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Effectiveness of hand-arm bimanual intensive therapy including lower extremities in the rehabilitation of children with cerebral palsy: a systematic review protocol

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ABSTRACT

Introduction Cerebral palsy (CP) is a paediatric disorder with permanent impairment of movement and posture with a prevalence of about 2.11 in 1000 births in the world. Given the therapeutic effect of hand-arm bimanual intensive therapy including lower extremities (HABIT-ILE) in children with CP, a systematic review of the available literature on this topic is warranted. The objective of this study is to systematically review the effectiveness of HABIT-ILE on upper extremity, lower extremity and trunk outcomes within the domains of body functions and structures, activity and participation of the International Classification of Functioning, Disability and Health in children with CP.

Methods and analysis This study will be conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Searches will be conducted in six databases: MEDLINE, PubMed, Cochrane Library, Scopus, OT seeker and Web of Science for available published literature. The grey literature sources will include WorldCat, National Technical Information Service, Agency for Healthcare Research and Quality, Open Grey, WHO and OpenDOAR. Manual searches of citations of included papers will be performed to collect all experimental studies of HABIT-ILE in children with CP. The level of evidence for included articles will be classified according to the level of evidence in the guidelines for systematic reviews on the American Occupational Therapy Association website. Based on the study design of the included articles, the risk of bias will be assessed using the revised Cochrane risk-of-bias tool, the Cochrane Risk Of Bias In Non-randomised Studies – of Interventions tool and the quality assessment tool recommended by the American Occupational Therapy Association. In order to synthesise the data, narrative synthesis will be used, along with meta-analysis, if available.

Ethics and dissemination As this study only reviewed previously published articles, ethical approval was not required. The findings will be published in a peer-reviewed scientific journal.

PROSPERO registration number CRD42024518179.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Multiple databases were searched, enhancing the comprehensiveness and reliability of the review.
⇒ Independent screening and data extraction by two reviewers minimise selection and extraction bias.
⇒ Inclusion of all experimental study designs increases the applicability of findings but may introduce heterogeneity.
⇒ As the review will include studies in English, Portuguese, French, German and Spanish, articles in other languages will not be searched or included, potentially resulting in language bias.

INTRODUCTION

Cerebral palsy (CP) is a paediatric disorder that leads to permanent impairment of movement and posture due to non-progressive brain damage occurring from the fetal or neonatal period up to age 3.[1 2] It is estimated that the prevalence of CP is approximately 2.11 per 1000 births globally.[3] CP presents with motor dysfunctions such as spasticity, dyskinesia, ataxia, weakness and contractures, impacting the upper and lower limbs and the trunk.[4] These symptoms affect the International Classification of Functioning, Disability and Health (ICF) domains: body functions and structures, activities, and participation.[5] Specifically, spasticity and ataxia impair fine motor skills, mobility, and postural control, limiting tasks such as writing and walking.[6] Consequently, children with CP may struggle with activities such as writing a greeting card or walking a dog with a friend, leading to reduced participation at home, school and community.[7]

Hand-arm bimanual intensive therapy (HABIT), developed by Charles and Gordon in 2006, is an intervention based on motor learning and neuroplasticity principles for children with unilateral spastic cerebral palsy (USCP).[8] Compared with constraint-induced movement therapy (CIMT), which is also

designed for children with USCP, this type of bimanual therapy emphasises the functional use of both hands rather than unimanual practice, providing extensive, child-friendly practice without physically constraining the child's less-affected hand.[8 9] HABIT consists of a structured practice of functional and playful activities with increasing complexity to improve two-handed coordination using upper extremities.[8] This therapy results in improvements in bimanual ability, unilateral dexterity, self-care function, functional goal performance and satisfaction.[10 11] In HABIT, children are predominantly seated and primarily trained on their upper extremities, without targeting their lower extremities.[8]

