR-2 assessment
ADL (FIM, BI)							
d550, d5202, d540, d510, d530, d420	Mehrholz 2018	electromechanical and RT vs OI	Statistically significant improvement in experimental group**	SMD 0.31 (0.09 to 0.52)	59%	24 (957)	High
	Veerbeek 2017	RT vs any type of control	no statistically significant difference between groups	SMD 0.27 (-0.05 to 0.59)	56%	14 (427)	Low
	Lo K 2017	RT vs CT	no statistically significant difference between groups	SMD 0.11 (-0.11 to 0.33)	66%	31 (1120)	Moderate
	Kwakkel 2008	RT vs CT	no statistically significant difference between groups	SES 0.13 (-0.23 to 0.50)	N/A	5 (139)	Low
Arm use (ARAT, AMAT, WMFT, BBT, MAL)							
d440, d4401, d4400, d550, d445, d4459, d2101, d540, d2102, d2100, d5202	Veerbeek 2017	RT vs any type of control	no statistically significant difference between groups	SMD 0.04 (-0.12 to 0.19)	2%	20 (682)	Low
	Da Silva 2018	Self-directed RT vs N/A	no statistically significant difference between groups	MD -0.10 (-0.49 to 0.29)	N/A	1 (19)	Critically Low
	Da Silva 2018	Self-directed RT vs N/A	no statistically significant difference between groups	MD -0.25 (-0.51 to 0.02)	41%	2 (35)	Critically Low

Abbreviations: d550= hand to mouth/eating; d5202= comb hair; d540=grooming, dressing, put on shirt; d510= bathing; d530= toileting, bowel, bladder; d420= transfer; d440= fine hand use; d4401= grasping; d4400= pick and lift objects; d445= hand and arm use; d4459= contribution to bilateral activity; d2101= undertaking a complex task; d2102= undertaking a single task independently; d2100= undertaking a simple task; ADL= activities of daily living; AMAT= Arm Motor Ability Test; ARAT= Action Research Arm Test; BI= Barthel Index; BBT= Box and Block Test; CI= confidence interval; CT= conventional therapy; FIM= Functional Independence Measure; ICF= International Classification of Functioning, Disability and Health; MAL= Motor Activity Log; RT= robot-assisted therapy; MD= mean difference; SES= summary effect size; SMD= standardized mean difference; OI= other intervention; N/A= not available; WMFT= Wolf Motor Function Test; ** p<0.01

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Supplementary Table 1. Extensive search strategy.

Database	Search strings
CINAHL	1. Stroke OR "Brain Ischemia" 2. stroke OR "Cerebrovascular Accident" OR ((brain OR cerebral) AND (infarct* OR ischemi* OR ischaemi* OR hemorrhag*)) 3. Hemiplegia OR Paresis 4. hemiplegi* OR hemipare* OR paresis OR plegia OR paretic OR plegic 5. #1 OR #2 OR #3 OR #4 6. Robotics OR Automation 7. robot* OR "robot assisted" OR electromechani* OR electro-mechani* 8. "Exoskeleton Device" 9. exoskelet* OR "end effector*" 10. "Therapy, Computer-Assisted" 11. "computer aided" OR "computer assisted" 12. "Man-Machine Systems" 13. "Orthotic Devices" 14. orthos* OR orthotic 15. #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 16. “Upper Extremity" OR "upper limb" OR Shoulder OR Arm OR Elbow OR Forearm OR Wrist OR Hand OR finger* 17. Rehabilitat* OR physiotherap* OR recovery 18. "systematic review" OR "Meta analysis" OR meta-analysis 19. #5 AND #15 AND #16 AND #17 AND #18
Cochrane Library	1. MeSH descriptor: [Stroke] explode all trees 2. MeSH descriptor: [Brain Ischemia] explode all trees 3. #1 OR #2 4. “stroke” OR “Cerebrovascular Accident” OR ((“brain” OR “cerebral”) AND (“infarct*” OR “ischemi*” OR “ischaemi*” OR “hemorrhag*”)) 5. MeSH descriptor: [Hemiplegia] explode all trees 6. MeSH descriptor: [Paresis] explode all trees 7. #5 OR #6 8. “hemiplegi*” OR “hemipare*” OR “paresis” OR “plegia” OR “paretic” OR “plegic” 9. #3 OR #4 OR #7 OR #8 10. MeSH descriptor: [Robotics] explode all trees 11. MeSH descriptor: [Automation] explode all trees 12. “robot*” OR "robot assisted" OR “electromechani*” OR “electro-mechani*” 13. MeSH descriptor: [Exoskeleton Device] explode all trees 14. "exoskelet*" OR "end effector*" 15. MeSH descriptor: [Therapy, Computer-Assisted] explode all trees 16. "computer aided" OR "computer assisted" 17. MeSH descriptor: [Man-Machine Systems] explode all trees 18. MeSH descriptor: [Orthotic Devices] explode all trees 19. “orthos*” OR “orthotic” 20. #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 21. MeSH descriptor: [Upper Extremity] explode all trees 22. MeSH descriptor: [Shoulder] explode all trees 23. MeSH descriptor: [Arm] explode all trees 24. MeSH descriptor: [Elbow] explode all trees 25. MeSH descriptor: [Forearm] explode all trees 26. MeSH descriptor: [Wrist] explode all trees 27. MeSH descriptor: [Hand] explode all trees

	28. “upper extremity” OR “upper limb” OR “shoulder” OR “arm” OR “elbow” OR “forearm” OR “wrist” OR “hand” OR “finger*” 29. #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 30. MeSH descriptor: [Rehabilitation] explode all trees 31. MeSH descriptor: [Physical Therapy Modalities] explode all trees 32. MeSH descriptor: [Recovery of Function] explode all trees 33. “Rehabilitat*” OR “physiotherap*” OR “recovery” 34. #30 OR #31 OR #32 OR #33 35. #9 AND #20 AND #29 AND #34 in Cochrane Reviews
Embase	1. 'Stroke'/exp OR 'Brain Ischemia'/exp 2. stroke OR ‘Cerebrovascular Accident’ OR ((brain OR cerebral) AND (infarct* OR ischemi* OR ischaemi* OR hemorrhag*)) 3. 'Hemiplegia'/exp OR 'Paresis'/exp 4. ‘hemiplegi*’ OR ‘hemipare*’ OR ‘paresis’ OR ‘plegia’ OR ‘paretic’ OR ‘plegic’ 5. #1 OR #2 OR #3 OR #4 6. 'Robotics'/exp OR 'Automation'/exp 7. robot* OR ‘robot assisted’ OR electromechani* OR electro-mechani* 8. 'Exoskeleton Device'/exp 9. exoskelet* OR ‘end effector*’ 10. 'Therapy, Computer-Assisted'/exp 11. ‘computer aided’ OR ‘computer assisted’ 12. 'Man-Machine Systems'/exp 13. 'Orthotic Devices'/exp 14. orthos* OR orthotic 15. #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 16. 'Upper Extremity'/exp OR 'Shoulder'/exp OR 'Arm'/exp OR 'Elbow'/exp OR 'Forearm'/exp OR 'Wrist'/exp OR 'Hand'/exp 17. ‘upper extremity’ OR ‘upper limb’ OR shoulder OR arm OR elbow OR forearm OR wrist OR hand OR finger* 18. #16 OR #17 19. 'Rehabilitation'/exp OR 'Physical Therapy Modalities'/exp OR 'Recovery of Function'/exp 20. Rehabilitat* OR physiotherap* OR recovery 21. #19 OR #20 22. [systematic review]/lim OR [meta analysis]/lim 23. [humans]/lim 24. #5 AND #15 AND #18 AND #21 AND #22 AND #23
Epistemonikos	1. stroke OR "cerebrovascular accident" OR “hemiplegi*” OR “hemipare*” OR “paresis” OR “plegia” OR “paretic” OR “plegic” 2. robotic* OR "robot assisted" OR "electromechani*" OR "electro-mechani*" OR "exoskelet*" OR "end effector*" OR "computer aided" OR "computer assisted" OR "orthos*" OR "orthotic" 3. "upper extremity" OR "upper limb" OR "shoulder" OR "arm" OR "elbow" OR "forearm" OR "wrist" OR "hand" OR "finger*" 4. "Rehabilitat*" OR "physiotherap*" OR "recovery" 5. Publication type: Systematic review 6. #1 AND #2 AND #3 AND #4 AND #5
PEDro	1. stroke robot* upper 2. stroke computer* upper 3. stroke electromechani* upper 4. stroke robot* arm 5. stroke computer* arm 6. stroke electromechani* arm

