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Early Goal Directed Training vs Passive Therapy for Functional Independence of Infants with Cerebral Palsy: Systematic Review and Meta-Analysis

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Background: Cerebral palsy (CP) is the leading cause of childhood motor disability, especially in LMICs. Early intervention is critical, yet the efficacy of goal-directed training compared to passive/standard therapies remains debated.

Objective: This study aims to evaluate the effectiveness of early goal-directed interventions on improving functional independence in infants and children with or at high risk of CP.

Methods: This systematic review and meta-analysis were conducted in accordance with PRISMA guidelines. A comprehensive literature search was performed to identify randomized controlled trials (RCTs) comparing goal-directed training with passive therapy or standard care. Methodological quality was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool. Data were synthesized using a random-effects model to calculate the Standardized Mean Difference (SMD).

Results: Five RCTs involving 302 participants were included. Meta-analysis revealed that goal-directed training showed a positive trend toward improved functional outcomes compared to passive therapy, although it did not reach statistical significance (SMD 0.19; 95% CI -0.09 to 0.47; p=0.1398). Heterogeneity across studies was remarkably low (I2 = 0), indicating a consistent intervention effect across diverse age groups and therapeutic modalities. Risk of bias assessment identified "some concerns" in three studies primarily due to missing outcome data, while two trials were rated as low risk.

Conclusion: Goal-directed training demonstrates a promising and consistent clinical trend in enhancing functional independence for children with CP. Despite the current lack of statistical significance, the negligible heterogeneity supports the integration of active, goal-focused exercises as a potentially effective and stable strategy for early neurorehabilitation.

Keywords: Cerebral palsy, early intervention, goal-directed training, functional independence, meta-analysis

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Introduction

Cerebral palsy (CP) is the most common permanent motor disability in children worldwide. The prevalence of CP ranges from 1.6 cases per 1,000 people in high-income countries to 4 cases per 1,000 people in lower-middle-income countries (LMICs). Many children with CP still do not receive adequate intervention or therapy.[1] The global impact of this condition has far exceeded expectations. According to data from the World Health Organization (WHO) and the 2019 Global Burden of Disease Study, approximately 8 million children in 204 countries live with Cerebral Palsy (CP). The majority of these children, 96%, are concentrated in LMICs.[1] This condition shows that CP is not only a clinical problem for each individual country, but rather an urgent global problem that needs to be addressed, especially in developing countries.

The effects of Cerebral Palsy (CP) are not limited to motor skills but encompass the entire spectrum of a child's life. According to the International Classification of Functioning, Disability and Health (ICF) framework, this condition disrupts bodily functions and limits a child's involvement in daily activities, education, and social interactions. Collectively, these barriers reduce the quality of life for both the child and their family.[2] Furthermore, there is significant evidence that increasing the autonomy of children with CP in daily activities contributes to reducing the psychological burden on caregivers. This directly impacts the overall quality of life of the family.[3] Thus, functional independence is a central clinical outcome that should be the primary goal in any rehabilitation program for children with CP.

The strongest scientific basis for early intervention in CP is neuroplasticity. Evidence shows that the developing brain is highly responsive to the quality, quantity, and timing of early sensorimotor experiences, and the infant's active participation is an indispensable element in promoting this neuroplasticity.[4] Most lesions underlying CP occur in the second half of gestation, when brain development is at its peak the variations in the timing of injury result not only in different lesions but also in different neuroplastic responses.[5] Interventions initiated early, during the critical period of brain plasticity and before musculoskeletal and central nervous system maladaptations occur, are believed to offer the best opportunity to optimize the developmental trajectory of children with CP.[6]

For decades, the dominant rehabilitation approach used in infants and children with CP has been passive therapy, particularly Bobath-based Neurodevelopmental Therapy (NDT), which focuses on normalizing muscle tone and providing external movement facilitation by a therapist. However, the effectiveness of this approach has been increasingly questioned. A meta-analysis published in the journal Pediatrics (2022) concluded that activity-based interventions were more effective than NDT in improving motor function, NDT was no more effective than a control group, and increasing the dose of NDT did not result in greater improvement; a strong recommendation was made to discontinue the use of NDT in the management of CP.[7] Similarly, global CP experts have unequivocally stated that the available evidence indicates Bobath/NDT is ineffective and should therefore be de-implemented in clinical practice.[8] Such passive approaches also align with the principles of neuroplasticity, as evidence suggests that excessive use of external facilitation or physical guidance during children's movement is not recommended, and treatment techniques aimed at inhibiting muscle tone have not been shown to be effective.[9]

In response to these limitations, the rehabilitation paradigm has shifted to active, goal-directed training (GDT) approaches. Current literature positions GDT as a method for improving function in children with CP, in which the child actively practices a desired goal or task; this approach uses varied and repetitive activities to promote neuroplasticity and functional improvement and is now considered a standard of care for CP.[9] One GDT program specifically designed for infants is GAME (Goals–Activity–Motor Enrichment), which combines intensive goal-based motor training, parent education, and environmental enrichment. Unlike NDT, this program focuses on task feasibility and environmental context, with the therapist acting as a "change agent" facilitating the infant's exploration of motor solutions.[10] The LEAP-CP RCT, published in Pediatrics (2024), in infants with CP in a low-income country, found that although there was no overall effect size, a modified intention-to-treat analysis showed that the goal-directed intervention resulted in significant improvements in motor skills in ambulatory children with CP, consistent with what is known about targeted goal-based training.[11]

However, several critical gaps in scientific evidence remain unaddressed. To date, data on the efficacy of early intervention in infants with CP remains very limited, as the diagnosis of CP is typically not made until between 12 and 24 months of age, often missing the most critical intervention window.[12] More importantly, despite the proven effectiveness of GDT, variability in

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its implementation has contributed to the gap between research evidence and daily clinical practice.[13] Research directly and head-to-head comparing early goal-directed training with passive therapy in infants with CP particularly with functional independence as the primary focus remains very limited, particularly in LMIC contexts. Recent guidelines from China (2024) also emphasize that structured, goal-based rehabilitation is the backbone of CP management, but its implementation remains uneven.[14]

This gap is the primary justification for this research. The current situation reflects a reality where passive therapy is still widely practiced in various rehabilitation facilities, while scientific evidence consistently and increasingly demonstrates that active, goal-based approaches from an early age are superior in maximizing neuroplasticity and increasing functional independence. This study aims to generate stronger comparative evidence regarding the superiority of early goal-directed training over passive therapy for functional independence in infants with CP, thus providing a basis for updating clinical guidelines and pediatric rehabilitation practices globally.

