



# Robot-Assisted Therapy for Upper Extremity Motor Impairment After Stroke: A Systematic Review and Meta-Analysis

Jingyi Wu, BSc<sup>1,2</sup>, Hao Cheng, BSc<sup>1,2,†</sup>, Jiaqi Zhang, MSc<sup>3,†</sup>, Shanli Yang, MD<sup>1,2</sup>, Sufang Cai, MSc<sup>1,2,\*</sup>

<sup>1</sup>Rehabilitation Hospital affiliated to Fujian University of Traditional Chinese Medicine, Fuzhou, Fujian, China
 <sup>2</sup>Fujian Key Laboratory of Rehabilitation Technology, Fuzhou, Fujian, China
 <sup>3</sup>Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, Hong Kong SAR, China
 \*Address all correspondence to Mrs. Cai at sufang\_kangfu01@163.com or Mr. Zhang at jack-jq.zhang@connect.polyu.hk

<sup>+</sup>H. Cheng and J. Zhang contributed equally to this work.

# Abstract

**Objective.** The purpose of this study was to review the effects of robot-assisted therapy (RT) for improving poststroke upper extremity motor impairment.

**Methods.** The PubMed, Embase, Medline, and Web of Science databases were searched from inception to April 8, 2020. Randomized controlled trials that were conducted to evaluate the effects of RT on upper extremity motor impairment poststroke and that used Fugl-Meyer assessment for upper extremity scores as an outcome were included. Two authors independently screened articles, extracted data, and assessed the methodological quality of the included studies using the Physiotherapy Evidence Database (PEDro) scale. A random-effects meta-analysis was performed to pool the effect sizes across the studies.

**Results.** Forty-one randomized controlled trials with 1916 stroke patients were included. Compared with dose-matched conventional rehabilitation, RT significantly improved the Fugl-Meyer assessment for upper extremity scores of the patients with stroke, with a small effect size (Hedges g = 0.25; 95% Cl, 0.11-0.38;  $l^2 = 45.9\%$ ). The subgroup analysis revealed that the effects of unilateral RT, but not that of bilateral RT, were superior to conventional rehabilitation (Hedges g = 0.32; 95% Cl, 0.15-0.50;  $l^2 = 55.9\%$ ). Regarding the type of robot devices, the effects of the end effector device (Hedges g = 0.22; 95% Cl, 0.09–0.36;  $l^2 = 35.4\%$ ), but not the exoskeleton device, were superior to conventional rehabilitation. Regarding the stroke stage, the between-group difference (ie, RT vs convention rehabilitation) was significant only for people with late subacute or chronic stroke (Hedges g = 0.33; 95% Cl, 0.16-0.50;  $l^2 = 34.2\%$ ).

**Conclusion.** RT might be superior to conventional rehabilitation in improving upper extremity motor impairment in people after stroke with notable upper extremity hemiplegia and limited potential for spontaneous recovery.

Keywords: Stroke, Upper Extremity, Unilateral/Bilateral Robot-Assisted Therapy, Meta-Analysis, Randomized Controlled Trial

Received: April 30, 2020. Accepted: December 6, 2020

© The Author(s) 2021. Published by Oxford University Press on behalf of the American Physical Therapy Association. All rights reserved. For permissions, please e-mail: journals.permissions@oup.com

#### Introduction

Stroke is one of the most common causes of adult-onset neurological disability.<sup>1</sup> According to the Global Burden of Disease study in 2016,<sup>2</sup> stroke is one of the leading causes of the loss of disability-adjusted life-years worldwide. Upper extremity hemiplegia is the most common and stable symptom of stroke survivors.<sup>3</sup> Physical therapy and occupational therapy interventions delivered by therapists are the mainstream rehabilitation treatments for poststroke upper extremity motor impairment. Various rehabilitation approaches focusing on upper extremity motor rehabilitation, such as constraintinduced movement training, task-oriented training, mental practice, and mirror therapy, have been widely applied in clinical practice.<sup>3</sup> Robot-assisted therapy (RT) has been developed as an approach for hemiplegia rehabilitation in the upper extremities in recent decades.<sup>4</sup> RT is defined as "an electronic computer-controlled system that can be used with a device to assist in functional rehabilitation of humans; these can be divided into therapeutic and assistive robots."5 Compared with conventional therapist-led rehabilitation, RT can provide high-intensity, repetitive, and highly reproducible motor training to facilitate the restoration of hemiplegic upper extremity function and neuroplasticity after stroke.<sup>6</sup>,

Therapeutic robots can be broadly categorized into end effector and exoskeleton devices. An end effector device is a tool that interacts with the environment and connects to the individual at a solitary point, whereas an exoskeleton device is connected to the individual at multiple points that match the joint axes.<sup>8</sup> In clinical practice, RT is used on the paretic arm only or both arms and is therefore referred to as unilateral robot-assisted therapy (URT) or bilateral robot-assisted therapy (BRT), respectively. URT aims to train the hemiplegic arm through repeated active or passive exercise. Turner et al<sup>9</sup> reported that URT was associated with the activation of the ipsilesional primary motor cortex in stroke patients, consequently facilitating the recovery of upper extremity motor impairment. BRT aims to train both arms, with the most impaired arm mimicking the unimpaired or less impaired arm to perform synchronous movements assisted by the robot device.<sup>10</sup> Studies have also examined the usefulness of bilateral asymmetrical movements for stroke rehabilitation, although these are seldom practiced with robotic devices.

Some researchers postulate that bilateral arm training is superior to unilateral arm training in improving hemiplegic arm function. Indeed, some studies with functional magnetic resonance imaging<sup>11,12</sup> showed that the effect of bilateral arm training may be superior to that of unilateral arm training in terms of activating the ipsilesional primary motor cortex and supplementary motor area, thus rebalancing the abnormal interhemispheric transcallosal inhibition caused by stroke. Such movement also improves interlimb coordination and enhances intra- and interhemisphere coupling. With the support of the bilateral recovery theory, BRT has been developed and applied in several clinical studies with stroke patients.<sup>13–15</sup>

Previous reviews investigated the effects of RT in upper extremity motor rehabilitation. A review conducted by Veerbeek et al<sup>16</sup> in 2016 showed that RT significantly improved Fugl-Meyer assessment for upper extremity (FMA-UE) scores, and subgroup analyses revealed that the type of robot device, stroke stage, and the type of control therapy may impact the effect size. Similar results were found in a Cochrane review conducted by Mehrholz et al,<sup>17</sup> in which high-level evidence was found to support the effects of electromechanical and RT for improving hemiplegic arm functions, as measured with the FMA-UE scores, in stroke patients. However, neither review included statistical comparisons between the different subgroups. Another meta-analysis by Zhang et al<sup>18</sup> was also published on this topic; however, various outcome measurements may lead to high heterogeneity among their analyses. Because a substantial number of studies have been published in this area, it is time to conduct detailed subgroup analyses with appropriate statistical comparisons to examine the potential influence of the patient characteristics and the interventional methodology on the treatment effect.

Thus, the objective of the present review was to answer the following questions: (1) Does RT have a superior effect on the improvement of upper extremity motor impairment in stroke patients compared with the conventional, therapist-led rehabilitation training, in terms of short-term (immediately after intervention) or long-term (follow-up) outcomes? (2) Is there any difference in effects between BRT and URT? (3) Could the patient characteristics such as stroke stage or the baseline level of upper extremity motor impairment measured with the FMA-UE scores<sup>19,20</sup> influence the effect size associated with the treatment? Finally, (4) could the type of robot device (e.g., end effector or exoskeleton) influence the effect sizes associated with the treatment? By answering these questions, this review aims to provide an overall picture of the currently available evidence regarding the clinical application of RT in poststroke upper extremity rehabilitation.

#### Methods

#### Data Sources and Search Terms

This review was performed in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).<sup>21</sup> Two authors (J.W. and H.C.) independently searched the PubMed, Embase, Medline, and Web of Science databases to identify any randomized controlled trials (RCTs) about the effects of RT on the rehabilitation of upper extremity motor impairment in patients with stroke. Studies were collected from inception up to April 8, 2020. In each database, the search was conducted using a combination of the keywords: "stroke OR hemiplegic OR paresis OR cerebrovascular disorder OR cerebrovascular accident" AND "upper limb OR upper extremity OR arm OR forearm OR hand OR shoulder OR elbow" AND "robot-assisted OR robotics OR exoskeleton OR robotic aided OR robot assisted OR robotic device" AND "randomized controlled trial OR controlled trial." These terms were searched for in the whole article. Any disagreement was settled by discussion with the third author (J.Z.). The detailed search strategy is presented in Supplementary Table 1.

#### Study Selection

Studies that met all of the following criteria were included in this review: (1) studies designed as an RCT with either a crossover or parallel design; (2) studies with participants who were adults (aged over 18 years) diagnosed as having a unilateral hemispheric stroke; (3) studies that used a robotassisted device for intervention; (4) studies with at least 1 control group in which participants received dose-matched conventional physical/occupational therapy led by therapists (the experimental and control groups had equal treatment times); and (5) studies that used the FMA-UE scores to assess hemiplegic upper extremity impairment, which is the most widely used primary outcome of patients with poststroke upper extremity motor impairment.<sup>22</sup> We restricted the outcome of interest to hemiplegic upper extremity impairment because it could reduce the potential heterogeneity during the subgroup analyses and statistical comparisons among different subgroups.

Studies that met any of the following criteria were excluded from this review: (1) studies published as conference abstracts, conference proceedings, or research protocols; (2) studies in which the reported data were insufficient for effect size calculation; (3) studies that used similar robot devices for intervention in both groups, except for those that compared BRT and URT, or end effector and exoskeleton devices; (4) studies that combined RT with other interventional modalities such as functional electrical stimulation, transcutaneous electrical nerve stimulation, or noninvasive brain stimulation; (5) studies that were not published in the English language (the English language restriction did not significantly affect the results of the meta-analysis, as demonstrated in a previous study<sup>23</sup>); and (6) non-RCTs or single-group pre/post-repeatedmeasures studies.

#### **Data Extraction**

After identifying the relevant studies, 2 authors (J.W. and H.C.) independently extracted the following information from each article: (1) the first author and publication year; (2) the characteristics of the participants (eg, age, time since stroke, and baseline motor impairment level); (3) the intervention in both groups, including the involved body parts in the RT (U = unilateral arm, B = bilateral arm), the joints involved in the RT (ie, whole upper extremity, shoulder/elbow, or forearm/wrist/hand), type of robot device (ie, exoskeleton or end effector robotic device), and intervention duration; and (4) the short- and long-term outcome data, including the mean and SD for each group. When the SDs were not available, estimates were made based on the sample size, median, interquartile range,<sup>24–27</sup> 95% CI,<sup>20,28</sup> SE,<sup>29,30</sup> and correlation coefficient (r).<sup>13–15,31–41</sup> For calculating the SD of the change in scores, we initially used a r of 0.8. Subsequently, different levels of r (0.3 and 0.5) were replaced in the calculation to examine the robustness of our results as a sensitivity analysis.<sup>42</sup> Any disagreement was settled by discussion with the third author (J.Z.).

#### **Quality Assessment**

The methodological quality of the included studies was independently assessed by 2 authors using the Physiotherapy Evidence Database (PEDro) scale. The items in the PEDro scale include random allocation, concealment of allocation, baseline equivalence, blinding procedure, intention-to-treat analysis, adequate follow-up, between-group statistical analysis, measurement of data variability, and point estimates. A PEDro score greater than or equal to 6 indicated good methodological quality.<sup>43</sup> We removed studies with a PEDro score less than 6 after every primary meta-analysis to test the robustness of the results, as another sensitivity analysis.

#### Data Synthesis and Analysis

Stata version 15.0 software (StataCorp LLC., College Station, TX, USA) was used for the meta-analysis, and Comprehensive

Meta-Analysis version 3.0 software (Biostat, Englewood, NJ, USA) was used for the statistical analysis, including metaregression and the *Q* test for the between-subgroup variance. The Hedges g was used to calculate the effect size, because it could correct the potential bias caused by studies with small sample size. A random-effects meta-analysis was performed because of the obvious clinical and methodological heterogeneity among the included studies.44 Between-study heterogeneity was examined using the Higgins  $I^2$  statistic. Studies with an  $I^2$  of 25%-50% were considered to have low heterogeneity, and those with an  $I^2$  of 50% to 75% and greater than 75% were considered as having moderate and high levels of heterogeneity, respectively.<sup>45</sup> Publication bias was assessed using funnel plots and Egger tests. Subgroup analyses were used to examine the moderating effects of the RT design (ie, URT vs BRT), type of robot device (ie, end effector vs exoskeleton), stroke stage (ie, <3 months vs  $\geq 3$  months, or <6 months vs  $\geq 6$  months),  $^{46}$  and baseline severity of arm hemiplegia (ie, mildly impaired: FMA-UE score >50; moderately impaired: FMA-UE score 18-50; and severely impaired: FMA-UE score < 18).<sup>19,20</sup> After the subgroup analyses, we further performed a Q test based on the analysis of variance to test the between-subgroup portion of the variance.<sup>47</sup> The potential dose-dependent effect of the RT was assessed using a univariable meta-regression. In the meta-regression, we treated the total training time, the number of training sessions, and average training time per session as the independent variables, and effect size as the dependent variable. Because the dose is likely to be an important modulator of the treatment effects, we further included significant dose parameters and categorical variables in the multivariable meta-regression model, when appropriate. The statistical threshold was set at P < .05 (2-tailed), with the exception that a threshold of P < .1 (2-tailed) was used for the Egger test.48

#### Role of the Funding Source

This work was supported by the Central Guide to Local Science and Technology Development (grant no. 2018 L3009) and the Science and Technology Platform Construction Project of the Fujian Science and Technology Department (grant no. 2015Y2001–40). This funding source had no role in the design of this study, its execution, analyses, interpretation of the data, or decision to submit results

#### Results

### **Study Selection**

The search resulted in 1018 citations. After removing duplicates, 548 records were screened, of which 356 citations were excluded for the following reasons: the studies were irrelevant (n = 233); the studies were reviews or meta-analyses (n = 29); the studies focused on infants, children, or adolescents (n = 19); technical papers (n = 64); or the studies enrolled healthy individuals exclusively (n = 11). The remaining 192 articles were subjected to full-text screening, of which 151 were removed for the following reasons: RCTs applied similar RTs in both the experiment and control groups (n = 17); the studies were not designed as RCTs (n = 44); the reported data for the meta-analysis were insufficient (n = 7); the studies were conference abstracts or study protocols (n = 19); the studies did not use FMA-UE scores as the outcome (n = 15); the studies compared brain-computer interfaceguided/electronic-based/electromyography-driven RT with pure RT (n = 36); or the studies did not use a dose-matched conventional rehabilitation as the control or used different conventional rehabilitations in the experiment and control groups (n = 13). Finally, 41 studies with 1916 stroke patients satisfied the inclusion criteria and were included in the present systematic review. Supplementary Figure 1 shows the flowchart of the study selection, and the characteristics of the included studies are presented in Supplementary Table 2. The methodological quality of the included studies is presented in Supplementary Table 3.