	7. stroke robot* hand 8. stroke computer* hand 9. stroke electromechani* hand 10. OR #1 - #6 AND Method: systematic review
Pubmed	1. "Stroke"[Mesh] OR "Brain Ischemia"[Mesh] 2. “stroke” OR “Cerebrovascular Accident” OR ((“brain” OR “cerebral”) AND (“infarct*” OR “ischemi*” OR “ischaemi*” OR “hemorrhag*”)) 3. “Hemiplegia"[Mesh] OR "Paresis"[Mesh] 4. “hemiplegi*” OR “hemipare*” OR “paresis” OR “plegia” OR “paretic” OR “plegic” 5. #1 OR #2 OR #3 OR #4 6. "Robotics"[Mesh] OR "Automation"[Mesh] 7. “robot*” OR "robot assisted" OR “electromechani*” OR “electro-mechani*” 8. "Exoskeleton Device"[Mesh] 9. “exoskelet*” OR "end effector*” 10. "Therapy, Computer-Assisted"[Mesh] 11. "computer aided" OR "computer assisted" 12. "Man-Machine Systems"[Mesh] 13. "Orthotic Devices"[Mesh] 14. “orthos*” OR “orthotic” 15. #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 16. "Upper Extremity"[Mesh] OR "Shoulder"[Mesh] OR "Arm"[Mesh] OR "Elbow"[Mesh] OR "Forearm"[Mesh] OR "Wrist"[Mesh] OR "Hand"[Mesh] 17. “upper extremity” OR “upper limb” OR “shoulder” OR “arm” OR “elbow” OR “forearm” OR “wrist” OR “hand” OR “finger*” 18. #16 OR #17 19. "Rehabilitation"[Mesh] OR "Physical Therapy Modalities"[Mesh] OR "Recovery of Function"[Mesh] 20. “Rehabilitat*” OR “physiotherap*” OR “recovery” 21. #19 OR #20 22. "Systematic Review" [Publication Type] OR "Systematic Reviews as Topic"[Mesh] 23. “systematic review” 24. "Meta-Analysis" [Publication Type] OR "Meta-Analysis as Topic"[Mesh] 25. “Meta analysis” OR meta-analysis 26. #22 OR #23 OR #24 #25 27. "Humans"[Mesh] 28. #5 AND #15 AND #18 AND #21 AND #26 AND #27
Scopus	1. Stroke OR "Brain Ischemia" 2. stroke OR "Cerebrovascular Accident" OR ((brain OR cerebral) W/2 (infarct* OR ischemi* OR ischaemi* OR hemorrhag*)) 3. Hemiplegia OR Paresis 4. hemiplegi* OR hemipare* OR paresis OR plegia OR paretic OR plegic 5. #1 OR #2 OR #3 OR #4 6. Robotics OR Automation 7. robot* OR "robot assisted" OR electromechani* OR electro-mechani* 8. "Exoskeleton Device" 9. exoskelet* OR "end effector*" 10. "Therapy, Computer-Assisted" 11. "computer aided" OR "computer assisted" 12. "Man-Machine Systems" 13. "Orthotic Devices" 14. orthos* OR orthotic 15. #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14

	16. “Upper Extremity" OR "upper limb" OR Shoulder OR Arm OR Elbow OR Forearm OR Wrist OR Hand OR finger* 17. Rehabilitat* OR physiotherap* OR recovery 18. "systematic review" OR "Meta analysis" OR meta-analysis 19. TITLE-ABS-KEY(#5 AND #15 AND #16 AND #17 AND #18)
Web of Science	1. Stroke OR "Brain Ischemia" 2. stroke OR "Cerebrovascular Accident" OR ((brain OR cerebral) NEAR (infarct* OR ischemi* OR ischaemi* OR hemorrhag*)) 3. Hemiplegia OR Paresis 4. hemiplegi* OR hemipare* OR paresis OR plegia OR paretic OR plegic 5. TS=(#1 OR #2 OR #3 OR #4) 6. Robotics OR Automation 7. robot* OR "robot assisted" OR electromechani* OR electro-mechani* 8. "Exoskeleton Device" 9. exoskelet* OR "end effector*" 10. "Therapy, Computer-Assisted" 11. "computer aided" OR "computer assisted" 12. "Man-Machine Systems" 13. "Orthotic Devices" 14. orthos* OR orthotic 15. TS=(#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14) 16. TS=("Upper Extremity" OR "upper limb" OR Shoulder OR Arm OR Elbow OR Forearm OR Wrist OR Hand OR finger*) 17. TS=(Rehabilitat* OR physiotherap* OR recovery) 18. TS=("systematic review" OR "Meta analysis" OR meta-analysis) 19. #5 AND #15 AND #16 AND #17 AND #18

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Supplementary Table 2. List of excluded reviews.

Author	Title	Journal	Year	Exlusion reason
D'Anci, K E; Uhl, S; Oristaglio, J; Sullivan, N; Tsou, A Y	Treatments for poststroke motor deficits and mood disorders: A systematic review for the 2019 U.S. Department of Veterans Affairs and U.S. Department of Defense guidelines for stroke rehabilitation	Annals of Internal Medicine	2019	no SR
van Delden, A Lex E Q; Peper, C Lieke E; Kwakkel, Gert; Beek, Peter J	A systematic review of bilateral upper limb training devices for poststroke rehabilitation.	Stroke research and treatment	2012	no outcome of interest
Lo, K; Stephenson, M; Lockwood, C	The economic cost of robotic rehabilitation for adult stroke patients: a systematic review.	JBI Database of Systematic Reviews and Implementation Reports	2019	no outcome of interest
Langhorne, Peter; Coupar, Fiona; Pollock, Alex	Motor recovery after stroke: a systematic review.	The Lancet Neurology	2009	no SR
E, Pulman J; Buckley	Assessing the efficacy of different upper limb hemiparesis interventions on improving health-related quality of life in stroke patients: a systematic review	Topics in Stroke Rehabilitation	2013	no outcome of interest
Hatem, Samar M; Saussez, Geoffroy; della Faille, Margaux; Prist, Vincent; Zhang, Xue; Dispa, Delphine; Bleyenheuft, Yannick	Rehabilitation of motor function after stroke: A multiple systematic review focused on techniques to stimulate upper extremity recovery	FRONTIERS IN HUMAN NEUROSCIENCE	2016	no SR
Winser, Stanley; Lee, Sing Hong; Law, Hung Sing; Leung, Hei Yuen; Bello, Umar Muhammad; Kannan, Priya	Economic evaluations of physiotherapy interventions for neurological disorders: a systematic review	DISABILITY AND REHABILITATION	2020	no outcome of interest
Parker, Jack; Powell, Lauren; Mawson, Susan	Effectiveness of Upper Limb Wearable Technology for Improving Activity and Participation in Adult Stroke Survivors: Systematic Review	JOURNAL OF MEDICAL INTERNET RESEARCH	2020	no intervention of interest
Rehmat, Naqash; Zuo, Jie; Meng, Wei; Liu, Quan; Xie, Sheng Q; Liang, Hui	Upper limb rehabilitation using robotic exoskeleton systems: a systematic review	INTERNATIONAL JOURNAL OF INTELLIGENT ROBOTICS AND APPLICATIONS	2018	no SR
Aguiar, Larissa Tavares; Nadeau, Sylvie; Martins, Julia Caetano; Teixeira-Salmela, Luci Fuscaldi; Britto, Raquel Rodrigues; Faria, Christina Danielli Coelho de Morais	Efficacy of interventions aimed at improving physical activity in individuals with stroke: a systematic review	DISABILITY AND REHABILITATION	2020	no intervention of interest
Bertani, Rachele; Melegari, Corrado; De Cola, Maria C;	Effects of robot-assisted upper limb rehabilitation in stroke patients: a systematic review with meta-analysis.	Neurological Sciences	2017	no SR

Bramanti, Alessia; Bramanti, Placido; Calabro, Rocco Salvatore

Abbreviations: SR= Systematic Review.

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Supplementary Table 3. Primary studies included in the systematic reviews.

Primary study					**Systematic Reviews**																		
Author	**Year**	**Title**	**N. of participants**	**Study design**	**Mubin 2019**	**Veerbeek 2017**	**Zhang 2017**	**Lo K 2017**	**Norouzi-Gheidari 2012**	**Mehrholz 2018**	**Ferreira 2018**	**Dixit & Tedla 2019**	**Kim 2017**	**Peter 2011**	**Prange 2006**	**Hayward 2011**	**Kwakkel 2008**	**Wolf 2014**	**Lin 2018**	**Da Silva 2018**	**Arya 2017**	**Pelton 2012**
Sale et al	2014	Effects of upper limb robot-assisted therapy on motor recovery in subacute stroke patients	53	RCT		1	1	1		1	1		1						1			
Klamroth-Marganska et al	2014	Three-dimensional, task-specific robot therapy of the arm after stroke: a multicentre, parallel-group randomized trial	73	RCT	1	1	1	1		1	1											
Brokaw et al	2014	Robotic therapy provides a stimulus for upper limb motor recovery after stroke that is complementary to and distinct from conventional therapy	12	RCT		1		1		1	1											
Liao et al	2012	Effects of robot-assisted upper limb rehabilitation on daily function and real-world arm activity in patients with chronic stroke: a randomized controlled trial	20	RCT	1	1	1	1		1	1											
Burgar et al	2011	Robot-assisted upper-limb therapy in acute rehabilitation setting following stroke: Department of Veterans Affairs multisite clinical trial	54	RCT		1		1		1	1								1			
Masiero et al	2011	Upper-limb robot-assisted therapy in rehabilitation of acute stroke patients: focused review and results of new randomized controlled trial	21	RCT		1		1		1									1			
Hsieh et al	2011	Effects of treatment intensity in upper limb robot-assisted therapy for chronic stroke: a pilot randomized controlled trial	18	RCT	1	1		1		1	1											
Lo et al	2010	Robot-assisted therapy for long-term upper-limb impairment after stroke	127	RCT		1		1	1	1	1	1		1								
Housman Sarah J et al	2009	A randomized controlled trial of gravity-supported, computer-enhanced arm exercise for individuals with severe hemiparesis	28	RCT		1	1		1	1	1	1										
Volpe et al	2008	Intensive sensorimotor arm training mediated by therapist or robot improves hemiparesis in patients with chronic stroke	21	RCT		1	1	1	1	1	1			1		1						
Masiero et al	2007	Robotic-assisted rehabilitation of the upper limb after acute stroke	35	RCT		1	1		1	1		1		1		1			1			
Lum et al	2006	MIME robotic device for upper-limb neurorehabilitation in	30	RCT		1		1	1	1	1	1		1		1	1	1				