Method

Study Design and Protocol Registration

This study was designed as a systematic review and meta-analysis to compare the effectiveness of early goal-directed training with passive therapy for functional independence in infants with cerebral palsy. This review integrates evidence from randomized controlled trials to provide a comprehensive summary of the existing data. Reporting of the study results follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to ensure transparency, completeness, and reproducibility of the methods.[15]

The review protocol was established in advance to guide the methodological approach of this study. It was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number (CRD420261394788). The protocol was registered to ensure transparency throughout the review process and to limit the possibility of reporting bias. Any modifications to the original protocol were clearly stated and justified in the final report.[16]

Eligibility Criteria

Studies were selected according to the Population, Intervention, Comparison, Outcome, and Study Design (PICOS) framework. Eligible studies were randomized controlled trials involving infants and children diagnosed with cerebral palsy or identified as being at high risk of developing cerebral palsy. The intervention group consisted of early goal-directed or activity-based rehabilitation programs aimed at improving motor function and functional independence. These interventions included structured active therapies such as Goals–Activity–Motor Enrichment (GAME), Baby-CIMT, Baby-BIM, LEAP-CP, and other task-oriented training approaches.

Comparator groups included passive therapy, conventional neurodevelopmental treatment, standard rehabilitation, or other non-goal-directed therapeutic approaches. The primary outcomes assessed were functional independence, activity performance, participation, and motor function measured using validated assessment instruments, including the Gross Motor Function Measure (GMFM), Pediatric Evaluation of Disability Inventory (PEDI/PEDI-CAT), Hand Assessment for Infants (HAI), Canadian Occupational Performance Measure (COPM), or comparable standardized functional outcome tools.

Only full-text articles published in English between January 2016 and May 2026 were included. Conference abstracts, review articles, case reports, editorials, study protocols, animal studies, and non-comparative studies were excluded. Studies with insufficient quantitative data for effect size calculation were also excluded from the meta-analysis.

Information Sources and Search Strategy

Relevant studies were identified through searches of multiple electronic databases, including PubMed, ScienceDirect, ProQuest, Wiley Online Library, and MedRxiv. MedRxiv was included to capture gray literature, identify emerging evidence, and minimize potential publication bias. To systematically address the lack of peer review in preprint studies, a sensitivity analysis using a leave-one-out approach was planned a priori to evaluate whether the inclusion of these preprint data significantly or systematically distorted the primary pooled meta-analysis findings. Studies published from January 2016 until the final search date (7 May 2026) were considered for inclusion. To ensure comprehensiveness, the reference lists of all included studies and relevant review articles were manually screened, and a snowballing approach was applied to identify additional eligible studies.

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The search strategy was developed using database-specific search strings that incorporated controlled vocabulary (where applicable), free-text terms, and Boolean operators ("AND" and "OR"). Search terms were related to cerebral palsy, high-risk infants, goal-directed interventions, and functional independence outcomes. Search strategies were adapted according to the indexing structure and search requirements of each database. The complete database-specific search strategies, including all search terms, Boolean operators, and MeSH headings, are presented in Supplementary Appendix 1.

Study Selection and Data Collection

Two reviewers independently screened titles and abstracts of all retrieved records according to the predefined eligibility criteria. Potentially eligible studies subsequently underwent full-text assessment by the same reviewers. Any disagreements regarding study selection were resolved through discussion and consensus.

Data extraction was performed independently by two reviewers using a standardized extraction form. Extracted data included study characteristics, participant demographics, intervention details, outcome measures, and study outcomes. Any discrepancies were resolved through discussion and review of the original articles until consensus was reached. Risk of bias assessment was conducted independently by two reviewers using the Cochrane Risk of Bias 2 (RoB 2) tool. Disagreements were resolved through discussion and consensus.

Risk of Bias Assessment

The RCT study was assessed using the Cochrane Risk of Bias tool version 2 (RoB 2.0) and visualized using the ROBVIS visualization.[17,18] The assessment covered five key domains, including the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported results. The results of the assessment were explicitly used to interpret the strength of the clinical evidence and were visualized using specialized tools to maintain transparency in the quality of the included studies.

Statistical Analysis

A quantitative synthesis was performed using meta-analysis to evaluate the effectiveness of early goal-directed and activity-based interventions on functional independence and motor outcomes in infants and children with or at high risk of cerebral palsy. All statistical analyses and quantitative poolings were conducted using Review Manager (RevMan) software, version 5.4 (The Cochrane Collaboration, 2020). To evaluate the overall impact of the intervention on functional capacity, data from diverse outcome measures (including GMFM for gross motor function, HAI for upper limb function, and PEDI-CAT or COPM for comprehensive functional domains) were pooled using the Standardized Mean Difference (SMD) with corresponding 95% confidence intervals (CI). The use of SMD is justified as it standardizes heterogeneous scales into a uniform metric, allowing for an aggregate estimation of global functional improvement. To minimize conceptual bias, data were hierarchically selected based on the primary domain targeted by the intervention when a study reported multiple scales.

A random-effects model was applied to account for anticipated clinical and methodological heterogeneity among studies, including differences in intervention protocols, treatment duration, participant characteristics, and outcome measurement tools. Statistical heterogeneity was assessed using the I^2 statistic, with values above 50% considered indicative of substantial heterogeneity. Statistical significance was defined as a two-tailed p-value < 0.05.

As an exploratory measure, publication bias was evaluated qualitatively through visual inspection of funnel plot asymmetry. Although visual inspection of the plot may demonstrate relative symmetry, this interpretation must be treated with extreme caution. Standard methodological guidelines indicate that publication bias assessments using funnel plots are unreliable and lack statistical power when a meta-analysis includes fewer than 10 studies. Therefore, the presence of small-study effects or selective publication cannot be definitively ruled out based on our limited sample size. Sensitivity analysis was conducted using a leave-one-out approach to assess the robustness and stability of the pooled effect estimates.