As components of everyday activities, certain tasks may demand coordinated utilisation of upper and lower limbs alongside the trunk, exemplified by carrying a tray to a table. Two studies using modified CIMT reported improvements in gait variables despite the training not being specifically designed for the lower extremities, potentially due to the combination of upper and lower extremity tasks during intervention.[12 13] Treadmill training demonstrated improved walking speed in children with CP; however, it lacked intensive, tailored training for those with bilateral CP, which can be perceived as monotonous and frustrating.[14 15] Considering the integration of upper and lower limbs and trunk activities in daily life and the lack of lower extremity-friendly intensive training for children, Bleyenheuft and Gordon developed HABIT including lower extremities (HABIT-ILE) in 2014, marking the first intervention to simultaneously target both upper and lower extremity control in children with CP.[16]

HABIT-ILE builds on the HABIT methodology by integrating structured bimanual tasks and activities of daily living that progressively increase in motor difficulty, targeting both the upper and lower extremities and the trunk.[16–19] HABIT-ILE emphasises simultaneous control of the upper and lower extremities, with a child-friendly design that aligns with functional goals.[16] There will be changes in the trunk and lower extremity positions in HABIT-ILE as the lower extremities perform better, changing from easy to difficult positions and standing on unstable supports, for instance.[16] Studies reported that children with unilateral spastic CP and children with bilateral CP exhibit significantly improved upper and lower extremity motor abilities following HABIT-ILE.[17–19] In comparison with HABIT, HABIT-ILE did not reduce the promotion of upper extremity training in children with unilateral spastic CP;[20] conversely, they even demonstrated more significant improvements in daily life activities with better performance on measures like the Paediatric Evaluation of Disability Inventory and the Canadian Occupational Performance Measure (COPM).[20] These superior outcomes may be attributed to the inclusion of lower extremity training, which enhances upper-lower limb coordination. Since many self-care tasks, such as dressing, toileting and body washing, require both upper and lower limb involvement, this additional component likely contributed to greater functional gains.[20] Furthermore, the dynamic nature of HABIT-ILE, incorporating activities like sitting on a ball, standing, balancing, walking and jumping while performing bimanual tasks, may have further supported improvements in functional independence.[16 20]

A systematic review on the effectiveness of HABIT for improving upper-limb function in children with CP included HABIT-ILE as a distinct category under 'HABIT-added component', which integrates lower extremity training while maintaining intensive upper extremity practice. This review focused specifically on the impact of HABIT-ILE on upper-limb function and included only three studies published between 2015 and 2017: one quasirandomised controlled trial (RCT),[19] one crossover-RCT[18] and one retrospective study.[10 20] To our knowledge, there have been no systematic reviews encompassing all types of studies investigating the effects of HABIT-ILE on both upper and lower limb function in children with CP. In this systematic review, we will focus mainly on HABIT-ILE effectiveness on upper extremity, lower extremity and trunk outcomes at the level of body functions and structures, activity and participation in children with CP according to the ICF.

METHODS AND ANALYSIS

Protocol registration

This systematic review protocol was developed based on the 2015 statement of Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P).[21] The protocol is registered on the International Prospective Register of Systematic Reviews (PROSPERO) website (CRD42024518179).

Eligibility criteria

The inclusion and exclusion criteria are listed below based on the participants, intervention, comparison and outcome (PICO) framework.[22] Articles will be included if they satisfy the following criteria: (1) Participants diagnosed with CP. (2) Participants aged 0–18 years will be included, based on the ICF for Children and Youth, which defines childhood as from birth to 18 years of age.[23] However, we acknowledge that different studies may use varying age definitions. Studies that exclusively include participants aged 0–18 years will be eligible for inclusion. Studies including both children (<18 years) and adults (≥18 years) will be included only if separate data for the 0–18 age group can be extracted. Studies covering a broader age range (eg, 0–19 years) without separate data for 0–18 years will be excluded. If the age range is unclear, inclusion will be determined on a case-by-case basis through discussion among the reviewers. (3) All levels of experimental studies related to the effectiveness of HABIT-ILE. (4) There is no restriction of setting. (5) There is no restriction of the control group. The control group could be usual care or other interventions. Articles without control groups are also acceptable. (6)

Outcomes with changes in upper and lower extremity function, occupational performance and occupational satisfaction from baseline to last follow-up. In addition to the outcomes mentioned above, other rehabilitation outcomes will also be acceptable. (7) There are no restrictions on the types of study. Pilot and feasibility trials will also be included. (8) Studies published as original articles with full text. Relevant grey literature will be included. (9) Studies published in English, Portuguese, French, German and Spanish languages. (10) Articles published from 2014 to 2024 to include the more recent evidence from the literature. In 2014, the developer of HABIT-ILE published the first original research on the project.[16] Articles will be excluded if full text could not be found through interlibrary loan.

