

BMJ Open Children with Hemiparesis Arm and Movement Project (CHAMP): protocol for a multisite comparative efficacy trial of paediatric constraint-induced movement therapy (CIMT) testing effects of dosage and type of constraint for children with hemiparetic cerebral palsy

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ABSTRACT

Introduction The Children with Hemiparesis Arm and Movement Project (CHAMP) addresses two pressing issues concerning paediatric constraint-induced movement therapy (CIMT): effects of two dosages and two types of constraint on functional outcomes. Systematic reviews conclude that CIMT is one of the most efficacious treatments, but wide variations in treatment protocols, outcome measures and patient characteristics have prevented conclusions about potential effects of dosage levels and constraint methods.

Methods and analysis CHAMP is a multisite comparative efficacy randomised controlled trial of 135 children (2–8 years) with hemiparetic cerebral palsy. The 2×2 factorial design tests two dosage levels—60 hours (3.0 hours/day, 5 days/week × 4 weeks) and 30 hours (2.5 hours/day, 3 days/week × 4 weeks) and two constraint conditions—full-arm, full-time cast and part-time splint, plus usual and customary (UCT) controls, yielding five groups: (1) 60 hours CIMT+full-time cast, (2) 60 hours CIMT+part-time splint, (3) 30 hours CIMT+full-time cast, (4) 30 hours CIMT+part-time splint and (5) UCT. Trained therapists deliver the standardised ACQUIREc protocol for CIMT. Blinded assessments at baseline, end of treatment, and 6 and 12 months post treatment include the Assisting Hand Assessment, and subscales from the Peabody Developmental Motor Scales-2 and modified Quality of Upper Extremity Skills Test. Parents complete the Pediatric Motor Activity Log and Pediatric Evaluation of Disability Inventory. A new Fidelity of Implementation Rehabilitation Measure monitors treatment delivery. Data analyses involve repeated-measures multivariate analysis of covariance controlling for selected baseline variables.

Ethics and dissemination Ethics boards at site universities approved the study protocol. To promote equipoise, parents of UCT controls are offered ACQUIREc after 6 months. A Data Safety and Monitoring Committee reviews results regularly, including measures of child and family stress. We will disseminate CHAMP results via peer-

Strengths and limitations of this study

- Children with Hemiparesis Arm and Movement Project is the first adequately powered comparative efficacy trial to test the effects of variation in two core components of paediatric constraint-induced movement therapy (CIMT)—dosage level and type of constraint in multiple combinations.
- A strength is that the CIMT treatment protocol—ACQUIREc—adheres to a published administration guide and is monitored for fidelity of treatment implementation (with a new standardised method).
- Parent and child stress is measured prospectively (before, during and after treatment) to address concerns about subjective stress from high-intensity treatments and use of a full-time cast. (Note: other objective measures independently assess potential effects of both forms of constraint being studied.)
- Study design limitations are that a wide range of ages (2–8 years) and baseline ability levels are included, only two dosage levels are compared—with the lower dose of 7.5 hours per week × 4 weeks still considered to be high-intensity compared with UCT and limited information (only dosage and type) about the UCT interventions.

reviewed publications and presentations to professional and advocacy organisations.

Trial registration number NCT01895660; Pre-results.

INTRODUCTION

Background and rationale

Constraint-induced movement therapy (CIMT) for children with hemiparetic cerebral palsy is an intensive form of rehabilitation that many scientists and clinicians have

tested and applied. Paediatric CIMT was initially based on a similar treatment approach for adults with chronic stroke.^{1 2} Well over 55 independent clinical reports and trials on paediatric CIMT have been conducted^{3 4} yielding >100 publications. Classical or signature CIMT is distinguished by three essential core components: (1) constraint of the unimpaired or less impaired upper extremity; (2) a high and concentrated dosage of the therapy (often for many hours per day for at least 10 days) and (3) systematic application of principles of reinforcement, behavioural shaping and massed practice to elicit and improve neuromotor control of the hemiparetic upper extremity. When all three components are not present, the treatment often is referred to as ‘modified CIMT (mCIMT)’ or ‘alternative CIMT’²⁻⁶ which has been tested more often than the signature or classical form of CIMT in children.⁷

Multiple systematic and independent reviews^{4 7-12} strongly support the conclusion that CIMT, in both the signature and modified forms, is one of the few therapies that produces clinically meaningful and sustained benefits for children with hemiparesis. This consensus about CIMT efficacy is especially noteworthy because the large majority of current treatments used for children with cerebral palsy have been deemed ineffective, uncertain or sometimes even harmful.⁹ Despite the strong endorsement for paediatric CIMT, many of these reviews have identified the following serious limitation: the research studies have varied so widely in terms of their specific CIMT treatment protocols (including varied dosage levels and types of constraint), the characteristics of the children treated (eg, age and ability levels) and in outcome measures that formal meta-analyses and meaningful cross-study comparisons are precluded. This limitation thus prevents clinicians and families from having a strong evidence basis for deciding which treatment protocol to use.