#### Meta-Analysis

Among the included studies, 34 compared the effect of RT and dose-matched conventional rehabilitation<sup>14,15,20,24,26–28</sup>, <sup>30–41,49–62</sup> (except in 1 study, the duration in the control group seemed to be longer than that in the RT group<sup>63</sup>). Three studies had 3 groups, namely, the BRT, URT, and dose-matched conventional rehabilitation, and we therefore divided the comparisons into 2 units of analysis.<sup>13,25,64</sup> Two studies compared the effect of the sequential use of BRT and URT with that of dose-matched conventional rehabilitation.<sup>29,65</sup> One study had 4 groups, namely, the combined URT and BRT, URT, BRT, and dose-matched conventional rehabilitation and therefore, the comparisons were divided into 3 units of analysis.<sup>66</sup> One study directly compared the effects of BRT and dose-matched URT without conventional rehabilitation.<sup>67</sup>

Seventeen studies were included to estimate both the shortterm effects immediately after the intervention and the longterm retention effects at follow-up (mean [SD] = 22.0 [7.4] weeks). When a study had several follow-up time points, the longest one was selected, <sup>24,26,27,29,30,34,39–41,50,51,53–55,59</sup>,  $^{65,66}$  and 24 studies only estimated the short-term effects immediately after the intervention.  $^{13-15,20,25,28,31-33,35-38}$ , 49,52,56-58,60-64,67 A statistically significant difference was observed in favor of RT over conventional rehabilitation immediately after the training (n = 1906; Hedges g = 0.25; 95% CI, 0.11–0.38;  $P < .001; I^2 = 45.9\%$  (Fig. 1) but not at the follow-up assessment (n = 897; Hedges g = 0.16; 95% CI, -0.03 to 0.34; P = .092;  $I^2 = 26.9\%$ ) (Supplementary Figure 2). No evidence of publication bias was found in the retention effects (P = .31) among the included studies, but we found a publication bias immediately after intervention (P = .04), as suggested by the Egger test (Supplementary Figures 3 and 4).

#### **Meta-Regression With Dose Parameters**

In the meta-regression with dose parameters, total training time, number of training sessions, and average training time per session were not significantly associated with the effect sizes in the short term (P = .127, .717, and .079, respectively) and long term (P = .878, .978, and .093, respectively).

#### Subgroup Meta-Analysis

This study then analyzed 5 subgroups based on the type of RT (i.e., URT, BRT, or combined URT and BRT), stroke stage (using either 3 or 6 months as the cutoff value), baseline motor impairment level (ie, moderate to severe or mild to moderate), type of robot device (ie, end effector or exoskeleton), and trained part (ie, proximal or distal joints). Owing to the limited number of studies with follow-up assessments, the

subgroup analyses were performed on the basis of the effects immediately after RT.

# Comparison of URT/BRT With Conventional Rehabilitation

In total, 33 units of analysis compared URT with conventional rehabilitation, 14 units of analysis compared BRT with conventional rehabilitation, and 3 units of analysis compared combined URT and BRT with conventional rehabilitation. The results indicated that URT was superior to conventional rehabilitation (n = 1548; Hedges g = 0.32; 95% CI, 0.15– 0.50; P < .001;  $I^2 = 55.9\%$ ).<sup>13,20,24–28,30,31,35,36,38–40</sup>, <sup>49-64,66</sup> When BRT was compared with conventional rehabilitation, the overall effect was not significant (n = 312; Hedges g = 0.07; 95% CI, -0.15 to 0.28; P = .542;  $I^2 = 0\%$ ).<sup>13-15,25,32-34,37,41,64,66</sup> Combined URT and BRT was also not superior to conventional rehabilitation (n = 80;Hedges g = 0.22; 95% CI, -0.71 to 1.15; P = .645;  $I^2 = 74.5\%$  (Fig. 1).<sup>29,65,66</sup> No statistically significant difference was detected by the Q test when either 2 subgroups (ie, URT and BRT) (Q = 2.46; P = .12) or 3 subgroups (ie, URT, BRT, and URT plus BRT) (Q = 2.48; P = .29) were compared.

#### Comparison of URT and BRT

Five studies directly compared the effects of BRT with those of URT.<sup>13,25,64,66,67</sup> The results showed that URT was better than BRT in terms of improved FMA-UE scores (n = 68; Hedges g = -0.53; 95% CI, -1.02 to -0.04; P = .035;  $I^2 = 0\%$ ) (Fig. 2).

#### Influence of Stroke Stage

The subgroup analysis based on 35 studies revealed that RT significantly improved the FMA-UE scores in patients who had had a stroke at least 3 months before the assessment (n = 809; Hedges g = 0.33; 95% CI, 0.16–0.50; P < .001;  $I^2 = 34.2\%$ )<sup>13–15,20,25,27,30,32,33,36,38,41,49–52,54–57,59,63–65</sup> but not in those who had had a stroke less than 3 months before (n = 457; Hedges g = 0.21; 95% CI, -0.12 to 0.54; P = .220;  $I^2 = 64.8\%$ ) (Fig. 3).<sup>24,26,29,31,34,35,40,53,58,60,61</sup> Similarly, when using 6 months as the cutoff, RT significantly improved the FMA-UE scores in patients who had had a stroke at least 6 months before the assessment (n = 826; Hedges g = 0.26; 95% CI, 0.12–0.41; P < .001;  $I^2 = 2.3\%$ )<sup>13–15,20,25,27,30,32,33,36,38,41,49–52,56,57,59,64,65</sup> but not in those who had had a stroke less than 6 months before (n = 518; Hedges g = 0.17; 95% CI, -0.08 to 0.42; P = .177;  $I^2 = 53.2\%$ ).<sup>24,26,28,29,31,34,35,37,40,53,58,60,61,66</sup> However, no statistically significant difference between the subgroups was detected by the Q test when either 3 months (P = .473) or 6 months (P = .471) was used as the cutoff.

#### Influence of Baseline Motor Impairment Level

We found that RT significantly improved the FMA-UE scores in the patients with moderate to severe motor impairment, compared with the control (n = 1295; Hedges g = 0.27; 95% CI, 0.08–0.46; P = .004;  $I^2 = 53.0\%$ ).<sup>24–26,29–31,34–36,38,39</sup>, <sup>49–57,59,61,64–66</sup> However, no significant between-group difference (RT vs control) was identified in the patients with mild to moderate motor impairment (n = 316; Hedges g = 0.19; 95% CI, -0.01 to 0.40; P = .063;  $I^2 = 0\%$ )

