CRITICALLY APPRAISED TOPIC

FOCUSED CLINICAL QUESTION

For a child with hemiplegic cerebral palsy (P), is constraint induced movement therapy (I) more effective in improving upper extremity strength and function (O) when compared with bimanual therapy (C)?

AUTHOR

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CLINICAL SCENARIO

The patient is an 8-year-old female diagnosed with right hemiplegic cerebral palsy. Her right upper extremity and lower extremity are primarily impacted by her diagnosis. Her physical and occupational therapists recommended she attend UNC Hospital's *Helping Kids with Hemiplegia* summer camp given her gross and fine motor impairments. This 8-day camp provides patient-centered, age-appropriate, goal-directed, and activity-based interventions aimed at improving gross and fine motor skills. Constraint-induced movement therapy (CIMT), bimanual intensive therapy (BIT), and therapeutic handling intervention strategies are implemented to enhance upper extremity function. The patient and her parents would like to increase her independence with activities of daily living, such as putting her right shoe on over her ankle foot orthosis (AFO), zipping her jacket, and opening her water bottle. In order to help this patient achieve her goals, I would like to know whether constraint-induced movement therapy results in improved upper extremity gross and fine motor function compared to bimanual therapy intervention strategies.

SUMMARY OF SEARCH

From a literature search conducted in 3 electronic databases, 8 studies met the inclusion and exclusion criteria, including 3 systematic reviews and 5 randomized controlled trials (RCTs). Among these 8 studies, 2 were considered to be best evidence for the clinical question based on relevance, validity, and overall quality.

Key findings from the two appraised studies include:

➢ Both CIMT and BIT interventions effectively improve the function of the involved upper extremity in children with hemiplegia.
➢ Typically, CIMT improves unimanual capacity in children with hemiplegia, whereas BIT often demonstrates equivalent or greater improvements in bimanual performance, spontaneous hand use, and functional goal attainment.
➢ Although CIMT significantly improves unimanual capacity and bimanual performance compared to low-dose interventions, it yields equivalent functional gains for the hemiplegic upper extremity as high-dose and dose-matched comparisons.

CLINICAL BOTTOM LINE

Current literature indicates that children with hemiplegic cerebral palsy benefit from both CIMT and BIT interventions. The two appraised articles found that while CIMT can lead to greater unimanual functional capacity of the hemiplegic upper extremity, BIT demonstrates equivalent improvements in bimanual performance, movement quality, and participation in activities of daily living. Since existing evidence has found CIMT and BIT to be equally beneficial when implemented individually, future research should be directed towards determining best practice for a combined CIMT and BIT approach. Evidence also suggests that CIMT more effectively improves unimanual and bimanual function compared to low-dose interventions. Based on the literature, clinicians can infer CIMT and BIT are effective adjunct interventions for children with hemiplegia receiving traditional therapy services. The evidence presented in these studies can be used by clinicians to conduct CIMT and BIT intervention programs or refer patients to existing programs, such as UNC Children's *Helping Kids with Hemiplegia* summer camp described in the clinical scenario above.

SEARCH STRATEGY

Terms used to guide the search strategy			
Patient/Client Group	**I**ntervention (or Assessment)	**C**omparison	**O**utcome(s)
Child* Pediatric* Youth Hemip* Unilateral cerebral palsy Unilateral paralysis	Constraint-induced movement therapy CIMT	Bimanual therapy Bimanual intensive therapy	Upper extremity Arm Hand Function Strength

Final search strategy (history):

PubMed:

1. Child* OR pediatric* OR youth
2. Hemip* OR Unilateral cerebral palsy OR Unilateral paralysis
3. Constraint induced movement therapy OR CIMT
4. Bimanual therapy OR Bimanual intensive therapy
5. Upper extremity
6. Hand
7. Arm
8. Strength
9. Function
10. Function*
11. Upper limb

#1 AND #2 AND #3 AND #4 AND (#5 OR #6 OR #7) AND (#8 OR #9) *(59 results)*

#1 AND #2 AND #3 AND #4 AND (#5 OR #6 OR #7 OR #11) AND (#8 OR #9) *(61 results)*

#1 AND #2 AND #3 AND #4 AND (#5 OR #6 OR #7 OR #11) AND (#8 OR #10) *(56 results)*

Databases and Sites Searched	Number of results	Limits applied, revised number of results (if applicable)
PubMed	**56**	Filters were applied to limit results to meta-analyses, randomized controlled trials, and systematic reviews published in the last 10 years. **25 results**
CINHAL	**31**	Filters were applied to limit results to English publications. **30 results**
EMBASE	**44**	The following filters were applied and yielded **18 results** - age (infant, child, preschool child, school child, adolescent) - diseases (cerebral palsy, hemiplegia, spasticity, hemiparesis, motor dysfunction) - study types (randomized controlled trial, controlled study, systematic review, meta-analysis) - publication years (2010-2020)

INCLUSION and EXCLUSION CRITERIA

Inclusion Criteria
- Pediatric population (<21 years old)   - Diagnosis of hemiplegic cerebral palsy   - Studies that have a clearly defined constraint induced movement therapy protocol   - High level evidence including randomized controlled trials, systematic reviews, and meta-analyses
Exclusion Criteria
- Not published in English   - Low level evidence including poster presentations, case studies, case-series, and narrative review articles   - Adult population (>21 years old)   - Studies focused on subjects with a diagnosis other than hemiplegic cerebral palsy

RESULTS OF SEARCH

Summary of articles retrieved that met inclusion and exclusion criteria

Author (Year)	Risk of bias (quality score)*	Level of Evidence**	Relevance	Study design
Hoare et al. (2019)	**AMSTAR - 10/11**	**Level 1a**	**High**	**Systematic Review**
Tervahauta et al. (2017)	**AMSTAR - 7/11**	**Level 1a**	**High**	**Systematic Review**
Dong et al. (2013)	**AMSTAR - 5/11**	**Level 1a**	**High**	**Systematic Review**
Sakzewski et al. (2011) Randomized trial of constraint-induced movement therapy and bimanual training on activity outcomes for children with congenital hemiplegia	**PEDro – 9/11**	**Level 1b**	**High**	**Single-blind, matched pairs RCT**
Gordon (2011)	**PEDro – 8/11**	**Level 1b**	**High**	**Single-blind RCT**
Deppe et al. (2013)	**PEDro – 8/11**	**Level 1b**	**Moderate**	**Single-blind RCT**
Sakzewski et al. (2011) Participation outcomes in a randomized trial of 2 models of upper-limb rehabilitation for children with congenital hemiplegia	**PEDro – 8/11**	**Level 1b**	**Moderate**	**RCT**
de Brito Brandão et al. (2012)	**PEDro – 7/11**	**Level 1b**	**Moderate**	**Matched pairs RCT**

*Indicate tool name and score

**Use Portney & Watkins Table 16.1 (2009); if downgraded, indicate reason why

BEST EVIDENCE

The following 2 studies were identified as the 'best' evidence and selected for critical appraisal. Rationale for selecting these studies were:

- ➢ **Sakzewski et al. Randomized trial of constraint-induced movement therapy and bimanual training on activity outcomes for children with congenital hemiplegia. (2011)**
  - ○ This single-blind, matched pairs randomized controlled trial is classified as level 1b evidence and directly compared constraint-induced movement therapy with bimanual training in the treatment of pediatric hemiplegic cerebral palsy. It has high methodological quality, as indicated by a score of 9/11 on the PEDro scale. The study lost two points for not blinding the subjects or therapists administering the intervention; however, this would have been difficult to accomplish given the study design and nature of the intervention. Researchers provided a thorough statistical analysis, consisting of between-group comparisons, point measures, and measures of validity. Study limitations and directions for future research were addressed by the researchers.
- ➢ **Hoare et al. Constraint-induced movement therapy in children with unilateral cerebral palsy. (2019)**
  - ○ This systematic review is classified as level 1a evidence and directly addresses the clinical question by comparing CIMT to low-dose, dose matched, and high dose physical, occupational, bimanual, and Hand Arm Bimanual Intensive therapy. It has high methodological quality as indicated by a score of 10/11 on the AMSTAR. The study lost one point for publication bias. Researchers conducted a comprehensive search and thorough analysis of the literature, addressing the publication status, scientific quality, methodological rigor, and conflicts of interest of all studies.