Specifically, two of the central distinguishing features of CIMT that vary widely in practice and in previous randomised controlled trials (RCTs) are (1) the type of constraint applied to the more functional, less impaired upper extremity (eg, how it is constructed and the amount of time the child wears the constraint per day or throughout the treatment period) and (2) the dosage or amount of CIMT measured in terms of the treatment hours per session and total number of treatment sessions within a specified treatment period. Accordingly, we designed the Children with Hemiparesis Arm and Movement Project (CHAMP) as a multisite, RCT to be a comparative efficacy trial with a primary goal of testing the effects of alternative types of constraint and dosage levels (in different combinations) on short-term and longer-term outcomes in children’s neuromotor competence and functional use of the hemiparetic upper extremity. We chose to test a signature or classical form of CIMT—specifically ACQUIREc—in which the treatment is administered one-on-one to children by protocol-trained paediatric rehabilitation occupational therapists or physical therapists. Although

our rationale for conducting this study is strongly pragmatic—that is, to provide rigorous clinical trial outcome data to help inform clinical practice—we also designed this trial to further advance theory in the emerging field of therapy-induced neuroplasticity.¹³⁻¹⁶

Rationale for different forms of constraint in CIMT

Concerning the form and use of constraint for children, DeLuca and colleagues¹⁷⁻²¹ were the first to develop and test a full-arm casting protocol for use in paediatric CIMT. The rationale was that a full-arm cast would be effective as a means to help young children overcome what they labelled as ‘developmental disregard’—that is, a behavioural pattern observed in many children with hemiparesis that involves the child appearing to neglect the hemiparetic upper extremity and thus seldom or almost never trying to use the hemiparetic arm and hand in everyday functioning.^{2 22} Accordingly, for those children who have little or no voluntary control of their hemiparetic upper extremity prior to treatment, wearing the full-arm cast on their functional upper extremity creates a natural environmental impetus for them to notice and then to have a strong reason to use their hemiparetic side. The cast also appears to reduce competing movement and sensations from the non-hemiparetic side. The cast is designed to be worn throughout most or all of a multiweek treatment period. Early phase I testing with a toddler²¹ showed that this form of constraint was acceptable and safe, producing no short-term or long-term negative effects on the casted arm and hand. Further, the first child adapted rapidly to the cast and showed a marked new interest in trying to do things with previously neglected hemiparetic upper extremity, both during formal CIMT treatment sessions and during non-treatment times as well. Theoretically, wearing the cast continuously for three or four consecutive weeks of treatment serves to promote a new habit pattern of engaging the hemiparetic arm and hand on a routine and natural basis—but *if and only if* use of the cast is combined with systematic therapy that effectively elicits new voluntary control and functional use of the hemiparetic upper extremity. Prior research on the use of casting or splints alone as a sole therapy intervention for treating hemiparesis showed it did not improve functional outcomes,^{4 23} and similar results occurred even when casting was combined with neurodevelopmental therapy.¹¹ After the initial case history using full-time constraint in CIMT, multiple RCTs with larger samples demonstrated consistently the feasibility, acceptability and lack of harm to the casted extremity, along with positive behavioural outcomes associated with full-arm casting (as specified by the research protocol for individualising the cast for each child)^{3 20} combined with high-intensity shaping techniques provided by protocol-trained occupational therapists or physical therapists administering the CIMT.

Independent other RCTs and clinical case series studies also tested CIMT protocols that used forms of constraint that were worn only part-time—sometimes just during

