Effect of Motor Intervention for Infants and Toddlers With Cerebral Palsy: A Systematic Review and Meta-analysis

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Purpose: To conduct a systematic review and meta-analysis on the effect of motor intervention on motor function of infants and toddlers with cerebral palsy (CP).

Methods: Four databases were searched for randomized controlled trials (RCTs) of motor interventions for children with or at high risk of CP younger than 36 months. Studies were excluded if less than 50% of children developed CP.

Results: Eleven RCTs included 363 children; 85% diagnosed with CP. Very low-quality evidence supports that: (1) task-specific motor training was more effective than standard care for improving motor function (small effect), (2) constraint-induced movement therapy (CIMT) may be more effective than bimanual play or massage for improving function of the more affected hand (moderate effect), and high-intensity treadmill training is no more effective than low-intensity for improving walking.

Conclusions: Very low-quality evidence supports that task-specific motor training and CIMT may improve motor function of infants and toddlers with CP.

The Supplemental Digital Content Video Abstract is available at: http://links.lww.com/PPT/A382. (Pediatr Phys Ther 2022;34:297–307)

Key words: cerebral palsy, infant, meta-analysis, motor intervention, systematic review, toddler

INTRODUCTION

Recent advancements in the early detection of cerebral palsy (CP) support that children can be diagnosed with or at high risk of CP as early as 3 to 4 months of age.[1] This breakthrough provides an opportunity for infants and toddlers with or at high risk of CP to participate in CP-specific motor intervention in early infancy[2] when there is the greatest potential for neuroplastic change to maximize lifelong motor function.[3]

The potential of early motor intervention to optimize functional outcomes by harnessing the greater neuroplasticity of the developing brain and neuromotor system is particularly relevant to CP. Cerebral palsy is a disorder of movement caused by a malformation or lesion to the developing brain.[4] It is the most common physical disability in childhood[5] and affects over 17 million people worldwide.[6] The functional outcome of CP is the result not only of the direct effects of the malformation or lesion, but also the activity-dependent neural reorganization that occurs in response to environmental experiences, including motor intervention. Recognizing that children with CP reach 90% of their gross motor potential by age 5, with most potential achieved by 3 years,[7] motor intervention during the early years of life is considered critical to optimize the activity-dependent neuroplasticity and functional outcome of infants and toddlers with CP. Since activity-dependent reorganization can be adaptive or maladaptive, one needs to consider not only the positive, adaptive plasticity that can result from early intervention, but also the negative, maladaptive plasticity that can result from not providing intervention early enough or providing suboptimal intervention in terms of content or dose.

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What This Article Adds

For infants and toddlers with or at high risk of cerebral palsy, very low-quality evidence supports that:

- task-specific motor training based on motor learning principles may have a small effect on motor function,
- constraint-induced movement therapy may have a moderate effect on function of the more affected hand, and
- high-intensity treadmill training is no more effective than low-intensity treadmill training for improving walking function.

To optimize positive activity-dependent neuroplasticity and functional outcomes, it is critical to determine the efficacy of specific types of intervention for infants and toddlers with or at high risk of CP. Three systematic reviews have investigated the efficacy of early motor intervention for infants and toddlers with or at high risk of CP younger than 3 years.[8-10] One review included infants younger than 12 months,[9] 1 included children younger than 2 years,[10] and 1 included children younger than 3 years.[8] The reviews have 3 limitations. All 3 reviews included studies in which less than 50% of children developed CP by follow-up, which limits the applicability of the findings to children with CP. The reviews did not assess the research literature quantitatively using a meta-analysis to determine the efficacy of specific motor interventions, such as task-specific motor training and constraint-induced movement therapy (CIMT). In addition, the previous reviews did not include the recently published randomized controlled trials (RCTs) on CIMT. This systematic review with meta-analysis addresses these gaps in the literature by quantitatively investigating the effect of specific motor interventions on motor function of infants and toddlers with or at high risk of CP younger than 3 years using the highest-quality studies, RCTs, in which more than 50% of children developed CP by follow-up.

METHODS

Protocol and Registration

This systematic review and meta-analysis was prepared according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[11] The A MeaSurement Tool to Assess systematic Reviews-2 (AMSTAR-2) checklist was used for the critical appraisal of this review.[12] The protocol was prospectively registered with the PROSPERO International Prospective Register of Systematic Reviews (CRD42021250548).

Search Strategy

A comprehensive literature search was completed from inception to February 2021 and rerun in July 2021 by an information services librarian of 4 databases: CINAHL, Embase, PubMed, and Web of Science. Searches were not restricted by publication date or language. Search terms included cerebral palsy, children, motor intervention, physical therapy, and occupational therapy. References of included studies were examined and experts in the field were contacted to identify additional relevant studies. The full search strategy by database is provided in Supplemental Digital Content 1 (available at: http://links.lww.com/PPT/A383).

Eligibility Criteria and Study Selection

Included studies fulfilled the following criteria: (1) RCT and quasi-RCTs; (2) participants were children younger than 36 months with a diagnosis of CP or at high risk of CP based on neuroimaging, abnormal General Movement Assessment or abnormal Hammersmith Infant Neurological Examination, consistent with the early detection guidelines for CP[1]; (3) intervention targeted motor function and occurred in the outpatient, home, or community setting; (4) comparison group consisted of standard care or a different motor intervention; and (5) one or more outcome measures assessed motor function using a standardized test. Only RCTs were included to report findings from the highest quality of evidence.

Studies were excluded if: (1) they were review papers, abstracts, protocols, conference proceedings, or dissertations; (2) they were published in a language other than English and an adequate English translation could not be obtained; (3) less than 50% of participants had a diagnosis of CP by follow-up; (4) all or part of the intervention occurred in the inpatient setting, including the neonatal intensive care unit; (5) the study assessed the effect of an adjunct by comparing motor intervention alone to the same motor intervention plus an adjunct, such as electrical stimulation or Kinesio tape.

Studies were screened using a web-based screening and data extraction tool, Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia), based on title and abstract, using the inclusion and exclusion criteria. If necessary, a full-text review of studies was completed. During the screening and full-text review, 2 of 3 authors independently reviewed the studies, data were compared for agreement, and disagreements were resolved by discussion. Studies that were read in full text but excluded are listed in Supplemental Digital Content 2 (available at: http://links.lww.com/PPT/A384); abstracts are not included in this table.

Level of Evidence and Risk of Bias

Three authors independently appraised the studies using the Oxford Center for Evidence-Based Medicine levels of evidence[13] and the Revised Cochrane risk-of-bias Tool (ROB-2) for randomized trials.[14] Discrepancies were resolved through discussion.