SUMMARY OF BEST EVIDENCE

(1) Description and appraisal of "Randomized trial of constraint-induced movement therapy and bimanual training on activity outcomes for children with congenital hemiplegia" by Sakzewski et al. (2011)

Aim/Objective of the Study/Systematic Review:
The aim of the study by Sakzewski et al. was to determine whether constraint induced movement therapy (CIMT) is more effective at improving upper limb function in children with hemiplegic cerebral palsy compared to bimanual training (BIM).
Study Design
This study by Sakzewski et al. is a single-blind, matched pairs, randomized controlled trial that consisted of 64 children ages 5 to 16 years with a diagnosis with congenital hemiplegia. Participants were allocated into matched pairs based on their age, sex, diagnosis of right- or left-sided hemiplegia, and their score on the Melbourne Assessment of Unilateral Upper Limb Function (MUUL). Randomization occurred using a computer-generated list and concealed envelopes. Given the nature of the intervention, participants and the therapists who administered the intervention were not blinded to group allocation.
Outcomes were measured at baseline, 3-weeks postintervention, and 26-weeks postintervention. The four occupational and physical therapists who obtained the outcome measures were aware of group allocation. Trained occupational therapists masked to group allocation scored primary outcome measures from video recordings in random order.
Setting
Children were recruited from public and private medical specialists in Queensland and Victoria, Australia. Interventions were administered in the form of a 10-day, circus-themed, intensive day camp at community sporting facilities in Melbourne and Brisbane, Australia.
Participants
A total of 64 children with hemiplegic cerebral palsy were recruited to the study from public and private medical specialists in Queensland and Victoria, Australia and randomly allocated to CIMT or BIM intervention groups. Eligibility criteria were a diagnosis of congenital hemiplegia, age between 5 to 16 years, ability to follow commands, and spasticity between grades 1 to 3 on the modified Ashworth Scale (MAS) that interferes with upper extremity function. Participants with predominant dystonia or muscle contracture (MAS >3), history of upper limb orthopedic surgery, and serial casting or botulinum toxin injection within the previous 6-months were excluded from the study. There was 100% compliance with the CIMT intervention and 97% compliance with the BIM intervention. Of the initial 64 patients, one was injured prior to baseline and one withdrew on day 2 due to pre-existing behavioral problems leaving 62 participants. Overall, there was no difference between groups at baseline with regards to demographics or measures assessed.

Compliance:

- ❖ CIMT Group
  - o Enrollment: n=32
  - o Allocation: n=32
  - o 3-weeks follow-up: n=31
    - ▪ 1 participant missing baseline primary outcome data due to video recording error
  - o 26-weeks follow-up: n=28
    - ▪ 1 participant missing baseline primary outcome data due to video recording error
    - ▪ 2 participants failed to attend
    - ▪ 1 participant was unable to be contacted
- ❖ BIM Group
  - o Enrollment: n=32
  - o Allocation: n=30
    - ▪ 1 participant injured prior to baseline
    - ▪ 1 participant did not return due to behavioral issues
  - o 3-weeks follow-up: n=30
  - o 26-weeks follow-up: n=29
    - ▪ 1 participant broke an arm

Baseline Demographics and Measures:

- ❖ CIMT Group (n=32)
  - o Mean age: 10 years, 1 month
  - o Sex: 17 males, 15 females
  - o Left-side hemiplegia: 50%
  - o Motor type (dystonia and spasticity): 3%
  - o Epilepsy: 16%
  - o Learning Disability: 31%
  - o Manual Ability Classification System (MACS): 25% Level I, 72% Level II, 3% Level III
  - o Gross Motor Function Classification System (GMFCS): 25% Level I, 75% Level II
  - o Zancolli scale: 56% Level I, 28% Level IIa, 16% Level IIb
  - o House scale: 9% Spontaneous use, 75% Active assist, 16% Passive Assist
  - o School: 91% typical school, 9% special school
  - o Concurrent occupational therapy services: 6% weekly/fortnightly, 16% monthly, 28% other
  - o Concurrent physical therapy services: 19% weekly/fortnightly, 12% monthly, 16% other
- ❖ BIM Group (n=31)
  - o Mean age: 10 years, 2 months
  - o Sex: 16 males, 15 females
  - o Left-side hemiplegia: 36%
  - o Motor type (dystonia and spasticity): 10%
  - o Epilepsy: 26%
  - o Learning Disability: 29%
  - o MACS: 26% Level I, 74% Level II, 0% Level III
  - o GMFCS: 26% Level I, 74% Level II
  - o Zancolli scale: 48% Level I, 36% Level IIa, 16% Level IIb
  - o House scale: 13% Spontaneous use, 81% Active assist, 6% Passive assist
  - o School: 94% typical school, 6% special school
  - o Concurrent occupational therapy services: 13% weekly/fortnightly, 10% monthly, 26% other
  - o Concurrent physical therapy services: 10% weekly/fortnightly, 3% monthly, 29% other

Intervention Investigated

CIMT Group (Experimental)

Participants attended an intensive day camp where they received 6 hours of CIMT interventions for 10 consecutive days. The mode of constraint was a tailor-made glove worn on the non-involved upper extremity that prevented grasp but allowed the hand to be used for support and safety. Children were instructed to wear the glove for the duration of the day camp, with the exception of toileting and activities that required two hands for safety. If the glove needed to be removed for safety, the fingers of the non-involved hand were taped together with Elastoplast tape to provide an alternative method of constraint. Use of the involved upper extremity was encouraged throughout the duration of the camp.

The day camp was circus themed to maximize engagement, motivation, and participation. All interventions were fun, age-appropriate, goal-oriented, and activity-based. Specific intervention strategies included games and activities to promote fine and gross motor skill acquisition, proper utensil use during meals, and de-briefing for self-reflection at the end of the day.

Participants were supervised by trained occupational therapists, physical therapists, and camp volunteers.

Participants in the BIM group attended an intensive day camp where they were encouraged to use both their involved and non-involved upper extremities throughout the day. The intervention dose was matched to that of the experimental group.

The day camp was circus themed to maximize engagement, motivation, and participation. All interventions were fun, age-appropriate, goal-oriented, and activity-based. Specific intervention strategies included games and activities to promote fine and gross motor skill acquisition, proper utensil use during meals, and de-briefing for self-reflection. Instructions were provided on how each hand should be used prior to beginning the activity.

Participants were supervised by trained occupational therapists, physical therapists, and camp volunteers.

Outcome Measures

Outcomes measures were obtained at baseline, 3-weeks postintervention, and 26-weeks postintervention. The four occupational and physical therapists administering the outcome measures were aware of group allocation. Trained occupational therapists, who were unaware of group allocation, scored the primary outcome measures in random order.

- ❖ Primary Outcome Measures
  - o Melbourne Assessment of Unilateral Upper Limb Function (MUUL)
    - ▪ Used to assess function and quality of movement of the impaired upper extremity
    - ▪ Considered the best measure of unimanual capacity
    - ▪ MCID = 7.4%
  - o The Assisting Hand Assessment (AHA)
    - ▪ Valid and reliable measure of function and performance of bilateral upper extremities
- ❖ Secondary Outcome Measures
  - o Grip strength via hand-held dynamometer
    - ▪ Assessed bilaterally
  - o Moving two-point discrimination (M2PD) of the index finger via Disk-criminator
  - o Stereognosis
  - o Jebsen Taylor Test of Hand Function (JTTHF)
    - ▪ Used to measure movement efficiency of the impaired upper limb
    - ▪ Performed on both the impaired and unimpaired upper extremities

Main Findings

Table 1. Outcomes for CIMT and BIM groups at baseline, 3, and 26 weeks [4]

