https://doi.org/10.1016/j.ejpn.2019.12.017

Title: Effectiveness of Hand-Arm Bimanual Intensive Training on upper extremity function in children with cerebral palsy: A systematic review

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Declarations of interest: none

Effectiveness of Hand-Arm Bimanual Intensive Training on upper extremity function in children with cerebral palsy: A systematic review

Abstract

Objective: To systematically review the effectiveness of Hand-Arm Bimanual Intensive Training (HABIT) on upper limb function in children with cerebral palsy.

Methods: Six databases (MEDLINE, CINAHL, PubMed, Embase, Cochrane Library, and PsycINFO) were searched for HABIT-related studies published in English between 2007 and 2017. The methodological quality of the included studies was classified based on the Levels of Evidence of the American Occupational Therapy Association guidelines. If the included studies were randomized controlled trials (RCTs), the methodological quality was evaluated using the Revised Cochrane risk of bias tool. Cohen's *d* effect sizes were computed and synthesized to assess the effectiveness.

Results: Among 646 studies, 15 fulfilled the inclusion criteria. Eleven studies were RCTs, 64% of which were rated as having a high risk of bias; one was a quasi-RCT, one was a retrospective study, and two were longitudinal studies. Nearly half of the included studies used HABIT for 6 hours a day for three consecutive weeks (totaling 90 hours), and some studies used different doses/schedules or added training components to HABIT. Synthesis of the results demonstrated a significantly small effect size ($d = 0.36$, $P = 0.017$) for improving upper limb function immediately after the interventions, and the improvements were maintained at follow-up. Similarly, significantly moderate or large effect sizes were found for self-care function ($d = 0.52$, $P = 0.003$) and goal improvements ($d = 1.78–2.28$, $P < 0.001$).

Conclusion: This review supports the effectiveness of HABIT as an intervention for improving upper limb function in children with cerebral palsy.

Keywords

Hand-Arm Bimanual Intensive Training (HABIT); Cerebral palsy; Upper extremity; Children; Systematic review

Abbreviations

ADL, activities of daily living; AHA, Assisting Hand Assessment; CI, confidence interval; CIMT, constraint-induced movement therapy; COPM, Canadian Occupational Performance Measure; CP, cerebral palsy; HABIT, Hand-Arm Bimanual Intensive Training; JTTHF, Jebsen-Taylor Test of Hand Function; MACS, Manual Ability Classification System; PEDI, Pediatric Evaluation of Disability Inventory; RCT, randomized controlled trial; RoB 2.0, Revised Cochrane risk of bias tool

1. Introduction

Cerebral palsy (CP) is the most common physical dysfunction disease in children.[1] The prevalence of CP is 1.5 to 4 per 1,000 births.[2] CP is a disorder caused by non-progressive damage or abnormal development in parts of the brain during the fetal or infant phase.[3] More than 80% of children with CP have an upper extremity impairment,[4] which significantly affects their activities of daily living (ADL) and quality of life. Due to damage to the motor cortex and corticospinal pathways, children with CP demonstrate difficulties in precise grasping and fine motor control[5,6] and will develop an abnormal movement pattern.

Recent evidence has shown that children with CP could benefit from constraint-induced movement therapy (CIMT) for unimanual hand ability.[7] CIMT was originally developed to address learned non-use in hemiplegic adults.[8] CIMT focuses on the practice of the involved hand, and it restrains the use of the non-involved hand during treatment. Many studies have illustrated the positive effects of CIMT on hand function in children with CP;[9,10] however, CIMT focuses only on the affected hand. This may be impractical for children to perform ADL since most ADL tasks require two hands working together for activities such as opening bottles, dressing, and folding clothes. While CIMT is commonly used in clinical practice,[7,11] the concept of the non-use hand in children with CP could be different from that in hemiplegic adults. CP is an early brain damage disorder; children with CP never have the chance to learn normal movement patterns and often develop ineffective compensation movements. Physical constraint of the non-involved hand seems to be invasive for children and may lead to psychological frustration.[12] Furthermore, the bimanual coordination deficit could be more critical than unilateral impairment in children with CP.[13,14] The

aforementioned challenges and concerns regarding CIMT for children with CP urge an alternative therapy and, therefore, bimanual therapy has gained increasing attention in both research and clinical settings.

Bimanual therapy is a general term for repetitive task practice using two hands, rather than one hand, to complete functional activities. It is a child-friendly technique without the physical constraint of the less-affected hand. Rehabilitation therapists have routinely used this intervention approach to manage upper limb dysfunction in children with CP. However, the guiding principles, structure, and administration of bimanual therapy are often not standardized and could be varied across clinical settings. To address these issues, Hand-Arm Bimanual Intensive Training (HABIT), which is a specific type of bimanual therapy, was introduced by Charles and Gordon[15] in 2006. The HABIT process involves prioritization of the bimanual coordination skills of hands, and it maintains the intensive quality of constraint therapy. The basic principle of HABIT concerns maintaining the intensity of constraint therapy and improving the deficiency of bimanual coordination (including temporal and spatial coordination) based on the principles of motor learning and neuroplasticity.[16,17] Accordingly, intervention by HABIT involves a structured practice for bimanual hand function through child-friendly activities which are chosen by children according to their goals and preferences. The structured practice includes two specific types: one is the whole-task practice (e.g., performing the activity for at least 15 to 20 minutes) and the other is the part-task practice (e.g., practicing target movements repeatedly).[15] Children are asked to use the involved limb in the same manner as that of the non-dominant hand of a typically developing child.[15] Thus, the training requires children to have a normal cognitive level so as

to understand the purpose of each activity and avoid the use of compensatory strategies. The intervention can be conducted individually or in groups. Task difficulty is graded according to the speed, accuracy, or extent of using the involved hand in each activity.[15] A training protocol including the 60-hour intensive training plus 1-hour daily home practice was initially documented[15] and then trialed in Gordon et al.'s study.[18]

A more intensive 90-hour training protocol for HABIT (i.e., 6 hours each day with a 1-hour home practice for 15 continuous weekdays) was subsequently used in most studies.[19-23] Some researchers also started to adopt different training dosages and schedules (e.g., increasing to 96 hours for a longer duration of 8 weeks)[24] to accommodate the needs in different clinical and educational settings. Investigators also added other training components (e.g., lower extremity training)[25-27] to HABIT to study the additional effects. Considering that HABIT comprises the advantages of intensive training in a more child-friendly way and pays attention to bimanual training which is highly related to most ADL tasks, there is a need to systematically evaluate the effectiveness of HABIT-related interventions in children with CP to support evidence-based practice.