Studies were assigned a level of design rigor using criteria from the Oxford Center for Evidence-Based Medicine levels of evidence.[13] Levels of evidence range from level I through level V, with level I as the highest level of evidence and level V as the lowest level of evidence.

Risk of bias was assessed using the ROB-2.[14] This tool assesses bias resulting from 5 domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. The risk of bias was classified as low, some concerns, or high for each domain and for the entire study.

Data Extraction

Data were independently extracted by 2 of 3 reviewers, data were compared for agreement, and discrepancies were resolved through discussion.[15] Sources of funding were assessed to determine whether they represented a conflict of interest.

Quantitative Data Synthesis

Vote counting based on statistical significance was used to synthesize results for all studies based on type of intervention. For each type of intervention with multiple studies, 1 motor outcome measure from each study was pooled for meta-analysis. If a study reported multiple motor outcome measures, the primary outcome measure was used. If the primary outcome measure was not a standardized motor assessment, then data from the standardized motor assessment were used. All studies reported outcomes immediately after intervention; therefore, means and standard deviations (SD) of postintervention scores were used to obtain the pooled estimates. Authors of studies that did not report means and SDs were contacted to obtain this information. For studies reporting medians and quartiles due to violation of normality assumptions, means and SDs were manually estimated using the method of Wan et al.[16]

Using Review Manager (RevMan 5.4.1 Cochrane Collaboration, Copenhagen, Denmark), standard mean differences (SMD) with 95% confidence intervals (CI) were calculated. A random-effects model was used with inverse-variance weighting. For SMD effect size interpretation, 0.2 was considered small, 0.5 moderate, and 0.8 large.[17] Heterogeneity was investigated using the I^2 statistic and the tau statistic.[2] Heterogeneity was considered substantial when I^2 was greater than 50%, and the tau statistic[2] was greater than 0.05. If heterogeneity was high, a sensitivity analysis was performed to assess the cause of the heterogeneity; this may result in removal of a study from the meta-analysis. If a study was removed from the meta-analysis, the reason for removal was documented. Results of the meta-analysis for each type of intervention were graphically represented using forest plots.

Quality of Evidence

The grading of the quality of evidence was based on the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach for systematic reviews of clinical trials. The quality of evidence refers to the confidence in the estimates of effect. It is graded as high, moderate, low, or very low. The effect of each type of motor intervention with results from RCTs with risk of bias rated as low or some concerns were used. The quality of evidence was assumed to be high, but then was rated down 1 level if there were study limitations, inconsistency of results, indirectness of evidence, and imprecision. The level of evidence was then rated up 1 level if there was a large magnitude of effect or dose-response gradient. Two of 3 authors independently appraised for GRADE and discrepancies were resolved through discussion.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

RESULTS

Studies Included

Search strategy and selection details are in Figure 1.[18] Twelve studies were eligible for inclusion, but 2 studies used the same sample; thus, the results of these studies were combined

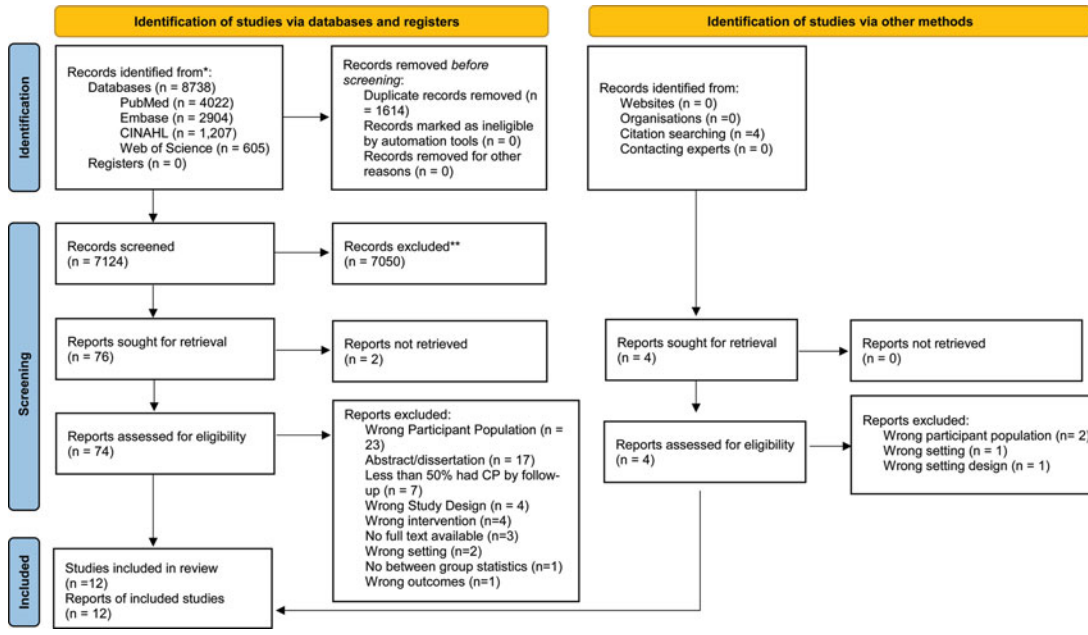

Fig. 1. PRISMA flow diagram.

as 1 study.[19,20] Eleven studies were included in this review.[19-30] All 11 studies were level II RCTs.[19-30] Risk of bias was low for 5 studies,[19,20,22,23,25,30] some concerns for 5 studies,[24,26-29] and high for 1 study.[21] The most common reasons for some concerns or high risk of bias included bias due to deviations from intended intervention, selection of reported results, and the randomization process. The level of evidence, study design, overall risk of bias, number of participants, interventions, and intervention parameters are in Table 1. Full risk-of-bias assessments are in Supplemental Digital Content 3 (available at: http://links.lww.com/PPT/A390). Sources of funding are in Supplemental Digital Content 4 (available at: http://links.lww.com/PPT/A391).

Participants

A total of 363 children with or at high risk of CP ranging in age from 0 to 32 months participated in the studies; 85% were diagnosed with CP by follow-up.[19-30] The characteristics of the participants are in Supplemental Digital Content 5 (available at: http://links.lww.com/PPT/A392).

Motor Outcome Measures

Results of motor outcome measures are in Table 2. Motor participation was measured in 4 of 11 studies (36%).[19,26-29] Outcomes included the Canadian Occupational Performance Measure, Pediatric Evaluation of Disability Index (PEDI), and Vineland Adaptive Behavior Scales (VABS).