	Outcome	CIMT	BIM
Grip strength (kg)	Impaired, median (95% CI) Baseline 3 wk 26 wk	 5.2 (2.7 to 6.6) 4.8 (4.5 to 6.3) 5.0 (4.5 to 7.8)	 4.8 (3.6 to 7.1) 5.5 (4 to 6.9) 4.7 (2.7 to 8.7)
	Unimpaired, median (95% CI) Baseline 3 wk 26 wk	 16 (11.9 to 18.6) 14.7 (13.1 to 18.0) 17 (13.2 to 20.8)	 14.7 (12.3 to 17.4) 16.8 (13.9 to 19.4) 17.2 (13.8 to 21.3)
Sensation	Stereognosis (/9), median (95% CI) Baseline 3 wk 26 wk	 5 (4 to 7) 6 (3 to 7) 6 (2.7 to 7)	 6 (3 to 8) 4 (3 to 7) 7 (3 to 7)
	M2PD (mm), median (95% CI) Baseline 3 wk 26 wk	 5 (3 to 7.8) 5 (3.5 to 8) 5 (3 to 10)	 5 (3 to 7) 4 (3 to 7) 4 (3 to 7.4)
Activity	MUUL, mean (95% CI) Baseline 3 wk 26 wk	 67.1 (62.5 to 71.6) 69.8 (65.2 to 74.3) 71.1 (66.6 to 75.6)	 70.8 (66.7 to 74.9) 71.5 (67.9 to 75.1) 71.0 (66.9 to 75.1)
	AHA, mean logits (95% CI) Baseline 3 wk 26 wk	 61.7 (57 to 66.4) 64.8 (60.0 to 69.6) 63.0 (57.7 to 68.4)	 63.0 (58.4 to 67.6) 64.9 (60.7 to 69.1) 65.3 (61.0 to 69.6)
	JTTHF (impaired), mean (95% CI) Baseline 3 wk 26 wk	 365.7 (294.1 to 437.3) 337.5 (264.0 to 411.0) 307.9 (235.6 to 380.2)	 323 (261.2 to 384.8) 306.8 (240.8 to 372.7) 287.4 (221.2 to 353.6)
	JTTHF (unimpaired), median (95% CI) Baseline 3 wk 26 wk	 48.5 (41.0 to 57/0) 42 (39 to 47.2)	 44 (36.4 to 51.4) 43 (36 to 45.3)

Table 2. Results of comparison of activity outcomes for the CIMT and BIM training groups at 3 and 26 weeks[4]

Factors	Model regression coefficienct (95% CI)	p value
Model 1: MUUL		
Constant	68.8	
Treatment	-3.2 (-8.7 to 2.4)	0.3
Timing 1 (3wks)	0.9 (-0.6 to 2.5)	0.2
Timing 2 (26wks)	0.0 (-1.5 to 1.6)	0.9
Treatment by time 1	1.8 (-0.4 to 4.0)	0.1
Treatment by time 2	4.5 (2.2 to 6.7)	<0.0001
Model 1: AHA		
Constant	69.0	
Treatment	-0.4 (-6.4 to 5.7)	0.9
Timing 1 (3wks)	1.9 (0.2 to 3.6)	0.03
Timing 2 (26wks)	2.3 (0.6 to 4.0)	0.008
Treatment by time 1	1.2 (-1.2 to 3.5)	0.3
Treatment by time 2	-0.7 (-3.1 to 1.8)	0.6
Model 3: JTTHF		
Constant	505.5	
Treatment	30.7(-58.4 to 119.9)	0.7
Timing 1 (3wks)	-14.9 (-36.5 to 6.8)	0.2
Timing 2 (26wks)	-34.3 (-56.2 to -12.5)	0.002
Treatment by time 1	-11.1 (-41.7 to 19.4)	0.5
Treatment by time 2	-25.6 (-57 to 5.7)	0.1

Table 3. Difference and changes over time for activity outcomes between CIMT and BIM intervention groups [4]

	Difference between groups		Change in CIMT		Change in BIM	
Baseline to	3wks	26wks	3wks	26wks	3wks	26wks
Estimated mean difference (95% CI)						
MUUL	1.8(-0.3 to 4.0) 0.1	4.4(2.2 to 6.7) <0.001	2.8(1.2 to 4.3) <0.0001	4.5(2.8 to 6.1) 0.3	0.9(-0.6 to 2.5) 0.3	0.0(-1.5 to 1.6) 0.9
AHA	1.2(-1.2 to 3.5) 0.3	-0.7(-3.1 to 1.7) 0.6	3.1(1.4 to 4.7) <0.0001	1.9(0.2 to 3.6) 0.03	1.9(0.2 to 3.6) 0.003	2.3(0.6 to 4.0) 0.008
JTTHF	-11.1(-41.7 to 19.4) 0.5	-25.7(-57.0 to 5.7) 0.1	-26(-47.6 to -4.4) 0.02	-14.9(-36.3 to 6.5) 0.2	-14.9(-36.3 to 6.5) 0.2	-34.3(-56.2 to -12.5) 0.002

The researchers found a significant group by time interaction that favored the CIMT group on the MUUL at 26-weeks, indicating that CIMT resulted in significantly greater improvements in hemiplegic upper extremity function and quality of movement overtime than the BIM training group. No other significant between group differences were observed for primary or secondary outcome measures at either 3- or 26-weeks postintervention. At 3-weeks follow-up, the CIMT group demonstrated significant improvement in MUUL and JTTHF scores compared to baseline that were further improved at 26-weeks postintervention. Additionally, there was a significant initial improvement in AHA scores for the CIMT group at 3-weeks; however, this gain was not retained at 26-weeks. At 3-weeks, the BIM group demonstrated significant change in AHA scores that continued to improve at 26-weeks. Additionally, there was a significant improvement in JTTHF scores at 26-weeks compared to baseline in the BIM group. No significant differences in grip strength or sensation were observed among the CIMT group.

Original Authors' Conclusions

The authors conclude that both CIMT and BIM interventions effectively improve the function of the involved upper extremity in children with congenital hemiplegia. While CIMT results in enhanced unimanual functional capacity and BIM training leads to greater improvements in bilateral performance, the differences in outcomes are not clinically significant. The authors identify the need for future research to determine if combined CIMT and BIM training protocols result in further improvements in upper limb outcomes compared to traditional intervention strategies.

Critical Appraisal

Validity

- ❖ This single-blind, matched pairs randomized controlled trial by Sakzewski et al. is classified as level 1b evidence and demonstrates high methodological quality.
    - o The study scored a total score of 9/11 points on the PEDro scale, with 2 points deducted for lack of blinding of subjects and therapists who administered the intervention.

- ❖ **Internal and External Validity**
    - o The eligibility criteria were specified by the authors which enhances the external validity of the study. While the majority of the children in the study were GMFCS level II, MACS level II, Zancolli scale level I, active assist on the House scale, and had left-side hemiplegia, participants with both right- and left-sided hemiplegia at a variety of functional levels were included which increases the generalizability of the study. Additionally, the inclusion of children with learning disabilities from a variety of educational settings, co-morbidities (i.e. epilepsy), and those receiving concurrent therapy services further enhance the generalizability and external validity.
    - o Randomized and concealed allocation of participants using computer-based distribution and concealed envelopes increases the internal and external validity of the study by ensuring that two intervention groups are comparable and reducing risk of systematic bias.
    - o The study demonstrates good internal validity as indicated by items 2-9 on the PEDro scale. Both the CIMT and BIM groups were similar at baseline in terms of demographic characteristics and outcome measures which indicates adequate randomization and enhances the validity of the study. The occupational therapists who scored the outcome measures were blinded to eliminate potential bias. Primary outcome measures were assessed for 100% of the CIMT group and 97% of the BIM training group which reduces potential bias from systematic differences among participants who were not followed up with compared to those who were. Additionally, intention-to-treat analysis was performed. Blinding of participants and therapists administering the intervention would have further increased the internal validity; however, this would have been difficult to accomplish given the study design and nature of the intervention.
    - o Results for between group statistical comparisons, point measures, and measures of validity are reported for key outcomes which supports the interpretability of the study.

- ❖ **Strengths**
    - o The matched pairs randomized controlled design of this study eliminates the risk of bias due to baseline differences between groups and indicates that it is high-level.
    - o The external validity, internal validity, and interpretability indicate high methodological quality.
    - o The results are generalizable to patients with congenital hemiplegia given the eligibility criteria.

- ❖ **Weaknesses**
    - o Lack of blinding of subjects and therapists administering the interventions introduced potential sources of bias and decreases the internal validity of the study.
    - o Lack of a control group receiving standard, non-intensive doses of therapeutic interventions to serve as a comparison to the intensive CIMT and BIM protocols.
    - o Use of impairment-based outcome measures (grip strength, sensation) for activity- and participation-based interventions

- ❖ **Overall Quality of Evidence**
    - o In conclusion, this is a high-quality study, despite the limitations in study design mentioned above, as the authors identified a gap in the literature and conducted a trial of high methodological quality to help influence best practice.

Interpretation of Results

The results of this study indicate that both CIMT and BIM intervention-based camps effectively improve upper extremity function and movement quality, as well as overall participation during bimanual tasks in children with congenital hemiplegia. Strengths of the article include the high level of evidence and high methodological quality, as well as the ease of interpretability. The single-blind, matched pairs randomized controlled trial design enhances study validity and reduces systematic bias. The outcome measures utilized to assess upper extremity function were both valid, reliable, and appropriate to use with this patient population.