Many systematic reviews have investigated the effectiveness of interventions targeted at improving upper extremity function in children with hemiplegic CP, and some of the reviews included bimanual therapies.[28-32] For example, Novak and colleagues investigated the efficacy of evidence-based bimanual therapies in supporting the effectiveness of interventions targeted at improving upper extremity function in children with hemiplegic CP and included various types of bimanual therapies.[29,31] Various bimanual therapies were also included in the other reviews,[28,30,32] and this may be one reason for their inconclusive

findings on the comparative efficacy of bimanual therapy to that of CIMT. To unravel the benefit of bimanual therapy, it is necessary to focus on one specific type of bimanual therapy with an exact structure (i.e., HABIT). Therefore, this systematic review aimed to investigate the effectiveness of HABIT in improving upper extremity function in children with CP.

2. Methods

2.1 Search strategy

A literature search was conducted for articles about the effectiveness of HABIT on upper extremity function in children with CP. Six databases, including MEDLINE, CINAHL, PubMed, Embase, Cochrane Library, and PsycINFO, were searched. Search strategies included the title, abstract, and content of articles using the keywords "hand-arm bimanual intensive training or bimanual (or bilateral) intervention/training/therapy/treatment," "HABIT or HABIT including lower extremity (HABIT-ILE)," "cerebral palsy, CP, hemiplegia, congenital hemiplegia, or hemiplegic cerebral palsy," "child or children," and "upper limb, upper extremity, hand, or arm." The titles and abstracts of eligible articles were simultaneously screened by the first three authors. Full texts were also screened when the title and abstract did not provide sufficient detail.

2.2 Inclusion and exclusion criteria

Articles were included if they satisfied the following inclusion criteria: 1) all levels of experimental studies related to the effectiveness of HABIT for improving upper extremity function; 2) participants needed to be diagnosed with CP and aged between 1 and 18 years old; and 3) articles were published in English between 2007 and 2017, considering that the

first study of HABIT[18] was published in 2007. Articles were excluded if they were case studies or conference papers, full texts were not available through the interlibrary loan services, or interventions combined the use of HABIT with CIMT as this review focused specifically on HABIT.

2.3 Methodological quality assessment

The quality of the included studies was classified according to the Levels of Evidence of the American Occupational Therapy Association guidelines.[33] Randomized controlled trials (RCTs) were assessed using the Revised Cochrane risk of bias tool (RoB 2.0),[34] which contains six domains for the methodological quality for RCTs: 1) risk of bias arising from the randomization process, 2) risk of bias due to deviations from the intended intervention (effect of assignment to the intervention), 3) risk of bias due to deviations from the intended intervention (effect of adhering to the intervention), 4) missing outcome data, 5) risk of bias in the measurement of the outcome, and 6) risk of bias in the selection of the reported results. Specifically, in domain 5, primary outcome measures in relation to upper extremity function were targeted in the evaluation. If primary outcome measures were not stated or unrelated to upper extremity function in certain studies, alternative measures with the specific focus on upper extremity function were used. An overall risk of bias was assigned to each study based on the RoB 2.0 guideline.[34] For example, "low risk of bias" indicates a low risk of bias for all domains; "some concerns" indicates at least one domain that may raise some concerns and without a high risk of bias for any other domains; and "high risk of bias" indicates a high risk of bias in at least one domain or multiple domains judged to have some concerns. The evidence level and/or risk of bias for each study were rated independently by two authors

using the criteria outlined in the guidelines.[33,34] In case of a disagreement about the evaluation results, a consensus was reached based on a discussion among all the authors.

2.4 Computation and synthesis of effect sizes

Effect sizes for HABIT and control interventions in each included study were calculated using Cohen's *d* formula. This effect size calculation is based on the difference between pre- and post-treatment scores divided by the pooled standard deviation.[35] Means and standard deviations were retrieved from the tables published in the included studies. When only graphs were reported, we used WebPlotDigitizer 4.1 (Ankit Rohatgi, Austin, TX, USA) to extract the data. Because two of the included studies used a crossover or multiple dosing design,[21,25] one additional effect size was calculated for the delayed HABIT or that with more dosages. Moreover, we calculated the effect sizes of both HABIT and control interventions for short-term (i.e., between pre- and post-treatment) and long-term perspectives (i.e., between post-treatment and follow-up). The direction of all effect sizes was coded uniformly, such that a positive value indicated a great treatment benefit to the children from the intervention, and vice versa. According to Cohen's classification,[36] effect sizes were divided into five levels: trivial (<0.2), small (>0.2), medium (>0.5), large (>0.8), and very large (>1.3).

To determine the overall effects of HABIT, common outcome measures among the identified studies were selected. Four common tests were reported as outcome measures: 1) Assisting Hand Assessment (AHA), 2) Jebsen-Taylor Test of Hand Function (JTTHF), 3) Pediatric Evaluation of Disability Inventory (PEDI), and 4) Canadian Occupational Performance Measure (COPM). When more than one study had data available for analysis, computation of the overall effect sizes was performed with StatsDirect statistical analysis

software (StatsDirect Ltd., Cambridge, UK) for each outcome measure using the random-effects models (i.e., weighting effect sizes by the inverse of their variance).

Different training protocols and contents of HABIT have been tested in previous studies by altering training hours or adding components. These variables might confound the overall analysis. Therefore, we decided to classify HABIT-related interventions into three categories. Based on the dosages and training focus, the three categories were: 1) HABIT-standard that provided a total of 90 hours of training specific to upper extremity function within three continuous weeks, used in most of the previous studies; 2) HABIT-other dosage that adopted different training hours (e.g., fewer total hours) or schedules (e.g., within more weeks) from the above standard protocol; and 3) HABIT-added component that adopted the same or similar training hours to the above standard form (e.g., between 80 and 90 hours within consecutive weeks) but added other training components (e.g., lower extremity) to the intervention for upper extremity function. If a study compared HABIT-other dosage with HABIT-standard, this study was classified into multiple categories and the data were retrieved to calculated effect sizes for their corresponding categories. Analyses were conducted separately for each of the three categories as well as for other control interventions (e.g., CIMT or usual care) if sufficient data were available.

3. Results

3.1 Methodological quality of reviewed articles

In total, 15 studies were included from 646 identified articles (see Fig. 1). Among these studies, 11 papers were level I RCTs, two were level II quasi-RCT or retrospective study, and

two were level III longitudinal studies without a control group (Table 1). The risk of bias of the 11 RCTs is summarized with the ratings for each domain in Fig. 2 and 3. Three RCTs had a low risk of bias,[19,22,24] whereas the remaining eight were rated as having a high risk of bias or some concerns regarding the overall results.[18,20,21,23,25,37-39]

Specifically, 'the randomization process' (domain 1), 'deviation from the effect of adhering to the intervention' (domain 3), and 'the measurement of the outcome' (domain 5) were the three main areas for low methodological quality among the included studies (Fig. 2 and 3). For the randomization process, one study[18] raised a high risk of bias due to imbalances between the experimental and control groups at pre-test. The other two studies[37,39] had some risk-of-bias concerns because no sufficient information regarding concealment or randomization technique was provided. Three studies[21,37,39] were rated as having a high risk of bias or some concerns in the domain of deviation from the intended intervention regarding adhering to the intervention. These studies did not elaborate on the protocol of co-intervention for the experimental group and/or control group, nor provided evidence of the analysis to estimate the adherence effect. A high risk of bias in the measurement of the outcome was assigned to three studies[20,25,37] that did not blind the assessors for measuring the outcome specifically related to upper extremity function or did not provide information in blind scoring of the outcome measures.