Activity was measured in 11 of 11 studies (100%).[19-30] Fine motor outcomes included the Assisting Hand Assessment (AHA) and Mini-AHA; Bayley Scales of Infant and Toddler Development fine motor subscale (BSITD-fm); Functional Inventory bilateral hand use (FI-bhu) and unilateral hand use (FI-uhu); Hand Assessment of Infants of the more affected hand (HAI more-affected), less affected hand (HAI less-affected), and both hands (HAI-bim). Gross motor outcomes included the Alberta Infant Motor Scale, average active minutes, BSITD-gross motor composite, Functional Inventory gross motor (FI-gm), Gross Motor Function Measure (GMFM), Infant Motor Profile, Peabody Developmental Motor Scale, 2nd edition (PDMS-2), Pediatric Evaluation of Disability Index mobility score (PEDI-m), and 10-m walk test (10 MWT). Motor outcomes were measured using the Bayley Scales of Infant Development motor composite (BSID-pdi) and Goal Attainment Scale.

Body structure and function (BSF) was measured in 2 of 11 studies (18%).[21,26,29] Outcomes included the Modified Ashworth Scale (MAS), primitive reflexes, and 1-minute walk test (1 MWT) to assess endurance.

Motor Interventions

Motor interventions were categorized into 4 groups: (1) task-specific motor training based on motor learning principles (n = 5 studies), (2) CIMT (n = 4 studies), (3) neurofacilitation of developmental reaction approach (n = 1 study), and (4) treadmill training (n = 1 study). Supplemental Digital Content 6 (available at: http://links.lww.com/PPT/A393) includes principles of each experimental intervention, including goals, motor intervention principles, and family coaching.

Task-Specific Motor Training Based on Motor Learning Principles

Five RCTs assessed outcomes of task-specific motor training based on motor learning principles compared with standard care or another motor intervention.[19,20,24,27-29] Task-specific motor training based on motor learning principles was defined as intensive, targeted motor training of task and context-specific goals that incorporated motor learning principles of trial-and-error learning, movement exploration, and embedding practice into daily routines. Two studies assessed outcomes of Goals Activity Motor Enrichment (GAME),[27,28] 1 study assessed outcomes of Coping with and Caring for Infants with Special Needs (COPCA),[19,20] 1 study assessed *Learninggames*,[29] and 1 study assessed outcomes of a perceptual motor intervention.[24] Participants ranged in age from 0 to 24 months; 73% of infants were diagnosed with CP. Types of CP included unilateral and bilateral spastic CP and athetoid CP with function ranging from Gross Motor Function Classification System levels I to V. The experimental intervention dose ranged from 8 weeks to 12 months, with a frequency of 2 times per week to every other week for 30 to 90 minutes. Two of 5 studies used control interventions that were dose-matched with the experimental groups,[19,20,29] and the other 3 used a lower dose.[24,27,28] No adverse events were reported.

The 5 task-specific motor training interventions reported participation and activity outcomes.[19,20,24,27-29] Between the experimental and control groups, 17 outcomes were compared after intervention, with 0 of 3 participation outcomes and 4 of 14 activity outcomes (PDMS-2, BSID-pdi) reaching statistical significance. One study reported within-group comparisons.[19,20] Within the experimental and control groups, 2 of 2 participation outcomes (PEDI, VABS) reached statistical significance in the intended direction in both groups.

Four studies, with a total of 121 children with or at high risk of CP, reported sufficient data on motor function to be pooled for meta-analysis.[24,27-29] The meta-analysis supported that infants and toddlers with or at high risk of CP who received task-specific motor training based on motor learning principles (n = 59) scored an SMD of 0.41 (95% CI 0.05 to 0.78, P = .03; small effect) higher on motor function compared with children who received standard care or another motor intervention (n = 62). The effect was small, the meta-analysis was significant, and heterogeneity was low (I^2 = 0%, tau^2 = 0). Figure 2 is the forest plot. An initial meta-analysis was performed with 5 studies (see Supplemental Digital Content 7, available at: http://links.lww.com/PPT/A394, and Supplemental Digital Content 8, available at: http://links.lww.com/PPT/A395, for details).

There is very low-quality evidence (downgraded for risk of bias, indirectness, imprecision) that, immediately post-intervention, task-specific motor training based on motor learning principles may be more effective than standard care for improving motor function of infants and toddlers with or at high risk of CP. Supplemental Digital Content 9 (available at: http://links.lww.com/PPT/A396) is the GRADE Evidence Profile.

TABLE 1
Study Characteristics

Author	Level of Evidence	Study Design	Overall Risk of Bias	Experimental Group vs Control Group With Number of Participants	Experimental Frequency Intensity Time Duration	Control Frequency Intensity Time Duration	Home Program
Constraint-induced movement therapy							
Chamudot et al[22]	II	RCT	Low	CIMT (n = 17) vs BIM (n = 16)	*Home-based OT:* F: 1x/wk I/T: NR D: 8 wk	*Home-based OT:* F: 1x/wk I/T: NR D: 8 wk	F: 7x/wk I: NR T: 60 min D: 8 wk
Eliason et al[23]	II	RCT	Low	CIMT (n = 18) vs IM (n = 13)	*Home-based OT:* F:1x/wk I: NR T: NR D: 12 wk	*Home-based OT:* F: 3 sessions I: NR T: NR D: N/A	F: 6x/wk I: NR T: 30 min (CIMT) T: 5-30 min (IM) D: 12 wk
Maitre et al[25]	II	RCT	Low	CIMT (n = 37) vs BIM (n = 36)	*Home-based therapy:* F: 1x/wk I: NR T: 60 min D: 28 d	*Home-based therapy:* F: 1x/d I: NR T: 20 min D:28 d	*CIMT:* F: 1x/d I: NR T: 6 h (CIMT) T: 20 min (BIM) D: 28 d
Pietruszewski et al[30]	II	RCT	Low	CIMT (n = 7) vs BIM (n = 6)	*Telehealth therapy:* F: 1x/wk I: NR T: 15-45 min D: 28 d	*Telehealth therapy:* F: 1x/wk I: NR T: 15-45 min D: 28 d	F: 5x/wk I: NR T: 6 h (CIMT) T: 20 min (BIM) D: 28 d
Task-specific motor training based on motor learning principles							
Harbourne et al[24]	II	RCT	Some concerns	Perceptual motor intervention (n = 15) vs home program (n = 15)	*Clinic-based PT:* F: 2x/wk I: NR T: 1 h D: 8 wk	*Home-based therapy:* F: 1x/wk I: NR T: 30-60 min D:8 wk	F: daily I/T: NR D: 8 wk
Hielkema et al[19,20]	II	RCT	Low	COPCA (n = 23) vs SC (n = 20)	*Home-based PT:* F: 1x/wk I: NR T: 30-60 min D: 1 y	*Home-based /clinic-based PT:* F: 1x/wk I: NR T: 30-60 min D: 1 y	NR
Morgan et al[27]	II	RCT	Some concerns	GAME (n = 6) vs SC (n = 7)	*Home-based therapy:* F: 1x/wk initially, decreased I: NR T: 60-90 min D: 12 wk	*Clinic-based therapy:* F: 1-2x/mo I/T: NR D: 12 wk	F/I/T: NR D: 12 wk
Morgan et al[28]	II	RCT	Some concerns	GAME (n = 15) vs SC (n = 15)	*Home-based therapy:* F: at least fortnightly I: NR T: 30-90 min D: 16 wk	*Home-based or clinic-based therapy:* F: NR I: NR T: 15-90 min D: 16 wk	F/I/T: NR D: 16 wk
Palmer et al[29]	II	RCT	Some concerns	*Learninggames* (n = 23) vs NDT (n = 25)	*Clinic-based child development specialist:* F: every 2 wk I: NR T: 1 h D: 6 mo	*Clinic-based PT:* F: every 2 wk I: NR T: 1 h D: 6 mo *Clinic-based PT*: F: daily I/T: NR D: until transition to sit independently	F: daily I/T: NR D: 6 mo