Search strategy and information sources

Six databases will be searched: MEDLINE, PubMed, Cochrane Library, Scopus, OTseeker and Web of Science for published literature. The grey literature sources will include WorldCat, National Technical Information Service, Agency for Healthcare Research and Quality, Open Grey, WHO and OpenDOAR. Filters will be applied to limit the search to articles written in English, Portuguese, French, German and Spanish from 2014 to 2024. Citation manual searches of included papers will be conducted for further relevant research. Study authors will be contacted for unclear or incomplete important data. The selection of electronic databases and the search strategy will be based on the search strategies of previous reviews of the CP literature.[10 24] The medical subject headings 'child', 'teenager' and 'cerebral palsy' were searched for synonyms and related terms to generate a comprehensive list of keywords. The search strategy also includes keywords 'Hand-arm bimanual intensive therapy including lower extremities or HABIT-ILE', within the title and abstract. Online supplemental appendix 1 illustrates an example search strategy.

Screening and study selection

The literature search results will be imported into EndNote V.21 and include information such as the title, author and abstract of the article. Next, the EndNote V.21 software's function of removing duplicate articles will be used. The first reviewer will carefully compare the information in the pop-up window. By reading the title, abstract, Digital Object Identifier and other information in the article, only one of the same documents will be retained and the rest will be deleted. Then, the first reviewer observes the title directory to ensure again that duplicate articles have been deleted. The EndNote file containing the remaining papers will be shared. Two reviewers will read titles and abstracts, respectively, and screen articles based on inclusion and exclusion criteria. If it is not possible to determine whether the paper is included in the systematic review after reading the title and abstract, the full text will be read and screened to further identify whether the revised paper is included in this systematic review. Relevant papers will be copied to a new literature group in EndNote software. Finally, the two reviewers will compare their screening results. If the results of the two reviewers are inconsistent, discussion and negotiation will be held to reach a consensus. If an agreement cannot be reached, a third reviewer will be consulted. The third reviewer will act as the final decision-maker to determine whether the study meets the inclusion criteria. A PRISMA flow diagram will be used to illustrate the review process (figure 1).

Data extraction

The included articles at the end of this process will ultimately be subject to further full-text reading. The data extraction table refers to the guidelines for systematic reviews on the American Occupational Therapy Association website.[25] The content of the evidence table includes author/year, level of evidence, study design, risk of bias (quality assessment), participants (age, gender and location), inclusion criteria, study setting, interventions (treatment modality and the amount, duration, frequency and intensity used in experimental and control groups), outcome measures and results (including significance of findings). The above information from the article will be extracted. The two reviewers will work together to extract and synthesise data. If inconsistencies are encountered, a third reviewer will be invited to join the discussion to reach consensus. During the systematic review, if necessary, the initial data extraction evidence table derived from the Guidelines for Systematic Reviews on the American Occupational Therapy Association website will be revised following a unanimous decision.

Outcomes and prioritisation

The primary outcomes focus on gross motor and bimanual hand function, as these domains are critical for enhancing independence and participation in children with CP. For example,

- Gross Motor Function Measure-66, b710/b755/b760/d410/d415/d450/d455: evaluates changes in gross motor abilities, such as sitting, standing and walking, reflecting activity and mobility levels (eg, mobility and posture control) within the ICF framework.[26]
- ABILHAND-Kids (d510/d520/d540/d550/d560): assesses the quality and effectiveness of bimanual hand use in performing everyday functional tasks, linking activity and participation domains within the ICF.[27]

The secondary outcomes complement the primary measures by capturing additional dimensions of motor function, participation and client-centred care. For example,