3.2 Characteristics of the included participants

The sample sizes of the included studies ranged from 12 to 86 (Table 1). In total, 412 participants were included in this review, and 199, 163, 30, and 20 subjects were diagnosed with unilaterally spastic, hemiplegic, spastic, and bilateral CP, respectively. The age of the

subjects ranged from 1.5 to 18 years old, and most of the studies included children aged 3 or older.[18-23,25-27,37-41]

Among the selected studies, nine reported that the children's manual ability ranged from level I to III with mild or moderate functional limitations according to the Manual Ability Classification System (MACS).[20-25,38,40] Khan et al.'s study included participants with hand function ranging from MACS level III to IV.[41] Seven studies applied other assessments to characterize the children's hand function. For example, the children included in Gordon et al.'s study were able to extend their wrist joint above twenty degrees and the metacarpophalangeal joints at the fingers greater than ten degrees at full fist, and had the required score difference of over 50% between the involved and non-involved hand on the JTTHF at the baseline assessment.[18,22] Brandao et al.'s,[19] Bleyenheuft et al.'s,[26] Kumar et al.'s,[39] and Saussez et al.'s[27] studies required participants to have the manual ability to lift their hand from a surface and/or grasp light objects. Abd El Wahab et al.'s study required children with a level of hand spasticity ranging between 1 and 1+ in the Modified Ashworth Scale.[37]

Apart from hand function, the children included in nine studies[18-20,22-26,38] were reported to have a normal cognitive ability, whereas the other five articles recruited children who were able to follow simple instructions.[21,27,39-41] One study did not convey the participants' cognitive requirement.[37]

3.3 Intervention characteristics

Of the 15 included studies, seven[19-23,27,38] adopted the protocol of a total of 90 hours (6 hours per day) for three consecutive weeks, as either the experimental or control

intervention (see Table 1A). Different dosages and dosing schedules were found in seven studies (Table 1B). Gordon et al.'s[18] and Green et al.'s[40] studies both adopted 6 hours per day for 10 days, totaling 60 hours. Brandao et al.'s[21] study divided the total 90-hour practice into two phases (45 hours each) with a six-month interval in between, whereas Khan et al.'s[41] study adopted a total of 90 hours for nine weeks. Three studies[24,37,39] used fewer training hours per day (e.g., 40 minutes, 2 hours, or 3 hours) and varying durations (e.g., four to twelve weeks).

In addition, some components were added to HABIT in five studies (Table 1C). Three studies[25-27] included lower limb practice in the training, and tactile training was included in one study.[38] Brandao et al.'s study[19] replaced the structured practice with unstructured practice as the control intervention.

Regarding the control interventions used in the studies, four studies compared HABIT-related interventions with CIMT or the modified version.[20,22-24] Three studies adopted usual care (e.g., occupational therapy or neurodevelopmental theory intervention) as the control intervention for comparison with HABIT-related interventions.[18,25,26] One study compared HABIT and unimanual treatment.[37] The remaining five studies compared the effects of different HABIT-related interventions by altering the doses/schedules or adding/replacing training components.[19,21,27,38,39]

HABIT interventions were found to be conducted in either individualized training, group-based training, or both. Of the included studies, four provided individual treatment in combination with group sessions.[19,20,24,40] For the group sessions, the ratio of interventionists to participants ranged from 1:1 to 1:2, although the number of children in each group was not

clarified. The remaining 11 studies provided individual-based training.[18,21-23,25-27,37-39,41] In addition, five studies explicitly stated the provision of a 1-hour home program during the HABIT intervention period.[18-22] Gordon et al.[18] adopted an increased time of 2 hours for the home program during the follow-up period in their study.

3.4 Outcome measures

For the outcome measure related to upper extremity function, nine out of 15 studies (60%) used the AHA to assess bimanual ability.[18,19,21,22,24,25,27,38,40] Seven studies (47%) used the JTTHF to assess unilateral dexterity.[19,21,22,26,27,38,40] Five studies (33%) used the ABILHAND-Kids questionnaire to measure manual ability.[19,25-27,41] The Box and Block Test for gross manual dexterity,[25,26] the Quality of Upper Extremity Skills Test for upper extremity function,[22,24] and accelerometry for the frequency of hand use during the task[22,24] were each used in two studies (13%). In addition, four (27%) and six (40%) of the included studies used the COPM and PEDI to evaluate children's functional goals[19-21,27] and self-care function,[19-21,25-27] respectively.

3.5 Intervention effects

The effect sizes of the interventions for each study on each upper extremity-related measure are summarized in Table 2. Table 3 summarizes the mean overall effect sizes, associated 95% confidence intervals (CIs), and the *P*-values for each of the four common outcome measures, according to the categories of HABIT-related and control interventions.

For bimanual ability as measured by the AHA, 12 out of 15 effect sizes for HABIT-related interventions were found to be small to large (range of $d = 0.22–1.18$, Table 2) at the post-treatment period. After being classified into different HABIT-related categories

and combined for analysis, significantly small effect sizes were found for HABIT-standard (d = 0.36, 95% CI [0.06, 0.66], P = 0.016) and HABIT-other dosage (d = 0.44, 95% CI [0.08, 0.81], P = 0.017). There were no significant short-term effect sizes for HABIT-added component, CIMT, and usual care (Table 3). There were also no significant negative effect sizes between the post-treatment and follow-up periods for bimanual ability in any types of HABIT-related interventions.

For unilateral dexterity as measured by the JTTHF, the effect sizes for HABIT-related interventions ranged from small to medium (d = 0.25–0.64, Table 2) in seven out of 12 comparisons at the post-treatment period. The results of the combined analysis revealed a significantly small, short-term effect size for HABIT-standard (d = 0.41, 95% CI [0.12, 0.71], P = 0.005). The effect sizes between the pre- and post-treatment periods for HABIT-other dosage and HABIT-added component were not significant (Table 3). In addition, there were no significant negative, long-term effect sizes for any types of HABIT-related interventions. For CIMT and usual care, no sufficient data were available to calculate the overall, short-, or long-term effect sizes.

For self-care function as measured by the PEDI, all effect sizes for HABIT-related interventions, except for one,[19] at the post-treatment period were found to be small to large (range of d = 0.21–1.21, Table 2). Considering the combined analysis, there were significantly medium, short-term effect sizes for self-care function in HABIT-standard (d = 0.53, 95% CI [0.19, 0.87], P = 0.002) and HABIT-added component (d = 0.57, 95% CI [0.26, 0.89], P = <0.001). There were no significant short-term effect sizes for HABIT-other dosage and usual care (Table 3). There were also no significant negative, long-term effect sizes for

any types of HABIT-related interventions. No sufficient data for the overall effect size calculation were available for CIMT.