Lum et al. 2002 Lum et al. 2006 Burgar et al. 2011 Subtotal (l-squared = 74.5%, p = 0.020) - Ulaterial robot-assisted Lum et al. 2006 Housman et al. 2007 Rabadi et al. 2008 Housman et al. 2007 Rabadi et al. 2008 Housman et al. 2007 Rabadi et al. 2008 Corncy et al. 2011 Conroy et al. 2012 Subtotal (l-squared = 55.9%, p = 0.020) - Elabor et al. 2019 Capited at al. 2016 Capited at al. 2017 Takabadi et al. 2016 Capited at al. 2016 Capited at al. 2018 Capited at al. 2018 Capited at al. 2019 Capited Capited at al. 2019 Capited at al. 2	Study ID	Hedges' g (95% CI)	% Weight
Lum et al. 2006 Burgar et al. 2011 Subtoal (I-squared = 74.5%, p = 0.020) Uilateral robot-assisted Lum et al. 2006 Housman et al. 2007 Anabadi et al. 2007 Anabadi et al. 2008 Use et al. 2018 Corroy et al. 2014 Corroy et al. 2018 Corroy et al. 2014 Corroy et al. 2014 Corroy et al. 2014 Corroy et al. 2014 Corroy et al. 2016 Corroy et al. 2014 Corroy et al. 2016 Corroy et al. 2017 Corroy et al. 2018 Corroy et al. 2014 Corroy et al. 2016 Corroy et al. 2018 Corroy et al. 2019 Corroy corroy Corrow corroy Corrow corrow cor	Uilateral+Bilateral robot-assisted		
Burgar et al. 2011 Burgar et al. 2014 Lum et al. 2005 Housman et al. 2007 Rabadi et al. 2008 Housman et al. 2007 Housman et al. 2007 Housman et al. 2007 Housman et al. 2008 Housman et al. 2009 Correy et al. 2012 Wage et al. 2014 Masiero et al. 2014 Kamroth et al. 2014 Kamroth et al. 2014 Housh et al. 2015 Susanto et al. 2014 Kamroth et al. 2015 Housh et al. 2016 Hube et al. 2018 Hube	Lum et al. 2002	• 0.81 (0.02, 1.60)	1.86
Subtoral (I-squared = 74.5%, p = 0.020) Uitater al 2006 Housman et al. 2007 Habei et al. 2008 Housman et al. 2007 Habei et al. 2008 Housman et al. 2007 Habei et al. 2008 Housman et al. 2008 Housman et al. 2007 Habei et al. 2008 Housman et al. 2008 Housman et al. 2008 Housman et al. 2008 Housman et al. 2007 Habei et al. 2018 Cornory et al. 2011B Cornory et al. 2011B Cornory et al. 2011B Cornory et al. 2014 Housman et al. 2015 Housman et al. 2016 Tormo et al. 2017 Habeh et al. 2018 Carbor et al. 2018 Habeh et al. 2018 Habeh et al. 2018 Habeh et al. 2018 Carbor et al. 2017 Habeh et al. 2018 Carbor et al. 2018 Carbor et al. 2017 Habeh et al. 2018 Carbor et al. 2019 Carbor et al. 2017 Habeh et al. 2018 Habeh	Lum et al. 2006a	0.54 (-0.49, 1.58)	1.28
Uilleteral robot-assisted       0.53 (0.52, 1.59)       1.24         Lum et al. 2007       0.38 (0.44, 1.15)       1.25         Rabadi et al. 2008       0.22 (1.66, 0.60)       1.61         Voge et al. 2001       0.21 (0.65, 1.59)       1.24         Massino et al. 2011       0.21 (0.65, 1.59)       1.24         Cornoy et al. 2011       0.21 (0.65, 1.59)       1.24         Massino et al. 2014       0.41 (0.13, 0.66)       1.67         Aring et al. 2014       0.49 (0.15, 1.56)       1.22         Massino et al. 2014       0.49 (0.63, 1.55)       1.27         Massino et al. 2014       0.66 (0.76, 0.62)       1.37         Aring et al. 2014       0.51 (0.52, 1.59)       1.27         Massino et al. 2014       0.51 (0.53, 1.55)       1.27         Massino et al. 2015       0.54 (0.11, 0.9)       2.77         Massino et al. 2015       0.54 (0.00, 0.93)       3.18         Daumoravicience et al. 2016       0.44 (0.33, 1.14)       2.66         Calabo et al. 2017       0.33 (0.44, 0.38)       3.49         Daumoravicience et al. 2018       0.44 (0.33, 1.14)       2.66         Calabo et al. 2019       0.44 (0.33, 1.14)       2.66         Daumoravicience et al. 2017       0.33 (0.44, 0.15)       1.55 <td>Burgar et al. 2011</td> <td>-0.58 (-1.24, 0.08)</td> <td>2.30</td>	Burgar et al. 2011	-0.58 (-1.24, 0.08)	2.30
Lum et al. 2006b Housman et al. 2007 Rabadi et al. 2008 Wope et al. 2008 Housman et al. 2009 Lo et al. 2010 Masiero et al. 2011 Corncy et al. 2011a Corncy et al. 2011a Corncy et al. 2012 Corncy et al. 2014 Ang et al. 2014 Ang et al. 2014 Corncy et al. 2015 Corncy et al. 2015 Corncy et al. 2016 Corncy et al. 2018 Corncy et al. 2019 Corncy et al. 2019 Corncy et al. 2018 Corncy et al. 2019 Corncy et al. 2019 Corncy et al. 2019 Corncy et al. 2018 Corncy et al. 2	Subtotal (I-squared = 74.5%, p = 0.020)	0.22 (-0.71, 1.15)	5.44
Lum et al. 2006b Housman et al. 2007 Rabadi et al. 2008 Wope et al. 2008 Housman et al. 2009 Lo et al. 2010 Masiero et al. 2011 Corncy et al. 2011a Corncy et al. 2011a Corncy et al. 2012 Corncy et al. 2014 Ang et al. 2014 Ang et al. 2014 Corncy et al. 2015 Corncy et al. 2015 Corncy et al. 2016 Corncy et al. 2018 Corncy et al. 2019 Corncy et al. 2019 Corncy et al. 2018 Corncy et al. 2019 Corncy et al. 2019 Corncy et al. 2019 Corncy et al. 2018 Corncy et al. 2	Uilateral robot-assisted		
Housman et al. 2007 Housman et al. 2008 Vippe et al. 2008 Vippe et al. 2009 Housman et al. 2009 Lot et al. 2010 Conroy et al. 2011 Conroy et al. 2011 Conroy et al. 2011 Conroy et al. 2012 Yang et al. 2012 Yang et al. 2014 Arag et al. 2015 Susanto et al. 2015 Susanto et al. 2018 Arachashet et al. 2018 Arachashet al. 2016 Arachashet al. 2018 Branceschini et al. 2019 Branceschini et al. 2019 Branceschini et al. 2019 Branceschini et al. 2019 Branceschini et al. 2018 Capited et al. 2019 Capited et al. 2019 Capited et al. 2019 Capited et al. 2019 Capited et al. 2018 Capited et al. 2019 Capited et al. 2018 Capited et al. 2018 Capited et al. 2019 Capited et al. 2019 Capited et al. 2018 Capited et al. 2018 Capited et al. 2018 Capited et al. 2018 Capited et al. 2019 Capited et al. 2019 Capited et al. 2018 Capited et al. 2018 Capited		0.53 (-0.52, 1.59)	1.24
Rabadi et al. 2008 Housena et al. 2009 Lot at al. 2010 Masiero et al. 2011 Corroy et al. 2011a Corroy et al. 2012 Yang et al. 2012 Yang et al. 2014 Ang et al. 2015 Ang et al. 2015 Ang et al. 2015 Ang et al. 2016 Ang et al. 2018 Ang et al. 2018 Ang et al. 2018 Ang et al. 2018 Ang et al. 2019 Ang et al. 2018 Ang et al. 2019 Ang et al. 2018 Ang	Housman et al. 2007		1.75
Vispe et al. 2008 Housman et al. 2019 Conroy et al. 2011 Conroy et al. 2011 Conroy et al. 2011 Conroy et al. 2011 Conroy et al. 2012 Wang et al. 2012 Wang et al. 2012 Wang et al. 2014 Ang et al. 2015 Subto et al. 2015 Built et al. 2015 Built et al. 2016 Ang et al. 2018 Consol et al. 2017 Ang et al. 2018 Ang et al. 2019 Ang et al. 2018 Ang et al. 2019 Ang et al. 2018 Ang et al. 20	Rabadi et al. 2008		1.61
La et al. 2010 Masiero et al. 2011 Conroy et al. 2011a Conroy et al. 2011a Conroy et al. 2012a Wang et al. 2012a Wag et al. 2012a Wag et al. 2014 Sale et al. 2014 Masiero et al. 2015 Subanto et al. 2015 Subanto et al. 2015 Trance et al. 2016 Corrow et al. 2017 Hashe et al. 2018 Cataloro et al. 2018 Cataloro et al. 2019 Cataloro et al. 2018 Cataloro et al. 2019 Cataloro et al. 2019 Hashe et al. 2019 Dauroraviciene et al. 2019 Dauroraviciene et al. 2019 Dauroraviciene et al. 2019 Dauroraviciene et al. 2019 Hashe et al. 2019 Hashe et al. 2019 Dauroraviciene et al. 2019 Hashe et al. 2019 Hashe et al. 2017 Hashe et al. 2018 Cataloro et al. 2019 Hashe et al. 2019 Hashe et al. 2019 Dauroraviciene et al. 2019 Hashe et al. 2019 Hashe et al. 2017 Hashe et al. 2018 Cataloro bet al. 2019 Hashe et al. 2018 Cataloro bet al. 2019 Hashe et al. 2017 Hashe et al. 2017 Hashe et al. 2018 Hashe et al. 2019 Hashe et al. 2019 Hashe et al. 2017 Hashe et al. 2017 Hashe et al. 2017 Hashe et al. 2018 Hashe et al. 2017 Hashe et al. 2018 Hashe et al. 2019 Hashe et al. 2017 Hashe et al	Vlope et al. 2008		1.67
Masiero et al. 2011 Cornor y et al. 2012 Cornor y et al. 2012 Cornor y et al. 2012 Cornor y et al. 2012 Timmemans et al. 2014 Ang et al. 2013 Timmemans et al. 2014 Ang et al. 2014 Brokaw et al. 2014 Brokaw et al. 2014 Sale et al. 2014 Masiero et al. 2014 Masiero et al. 2014 Masiero et al. 2015 Susanto et al. 2015 Susanto et al. 2016 Takanashi et al. 2016 Takanashi et al. 2017 Haieh et al. 2018 Daunoraviciene et al. 2019 Daunoraviciene et al. 2019 Dauno	Housman et al. 2009	0.43 (-0.29, 1.14)	2.11
Concy et al. 2011a Concy et al. 2011b Beinkensmeyer et al. 2012 Yang et al. 2013a By let al. 2013a By let al. 2014 Ang et al. 2014 Ang et al. 2014 By let al. 2015 By let al. 2015 By let al. 2016 Carpinelia et al. 2018 By let al. 2017 Hsieh et al. 2019 Bother al. 2019 By let al. 2019 By let al. 2019 By let al. 2019 Carpinelia et al. 2016 Carpinelia et al. 2018 By let al. 2017 Hsieh et al. 2019 By let al. 2019 By let al. 2017 Hsieh et al. 2018 Carpinelia et al. 2019 By let al. 2019 By let al. 2017 Hsieh et al. 2019 Carpinelia et al. 2019 By let al. 2019 By let al. 2017 Hsieh et al. 2019 Carpinelia et al. 2019 By let al. 2018 Carpinelia et al. 2019 Hsieh et al. 2019 By let al. 2018 Carpinelia et al. 2019 Hsieh et al. 2019 Carpinelia et al. 2017 Hsieh et al. 2017 Hsieh et al. 2017 Hsieh et al. 2018 Carpinelia et al. 2019 Carpinelia et al. 2019 Carpineli	Lo et al. 2010	-0.01 (-0.42, 0.39)	3.50
Concy et al. 2011b Benkresmeyer et al. 2012 Yang et al. 2013b Timmermans et al. 2014 Ang et al. 2015 Susance et al. 2014 Ang et al. 2015 Builden et al. 2016 Tomic et al. 2017 Hsieh et al. 2018 Builden et al. 2019 Dehem et al. 2019 Dehem et al. 2019 Dehem et al. 2019 Builden et al. 2019 Dehem et al. 2019 Builden et al. 2017 Hsieh et al. 2019 Ang et al. 2018 Ang et al. 2019 Ang et al. 2018 Ang et al. 2017 Ang et al. 2019 Ang et al. 2017 Ang et al. 2018 Ang et al. 2018 An	Masiero et al. 2011	-0.18 (-1.03, 0.68)	1.67
Reinkensmeyer et al. 2012 Yang et al. 2013a By et al. 2013a Ang et al. 2014 Ang et al. 2015 Trances at al. 2014 Ang et al. 2015 Trances at al. 2015 Trance at al. 2017 Hsieh et al. 2018 Daumoraviciene et al. 2018 Daumoraviciene et al. 2019 Praneg et al. 2019 Dehmer et al. 2019 Denmer et al. 2012 Denmer et al. 2014 Denmer et al. 2014 Denmer et al. 2014 Denmer et al. 2014 Denmer et al. 2015 Denmer et al. 2014 Denmer et al. 2015 Denmer et al.	Conroy et al. 2011a		2.39
Yang et al. 2012a Timmermans et al. 2014 Ang et al. 2014 Brokaw et al. 2014 Brokaw et al. 2014 Sale et al. 2014 Missiero et al. 2014 Kiamroth et al. 2015 Susanto et al. 2015 Susanto et al. 2015 Susanto et al. 2015 Susanto et al. 2015 Brokaw et al. 2015 Susanto et al. 2015 Brokaw et al. 2015 Susanto et al. 2015 Brokaw et al. 2016 Transe et al. 2016 Transe et al. 2017 Heish et al. 2018 Brainer et al. 2019 Dehem et al. 2019 Dehem et al. 2019 Dehem et al. 2019 Bialferal robot-assisted Lum et al. 2020 Subtotal (I-squared = 55.9%, p = 0.000) Heish et al. 2012a Heish et al. 2012a Heish et al. 2012a Heish et al. 2012a Heish et al. 2012b Heish et al. 2012b Heish et al. 2012b Heish et al. 2012b Hung et al. 2012a Heish et al. 2012b Heish et al. 2014b Heish et al. 2012b Heish et al. 2017b Heish et al. 2017b	Conroy et al. 2011b		2.36
By et al. 2013b Timmermane tal. 2014 Ang et al. 2014 Sale et al. 2014 Masiero et al. 2014 Masiero et al. 2014 Klamroth et al. 2014 Masiero et al. 2014 Klamroth et al. 2014 Klamroth et al. 2014 Klamroth et al. 2014 Klamroth et al. 2015 Tomic et al. 2015 Takahashi et al. 2016 Tomic et al. 2017 Hsieh et al. 2018 Daunoraviciene et al. 2019 Data 2019 Catabrot et al. 2019 Data 2019 Bilateral robot-assisted Lum et al. 2020 Subtotal (I-squared = 5.9%, p = 0.000) Theisen et al. 2012 Hsieh et al. 2013 Hsieh et al. 2019 Data 2019 Data 2019 Data 2012 Hsieh et al. 2019 Data 2019 Data 2012 Hsieh et al. 2014 Hung et al. 2019 Data 2015 Hsieh et al. 2017 Hsieh et al. 2018 Data 2012 Hsieh et al. 2019 Data	Reinkensmeyer et al. 2012		1.87
Timmerans et al. 2014       0.06 (0.76, 0.92)       1.73         Ang et al. 2014       0.27 (0.08, 1.43)       1.08         Sale et al. 2014       0.27 (0.08, 1.43)       1.08         Masiero et al. 2014       0.27 (0.08, 1.43)       1.08         Viamo et al. 2014       0.44 (0.03, 1.14)       2.06         Masiero et al. 2014       0.47 (0.00, 0.93)       3.18         Prange et al. 2015       -0.27 (1.08, 1.43)       1.08         Susanto et al. 2015       -0.27 (1.00, 0.80)       1.74         Wolf et al. 2015       -0.47 (1.30, 0.30)       1.74         Wolf et al. 2016       -0.38 (0.44, 0.38)       3.49         Takahashi et al. 2018       -0.86 (0.78, 0.22)       1.87         Dauroraviciene et al. 2019       -0.38 (0.44, 0.38)       1.86         Pranceschnic et al. 2019       -0.86 (0.28, 0.18)       1.86         Calabro et al. 2019       -0.86 (0.28, 0.13)       1.87         Calabro et al. 2019       -0.86 (-0.78, 1.51)       2.14         Hung et al. 2019       0.34 (0.26, 0.14)       2.50         Calabro et al. 2012       0.32 (0.15, 0.50)       70.07         Hsieh et al. 2012       0.35 (0.31, 1.01)       2.31         Liao et al. 2012       0.35 (0.31, 1.01)       2.31 <td></td> <td></td> <td></td>			
Ang et al. 2014 Sale et al. 2014 Masiero et al. 2014 Masiero et al. 2014 Masiero et al. 2014 Masiero et al. 2015 Susanto et al. 2015 MoCabe et al. 2015 Tomic et al. 2017 Hsieh et al. 2018 Daunoraviciene et al. 2019 Daunoraviciene et al. 2010 Dilia et al. 2012 Hsieh et al. 2012b Haieh et al. 2012b Haieh et al. 2013 Heisen et al. 2014 Hung et al. 2019 Daunoraviciene et al. 2014 Hung et al. 2019 Daunoraviciene et al. 2019 Daunor			
Brokaw et al. 2014 Brokaw et al. 2014 Masiero et al. 2014 Kiamroth et al. 2014 Kiamroth et al. 2014 Kiamroth et al. 2015 Susanto et al. 2015 Wolf et al. 2015 Tomic et al. 2015 Takahashi et al. 2016 Tomic et al. 2017 Hsieh et al. 2018 Calabrò et al. 2018 Calabrò et al. 2019 Denem et al. 2010 Denem et al. 2019 Denem et al. 2019 Denem et al. 2010 Denem et al. 2019 Denem et al. 2019 Denem et al. 2010 Denem et al. 2019 Denem et al. 2019 Denem et al. 2019 Denem et al. 2019 Denem et al. 2010 Denem et al. 2019 Denem et al. 2010 Denem et a			
Sale et al. 2014 Masiero et al. 2014 Klamroth et al. 2014 Klamroth et al. 2014 Volf et al. 2015 McCabe et al. 2015 McCabe et al. 2015 McCabe et al. 2015 Tanke absi et al. 2016 Tomic et al. 2017 Hsieh et al. 2018 Dehem et al. 2018 Dehem et al. 2019 Franceschini et al. 2019 Dehem et al. 2019 Dehem et al. 2019 Dehem et al. 2019 Bilateral robot-assisted Lum et al. 2012a Wu et al. 2012a Wu et al. 2012a Yang et al. 2012 Hsieh et al. 2012a Wu et al. 2012a Yang et al. 2012 Hsieh et al. 2012a Wu et al. 2012b Hsieh et al. 2012a Wu et al. 2012b Hsieh et al. 2014b Hsieh et al. 2012b Hsieh et al. 2014b Hsieh et al. 2012b Hsieh et al. 2014b Hsieh et al. 2014b Hsieh et al. 2014b Hsieh et al. 2015b Hsieh et al. 2014b Hsieh et al. 2014			
Masiero et al. 2014 Kiamroth et al. 2014 Frange et al. 2015 Susanto et al. 2015 Susanto et al. 2015 Susanto et al. 2015 Tomic et al. 2015 Takahashi et al. 2016 Takahashi et al. 2017 Tomic et al. 2018 Hsieh et al. 2018 Calabró et al. 2019 Daunoraviciene et al. 2019 Daunoraviciene et al. 2019 Daunoraviciene et al. 2019 Daunoraviciene et al. 2019 Dataprotect et al. 2010 Dataprotect et al. 2010 Dataprotect et al. 2010 Dataprotect et al. 2010 Dataprotect et al. 2012 Dataprotect et al. 2014 Hsieh et al. 2012 Dataprotect et al. 2014 Hsieh et al. 2017 Hsieh et al. 2017 Hsieh et al. 2017 Hsieh et al. 2018 Dataprotect et al. 2019 Dataprotect et al. 2014 Hsieh et al. 2017 Hsieh et al. 2017 Hsieh et al. 2017 Dataprotect et al. 2019 Dataprotect et al. 2014 Dataprotect et al. 2019 Dataprotect et al. 2014 Datapro			
Klamoth et al. 2014 Prange et al. 2015 Susanto et al. 2015 Susanto et al. 2015 Susanto et al. 2015 Susanto et al. 2016 Tranic et al. 2017 Hsieh et al. 2018 Calabrò et al. 2018 Calabrò et al. 2019 Randerschini et al. 2018 Calabrò et al. 2019 Randerschini et al. 2019 Randerschini et al. 2019 Branceschini et al. 2010 Branceschini et al. 2012 Branceschini et al. 2012 Branceschini et al. 2014 Branceschini et al. 2012 Branceschini et al. 2014 Branceschini et al. 2012 Branceschini et al. 2012 Branceschini et al. 2014 Brieh et al. 2012 Branceschini et al. 2014 Brieh et al. 2012 Branceschini et al. 2014 Brieh et al. 2014 Brie			
Prange et al. 2015 Susanto et al. 2015 MoCabe et al. 2015 MoCabe et al. 2015 Tomic et al. 2016 Tomic et al. 2017 Hsieh et al. 2018 Daunoraviciene et al. 2018 Calabrò et al. 2019 Pranceschini et al. 2019 Pranceschini et al. 2019 Dehem et al. 2019 Bilateral robot-assisted Lum et al. 2012b Hsieh et al. 2013A Hsieh et al. 2014 Hsieh et al. 2015A Hsieh et al. 2014 Hsieh et al. 2017A Hsieh et al. 2018b Domonov DTE: Weights are from random effects analysis 			