(*continues*)

TABLE 1
Study Characteristics (*Continued*)

Author	Level of Evidence	Study Design	Overall Risk of Bias	Experimental Group vs Control Group With Number of Participants	Experimental Frequency Intensity Time Duration	Control Frequency Intensity Time Duration	Home Program
Neurofacilitation of developmental reaction approach							
Batra et al[21]	II	RCT	High	NFDR vs NDT (total = 30[a])	*Home-based therapy:* F: 3x/wk I: NR T: 40 min D: 3 mo	*Home-based therapy:* F: 3x/wk I: NR T: 40 min D: 3 mo	F/I/T/D: NR
Treadmill training							
Mattern-Baxter et al[26]	II	RCT	Some concerns	TT 10x/wk (n = 9) vs TT 2x/wk (n = 10)	*Home-based therapist instruction:* F: 1x/wk I/T: NR D: 6 wk	*Home-based therapist instruction:* F: 1x/wk I/T: NR D: 6 wk	F: 10x/wk (EG) or 2x/wk (CG) I: fastest speed a child could walk T: 20 min D: 6 wk

Abbreviations: BIM, bimanual training; CG, control group; CIMT, constraint-induced movement therapy; COPCA, Coping With and Caring for Infants With Special Needs; D, duration; EG, experimental group; F, frequency; GAME, Goals Activity Motor Enrichment; I, intensity; IM, infant massage; NDT, neurodevelopmental treatment; NFDR, neurofacilitation of developmental reactions; NR, not reported; OT, occupational therapy; PT, physical therapy; RCT, randomized control trial; SC, standard care; T, time; TT, treadmill training.
[a]Study did not report number of participants per group.

Constraint-Induced Movement Therapy

Four RCTs assessed outcomes of CIMT compared with bimanual play or infant massage.[22,23,25,30] CIMT was defined as intensive, structured motor training of the more affected upper extremity while restricting use of the less affected upper extremity. In all 4 studies a soft custom mitt was used to restrict use of the less affected upper extremity. Participants ranged in age from 3 to 24 months, and all were diagnosed with unilateral or bilateral asymmetric spastic CP. The experimental intervention dose ranged from 28 days to 12 weeks, 1 to 6 times per week for 30 minutes to 6 hours. Two of 4 studies used control interventions that were dose-matched with the experimental groups,[22,23] and the other 2 used a lower dose.[25,30] No adverse events were reported.

The 4 CIMT studies reported activity outcomes.[22,23,25,30] Between the experimental and control groups, 13 outcomes were compared after intervention with 3 of 13 activity outcomes (BSITD-fm more-affected, HAI more-affected) reaching statistical significance. Two studies reported within-group comparisons.[22,23] Within the experimental and control groups, 7 activity outcomes were compared after intervention with 6 outcomes reaching statistical significance in both groups (Mini-AHA, FI-bhu, FI-uhu, FI-gmu, HAI more-affected, HAI less-affected) and 1 reaching statistical significance in the experimental group only (HAI-bim).

All 4 studies with a total of 150 children with CP reported sufficient data on unimanual function of the more affected hand to be pooled for meta-analysis.[22,23,25,30] The meta-analysis supported that children with unilateral CP who received CIMT (n = 79) scored an SMD of 0.59 (95% CI −0.18 to 1.37, P = .13; moderate effect) higher on unimanual function of the more affected hand compared with children with unilateral CP who received bimanual play or infant massage (n = 71). Although the combined pooled effect was moderate, it only trended toward significance and there was substantial heterogeneity (I^2 = 75%, tau^2 = 0.42). Figure 3 is the forest plot. A sensitivity analysis was performed and the Pietruszewski et al[30] study contributed to the high heterogeneity. Refer to Supplemental Digital Content 7 (available at: http://links.lww.com/PPT/A394 for details).

There is very low-quality evidence (downgraded for inconsistency, indirectness, imprecision) that, immediately post-intervention, CIMT may be more effective than bimanual play or infant massage for improving unimanual function of the more affected hand in infants with unilateral CP.

Neurofacilitation of Developmental Reaction Approach

One RCT assessed outcomes of the neurofacilitation of developmental reaction approach compared with neurodevelopment treatment.[21] Participants ranged in age from 6 months to 2 years and all were diagnosed with CP. The intervention dose was 3 months, 3 times per week for 40 minutes. No adverse events were reported. Between the experimental and control groups, 3 outcomes were compared after intervention with 1 of 1 activity outcomes (GMFM) and 1 of 2 BSF outcomes (MAS) reaching statistical significance. The outcomes of this RCT were not assessed using GRADE because the study had a high risk of bias.