- Jebsen-Taylor Test of Hand Function (b760/d430–39): evaluates hand dexterity and fine motor skills across both hands.[28]
- 6-Minute Walk Test (b147/d410–429/d450/d455): measures walking endurance and mobility, reflecting participation in physical activities.[29]

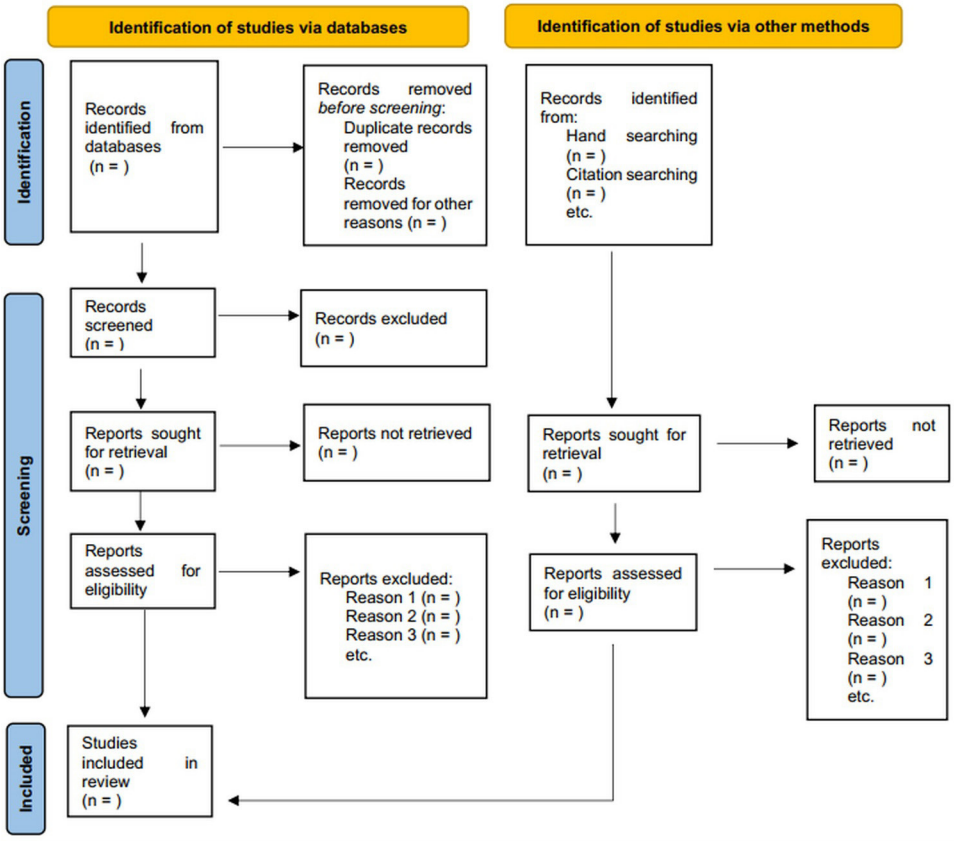

Figure 1 Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) flow diagram.

- COPM (d1–9): captures parent-reported performance and satisfaction with functional goals, offering insights into participation and caregiver perspectives.[30]
- CP Quality-of-Life Questionnaire (d760/d770/d910/d920): assesses quality-of-life dimensions relevant to children with CP, linking participation and environmental factors within the ICF framework.[31 32]

The rationale for prioritising the primary outcomes lies in their alignment with the intervention's core objectives to enhance gross motor and bimanual hand function. These areas are foundational for achieving independence and active participation in daily life. Secondary outcomes were chosen to provide a broader understanding of the intervention's effects, including functional gains in hand dexterity, walking endurance and caregiver-reported outcomes. This comprehensive evaluation ensures that the intervention's impact is assessed across multiple dimensions of activity, body function and participation, adhering to the ICF framework and principles of client-centred care.