		subacute stroke subjects: a follow-up study																
Hesse et al	2005	Computerized arm training improves the motor control of the severely affected arm after stroke: a single-blinded randomized trial in two centers	39	RCT		1				1	1	1	1		1	1		
Lum et al	2002	Robot-assisted movement training compared with conventional therapy techniques forthe rehabilitationofupper-limb motor function after stroke	27	RCT		1	1	1	1	1		1	1	1	1	1		
Lambercy et al	2011	Effects of a robot-assisted training of grasp and pronation/supination in chronic stroke: a pilot study	15	NRCT	1													
Khor et al	2017	Portable and Reconfigurable Wrist Robot Improves Hand Function for Post-Stroke Subjects	7	NRCT	1													
Acosta et al	2011	Pilot study to test effectiveness of video game on reaching performance in stroke	7	NRCT	1													
Wolf et al	2015	The HAAPI (Home Arm Assistance Progression Initiative) Trial: A Novel Robotics Delivery Approach in Stroke Rehabilitation	99	RCT	1					1							1	1
Ueki et al	2012	Development of a Hand-Assist Robot With Multi-Degrees-of-Freedom for Rehabilitation Therapy	12	NRCT	1													
Grimm et al	2016	Closed-Loop Task Difficulty Adaptation during Virtual Reality Reach-to-Grasp Training Assisted with an Exoskeleton for Stroke Rehabilitation	5	NRCT	1													
Comani et al	2015	Monitoring Neuro-Motor Recovery From Stroke With High-Resolution EEG, Robotics and Virtual Reality: A Proof of Concept	3	NRCT	1													
Connely et al	2010	A pneumatic glove and immersive virtual reality environment for hand rehabilitative training after stroke	16	NRCT	1													
Delbressine et al	2012	Motivating arm-hand use for stroke patients by serious games	12	N/A	1													
Gijbels et al	2011	The Armeo Spring as training tool to improve upper limb functionality in multiple sclerosis: a pilot study	10	NRCT	1													
House et al	2016	Integrative rehabilitation of residents chronic post-stroke in skilled nursing facilities: the design and evaluation of the BrightArm Duo	13	RCT	1													

Buschfo et al	2010	Arm studio to intensify the upper limb rehabilitation after stroke: concept, acceptance, utilization and preliminary clinical results	119	NRCT	1
Cameirao et al	2012	The combined impact of virtual reality neurorehabilitation and its interfaces on upper extremity functional recovery in patients with chronic stroke	48	RCT	1
Da Silva Cameirao et al	2011	Virtual reality based rehabilitation speeds up functional recovery of the upper extremities after stroke: a randomized controlled pilot study in the acute phase of stroke using the rehabilitation gaming system	16	RCT	1
Zhang et al	2011	Feasibility studies of robot-assisted stroke rehabilitation at clinic and home settings using RUPERT	8	NRCT	1
Frisoli et al	2012	Positive effects of robotic exoskeleton training of upper limb reaching movements after stroke	9	NRCT	1
Mihelj et al	2012	Virtual Rehabilitation Environment Using Principles of Intrinsic Motivation and Game Design. Presence: Teleoperators and Virtual Environments	16	N/A	1
Sivan et al	2014	Home-based Computer Assisted Arm Rehabilitation (hCAAR) robotic device for upper limb exercise after stroke: results of a feasibility study in home setting	19	NRCT	1
Amirabdollahian et al	2014	Design, development and deployment of a hand/wrist exoskeleton for home-based rehabilitation after stroke - SCRIPT project	23	NRCT	1
Stein et al	2011	A pilot study of robotic-assisted exercise for hand weakness after stroke	12	NRCT	1
Dovat et al	2010	A technique to train finger coordination and independence after stroke	2	NRCT	1
Novak et al	2014	Increasing motivation in robot-aided arm rehabilitation with competitive and cooperative gameplay	38	NRCT	1
Merians et al	2010	Integrated arm and hand training using adaptive robotics and virtual reality simulations. In: 8th Annual International Conference on Dissability, Virtual	11	N/A	1

		Reality and Associated Technologies														
Kan et al	2011	The development of an adaptive upper-limb stroke rehabilitation robotic system	2	NRCT	1											
Simkins et al	2012	Robotic Rehabilitation Game Design for Chronic Stroke	10	NRCT	1											
Aisen et al	1997	The effect of robot-assisted therapy and rehabilitative training on motor recovery following stroke	20	NRCT		1			1		1		1	1	1	1
Burgar et al	2000	Development of robots for rehabilitation therapy: the Palo Alto VA/Standford experience	21	NRCT		1	1				1				1	
Kahn et al	2000	Comparison of robot-assisted reaching to free reaching in promoting recovery from chronic stroke	10	N/A		1									1	
Volpe et al	2000	A novel approach to stroke rehabilitation: robot-aided sensorimotor stimulation	56	RCT		1	1		1	1		1		1	1	1
Daly et al	2005	Response to upper-limb robotics and functional neuromuscular stimulation following stroke	12	RCT		1				1	1	1	1		1	
Kahn et al	2006	Robot assisted reaching exercise promotes arm movement recovery in chronic hemiparetic stroke: a randomized controlled pilot study	19	RCT		1		1	1	1	1	1	1		1	
Masiero et al	2006	A novel robot device in rehabilitation of post-stroke hemiplegic upper limbs	20	NRCT		1	1							1		1
Amirabdollahian et al	2007	Multivariate analysis of the FuglMeyer outcome measures assessing the effectiveness of GENTLE/S robot-mediated stroke therapy	31	NRCT		1				1						
Rabadi et al	2008	A pilot study of activity-based therapy in the arm motor recovery post stroke: a randomized controlled trial	20	RCT		1	1	1	1	1	1	1	1	1		1
Hu et al	2009	A comparison between electromyography-driven robot and passive motion device on wrist rehabilitation for chronic stroke	27	RCT		1										
Kutner et al	2010	Quality-of-life change associated with robotic-assisted therapy to improve hand motor function in patients with subacute stroke: a randomized clinical trial	17	RCT		1				1		1				
Abdullah et al	2011	Results of clinicians using a therapeutic robotic system in an inpatient stroke rehabilitation unit	20	RCT		1				1	1					
De Araujo et al	2011	Effects of intensive arm training with an	12	NRCT		1					1					

		electromechanical orthosis in chronic stroke patients: a preliminary study								
Conroy et al	2011	Effect of gravity on robot-assisted motor training after chronic stroke: a randomized trial	62	RCT	1		1	1	1	
Hollenstein et al	2011	Additional therapy with computeraided training system compared to occupational therapy arm group therapy [Zusatztherapie mit computerunterstütztem trainingssystem im vergleich zu ergotherapeutischer armgruppentherapie]	13	NRCT	1			1		
Hwang et al	2012	Individual finger synchronized robot-assisted hand rehabilitation in subacute to chronic stroke: a prospective randomized clinical trial of efficacy	17	RCT	1			1		
Reinkensmeyer et al	2012	Comparison of three-dimensional, assist- as-needed robotic arm/hand movement training provided with Pneu-WREX to conventional tabletop therapy after chronic stroke	26	RCT	1	1	1		1	
Wu et al	2012	Effect of therapist-based versus robot-assisted bilateral arm training on motor control, functional performance, and quality of life after chronic stroke: a clinical trial	42	RCT	1		1	1	1	1
Yang et al	2012	Pilot comparative study of unilateral and bilateral robot-assisted training on upper-extremity performance in patients with stroke	21	RCT	1				1	
Byl et al	2013	Chronic stroke survivors achieve comparable outcomes following virtual task specific repetitive training guided by a wearable robotic orthosis (UL-EXO7) and actual task specific repetitive training guided by a physical therapist	15	RCT	1		1		1	
Page et al	2012	Portable upper extremity robotics is as efficacious as upper extremity rehabilitative therapy: a randomized controlled pilot trial	16	RCT	1				1	
Wu et al	2013	Unilateral versus bilateral robot-assisted rehabilitation on arm-trunk control and functions post stroke: a randomized controlled trial	53	RCT	1		1			
Yoo et al	2013	Effect of three-dimensional robot-assisted therapy on upper	22	RCT	1			1	1	