For functional goal performance and satisfaction as measured by the COPM, large or very large individual effect sizes for HABIT-related interventions (range of d = 1.18–4.26, Table 2) were found in all 12 comparisons at the post-treatment periods. The results of the combined analysis demonstrated that the short-term effect sizes for all HABIT-related interventions were very large and significant (Table 3). The effect sizes also tended to increase with the use of added components. In addition, a significant negative and medium effect size for goal satisfaction between the post-treatment and follow-up periods were found for HABIT-standard (d = -0.47, 95% CI [-0.83, -0.11], P = 0.011), but not for the other two HABIT-related interventions. For CIMT and usual care, no sufficient data were available to calculate the overall, short-, or long-term effect sizes.

4. Discussion

This study is the first review to specifically and systematically evaluate the effectiveness of HABIT for improving upper extremity function in children with CP. Overall, 11 level I studies, two level II, and two level III studies were included in the review, and seven (64%) of the 11 RCTs were rated as having a high risk of bias. Among the included studies, HABIT was mostly used for children with hemiplegic CP who were older than 3 years. Nearly half of the included studies used HABIT for 6 hours a day for three consecutive weeks (totaling 90 hours). HABIT using other doses/schedules and with added training components were also found. For these interventions related to HABIT, there were small and significant

improvements in bimanual ability and unilateral dexterity immediately after the interventions (especially for the standard HABIT), and improvements during the follow-up period were maintained. Similarly, moderate or large effect sizes were found for self-care function and goal improvements immediately after HABIT, and these were sustained at follow-up. Some discrepancies among the three categories of HABIT-related interventions were identified and discussed.

Compared to other forms of HABIT, the standard 90-hour protocol for three consecutive weeks demonstrated consistently small and significant effect sizes for bimanual ability and unilateral dexterity. The findings indicate that the standard form of HABIT is effective to improve upper extremity function in children with CP. In particular, when compared to the trivial/small and insignificant effect sizes of CIMT and usual care, the standard HABIT appeared to be superior. This differs from the findings of previous reviews that reported similar efficacy of CIMT to that of bimanual therapy.[28,30,32] We speculate that this disparity in the findings may be attributed to the advantage of the detailed training protocols of HABIT over those of the other types of bimanual therapies with less-structured training and varied intensity. Also, HABIT adopts a child-friendly approach to motivating children to engage in the treatment program. In contrast to CIMT, HABIT does not require a child's unaffected hand to be constrained for six hours. Furthermore, HABIT involves an intensive form of whole- and part-task practice, which covers target movement proficiency and whole-task accomplishment to provide more opportunities for children to practice various tasks requiring bimanual use. Practicing various bimanual tasks is considered to be a powerful element of children's motor learning, because it focuses on task accomplishment, and helps generalize

the ability of children to perform new tasks in their daily lives.[20,42,43] Accordingly, this generalization effect may explain why HABIT and related interventions (i.e., those with other dosages or added training components) demonstrated moderate or even large immediate effects on improving self-care and functional goals. However, the level of goal satisfaction was significantly decreased at follow-up for the standard HABIT only and not for the other forms. An interpretation of this finding is difficult and beyond the scope of this review. Perhaps parents' expectations might have changed over time and became higher when their children grew older. As the standard HABIT provided training within a relatively short period of three intensive weeks, parents' attenuated perception about goal satisfaction may be reasonable.

On the AHA, HABIT with other dosages demonstrated a similar small effect size to the standard HABIT, implying that a decreased dosage might have a comparable effect on improving bimanual ability. However, unlike the standard HABIT, HABIT with other dosages did not affect unilateral dexterity and self-care function. This may be related to the shorter training duration per day or in total in which bimanual ability was the main focus of the intervention, resulting in a decrease in the practicing time and opportunities for unilateral dexterity or self-care activities. Home practice of functional activities to extend the effect on self-care function was also not used in most studies of HABIT with other dosages. Thus, the use of shorter training hours or different dosing schedules could have trade-off effects, although it may suit busy clinical practice. More research may be needed to investigate the optimal dosage and schedule of HABIT if implementation of the standard form of training is not feasible in certain clinical settings or cultural contexts.

Compared to the standard HABIT, HABIT with added training components had very large immediate effects on self-care function and functional goals but, surprisingly, no significant effects on improving bimanual ability and unilateral dexterity. It is speculated that progress of self-care activities may be related to the added component of the training such as training of the lower limb in HABIT-ILE.[25-27] The reasons could be that lower limbs are largely involved in some daily activities (e.g., walking or transferring from bed to chair) and that good postural control is also needed when performing self-care activities.[44] Thus, the improvement of self-care activities is likely to be highly prioritized by children and parents in their goals and expectations,[19,45] resulting in higher satisfaction and performance scores for the COPM after undergoing HABIT-ILE.

In contrast, multiple factors such as the involvement of the lower limbs in activities and the age of participating children might also lead to the lack of improvement of bimanual ability and unilateral dexterity. The involvement of the lower extremities in training may cause dual-task interference and, thus, attenuate the improvement of upper limb function.[46] We also found that children who participated in studies using HABIT with added training components were generally older than those who underwent other forms of HABIT. This finding is consistent with a study[47] that found no improvement in the AHA following CIMT in children aged between 8 and 17 years. Older children may develop compensation strategies to perform bimanual and unilateral activities leading to a reduced possibility of improvement in their bimanual ability; these compensation strategies could be difficult to change within a short time. Furthermore, the plasticity of the brain reaches its maximum in the first few years of life and it decreases with increasing age.[48]

In addition, we noticed that some studies that were categorized as HABIT with added training components adopted HABIT-ILE. HABIT-ILE is a new intervention that was developed in recent years. In all related studies, there was insufficient information on the allocation and proportion of upper extremity and lower extremity training time, which may possibly interfere with the treatment intensity for bimanual ability and unilateral dexterity. As Bleyenheuft et al.[25] stated, intensity is the key to develop neuroplasticity and improve children's activities; therefore, reducing practice time for upper extremity-related activities might account for the lack of improvement of upper limb function. More studies are needed to investigate the influence of added training components on HABIT (especially for HABIT-ILE) for improving bimanual ability and unilateral dexterity.

4.1 Study limitations

This review has some limitations. Only studies published in English were included in the review. We also eliminated ten studies because they were conference proceedings or case studies. In addition, studies combining CIMT with HABIT for the intervention were also excluded because the focus of this review was specifically on HABIT as the primary intervention. Furthermore, this review consisted of 11 RCTs, 64% of which were rated as having a high risk of bias. Different outcome measures were used in the included studies, and one study[41] did not provide the necessary data. Thus, it was not possible to obtain sufficient data to synthesize the effect sizes for some measures (e.g., ABILHAND-Kids) and control interventions (e.g., CIMT and usual care) for comparison.