Quality assessment

The level of evidence for included articles will be classified according to the level of evidence in the guidelines for systematic reviews on the American Occupational Therapy Association website.[25] The bias risk for RCTs will be evaluated by using the revised Cochrane risk-of-bias tool,[33] which contains and assesses five risk domains for methodological quality, namely: (1) the process of randomisation; (2) deviations from the intended intervention (assignment and adhering to the intervention); (3) missing outcome data; (4) outcome measurement and (5) selection of the reported result. A Cochrane Risk Of Bias In Non-randomised Studies – of Interventions tool[34] will be used to evaluate bias risks in non-randomised studies, which assesses biases based on: (1) confounding factors; (2) selection of participants into study; (3) intervention classification; (4) deviations from intended intervention; (5) missing outcome data; (6) outcome measurement and (7) selection of which results are reported. Risk of bias for before-after (pre-post) studies with no control group will be assessed using the quality assessment tool adapted from the National Heart Lung and Blood Institute recommended by the American Occupational Therapy Association.[25] The risk of bias will be evaluated based on the following factors: (1) clear description of research questions or objectives; (2) clear description of eligibility; (3) whether participants are representative and reasonable; (4) clear description of the intervention; (5) outcome measurement; (6) blinding the evaluators; (7) loss rate of follow-up studies and (8) statistical method.

Data synthesis

A narrative synthesis of the findings will be conducted based on the review objectives. In this case, quantitative results from each study will be reported and summarised descriptively. If at least three efficacy and effectiveness studies are comparable regarding intervention,

comparator(s) and outcome(s),[35] the reviewers will decide whether a meta-analysis is appropriate and report the rationale (eg, the rationale for inappropriateness is that a small number of studies meet the eligibility criteria or there is significant heterogeneity). Meta-analyses will be conducted using random-effects modelling with RevMan software V.5.3. The mean difference and 95% CI will be calculated for continuous data if the outcome measures use the same scales. The standardised mean difference and 95% CI will be calculated for different outcome measurement scales. A small effect size is defined as one between 0 and 0.2, a medium effect size as one between 0.2 and 0.5, and a large effect size as one ranging from >0.5 to 0.8.[36] Heterogeneity will be assessed using the I^2 statistic, with 25%, 50% and 75% I^2 values representing low, medium and high heterogeneity degrees, respectively.[37] Study quality will be taken into account in sensitivity analyses. An inspection of funnel plots will be performed if the meta-analysis includes more than 10 studies.[38] During the meta-analysis, Egger's test will be used to detect publication bias.[39] When possible, subgroup analyses will be conducted based on the type of CP (eg, unilateral CP, bilateral CP). A subgroup analysis and sensitivity analysis will be conducted to identify heterogeneity sources and assess findings' robustness.[35]

Confidence in cumulative evidence

To evaluate the quality of evidence, grade of recommendation, assessment, development and evaluation (GRADE) will be used, which categorises evidence based on study limitations (domain bias risk), inconsistency, imprecision of indirect evidence and publication bias.[40–42] The GRADE approach systematically classifies evidence into four distinct quality levels—high, moderate, low and very low—with RCTs initially rated as high-quality evidence, subject to possible downgrading based on certain criteria to moderate, low or very low certainty.[40–42]

Patient and public involvement

There will be no direct involvement of patients or members of the public in the study.

DISCUSSION

This is the first systematic review on the effectiveness of HABIT-ILE on upper extremity, lower extremity and trunk outcomes at the level of body functions and structures, activity and participation in children with CP according to the ICF. This systematic review will encompass all studies using any experimental design published from 2014 onwards, including the first original research on the HABIT-ILE project by its developer in 2014. In addition, pilots and feasibility studies will also be included. The proposed systematic review study will provide a comprehensive reference of HABIT-ILE. It will increase our knowledge of the effectiveness of HABIT-ILE, thus providing more intervention options for the therapist, parents and caregivers to choose from. Ultimately, this will support the clinical usage of HABIT-ILE for the rehabilitation of children with CP, allowing the service providers to deliver effective and high-quality interventions to benefit the service recipients. For managers of hospitals, rehabilitation departments or rehabilitation institutions, this article can serve as a reference when making decisions about rehabilitation for children with CP.