Treadmill Training

One RCT assessed outcomes of high- versus low-intensity treadmill training.[26] Participants ranged in age from 14 to 32 months; 74% were diagnosed with spastic diplegic CP. The intervention dose was 6 weeks of 20-minute sessions, implemented

TABLE 2

Summary of Results

Author	Experimental vs Control Adherence	Timing of Outcome Measures	ICF Model	Outcome Measures	Between-Group Differences EG vs CG	Within-Group Differences EG and CG	Clinical Implications
Constraint-induced movement therapy							
Chamudot et al[22]	CIMT: 75% h BIM: 81% h	Pre, post	A A A A	Mini-AHA FI-GMS FI-UHU FI-BHU	NS, ES: 0.17[a] NS NS, ES: 0.00[a] NS	NS NS NS NS NS NS NS NS	For infants with CP, 8 wk of CIMT compared with BIM resulted in similar improvements in hand and gross motor function.
Eliason et al[23]	CIMT: 97% h Massage: 72% sessions	Pre, 6 wk, 12 wk, post, 18 mo of age	A A A	HAI-A HAI-NA HAI-B	↑, ES: 0.43[a] NS NS, ES: 0.57[a]	↑ NS NR NR NS NS	For infants with UCP, 12 wk of CIMT compared with infant massage resulted in improved function of the affected hand. During follow-up at 18 wk, results were maintained.
Maitre et al[25]	CIMT: 38 h/wk BIM: NR	Pre, post	A A A A	BSITD-UFM-A BSITD-UFM-NA BSITD-BI BSITD-GM	↑, ES: 0.35 NS NS, ES: 0.02 NS	NR NR NR NR NR NR NR NR	For infants with asymmetric CP, 28 d of CIMT compared with a waitlist control resulted in improved fine motor skills of the more affected hand.
Pietruszewski et al[30]	CIMT: 21 h/wk BIM: NR	Pre, post	A A A	BSITD UFM BSITD BFM BSITD GM	↑, ES: 3.91[a] NS, ES: 2.1[a] NS	NR NR NR NR NR NR	For infants with hCP or asymmetric CP, 28 d of CIMT compared with a waitlist control resulted in improved fine motor skills of the more affected hand.
Task-specific training based on motor learning principles							
Harbourne et al[24]	Perceptual motor intervention: NR Home program: NR	Pre, 1 mo post	A	GMFM-sitting	NS, ES: 0.07[a]	NR NR	For infants with or at high risk of CP, 8 wk of perceptual-motor intervention compared with a home program had resulted in similar effects on sitting function.
Hielkema et al[19,20]	COPCA: median 3.0 session/mo TIP: median 2.5 sessions/mo	Pre, 3 mo, 6 mo, post, at 21 mo CA	A A A A A A A P	IMP-perf GMFM-88 GMFM-66 GMFM (adapted) AIMS BSID-II: PDI PEDI VABS	NS, ES: 0.29[a] NS, ES: 0.11[a] NS, ES: 0.36[a] NS NS, ES: 0.08[a] NS, ES: 0.10[a] NS NS	NR NR NR NR NR NR NR NR NR NR NR NR ↑ ↑ ↑ ↑	For infants with or at high risk of CP, 1 y of COPCA intervention compared with typical infant physiotherapy resulted in similar developmental outcomes.
Morgan et al[27]	GAME: mean 140.58 h SC: mean 54.17 h	Pre, post	A P A A	GAS COPM: perf PDMS-2: TMQ PDMS-2 total motor SS	NS NS ↑, ES: 0.68[a] ↑, ES: 0.67[a]	NR NR NR NR NR NR NR NR	For infants with or at high risk of CP, 12 wk of GAME intervention compared with standard care resulted in improved motor skills.

(*continues*)

TABLE 2

Summary of Results (*Continued*)

Author	Experimental vs Control Adherence	Timing of Outcome Measures	ICF Model	Outcome Measures	Between-Group Differences EG vs CG	Within-Group Differences EG and CG	Clinical Implications
Morgan et al[28]	GAME: mean 21.91 h SC: mean 12.82 h	Pre, post, 12 mo of age	A A P	PDMS-2: TMQ PDMS-2: RS COPM: perf	NS, ES: 0.44[a] ↑, ES: −0.10[a] NS, ES: 0.25[a]	NR NR NR NR NR NR	For infants with or at high risk of CP, 16 wk of GAME intervention compared with standard care resulted in improved motor skills.
Palmer et al[29]	*Learninggames*: >90% compliance NDT: >90% compliance	Pre, post, 6 mo post	A	BSID-PDI	↑, ES: 0.57[a]	NR NR	For infants with CP, 6 mo of *Learninggames* intervention compared with NDT intervention resulted in improved motor skills.
Neurofacilitation of developmental reaction approach							
Batra et al[21]	NFDR: NR NDT: NR	Pre, post	BSF BSF A	MAS PR GMFM	↑ NS ↑	NR NR NR NR NR NR	For infants with CP, 3-mo of NFDR program compared to NDT resulted in improved motor function.
Treadmill training							
Mattern-Baxter et al[26]	TT 2x/wk: 183 ± 46 m TT 10x/wk: 762 ± 213 m	Pre, post, 1 mo and 4 mo post	A A A A A BSF A A	GMFM D GMFM E PDMS-2 loc PEDI mob 10 MWT 1-MWT Average steps Average active minutes	NS, ES: 0.34[a] NS, ES: 0.25[a] NS, ES: 0.28[a] NS NS NS NS NS	↑ ↑ NS ↑ ↑ ↑ ↑ ↑ ↑ ↑ ↑ ↑ NS NS NS NS	For toddlers with CP, 6 wk of TT intervention delivered 2x/wk or 10x/wk resulted in similar improvement of walking skills.

Abbreviations: ↑, statically significant increase; ↓, statistically significant decrease; A, activity; AIMS, Alberta Infant Motor Scale; BIM, bimanual training; BSF, Body Structure Function; BSID-II, Bayley Scales of Infant Development-second edition; BSITD-BI, Bayley Scales of Infant and Toddler Development bilateral hand function; BSITD-GM, Bayley Scales of Infant and Toddler Development gross motor; BSITD-UMF-A, Bayley Scales of Infant and Toddler Development unilateral motor function of the more affected hand; BSITD-UFM-NA, Bayley Scales of Infant and Toddler Development unilateral motor function of the less affected hand; CA, corrected age; CG, control group; CIMT, constraint-induced movement therapy; COPCA, Coping With and Caring for Infants With Special Needs; COPM, Canadian Occupational Performance Measure; CP, cerebral palsy; EG, experimental group; ES, effect size; FI-BHU, Functional Inventory bilateral hand use; FI-GMS, Functional Inventory gross motor subtest; FI-UHU, Functional Inventory unilateral hand use; GAME, Goals Activity Motor Enrichment; GAS, Goal Attainment Scale; GMFM, Gross Motor Functional Measure; GMFM D, Gross Motor Function Measure-subscale D; GMFM E, Gross Motor Function Measure-subscale E; HAI-A, Hand Assessment of Infants of the more affected hand; HAI-B, Hand Assessment of Infants of both hands; HAI-NA, Hand Assessment of Infants of the less affected hand; hCP, hemiplegic cerebral palsy; ICF, International Classification of Functioning; IMP-perf, Infant Motor Profile-performance subtest; MAS, Modified Ashworth Scale; Mini-AHA, Mini-Assisting Hand Assessment; NDT, neurodevelopmental treatment; NFDR, neurofacilitation of developmental reactions; NR, not reported; NS, nonsignificant; 1 MWT, 1 m walk test; P, participation; PDI, Pain Disability Index; PDMS, Peabody Developmental Motor Scales; PEDI, Pediatric Evaluation of Disability Inventory; PR, primitive reflex; S, significant; SC, standard care; SS, standard score; 10 MWT, 10-meter walk test; TIP, traditional infant physical therapy; TMQ, Total Motor Quotient; TT, treadmill training; UCP, unilateral cerebral palsy; VABS, Vineland Adaptive Behavior Scales.