Result

Study Selection

A systematic literature search was conducted across five electronic databases, including PubMed, ScienceDirect, Wiley Online Library, ProQuest, and medRxiv. A total of 314 records were identified through database searching, consisting of 191 records from ProQuest, 99 from ScienceDirect, 12 from Wiley, 10 from medRxiv,

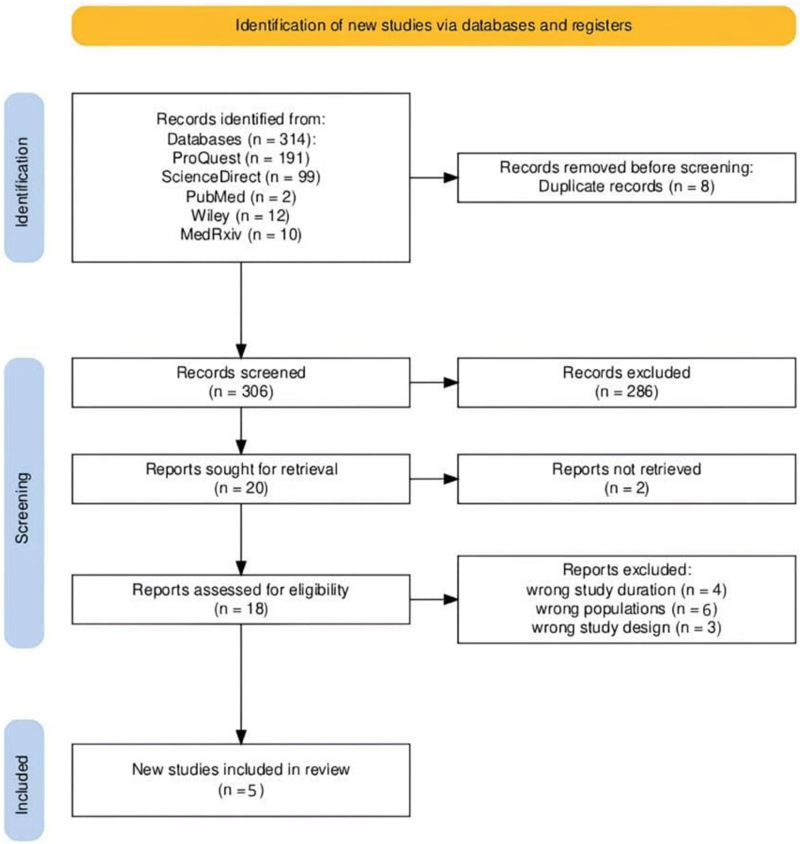

Figure 1: PRISMA Flowchart

and 2 from PubMed.

After removal of 8 duplicate records, 306 studies underwent title and abstract screening. Of these, 286 records were excluded due to irrelevance to the study objectives. Subsequently, 20 full-text articles were sought for retrieval, of which 18 articles were successfully assessed for eligibility, while 2 reports could not be retrieved.

During full-text assessment, 12 studies were excluded for the following reasons: inappropriate study duration (n = 4), irrelevant population (n = 6), and unsuitable study design (n = 3). Ultimately, 5 studies met the eligibility criteria and were included in the systematic review and meta-analysis. The study selection process is summarized in the PRISMA flow diagram (Figure 1).

Study Characteristics

The baseline and methodological characteristics of the five included trials are systematically summarized in Table 1.

Risk of Bias Analysis

The methodological quality and risk of bias included randomized controlled trials were independently assessed by the Cochrane Risk of Bias 2 (RoB 2) tool.[19] Each study was evaluated across five distinct domains: (1) bias arising from the randomization process; (2) bias due to deviations from intended interventions; (3) bias due to missing outcome data; (4) bias in measurement of the outcome; and (5) bias in selection of the reported result. The assessment of the risk of bias for the five included studies was conducted using the Cochrane Risk of Bias 2 (RoB 2) tool, as illustrated in Figures 2 and 3.

Overall, the studies demonstrated a high level of methodological quality, with two trials (Boyd et al., 2025 and Armstrong et al., 2020) achieving a “low risk of bias” across all evaluated domains. These studies implemented robust randomization and allocation concealment procedures, alongside effective blinding of outcome assessors.

In contrast, three studies (Morgan et al., 2016; Eliasson et al., 2018; Benfer et al., 2024) were identified as having

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Table 3. Characteristics of Included Trials

Author, Year	Study Location	Sample (n)	Study Design	Age	Diagnosis/ Risk	Type of Cerebral Palsy	Dose (Frequence or Duration of Intervention)	Setting	Intervention	Comparison	Primary Outcome (measurement tool)	Secondary Outcome
Benfer, et al. (2024)	India (West Bengal, LMIC)	n = 153 (LEAP-CP = 77, HA = 76)	RCT (single-blind, multisite)	12–40 weeks corrected age (CA), Mean 7.1 ± 2.7 months CA	High Risk of CP	Not Classified	15 fortnightly home visits (≈7. 5 months) until 18 months CA Peer-delivered; dose-matched between arms	Home-based	LEAP-CP (goal-directed, parent-delivered, multidomain)	Health Advice (WHO Key Family Practices)	PEDI-CAT Mobility domain + DASS (caregiver mental health)	PDMS-2, BSID-III, COPM, HINE, PSOC, Near Detection Scale, HOME Inventory
Morgan, et al. (2016)	Australia (Sydney)	n = 30 (GAME = 15, SC = 15)	RCT (single-blind, parallel group)	3–6 months CA at enrolment, Mean enrolment: 15.7–20.1 weeks CA	High Risk of CP	Not Classified	16 weeks, weekly home visits by therapist	Home-based + hospital visit for assessments	GAME (Goals–Activity–Motor Enrichment; motor learning + enrichment)	Standard Care (routine community therapy)	PDMS-2 (Peabody Developmental Motor Scales-2)	BSID-III, GMFM-66, COPM
Elliason, et al. (2018)	Sweden (Stockholm)	n = 37 (Baby CMIT: 18, Massage: 13)	Exploratory RCT (evaluator linded, parallel group)	3–8 months CA at entry Baby-CIMT: mean 6.1 ± 1.7 months Massage: mean 5.0 ± 1.6 months	High Risk of CP	Unilateral Cerebral Palsy	2 × 6-week training periods separated by 6-week pause (18 weeks total)	Home-based	Baby-CIMT (non-affected hand restrained; parent-led, OT-coached)	Baby-Massage (full-body massage, 1×/day, parent-led)	HAI Affected Hand Score	AHA, PSCS, Feasibility Questionnaire
Boyd, et al. (2025)	Australia and US (not specified)	n = 144 (72 for each group) --> 96/144 joined because recruitmentnya prematurely because of the COVID-19 pandemic.	Single-blinded RCT	3-9 months of corrected age	High Risk of CP	Unilateral Cerebral Palsy	1-3 sessions/day, 5 days/week for 6-9 months, according to age at study entry. Bimonthly home visits by pediatric therapist	Home-based	Baby-CMIT	Baby-BIM	HAI Affected Hand Score	Mini-AHA, AHA, BSID-III, PEDI-CAT, EA-SR, DASS-21,
Armstrong, et al. (2020)	Brisbane, Australia	n = 21 (11 with intervention, 11 usual care)	Parallel grouped RCT	6-18 years old	CP (GMFCS level II until IV)	Not Classified	1 hour sessions at a tertiary children's hospital and 1 hour home exercise programme (HEP) for 8 weeks. Included 30 minutes of goal-directed training programme from Canadian Occupational Performance Measure (COPM) and 30 minutes of FES cycling	home and hospital based??	Goal-directed training and FES cycling	Usual care (physiotherapy, speech therapy, occupational therapy)	GMFM (Gross Motor Function Measure) and COPM (Canadian Occupational Performance Measure)	Peak cycling powe and resistance, Peadiatric Evaluation of Disability Inventory Computer Adaptive Test (PEDI-CAT), and Participation and Environment Measure – Child and Youth (PEMCY)