When interpreting the results of this study, it is important to take effect size into account. While the CIMT group experienced statistically significant improvements in MUUL scores compared to the BIM training group, the gains on the MUUL cannot be considered clinically significant as they are not greater than the minimal clinical important difference of 7.4%. This indicates a need for further research to determine an appropriate intervention dose that is able to produce clinically significant changes in upper extremity function. Additionally, there was minimal difference in scores on the AHA and JTTHF between the CIMT and BIM groups at both 3- and 26-weeks follow-up. These small effect sizes indicate that both CIMT and BIM are favorable intervention strategies to improve upper extremity outcomes.

Another disadvantage of this study is that the high-dose, camp-based therapeutic intervention does not translate into standard clinical practice. In order to replicate the results of this study, patients would need to receive 60-hours of therapy over the course of 10 days. While intensive CIMT or BIM training may be beneficial as a form of adjunct therapy, most clinicians will not be able to meet the intensity, frequency, and duration within a patient's plan of care due to time, scheduling, and financial reimbursement constraints. Given the results of this study, therapists can feel confident referring their patients to intensive CIMT programs; however, further research is needed to understand the effects of CIMT on upper extremity function when it is delivered at a lower dose.

Overall, this is valid and reliable study supporting the use of intensive CIMT and BIM intervention strategies to improve upper extremity function in children with congenital hemiplegia; however, further research is necessary in order enhance applicability to clinical practice.

Applicability of Study Results

The study by Sakzewski et al. is relevant and applicable to the clinical question and scenario. The patient in the clinical scenario is an 8-year-old female with a diagnosis of hemiplegic cerebral palsy who is currently receiving outpatient occupational and physical therapy services. She is referred to participate in a camp, similar to that of the study, that incorporates the principles of intensive CIMT and BIM training through engaging, age-appropriate, goal-based activities. Since she meets the eligibility criteria for the study, we can infer that attending camp will help her progress towards her goals of increased independence, function, movement quality, and participation with activities of daily living involving use of bimanual upper extremities.

The clinical question sought to determine whether CIMT or BIM results in greater improvements in upper extremity function. This study indicates that both interventions lead to positive outcomes in participation and upper extremity function. Further research is necessary to explore the impact of a combined CIMT and BIM training approach on upper extremity function in children with hemiplegic cerebral palsy.

While implementing an intensive constraint induced movement therapy regimen may not be feasible in traditional practice settings, administering CIMT is practical and feasible in this clinical scenario given the existence of UNC Children's *Helping Kids with Hemiplegia Camp*. Given the effectiveness of CIMT in improving unimanual function and self-care in children with hemiplegia, I believe that a referral to the *Helping Kids with Hemiplegia Camp* is appropriate for my patient.

(2) Description and appraisal of "Constraint-induced movement therapy in children with unilateral cerebral palsy" by Hoare et al. (2019)

Aim/Objective of the Study/Systematic Review:

Hoare et al. conducted a systematic review and meta-analysis in order to determine if constraint-induced movement therapy improves hemiplegic upper extremity function in children with unilateral cerebral palsy.

Study Design

This study is a systematic review and meta-analysis of randomized controlled trials (RCTs) and cluster-RCTs.

- ❖ **Search Strategy:** The following online databases were searched for relevant articles published through March 2018: the Central Register of Controlled Trials in the Cochrane Library, MEDLINE, MEDLINE In-Process & other Non-Indexed Citation Ovid, MEDLINE Epub Ahead of Print Ovid, Embase Ovid, CINAHL EBSCO*host*, PsychInfo OVID, Science Citation Index, PEDro, OT seeker, *Cochrane Database of Systematic Reviews*, ClinicalTrial.gov, WHO International Clinical Trials Registry Platform, and Australian New Zealand Clinical Trials Registry.
    - o Searches combined keywords related to cerebral palsy, hemiplegia, CIMT, forced use, and massed practice. Specific search terms and syntax were adapted for each database and are published by the authors in Appendix 1. No restrictions were applied based on language, date, or publication status.
    - o Additional search strategies included:
        - ▪ Conversations with key authors and colleagues in the field
        - ▪ Review of reference lists of included studies, as well as relevant articles, systematic reviews, and conference abstracts
        - ▪ Google Scholar search with the terms "cerebral palsy" and "constraint therapy"
        - ▪ Hand searching the following journals from 2007 to 2018: Developmental Medicine and Child Neurology; Physical and Occupational Therapy in Pediatrics; Archives of Physical Medicine and Rehabilitation; Journal of Child Neurology; Journal of Rehabilitation Medicine; Pediatric Physical Therapy; American Journal of Occupational Therapy; NeuroRehabilitation and Clinical Rehabilitation
    - o This search strategy yielded 1290 results when combining results from each database and eliminating duplicates.

- ❖ **Selection Criteria:** Two review authors screened titles and abstracts and reviewed full-text papers for relevance using the selection criteria below. A third review author was not required as the two review authors did not disagree on the inclusion or exclusion criteria for any abstracts or articles.
  - o **Inclusion criteria:** Randomized controlled trials (RCTs), cluster-RCTs, or clinically controlled trials comparing signature CIMT (cCIMT), modified CIMT (mCMIT), hybrid CIMT (hCIMT), or forced used therapy to low-dose, high-dose, of dose-matched bimanual therapy, standard care, different forms of CIMT, and/or no intervention; Subjects were children ages birth to 19 years with a diagnosis of unilateral cerebral palsy; Primary outcomes measured bimanual performance, unimanual capacity, and manual ability; Secondary outcomes included self-care, body function, participation, and quality of life measures.
  - o **Exclusion criteria**: CIMT was combined with lower limb interventions; CIMT could not be isolated from co-interventions

- ❖ **Methods**
  - o Five review authors were paired and allocated included trials. Reviewers independently extracted data on the study population, environment, intervention, methodology, and outcomes. Disagreements between pairs of review authors were resolved through discussion and, if necessary, a third review author was consulted. Multiple publications of the same trial were compared to ensure completes and assess for contradictions. Study authors were contacted if additional information was needed.
  - o CIMT was compared to low dose, high dose and dose-matched interventions, as well as other forms of CIMT. Mean change scores, standard deviations of the mean differences, and 95% confidence intervals were analyzed for all primary outcomes. Data from individual comparisons were not pooled in a single meta-analysis due to variability in treatment dosages. A random effects model was used when there was sufficient data to conduct a meta-analysis. Data that could not be pooled was presented in tables. Heterogeneity of each meta-analysis was assessed using forest plots, I^2, and Tau^2 statistics.
  - o The GRADE approach was used by two review authors to assess the quality of evidence for each comparison and all outcomes where there was sufficient evidence for a meta-analysis. The level of evidence was downgraded if there is evidence of publication bias, there are less than 400 participants for continuous data, >50% of participants are outside the target group, less than 75% of included studies are low risk across all risk of bias domains, data is from a single study only, and/or there is statistically significant heterogeneity (p <0.10) and I^2 >40%.
  - o Risk of bias was independently assessed by the pairs of review authors using the *Cochrane Handbook for Systematic Reviews of Interventions* criteria. Pairs of authors resolved disagreement by discussion, consulting a third author if required.

Setting

The majority of interventions were delivered in clinical treatment centers (9 studies) or a combination of clinical treatment centers and home settings (8 studies). Additional treatment locations included theme camps; home-based; and home and community, preschool, or camp settings. The trials included in this systematic review were conducted in the following countries: Australia (5 studies), United States (5), Iran (4), Italy (2), China (2), South Korea (2), Sweden (2), the Netherlands (1), Germany (1), Switzerland (1), Brazil (1), Canada (1), Jordan (1), Egypt (1), Israel (1), Taiwan (1), India (1), and Pakistan (1).

Participants

This systematic review included a total of 36 studies: 35 RCTs and 1 cluster-RCT.