[a]Effect size was calculated by authors (Hedges' g).

10 sessions per week for the high-intensity group and 2 sessions per week for the low-intensity group. No adverse events were reported. Between the experimental and control groups, no outcomes reached statistical significance. Within the experimental and control groups, 8 outcomes were compared after intervention with 5 outcomes reaching statistical significance in both groups: 4 activity outcomes (GMFM-standing dimension, PDMS-2 locomotion subtest, PEDI-m, and 10 MWT) and 1 BSF outcome (1 MWT). One activity outcome (GMFM-walking, running, and jumping dimension) reached statistical significance in the control group only.

There is very low-quality evidence (downgraded for risk of bias, imprecision) that, immediately post-intervention, high-intensity treadmill training is no more effective than low-intensity treadmill training for improving gait function of toddlers with spastic diplegic CP.

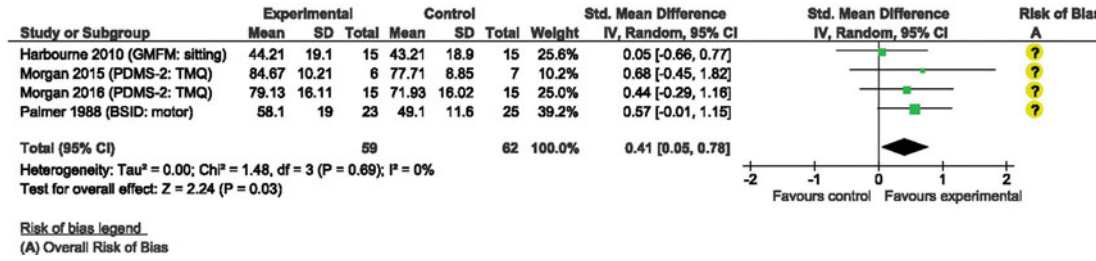

Fig. 2. Task-specific motor learning based on motor learning principles forest plot. Infants and toddlers with or at high risk of cerebral palsy who received task-specific motor training based on motor learning principles (n = 59) scored an SMD of 0.41 (95% CI 0.05 to 0.78, $P = .03$; small effect) higher on motor function compared with children who received standard care or another motor intervention (n = 62). The meta-analysis was significant, and heterogeneity was low. BSID indicates Bayley Scales of Infant Development; CI, confidence interval; GMFM, Gross Motor Function Measure; PDMS-2, Peabody Developmental Motor Scales, 2nd edition; SD, standard deviation; SMD, standard mean difference; Std, standard; TMQ, total motor quotient.

DISCUSSION

This systematic review found 11 RCTs that investigated the effects of motor intervention on motor outcomes of infants and toddlers with or at high risk of CP; 85% of children developed CP. Interventions with the strongest evidence were task-specific motor training based on motor learning principles and CIMT although the evidence was of very low quality. This review compares findings from this review to other systematic reviews published in the literature. Recommendations to strengthen the quality of future research evidence and to improve clinical application of this evidence are discussed.

This review found very low-quality evidence from 4 RCTs with moderate risk of bias that, immediately post-intervention, task-specific motor training based on motor learning principles may improve motor function of children with or at high risk of CP compared with standard care or another motor intervention (SMD 0.41, 95% CI 0.05 to 0.78, $P = .03$; small effect). This finding is consistent with the 3 systematic reviews on motor intervention for infants and toddlers with or at high risk of CP [8-10] and the motor recommendations from the international clinical practice guideline.[2] All 4 reviews supported motor intervention that included task and context-specific goals, child-initiated movement, task-specific motor training with high repetition and practice, trial-and-error learning with encouragement of movement exploration and variability, and avoiding passive handling techniques. They also supported prioritizing the child-parent relationship, embedding practice into daily routines, and enriching the environment. All studies on task-specific motor training based on motor learning principles included in this review documented the use of at least 60% of these principles.

This review found very low-quality evidence from 4 RCTs with low risk of bias that, immediately post-intervention, CIMT compared with bimanual therapy or infant massage may improve unimanual function of the more affected hand of children with unilateral CP (SMD 0.59, 95% CI −0.18 to 1.37, $P = .13$; moderate effect). This finding is consistent with a recent systematic review and meta-analysis on CIMT for children with unilateral CP ages 3 months to 19 years.[31] Similar to this review, the review reported low to very low-quality evidence that CIMT was more effective than low-dose occupational therapy for improving unimanual capacity of the more affected hand of children with CP. However, the review found no difference in unimanual capacity when CIMT was compared with high-dose or dose-matched occupational therapy or bimanual therapy.[31] Consistent with this finding, 2 studies in this review found significant differences in unimanual capacity of the more affected hand when CIMT was compared with low-dose bimanual therapy.[25,30] One study in this review found no difference in unimanual capacity of the more affected hand when CIMT was compared with dose-matched bimanual therapy.[22] However, when CIMT was dose-matched with infant massage, CIMT was more effective for improving unimanual capacity of the more affected hand.[23] This supports that active child-initiated motor interventions, such as CIMT and bimanual therapy, may be more effective than passive interventions such as massage. Further research is needed to determine the effect of dose versus content of the intervention, such as CIMT or bimanual therapy, on unimanual and bimanual outcomes of infants and toddlers with unilateral CP.