5. Conclusions

HABIT is a child-friendly, intensive training intended for children with CP which focuses on promoting bimanual coordination. The findings of this systematic review suggest that HABIT in the form of 6 hours a day for three consecutive weeks (totaling 90 hours) led to the improvement of bimanual ability, unilateral dexterity, self-care function, and functional goals after the intervention and that the improvements were mostly maintained during the follow-up period. In addition, other forms of HABIT with different dosages or added training components have been investigated for effectiveness in children with CP. While these modified forms of HABIT showed evidence for improving self-care function and functional goals, there was little impact on upper extremity function. More studies of good methodological quality are warranted to investigate the effect of these HABIT-related interventions on upper extremity function in children with CP.

Acknowledgments

The authors acknowledged the editing support of the Taylor & Francis Editing Services in this manuscript.

Declaration of interest: None.

Funding: The work was supported by the New Staff Start-up Fund from the Department of Rehabilitation Sciences, The Hong Kong Polytechnic University (grant number: 1-ZE4E).

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Table 1 – Summary of the characteristics of the studies by the categories of HABIT-related interventions

Study	Participants					Intervention				
	Evidence level (study design)	Diagnosis	Affected hand function	Cognitive function	Age (y)	Group (n)	Type	Protocol	Setting	Home program
A. HABIT-standard										
Gordon et al.[22]	I (RCT)	Hemiplegic, mild-moderate spasticity	Extend hand slightly, lift a hand from a surface, and grasp light objects	Age-matched and FSI	3.5-10	TG: 21 CG: 21	HABIT CIMT	6 hrs a day, 15 days, 1- and 6-month follow-up	Camp at university	1 hr
Hung et al.[23]	I (RCT)	Hemiplegic	Extend hand slightly	Age-matched	4-10	TG: 10 CG: 10	HABIT CIMT	6 hrs a day, 15 days	NS	NA
Brandão et al.[20]	I (RCT)	Hemiplegic	Extend hand slightly	Age-matched	3-10	TG: 8 CG: 8	HABIT CIMT	6 hrs a day, 15 days	University	1 hr
Brandão et al.[21]	I (RCT)	Hemiplegic, spasticity	Extend hand slightly	FSI	4-12	TG: 9 CG: 9	HABIT HABIT (45 hrs x 2)[a]	6 hrs a day, 15 days, 6-month follow-up	Camp in center	1 hr

Brandão et al.[19]	I (RCT)	Hemiplegic, spasticity	Grasp light objects, lift a hand from a surface	Age-matched	6-13	TG:11 CG:11	HABIT HABIT-UP	6 hrs per day 15 days	Day camp	1 hr
Kuo et al.[38]	I (RCT)	Hemiplegic, spasticity	Lift hand from a surface, grasp light objects	Age-matched and FSI	6-18	TG: 10 CG: 9	HABIT HABIT-TT	6 hrs a day, 15 days	Camp at university	NA
Saussez et al.[27]	II (retrospective study)	Hemiplegic, spasticity	Grasp light objects, lift a hand from a surface	FSI	5-18	CG: 42 TG: 44	HABIT HABIT-ILE	6 hrs per day 15 days	Day camp	NA
B. HABIT-other dosage										
Brandão et al.[21]	I (RCT)	Unilateral spasticity cerebral palsy	Extend hand slightly	FSI	4-12	CG: 9 TG: 9	HABIT (45 hrs x 2)[a] HABIT	6 hrs a day, 15 days, 6-month follow-up	Camp in center	1 hr

Gordon et al.[18]	I (RCT)	Hemiplegic, mild-moderate spasticity	Extend hand slightly, lift a hand from a surface	Age-matched	3-15	TG: 10 CG: 10	HABIT (60 hrs) Usual care	6 hrs a day, 10 days, 1-month follow-up	University	1 hr[b] 2 hrs[b]
Gelkop et al.[24]	I (RCT)	Hemiplegic	Extend hand slightly, release objects	Age-matched	1.5-7	TG: 6 CG: 6	HABIT (96 hrs) mCIMT	2 hrs a day, 6 days a week, 8 weeks, 2-month follow-up	Preschool	NR
Abd El Wahab et al.[37]	I (RCT)	Hemiplegic, mild spasticity	Hand spasticity: MAS	NS	3-7	TG: 15 CG: 15	HABIT (108 hrs) Unimanual treatment	3 hrs a day, 3 times a week, 12 weeks	Clinic	NA
Khan et al.[41]	III (longitudinal study)	Spastic	Grasp light objects	FSI	6-12	30	HABIT (90 hrs)	90 hrs in 9 weeks	Hospital	NA

Green et al.[40]	III (longitudinal study)	Hemiplegic	NS	Simple sequences of actions	7-15	23	HABIT (90 hrs)	6 hrs a day, 10 days, 3-month follow-up	Camp in hospital	NS
Kumar et al.[39]	I (RCT)[c]	Hemiplegic, mild spasticity	Grasp light objects	FSI	4-8	TG: 15 CG: 15	HABIT (16 hrs) HABIT-SOM	40 mins per session, 6 days a week, 4 weeks	Hospital and clinic	NA
C. HABIT-added component										
Brandão et al.[19]	I (RCT)	Hemiplegic, spasticity	Grasp light objects, lift hand from a surface	Age-matched and FSI	6-13	CG:11 TG:11	HABIT-UP HABIT	6 hrs per day 15 days	Day camp	1 hr
Kuo et al.[38]	I (RCT)	Hemiplegic, spasticity	Lift hand from a surface, grasp light objects	Age-matched and FSI	6-18	CG: 9 TG: 10	HABIT-TT HABIT	6 hrs a day, 15 days	Camp at university	NA

Saussez et al.[27]	II (retrospective study)	Hemiplegic, spasticity	Grasp light objects, lift hand from a surface	FSI	5-18	TG: 44 CG: 42	HABIT-ILE HABIT	6 hrs a day, 15 days	Day camp	NA
Bleyenheuft et al.[25]	I (crossover RCT)	Hemiplegic, spasticity	Lift hand from a surface, grasp light objects	Age-matched and FSI	6-13	TG: 12 CG: 12	HABIT-ILE Usual care[d]	9 hrs a day, 10 days, 10-day follow-up	Sleepover camp	NA
Bleyenheuft et al.[26]	II (quasi-RCT)	Bilateral	Lift hand from a surface, grasp light objects	Age-matched and FSI	6-16	TG: 10 CG: 10	HABIT-ILE Usual care	6.5 hrs a day, 13 days	Day camp	NA

CG = control group; CIMT = constraint-induced movement therapy; CP = cerebral palsy; FSI = follow simple instruction; HABIT = Hand-Arm Bimanual Intensive Training; UP = unstructured practice; TT = tactile training; ILE = including lower extremity; SOM = same object manipulation; mCIMT = modified constraint-induced movement therapy; MAS = Modified Ashworth Scale; NA = not applicable; NS = not specified; NR = not reported; RCT = randomized controlled trial; TG = treatment group.

[a] Two 45-hr sessions were given within a 6-month interval in between.