Susamo et al. 2015 McCabe et al. 2015 McCabe et al. 2015 McCabe et al. 2016 Tomic et al. 2017 Hsieh et al. 2018 Daunoraviciene et al. 2018 Calabro et al. 2019 Rodgers et al. 2019 Pranceschini et al. 2019 Dehem et al. 2019 Dehem et al. 2019 Dehem et al. 2019 Dehem et al. 2019 Delem et al. 2019 Delem et al. 2019 Dilateral robot-assisted Lum et al. 2012a Mung et al. 2012b Hsieh et al. 2013a Hsieh et al. 2013a Hsieh et al. 2014b Hsieh et al. 2015b Hsieh et al. 2015b Hsieh et al. 2016b Hsieh et al. 2017b Hsieh et al. 2019a Hsieh et al. 20			
McCabe et al. 2015 Wolf et al. 2015 Takkhashi et al. 2016 Takkhashi et al. 2018 Calabro et al. 2019 Pranceschini et al. 2019 Braneschini et al. 2019 Braneschini et al. 2019 Braneschini et al. 2019 Braneschini et al. 2019 Bilateral robot-assisted Lum et al. 2012b Hsieh et al. 2014b Hsieh et al. 2017b Hsieh et al			
Wolf et al. 2015 Takahashi et al. 2016 Takahashi et al. 2017 Hsieh et al. 2018 Calabrò et al. 2019 Rodgers et al. 2019 Rodgers et al. 2019 Pranceschini et al. 2019 Dehem et al. 2019 Delataral robot-assisted Lum et al. 2012b Hsieh et al. 2011a Hsieh et al. 2012b Hsieh et al. 2013a Hesse et al. 2014 Hsieh et al. 2017a Hsieh et al. 201			
Takahashi et al. 2016       0.31 (-0.22, 0.84)       2.87         Tomic et al. 2017       1.32 (0.46, 2.18)       1.66         Hsieh et al. 2018       0.08 (-0.68, 0.44)       1.95         Daunoravicine et al. 2019       0.23 (-0.56, 1.02)       1.87         Pranceschini et al. 2019       1.64 (-1.87, 0.60)       0.97         Calabrò et al. 2019       0.44 (-0.26, 1.15)       2.14         Dehem et al. 2019       0.44 (-0.26, 1.15)       2.14         Carpinella et al. 2020       0.10 (-0.54, 0.73)       2.40         Subtotal (I-squared = 55.9%, p = 0.000)       0.97       0.36 (-0.78, 1.51)       1.09         Hsieh et al. 2011a       0.36 (-0.78, 1.51)       1.09       0.36 (-0.78, 1.51)       1.09         Hsieh et al. 2012a       0.35 (-0.31, 1.01)       2.31       0.35 (-0.31, 1.01)       2.31         Wu et al. 2012a       0.36 (-0.78, 1.51)       1.09       0.36 (-0.78, 0.50)       70.77         Wu et al. 2012a       0.36 (-0.78, 0.51)       1.09       0.36 (-0.78, 0.51)       1.09         Wu et al. 2012a       0.36 (-0.78, 0.51)       1.09       0.36 (-0.78, 0.51)       1.01         Hsieh et al. 2013a       0.57 (-0.21, 1.61)       1.54       0.25 (-0.37, 0.42)       2.51         Hung et al. 2017       0.55			
Tomic et al. 2017       1.32 (0.46, 2.18)       1.66         Hsieh et al. 2018       0.08 (-0.68, 0.84)       1.95         Hsieh et al. 2018       0.28 (-0.56, 1.02)       1.87         Daunoraviciene et al. 2019       0.26 (-0.5, 0.12)       4.69         Rodgers et al. 2019       0.06 (-0.25, 0.12)       4.69         Pranceschini et al. 2019       0.94 (0.34, 1.54)       2.51         Dehem et al. 2019       0.44 (-0.26, 1.15)       2.14         Hung et al. 2019       0.44 (-0.26, 1.15)       2.14         Hung et al. 2019       0.44 (-0.26, 1.15)       2.14         Uhm et al. 2010       0.87 (-0.06, 1.80)       1.50         Uhm et al. 2012a       0.35 (-0.31, 1.01)       2.31         Hsieh et al. 20112       -0.64 (-1.87, 0.60)       0.97         Uh et al. 2012a       -0.64 (-1.87, 0.60)       0.97         Hsieh et al. 2012b       -0.64 (-1.87, 0.60)       0.97         Uhe et al. 2012b       0.03 (-0.62, 0.68)       2.33         Yang et al. 2012b       0.35 (-0.31, 1.01)       2.31			
Heich et al. 2018a Holeh et al. 2018b Daunoravicine et al. 2019 Franceschini et al. 2019 Franceschini et al. 2019 Franceschini et al. 2019 Dehem et al. 2019 Bilateral robot-assisted Lum et al. 2006c Um et al. 2002 Um et al. 2002 Um et al. 2002 Hsieh et al. 2011a Hsieh et al. 2012a Hsieh et al. 2012b Hsieh et al. 2012b Hoise et al. 2014b Hung et al. 2017b Hung et al. 2019a Gord (-1.05, 1.05) L25 L25 Hole Et al. 2017b Hung et al. 2019a Hong et al. 2019a Hon			
Hsieh et al. 2018b Daunoraviciene et al. 2018 Calabrò et al. 2019 Franceschini et al. 2019 Pranceschini et al. 2019 Dehem et al. 2019 Dubem et al. 2020 Subtotal (I-squared = 55.9%, p = 0.000) Hsieh et al. 2012a Hung et al. 2012b Hsieh et al. 2012b Hung et al. 2017 Hsieh et al. 2019 Subtotal (I-squared = 0.0%, p = 0.783) Coverall (I-squared = 45.9%, p = 0.000) NOTE: Weights are from random effects analysis 			
Daunoraviciene et al. 2018 Calabri et al. 2019 Rodgers et al. 2019 Franceschini et al. 2019 Franceschini et al. 2019 Franceschini et al. 2019 Dehem et al. 2019 Carpinella et al. 2020 Subtotal (I-squared = 55.9%, p = 0.000) Bilateral robot-assisted Lum et al. 2012b Hsieh et al. 2011b Wu et al. 2012b Hsieh et al. 2014 Hsieh et al. 2017 Hsieh et al. 2017 Hsieh et al. 2017 Hsieh et al. 2017 Hsieh et al. 2019a Subtotal (I-squared = 0.0%, p = 0.783) Hore: Weights are from random effects analysis Hore: Hsights are from random effects analysis Hore: Weights are from random effects analysis Hore: Hsights are from random effe			
Calabrò et al. 2019 Rodgers et al. 2019 Franceschini et al. 2019 Pranceschini et al. 2019 Hung et al. 2019 Carpinella et al. 2020 Subtotal (I-squared = 55.9%, p = 0.000) Bilateral robot-assisted Lum et al. 2016 Hsieh et al. 2011a Hsieh et al. 2011a Hsieh et al. 2012a Hsieh et al. 2012b Hase et al. 2012b Hsieh et al. 2014b Hsieh et al. 2017b Hsieh et al. 2019a Subtotal (I-squared = 0.0%, p = 0.783) Hsieh et al. 2019a Hsieh e			
Rodgers et al. 2019       -0.06 (-0.25, 0.12)       4.69         Franceschini et al. 2019       0.94 (0.34, 1.54)       2.55         Dehem et al. 2019       0.44 (0.26, 1.15)       2.14         Hung et al. 2019b       0.87 (-0.06, 1.80)       1.50         Carpinella et al. 2020       0.10 (-0.54, 0.73)       2.40         Subtotal (I-squared = 55.9%, p = 0.000)       0.32 (0.15, 0.50)       70.07         Hum et al. 2006c       -0.64 (-1.87, 0.60)       0.97         Hsieh et al. 2011a       -0.03 (-0.78, 1.51)       1.09         Hsieh et al. 2012b       -0.03 (-0.73, 1.21)       1.11         Wu et al. 2012b       -0.07 (-1.20, 1.07)       1.11         Hsieh et al. 2012b       -0.03 (-0.21, 6.68)       2.33         Yang et al. 2012b       -0.03 (-0.22, 6.02)       2.14         Hsieh et al. 2017       -0.58 (-0.37, 1.42)       1.58         Pyl et al. 2017       -0.29 (-0.86, 0.27)       2.71         Hsieh et al. 2017       -0.26 (-0.37, 1.42)       1.58         Hung et al. 2019a       -0.07 (-0.21, 1.61)       1.54         Hsue et al. 2017       -0.26 (-0.35, 0.85)       2.54         Hung et al. 2019a       -0.05 (-0.66, 0.75)       2.14         Hsue et al. 2019a       -0.26 (-0.35, 0.85)			
Franceschini et al. 2019       0.94 (0.34, 1.54)       2.55         Dehem et al. 2019       0.44 (-0.26, 1.15)       2.14         Hung et al. 2020       0.10 (-0.54, 0.73)       2.40         Subtotal (I-squared = 55.9%, p = 0.000)       0.32 (0.15, 0.50)       70.07          0.36 (-0.78, 1.51)       1.09         Hsieh et al. 2011a       0.36 (-0.78, 1.51)       1.09         Hsieh et al. 2012a       0.36 (-0.78, 1.51)       1.09         Wu et al. 2012b       0.36 (-0.78, 1.51)       1.09         Hsieh et al. 2012b       0.33 (-0.62, 0.68)       2.33         Yang et al. 2012b       0.03 (-0.62, 0.68)       2.33         Yang et al. 2012b       0.00 (-1.05, 1.05)       1.25         Liao et al. 2017       Hsu et al.2017       1.54         Hsue et al. 2017       0.05 (-0.66, 0.75)       2.14         Hsu et al. 2017       0.05 (-0.68, 0.27)       2.71         Hsue et al. 2014       0.25 (0.37, 1.10)       1.58         Urrer et al. 2019       0.07 (-0.15, 0.28)       24.49         Overall (I-squared = 45.9%, p = 0.000)       0.25 (0.11, 0.38)       100.00         NOTE: Weights are from random effects analysis       0       3.03			
Dehem et al. 2019 Hung et al. 2020 Subtotal (I-squared = 55.9%, p = 0.000) Bilateral robot-assisted Lum et al. 2006c Hsieh et al. 2011a Hsieh et al. 2011a Hsieh et al. 2012a Hsieh et al. 2012a Hsieh et al. 2012b Hsieh et al. 2017b Hsieh et al. 2019a Subtotal (I-squared = 0.0%, p = 0.783) 			
Hung et al. 2019b Carpinella et al. 2020 Subtotal (I-squared = 55.9%, p = 0.000) Bilateral robot-assisted Lum et al. 2016 Hsieh et al. 2011a Hsieh et al. 2011b Wu et al. 2012b Hsieh et al. 2012b Hung et al. 2014 Hsieh et al. 2017 Hsieh et al. 2017 Hsieh et al. 2017b Hung et al. 2019 Hung et al. 2019 Hung et al. 2019a Hung et			
Carpinella et al. 2020 Subtotal (I-squared = 55.9%, p = 0.000) Histeh et al. 2010 Hue et al. 2010 Wu et al. 2012b Husteh et al. 2012b Husteh et al. 2012b Hung et al. 2012b Hung et al. 2017 Husteh et al. 2017 Hung et al. 2019a Subtotal (I-squared = 0.0%, p = 0.783) -3.03 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			
Subtotal (I-squared = 55.9%, p = 0.000) Bilateral robot-assisted Lum et al. 2006c Hsieh et al. 2011a Hsieh et al. 2011a Wu et al. 2012a Wu et al. 2012b Hsieh et al. 2012b Liao et al. 2012 By I et al. 2013a Hesse et al. 2014 Hsieh et al. 2017 Hsu et al. 2017 Hsu et al. 2017 Hsieh et al. 2019a Subtotal (I-squared = 0.0%, p = 0.783) NOTE: Weights are from random effects analysis -3.03 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			
Lum et al. 2006c Hsieh et al. 2011a Hsieh et al. 2011b Wu et al. 2012a Wu et al. 2012b Hsieh et al. 2012b Hsieh et al. 2012b Yang et al. 2012b Hsieh et al. 2012b Yang et al. 2012b Hsieh et al. 2012b Hsieh et al. 2012b Hsieh et al. 2012b Hsieh et al. 2012b U of et al. 2012b Hsieh et al. 2012b Hsieh et al. 2014 Hsieh et al. 2017 Hsue et al. 2019 Hung et al. 2019a Subtotal (I-squared = 0.0%, p = 0.783)  Overall (I-squared = 45.9%, p = 0.000) NOTE: Weights are from random effects analysis -3.03 0 0 0 0 0 0 0 0 0 0 0 0 0	Subtotal (I-squared = 55.9%, p = 0.000)		
Lum et al. 2006c Hsieh et al. 2011a Hsieh et al. 2011b Wu et al. 2012a Wu et al. 2012b Hsieh et al. 2012b Hsieh et al. 2012b Yang et al. 2012b Hsieh et al. 2012b Yang et al. 2012b Hsieh et al. 2012b Hsieh et al. 2012b Hsieh et al. 2012b Hsieh et al. 2012b U of et al. 2012b Hsieh et al. 2012b Hsieh et al. 2014 Hsieh et al. 2017 Hsue et al. 2019 Hung et al. 2019a Subtotal (I-squared = 0.0%, p = 0.783)  Overall (I-squared = 45.9%, p = 0.000) NOTE: Weights are from random effects analysis -3.03 0 0 0 0 0 0 0 0 0 0 0 0 0	Pilotoral robot assisted		
Hsieh et al. 2011a Hsieh et al. 2011b Wu et al. 2012a Wu et al. 2012b Hsieh et al. 2012b Hsieh et al. 2012b Hsieh et al. 2012b Liao et al. 2012 By let al. 2013a Hesse et al. 2014 Hsieh et al. 2017 Hsieh et al. 20170 Hung et al. 2019a Overall (I-squared = 0.0%, p = 0.783) Overall (I-squared = 45.9%, p = 0.000) NOTE: Weights are from random effects analysis -3.03 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Lum et al. 2006c	-0.64 (-1.87, 0.60)	0.97
Hsieh et al. 2011b Wu et al. 2012a Wu et al. 2012b Hsieh et al. 2012a Hsieh et al. 2012b Hsieh et al. 2012b Hsieh et al. 2012b Hesse et al. 2012 Hung et al. 2017 Hsue et al. 2018a Overall (I-squared = 0.0%, p = 0.783) -3.03 0	Hsieh et al. 2011a		
Wu et al. 2012a       0.11 (-0.63, 0.85)       2.01         Wu et al. 2012b       -0.20 (-0.95, 0.54)       2.01         Hsieh et al. 2012a       0.35 (-0.31, 1.01)       2.31         Yang et al. 2012b       0.03 (-0.62, 0.68)       2.33         Yang et al. 2012b       0.00 (-1.05, 1.05)       1.25         Liao et al. 2012       0.70 (-0.21, 1.61)       1.54         Byl et al. 2013a       -0.68 (-1.97, 0.62)       0.89         Hesse et al. 2014       -0.25 (-0.36, 0.85)       2.54         Hung et al. 2019a       0.07 (-0.15, 0.28)       24.49         Overall (I-squared = 0.0%, p = 0.783)       0       0.25 (0.11, 0.38)       100.00         NOTE: Weights are from random effects analysis       -3.03       0       3.03	Hsieh et al. 2011b		
Wu et al. 2012b       -0.20 (-0.95, 0.54)       2.01         Hsieh et al. 2012a       0.35 (-0.31, 1.01)       2.31         Yang et al. 2012b       0.03 (-0.62, 0.68)       2.33         Yang et al. 2012b       0.00 (-1.05, 1.05)       1.25         Liao et al. 2012       0.70 (-0.21, 1.61)       1.54         Byl et al. 2013a       -0.29 (-0.86, 0.27)       2.71         Hsieh et al. 2017       -0.29 (-0.86, 0.27)       2.71         Hsieh et al. 2017       0.05 (-0.66, 0.75)       2.14         Hsieh et al. 2019       0.25 (-0.37, 1.42)       1.58         Subtotal (I-squared = 0.0%, p = 0.783)       0.07 (-0.15, 0.28)       24.49          0.025 (0.11, 0.38)       100.00         NOTE: Weights are from random effects analysis       -3.03       0       3.03	Wu et al. 2012a		2.01
Hsieh et al. 2012b Yang et al. 2012b Liao et al. 2012 Byl et al. 2013a Hesse et al. 2014 Hsieh et al. 2017 Hsu et al. 2017 Hsu et al. 2019 Subtotal (I-squared = 0.0%, p = 0.783) Overall (I-squared = 45.9%, p = 0.000) NOTE: Weights are from random effects analysis -3.03 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	Wu et al. 2012b		2.01
Yang et al. 2012b       0.00 (-1.05, 1.05)       1.25         Liao et al. 2012       0.70 (-0.21, 1.61)       1.54         Byl et al. 2013a       -0.68 (-1.97, 0.62)       0.89         Hesse et al. 2014       -0.29 (-0.86, 0.27)       2.71         Hsieh et al. 2017       0.05 (-0.66, 0.75)       2.14         Hung et al. 2019a       0.52 (-0.37, 1.42)       1.58         Subtotal (I-squared = 0.0%, p = 0.783)       0.77 (-0.15, 0.28)       24.49         .       0.07 (-0.15, 0.28)       24.49         .       -3.03       0       3.03	Hsieh et al. 2012a	0.35 (-0.31, 1.01)	2.31
Liao et al. 2012 By let al. 2013 Hesse et al. 2014 Hsich et al. 2017 Hsu et al. 2017 Hsu et al. 2017 Hung et al. 2019 Overall (I-squared = 0.0%, p = 0.783) 	Hsieh et al. 2012b		2.33
Byl et al. 2013a       -0.68 (-1.97, 0.62)       0.89         Hesse et al. 2014       -0.29 (-0.86, 0.27)       2.71         Hsieh et al. 2017       0.05 (-0.66, 0.75)       2.54         Hung et al. 2019a       0.52 (-0.37, 1.42)       1.58         Subtotal (I-squared = 0.0%, p = 0.783)       0.25 (0.11, 0.38)       100.00         NOTE: Weights are from random effects analysis       -3.03       0       3.03	Yang et al. 2012b	0.00 (-1.05, 1.05)	1.25
Hesse et al. 2014 Hsich et al. 2017 Hsu et al. 2019 Hung et al. 2019a Subtotal (I-squared = 0.0%, p = 0.783) Overall (I-squared = 45.9%, p = 0.000) NOTE: Weights are from random effects analysis - 3.03 0 -0.29 (-0.86, 0.27) 2.71 0.05 (-0.66, 0.75) 2.14 0.52 (-0.37, 1.42) 1.58 0.07 (-0.15, 0.28) 24.49 0.25 (0.11, 0.38) 100.00 3.03	Liao et al. 2012	• 0.70 (-0.21, 1.61)	1.54
Hsieh et al. 2017       0.05 (-0.66, 0.75)       2.14         Hsu et al. 2019       0.25 (-0.35, 0.85)       2.54         Hung et al. 2019a       0.52 (-0.37, 1.42)       1.58         Subtotal (I-squared = 0.0%, p = 0.783)       0.07 (-0.15, 0.28)       24.49         Overall (I-squared = 45.9%, p = 0.000)       0.25 (0.11, 0.38)       100.00         NOTE: Weights are from random effects analysis       1       1         -3.03       0       3.03	Byl et al. 2013a	-0.68 (-1.97, 0.62)	0.89
Hsu et al.2019 Hung et al. 2019a Subtotal (I-squared = 0.0%, p = 0.783) Overall (I-squared = 45.9%, p = 0.000) NOTE: Weights are from random effects analysis 	Hesse et al. 2014		
Hung et al. 2019a       0.52 (-0.37, 1.42)       1.58         Subtotal (I-squared = 0.0%, p = 0.783)       0.77 (-0.15, 0.28)       24.49         Overall (I-squared = 45.9%, p = 0.000)       0.25 (0.11, 0.38)       100.00         NOTE: Weights are from random effects analysis       0       3.03	Hsieh et al. 2017		
Subtotal (I-squared = 0.0%, p = 0.783)       0.07 (-0.15, 0.28)       24.49         .       0       0.25 (0.11, 0.38)       100.00         NOTE: Weights are from random effects analysis       1       1       1         -3.03       0       3.03       3.03       100.00	Hsu et al.2019		
Overall (I-squared = 45.9%, p = 0.000)     0.25 (0.11, 0.38)     100.00       NOTE: Weights are from random effects analysis     1     1       -3.03     0     3.03	Hung et al. 2019a		
NOTE: Weights are from random effects analysis	Subtotal (I-squared = 0.0%, p = 0.783)	0.07 (-0.15, 0.28)	24.49
NOTE: Weights are from random effects analysis	Overall (I-squared = 45.9%, p = 0.000)	0.25 (0.11, 0.38)	100.00
	NOTE: Weights are from random effects analysis	,	
control group experiment group	-3.03 0	3.03	
	control group	experiment group	