This review found very low-quality evidence from one RCT with moderate risk of bias that high-intensity treadmill training

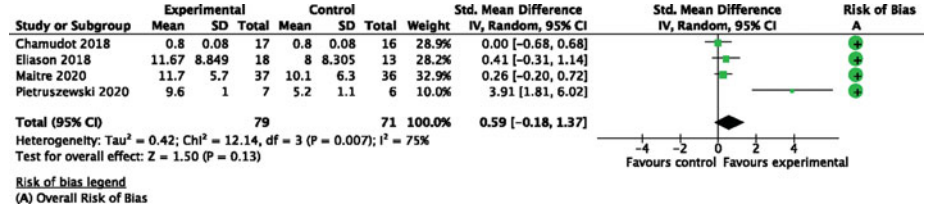

Fig. 3. Constraint-induced movement therapy forest plot. Infants and toddlers with or at high risk of cerebral palsy who received constraint-induced movement therapy (n = 79) scored an SMD 0.59 (95% CI −0.18 to 1.37, $P = .13$, moderate effect) higher on unimanual function of the more affected hand compared with children with unilateral CP who received bimanual play or infant massage (n = 71). Although the combined pooled effect was moderate, it only trended toward significance and there was substantial heterogeneity. CI indicates confidence interval; SD, standard deviation; SMD, standard mean difference; Std, standard.

is no more effective than low-intensity treadmill training for improving gait function of toddlers with spastic diplegic CP. This finding is consistent with a systematic review and meta-analysis on treadmill training for children younger than 6 years at risk for neuromotor delay that found no difference of high- and low-intensity treadmill training on onset of independent walking for children with Down syndrome[32]; however, they did find moderate-quality evidence that treadmill training compared with no treadmill training promoted earlier independent walking attainment for children with Down syndrome.[32] An area for future research may be to determine whether treadmill training or another type of intensive walking training promotes earlier independent walking attainment for children with CP.

In limiting the inclusion criteria to only RCTs in which over 50% of infants and toddlers developed CP by follow-up, the applicability of the results of this systematic review to children with CP is strengthened, but many motor interventions were not included. Other promising motor interventions for infants and toddlers with or at high risk of CP include the CareToy,[33] iMOVE with dynamic weight support,[34,35] Self-Initiated Prone Progression Crawler (SIPPC),[36] Sitting Together And Reaching to Play (START-Play),[37] Small Step Program,[38] and whole body vibration.[39] In addition, large efficacy trials of many interventions included in this review or noted earlier are ongoing and likely to provide more information within the next 5 years on the efficacy of motor intervention on motor outcomes of infants and toddlers with or at high risk of CP. The trials include: GAME, ACTRN12617000006347; SIT-PT, NCT04230278; early locomotor training, NCT04561232; CIMT/I-AQUIRE, NCT03910075; and CIMT/APPLES, NCT02567630.

Implications for Research

The following 4 recommendations are proposed to improve the quality of research on early motor intervention for infants and toddlers with or at high risk of CP. First, to increase the number of infants with CP in research studies, it is recommended that infants at high risk of CP be identified using the early detection guidelines[1] and followed for the first 2 years to confirm that the infants developed CP and to quantify the type, topography, and functional level of CP. This may allow for subgroup analyses that could strengthen applicability of the results to children with specific types and functional levels of CP.

Second, it is recommended to quantify the content, dose, fidelity, and adherence of not only the experimental and control interventions, but also the standard care that the child is receiving and the parents' implementation of the motor intervention into the children's daily routines. Most studies in this review (81%) reported content, dose, and adherence in the experimental groups, but this was only reported in 63% of studies for the control groups. Far fewer studies assessed fidelity to the intervention or quantified the parents' implementation of intervention principles into daily routines. This is critical since there is a growing appreciation of the importance of dose and the families' potential role in supporting an adequate dose of daily motor practice for positive activity-dependent neuroplasticity and improved functional outcomes.

Third, it is recommended to use primary outcome measures that are responsive to change for infants and toddlers with or at high risk of CP. The GMFM is the only outcome measure developed and validated to evaluate change in the gross motor function of children with CP,[7] yet it has not been validated for infants younger than 5 months. New outcome measures may need to be developed or current outcome measures modified to better quantify change with intervention for infants and toddlers with CP.

Fourth, it is recommended that characteristics of the family that may impact the outcome of intervention are collected and analyzed to determine barriers or opportunities for improved infant and family outcomes. The recommended home programs in the included studies ranged from twice a week to daily and up to 6 hours a day. Contextual factors such as maternal and paternal stress, age, socioeconomic status, or education[19,20,27,28] may contribute to a family's ability to incorporate intervention principles into daily routines. Understanding these contextual factors may allow improved ability to determine the optimal interventions for specific infant and family contexts and the most effective ways to coach parents to support the child-parent relationship, strengthen the infant and parents' sense of efficacy, and organize the environment to feasibly incorporate motor practice into daily activities.

Implications for Clinical Practice

This review supports the clinical recommendations from the 3 previous systematic reviews and the recent international clinical practice guideline for infants and toddlers at high risk of CP: initiate early intervention at the time of suspected diagnosis, focus on task-specific motor training based on motor learning principles, initiate CIMT and/or bimanual training when a unilateral CP diagnosis is suspected, and avoid the use of passive handling techniques.[2,8-10] This review adds that there is very low-quality evidence that task-specific training based on motor learning principles and CIMT may have, respectively, a small and moderate effect on motor function.

Limitations

This review's ability to quantify the efficacy of motor intervention for infants and toddlers with or at high risk of CP was limited by the small number of high-quality studies, small sample sizes within studies, and heterogeneity of interventions and outcome measures, which contributed to a meta-analysis with substantial heterogeneity. In addition, fewer than 10 studies were included for each meta-analysis, which precluded an assessment for publication bias.

CONCLUSIONS

A growing body of evidence supports the feasibility, safety, and efficacy of motor intervention for infants and toddlers with CP. Task-specific training based on motor learning principles and CIMT has the strongest quality of evidence; however, the overall quality of evidence is very low. Further rigorous research is needed.