		limb function of patients with stroke											
Ang et al	2014	Brain-computer interface based robotic end effector system for wrist and hand rehabilitation: results of a three-armed randomized controlled trial for chronic stroke	21	RCT	1		1	1	1				
Hesse et al	2014	Effect on arm function and cost of robot-assisted group therapy in subacute patients with stroke and a moderately to severely affected arm: a randomized controlled trial	50	RCT	1		1	1		1	1		1
Masiero et al	2014	Randomized trial of a robotic assistive device for the upper extremity during early inpatient stroke rehabilitation	30	RCT	1	1	1		1	1	1		
Sale et al	2014	Recovery of hand function with robot-assisted therapy in acute stroke patients: a randomized-controlled trial	20	RCT	1	1	1		1		1		
Timmermans et al	2014	Effects of task-oriented robot training on arm function, activity, and quality of life in chronic stroke patients: a randomized controlled trial	22	RCT	1	1		1	1				
McCabe et al	2015	Comparison of robotics, functional electrical stimulation, and motor learning methods for treatment of persistent upper extremity dysfunction after stroke: a randomized controlled trial	35	RCT	1		1	1	1	1			
Susanto et al	2015	Efficacy of robot assisted fingers training in chronic stroke survivors: a pilot randomized-controlled trial	19	RCT	1		1	1	1				
Rosati et al	2007	Design, implementation and clinical tests of a wire-based robot for neurorehabilitation	24	RCT		1						1	
Hsieh et al	2012	Dose–Response Relationship of Robot-Assisted Stroke Motor Rehabilitation: The Impact of Initial Motor Status	54	RCT			1						
Hsieh et al	2014	Sequential combination of robot-assisted therapy and constraint-induced therapy in stroke rehabilitation: a randomized controlled trial	48	RCT			1	1					
Hsieh et al	2016	Bilateral robotic priming before task-oriented approach in subacute stroke rehabilitation: a pilot randomized controlled trial	31	RCT			1						1

Orihuela-Espina et al	2016	Robot training for hand motor recovery in subacute stroke patients: A randomized controlled trial	17	RCT	1		1		1					
Vanoglio	2016	Feasibility and efficacy of a robotic device for hand rehabilitation in hemiplegic stroke patients: a randomized pilot controlled study	30	RCT	1		1							
Fazekas et al	2007	Robot-mediated upper limb physiotherapy for patients with spastic hemiparesis: a preliminary study	30	RCT		1	1		1		1			
Volpe et al	1999	Robot training enhanced motor outcome in patients with stroke maintained over 3 years	12	N/A		1		1				1		
Bustamante Valles et al	2016	Technology-assisted stroke rehabilitation in Mexico: a pilot randomized trial comparing traditional therapy to circuit training in a robot/technologyassisted therapy gym.	20	RCT			1		1					
Grigoras et al	2016	Testing of a hybrid FES-robot assisted hand motor training program in sub-acute stroke survivors.	25	RCT			1							
Lee et al	2016	Effect of upper extremity robot-assisted exercise on spasticity in stroke patients	58	RCT			1							1
Mayr et al	2008	ARMOR: an electromechanical robot for upper limb training following stroke. A prospective randomised controlled pilot study	8	RCT			1							
NCT03020576	2017	Robotic and conventional hand therapy after stroke.	31	RCT			1							
Takahashi et al	2016	Efficacy of upper extremity robotic therapy in subacute poststroke hemiplegia: an exploratory randomized trial	60	RCT			1		1	1				1
Taveggia et al	2016	Efficacy of robot-assisted rehabilitation for the functional recovery of the upper limb in post-stroke patients: a randomized controlled study	54	RCT			1							
Tomic et al	2017	ArmAssist robotic system versus matched conventional therapy for poststroke upper limb rehabilitation: a randomized clinical trial	26	RCT			1							
Villafane et al	2017	Efficacy of short-term robot-assisted rehabilitation in patients with hand paralysis after stroke: a randomized clinical trial	32	RCT			1							
Fasoli et al	2004	Does shorter rehabilitation limit potential recovery poststroke?	56	RCT				1			1	1	1	1

Lin et al	2015	Effects of computer-aided interlimb force coupling training on paretic hand and arm motor control following chronic stroke: a randomized controlled trial	33	RCT	1				
Ramos-Murguialday et al	2013	Brain-machine-interface in chronic stroke rehabilitation: a controlled study	30	RCT	1				
Simkins et al	2013	Robotic unilateral and bilateral upper-limb movement training for stroke survivors afflicted by chronic hemiparesis	15	NRCT	1				
Xu et al	2012	Adaptive hierarchical control for the muscle strength training of stroke survivors in robot-aided upper-limb rehabilitation	18	RCT	1				
Xu et al	2014	Clinical experimental research on adaptive robot-aided therapy control methods for upper-limb rehabilitation	45	RCT	1				
Prange et al	2015	The effect of arm support combined with rehabilitation games on upper-extremity function in subacute stroke: a randomized controlled trial	68	RCT		1			
Fasoli et al	2004	Robotic therapy for chronic motor impairments after stroke: follow-up results	42	NRCT			1	1	
Fasoli et al	2003	Effects of robotic therapy on motor impairment and recovery in chronic stroke	20	NRCT			1		
Krebs et al	2004	Rehabilitation robotics: pilot trial of a spatial extension for MIT-Manus	10	NRCT			1	1	
MacClellan	2005	Robotic upper-limb neurorehabilitation in chronic stroke patients	27	NRCT			1		
Posteraro et al	2009	Robot-mediated therapy for paretic upper limb of chronic patients following neurological injury	20	NRCT			1		
Hesse et al	2003	Robot assisted arm trainer for the passive and active practice of bilateral forearm and wrist movements in hemiparetic subjects	12	NRCT			1		
Fazekas et al	2007	Steps in the development of robot aided upper limb physiotherapy with the REHAROB System. Proceedings of 9th congress of the European federation for research in rehabilitation, Budapest, 26–29 August 2007	N/A	NRCT			1		
Chang et al	2007	Effects of robot-aided bilateral force-induced isokinetic arm training combined with conventional	20	NRCT			1		1

		rehabilitation on arm motor function in patients with chronic stroke				
Coote et al	2008	The effect of the GENTLE/s robot-mediated therapy system on arm function after stroke	20	NRCT	1	
Treger et al	2008	Robot-assisted therapy for neuromuscular training of sub-acute stroke patients: a feasibility study.	10	NRCT	1	
Bovolenta et al	2009	Robot therapy for functional recovery of the upper limbs: a pilot study on patients after stroke	14	NRCT	1	
Casadio et al	2009	A proof of concept study for the integration of robot therapy with physiotherapy in the treatment of stroke patients	14	NRCT	1	
Colombo et al	2010	Measuring changes of movement dynamics during robot-aided neurorehabilitation of stroke patients	18	NRCT	1	
Song et al	2008	Assistive control system using continuous myoelectric signal in robot-aided arm training for patients after stroke	8	NRCT	1	
Hu et al	2007	Variation of muscle coactivation patterns in chronic stroke during robot-assisted elbow training	7	NRCT	1	
Hu et al	2009	Quantitative evaluation of motor functional recovery process in chronic stroke patients during robot-assisted wrist training	15	NRCT	1	
Stein et al	2007	Electromyography controlled exoskeletal upper-limb-powered orthosis for exercise training after stroke	6	NRCT	1	
Frisoli et al	2009	Robotic assisted rehabilitation in virtual reality with the L-EXOS	9	NRCT	1	
Reinkensmeyer et al	2000	Understanding and treating arm movement impairment after chronic brain injury: progress with the ARM guide	3	NRCT		1
Krebs et al	2000	Increasing productivity and quality of care: Robot-aided neuro-rehabilitation	76	NRCT		1
Ferraro et al	2003	Robot-aided sensorimotor arm training improves outcome in patients with chronic stroke	30	NRCT		1
Stein et al	2004	Comparison of two techniques of robot-aided upper limb exercise training after stroke. Am J Phys Med Rehabil	46	NRCT		1
Lum et al	2004	Evidence for improved muscle activation	13	NRCT		1

		patterns after retraining of reaching movements with the MIME robotic system in subjects with poststroke hemiparesis							
Hesse et al	2008	Mechanical arm trainer for the treatment of the severely affected arm after a stroke	54	RCT	1				
Qian et al	2017	Early stroke rehabilitation of the upper limb assisted with an electromyography driven neuromuscular electrical stimulation-robotic arm	24	RCT		1			
Nijenhuis et al	2017	Effects of training with a passive hand orthosis and games at home in chronic stroke: a pilot randomised controlled tria	19	RCT			1		
Stinear et al	2008	Priming the motor system enhances the effects of upper limb therapy in chronic stroke	37	RCT			1		
Zondervan et al	2015	Machine-based, self-guided home therapy for individuals with severe arm impairment after stroke: a randomized controlled trial	16	RCT			1		
Dohle et al	2013	Pilot study of a robotic protocol to treat shoulder subluxation in patients with chronic stroke	18	NRCT				1	
Krebs et al	2008	A comparison of functional and impairment-based robotic training in severe to moderate chronic stroke: a pilot study.	47	NRCT					1
Merians et al	2006	Sensorimotor training in a virtual reality environment: does it improve functional recovery poststroke?	8	NRCT					1
Qiu et al	2009	Coordination changes demonstrated by subjects with hemiparesis performing hand-arm training using the NJIT-RAVR robotically assisted virtual rehabilitation system	8	NRCT					1

Abbreviations: N/A= not available; NRCT= non-randomized controlled trial; RCT= randomized controlled trial.

Supplementary Table 4. Comprehensive report of outcome reported for robot-assisted arm rehabilitation.