**Figure 1.** Meta-analysis of short-term changes in FMA-UE score between RT and the control group, URT and the control group, BRT and the control group, and combined URT and BRT and the control group. BRT = bilateral robot-assisted therapy; FMA-UE = Fugl-Meyer assessment for upper extremity; RT = robot-assisted therapy; URT = unilateral robot-assisted therapy.

(Fig. 4).<sup>13–15,20,27,32,33,41,60</sup> Moreover, no statistically significant difference among the subgroups was detected by the Q test (Q = 0.24; P = .889).

# Influence of the Type of Robot Device

We found that end effector robots (n = 1605; Hedges g = 0.22; 95% CI, 0.09–0.36; P = .001;  $I^2 = 35.4\%$ ) <sup>13–15,20,24–41,50,52,53,55,60–62,65,66</sup> but not exoskeleton robots (n = 301; Hedges g = 0.31; 95% CI, -0.14 to 0.76;

 $P = .171; I^2 = 68.9\%)^{49,51,54,56-59,63,64}$  were superior to conventional rehabilitation in terms of improving the FMA-UE scores (Fig. 5). However, no statistically significant difference between the subgroups was detected by the Q test (Q = 0.25; P = .616).

## Influence of the Trained Part

The subgroup analysis based on 30 studies revealed that shoulder/elbow robotics (n = 1097; Hedges g = 0.27; 95% CI,

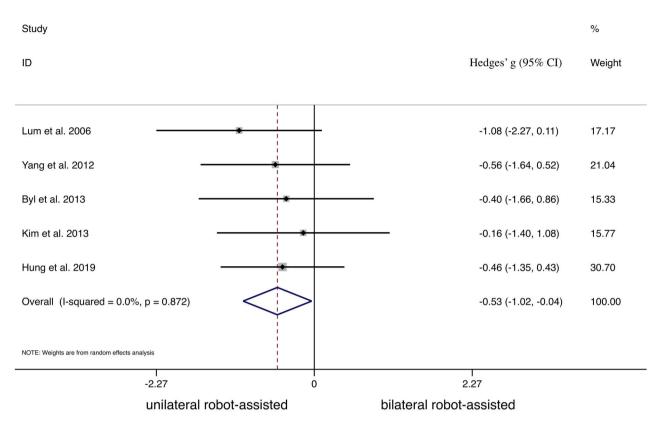


Figure 2. Meta-analysis of changes in FMA-UE score between URT and BRT. BRT = bilateral robot-assisted therapy; FMA-UE = Fugl-Meyer assessment for upper extremity; URT = unilateral robot-assisted therapy.