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REFERENCES

1. Novak I, Morgan C, Adde L, et al. Early, accurate diagnosis and early intervention in cerebral palsy: advances in diagnosis and treatment. *JAMA Pediatr*. 2017;171(9):897-907.
2. Morgan C, Fetters L, Adde L, et al. Early intervention for children aged 0 to 2 years with or at high risk of cerebral palsy: international clinical practice guideline based on systematic reviews. *JAMA Pediatr*. 2021; 175(8):846-858.
3. Cioni G, D'Acunto G, Guzzetta A. Perinatal brain damage in children: neuroplasticity, early intervention, and molecular mechanisms of recovery. *Prog Brain Res*. 2011;189:139-154.
4. Rosenbaum P, Paneth N, Leviton A, et al. A report: the definition and classification of cerebral palsy April 2006. *Dev Med Child Neurol Suppl*. 2007;109:8-14.
5. Stanley F, Blair E, Alberman E. *Cerebral Palsies: Epidemiology and Causal Pathways*. London, England: Mac Keith; 2000.
6. Graham HK, Rosenbaum P, Paneth N, et al. Cerebral palsy. *Nat Rev Dis Primers*. 2016;2:15082.
7. Rosenbaum PL, Walter SD, Hanna SE, et al. Prognosis for gross motor function in cerebral palsy: creation of motor development curves. *JAMA*. 2002;288(11):1357-1363.
8. Damiano DL, Longo E. Early intervention evidence for infants with or at risk for cerebral palsy: an overview of systematic reviews. *Dev Med Child Neurol*. 2021;63(7):771-784.
9. Hadders-Algra M, Boxum AG, Hielkema T, Hamer EG. Effect of early intervention in infants at very high risk of cerebral palsy: a systematic review. *Dev Med Child Neurol*. 2017;59(3):246-258.
10. Morgan C, Darrah J, Gordon AM, et al. Effectiveness of motor interventions in infants with cerebral palsy: a systematic review. *Dev Med Child Neurol*. 2016;58(9):900-909.
11. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. 2009;339:b2535.
12. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ*. 2017;358:j4008.
13. Howick J, Chalmers I, Glasziou P, Greenhalgh T, et al. *The Oxford 2011 Level of Evidence*. Oxford Centre for Evidence-Based Medicine; 2011.
14. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:l4898.
15. Hoffmann TC, Glasziou PP, Boutron I, et al. Better reporting of interventions: Template for Intervention Description and Replication (TIDieR) checklist and guide. *BMJ*. 2014;348:g1687.
16. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol*. 2014;14:135.
17. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.
18. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372: n71.
19. Hielkema T, Boxum AG, Hamer EG, et al. LEARN2MOVE 0-2 years, a randomized early intervention trial for infants at very high risk of cerebral palsy: family outcome and infant's functional outcome. *Disabil Rehabil*. 2020;42(26):3762-3770.
20. Hielkema T, Hamer EG, Boxum AG, et al. LEARN2MOVE 0-2 years, a randomized early intervention trial for infants at very high risk of cerebral palsy: neuromotor, cognitive, and behavioral outcome. *Disabil Rehabil*. 2020;42(26):3752-3761.
21. Batra M, Sharma VP, Batra V, Malik GK, Pandey RM. Neurofacilitation of developmental reaction (NFDR) approach: a practice framework for integration /modification of early motor behavior (primitive reflexes) in cerebral palsy. *Indian J Pediatr*. 2012;79(5):659-663.
22. Chamudot R, Parush S, Rigbi A, Horovitz R, Gross-Tsur V. Effectiveness of modified constraint-induced movement therapy compared with bimanual therapy home programs for infants with hemiplegia: a randomized controlled trial. *Am J Occup Ther*. 2018;72(6):7206205010p1-7206205010p9.
23. Eliasson AC, Nordstrand L, Ek L, et al. The effectiveness of Baby-CIMT in infants younger than 12 months with clinical signs of unilateral-cerebral palsy: an explorative study with randomized design. *Res Dev Disabil*. 2018;72:191-201.
24. Harbourne RT, Willett S, Kyvelidou A, Deffeyes J, Stergiou N. A comparison of interventions for children with cerebral palsy to improve sitting postural control: a clinical trial. *Phys Ther*. 2010;90(12):1881-1898.
25. Maitre NL, Jeanvoine A, Yoder PJ, et al. Kinematic and somatosensory gains in infants with cerebral palsy after a multi-component upper-extremity intervention: a randomized controlled trial. *Brain Topogr*. 2020;33(6):751-766.
26. Mattern-Baxter K, Looper J, Zhou C, Bjornson K. Low-intensity vs high-intensity home-based treadmill training and walking attainment in young children with spastic diplegic cerebral palsy. *Arch Phys Med Rehabil*. 2020;101(2):204-212.
27. Morgan C, Novak I, Dale RC, Badawi N. Optimising motor learning in infants at high risk of cerebral palsy: a pilot study. *BMC Pediatr*. 2015; 15:30.
28. Morgan C, Novak I, Dale RC, Guzzetta A, Badawi N. Single blind randomised controlled trial of GAME (Goals-Activity-Motor Enrichment) in infants at high risk of cerebral palsy. *Res Dev Disabil*. 2016;55:256-267.
29. Palmer FB, Shapiro BK, Wachtel RC, et al. The effects of physical therapy on cerebral palsy. A controlled trial in infants with spastic diplegia. *N Engl J Med*. 1988;318(13):803-808.
30. Pietruszewski L, Burkhardt S, Yoder PJ, Heathcock J, Lewandowski DJ, Maitre NL. Protocol and feasibility-randomized trial of telehealth delivery for a multicomponent upper extremity intervention in infants with asymmetric cerebral palsy. *Child Neurol Open*. 2020;7: 2329048X20946214.
31. Hoare BJ, Wallen MA, Thorley MN, Jackman ML, Carey LM, Imms C. Constraint-induced movement therapy in children with unilateral cerebral palsy. *Cochrane Database Syst Rev*. 2019;4(4):CD004149.
32. Valentín-Gudiol M, Mattern-Baxter K, Girabent-Farrés M, Bagur-Calafat C, Hadders-Algra M, Angulo-Barroso RM. Treadmill interventions in children under 6 years of age at risk of neuromotor delay. *Cochrane Database Syst Rev*. 2017;7(7):CD009242.
33. Sgandurra G, Lorentzen J, Inguaggiato E, et al. A randomized clinical trial in preterm infants on the effects of a home-based early intervention with the "CareToy System." *PLoS One*. 2017;12(3):e0173521.
34. Pierce SR, Skorup J, Alcott M, Bochnak M, Paremski AC, Prosser LA. The use of dynamic weight support with principles of infant learning in a child with cerebral palsy: a case report. *Phys Occup Ther Pediatr*. 2021; 41(2):166-175.
35. Prosser LA, Pierce SR, Dillingham TR, Bernbaum JC, Jawad AF. iMOVE: intensive mobility training with variability and error compared to conventional rehabilitation for young children with cerebral palsy: the protocol for a single blind randomized controlled trial. *BMC Pediatr*. 2018;18(1):329.
36. Kolobe THA, Fagg AH. Robot reinforcement and error-based movement learning in infants with and without cerebral palsy. *Phys Ther*. 2019; 99(6):677-688.
37. Harbourne RT, Dusing SC, Lobo MA, et al. START-Play physical therapy intervention impacts motor and cognitive outcomes in infants with neuromotor disorders: a multisite randomized clinical trial. *Phys Ther*. 2021;101(2):pzaa232.
38. Holmström L, Eliasson AC, Almeida R, et al. Efficacy of the small step program in a randomized controlled trial for infants under 12 months old at risk of cerebral palsy (CP) and other neurological disorders. *J Clin Med*. 2019;8(7):1016.
39. Stark C, Herkenrath P, Hollmann H, et al. Early vibration assisted physiotherapy in toddlers with cerebral palsy—a randomized controlled pilot trial. *J Musculoskelet Neuronal Interact*. 2016;16(3):183-192.