Outcome	Outcome measure	Contributing reviews	Intervention and comparison	Relative effect	Heterogeneity (I^2)	Number of participants (studies)
Cochrane Reviews (CSRs)						
ADL	FIM, BI	**Merholz 2018**	electromechanical and robot-assisted arm training versus any other intervention	statistically significant improvement in experimental group p=0,005	59%	24 (957)
ADL	FIM, BI	**Merholz 2018**	RT vs any other intervention in acute phase	statistically significant improvement in experimental group p=0,009	63%	13 (532)
ADL	FIM, BI	**Merholz 2018**	RT vs any other intervention in chronic phase	NO statistically improvement in experimental group p=0,24	54%	11 (425)
ADL	test for subgroup differences	**Merholz 2018**	acute/subacute phase vs chronic phase	NO significant difference	0%	N/A
Arm Function	FM	**Merholz 2018**	electromechanical and robot-assisted arm training versus any other intervention	statistically significant improvement in experimental group p<0,0001	36%	41 (1452)
Muscle strength	MI, MRC	**Merholz 2018**	electromechanical and robot-assisted arm training versus any other intervention	statistically significant improvement in experimental group p=0,003	76%	23 (826)
Acceptability	dropouts during the intervention period	**Merholz 2018**	electromechanical and robot-assisted arm training versus any other intervention	The use of electromechanical and robot-assisted arm training in people after stroke did not increase the risk of participants dropping out p=0,93	0%	45 (1619)
Sensitivity analysis ADL	adequate description of the randomization procedure	**Merholz 2018**	electromechanical and robot-assisted arm training versus any other intervention	statistically significant improvement in experimental group p=0,0002	9%	15 (661)
Sensitivity analysis ADL	adequately concealed allocation	**Merholz 2018**	electromechanical and robot-assisted arm training versus any other intervention	statistically significant improvement in experimental group p=0,03	30%	10 (392)
Sensitivity analysis ADL	blinded outcome assessors	**Merholz 2018**	electromechanical and robot-assisted arm training versus any other intervention	statistically significant improvement in experimental group p=0,004	41%	20 (808)
Sensitivity analysis Arm Function	adequate description of the randomization procedure	**Merholz 2018**	electromechanical and robot-assisted arm training versus any other intervention	statistically significant improvement in experimental group p<0,0001	28%	28 (1048)

Sensitivity analysis Arm Function	adequately concealed allocation	**Merholz 2018**	electromechanical and robot-assisted arm training versus any other intervention	statistically significant improvement in experimental group p=0,0001	21%	12 (462)
Sensitivity analysis Arm Function	blinded outcome assessors	**Merholz 2018**	electromechanical and robot-assisted arm training versus any other intervention	statistically significant improvement in experimental group p<0,0001	37%	32 (220)
ADL	FIM, BI	**Merholz 2018**	RT vs any other intervention (distal training)	statistically significant improvement in experimental group p=0,013	23%	8 (255)
ADL	FIM, BI	**Merholz 2018**	RT vs any other intervention (proximal training)	statistically significant improvement in experimental group p=0,056	68%	16 (702)
ADL	test for subgroup differences	**Merholz 2018**	training for the distal arm and the hand vs training of the proximal arm	NO significant difference	0%	N/A
Arm Function	FM	**Merholz 2018**	RT vs any other intervention (distal training)	statistically significant improvement in experimental group p=0,0085	48%	16 (547)
Arm Function	FM	**Merholz 2018**	RT vs any other intervention (proximal training)	statistically significant improvement in experimental group p=0,0002	27%	24 (905)
Arm Function	test for subgroup differences	**Merholz 2018**	training for the distal arm and the hand vs training of the proximal arm	NO significant difference	0%	N/A
Non-Cochrane Reviews (non-CSRs)						
Motor Function	N/A	**Mubin 2019**	N/A	N/A	N/A	N/A
Motor Control	FMA arm	**Veerbeek 2017**	Robot-assisted therapy vs any type of control	statistically significant improvement in experimental group p=0,001	30%	28 (884)
Motor Control	FMA-SEC	**Veerbeek 2017**	Robot-assisted therapy vs any type of control	statistically significant improvement in experimental group p<0,00001	34%	14 (369)
Motor Control	FMA-WH	**Veerbeek 2017**	Robot-assisted therapy vs any type of control	NO statistically significant difference between groups p=0,19	75%	17 (443)
Motor Control	FMA arm	**Veerbeek 2017**	Shoulder/elbow robotics vs shoulder/ elbow comparisons	Statistically significant improvement in experimental group p=0,008	14%	14 (528)
Motor Control	FMA-SEC	**Veerbeek 2017**	Shoulder/elbow robotics vs shoulder/ elbow comparisons	statistically significant improvement in experimental group p=0,003	31%	8 (228)
Motor Control	FMA-WH	**Veerbeek 2017**	Shoulder/elbow robotics vs shoulder/ elbow comparisons	NO statistically significant difference between groups p=0,22	33%	10 (290)
Motor Control	FMA arm	**Veerbeek 2017**	whole arm robotics vs any type of control	NO statistically significant difference between groups p=0,76	81%	2 (62)

Motor Control	FMA arm	**Veerbeek 2017**	shoulder/elbow/wrist robotics vs any type of control	NO statistically significant difference between groups p=0,82	0%	3 (102)
Motor Control	FMA arm	**Veerbeek 2017**	elbow/wrist robotics vs any type of control	statistically significant improvement in experimental group p=0,001	46%	5 (131)
Motor Control	FMA-SEC	**Veerbeek 2017**	elbow/wrist robotics vs any type of control	statistically significant improvement in experimental group p=0,007	44%	2 (65)
Motor Control	FMA-WH	**Veerbeek 2017**	elbow/wrist robotics vs any type of control	NO statistically significant difference between groups p=0,12	53%	2 (65)
Motor Control	FMA-SEC	**Veerbeek 2017**	wrist /hand robotics vs any type of control	NO statistically significant difference between groups p=0,12	0%	2 (30)
Motor Control	FMA-WH	**Veerbeek 2017**	wrist /hand robotics vs any type of control	NO statistically significant difference between groups p=0,42	0%	2 (30)
Upper Limb Capacity	laboratory measures	**Veerbeek 2017**	robot assisted therapy vs any type of control	NO statistically significant difference between groups p=0,64	2%	20 (682)
Upper Limb Capacity	laboratory measures	**Veerbeek 2017**	whole arm robotics vs any type of control	NO statistically significant difference between groups p=0,49	17%	2 (62)
Upper Limb Capacity	laboratory measures	**Veerbeek 2017**	shoulder/elbow robotics vs any type of control	NO statistically significant difference between groups p=0,49	17%	12 (413)
Upper Limb Capacity	laboratory measures	**Veerbeek 2017**	hand robotics vs any type of control	NO statistically significant difference between groups p=0,56	0%	2 (39)
ADL	FIM, mRS, BI	**Veerbeek 2017**	Robot-assisted therapy vs any type of control	NO statistically significant difference between groups p=0,09	56%	14 (427)
ADL	FIM, mRS, BI	**Veerbeek 2017**	shoulder/elbow robotics vs any type of control	NO statistically significant difference between groups p=0,25	64%	11 (330)
Muscle strength	MRC, MI-arm, MPS	**Veerbeek 2017**	Robot-assisted therapy vs any type of control	NO statistically significant difference between groups p=0,22	56%	15 (494)
Muscle strength	MRC, MI-arm, MPS	**Veerbeek 2017**	shoulder/elbow robotics vs any type of control	statistically significant improvement in experimental group p=0,006	44%	7 (254)
Muscle strength	MRC-shoulder abductor strength	**Veerbeek 2017**	shoulder/elbow robotics vs any type of control	NO statistically significant difference between groups p=0,98	38%	3 (71)
Muscle strength	MRC-elbow flexor strength	**Veerbeek 2017**	shoulder/elbow robotics vs any type of control	NO statistically significant difference between groups p=0,74	0%	3 (71)