[b] One hour was used during the intervention period, whereas 2 hours were used during the following-up period.

[c] The author used a single blind RCT design but did not clarify if participants or assessors were blinded.

[d] HABIT-ILE was implemented in the control group after receiving 90 hrs of usual care.

Table 2 – Outcome measures and effect sizes of the interventions in the 15 studies

Study	Outcome measures[a]	Interventions[b]	Effect size (*d*)	
			Short-term[c]	Long-term[d]
Gordon et al.[18]	AHA*	HABIT (60 hrs)	0.53	-0.32
		Usual care	-0.15	0.23
	JTTHF	HABIT (60 hrs)	NR	NR
		Usual care	NR	NR
	BOTMP	HABIT (60 hrs)	0.21	0.41
		Usual care	-0.07	0.04
	CFUS frequency	HABIT (60 hrs)	0.72	0.01
		Usual care	-0.33	0.42
	CFUS quality	HABIT (60 hrs)	1.06	0.05
		Usual care	-0.10	0.31
	Accelerometry	HABIT (60 hrs)	1.24	0.08
		Usual care	-0.10	-0.71
	Goal synchronization duration	HABIT (60 hrs)	0.63	0.46
		Usual care	-0.31	0.58
Gordon et al.[22]	AHA*	HABIT	0.32	0.03
		CIMT	0.26	0.15
	JTTHF*	HABIT	0.64	0.16
		CIMT	0.08	0.07
	QUEST* dissociated movement	HABIT	0.53	-0.06
		CIMT	0.52	-0.22
	QUEST* grasp	HABIT	0.91	-0.27
		CIMT	0.41	0.05
	GAS	HABIT	1.01	0.63
		CIMT	0.06	1.09
	Accelerometry	HABIT	2.12	-0.08
		CIMT	0.95	0.18
Hung et al.[23]	Movement overlap†	HABIT	0.03	–
		CIMT	0.19	–
	Goal synchronization duration†	HABIT	1.49	–
		CIMT	1.21	–
	Movement time†	HABIT	-0.24	–
		CIMT	0.86	–
	Peak reaching tangential velocity†	HABIT	0.31	–
		CIMT	-0.18	–
Brandão et al.[20]	COPM performance	HABIT	3.14	–
		CIMT	1.18	–
	COPM satisfaction	HABIT	2.07	–
		CIMT	0.85	–
	PEDI self-care	HABIT	0.60	–
		CIMT	0.18	–
	PEDI assistance	HABIT	0.27	–
		CIMT	0.02	–
Green et al.[40]	AHA*	HABIT (60 hrs)	0.55	0.07
	CHEQ*	HABIT (60 hrs)	0.50	-0.12
	JTTHF	HABIT (60 hrs)	0.35	-0.03

Brandão et al.[19]	AHA*	HABIT	0.22	-0.17
		HABIT-UP	0.11	-0.34
	JTTHF*	HABIT	0.48	0.11
		HABIT-UP	0.07	-0.05
	ABILHAND-Kids	HABIT	0.62	0.37
		HABIT-UP	0.46	0.15
	COPM performance	HABIT	2.86	-0.09
		HABIT-UP	2.21	0.83
	COPM satisfaction	HABIT	2.24	-1.04
		HABIT-UP	1.69	0.25
	PEDI self-care	HABIT	0.90	0.17
		HABIT-UP	0.39	0.72
	PEDI assistance	HABIT	-0.04	0.74
		HABIT-UP	0.28	0.70
Abd El Wahab et al.[37]	PDMS-2 grasping	HABIT (36 hrs)	2.49	–
		Usual care	2.84	–
	Dynamometer	HABIT (36 hrs)	2.34	–
		Usual care	1.37	–
Gelkop et al.[24]	AHA	HABIT (96 hrs)	0.73	-0.03
		mCIMT	0.37	-0.16
	QUEST* total	HABIT (96 hrs)	0.78	-0.03
		mCIMT	0.38	-0.06
	QUEST* dissociated movement	HABIT (96 hrs)	0.36	0.33
		mCIMT	0.68	-0.55
	QUEST* grasp	HABIT (96 hrs)	0.82	0.21
		mCIMT	0.36	0.31
	QUEST* protective extension	HABIT (96 hrs)	0.33	0.08
		mCIMT	0.23	-0.11
	QUEST* weight bearing	HABIT (96 hrs)	0.95	-0.43
		mCIMT	0.23	-0.02
Bleyenheuft et al.[25]	AHA*	HABIT-ILE immed.	0.37	0
		Usual care	0	–
		HABIT-ILE delayed	0.53	–
	ABILHAND-Kids	HABIT-ILE immed.	1.02	-0.19
		Usual care	0	–
		HABIT-ILE delayed	1.09	–
	PEDI self-care	HABIT-ILE immed.	1.21	0.21
		Usual care	0.06	–
		HABIT-ILE delayed	0.68	–
	BBT†	HABIT-ILE immed.	0.51	-0.15
		Usual care	0.06	–
		HABIT-ILE delayed	0.35	–
	Finger strength†	HABIT-ILE immed.	0.61	0.39
		Usual care	-0.69	–
		HABIT-ILE delayed	0.73	–
Khan et al.[41]	ABILHAND-Kids	HABIT	NR	–
Kuo et al.[38]	AHA	HABIT	0.39	–
		HABIT-tactile training	0.28	–
	JTTHF	HABIT	0.54	–

		HABIT-tactile training	0.01	–
Kumar et al.[39]	MAS	HABIT (16 hrs)	1.82	–
		HABIT-SOM (16 hrs)	2.93	–
	MACS	HABIT (16 hrs)	2.77	–
		HABIT-SOM (16 hrs)	2.93	–
	PMAL-R	HABIT (16 hrs)	3.49	–
		HABIT-SOM (16 hrs)	3.59	–
Bleyenheuft et al.[26]	ABILHAND-Kids*	HABIT-ILE	0.69	0.37
		Usual care	0	-0.05
	JTTHF	HABIT-ILE	0.25	0.06
		Usual care	0	-0.01
	BBT†	HABIT-ILE	0.23	0
		Usual care	0.06	-0.06
	PEDI self-care	HABIT-ILE	0.42	0.27
		Usual care	0	0
Saussez et al.[27]	AHA*	HABIT	0.26	-0.10
		HABIT-ILE	0.09	0.01
	ABILHAND-Kids*	HABIT	0.53	0.24
		HABIT-ILE	0.80	0.06
	JTTHF	HABIT	0.26	-0.05
		HABIT-ILE	0.02	0.10
	PEDI self-care	HABIT	0.51	0.11
		HABIT-ILE	0.52	0.05
	COPM performance	HABIT	2.09	0.01
		HABIT-ILE	4.26	-0.08
	COPM satisfaction	HABIT	1.62	-0.31
		HABIT-ILE	3.77	-0.25
Brandão et al.[21]	AHA*	HABIT	1.18	-0.14
		HABIT (45 hrs)	0.13	0
		HABIT (45 hrs x 2)	0.36	-0.63
	JTTHF	HABIT	0.53	0.06
		HABIT (45 hrs)	0.07	0.06
		HABIT (45 hrs x 2)	0.11	-0.38
	COPM performance*	HABIT	2.78	-0.21
		HABIT (45 hrs)	1.91	0.28
		HABIT (45 hrs x 2)	3.46	-0.62
	COPM satisfaction*	HABIT	2.50	-0.63
		HABIT (45 hrs)	2.52	0.05
		HABIT (45 hrs x 2)	2.13	-0.96
	PEDI self-care	HABIT	0.27	0.13
		HABIT (45 hrs)	0.15	-0.01
		HABIT (45 hrs x 2)	0.21	-0.18
	PEDI assistance	HABIT	0.22	0.15
		HABIT (45 hrs)	0.19	-0.05
		HABIT (45 hrs x 2)	0.22	-0.08