- ❖ **Characteristics of Included Studies:**
  - o 789 articles were identified originally, resulting in 204 relevant articles for review that produced 36 studies that met the selection criteria
  - o 32 articles were published in English and 4 were published in Persian. An English manuscript was obtained for Hosseini 2010. Assessment and data extraction of the remaining three studies was performed by Persian speaking health professionals.
  - o The majority of trials were two-group designs evaluating CIMT and a comparison intervention, 3 of the included trials were three-group designs and 2 trials were a four-group design
  - o 2 of the included studies provided sCIMT, 24 provided mCIMT, and 10 provided hCIMT
  - o 17 of the included studies used low dose comparison, 17 studies used a dose-matched comparison, and 3 studies compared a different form of CIMT
  - o The review undertook 40 comparisons across the 36 included trials:
    - CIMT versus low dose (17 comparisons)
    - CIMT versus high dose (4 comparisons)
    - CIMT versus dose-matched (16 comparisons)
    - CIMT versus different form of CIMT (3 comparisons)
  - o Sample size of included studies ranged from 11 to 105 participants. 10% of studies includes less than 20 participants.

- ❖ **Characteristics of Participants:**
  - o Data was reported for 1195 of the 1264 participants across the 36 included studies.
    - ▪ 53% boys
    - ▪ 47% left-sided hemiplegia
  - o 35 studies reported the age of participants
    - ▪ Mean age of 5.95 years; range 3 months to 19.8 years
  - o 12 studies (415 participants) classified children using the Manual Ability Classification System (MACS)
    - ▪ 28.5% MACS Level I, 59.1% MACS Level II, 11.5% MACS Level III, and 0.05% MACS Level IV
  - o 8 studies (383 participants) classified children using the Gross Motor Function Classification System (GMFCS)
    - ▪ 65.3% (250 participants) GMFCS Level I, 34.5% (132 participants) GMFCS Level II, and 1 participant GMFCS Level 3
  - o Inclusion Criteria:
    - ▪ Active range of motion of least 20 degrees for wrist extension and at least 10 degrees from full flexion at the metacarpophalangeal joint (16 studies)
    - ▪ Ability to grasp and release with the affected hand (6 studies)
    - ▪ Ability to follow simple or one-stage commands (16 studies)
    - ▪ Intellectual quotient (IQ) >70 (4 studies)
    - ▪ Normal intellectual function (2 studies)
  - o Exclusion Criteria:
    - ▪ Upper-limb Botulinum toxin-A injections in the previous 6 months (20 studies)
    - ▪ History of recent or prior upper-limb surgery (17 studies)
    - ▪ Recent or uncontrolled seizures (14 studies)
    - ▪ Visual impairments (14 studies)
    - ▪ Contractures or spasticity as defined by a modified Ashworth Scale score of >3 points (11 studies)
    - ▪ Hearing impairments (4 studies)
    - ▪ 4 studies did not report exclusion criteria

Intervention Investigated

Control

The review authors evaluated trials that compared CIMT interventions to four comparison groups: low-dose interventions, high-dose interventions, dose-matched interventions, and different forms of CIMT. The comparison dosage consisted of the total number of therapist-led, parent-led, and other interventions. The intensity of low-dose, high-dose, and dose-matched comparison interventions were classified by the review authors as follows:

  - o *Low-dose:* 0 to 25 total hours of intervention with a significant difference from the experimental group, excluding forced-use dosage.
  - o *High-dose:* greater than 25 total hours of intervention but less than the CIMT-group dosage, excluding forced-use dosage
  - o *Dose-matched*: total dosage equal to that of the CIMT-group, excluding forced-use dosage

Below is a description of the methods, setting, and dosage for studies in each of the four comparison groups.
- ❖ **Low-Dose Comparison Groups**
  - o Low-dose comparisons, consisting of occupational therapy, usual care, conventional therapy, neuro-developmental therapy, infant massage, and no intervention, were delivered in 17 studies by occupational and physical therapists
  - o Interventions were provided for 20 to 60 minutes/day, 0 to 7 days/week for 2 to 10 weeks, averaging a total of 7.9 hours of intervention (range 0 to 16 hours).

- ❖ **High-Dose Comparison Groups**
  - o High-dose comparisons, consisting of intensive occupational therapy, bimanual occupational therapy, or intensive traditional physical therapy rehabilitation, were delivered in 4 studies by occupational and physical therapists
  - o Interventions were provided for 45 minutes to 4 hours per day, 1 to 2 days/week for 4 to 8 weeks, averaging a total of 37.5 hours of intervention (range 30 to 45 hours)

- ❖ **Dose-Matched Comparison Groups**
  - o Dose-matched comparisons, consisting of Hand Arm Bimanual Intensive Training (HABIT), bimanual interventions, or conventional care, were delivered in 15 studies by occupational and physical therapists

- o Interventions were provided for 30 minutes to 8 hours a day, from once every other week to 6 days per week, for 1 to 10 weeks. The total dose averaged 71.4 hours of intervention (range 6 to 210 hours).

- ❖ **Different Form of CIMT Comparison Groups**
  - o Different forms of CIMT, delivered at a different dose or in a different environment by occupational therapists and family members, were used as a comparison in 3 studies.
  - o Comparisons consisted of 6 hours/day of high-dose hCIMT versus 3 hours/day high-dose hCIMT, clinic-based CIMT versus home-based CIMT delivered by an occupational therapist, and prolonged constraint via semi-rigid casting with intermittent hand holding.
  - o The total dose across these studies averaged 91 hours of intervention (range 42 to 168 hours). Therapist led interventions were provided for 90 minutes to 3 hours per day, 5 to 7 days per week for 2 to 3 weeks, totaling 15-63 hours of intervention. Families provided hand-holding interventions for one hour/day, for a total of 42 hours, over a 10-week period.

Experimental

- ❖ **Intervention:** CIMT interventions in the included studies were administered individually, in a group-based model, or using a combined delivery method by therapists, teachers, parents, students, and other interventionists in a variety of settings including clinical treatment centers, home-based environments, theme camps, or a combination of clinical treatment centers and home, home and school, or camps and home.
  - o A variety of constraint methods were used on the non-involved upper limb including mitts, gloves, slings, splints, casts, and bandages.
  - o Interventions included fine and gross motor activities that implemented the principles of shaping or motor learning theories to improve upper extremity function.

- ❖ **Dosage:** The review authors defined the total dosage of CIMT interventions as the sum of therapist-led, parent-led, and other interventions. In the included studies, interventions were provided for 0.5 to 8 hours per day, 2 to 7 times a week, for an average of 5 weeks (range 1 to 12 weeks). The mean total dose of CIMT interventions across included studies was 129 hours (range 20 to 504 hours).
  - o Therapist led CIMT interventions averaged 56 hours (range 0 to 26 hours), while parent-led interventions averaged 34 hours (range 10 to 152 hours).
  - o Forced use (constraint outside of therapist- and parent-led interventions) was included in 11 studies with an average dosage of 161 hours (range 22 to 498 hours).
  - o A mean dosage of 6 hours of concurrent usual care (range 2 to 14 hours) was provided during the CIMT intervention period in 7 studies.

Outcome Measures

The 36 included trials assessed a total of 57 outcome measures, 52% of which were only used in 1 study. The range of outcomes used in each trial was 1 to 14, with a mean of 4 outcomes. The Assisting Hand Assessment, which was utilized in 15 studies, was the most commonly used outcome measure. Data from 5 studies was not included in the analysis due to inadequate reliability and/or validity for use with children with CP, adaptations to scoring or administration that invalidated the measure, and/or the data was not made available or reported. Outcomes analyzed by the review authors for each of the comparison groups are described below. All outcomes were measured at baseline and immediately postintervention (0-2 weeks).

- ❖ **Primary Outcome Measures**
  - o Kids-Assisting Hand Assessment (AHA)
    - ▪ Assessment of bimanual performance
    - ▪ Scale: 0-100, where higher score indicates improved in bimanual performance
    - ▪ Used in CIMT versus low-dose, high-dose, dose-matched, and different forms of CIMT comparisons
  - o Melbourne Assessment of Unilateral Upper Limb Function (MUUL)
    - ▪ Assessment of unimanual capacity
    - ▪ Scale: 0-100, where higher score indicates improved unimanual capacity
    - ▪ Used in CIMT versus low-dose, high-dose, and dose-matched comparisons
  - o Quality of Upper Extremity Skills Test (QUEST) – Grasps
    - ▪ Assessment of unimanual capacity
    - ▪ Scale: 0-100, where higher score indicates improved unimanual capacity
    - ▪ Used in CIMT versus low-dose, high-dose, dose-matched, and different forms of CIMT comparisons
  - o ABILHAND-Kids
    - ▪ Assessment of manual ability
    - ▪ Scale: -10 to 10, where higher score indicates improved manual ability
    - ▪ Used in CIMT versus dose-matched comparison

- ❖ **Secondary Outcome Measures**
  - o Pediatric Evaluation of Disability Inventory (PEDI) – Self Care Functional Skills Domain
    - ▪ Assessment of self-care
    - ▪ Scale: 0-73, where higher score indicates improved self-care
    - ▪ Used in CIMT versus high dose and dose-matched comparisons
  - o Canadian Occupational Performance Measure (COPM)– Performance
    - ▪ Parent-report performance measure
    - ▪ Scale: 0-10, where higher score indicates improved parent-rated occupational performance
    - ▪ Used in CIMT versus high dose and dose-matched comparisons

Main Findings

Tables 1-4 show the relevant differences in outcomes between the control and experimental groups immediately postintervention for each of the four comparison groups.