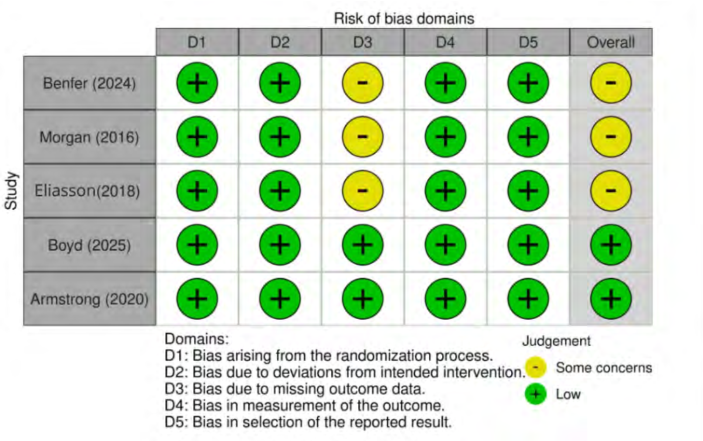

Figure 2: Risk of Bias domains of RCT studies

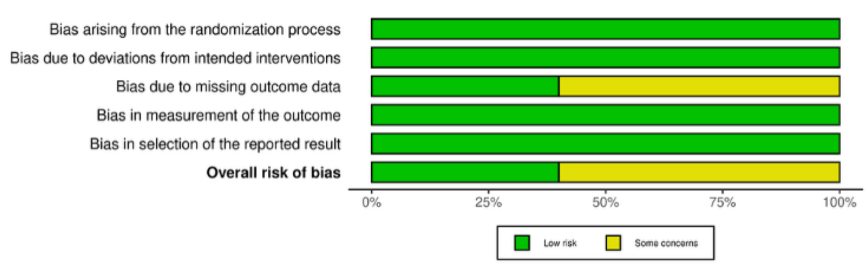

Figure 3: Overall risk of bias of RCT studies

"some concerns" in their overall judgment. In Benfer et al. (2024) and Eliasson et al. (2018), these concerns were primarily related to Domain 3 (bias due to missing outcome data) and Domain 2 (deviations from intended interventions), often due to participants being excluded after randomization or high attrition rates. Similarly, Morgan et al. (2016) was noted for "some concerns" in Domain 3 due to the loss of follow-up data in the intervention group. Despite these specific issues, none of the included studies were rated as "high risk," and the measurement of primary outcomes remained consistently at low risk of bias across the evidence base.

Quantitative Synthesis

Functional Motor Outcomes

A random-effects meta-analysis using standardized mean difference (SMD) was performed due to differences in outcome scales across studies. The pooled analysis demonstrated a small positive effect favoring early goal-directed and activity-based interventions compared with passive therapy or standard care (SMD = 0.19; 95% CI: -0.09 to 0.47). However, the overall effect was not statistically significant because the confidence interval crossed the null value (0). Heterogeneity among studies was low (I^2 = 0%), indicating consistent findings across included studies. These findings suggest that activity-based and goal-directed interventions demonstrate promising trends toward improving modest improvements in functional motor outcomes compared with passive therapy, although current evidence remains insufficient to demonstrate definitive effectiveness.

Forest Plot Interpretation

The forest plot demonstrated that most included studies favored the intervention group, as indicated by positive SMD values. According to Cohen's convention, the pooled estimate (SMD = 0.19; 95% CI: -0.09 to 0.47) represents a small effect size magnitude. The studies by Morgan et al. (2016) and Eliasson et al. (2018) showed the largest positive effects.[20,21] Visual inspection of the plot reveals a substantial overlap among the confidence intervals of individual trials, indicating statistical consistency. However, several studies exhibited wide confidence intervals crossing the line of no effect, reflecting limited statistical precision and uncertainty driven by the small cumulative sample size. The pooled diamond slightly favored the intervention group but crossed the null line, indicating non-significant overall findings. The study weights ranged from 7.3% to 33.4%, with Boyd et al. (2024) and Benfer et al. (2024)

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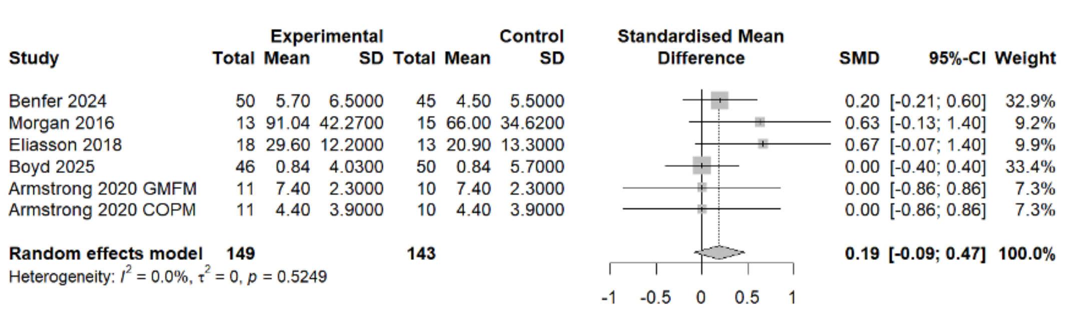

Figure 4: Forest Plot of Functional Motor Outcomes

CI: Confidence Interval; SMD: Standardized Mean Difference; SE: Standard Error.

contributing the greatest influence to the pooled analysis due to larger sample sizes.[22, 23]

Publication Bias

Visual inspection of the funnel plot did not demonstrate marked asymmetry. However, interpretation should be approached cautiously because the number of included studies was small (<10 studies), limiting the reliability of publication bias assessment.