AHA = Assisting Hand Assessment; BBT = Box and Blocks Test; BOTMP = Bruininks-Oeretsky Test of Motor Proficiency; CFUS = Caregiver Functional Use Survey; CHEQ = Children's Hand Experience Questionnaire; CIMT = constraint-induced movement therapy; COPM = Canadian Occupational Performance Measure; GAS = Goal Attainment

Scale; HABIT = Hand-Arm Bimanual Intensive Training; ILE = including lower extremity; immed. = immediate; JTTHF = Jebsen-Taylor Test of Hand Function; MACS = Manual Ability Classification System; MAS = Modified Ashworth Scale; mCIMT = modified constraint-induced movement therapy; NR = not reported; PDMS-2 = Peabody Developmental Motor Scales-Second edition; PEDI = Pediatric Evaluation of Disability Inventory; PMAL-R = Pediatric Motor Activity Log-Revised; QUEST = Quality of Upper Extremity Skills Test; SOM = same object manipulation; UP = unstructured practice.

[a] Only outcome measures related to upper extremity function are presented in the table.
[b] The values in the parenthesis indicates the training dosages used in the study, and the added training component is specified after HABIT (e.g., HABIT-ILE).
[c] indicates effect size between pre- and post-treatment periods.
[d] indicates effect size between post-treatment and follow-up periods.
* indicates primary outcome used in the study.
† indicates the results from the more affected hand.

Table 3 – Pooled effect sizes of the studies by outcome measures and the intervention categories

		Short-term effect[a]			Long-term effect[b]		
Outcome measure	Intervention category	No. of comparison	Cohen *d* (95% CI)	*P*	No. of comparison	Cohen *d* (95% CI)	*P*
AHA	HABIT[c]	5	0.36 (0.07, 0.66)	0.016	4	-0.08 (-0.39, 0.23)	0.601
	HABIT-other dosage[d]	5	0.44 (0.08, 0.81)	0.017	5	-0.12 (-0.49, 0.24)	0.493
	HABIT-added component[e]	5	0.19 (-0.11, 0.50)	0.204	3	-0.04 (-0.40, 0.30)	0.795
	CIMT/mCIMT	2	0.27 (-0.26, 0.81)	0.321	2	0.08 (-0.45, 0.62)	0.761
	Usual care	2	0.07 (-0.66, 0.52)	0.824	1	–	–
JTTHF	HABIT[c]	5	0.41 (0.12, 0.70)	0.005	4	-0.03 (-0.27, 0.34)	0.814
	HABIT-other dosage[d]	3	0.22 (-0.20, 0.64)	0.311	3	-0.09 (-0.51, 0.34)	0.692
	HABIT-added component[e]	4	0.06 (-0.29, 0.41)	0.738	3	0.06 (-0.31, 0.44)	0.733
	CIMT/mCIMT	1	–	–	0	–	–
	Usual care	1	–	–	1	–	–
PEDI self-care	HABIT[c]	4	0.53 (0.19, 0.87)	0.002	3	0.12 (-0.23, 0.47)	0.494
	HABIT-other dosage[d]	2	0.17 (-0.45, 0.80)	0.582	2	-0.09 (-0.72, 0.53)	0.765
	HABIT-added component[e]	5	0.57 (0.26, 0.89)	<0.001	4	0.19 (-0.14, 0.52)	0.263
	CIMT/mCIMT	1	–	–	0	–	–
	Usual care	2	0.03 (-0.56, 0.62)	0.916	1	–	–
COPM performance	HABIT[c]	4	2.22 (1.89, 2.76)	<0.001	3	-0.04 (-0.40, 0.31)	0.811
	HABIT-other dosage[d]	2	2.51 (1.06, 3.95)	<0.001	2	-0.16 (-1.00, 0.68)	0.710
	HABIT-added component[e]	2	3.39 (2.70, 4.08)	<0.001	2	0.11 (-0.31, 0.55)	0.593
	CIMT/mCIMT	1	–	–	0	–	–
	Usual care	0	–	–	0	–	–
COPM satisfaction	HABIT[c]	4	1.81 (1.42, 2.22)	<0.001	3	-0.47 (-0.83, -0.11)	0.011
	HABIT-other dosage[d]	2	2.21 (1.43, 3.00)	<0.001	2	-0.43 (-1.37, 0.52)	0.375
	HABIT-added component[e]	2	2.90 (2.27, 3.53)	<0.001	2	-0.13 (-0.56, 0.30)	0.560

CIMT/mCIMT	1	–	–	0	–	–
Usual care	0	–	–	0	–	–

AHA = Assisting Hand Assessment; COPM = Canadian Occupational Performance Measure; CIMT = constraint-induced movement therapy; HABIT = Hand-Arm Bimanual Intensive Training; JTTHF = Jebsen-Taylor Test of Hand Function; mCIMT = modified constraint-induced movement therapy; PEDI = Pediatric Evaluation of Disability Inventory.

[a] indicates effect size between pre- and post-treatment periods.

[b] indicates effect size between post-treatment and follow-up periods.

[c] indicates HABIT that adopted the standard dosage such as a three-week program (6 hours daily, totaling 90 hours).

[d] indicates HABIT that adopted the dosages other than the standard, e.g., 45 hours (in 1.5 weeks), 60 hours (in 2 weeks), 90 hours (in two 1.5-week programs within 6 months), or 96 hours (in 8 weeks).

[e] indicates HABIT that adopted the standard dosage but added training component(s), e.g., lower extremity training, unstructured practice procedure, or tactile training to the intervention.