Table 1. Effects of CIMT versus low-dose comparison immediately postintervention [1]

Outcomes	Anticipated absolute effects (95% CI)		Number of Participants	Certainty of Evidence
	Low-dose comparison	**Constraint induced movement therapy**		
Bimanual performance Assessed with: Kids-AHA	Mean bimanual performance ranged from **0.57 to 1.0 AHA units**	Mean bimanual performance was **5.44 AHA units higher** (range 2.37 to 8.51)	39 (2 RCTs)	Low
Unimanual capacity Assessed with: MUUL	Mean unimanual capacity was **-0.05 points**	Mean unimanual capacity was **1.98 points higher** (range -1.55 to 5.51)	23 (1 RCT)	Very low
Unimanual capacity Assessed with: QUEST – Grasp	Mean unimanual capacity ranged from **0.9 to 2.5 points**	Mean unimanual capacity was **7.57 points higher** (range 2.10 to 13.05)	103 (2 RCTs)	Very low

Pooled Results:

At follow-up immediately postintervention, the CIMT group demonstrated greater improvements in both bimanual performance and unimanual capacity than the low-dose comparison group, as indicated by improvements in Kids-AHA and QUEST-Grasp scores, respectively. Additionally, CIMT is more effective at improving unimanual capacity than low-dose comparisons in the two-weeks to four-months follow-up period, as indicated by statistically significant improvement on the QUEST dissociated movements (MD 5.80, 95% CI 2.29 to 9.31), grasp (MD 6.50, 95% CI 2.03 to 10.97), and protective extension (MD 11.10, 95% CI 6.22 to 15.98) domains.

Single-Study Results

- ❖ Eliasson 2018 reported no differences in bimanual or unimanual performance between CIMT and low-dose comparison groups.
  - o AHA at 18-months follow-up (MD 17.16 AHA units, 95% CI -2.59 to 36.91)
  - o HAI-Bimanual assessment scale, immediately postintervention (p=0.14, MD 5.27 HAI units, 95% CI -1.43 t0 11.97)
  - o HAI- Unimanual assessment scale, immediately postintervention (MD 2.52 HAI units, 95% CI -0.68 to 5.72)
- ❖ Eugester-Buesch 2012 found no difference in unimanual capacity assessed by the MUUL between groups postintervention (P=0.30, MD 1.98, 95% CI -1.55 to 5.51) or during the two-weeks to four-months follow-up period (MD 0.12, -4.02 to 4.26).
- ❖ Gharib 2010 found that CIMT is more effective at improving unimanual capacity immediately postintervention as assessed by the QUEST Grasp domain (MD 9.48, 95% CI 1.09 to 17.87).
- ❖ Yu 2012 reported greater improvements in unimanual capacity assessed by the Box and Blocks test immediately postintervention for the CIMT group (P < 0.05, MD 6.20, 95% CI 2.82 to 9.58).

- ❖ deBrito Brandão 2010 showed greater improvements in self-care on the PEDI-Self Care Functional Skills domain for the CIMT group than the low-dose comparison immediately postintervention (MD 5.64, 95% CI 0.82 to 10.46) and two-weeks to four-months follow-up (MD 6.87, 95% CI 3.58 to 10.16).

Adverse Events:

Of the 17 studies involving a low-dose comparison, 4 children across 3 studies were unable to tolerate constraint. Additionally, two studies reported minor skin irritation due to casting that was reversible.

Table 2. Effects of CIMT versus high-dose comparison immediately postintervention [1]

Outcomes	Anticipated absolute effects (95% CI)		Number of Participants	Certainty of Evidence
	High-dose comparison	Constraint induced movement therapy		
Bimanual performance Assessed with: Kids-AHA	Mean bimanual performance ranged from **0.8 to 7 AHA units**	Mean bimanual performance was **0.39 AHA units higher** (range -3.14 to 2.36)	126 (3 RCTs)	Low
Unimanual capacity Assessed with: MUUL	Mean unimanual capacity was **1.2 points**	Mean unimanual capacity was **2 points lower** (range -5.36 to 1.36)	43 (1 RCT)	Very low
Unimanual capacity Assessed with: QUEST – Grasp	Mean unimanual capacity was **3.31 points**	Mean unimanual capacity was **0.2 points lower** (range -11.84 to 11.44)	34 (1 RCT)	Very low
Self-care Assessed with: Pediatric Evaluation of Disability Inventory – Self-Care Functional Skills Domain	Mean self-care was **8.04 points**	Mean self-care was **1.52 points higher** (range -3.1 to 6.14)	34 (1 RCT)	Very Low
Individualized measures of performance Assessed with: Canadian Occupational Performance Measure – Performance	Mean individualized measure of performance ranged from **3.07 to 3.4 points**	Mean individualized measure of performance was **0.02 points lower** (range -0.72 to 0.69)	126 (3 RCTs)	Low

Pooled Results:

No differences in bimanual performance or occupational performance were observed between the CIMT and high-dose comparison groups immediately postintervention. The authors also found no difference in the two-weeks to four-months follow-up for bimanual performance (MD -0.91, 95% CI -5.06 to 3.23) and occupational performance (MD -0.22, 95% CI -0.87 to 0.43). Meta-analyses were unable to be conducted for unimanual capacity and self-care outcomes.

Single Study Results:

- ❖ Hoare 2013 reported no differences in unimanual capacity between groups on the QUEST- Grasp domain immediately postintervention (MD -0.20, 95% CI -11.84 to 11.44) and at two-weeks to four-months follow-up (MD 7.96, 95% CI -1.59 to 17.51). Additionally, no differences were found between CIMT and high-dose comparison interventions on self-care assessed by the PEDI- Self Care Functional skills domain (MD 1.52, 95% CI -3.10 to 6.14).
- ❖ Sakzewski 2015 observed no differences between groups in unimanual capacity assessed by the MUUL immediate postintervention (MD -2.30, 95% CI -5.56 to 0.96) and two-weeks to four-months follow-up (MD -2.00, 95% CI -5.36 to 1.36).

Two of the four studies reported that children experienced frustration with CIMT intervention, while two reported adverse events that were not related to CIMT.

Table 3. Effects of CIMT versus dose-matched comparison immediately postintervention

Outcomes	Anticipated absolute effects (95% CI)		Number of Participants	Certainty of Evidence
	High-dose comparison	**Constraint induced movement therapy**		
Bimanual performance Assessed with: Kids-AHA	Mean bimanual performance ranged from **1.2 to 9.5 AHA units**	Mean bimanual performance was **0.8 AHA units higher** (range -0.78 to 2.38)	229 (7 RCTs)	Low
Unimanual capacity Assessed with: MUUL	Mean unimanual capacity ranged from **-0.8 to 7.1 points**	Mean unimanual capacity was **1.48 points higher** (range -0.49 to 3.44)	203 (6 RCTs)	Low
Unimanual capacity Assessed with: QUEST – Grasp	Mean unimanual capacity ranged from **3.7 to 10.8 points**	Mean unimanual capacity was **6.63 points higher** (range -2.38 to 15.65)	124 (3 RCTs)	Very low
Manual ability Assessed with: ABILIHAND-Kids	Mean manual ability tanged from **-0.08 to 0.22 logits**	Mean manual ability was **0.52 logits higher** (range -0.41 to 1.46)	95 (3 RCTs)	Very low
Self-care Assessed with: Pediatric Evaluation of Disability Inventory (PEDI)– Self-Care Functional Skills Domain	Mean self-care was **1.4 to 3.4 points**	Mean self-care was **1.09 points lower** (range -2.42 to 0.24)	45 (2 RCTs)	Low
Individualized measures of performance Assessed with: Canadian Occupational Performance Measure (COPM) – Performance	Mean individualized measure of performance ranged from **1.2 to 3.4 points**	Mean individualized measure of performance was **0.08 points higher** (range -1.29 to 1.46)	191 (6 RCTs)	Very low

Pooled Results

There were no differences in bimanual performance assessed by the Kids-AHA between the CIMT and dose-matched comparison groups in the postintervention (MD 0.80 95% CI -0.78 to 2.38), two-week to four-month (MD 1.81, 95% CI -0.10 to 3.73), five- to six-month (MD -0.04, 95% CI -1.56 to 1.49), or seven- to twelve-month (MD 0.70, 95% CI -2.53 to 3.93) follow-up periods.