Sensitivity Analysis

Leave-one-out sensitivity analysis demonstrated stable pooled estimates across all iterations. Exclusion of individual studies did not substantially alter the overall effect size, suggesting that no single study disproportionately influenced the meta-analysis results. The pooled effect sizes after sequential omission of studies ranged from SMD 0.14 to 0.28, with all analyses remaining statistically non-significant. Heterogeneity remained consistently low (I^2 = 0%). The exact step-by-step omitted-study analysis, detailing the shifting SMD values and specific confidence intervals for each iteration, has been comprehensively tabulated and provided in Supplementary Table S1.

Overall Interpretation

Overall, early goal-directed and activity-based interventions demonstrated a trend toward improved functional motor outcomes in infants with cerebral palsy or high risk of cerebral palsy compared with passive therapy or standard care. Nevertheless, the pooled effect did not reach statistical significance.

Despite this, the consistently positive direction of effect and low heterogeneity \suggest potential clinical benefits of active, goal-oriented early intervention approaches. Additional high-quality randomized controlled trials with larger sample sizes and standardized outcome measures are needed to clarify the magnitude of benefit.

Discussion

The findings of this meta-analysis reveal a consistent and positive but non-significant trend toward the

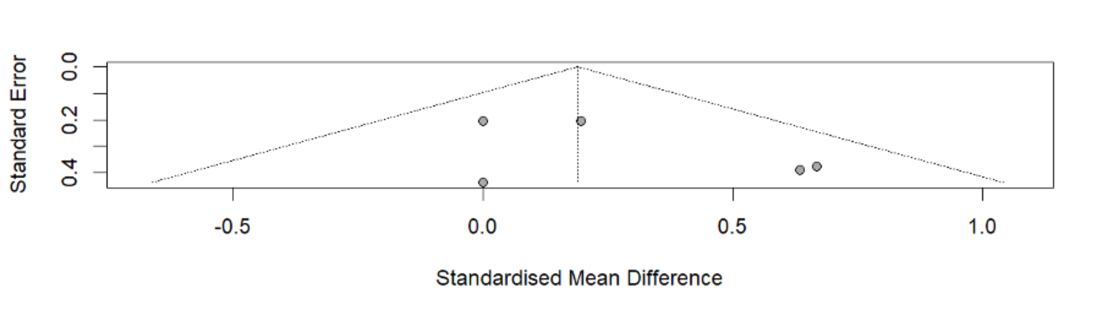

Figure 5: Funnel Plot for Publication Bias Assessment

Horizontal axis represents Standardized Mean Difference (SMD); vertical axis represents Standard Error (SE) to assess small-study effects.

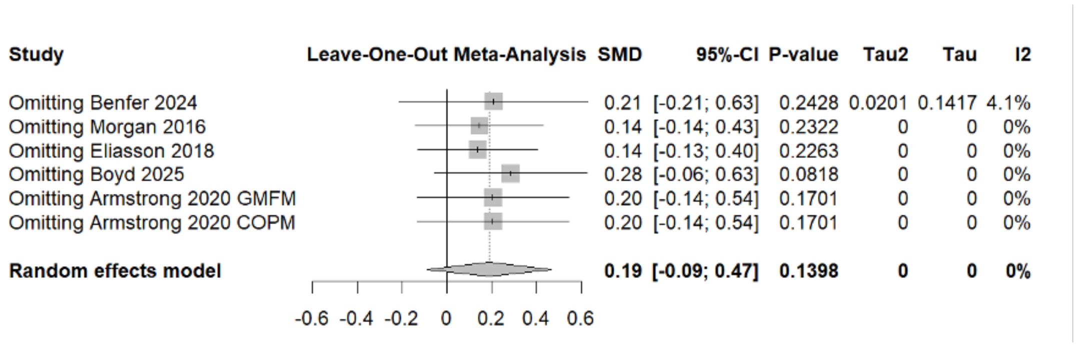

Figure 6: Sensitivity Analysis Chart

Omitted-study analysis applying a leave-one-out framework to assess the robustness of the pooled estimate.

efficacy of early active interventions for infants at high risk of cerebral palsy. Although the pooled analysis falls short of demonstrating definitive clinical superiority, several studies by Armstrong et al. (2020), Benfer et al. (2024), Choudhary et al. (2013), Boyd et al. (2025), Eliasson et al. (2018), and Morgan et al. (2016) Reported an undeniable increase in motor function, such as the upper limb movements and cognitive outcomes.[20-22,24,25] However, this therapeutic benefit may vary depending on the child's baseline functional severity, therefore an adjusted interpretation of result according to this study is mandatory. Benfer et al. (2024) reported that LEAD-CP appeared to provide greater benefits than HA, particularly in ambulant children with cerebral palsy.[23]

Application of Early Active Goal-based Intervention in Pathophysiology of Cerebral Palsy (CP)

The superiority of early active, goal-directed training (GDT) over passive modalities like Neurodevelopmental Treatment (NDT)/Bobath lies in its alignment with activity-dependent neuroplasticity. Cerebral palsy (CP) arises from a non-progressive injury to the developing brain during peak developmental activity, directly disrupting the normal activity-dependent synaptic competition of the corticospinal tract (CST). Variations in the timing of injury result not only in different lesions but also in different neuroplastic responses.[26] While passive therapies fail to trigger neural reorganization because they lack deliberate CST activation from the infant, active GDT explicitly exploits motor learning mechanisms. By motivating self-initiated, repetitive movements, GDT repeatedly activates remaining CST axons, thereby strengthening weak synaptic connections, inducing white and gray matter changes such as increased myelination, and preventing the pathological cycle of learned non-use.[26]