Muscle strength	MRC-wrist flexor strength	**Veerbeek 2017**	shoulder/elbow robotics vs any type of control	NO statistically significant difference between groups p=0,65	35%	3 (71)
Muscle strength	MRC, MI-arm, MPS	**Veerbeek 2017**	shoulder/elbow/wrist robotics vs any type of control	NO statistically significant difference between groups p=0,53	22%	2 (88)
Muscle strength	MRC, MI-arm, MPS	**Veerbeek 2017**	elbow/wrist robotics vs any type of control	NO statistically significant difference between groups p=0,22	59%	3 (82)
Muscle Tone	MAS	**Veerbeek 2017**	Robot-assisted therapy vs any type of control	statistically significant improvement in control group p=0,02	25%	13 (429)
Muscle Tone	MAS-elbow flexor	**Veerbeek 2017**	Robot-assisted therapy vs any type of control	NO statistically significant difference between groups p=0,41	46%	4 (107)
Muscle Tone	MAS-wrist flexor	**Veerbeek 2017**	Robot-assisted therapy vs any type of control	NO statistically significant difference between groups p=0,65	75%	3 (54)
Muscle Tone	MAS	**Veerbeek 2017**	shoulder/elbow robotics vs any type of control	NO statistically significant difference between groups p=0,06	50%	7 (206)
Muscle Tone	MAS	**Veerbeek 2017**	shoulder/elbow/wrist robotics vs any type of control	NO statistically significant difference between groups p=0,06	0%	2 (88)
Motor Control	FMA-arm	**Veerbeek 2017**	Exoskeleton vs any type of control	NO statistically significant difference between groups p=0,09	22%	9 (214)
Motor Control	FMA-WH	**Veerbeek 2017**	Exoskeleton vs any type of control	NO statistically significant difference between groups p=0,27	73%	2 (31)
Muscle strength	MRC, MI-arm, MPS	**Veerbeek 2017**	Exoskeleton vs any type of control	NO statistically significant difference between groups p=0,53	22%	2 (88)
Muscle Tone	MAS	**Veerbeek 2017**	Exoskeleton vs any type of control	NO statistically significant difference between groups p=0,06	0%	2 (88)
Upper Limb Capacity	laboratory measures	**Veerbeek 2017**	Exoskeleton vs any type of control	NO statistically significant difference between groups p=0,30	0%	4 (130)
Motor Control	FMA-arm	**Veerbeek 2017**	End-effector vs any type of control	Statistically significant improvement in experimental group p=0,005	35%	19 (670)
Motor Control	FMA-SEC	**Veerbeek 2017**	End-effector vs any type of control	statistically significant improvement in experimental group p<0,00001	34%	14 (369)
Motor Control	FMA-WH	**Veerbeek 2017**	End-effector vs any type of control	statistically significant improvement in experimental group p=0,02	74%	15 (412)

Muscle strength	MRC, MI-arm, MPS	**Veerbeek 2017**	End-effector vs any type of control	NO statistically significant difference between groups p=0,24	57%	12 (406)
Muscle Tone	MAS	**Veerbeek 2017**	End-effector vs any type of control	NO statistically significant difference between groups p=0,09	33%	11 (341)
Upper Limb Capacity	laboratory measures	**Veerbeek 2017**	End-effector vs any type of control	NO statistically significant difference between groups p=0,99	6%	17 (552)
ADL	FIM, mRS, BI	**Veerbeek 2017**	End-effector vs any type of control	NO statistically significant difference between groups p=0,09	56%	14 (427)
Motor Control	FMA arm	**Veerbeek 2017**	Early started (<3 months poststroke) RT-UL vs any type of control	NO statistically significant difference between groups p=0,27	62%	10 (360)
Motor Control	FMA arm	**Veerbeek 2017**	Late started (>3 months) RT-UL vs any type of control	NO statistically significant difference between groups p=0,6	0%	18 (506)
Motor Control	FMA-SEC	**Veerbeek 2017**	Early started RT-UL vs any type of control	statistically significant improvement in experimental group p<0,001	44%	8 (251)
Motor Control	FMA-SEC	**Veerbeek 2017**	Late started RT-UL vs any type of control	statistically significant improvement in experimental group p=0,04	23%	6 (118)
Motor Control	FMA-WH	**Veerbeek 2017**	Early started RT-UL vs any type of control	statistically significant improvement in experimental group p=0,02	85%	8 (251)
Motor Control	FMA-WH	**Veerbeek 2017**	Late started RT-UL vs any type of control	NO statistically significant difference between groups p=0,80	27%	9 (192)
Muscle strength	MRC, MI-arm, MPS	**Veerbeek 2017**	Early started RT-UL vs any type of control	NO statistically significant difference between groups p=0,35	69%	9 (396)
Muscle Tone	MAS	**Veerbeek 2017**	Early started RT-UL vs any type of control	NO statistically significant difference between groups p=0,08	47%	9 (299)
Upper Limb Capacity	laboratory measures	**Veerbeek 2017**	Early started RT-UL vs any type of control	NO statistically significant difference between groups p=0,99	40%	6 (195)
ADL	FIM, mRS, BI	**Veerbeek 2017**	Early started RT-UL vs any type of control	NO statistically significant difference between groups p=0,30	67%	10 (331)
Muscle strength	MRC, MI-arm, MPS	**Veerbeek 2017**	Late started RT-UL vs any type of control	NO statistically significant difference between groups p=0,82	0%	5 (148)
Muscle Tone	MAS	**Veerbeek 2017**	Late started RT-UL vs any type of control	NO statistically significant difference between groups p=0,10	0%	4 (130)

Upper Limb Capacity	laboratory measures	**Veerbeek 2017**	Late started RT-UL vs any type of control	NO statistically significant difference between groups p=0,58	0%	14 (487)
ADL	FIM, mRS, BI	**Veerbeek 2017**	Late started RT-UL vs any type of control	NO statistically significant difference between groups p=0,12	0%	4 (96)
Motor Control	FMA arm	**Veerbeek 2017**	dose-matched RT-UL trials versus any type of control	Statistically significant improvement in experimental group p=0,001	33%	26 (808)
Motor Control	FMA arm	**Veerbeek 2017**	non-dose-matched RT-UL trials versus any type of control	NO statistically significant difference between groups p=0,74	0%	2 (76)
Motor Control	FMA SEC	**Veerbeek 2017**	dose-matched RT-UL trials versus any type of control	statistically significant improvement in experimental group p=0,0003	40%	11 (263)
Motor Control	FMA SEC	**Veerbeek 2017**	non-dose-matched RT-UL trials versus any type of control	statistically significant improvement in experimental group p=0,02	0%	2 (50)
Motor Control	FMA WH	**Veerbeek 2017**	dose-matched RT-UL trials versus any type of control	NO statistically significant difference between groups p=0,23	75%	14 (337)
Motor Control	FMA WH	**Veerbeek 2017**	non-dose-matched RT-UL trials versus any type of control	Statistically significant improvement in experimental group p<0,00001	0%	3 (106)
Muscle strength	MRC, MI-arm, MPS	**Veerbeek 2017**	dose-matched RT-UL trials versus any type of control	NO statistically significant difference between groups p=0,47	50%	12 (418)
Muscle strength	MRC, MI-arm, MPS	**Veerbeek 2017**	non-dose-matched RT-UL trials versus any type of control	NO statistically significant difference between groups p=0,07	59%	2 (76)
ADL	FIM, mRS, BI	**Veerbeek 2017**	dose-matched RT-UL trials versus any type of control	NO statistically significant difference between groups p=0,47	32%	8 (279)
ADL	FIM, mRS, BI	**Veerbeek 2017**	non-dose-matched RT-UL trials versus any type of control	statistically significant improvement in experimental group p=0,002	54%	5 (148)
Muscle Tone	MAS	**Veerbeek 2017**	dose-matched RT-UL trials versus any type of control	statistically significant improvement in control group p=0,01	28%	12 (399)
Upper Limb Capacity	laboratory measures	**Veerbeek 2017**	dose-matched RT-UL trials versus any type of control	NO statistically significant difference between groups p=0,43	0%	19 (660)
Motor Function	FM-UE	**Zhang 2017**	Robot-assisted therapy vs conventional therapy	statistically significant improvement in experimental group p=0,003	68%	13 (426)
Motor Function	FM-UE	**Zhang 2017**	Robot-assisted therapy combined with conventional therapy	Statistically significant improvement in experimental group p<0,01	0%	4 (135)

			(additional RT) vs conventional therapy alone			
Motor Function	FM-UE	**Zhang 2017**	Robot-assisted therapy alone (substitutional RT) vs conventional therapy alone	NO statistically significant difference between groups p=0,08	78%	9 (291)
Motor Function	FM-UE	**Zhang 2017**	Robot-assisted therapy alone in chronic stage vs conventional therapy	Statistically significant improvement in experimental group p=0,01	74%	6 (198)
Motor Function	FM-UE	**Zhang 2017**	Robot-assisted therapy in acute/subacute stage vs conventional therapy	NO statistically significant difference between groups p=0,13	67%	7 (228)
Motor movement	FM-UE, MI	**Lo K 2017**	Robot-assisted therapy vs conventional therapy	NO statistically significant difference between groups p=0,45	41%	29 (860)
Motor movement	FM-UE, MI	**Lo K 2017**	Robot-assisted therapy in acute/subacute stage vs conventional therapy	NO statistically significant difference between groups p=0,93	N/A	N/A
Motor movement	FM-UE, MI	**Lo K 2017**	Robot-assisted therapy in chronic stage vs conventional therapy	NO statistically significant difference between groups p=0,22	N/A	N/A
Motor movement	FM-UE, MI	**Lo K 2017**	Robot-assisted therapy in severe impairment patients vs conventional therapy	NO statistically significant difference between groups p=0,34	N/A	N/A
Motor movement	FM-UE, MI	**Lo K 2017**	Robot assisted therapy in moderate/mild impairment patients vs conventional therapy	NO statistically significant difference between groups p=0,78	N/A	N/A
Motor movement	FM-UE, MI	**Lo K 2017**	Robot-assisted therapy alone vs conventional therapy	NO statistically significant difference between groups p=0,33	48%	16 (507)
Motor movement	FM-UE, MI	**Lo K 2017**	Robot-assisted therapy alone in acute/subacute stage vs conventional therapy	NO statistically significant difference between groups p=0,85	N/A	N/A
Motor movement	FM-UE, MI	**Lo K 2017**	Robot-assisted therapy alone in chronic stage vs conventional therapy	NO statistically significant difference between groups p=0,19	N/A	N/A
Motor movement	FM-UE, MI	**Lo K 2017**	Robot-assisted therapy alone in severe impairment patients vs conventional therapy	NO statistically significant difference between groups p=0,16	N/A	N/A
Motor movement	FM-UE, MI	**Lo K 2017**	Robot-assisted therapy alone in moderate/mild impairment patients vs conventional therapy	NO statistically significant difference between groups p=0,90	N/A	N/A
Sustainability (upperlimb movement)	N/A	**Lo K 2017**	Robot-assisted therapy vs conventional therapy (follow-up ≤ 3 months)	NO statistically significant difference between groups p=0,68	24%	9 (293)