0.05–0.50; P = .018;  $I^2 = 61.9\%)^{24,26,29–31,35,36,38,39,50,-53,54,58,60-62,65,66}$  and forearm/wrist/hand robotics (n = 417; Hedges g = 0.19; 95% CI, 0.01–0.37; P = .042;  $I^2 = 0.0\%)^{-13-15,25,28,32,33,37,40,41,55,59}$  were superior to conventional rehabilitation in terms of improving the FMA-UE scores (Fig. 6). However, no statistically significant difference between the subgroups was detected in the Q test (Q = 0.10; P = .755).

#### Sensitivity Analyses

The results of the sensitivity analysis are presented in Supplementary Table 4. The overall results of the analysis were robust when different levels of correlation coefficients were used to estimate the SD of the change scores, except the results of the 2-subgroup analyses (ie, URT vs BRT, and proximal joints vs distal joints). An additional sensitivity analysis was performed on the basis of the methodological quality of the included studies as measured with the PEDro scale. The overall results of the analysis were robust when only high-quality (PEDro score  $\geq 6$ ) studies were included.

## Discussion

This review suggests that RT was superior to conventional rehabilitation in terms of improving upper extremity motor impairment as assessed using the FMA-UE scores. A subsequent subgroup analysis revealed that URT, but not BRT, was superior to conventional rehabilitation, with a small effect size. Furthermore, URT seemed to be better than BRT in improving upper extremity motor impairment based on the meta-analysis of the 5 studies with direct comparisons. End effector robots, but not exoskeleton robots, seemed to be more useful for improving upper limb motor impairment after stroke than conventional rehabilitation. The subgroup analysis also revealed that the superiority of RT was more obvious when it was applied to patients with a limited potential for spontaneous biological recovery after stroke and patients with moderate to severe upper extremity motor impairment, although the statistical comparison did not reach significance in all the subgroup comparisons.

Learned nonuse is a common phenomenon whereby the movement of the hemiplegic arm is suppressed because of stroke, resulting in failure to use the hemiplegic arm during daily activities.<sup>68</sup> Along with the suppression of neural activities in the affected hemisphere, the unaffected hemisphere becomes overactivated, which leads to an interhemispheric asymmetry; however, this phenomenon could be overcome with appropriate behavioral training.<sup>69</sup> URT can be used to address learned nonuse by delivering high-intensity, repetitive training. Repetitive and high-intensity movement of the hemiplegic arm results in the reorganization of the affected motor cortex and consequently rebalances the interhemispheric asymmetry caused by unilateral stroke.<sup>70–72</sup> The results of this meta-analysis were in line with this theory and suggest that URT is an effective intervention for improving the upper extremity motor function of stroke patients. In addition, the theory on the recovery of bilateral hemispheric interaction after stroke suggests that bilateral arm training is potentially more effective than unilateral arm training in upper extremity rehabilitation. The underlying mechanisms may include the activation of the ipsilateral non-cross

Study ID	Hedges'g (95%CI)	% Weight
≥3 months		
Lum et al. 2002	0.81 (0.02, 1.60)	2.24
Housman et al. 2007	0.38 (-0.44, 1.21)	2.12
/lope et al. 2008	- 0.21 (-0.65, 1.07)	2.02
lousman et al. 2009	0.43 (-0.29, 1.14)	2.52
.o et al. 2010	-0.01 (-0.42, 0.39)	3.96
Isieh et al. 2011a	0.36 (-0.78, 1.51)	1.36
Isieh et al. 2011b	-0.07 (-1.20, 1.07)	1.38
Conroy et al. 2011a	0.49 (-0.15, 1.13)	2.82
Conroy et al. 2011b	0.14 (-0.50, 0.79)	2.79
Reinkensmeyer et al. 2012	0.55 (-0.23, 1.34)	2.26
Vu et al. 2012a	0.11 (-0.63, 0.85)	2.41
Vu et al. 2012b	-0.20 (-0.95, 0.54)	2.41
Isieh et al. 2012a	• 0.35 (-0.31, 1.01)	2.73
Hsieh et al. 2012b	0.03 (-0.62, 0.68)	2.76
/ang et al. 2012a	0.49 (-0.58, 1.56)	1.50
/ang et al. 2012b	- 0.00 (-1.05, 1.05)	1.55
iao et al. 2012	0.70 (-0.21, 1.61)	1.88
Byl et al. 2013a	-0.68 (-1.97, 0.62)	1.12
Byl et al. 2013b	-0.62 (-1.91, 0.67)	1.13
Timmermans et al. 2014	0.08 (-0.76, 0.92)	2.09
Ang et al. 2014	0.51 (-0.53, 1.55)	1.57
Brokaw et al. 2014	0.27 (-0.88, 1.43)	1.34
Klamroth et al. 2014	0.47 (0.00, 0.93)	3.65
Susanto et al. 2015	-0.10 (-1.00, 0.80)	1.90
McCabe et al. 2015	-0.47 (-1.30, 0.36)	2.11
Hsieh et al. 2018a	0.08 (-0.68, 0.84)	2.35
Hsieh et al. 2018b	- 0.23 (-0.56, 1.02)	2.25
Daunoraviciene et al. 2018	<b>2.16</b> (1.30, 3.03)	2.00
Calabrò et al. 2019	1.23 (0.62, 1.84)	2.95
Hsu et al.2019	0.25 (-0.35, 0.85)	2.99
Hung et al. 2019a	0.52 (-0.37, 1.42)	1.92
Hung et al. 2019b	0.87 (-0.06, 1.80)	1.84
Subtotal (I-squared = 34.2%, p = 0.032)	0.33 (0.16, 0.50)	69.95
<3 months		
Rabadi et al. 2008	-0.28 (-1.16, 0.60)	1.96
Burgar et al. 2011	-0.58 (-1.24, 0.08)	2.73
Masiero et al. 2011	-0.18 (-1.03, 0.68)	2.03
Hesse et al. 2014	-0.29 (-0.86, 0.27)	3.16
Sale et al. 2014	0.54 (-0.01, 1.09)	3.23
Masiero et al. 2014	0.41 (-0.31, 1.14)	2.47
Prange et al. 2015	-0.25 (-0.73, 0.22)	3.59
Takahashi et al. 2016	0.31 (-0.22, 0.84)	3.33
Tomic et al. 2017	▲ 1.32 (0.46, 2.18)	2.02
Franceschini et al. 2019	0.94 (0.34, 1.54)	2.99
Dehem et al. 2019	0.44 (-0.26, 1.15)	2.55
Subtotal (I-squared = 64.8%, p = 0.002)	0.21 (-0.12, 0.54)	30.05
Dverall (I-squared = 45.4%, p = 0.001)	0.29 (0.13, 0.44)	100.00
NOTE: Weights are from random effects analysis	I	
-3.03 0	3.03	
control group	experiment group	

Figure 3. Meta-analysis of changes in FMA-UE score between RT and control groups in the different stages of stroke. FMA-UE = Fugl-Meyer assessment for upper extremity; RT = robot-assisted therapy.

corticospinal pathway. Bilateral arm training may be better than unilateral arm training in terms of increasing the excitability of the ipsilesional motor cortex and transcallosal inhibition from the ipsilesional to the contralesional motor cortex, which results in the rebalance of interhemispheric activities in stroke patients.<sup>11,12</sup> However, in our review, we found that the effect of BRT was not superior to conventional rehabilitation. A potential reason for this finding may be the limited number of studies/the units of analysis (n = 11/n = 14) that used BRT. In addition, BRT can be varied according to symmetrical, asynchronous, and cooperative training modes with bilateral arms, compared with URT, which is important for neurological recovery. However, the included studies applied bilateral synchronous movements during BRT.

Study ID	Hedges' g (95% CI)	% Weight
moderate-severe		
Lum et al. 2002	0.81 (0.02, 1.60)	1.86
Lum et al. 2006a	0.54 (-0.49, 1.58)	1.28
Lum et al. 2006b	0.53 (-0.52, 1.59)	1.24
Lum et al. 2006c	-0.64 (-1.87, 0.60)	0.97
	0.38 (-0.44, 1.21)	1.75
Housman et al. 2007		
Rabadi et al. 2008	-0.28 (-1.16, 0.60)	1.61
Vlope et al. 2008	0.21 (-0.65, 1.07)	1.67
Housman et al. 2009	0.43 (-0.29, 1.14)	2.11
Lo et al. 2010	-0.01 (-0.42, 0.39)	3.50
Burgar et al. 2011	-0.58 (-1.24, 0.08)	2.30
Masiero et al. 2011	-0.18 (-1.03, 0.68)	1.67
Conroy et al. 2011a	0.49 (-0.15, 1.13)	2.39
Conroy et al. 2011b	0.14 (-0.50, 0.79)	2.36
Reinkensmeyer et al. 2012	0.55 (-0.23, 1.34)	1.87
Byl et al. 2013a	-0.68 (-1.97, 0.62)	0.89
Byl et al. 2013b	-0.62 (-1.91, 0.67)	0.90
Hesse et al. 2014	-0.29 (-0.86, 0.27)	2.71
Ang et al. 2014	0.51 (-0.53, 1.55)	1.27
Brokaw et al. 2014	0.27 (-0.88, 1.43)	1.08
Sale et al. 2014	0.54 (-0.01, 1.09)	2.77
Masiero et al. 2014	0.41 (-0.31, 1.14)	2.06
Klamroth et al. 2014	0.47 (0.00, 0.93)	3.18
Susanto et al. 2015	-0.10 (-1.00, 0.80)	1.56
McCabe et al. 2015	-0.47 (-1.30, 0.36)	1.74
Tomic et al. 2017	1.32 (0.46, 2.18)	1.66
Calabrò et al. 2019	1.23 (0.62, 1.84)	2.51
Rodgers et al. 2019	-0.06 (-0.25, 0.12)	4.69
Franceschini et al. 2019	0.94 (0.34, 1.54)	2.55
Hung et al. 2019a	0.52 (-0.37, 1.42)	1.58
Hung et al. 2019b	0.87 (-0.06, 1.80)	1.50
Subtotal (I-squared = 53.0%, p = 0.000)	0.27 (0.08, 0.46)	59.23
mild-moderate		
Hsieh et al. 2011a	0.36 (-0.78, 1.51)	1.09
Hsieh et al. 2011b	-0.07 (-1.20, 1.07)	1.11
Wu et al. 2012a	0.11 (-0.63, 0.85)	2.01
Wu et al. 2012b	-0.20 (-0.95, 0.54)	2.01
Hsieh et al. 2012a		2.31
	0.35 (-0.31, 1.01)	
Hsieh et al. 2012b	0.03 (-0.62, 0.68)	2.33
Yang et al. 2012a	0.49 (-0.58, 1.56)	1.22
Yang et al. 2012b	0.00 (-1.05, 1.05)	1.25
Liao et al. 2012	0.70 (-0.21, 1.61)	1.54
Timmermans et al. 2014	0.08 (-0.76, 0.92)	1.73
Takahashi et al. 2016	0.31 (-0.22, 0.84)	2.87
Hsieh et al. 2018a	0.08 (-0.68, 0.84)	1.95
Hsieh et al. 2018b	0.23 (-0.56, 1.02)	1.87
Hsu et al.2019 Subtotal (I-squared = 0.0%, p = 0.992)	0.25 (-0.35, 0.85) 0.19 (-0.01, 0.40)	2.54 25.83
mild-severe	(	
	0.05 / 0.79 .0.00	0 10
Prange et al. 2015	-0.25 (-0.73, 0.22)	3.12
Wolf et al. 2015	-0.03 (-0.44, 0.38)	3.49
Hsieh et al. 2017	0.05 (-0.66, 0.75)	2.14
Daunoraviciene et al. 2018	2.16 (1.30, 3.03)	1.65
Dehem et al. 2019	0.44 (-0.26, 1.15)	2.14
Carpinella et al. 2020	0.10 (-0.54, 0.73)	2.40
Subtotal (I-squared = 80.0%, p = 0.000)	0.34 (-0.21, 0.89)	14.93
Overall (I-squared = 45.9%, p = 0.000)	0.25 (0.11, 0.38)	100.00
	,/	
NOTE: Weights are from random effects analysis		
NOTE: Weights are from random effects analysis -3.03 0	 3.03	
-3.03 0	I 3.03 periment group	

Figure 4. Meta-analysis of changes in FMA-UE score between RT and control groups according to upper extremity motor impairment level. FMA-UE = Fugl-Meyer assessment for upper extremity; RT = robot-assisted therapy.

Thus, whether BRT may provide benefits to stroke patients with ipsilesional upper extremity dysfunction, which occurs in approximately one-third of stroke survivors, is unclear.<sup>73</sup> Further studies are needed to investigate these points.