The most relevant neuroplasticity mechanism in the context of CP rehabilitation is activity-dependent plasticity, the nervous system's capacity to reorganize itself structurally and functionally in response to active, repetitive motor experiences. The basic principles of experience-dependent neural plasticity have been comprehensively formulated by Kleim & Jones, encompassing specificity, repetition, intensity, and functional relevance. Understanding these principles is highly relevant for optimizing rehabilitation strategies after brain injury.[27] Motor interventions during the early years of life are considered critical for optimizing this activity-dependent neuroplasticity, but it is important to emphasize that activity-dependent reorganization can be both adaptive and maladaptive, so it is also the child's active role in the process.[9] This fundamentally differentiates active, goal-based therapy from passive therapy. In passive therapy approaches such as NDT/Bobath, the therapist physically guides or facilitates movement while the infant plays a passive role. This kind of approach fails to trigger activity-dependent plasticity because it does not produce a deliberate CST activation pattern from the child himself, and has been shown to be ineffective in harnessing neural plasticity.[28]

Neuroplasticity and the Response to Goal-Directed Training

The strongest pathophysiological argument for early intervention rests on the concept of the critical period of neuroplasticity, a specific window during early development where brain plasticity peaks and sensory experiences are necessary to build optimal cortical representations.[29] Outside this period, plasticity capacity is significantly reduced, and the same intervention produces a much weaker response. Data from gross motor function development curves indicate that the gross motor potential of most children

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with CP plateaus before age 5, depending on GMFCS level. For example, three-quarters of children with GMFCS levels I and II achieve 90% GMFM scores by age 5, while children with GMFCS level IV plateau at around 30% by the same age.[30] Plasticity in the motor system has been shown to be more robust in the early years than in later years, and maladaptive changes that occur after CNS injury are difficult to reverse once established.[30] Neuroimaging studies confirm that children with CP possess cortical plasticity that can be beneficial.[32] Delayed intervention, such as waiting until a definitive diagnosis at 12–24 months of age, pathophysiologically misses part of this critical window of greatest responsiveness.

Early goal-directed training (GDT) is explicitly designed to take advantage ofmotor learning mechanisms that optimally utilize neuroplasticity. The developing brain is highly responsive to the quality, quantity, and timing of early sensorimotor experiences, and the infant's active participation is essential to foster this process.[31] Evidence from experimental models suggests that early intensive rehabilitation reverses locomotor impairments, reduces brain inflammation, and induces neuroplasticity. Structural MRI confirms that activity-based and goal-directed interventions induce changes in gray and white matter properties in the brain, including increased myelination.[32] Conversely, without encouragement to actively move, infants with cerebral palsy are at risk of a learned non-use phenomenon in which infants learn not to use their weaker limbs due to the lack of positive reinforcement, which becomes increasingly difficult to correct with age. This condition can initiate a pathological cycle that deteriorates structure and function and produces maladaptive plasticity. Therefore, it is critical to initiate active interventions early to prevent permanent musculoskeletal and central nervous system maladaptations.[33]

Different Assessments through Different Measurement Tools

Motor function in children with cerebral palsy can be assessed using different types of interventions and outcome measures. Because each assessment tool examines different areas of function, the outcomes reported across studies may vary. This suggests that no single assessment can be regarded as the best overall tool, as each instrument has its own purpose and evaluates specific aspects of a child's abilities. Importantly, motor outcomes and functional independence should be interpreted as distinct but complementary constructs. In this review, motor outcomes primarily refer to improvements in gross motor abilities and upper-limb function, whereas functional independence reflects to broader domains, including participation and independence in activities of daily living.

Boyd et al. (2024) found that Baby-CIMT did not show greater effectiveness compared with Baby-BIM, as both interventions produced similar improvements in hand function and upper limb development.[22] These findings indicate that different intervention approaches may still lead to comparable outcomes in children with cerebral palsy. In addition, Armstrong et al. (2020) reported that GMFM was not necessarily superior to PEDI-CAT because both assessments measure different dimensions of motor function.[24] GMFM is mainly used to evaluate gross motor abilities, including movement-related activities such as cycling. Meanwhile, PEDI-CAT places greater emphasis on the child's ability to carry out everyday activities independently. Therefore, variations in study outcomes may be influenced not only by the intervention itself but also by the specific focus of the assessment tool used in each study.

Cerebral palsy affects not only motor function but also sensory function. A study conducted by Chorna et al. (2015) combined 6 hours of daily modified Constraint-Induced Movement Therapy (CIMT) with high-intensity tactile enrichment. Specifically, the intervention utilizes sensory-motor kits where infants search for objects in textured media and "sticky mittens" to facilitate successful reaching, providing the consistent, non-noxious afferent feedback required to rewire damaged thalamocortical pathways. To validate the impact of these therapies, the study employed several assessment tools, such as the use of high-density event-related potentials (ERP) and kinematic motion analysis. These measures quantify changes in cortical sensory processing and movement smoothness that traditional behavioral scales might overlook. By aligning parent-driven sensory exercises with objective cortical tracking, this approach suggests that the remediation of "developmental disregard" is best achieved when clinical therapy is paired withassessments capable of tracking the brain's evolving ability to register and utilize tactile information for motor control.[34]

Strengths and Limitations

A key strength of this systematic review and meta-analysis is its strict focus on the critical "window of opportunity" in early development, specifically targeting children. By evaluating goal-directed, activity-based interventions against traditional passive handling, this study provides a highly specialized synthesis of how active motor learning drives functional independence, measured through variations of standardized tools. Furthermore, the relationship between pathophysiology, neuroplasticity, and the response to early goal-directed training is clearly described. However, several limitations must be acknowledged. The overall number of pure randomized controlled trials in this specific age bracket remains relatively small, resulting in an underpowered pooled sample size that may limit the statistical power to detect significant differences. Moreover, there is a notable clinical heterogeneity across the literature; this is reflected in the high variability of intervention protocols—specifically the variations in total dosage, frequency, and duration—alongside the inclusion of mixed-severity populations and differing outcome measures. Finally, the short follow-up duration across the included studies limits our ability to determine whether the functional gains achieved in infancy are sustained into later childhood.