CIMT resulted in significant improvements in unimanual capacity assessed with the MUUL compared to dose-matched interventions at five- to six-months follow-up (MD 3.18, 95% CI 0.85 to 5.50). No differences were observed between groups during the postintervention (MD 1.48, 95% CI -0.49 to 3.44), two-week to four-month (MD 1.36, 95% CI -1.28 to 4.00), or seven- to twelve-month (MD -1.00, 95% CI -4.39 to 2.39) follow-up periods. Additionally, there were no significant differences in unimanual capacity as assessed by the QUEST-Grasp domain immediately postintervention (MD 6.63, 95% CI -2.38 to 15.65) or two-weeks to four-months (MD 1.18, 95% CI -5.12 to 7.49) and five- to six-months (MD 1.70, 95% CI -6.32 to 9.72) follow-up.

No differences in manual ability assessed by the ABILHAND-Kids were observed between groups immediately postintervention (MD 0.52, 95% CI -0.41 to 1.46) or at two to four months follow-up (MD 0.06, 95% CI -

0.51 to 0.62); however, CIMT was more effective than dose-matched comparisons at five- to six-months follow-up (MD 0.74, 95% CI 0.31 to 1.18).

There were no differences observed in occupational performance assessed by the COPM at the immediate postintervention (MD 0.08, 95% CI -1.29 to 1.46), two-weeks to four-months (MD 0.55, 95% CI -1.45 to 2.55), five- to six-months (MD -0.30, 95% CI -1.01 to 0.41), or seven- to twelve-months (MD 0.10, 95% CI -0.83 to 1.03) follow-up periods. Additionally, at immediate postintervention follow-up, there was no evidence that CIMT was more effective in improving self-care ability assessed with the PEDI Self Care Functional Skills domain (MD -1.09, 95% CI -2.42 to -0.24).

Single Study Results:

❖ Deppe 2013 found no difference in bimanual ability assessed by the AHA between CIMT and dose-matched comparison groups immediately postintervention (MD 1.00, 95% CI -2.63 to 4.63).
❖ Zafer 2016 reported no difference in unimanual capacity assessed by the QUEST-Grasp domain between groups immediately postintervention (MD 4.90, 95% CI 2.12 to 7.86).

Adverse Events:

Four studies reported adverse events, with two children unable to tolerate CIMT and complete the intervention in one study and three children having difficulty adjusting to CIMT in the beginning in a second study. Headache and side-effects of rTMS were reported by 11% of the participants receiving combined CIMT and rTMS intervention in Kirton 2016a and Kirton 2016b; however, no adverse effects were reported for the CIMT group.

Table 4. Effects of CIMT versus different form of CIMT immediately postintervention

Outcomes	Anticipated absolute effects (95% CI)		Number of Participants	Certainty of Evidence
	High-dose comparison	**Constraint induced movement therapy**		
Bimanual performance Assessed with: Kids-AHA* *Different scale units used prior to meta-analysis* *AHA Logit Scale from: -10.26 to 8.72*	Mean bimanual performance was 0.84 **AHA logits**	Mean bimanual performance was **2.19 AHA logits higher** (range -1.15 to 5.53)	60 (2 RCTs)	Very low
Bimanual performance Assessed with: Kids-AHA	Mean bimanual performance was **5.3 AHA units**	Mean bimanual performance was **3.70 AHA units higher** (range -1.27 to 8.67)	60 (1 RCT)	Very low
Unimanual capacity Assessed with: QUEST – Grasp	Mean unimanual capacity was **-0.05 points**	Mean unimanual capacity was **3.70 points higher** (range -1.91 to 8.71)	60 (1 RCT)	Very low

Pooled Results: Meta-analyses were unable to be conducted for any outcomes in this comparison group.

Single Study Results

❖ At immediate postintervention follow-up, DeLucca 2012 reported no difference in bimanual performance assessed with the Kids-AHA between children receiving 6 hours versus 3 hours of CIMT (MD 2.19 logit scores, 95% CI -1.15 to 5.53).
❖ Christmas 2019 found no difference immediately postintervention between prolonged CIMT and manual CIMT interventions in bimanual performance assessed by the AHA immediately (MD 3.70 AHA units, 95% CI -1.27 to 8.67) or unimanual capacity assessed by the QUEST - Grasp scale (MD 3.40, 95% CI -1.91 to 8.71). Prolonged CIMT more effectively improved manual ability assessed by the Birmingham Bimanual Questionnaire at the immediate post-intervention follow-up (P=0.019, MD 16.90, 95% CI 3.31 to 30.49). This improvement was not maintained at five- to six-months follow-up (P=0.87, MD 1.10, 95% CI -12.33 to 14.53).

Adverse Events:

Twelve non-serious adverse events were reported in one study: 2 children experienced minor bruising secondary to a fall and 10 had small areas of skin abrasion due to prolonged constraint.

Original Authors' Conclusions

The authors conclude that there is low quality evidence that CIMT results in greater improvements in unimanual capacity and bimanual performance in children with unilateral cerebral palsy compared to low-dose comparisons. There is no evidence that CIMT is more effective at improving bimanual performance or unimanual capacity than high-dose and dose-matched comparisons. The available evidence indicates that CIMT is a safe intervention for children with hemiplegic cerebral palsy.

Critical Appraisal

Validity

- ❖ This systematic review and meta-analysis by Hoare et al. is classified as level 1a evidence and demonstrates high methodological quality.
    - o **AMSTAR: 10/11**; a priori design provided: yes; duplicate study selection and data extraction: yes; comprehensive literature search: yes; inclusion of grey literature: yes; included/excluded studies provided: yes; characteristics of included studies provided: yes; quality of included studies: yes; quality assessment used in conclusions: yes; appropriate methods to combine studies: yes; assessment of publication bias: no; conflict of interest included: yes

- ❖ **Strengths**
    - o *Quality Assessment:* Quality assessment methods utilized by the authors are clearly described. The authors utilized the *Cochrane Handbook for Systematic Reviews of Interventions* to assess for risk of bias. The GRADE Working Group grades of evidence was used to assess the level of certainty of evidence. Pairs of reviewers assessed the risk of bias of each study, consulting a third reviewer as needed to resolved disagreements.
    - o *Selection Bias:* Two researchers screened titles, abstracts, and full-text articles for inclusion. The review authors performed a comprehensive literature search across 11 electronic databases and 3 trial registrars. In additional to electronic database searches, they hand-searched journals and reference lists, contacted experts, and searched Google Scholar.
    - o *Publication Bias:* Studies were not excluded based on language or publication status. Four studies published in Persian were included in the systematic review. The inclusion of grey literature in the search widens the available data for analysis.
    - o *Search Strategy:* The search strategy was both sensitive and relevant, using terms such as "constraint induced movement therapy," "cerebral palsy," and "hemiplegia". The authors provide a detailed description of the specific search strategies used in each electronic databased in Appendix 1.
    - o *Discussion of Results:* The authors acknowledge existing gaps in the literature and provide a thorough analysis of the best available evidence. They discuss future direction for research in order to improve quality of evidence. Data for primary outcomes are organized in tables in the text, with individual analysis plots for pooled data and tables containing additional information about included studies included in the appendices.
    - o *Quality of Selected Studies:* The quality of the included evidence was high, as all of the included studies were level I evidence. This greatly enhances the overall quality of the systematic review.
    - o *Discussion of Limitations:* The authors discuss potential sources of bias in the review process and address the strategies implemented to mitigate risk of bias.

- ❖ **Weaknesses**
    - o *Publication Bias Assessment:* The authors did not provide an assessment of likelihood of publication bias. Inclusion of graphical aids and/or statistical tests, such as a funnel plot, Egger regression test, or Hedges-Olken, would increase the reliability and validity of the study.