Fig. 1 – Flow chart of the selection process of the studies for inclusion in the review

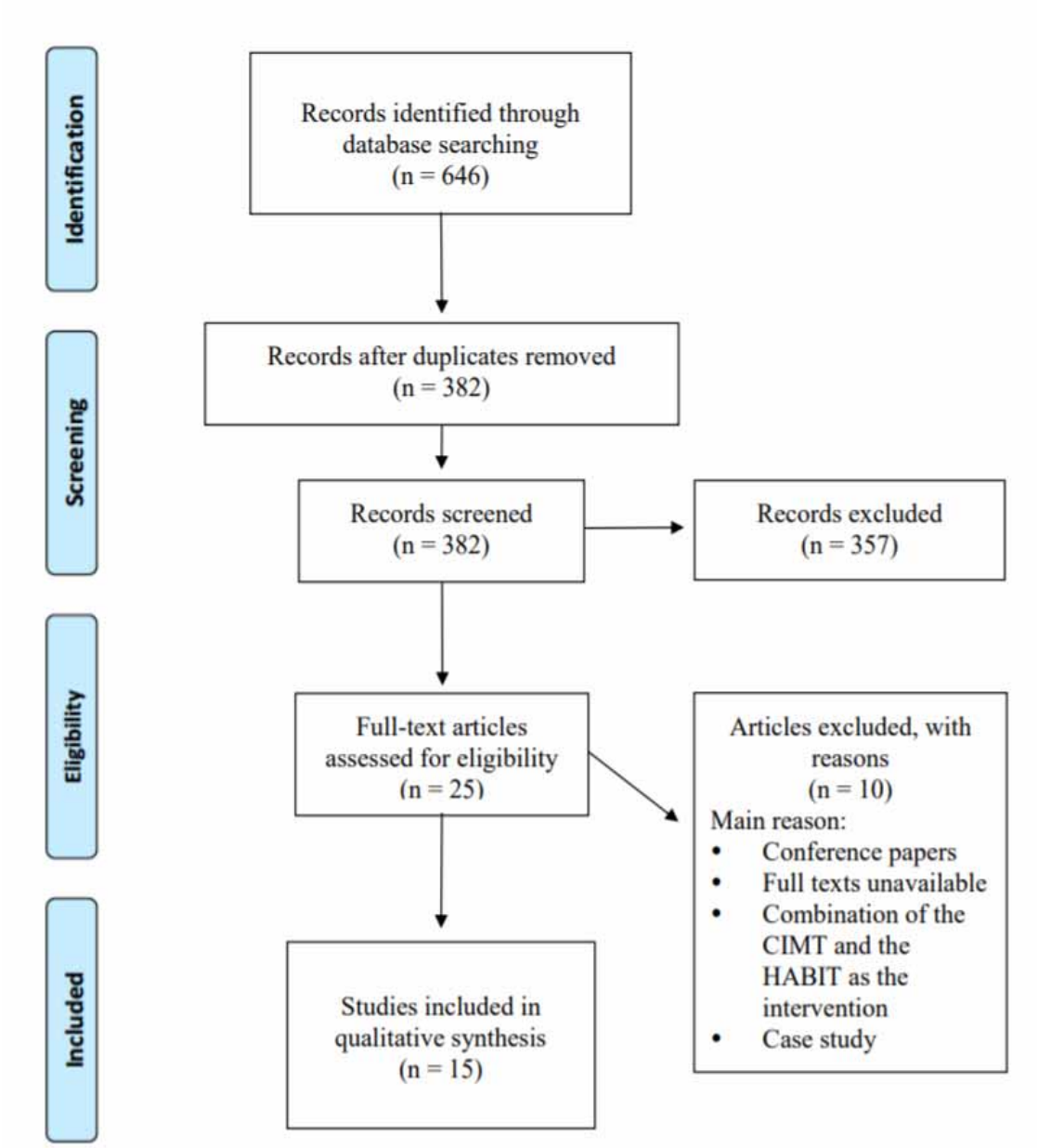

Fig. 2 – Risk of bias graph: review authors' judgments on each methodological quality item presented as percentages across all included studies (n=11)

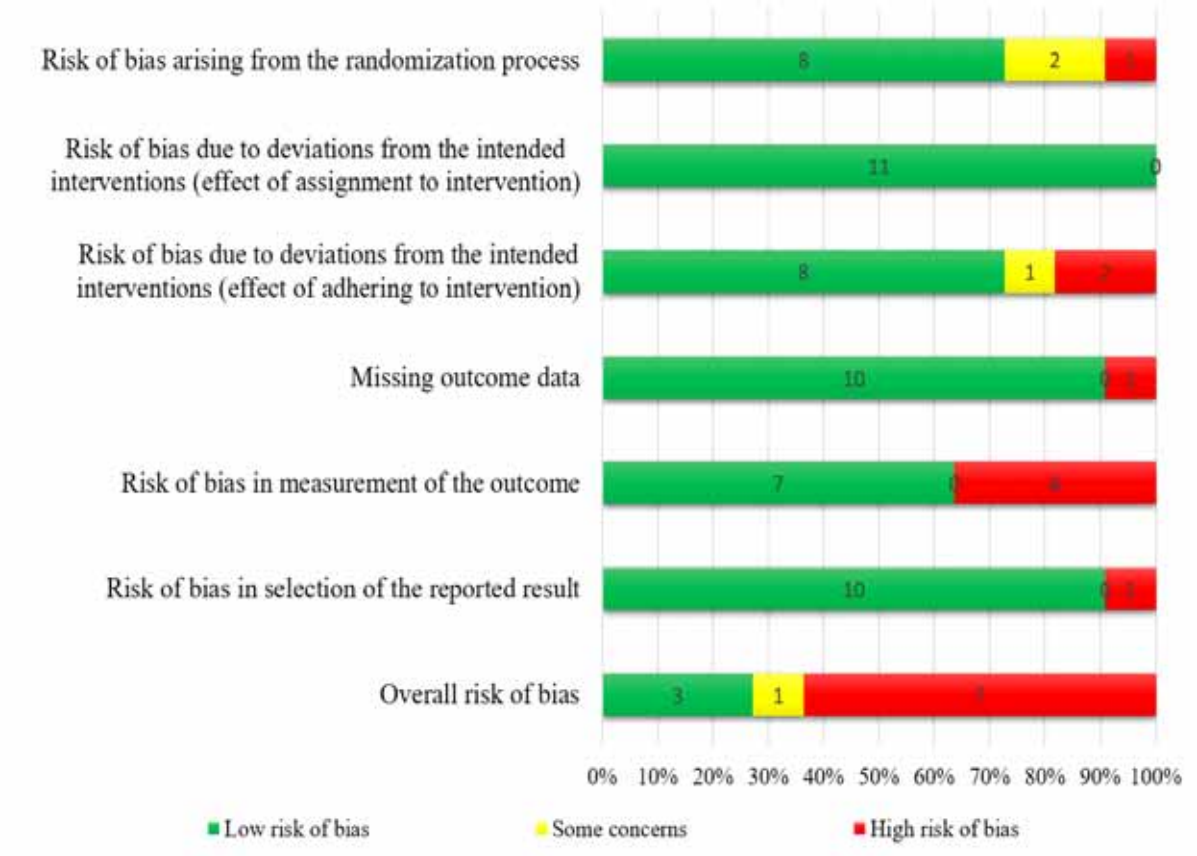

Fig. 3 – Risk of bias summary: review authors' judgments on each methodological quality item for each included study (n=11)