Sustainability (upperlimb movement)	N/A	**Lo K 2017**	Robot-assisted therapy vs conventional therapy (follow-up > 3 months)	NO statistically significant difference between groups p=1,00	59%	7 (217)
ADL	FIM [total], BI, MAL-QOM	**Lo K 2017**	Robot-assisted therapy vs conventional therapy	NO statistically significant difference between groups p=0,32	66%	31 (1120)
ADL	FIM [total], BI, MAL-QOM	**Lo K 2017**	Robot-assisted therapy in acute/subacute stage vs conventional therapy	NO statistically significant difference between groups p=0,95	N/A	N/A
ADL	FIM [total], BI, MAL-QOM	**Lo K 2017**	Robot-assisted therapy in chronic stage vs conventional therapy	NO statistically significant difference between groups p=0,08	N/A	N/A
ADL	FIM [total], BI, MAL-QOM	**Lo K 2017**	Robot-assisted therapy in severe impairment patients vs conventional therapy	NO statistically significant difference between groups p=0,19	N/A	N/A
ADL	FIM [total], BI, MAL-QOM	**Lo K 2017**	Robot assisted therapy in moderate/mild impairment patients vs conventional	NO statistically significant difference between groups p=0,68	N/A	N/A
ADL	FIM [total], BI, MAL-QOM	**Lo K 2017**	Robot-assisted therapy alone vs conventional therapy	NO statistically significant difference between groups p=0,99	82%	12 (345)
ADL	FIM [total], BI, MAL-QOM	**Lo K 2017**	Robot-assisted therapy alone in acute/subacute stage vs conventional therapy	NO statistically significant difference between groups p=0,26	N/A	N/A
ADL	FIM [total], BI, MAL-QOM	**Lo K 2017**	Robot-assisted therapy alone in chronic stage vs conventional therapy	NO statistically significant difference between groups p=0,09	N/A	N/A
ADL	FIM [total], BI, MAL-QOM	**Lo K 2017**	Robot-assisted therapy alone in severe impairment patients vs conventional therapy	NO statistically significant difference between groups p=1,28	N/A	N/A
ADL	FIM [total], BI, MAL-QOM	**Lo K 2017**	Robot-assisted therapy alone in moderate/mild impairment patients vs conventional therapy	NO statistically significant difference between groups p=0,98	N/A	N/A
Sustainability (ADL)	FIM [total], BI, MAL-QOM	**Lo K 2017**	Robot-assisted therapy vs conventional therapy (follow-up ≤ 3 months)	NO statistically significant difference between groups p=0,68	81%	11 (428)
Sustainability (ADL)	FIM [total], BI, MAL-QOM	**Lo K 2017**	Robot-assisted therapy vs conventional therapy (follow-up > 3 months)	NO statistically significant difference between groups p=0,50	76%	9 (481)
Motor Recovery	FM-UE	**Norouzi-Gheidari 2012**	Robot-assisted therapy used as additional therapy vs conventional therapy	statistically significant improvement in experimental group p=0,004	0%	4 (158)
Motor Recovery	FM-UE	**Norouzi-Gheidari 2012**	Robot-assisted therapy vs conventional therapy matching duration/intensity in RT and CT groups	NO statistically significant difference between groups p=0,28	13%	6 (204)

Motor Recovery	FM-UE	**Norouzi-Gheidari 2012**	RT vs CT with same duration/intensity in acute/subacute stage	NO statistically significant difference between groups p=0,83	4%	2 (35)
Motor Recovery	FM-UE	**Norouzi-Gheidari 2012**	RT vs CT with same duration/intensity in chronic stage	NO statistically significant difference between groups p=0,28	35%	4 (169)
Motor Recovery	FM-UE	**Norouzi-Gheidari 2012**	Additional RT vs CT in acute/subacute stage	statistically significant improvement in experimental group p=0,01	0%	3 (106)
Motor Recovery	FM-UE	**Norouzi-Gheidari 2012**	Additional RT vs CT in chronic stage	NO statistically significant difference between groups p=0,14	N/A	1 (52)
ADL	FIM	**Norouzi-Gheidari 2012**	Additional RT vs CT	NO statistically significant difference between groups p=0,07	77%	3 (106)
ADL	FIM	**Norouzi-Gheidari 2012**	RT vs CT with same duration/intensity	NO statistically significant difference between groups p=0,99	30%	3 (62)
Muscle strength	MPS out of 20	**Norouzi-Gheidari 2012**	Additional RT vs CT	statistically significant improvement in experimental group p< 0,001	0%	2 (76)
Muscle strength	MPS out of 70	**Norouzi-Gheidari 2012**	RT vs CT with same duration/intensity	NO statistically significant difference between groups p=0,56	0%	3 (56)
Motor Control	MSS	**Norouzi-Gheidari 2012**	Additional RT vs CT	statistically significant improvement in experimental group p=0,004	65%	2 (76)
Motor Control	MSS	**Norouzi-Gheidari 2012**	RT vs CT with same duration/intensity	NO statistically significant difference between groups p=0,82	N/A	1 (20)
Motor Recovery	FM-UE	**Norouzi-Gheidari 2012**	RT vs CT with same duration/intensity 6 months Follow-Up	NO statistically significant difference between groups p=0,11	0%	4 (160)
Motor Recovery	FM-UE	**Norouzi-Gheidari 2012**	Additional RT vs CT 8 months Follow-Up	statistically significant improvement in experimental group p=0,03	N/A	1 (30)
Motor Control	FM	**Ferreira 2018**	Robot-assisted therapy vs minimal intervention short term	NO statistically significant difference between groups p>0,05	0%	5 (137)
Motor Control	FM	**Ferreira 2018**	Robot-assisted therapy vs minimal intervention medium term	NO statistically significant difference between groups p>0,05	N/A	1 (19)
Motor Control	FM	**Ferreira 2018**	Robot-assisted therapy vs minimal intervention long term	NO statistically significant difference between groups p>0,05	N/A	1 (12)
Motor Control	FM	**Ferreira 2018**	Robot-assisted therapy vs other intervention short term	statistically significant improvement in experimental group p=0,001	45,68%	17 (595)

Motor Control	FM	**Ferreira 2018**	Robot-assisted therapy vs other intervention medium term	statistically significant improvement in experimental group p=0,01	17,64%	5 (205)
Motor Control	FM, CMSA	**Ferreira 2018**	additional effect of Robot-assisted therapy vs other intervention short term	NO statistically significant difference between groups p=0,23	0%	8 (184)
Motor Control	FM	**Ferreira 2018**	additional effect of Robot-assisted therapy vs other intervention medium term	NO statistically significant difference between groups p=0,39	0%	2 (52)
Spasticity	MAS	**Ferreira 2018**	Robot-assisted therapy vs minimal intervention short term	NO statistically significant difference between groups p=0,25	N/A	1 (30)
Spasticity	MAS	**Ferreira 2018**	Robot-assisted therapy vs other intervention short term	NO statistically significant difference between groups p=0,28	6,96%	6 (281)
Spasticity	MAS	**Ferreira 2018**	Robot-assisted therapy vs other intervention medium term	NO statistically significant difference between groups p=0,71	9,80%	2 (88)
Spasticity	MAS	**Ferreira 2018**	additional effect of Robot-assisted therapy vs other intervention short term	NO statistically significant difference between groups p=0,252	0%	3 (78)
Spasticity	MAS	**Ferreira 2018**	additional effect of Robot-assisted therapy vs other intervention medium term	NO statistically significant difference between groups p=0,076	N/A	1 (30)
Muscle strength	MRC, MPS, MMT, maximum resistive force	**Ferreira 2018**	Robot-assisted therapy vs other intervention short term	statistically significant improvement in experimental group p=0,002	32,08%	6 (203)
Muscle strength	MRC, MPS range 0-70	**Ferreira 2018**	Robot-assisted therapy vs other intervention medium term	NO statistically significant difference between groups p=0,474	0%	3 (110)
Muscle strength	MRC	**Ferreira 2018**	additional effect of Robot-assisted therapy vs other intervention short term	NO statistically significant difference between groups p=0,863	0%	1 (28)
Range of motion	goniometer, WAM control program, mean distance between a marker placed on the participant's wrist and five targets	**Ferreira 2018**	Robot-assisted therapy vs other intervention short term	NO statically significant difference between groups p=0,705	0%	3 (104)
Pain	VAS, Pain Scale of Fugl-Meyer, Chedoke McMaster Stroke Assessment Pain Inventory Scale	**Ferreira 2018**	Robot-assisted therapy vs other intervention short term	NO statistically significant difference between groups p=0,413	0%	5 (132)