Clinical Implication and Future Direction

The findings of this study support a significant trend shift in pediatric rehabilitation, moving away from traditional, passive neuromotor handling, such as passive stretching or isolated NDT without functional goals, toward active, task-specific, and goal-directed interventions. For clinicians and physical therapists, the evidence underscores that motor learning in infants is experience-dependent. Therefore, therapeutic sessions should be structured around self-initiated movements where the infant must actively solve a motor problem to achieve a rewarding outcome. Successful protocols like GAME and Small Steps heavily rely on environmental enrichment and parental coaching, so clinical practiceinto a more family-centered model is highly encouraged. Clinicians should prioritize training parents as active co-therapists who can seamlessly integrate goal-directed activities into the infant's daily home routine, thereby maximizing therapeutic dosage and enhancing the infant's real-world functional independence. [35,36]

To address the clinical heterogeneity observed in current literature, future studies should directly compare holistic, whole-body active interventions against targeted approaches, such as Baby-CIMT, to determine which protocols yield the highest efficacy for specific subgroups of cerebral palsy. Additionally, researchers should incorporate long-term longitudinal follow-ups to track the trajectories of functional independence and neuroplastic adaptation as these infants transition into school age. Furthermore, given the heavy reliance on home-based therapy, future studies should explore secondary outcomes more thoroughly, particularly looking into the cost-effectiveness of these interventions and their psychological impact on parental stress and quality of life

Conclusion

In conclusion, early goal-directed and activity-based interventions demonstrate a promising and consistent trend toward improving functional independence and motor outcomes in infants and children with or at high risk of cerebral palsy. Although the pooled meta-analysis did not reach statistical significance, the overall positive direction of effect, negligible heterogeneity, and robust sensitivity analysis support the potential clinical value of active, goal-oriented rehabilitation compared with passive therapy approaches. These findings reinforce the neuroplasticity-based rationale that early, repetitive, and self-initiated motor experiences are critical during the developmental window of maximal brain plasticity. Furthermore, the evidence highlights the importance of family-centered and environmentally enriched interventions, such as GAME and Baby-CIMT, in optimizing functional outcomes. Nevertheless, the limited number of high-quality randomized controlled trials, variations in intervention protocols, and lack of long-term follow-up data indicate that further large-scale and standardized studies are still required to establish definitive clinical recommendations and determine the long-term sustainability of these therapeutic benefits.

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could

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References

1. Olusanya BO, Nair MKC, Boo NY, Davis AC, Hadders-Algra M, Wright SM. Cerebral palsy in young children: bridging the global data gap. The Lancet Global Health. 2025 Aug 11
2. Africa LE, Human A, Tshabalala MD. Participation patterns of children with cerebral palsy: A caregiver's perspective. African Journal of Disability. 2023 Jan 31;12.
3. Faeze Alvandi, Amini M, Narges Ghafarzadeh Namazi. Factors Affecting the Independence Level of 4-6-Year-Old Children with Cerebral Palsy in Activities of Daily Living. PubMed [Internet]. 2023 Jan 1;17(4):93–104. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10704291/
4. Damiano DL. The E-words for promoting development and neuroplasticity for infants with or at high risk for cerebral palsy. Developmental Medicine & Child Neurology. 2025 Aug 22
5. Hadders-Algra M. Early diagnosis and early intervention in cerebral palsy. Frontiers in Neurology. 2014 Sep 24;5(185).
6. Spittle AJ, Morgan C. Early Intervention for Children with Cerebral Palsy. Cerebral Palsy. 2025;197–205.
7. te Velde A, Morgan C, Finch-Edmondson M, McNamara L, McNamara M, Paton MCB, et al. Neurodevelopmental Therapy for Cerebral Palsy: A Meta-analysis. Pediatrics. 2022 May 24;149(6).
8. Damiano D, Novak I. Bobath, NeuroDevelopmental Therapy, and clinical science: Rebranding versus rigor. Developmental Medicine & Child Neurology. 2024 Jan 12;66(5):668–8.
9. Damiano DL, Longo E. Early intervention evidence for infants with or at risk for cerebral palsy: an overview of systematic reviews. Developmental Medicine and Child Neurology [Internet]. 2021 Jul 1;63(7):771–84. Available from: https://pubmed.ncbi.nlm.nih.gov/33825199/
10. Morgan C, Novak I, Dale RC, Badawi N. Optimising motor learning in infants at high risk of cerebral palsy: a pilot study. BMC Pediatrics. 2015 Apr 1;15(1).
11. Benfer KA, Whittingham K, Ware RS, Asis Kumar Ghosh, Chowdhury S, Golam Moula, et al. Efficacy of Early Intervention for Infants With Cerebral Palsy in an LMIC: An RCT. Pediatrics. 2024 Mar 22;153(4).
12. Contemporarypediatrics.com. 2024 [cited 2026 May 15]. Available from: https://www.contemporarypediatrics.com/view/effect-of-goals-activity-motor-enrichment-in-infants-with-cerebral-palsy
13. Shierk A, Thias BB, Becker H, Allen B, Chaiprasert B, Lampe KC, et al. Defining Goal-Directed Training for Children with Cerebral Palsy: A Scoping Review and Framework for Implementation. Children. 2025 Aug 8;12(8):1039–9
14. Li Z, So KF, Chen L, Feng S, Hu Y, Cheng L, et al. Clinical guideline for neurorestorative therapy in pediatric cerebral palsy (2024 China version). Journal of Neurorestoratology [Internet]. 2025 Dec;13(6):100253. Available from: https://www.sciencedirect.com/science/article/pii/S2324242625000750?utm_source
15. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. British Medical Journal [Internet]. 2021;372(71). Available from: https://www.bmj.com/content/372/bmj.n71
16. Tricia Arella Taslim, Dhana Carissa Wangjaya, Deyra Maheswari Wistara, Febry Liana, Fadhlurrahman Ahmad Ariq Bachtiar. Early Goal Directed Training vs Passive Therapy for Functional Independence of Infants with Cerebral Palsy: Systematic Review and Meta-Analysis. PROSPERO 2026 CRD420261394788. Available from https://www.crd.york.ac.uk/PROSPERO/view/CRD420261394788.
17. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: A revised Cochrane risk-of-bias tool for randomized trials. 2019.
18. McGuinness LA, Higgins JPT. robvis: An R package and web app for visualising risk-of-bias assessments. Syst Rev. 2020;9(1):376.
19. McGuinness, LA, Higgins, JPT. Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. Res Syn Meth. 2020; 1- 7. https://doi.org/10.1002/jrsm.1411
20. 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. Research in Developmental Disabilities. 2016 Aug;55:256–67.
21. Eliasson AC, Nordstrand L, Ek L, Lennartsson F, Sjöstrand L, Tedroff K, 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. Research in Developmental Disabilities. 2018 Jan;72:191–201.
22. Boyd RN, Greaves S, Ziviani J, Novak I, Badawi N, Pannek K, et al. Randomized Comparison Trial of Rehabilitation Very Early for Infants with Congenital Hemiplegia. The Journal of Pediatrics. 2024 Oct 1;114381–1.
23. Benfer KA, Whittingham K, Ware RS, Asis Kumar Ghosh, Chowdhury S, Golam Moula, et al. Efficacy of Early Intervention for Infants With Cerebral Palsy in an LMIC: An RCT. Pediatrics. 2024 Mar 22;153(4).
24. Armstrong EL, Boyd RN, Horan SA, Kentish MJ, Ware RS, Carty CP. Functional electrical stimulation cycling, goal-directed training, and adapted cycling for children with cerebral palsy: a randomized controlled trial. Developmental Medicine & Child Neurology. 2020 Aug 9;62(12).
25. Choudhary A, Gulati S, Kabra M, Singh UP, Sankhyan N, Pandey RM, et al. Efficacy of modified constraint induced movement therapy in improving upper limb function in children with hemiplegic cerebral palsy: A randomized controlled trial. Brain and Development. 2013 Oct;35(9):870–6.
26. Hadders-Algra M. Early diagnosis and early intervention in cerebral palsy. Frontiers in Neurology. 2014 Sep 24;5(185).
27. Kleim JA, Jones TA. Principles of Experience-Dependent Neural Plasticity: Implications for Rehabilitation After Brain Damage. Journal of Speech, Language, and Hearing Research. 2008;51(1).
28. McIntyre S, Goldsmith S, Webb A, Ehlinger V, Hollung SJ, McConnell K, et al. Global Prevalence of Cerebral Palsy: a Systematic Analysis. Developmental Medicine & Child Neurology [Internet]. 2022 Aug 11;64(12):1494–506. Available from: https://onlinelibrary.wiley.com/doi/10.1111/dmcn.15346
29. Morgan C, Badawi N, Boyd RN, Spittle AJ, Dale RC, Kirby A, et al. Harnessing neuroplasticity to improve motor performance in infants with cerebral palsy: a study protocol for the GAME randomised controlled trial. BMJ Open. 2023 Mar;13(3):e070649.
30. Huroy M, Behlim T, Andersen J, Buckley D, Fehlings D, Kirton A, et al. Stability of the Gross Motor Function Classification System over time in children with cerebral palsy. Developmental Medicine & Child Neurology. 2022 Aug 8;64(12):1487–93.