- ❖ **Internal Validity**
    - o Overall, the included trials demonstrate moderate internal validity. The majority of the trials utilized random sequence generation and concealed allocation, which increase internal validity and reduces selection bias. The study demonstrates poor performance bias given the lack of blinding of participants and therapists due to the nature of the intervention. The blinding of outcome assessors reduced detection bias and enhances the internal validity of the study.

- ❖ **External Validity**
    - o The results can be generalized to a large population of children with hemiplegic cerebral palsy, as the participants in the included studies consist of children of various ages, genders, functional levels, and intellectual abilities.

- ❖ **Overall Quality of Evidence**
  - o Overall, this is a high-quality study, despite the limitations of the included studies mentioned above, as the authors identified a gap in the literature, performed a search of high methodological rigor, included studies of high-quality evidence, and made recommendations based on the best available evidence.

Interpretation of Results

The results of this study indicate that CIMT, high-dose bimanual training, and dose-matched bimanual interventions effectively improve unimanual capacity, bimanual performance, and manual ability, as well as self-care and overall participation, in children with unilateral cerebral palsy. Additionally, the results suggest that CIMT is more effective at improving bimanual performance and unimanual capacity than low-dose bimanual training and standard care, such as occupational therapy.

Strengths of the article include the high level of evidence and high methodological quality, as well as the ease of interpretability. The comprehensive literature search, including grey literature and publications in other languages, which was conducted by two authors, enhances the study quality and reduces risk of systematic bias. Additionally, the inclusion of level I evidence RCTs that utilized random and concealed allocation methods enhances the validity of the study and reduced risk of bias. The authors assess outcomes using measures that are valid, reliable, and appropriate for this patient population. Furthermore, a strength of this review is that authors made four different comparisons based on intensity, dosage, and intervention type which increases the applicability of the article.

Weaknesses of this review include that the quality of evidence was low to very low for all conclusions. CIMT generated statistically significant improvements in unimanual capacity only when compared to low-dose intervention. There were minimal differences in scores on all primary outcome measures for the CIMT versus high-dose, dose-matched, and different forms of CIMT comparisons. These small effect sizes indicate that CIMT, high-dose and dose-matched bimanual intervention, and different forms of CIMT produce positive upper extremity outcomes. The authors fail to report on clinical significance for all outcomes and comparisons, which decreases the applicability and practicality of implementing CIMT in clinical settings and emphasizes the need for further research.

Another disadvantage of this study is that intensive therapeutic interventions are difficult to implement in traditional physical therapy practice. In order to achieve the benefits of CIMT compared to traditional physical or occupational therapy plans of care demonstrated in this systematic review, patients would need to receive 129 total hours of intervention, 2 to 7 days/week for about 5 weeks. Most therapists will not be able to meet this dosage in a patient's plan of care due to time, scheduling, and financial reimbursement constraints. Based on the results of this review, physical therapists can feel comfortable referring pediatric patients with hemiplegic cerebral palsy to intensive CIMT programs; however, further research is needed to understand the clinical significance of CIMT compared to bimanual training on upper extremity function.

Overall, this is a valid and reliable systematic review supporting the use of intensive CIMT and BIM intervention strategies with children with hemiplegic cerebral palsy to improve unilateral capacity and bimanual performance; however, there is a need for further research to enhance clinical applicability.

Applicability of Study Results

The systematic review by Hoare et al. is relevant and applicable to the clinical question and scenario. It explores CIMT, bimanual therapy, and traditional therapeutic interventions of varying intensities and dosages similar to those implemented by UNC Children's *Helping Kids with Hemiplegia Camp* and the outpatient physical and occupational therapy clinics in my clinical question. The patient population includes children between the ages of 0 to 19 years with a diagnosis of hemiplegic cerebral palsy, which matches my patient description.

The clinical question sought to determine whether CIMT or bimanual training results in greater improvements in upper extremity function. This study indicates that although CIMT is more effective at improving upper extremity function with unimanual bimanual tasks when compared to low-dose intervention; there is no significant difference in unimanual capacity, bimanual performance, manual ability, self-care, and performance between CIMT, high-dose, and dose-matched comparisons. These results are applicable to the clinical question, indicating that the combined CIMT and bimanual intensive training camp protocol will result in positive outcomes for my patient. Additionally, intensive CIMT treatment will produce significant improvements in my patient's upper extremity function outside her traditional physical and occupational therapy plans of care.

While implementing an intensive constraint induced movement therapy regimen may not be feasible in traditional practice settings, administering CIMT is practical and feasible in this clinical scenario given the existence of UNC Children's *Helping Kids with Hemiplegia Camp*. Given the effectiveness of CIMT in improving unimanual function and self-care in children with hemiplegia, I believe that a referral to the *Helping Kids with Hemiplegia Camp* is appropriate for my patient.

SYNTHESIS AND CLINICAL IMPLICATIONS

Evidence Synthesis

The evidence analyzed in this literature review suggests that both Constraint Induced Movement Therapy (CIMT) and Bimanual Intensive Training (BIT) effectively improve functional capacity of the hemiplegic upper extremity in children with unilateral cerebral palsy. High quality evidence from Sakzewski et al. and Hoare et al. validates these findings and supports the consensus of prior research with similar target populations, study designs, aims, and objectives.

The single-blind, matched-pairs randomized controlled trial conducted by Sakzewski et al. in 2011 sought to determine the efficacy of CIMT compared to an equally intensive dosage of bimanual training (BIM). Children diagnosed with congenital hemiplegia in both intervention groups received a total of 60 hours of treatment over the course of 10 consecutive days. The Melbourne Assessment of Unilateral Upper Limb Function (MUUL) and the Assisting Hand Assessment (AHA) were administered at baseline, 3-weeks postintervention, and 26-weeks postintervention to assess movement quality of the impaired upper extremity and bimanual upper extremity performance, respectively. Researchers found that children receiving CIMT interventions demonstrated greater unimanual capacity, as indicated by higher scores on the MUUL, whereas those in the BIM group experienced increased bimanual performance, as indicated by higher scores on the AHA. Since the differences between groups were small and not clinically significant, the researchers suggest that the results reflect specificity of practice and conclude that both CIMT and BIT are effective interventions with this population.

Hoare et al. conducted a systematic review in 2011 that aimed to assess the effectiveness of CIMT as an intervention for the involved upper extremity of children with hemiplegic cerebral palsy. The review authors performed a comprehensive literature search and found 36 trials that were deemed to meet selection criteria. The included studies compared a mean total of 129 hours of CIMT delivered over an average of 4 weeks to low-dose, high-dose, and dose-matched interventions, as well as different forms of CIMT. Primary outcomes included bimanual performance (Kids-Assisting Hand Assessment), unimanual capacity (Melbourne Assessment of Unilateral Upper Limb Function and Quality of Upper Extremity Skills Test – Grasp), and manual ability (ABILHAND-Kids). The review authors concluded that although CIMT more effectively improves children's function use of bilateral upper extremities when compared to low-dose upper extremity interventions, it is not more effective when compared to bimanual interventions administered at equivalent or high doses.

Clinical Implications

The overall evidence presented by Sakzewski et al. and Hoare et al. indicates that children with hemiplegic cerebral palsy experience both short-term and long-term benefits from participation in CIMT and BIT interventions. Furthermore, research indicates that children receiving traditional, low-intensity therapeutic interventions benefit from adjunct CIMT to further improve bilateral upper extremity function. When implementing CIMT and BIT into clinical practice, all interventions should be individualized, age-appropriate, goal-oriented, and activity-based in order to optimize participation, engagement, and outcomes. Clinicians must also consider the intensity, frequency, and duration of the interventions. The therapeutic dose of CIMT in the appraised studies ranged from a total 60 to 129 hours over the course of 10 days to 10 weeks. Incorporating these interventions in the clinical practice setting at the dosage necessary to achieve functional benefits may be difficult to achieve given time and financial constraints. Therapists should consider conducting or referring patients to adjunct camps and programs that implement CIMT and BIT in a similar format to those described in the appraised studies by Sakzewski et al. and Hoare et al.

Future Implications

Future research should aim to evaluate the effectiveness of combined CIMT and BIT interventions, as well as determine the long-term of effects of both interventions in isolation and combination. There is great variability of parameters in the existing literature; therefore, researchers should seek to establish optimal intensities, frequencies, and durations of CIMT and BIT interventions in order to maximize functional improvements. While CIMT has been validated as a safe and effective intervention for pediatric patients with hemiplegia, participants in previous studies comprise a wide range of ages and functional abilities; therefore, future research should examine optimal parameters for groups of children based on age and level of function.

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