Pain	VAS, Pain Scale of Fugl-Meyer, Chedoke McMaster Stroke Assessment Pain Inventory Scale	**Ferreira 2018**	Additional effect of Robot-assisted therapy vs other intervention short term	NO statistically significant difference between groups p=0,615	N/A	1 (20)
Functional Independence	N/A	**Dixit & Tedla 2019**	N/A	N/A	N/A	N/A
Motor Control	N/A	**Dixit & Tedla 2019**	N/A	N/A	N/A	N/A
Quality of Life	N/A	**Dixit & Tedla 2019**	N/A	N/A	N/A	N/A
Motor Function	N/A	**Kim 2017**	N/A	N/A	N/A	N/A
ADL	N/A	**Kim 2017**	N/A	N/A	N/A	N/A
Motor control	FMA	**Peter 2011**	Robot-assisted therapy vs conventional therapy	FMA was used in 27 trial and showed statistically significant differences in motor function in 24 cases of these	N/A	24 (N/A)
Motor Control	MSS	**Peter 2011**	Robot-assisted therapy vs conventional therapy	MSS was applied in 13 trials, 10 of which showed significant changes	N/A	10 (N/A)
Motor Control	MP, MRC	**Peter 2011**	Robot-assisted therapy vs conventional therapy	MP/MRC were use in 13 trials and showed significant improvements in nine of these	N/A	9 (N/A)
Function	FIM	**Peter 2011**	Robot-assisted therapy vs conventional therapy	FIM was the main instrument of measure. Ten trials used these scales and there was significant change in five cases.	N/A	10 (N/A)
Function	Arm Motor Ability Test, Rancho Los Amigos Functional Test	**Peter 2011**	Robot-assisted therapy vs conventional therapy	The Arm Motor Ability Test was used in one trial, it changed significantly. Rancho Los Amigos Functional Test was performed in one trial; there was no significant change.	N/A	2 (N/A)
Spasticity	MAS	**Peter 2011**	Robot-assisted therapy vs conventional therapy	Spasticity showed a significant decrease in the experimental groups in nine trials.	N/A	9 (N/A)
Motor recovery	FM	**Prange 2006**	Robot-assisted therapy vs conventional therapy	From qualitative analysis robot-aided therapy improves several motor-control aspects (e.g., muscle activation patterns, selectivity, and speed of movement) and has long term effects of several months to several years, as measured at follow-up	N/A	8 (N/A)
Motor recovery	FM	**Prange 2006**	Robot-assisted therapy vs conventional therapy in chronic stroke	From quantitative analysis robot-aided therapy positively influenced FM scores p<0,05.	N/A	2 (70)

				statistically significant 6% increase in motor control after robot-aided therapy		
Functional abilities	FIM	**Prange 2006**	Robot-assisted therapy vs conventional therapy	No consistent influence of robot-aided therapy on improvement of functional abilities could be detected from the qualitative analysis	N/A	2 (57)
Impairments and activity	FMA, FIM	**Hayward 2011**	RT in proximal UL vs control intervention in acute phase	there is strong evidence that robotic therapy reduces impairments and increases activity of the proximal UL in stroke survivors with moderate to severe paresis	N/A	4 (115)
Impairments and activity	FMA, FIM	**Hayward 2011**	RT in proximal UL vs conventional therapy in subacute/chronic phase	limited evidence for stroke survivors with mild, moderate or severe paresis	N/A	2 (57)
Impairments and activity	FMA, FIM	**Hayward 2011**	RT in distal UL vs control intervention in subacute phase	limited evidence that robotic therapy reduces impairments in stroke survivors with subacute and severe paresis and no evidence that it improves activity	N/A	1 (39)
activity	ARAT	**Hayward 2011**	RT in proximal UL vs conventional therapy	There is no evidence that robotic therapy increases use of the arm in everyday tasks for either proximal or distal robotic therapy devices	N/A	1 (21)
Motor recovery	FM, CMSA	**Kwakkel 2008**	Robot assisted therapy vs conventional therapy	An overall statistically non-significant heterogeneous SES was found in favour of the robot-assisted therapy. p= 0,06	N/A	9 (218)
ADL	FIM	**Kwakkel 2008**	Robot assisted therapy vs conventional therapy	None of the studies reported significant effects for ADL in favour of the experimental group. P>0,05	N/A	5 (139)
Motor Recovery	FM-UE	**Wolf 2014**	Combined- Robot assisted therapy vs conventional therapy	RAT-C group had significantly greater reductions in impairments (proximal UEFM) than the conventional therapy group (P < .05), but these differences were not retained at 6 months	N/A	1 (30)
Motor Recovery	FM-UE	**Wolf 2014**	Bilateral- Robot assisted therapy vs conventional therapy	The RAT-B group demonstrated the least reduction in impairments, with the smallest gains in proximal and distal UEFM (no P values reported)	N/A	1 (30)

Motor Recovery	FM-UE	**Wolf 2014**	Bilateral- Robot assisted therapy vs conventional therapy	significant improvements in the subjects' UEFM from pre-test to post-test scores at 8 weeks (P < .001), but not between post-test and retention scores at 16 weeks (no P value reported)	N/A	1 (20)
Spasticity	MAS	**Wolf 2014**	Bilateral- Robot assisted therapy vs conventional therapy	NO statistically significant difference p=0,31	N/A	1 (20)
ADL	FAT	**Wolf 2014**	Bilateral- Robot assisted therapy vs conventional therapy	activity measure did not significantly change pre to post p= 0,33	N/A	1 (20)
ADL	FIM	**Wolf 2014**	Unilateral-Robotic or Combine robotic vs conventional therapy	FIM showed the least benefit as compared with combined, unilateral, or conventional interventions	N/A	1 (30)
Motor Recovery	FMA	**Lin 2018**	Robot-assisted training vs conventional therapy	statistically significant difference p= 0,0006	0%	5 (187)
Motor Recovery	FMA	**Lin 2018**	Robot-assisted training vs conventional therapy	NO statistically significant difference p=0,45	57%	10 (434)
Arm Function	ARAT, FMA	**Da Silva 2018**	Self-directed RT vs N/A	NO statistically significant difference p=0,80	76%	4 (171)
Arm use in ADL	MAL "amount of use scores"	**Da Silva 2018**	Self-directed RT vs N/A	NO statistically significant difference p=0,62	N/A	1 (19)
Arm use in ADL	MAL "quality of use scores"	**Da Silva 2018**	Self-directed RT vs N/A	No statistically significant difference p=0,07	41%	2 (35)
Subluxation reduction	non-radiological physical measurement (in mm)	**Arya 2017**	Linear robotic movement of the affected side with visual feedback on a screen	significant reduction of the subluxation	N/A	1 (18)
Improving coordination of reach to grasp after stroke	N/A	**Pelton 2012**	functional-based robot training vs impairment-based robot training.	Speculate that until a minimum set of abilities are present, robotic training might serve a patient best if it focuses on impairment reduction, leaving it to integrate motor gains into function during a later phase of treatment	N/A	1 (47)
Improving coordination of reach to grasp after stroke	Timing of hand opening relative to hand displacement. Coordination between timing of onset of arm movement and forearm pronation	**Pelton 2012**	computerised virtual reality exercise system (VE) with instrumented gloves, no control group	This experimental study without controls found more appropriate integration between hand shaping and arm transport after VE-based sensorimotor rehabilitation. Subject-specific benefits to hand and arm coordination during reach to grasp were reported following the experimental intervention	N/A	1 (8)

Improving coordination of reach to grasp after stroke	Time(s) after peak finger extension velocity	**Pelton 2012**	computerised virtual reality exercise system (VE) with instrumented gloves, no control group	Authors found no clinically significant improvements after robot-assisted VE therapy to the time(s) after peak finger extension velocity with robot-assisted therapy. the authors found the benefit of robot, VE therapy to improvements in hand and arm coordination to be inconclusive.	N/A	1 (8)

Abbreviations: ADL= activities of daily living; ARAT= Action Research Arm Test; CMSA= Chedoke-McMaster Stroke Assessment; BI= Barthel Index; FIM= Functional Independence Measure; FAT= Frenchay Arm Test; FMA= Fugl-Meyer Assessment; FMA-SEC= Fugl-Meyer Assessment shoulder/elbow coordination; FMA-WH= Fugl-Meyer Assessment wrist/hand; FM= Fugl-Meyer; FM-UE= Fugl-Meyer Upper Extremity; MAL= Motor Activity Log; MAL-QOM= Motor Activity Log- Quality of Movement; MAS= Modified Ashworth Scale; MI= Motricity Index; MMT= Manual Muscle Testing; MPS= Motor Power Scale; MRC= Medical Research Council; mRS= modified Rankin Scale; MSS= Motor Status Scale; N/A= not available; VAS= Visual Analogue Scale.

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Effectiveness of Robot-assisted Arm Therapy in Stroke Rehabilitation: an Overview of Systematic Reviews.

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Authors' contributions

SS, LB, MB, CA and SGL conceptualized paper and performed and/or supervised research. SS and LB drafted manuscript; MB and SS performed quality assessment of the systematic reviews; GM and SS, as organization committee and scientific technical committee of the CICERONE consensus conference supervises research, read and corrected manuscript. All authors read and approved the final version of the manuscript.