This systematic review may have some limitations. Only literature written in English, Portuguese, French, German and Spanish will be included in this systematic review. There may be studies in other languages that are useful and relevant but not taken into account. This review will also exclude non-full-text documents, such as conference abstracts, and this may cause the omission of some potential research. Additionally, while the inclusion of grey literature helps reduce publication bias and provides a more comprehensive review of available evidence, it may also introduce variability in study quality due to the lack of formal peer review. Furthermore, the inclusion of all experimental study designs increases the applicability of findings but may introduce heterogeneity due to variations in study methodologies, intervention protocols and outcome measures.

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REFERENCES

1 Balkrishnan R, Manuel JC, Smith BP, *et al*. Longitudinal examination of health outcomes associated with botulinum toxin use in children with cerebral palsy. *J Surg Orthop Adv* 2004;13:76–80.
2 Rosenbaum P, Paneth N, Leviton A. A report: the definition and classification of cerebral palsy April 2006. *Dev Med Child Neurol* 2007;49:8–14.
3 Oskoui M, Coutinho F, Dykeman J, *et al*. An update on the prevalence of cerebral palsy: a systematic review and meta-analysis. *Dev Med Child Neurol* 2013;55:509–19.
4 Patel DR, Neelakantan M, Pandher K, *et al*. Cerebral palsy in children: a clinical overview. *Transl Pediatr* 2020;9:S125–35.
5 Schiariti V, Klassen AF, Cieza A, *et al*. Comparing contents of outcome measures in cerebral palsy using the International Classification of Functioning (ICF-CY): a systematic review. *Eur J Paediatr Neurol* 2014;18:1–12.
6 Mutlu A, Akmese PP, Gunel MK, *et al*. The importance of motor functional levels from the activity limitation perspective of ICF in children with cerebral palsy. *Int J Rehabil Res* 2010;33:319–24.
7 Mei C, Reilly S, Reddihough D, *et al*. Activities and participation of children with cerebral palsy: parent perspectives. *Disabil Rehabil* 2015;37:2164–73.
8 Charles J, Gordon AM. Development of hand-arm bimanual intensive training (HABIT) for improving bimanual coordination in children with hemiplegic cerebral palsy. *Dev Med Child Neurol* 2006;48:931–6.
9 Chiu H-C, Ada L. Constraint-induced movement therapy improves upper limb activity and participation in hemiplegic cerebral palsy: a systematic review. *J Physiother* 2016;62:130–7.
10 Ouyang R-G, Yang C-N, Qu Y-L, *et al*. Effectiveness of hand-arm bimanual intensive training on upper extremity function in children with cerebral palsy: A systematic review. *Eur J Paediatr Neurol* 2020;25:17–28.
11 Alahmari K, Tedla JS, Sangadala DR, *et al*. Effectiveness of Hand-Arm Bimanual Intensive Therapy on Hand Function among Children with Unilateral Spastic Cerebral Palsy: A Meta-Analysis. *Eur Neurol* 2020;83:131–7.
12 Coker P, Karakostas T, Dodds C, *et al*. Gait characteristics of children with hemiplegic cerebral palsy before and after modified constraint-induced movement therapy. *Disabil Rehabil* 2010;32:402–8.
13 Zipp GP, Winning S. Effects of constraint-induced movement therapy on gait, balance, and functional locomotor mobility. *Pediatr Phys Ther* 2012;24:64–8.
14 Johnston TE, Watson KE, Ross SA, *et al*. Effects of a supported speed treadmill training exercise program on impairment and function for children with cerebral palsy. *Dev Med Child Neurol* 2011;53:742–50.
15 Beveridge B, Feltracco D, Struyf J, *et al*. "You gotta try it all": Parents' Experiences with Robotic Gait Training for their Children with Cerebral Palsy. *Phys Occup Ther Pediatr* 2015;35:327–41.
16 Bleyenheuft Y, Gordon AM. Hand-arm bimanual intensive therapy including lower extremities (HABIT-ILE) for children with cerebral palsy. *Phys Occup Ther Pediatr* 2014;34:390–403.