DOI: 10.52629/jamsa.v12i1.1105

31. Morgan C, Fetters L, Adde L, Badawi N, Bancale A, Boyd RN, 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 Pediatrics [Internet]. 2021 May 17;175(8). Available from: https://jamanetwork.com/journals/jamapediatrics/article-abstract/2780012

32. Omrani M, Rosaria Rita Chiarelli, Acquaviva M, Bassani C, Gloria Dalla Costa, Montini F, et al. Machine learning-driven diagnosis of multiple sclerosis from whole blood transcriptomics. Brain Behavior and Immunity [Internet]. 2024 Oct 1 [cited 2024 Aug 7];121:269–77. Available from: https://pubmed.ncbi.nlm.nih.gov/39097200/

33. Fabrizia Festante, Antonelli C, Mazzotti S, Guzzetta A. Early Intervention in Cerebral Palsy: From Theory to Current Practice. Springer eBooks. 2023 Jan 1;149–92.

34. Chorna O, Heathcock J, Key A, Noritz G, Carey H, Hamm E, et al. Early childhood constraint therapy for sensory/motor impairment in cerebral palsy: a randomised clinical trial protocol. BMJ Open [Internet]. 2015 Dec;5(12):e010212. Available from: https://bmjopen.bmj.com/content/5/12/e010212

35. Novak I, Morgan C, Adde L, Badawi N, Block S, Boyd RN, et al. Early, Intensive, Active, and Specific: Fractional Dose of Goal-Directed, Activity-Based Early Intervention for Infants at High Risk of Cerebral Palsy—A Systematic Review. J Clin Med. 2023;12(11):3621.

36. Novak I, Morgan C, McNamara L, Te Velde A, Badawi N, Bimanual and Constraint-Induced Movement Therapy Team. Baby-CIMT for infants with asymmetric brain lesions: a randomized controlled trial. Dev Med Child Neurol. 2022;64(9):1112-1121.

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Supplementary Files

Comparative Efficacy and Safety of Dual Orexin Receptor Antagonists (DORAs) Versus Z-Drugs for Insomnia in Older Adults : A Systematic Review

Appendix 1. Search Strategy

Database	Keywords	Records Retrieved
PubMed	((“Cerebral Palsy”[MeSH Terms] OR “Cerebral Palsy” OR “High Risk Infant” OR “High Risk Infants”)) AND ((“Goal-Directed Training” OR “goal-directed” OR “activity-based” OR “GAME intervention” OR “Small Step” OR “task-oriented”)) AND ((“PEDI” OR “PEDI-CAT” OR “functional independence” OR “functional outcome”))	19
ScienceDirect	(“Cerebral Palsy” OR “High Risk Infant”) AND (“goal directed” OR “activity-based” OR “task-oriented” OR “GAME intervention”) AND (“PEDI” OR “functional outcome”)	299
WILEY	(Abstract:”Cerebral Palsy” OR Abstract:”high risk infant”) AND (Abstract:”goal directed” OR Abstract:”activity-based” OR Abstract:”GAME”) AND (Abstract:”PEDI” OR Abstract:”functional”)	12
ProQuest	noft((“Cerebral Palsy” OR “High Risk Infant”) AND (“goal directed” OR “activity-based” OR “task-oriented” OR “GAME intervention”) AND (“PEDI” OR “functional outcome”))	232
MedRXiv	“Cerebral Palsy” AND “goal-directed” AND “infant”	10