In terms of disease stage, the results of this meta-analysis were consistent with those of a previous meta-analysis by Zhang et al<sup>18</sup> in that RT led to significant improvement in FMA-UE scores compared with the dose-matched conventional rehabilitation in chronic stroke patients. Spontaneous biological recovery is prominent within the first 3 months after stroke, and it is mostly diminished 6 months after stroke. The nonsignificant results may be due to the

Study ID	Hedges' g (95% CI)	% Weight
End-effector		
Lum et al. 2002	0.81 (0.02, 1.60)	1.86
Lum et al. 2006a	0.54 (-0.49, 1.58)	1.28
Lum et al. 2006b	0.53 (-0.52, 1.59)	1.24
Lum et al. 2006c	-0.64 (-1.87, 0.60)	0.97
Rabadi et al. 2008	-0.28 (-1.16, 0.60)	1.61
Vlope et al. 2008	0.21 (-0.65, 1.07)	1.67
Lo et al. 2010	-0.01 (-0.42, 0.39)	3.50
Hsieh et al. 2011a	0.36 (-0.78, 1.51)	1.09
Hsieh et al. 2011b	-0.07 (-1.20, 1.07)	1.11
Burgar et al. 2011	-0.58 (-1.24, 0.08)	2.30
Masiero et al. 2011	-0.18 (-1.03, 0.68)	1.67
Conroy et al. 2011a	0.49 (-0.15, 1.13)	2.39
Conroy et al. 2011b	0.14 (-0.50, 0.79)	2.36
Wu et al. 2012a	0.11 (-0.63, 0.85)	2.01 2.01
Hsieh et al. 2012a	0.35 (-0.31, 1.01)	2.31
Hsieh et al. 2012b	0.03 (-0.62, 0.68)	2.33
Yang et al. 2012a	0.49 (-0.58, 1.56) 0.00 (-1.05, 1.05)	1.22 1.25
Yang et al. 2012b		
Liao et al. 2012	0.70 (-0.21, 1.61)	1.54
Timmermans et al. 2014	0.08 (-0.76, 0.92)	1.73
Hesse et al. 2014	-0.29 (-0.86, 0.27)	2.71 1.27
Ang et al. 2014	0.51 (-0.53, 1.55)	2.77
Masiero et al. 2014	0.54 (-0.01, 1.09)	2.06
McCabe et al. 2015	0.41 (-0.31, 1.14) -0.47 (-1.30, 0.36)	1.74
Wolf et al. 2015	-0.03 (-0.44, 0.38)	3.49
Takahashi et al. 2016	0.31 (-0.22, 0.84)	2.87
Hsieh et al. 2017	0.05 (-0.66, 0.75)	2.14
Tomic et al. 2017	1.32 (0.46, 2.18)	1.66
Hsieh et al. 2018a	0.08 (-0.68, 0.84)	1.95
Hsieh et al. 2018b	◆ 0.23 (-0.56, 1.02)	1.87
Calabrò et al. 2019	1.23 (0.62, 1.84)	2.51
Rodgers et al. 2019	-0.06 (-0.25, 0.12)	4.69
Franceschini et al. 2019	0.94 (0.34, 1.54)	2.55
Dehem et al. 2019	0.44 (-0.26, 1.15)	2.14
Hsu et al.2019	0.25 (-0.35, 0.85)	2.54
Hung et al. 2019a	0.52 (-0.37, 1.42)	1.58
Hung et al. 2019b	0.87 (-0.06, 1.80)	1.50
Carpinella et al. 2020	0.10 (-0.54, 0.73)	2.40
Subtotal (I-squared = 35.4%, p = 0.016)	♦ 0.22 (0.09, 0.36)	81.88
· · · · · · · · · · · · · · · · · · ·	<b>1</b>	
Exoskeleton		
Housman et al. 2007	0.38 (-0.44, 1.21)	1.75
Housman et al. 2009	0.43 (-0.29, 1.14)	2.11
Reinkensmeyer et al. 2012	0.55 (-0.23, 1.34)	1.87
Byl et al. 2013a	-0.68 (-1.97, 0.62)	0.89
Byl et al. 2013b	-0.62 (-1.91, 0.67)	0.90
Brokaw et al. 2014	• 0.27 (-0.88, 1.43)	1.08
Klamroth et al. 2014	0.47 (0.00, 0.93)	3.18
Prange et al. 2015	-0.25 (-0.73, 0.22)	3.12
Susanto et al. 2015	-0.10 (-1.00, 0.80)	1.56
Daunoraviciene et al. 2018	2.16 (1.30, 3.03)	1.65
Subtotal (I-squared = 68.9%, p = 0.001)	0.31 (-0.14, 0.76)	18.12
Overall (I-squared = 45.9%, p = 0.000)	• 0.25 (0.11, 0.38)	100.00
NOTE: Weights are from random effects analysis		
		-
-3.03 0	3.03	
control group	experiment group	

Figure 5. Meta-analysis of changes in FMA-UE score between RT and control groups according to RT device. FMA-UE = Fugl-Meyer assessment for upper extremity; RT = robot-assisted therapy.

strong spontaneous biological recovery in stroke patients in the early stage. This may lead to a similar improvement in upper limb motor function regardless of the type of training provided. Therefore, poststroke patients with limited potential for spontaneous recovery may obtain more benefits from RT than from conventional rehabilitation. With regard to the severity of upper extremity motor impairment in stroke patients, the functional gains associated with RT were higher than those associated with conventional rehabilitation in stroke patients with moderate to severe upper limb impairment. Patients with notable upper limb hemiplegia likely obtain more benefits from RT, where their movements

Study ID	% Hedges'g (95%CI) Weig	ight
Proximal joints		
_um et al. 2002	• 0.81 (0.02, 1.60) 2.37	7
um et al. 2006a	0.54 (-0.49, 1.58) 1.58	
um et al. 2006b	• 0.53 (-0.52, 1.59) 1.53	
um et al. 2006c	-0.64 (-1.87, 0.60) 1.18	
abadi et al. 2008	-0.28 (-1.16, 0.60) 2.02	
lope et al. 2008	0.21 (-0.65, 1.07) 2.10	
urgar et al. 2011	-0.58 (-1.24, 0.08) 3.00	
lasiero et al. 2011	-0.18 (-1.03, 0.68) 2.10	
Conroy et al. 2011a	• 0.49 (-0.15, 1.13) 3.12	
conroy et al. 2011b	0.14 (-0.50, 0.79) 3.08	
einkensmeyer et al. 2012	● 0.55 (-0.23, 1.34) 2.38	
ale et al. 2014	• 0.54 (-0.01, 1.09) 3.70	
lasiero et al. 2014	• 0.41 (-0.31, 1.14) 2.66	
range et al. 2015	-0.25 (-0.73, 0.22) 4.25	
cCabe et al. 2015	-0.47 (-1.30, 0.36) 2.20	
akahashi et al. 2016	◆ 0.31 (-0.22, 0.84) 3.85	
omic et al. 2017	↓ 1.32 (0.46, 2.18) 2.09	
alabrò et al. 2019	1.23 (0.62, 1.84) 3.31	
odgers et al. 2019	-0.06 (-0.25, 0.12) 7.00	
ranceschini et al. 2019	◆ 0.94 (0.34, 1.54) 3.36	
arpinella et al. 2020	0.54 (0.54, 1.54) 3.50	
ubtotal (I-squared = 61.9%, p = 0.000)	> 0.10 (-0.54, 0.73) 3.14 > 0.27 (0.05, 0.50) 60.0	
ubiotal (Psquared = 01.5%, p = 0.000)	0.27 (0.03, 0.50) 00.0	12
Distal joints		
Isieh et al. 2011a	0.36 (-0.78, 1.51) 1.34	
sieh et al. 2011b	-0.07 (-1.20, 1.07) 1.36	
/u et al. 2012a	0.11 (-0.63, 0.85) 2.58	
Vu et al. 2012b	-0.20 (-0.95, 0.54) 2.57	
sieh et al. 2012a	• 0.35 (-0.31, 1.01) 3.01	
sieh et al. 2012b	0.03 (-0.62, 0.68) 3.04	
ang et al. 2012a	• 0.49 (-0.58, 1.56) 1.50	
ang et al. 2012b	0.00 (-1.05, 1.05) 1.55	
ao et al. 2012	0.70 (-0.21, 1.61) 1.93	3
ng et al. 2014	• 0.51 (-0.53, 1.55) 1.57	1
usanto et al. 2015	-0.10 (-1.00, 0.80) 1.95	
/olf et al. 2015	-0.03 (-0.44, 0.38) 4.85	5
sieh et al. 2017	0.05 (-0.66, 0.75) 2.76	3
ehem et al. 2019	• 0.44 (-0.26, 1.15) 2.76	3
Isu et al.2019	0.25 (-0.35, 0.85) 3.36	3
ung et al. 2019a	● 0.52 (-0.37, 1.42) 1.98	3
ung et al. 2019b	0.87 (-0.06, 1.80) 1.87	7
ubtotal (I-squared = 0.0%, p = 0.925)	> 0.19 (0.01, 0.37) 39.9	<del>)</del> 8
Overall (I-squared = 39.7%, p = 0.007)	> 0.25 (0.10, 0.39) 100.	.00
OTE: Weights are from random effects analysis		
-2.18 0	2.18	
control group	experiment group	

Figure 6. Meta-analysis of changes in FMA-UE score between RT and control groups according to training focus. FMA-UE = Fugl-Meyer assessment for upper extremity; RT = robot-assisted therapy.

can be assisted, than those with mild hemiplegia, who can perform most training tasks without robotic assistance.

We also demonstrated that the application of end effector robots could lead to better outcomes in the restoration of motor impairment after stroke than conventional rehabilitation. End effector robots allow multijoint coordination, which segment the arm movements, and may promote relearning of normal motor patterns of the affected limbs.<sup>74</sup> However, a recent clinical trial by Lee et al<sup>8</sup> reported no interaction effect on FMA-UE scores after training with end effector and exoskeleton robots. Because only 1 study was available for the direct comparison, a meta-analysis could not be performed to determine which type of robot device is potentially superior. Further studies are needed to investigate this point.

### Limitations

This study is not free from limitations. First, the present metaanalytic review only focused on the effects of RT on the outcome measures of upper extremity motor impairment to maintain the homogeneity of our meta-analysis and subgroup comparisons. Other important domains such as activities of daily living were not evaluated in the meta-analysis owing to the heterogeneity of the outcome measurements. Second, although this review examined the retention effects, the results should be considered as preliminary due to the differences in the follow-up lengths. Third, all the moderators remained insignificant in the statistical tests by meta-regression and Q test for the between-subgroup variance. Although O test has taken the weight of each study into account in the calculation, the fact that there are more studies in some subgroups may still influence the statistical comparisons. Also, we were unable to perform further multivariate meta-regression by including all significant modulators, with regards to the statistical insignificance. Therefore, the results of the subgroup analyses should be interpreted with caution. The numerically large effect sizes in the subgroup analyses may help determine the modulators when designing future studies about RT in stroke rehabilitation.

# Conclusion

RT is an effective intervention for improving upper extremity motor impairment in stroke patients. The superiority of RT compared with conventional methods might be more obvious when it is applied to stroke patients with notable upper limb hemiplegia and limited potential for spontaneous biological recovery. In addition, URT is likely to be superior to BRT.

# **Author Contributions**

Concept/idea/research design: J. Wu, J. Zhang, S. Cai

Writing: J. Wu, J. Zhang

Data collection: J. Wu, H. Cheng

Data analysis: J. Wu, H. Cheng, J. Zhang, S. Yang

Fund procurement: S. Yang

Consultation (including review of manuscript before submitting): J. Zhang, S. Cai

# Funding

This work was supported by the Central Guide to Local Science and Technology Development (grant no. 2018 L3009) and the Science and Technology Platform Construction Project of the Fujian Science and Technology Department (grant no. 2015Y2001–40).

# Disclosures

The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

# References

- 1. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the global burden of disease study 2010. *Lancet*. 2012;380:2095.
- 2. Mboi N, Surbakti IM, Trihandini I, et al. On the road to universal health care in Indonesia, 1990–2016: a systematic analysis for the global burden of disease study. *Lancet*. 2016;392:581–591.