17 Bleyenheuft Y, Arnould C, Brandão M, *et al*. Hand and arm bimanual intensive therapy including lower extremity (HABIT-ILE) in children with cerebral palsy: A randomized trial. *Dev Med Child Neurol* 2014;56:83–4.
18 Bleyenheuft Y, Arnould C, Brandao MB, *et al*. Hand and Arm Bimanual Intensive Therapy Including Lower Extremity (HABIT-ILE) in Children With Unilateral Spastic Cerebral Palsy: A Randomized Trial. *Neurorehabil Neural Repair* 2015;29:645–57.
19 Bleyenheuft Y, Ebner-Karestinos D, Surana B, *et al*. Intensive upper- and lower-extremity training for children with bilateral cerebral palsy: a quasi-randomized trial. *Dev Med Child Neurol* 2017;59:625–33.
20 Saussez G, Brandão MB, Gordon AM, *et al*. Including a Lower-Extremity Component during Hand-Arm Bimanual Intensive Training does not Attenuate Improvements of the Upper Extremities: A Retrospective Study of Randomized Trials. *Front Neurol* 2017;8:495.
21 Shamseer L, Moher D, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;350:g7647.
22 Schardt C, Adams MB, Owens T, *et al*. Utilization of the PICO framework to improve searching PubMed for clinical questions. *BMC Med Inform Decis Mak* 2007;7:1–6.
23 World Health Organization. *International classification of functioning, disability and health: children and youth version: ICF-CY*. Geneva, Switzerland: World Health Organization,
24 Zanon MA, Pacheco RL, Latorraca C de OC, *et al*. Neurodevelopmental Treatment (Bobath) for Children With Cerebral Palsy: A Systematic Review. *J Child Neurol* 2019;34:679–86.
25 Guidelines for Systematic Reviews American Occupational Therapy Association, 2020. Available: https://research.aota.org/DocumentLibrary/AOTA_AJOT_systematic%20reviews%20instructions.pdf
26 Russell DJ, Rosenbaum P, Wright M, *et al*. Gross motor function measure (GMFM-66 & GMFM-88) users manual. Mac keith press; 2002.
27 Arnould C, Penta M, Renders A, *et al*. ABILHAND-Kids: a measure of manual ability in children with cerebral palsy. *Neurology (ECronicon)* 2004;63:1045–52.
28 Tofani M, Castelli E, Sabbadini M, *et al*. Examining Reliability and Validity of the Jebsen-Taylor Hand Function Test Among Children With Cerebral Palsy. *Percept Mot Skills* 2020;127:684–97.
29 Maher CA, Williams MT, Olds TS. The six-minute walk test for children with cerebral palsy. *Int J Rehabil Res* 2008;31:185–8.
30 Verkerk GJQ, Wolf MJMAG, Louwers AM, *et al*. The reproducibility and validity of the Canadian Occupational Performance Measure in parents of children with disabilities. *Clin Rehabil* 2006;20:980–8.
31 Davis E, Mackinnon A, Davern M, *et al*. Description and psychometric properties of the CP QOL-Teen: a quality of life questionnaire for adolescents with cerebral palsy. *Res Dev Disabil* 2013;34:344–52.
32 Waters E, Davis E, Mackinnon A, *et al*. Psychometric properties of the quality of life questionnaire for children with CP. *Dev Med Child Neurol* 2007;49:49–55.
33 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.
34 Sterne JA, Hernán MA, Reeves BC, *et al*. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016;355:i4919.
35 Higgins JPT TJ, Chandler J, Cumpston M, eds. *Cochrane handbook for systematic reviews of interventions version 6.4*. 2023.
36 Cohen J. Statistical power analysis for the behavioral sciences. 2nd edn. 1988.
37 Higgins JPT. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557–60.
38 Sterne JAC, Sutton AJ, Ioannidis JPA, *et al*. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ* 2011;343:bmj.d4002.
39 Egger M, Smith GD, Schneider M, *et al*. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;315:629–34.
40 Bezerra CT, Grande AJ, Galvão VK, *et al*. Assessment of the strength of recommendation and quality of evidence: GRADE checklist. A descriptive study. *Sao Paulo Med J* 2022;140:829–36.
41 Guyatt GH, Oxman AD, Vist GE, *et al*. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924–6.
42 Guyatt GH, Oxman AD, Schünemann HJ, *et al*. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. *J Clin Epidemiol* 2011;64:380–2.