- 3. Gittler M, Davis AM. Guidelines for adult stroke rehabilitation and recovery. *JAMA*. 2018;319:820–821.
- 4. Maciejasz P, Eschweiler J, Gerlach-hahn K, Jansen-Troy A, Leonhardt S. A survey on robotic devices for upper limb rehabilitation. *J Neuroengineering Rehabil Rev.* 2014;11:1–29.
- 5. Pignolo L. Robotics in NEURO-rehabilitation. J Rehabil Med. 2009;41:955–960.
- 6. Dobkin BH. Strategies for stroke rehabilitation. *Lancet Neurol.* 2004;3:528–536.
- 7. Morone G, Cocchi I, Paolucci S, Iosa M. Robot-assisted therapy for arm recovery for stroke patients: state of the art and clinical implication. *Expert Rev Med Devices*. 2020;17:223–233.
- 8. Lee SH, Park G, Cho DY, et al. Comparisons between end-effector and exoskeleton rehabilitation robots regarding upper extremity function among chronic stroke patients with moderate-to-severe upper limb impairment. *Sci Rep.* 2020;10:1806.
- 9. Turner DL, Ramos-Murguialday A, Birbaumer N, Hoffmann U, Luft A. Neurophysiology of robot-mediated training and therapy: a perspective for future use in clinical populations. *Front Neurol.* 2013;4:184.
- Sheng B, Zhang Y, Meng W, Deng C, Xie S. Bilateral robots for upper-limb stroke rehabilitation: state of the art and future prospects. *Med Eng Phys.* 2016;38:587–607.
- 11. Luft AR, McCombe-Waller S, Whitall J, et al. Repetitive bilateral arm training and motor cortex activation in chronic stroke: a randomized controlled trial. *JAMA*. 2004;292:1853–1861.
- 12. Whitall J, McCombe Waller S, Sorkin JD, et al. Bilateral and unilateral arm training improve motor function through differing neuroplastic mechanisms: a single-blinded randomized controlled trial. *Neurorehabil Neural Repair*. 2011;25:118–129.
- 13. Yang C-L, Lin K-C, Chen H-C, WuC-Y, Chen C-L. Pilot comparative study of unilateral and bilateral robot-assisted training on upper-extremity performance in patients with stroke. *Am J Occup Ther.* 2012;66:198–206.
- 14. Wu C, Yang C, Chuang L, et al. 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. *Phys Ther.* 2012;92:1006–1016.
- 15. Hsieh YW, Wu CY, Lin KC, Yao G, Wu KY, Chang YJ. Dose-response relationship of robot-assisted stroke motor rehabilitation: the impact of initial motor status. *Stroke*. 2012;43: 2729–2734.
- 16. Veerbeek JM, Langbroek-Amersfoort AC, van Wegen EEHH, Meskers CGMM, Kwakkel G. Effects of robot-assisted therapy for the upper limb after stroke: a systematic review and meta-analysis. *Neurorehabil Neural Repair.* 2017;31:107–121.
- 17. Mehrholz J, Pohl M, Platz T, Kugler J, Elsner B. Electromechanical and robot-assisted arm training for improving activities of daily living, arm function, and arm muscle strength after stroke. *Cochrane Database Syst Rev.* 2018;9.
- Zhang C, Li-Tsang CWP, Au RKC. Robotic approaches for the rehabilitation of upper limb recovery after stroke: a systematic review and meta-analysis. *Int J Rehabil Res.* 2017;40:19–28.
- 19. See J, Dodakian L, Chou C, et al. A standardized approach to the Fugl-Meyer assessment and its implications for clinical trials. *Neurorehabil Neural Repair*. 2013;27:732–741.
- Hsieh Y-W, Lin K-C, Wu C-Y, et al. Comparison of proximal versus distal upper-limb robotic rehabilitation on motor performance after stroke: a cluster controlled trial. *Sci Rep.* 2018;8:2091.
- 21. Moher D, Liberati A, Tetzlaff J, Altman DG, for the PRISMA Group. Preferred reporting items for systematic reviews and metaanalyses: the PRISMA statement. *BMJ*. 2009;339:b2535.
- 22. Santisteban L, Térémetz M, Bleton J, Baron J. Upper limb outcome measures used in stroke rehabilitation studies: a systematic literature review. *PLoS One.* 2016;11:e0154792.
- 23. Morrison A, Polisena J, Husereau D, et al. The effect of Englishlanguage restriction on systematic review-based meta-analyses: a systematic review of empirical studies. *Int J Technol Assess Health Care*. 2012;28:138–144.

- Franceschini M, Mazzoleni S, Goffredo M, et al. Upper limb robotassisted rehabilitation versus physical therapy on subacute stroke patients: a follow-up study. J Bodyw Mov Ther. 2019;24:194–198.
- Hung C-S, Hsieh Y-W, Wu C-Y, et al. Comparative assessment of two robot-assisted therapies for the upper extremity in people with chronic stroke. *Am J Occup Ther.* 2019;73:7301205010p1– 7301205010p9.
- Masiero S, Armani M, Ferlini G, et al. Randomized trial of a robotic assistive device for the upper extremity during early inpatient stroke rehabilitation. *Neurorehabil Neural Repair.* 2014;28: 377–386.
- Timmermans AAA, Lemmens RJM, Monfrance M, et al. Effects of task-oriented robot training on arm function, activity, and quality of life in chronic stroke patients: a randomized controlled trial. J Neuroeng Rehabil. 2014;11:45.
- Wolf SL, Sahu K, Bay RC, et al. The HAAPI (home arm assistance progression initiative) trial: a novel robotics delivery approach in stroke rehabilitation. *Neurorehabil Neural Repair*. 2015;29: 958–968.
- Burgar CG, Lum PS, Scremin AME, et al. Robot-assisted upperlimb therapy in acute rehabilitation setting following stroke: Department of Veterans Affairs multisite clinical trial. J Rehabil Res Dev. 2011;48:445–458.
- Conroy SS, Whitall J, Dipietro L, et al. Effect of gravity on robotassisted motor training after chronic stroke: a randomized trial. *Arch Phys Med Rehabil.* 2011;92:1754–1761.
- Rabadi MH, Galgano M, Lynch D, et al. A pilot study of activitybased therapy in the arm motor recovery post stroke: a randomized controlled trial. *Clin Rehabil*. 2008;22:1071–1082.
- Hsieh YW, Wu CY, Liao WW, et al. Effects of treatment intensity in upper limb robot-assisted therapy for chronic stroke: a pilot randomized controlled trial. *Neurorehabil Neural Repair*. 2011;25: 503–511.
- 33. Liao W-W, Wu C-Y, Hsieh Y-W, et al. Effects of robot-assisted upper limb rehabilitation on daily function and real-world arm activity in patients with chronic stroke: a randomized controlled trial. *Clin Rehabil.* 2012;26:111–120.
- 34. Hesse S, Hess A, Werner CC, Kabbert N, Buschfort R. 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. *Clin Rehabil.* 2014;28:637–647.
- Sale P, Franceschini M, Mazzoleni S, et al. Effects of upper limb robot-assisted therapy on motor recovery in subacute stroke patients. J Neuroeng Rehabil. 2014;11:104.
- McCabe J, Monkiewicz M, Holcomb J, et al. Comparison of robotics, functional electrical stimulation, and motor learning methods for treatment of persistent upper extremity dysfunction after stroke: a randomized controlled trial. *Arch Phys Med Rehabil*. 2015;96:981–990.
- Hsieh Y, Wu C, Wang W, et al. Bilateral robotic priming before task-oriented approach in subacute stroke rehabilitation: a pilot randomized controlled trial. *Clin Rehabil.* 2017;31:225–233.
- Calabro RS, Accorinti M, Porcari B, et al. Does hand robotic rehabilitation improve motor function by rebalancing interhemispheric connectivity after chronic stroke? Encouraging data from a randomised-clinical-trial. *Clin Neurophysiol.* 2019;130:767–780.
- Rodgers H, Bosomworth H, Krebs HI, et al. Robot assisted training for the upper limb after stroke (RATULS): a multicentre randomised controlled trial. *Lancet*. 2019;394:51–62.
- Dehem S, Gilliaux M, Stoquart G, et al. Effectiveness of upperlimb robotic-assisted therapy in the early rehabilitation phase after stroke: a single-blind, randomised, controlled trial. *Ann Phys Rehabil Med.* 2019;62:313–320.
- 41. Hsu H-Y, Chiu H-Y, Kuan T-S, Tsai C-L, Su F-C, Kuo L-C. Robotic-assisted therapy with bilateral practice improves task and motor performance in the upper extremities of chronic stroke patients: a randomised controlled trial. *Aust Occup Ther J.* 2019;66:637–647.

- 42. Higgins JP, Green S. Cochrane Handbook for Systematic Reviews of Interventions: Cochrane Book Series. Hoboken, NJ, USA: John Wiley & Sons; 2008.
- Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. *Phys Ther.* 2003;83:713–721.
- 44. Borenstein M, Hedges LV, Higgins JP, et al. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Res Synth Methods*. 2010;1:97–111.
- Borenstein M, Higgins JPT, Hedges LV, Rothstein HR. Basics of meta-analysis: I2 is not an absolute measure of heterogeneity. *Res Synth Methods*. 2017;8:5–18.
- 46. Bernhardt J, Hayward KS, Kwakkel G, et al. Agreed definitions and a shared vision for new standards in stroke recovery research: the Stroke Recovery and Rehabilitation Roundtable Taskforce. *Int J Stroke*. 2017;12:444–450.
- Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Subgroup analysis. In: River ST, ed., *Introduction to Meta-Analysis*. Hoboken, NJ: John Wiley & Sons, Inc; 2009: 149–186.
- 48. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315:629–634.
- 49. Housman SJ, Le V, Rahman T, Sanchez RJ Jr, Reinkensmeyer DJ. Arm-training with T-WREX after chronic stroke: preliminary results of a randomized controlled trial. In: 2007 IEEE 10th International Conference on Rehabilitation Robotics. Noordwijk; 2007: 562–568.
- Volpe BT, Lynch D, Rykman-Berland A, et al. Intensive sensorimotor arm training mediated by therapist or robot improves hemiparesis in patients with chronic stroke. *Neurorehabil Neural Repair*. 2008;22:305–310.
- 51. Housman SJ, Scott KM, Reinkensmeyer DJ, et al. A randomized controlled trial of gravity-supported, computer-enhanced arm exercise for individuals with severe hemiparesis. *Neurorehabil Neural Repair.* 2009;23:505–514.
- Lo AC, Guarino PD, Richards LG, et al. Robot-assisted therapy for long-term upper-limb impairment after stroke. N Engl J Med. 2010;362:1772–1783.
- 53. Masiero S, Armani M, Rosati G, et al. Upper-limb robot-assisted therapy in rehabilitation of acute stroke patients: focused review and results of new randomized controlled trial. *J Rehabil Res Dev.* 2011;48:355–366.
- 54. Reinkensmeyer DJ, Wolbrecht ET, Chan V, et al. Comparison of three-dimensional, assist-as-needed robotic arm/hand movement training provided with pneu-wrex to conventional tabletop therapy after chronic stroke. *Am J Phys Med Rehabil.* 2012;91: 232–241.
- 55. Ang KK, Guan C, Phua KS, et al. Brain-computer interface-based robotic end effector system for wrist and hand rehabilitation: results of a three-armed randomized controlled trial for chronic stroke. *Front Neuroeng.* 2014;7:30.
- 56. Brokaw EB, Nichols D, Holley RJ, et al. Robotic therapy provides a stimulus for upper limb motor recovery after stroke that is complementary to and distinct from conventional therapy. *Neurorehabil Neural Repair*. 2014;28:367–376.
- Klamroth-Marganska V, Blanco J, Campen K, et al. Threedimensional, task-specific robot therapy of the arm after stroke: a multicentre, parallel-group randomised trial. *Lancet Neurol*. 2014;13:159–166.
- Prange GB, Kottink AIR, Buurke JH, et al. The effect of arm support combined with rehabilitation games on upper-extremity function in subacute stroke: a randomized controlled trial. *Neurorehabil Neural Repair.* 2015;29:174–182.
- Susanto EA, Tong RK, Ockenfeld C, et al. Efficacy of robot-assisted fingers training in chronic stroke survivors: a pilot randomizedcontrolled trial. J Neuroeng Rehabil. 2015;12:42.
- Takahashi K, Domen K, Sakamoto T, et al. Efficacy of upper extremity robotic therapy in subacute poststroke hemiplegia: an exploratory randomized trial. *Stroke*. 2016;47:1385–1388.

- Tomić TJDD, Savić AM, Vidaković AS, et al. ArmAssist robotic system versus matched conventional therapy for poststroke upper limb rehabilitation: a randomized clinical trial. *Biomed Res Int.* 2017;2017:7659893.
- 62. Carpinella I, Lencioni T, Bowman T, et al. Effects of robot therapy on upper body kinematics and arm function in persons post stroke: a pilot randomized controlled trial. *J Neuroeng Rehabil.* 2020;17:10.
- 63. Daunoraviciene K, Adomaviciene A, Grigonyte A, Griskevicius J, Juocevicius A. Effects of robot-assisted training on upper limb functional recovery during the rehabilitation of poststroke patients. *Technol Health Care.* 2018;26:533–542.
- 64. Byl NN, Abrams GM, Pitsch E, et al. 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. *J Hand Ther.* 2013;26:343–352.
- 65. Lum PS, Burgar CG, Shor PC, Majmundar M, der Loos M. Robotassisted movement training compared with conventional therapy techniques for the rehabilitation of upper-limb motor function after stroke. *Arch Phys Med Rehabil.* 2002;83:952–959.
- Lum PS, Burgar CG, Van der Loos M, et al. MIME robotic device for upper-limb neurorehabilitation in subacute stroke subjects: a follow-up study. *J Rehabil Res Dev.* 2006;43: 631–642.

- 67. Kim H, Miller LM, Fedulow I, et al. Kinematic data analysis for post-stroke patients following bilateral versus unilateral rehabilitation with an upper limb wearable robotic system. *IEEE Trans Neural Syst Rehabil Eng.* 2013;21:153–164.
- Taub E, Uswatte G, Pidikiti R. Constraint-induced movement therapy: a new family of techniques with broad application to physical rehabilitation—a clinical review. *Rehabil Res Dev.* 1999;36: 237–251.
- Ogden R, Franz SI. On cerebral motor control: the recovery from experimentally produced hemiplegia. *Psychobiology*. 1917;1: 33–49.
- 70. Langhorne P, Bernhardt J, Kwakkel G. Stroke rehabilitation. *Lancet*. 2011;377:1693–1702.
- Kwakkel G, Veerbeek JM, van Wegen EEH, Wolf SL. Constraintinduced movement therapy after stroke. *Lancet Neurol.* 2015;14: 224–234.
- 72. Di Pino G, Pellegrino G, Assenza G, et al. Modulation of brain plasticity in stroke: a novel model for neurorehabilitation. *Nat Rev Neurol.* 2014;10:597–608.
- Bustrén EL, Sunnerhagen KS, Alt Murphy M. Movement kinematics of the ipsilesional upper extremity in persons with moderate or mild stroke. *Neurorehabil Neural Repair*. 2017;31:376–386.
- Micera S, Caleo M, Chisari C, Hummel FC, Pedrocchi A. Advanced neurotechnologies for the restoration of motor function. *Neuron*. 2020;105:604–620.