treatment sessions⁴ and other times during treatment sessions and some of the child's waking hours. Often modified CIMT delivered in group settings at 5-day or 10-day summer camps had children wear constraint during most of the waking day. This use of part-time constraint replicates (with variation) the protocol for CIMT for adults who lose upper extremity control after stroke.¹ A widely used guideline in part-time constraint is that the patient wears the constraint for the majority of waking hours, often 80%.^{24–26} The types of part-time constraint used include a sling,^{27 28} a mitt or glove, and a part-arm splint⁴; and the amount of time the child is to wear these constraints varies widely. The common practice, however, has been that constraint is always worn during active treatment sessions. In theory, an advantage of using a mitt or splint only part-time is that this allows the child daily opportunities to integrate new or improved skills of the hemiparetic side while engaged in bilateral activities that are not restricted by a cast. (Note: even with a full-time cast, most children can engage in some bilateral activities, such as crawling or carrying a large object with two arms or engaging in large ball play, although these are somewhat limited.) Also, the child is able to engage in more bilateral activities with the part-time, less restrictive forms of constraint; and likely this is far less stressful or disruptive for parents. The above description identifies some of the practical differences associated with the full-time cast and the part-time constraint. Each constraint type has been used in CIMT trials and each has been associated with producing measurable benefits. Clinically, therapists and parents have reported that children adapt readily and positively to the full-time cast, including a marked, new interest in the hemiparetic upper extremity. Some mild concerns, however, are initial negativity in adjustment to the cast during the first 24 to 48 hours, and that some children develop minor pressure sores or skin irritations that are detected (and treated) during weekly removal of the cast.^{20 29} Despite lack of negative findings about use of a cast, initially many parents and therapists remain concerned that the cast could be a negative experience for the child. Parents also may need to help a child with everyday tasks more if the child is wearing a cast during non-treatment times. Alternatively, both parents and clinicians have reported that placing a part-time constraint on and off for therapy sessions is distressing to many children, resulting in a behavioural resistance and negativity which could possibly disrupt treatment processes. At the same time, the part-time constraint allows the child to quickly practice new skills with the hemiparetic upper extremity in conjunction with the non-hemiparetic upper extremity during the non-treatment hours. In the absence of systematically comparing potential differences in the effects of these alternative constraint protocols—when each is combined with the same therapeutic behavioural techniques to elicit, shape and practice new upper extremity skills—there is no empirical basis to inform treatment choice about which constraint to select. In this comparative efficacy trial, we selected the two approaches

that are used most commonly—the casting approach and a part-arm resting splint. Based on extensive clinical experience, we know that very young children easily and frequently try to remove a mitt or sling, whereas they are more accepting of the part-arm splint during a therapy session. Since children as young as 2 years are enrolled in CHAMP, the splint seemed the best choice to compare with the cast in terms of its effects on the therapy process and on measured outcomes. In CHAMP, we examine functional changes in the use of both upper extremities, throughout the treatment process (in weekly videotaped sessions) and at the end of 4 weeks of treatment and 6 and 12 months post treatment. Understanding both the short-term and long-term benefits and potential disadvantages of these types of constraint is crucial to implementing CIMT effectively and more broadly. The use of any constraint on the stronger arm and hand for a child with hemiparesis causes intentional limitations in function while in place, so the benefits/barriers ratio is an important consideration. Casting is particularly more constraining during the time it is worn and often requires parents and caregivers to provide more assistance to the child with daily living skills. At the same time, casting may facilitate the child's use throughout the day and night in using the hemiparetic upper extremity. Because of equally strong theoretical arguments in favour of each form of constraint, CHAMP is designed to provide new data about this variation in CIMT treatment protocols.

Scientific rationale for comparing different dosages of CIMT

Theoretically, a higher dose of therapy increases the opportunity (compared with a lower dose) for a child to acquire new and increasingly complex skills and movement patterns with the hemiparetic upper extremity, promoting improvements in both unilateral and bilateral use. Many models of neuroplasticity assume that changes in the structure and function of the central nervous system (with concomitant likely changes in muscle architecture and function) can be induced by active movement and/or voluntary use.^{13 30} Indeed, many developmental models highlight the advantages of enriched learning experiences on brain development and behavioural outcomes, with both short-term and long-term benefits. Prior to the invention of CIMT for adult patients with stroke, rehabilitation protocols rarely provided very high dosages of therapy per day. The usual and customary outpatient therapy session typically ranged from 1 to 3 hours per day and often was provided only once or twice a week; similarly, treatment interventions for children with neuro-motor impairments and cerebral palsy (CP) typically have been about 1–2 hours of treatment per week, delivered in either one or two treatment sessions.³¹ In theory, these conventionally low levels of treatment could produce frustration if a child experiences slow and only small or no progress, which could contribute to the phenomenon of 'learnt non-use' due to repeated failures when trying to control the hemiparetic upper extremity.^{24 25}

Classical learning theory that applies principles of operant conditioning to elicit and strengthen new behaviours further specifies that repetitive and varied practice of new learning yields more robust, enduring changes in an individual's behavioural repertoire.^{24,32} Accordingly, higher intensity treatments should yield greater benefits, on average, than do lower intensity interventions. When it comes to clinical implementation, however, a legitimate concern arises about whether a patient may have limits related to how high a dose can be tolerated, and whether high-dose treatment could itself produce fatigue, boredom and/or stress in the patient and/or the patient's family. In fact, there are virtually no empirically based guidelines about what comprises an 'optimal' dosage of rehabilitation for children, and the extent to which the dose might need to vary based on a child's characteristics (such as age, neuromotor impairment level, cognitive ability, attention span).^{5,12}

There have been a few studies that compared dosage levels.³³ One small-scale study compared two relatively high dosages of individually administered CIMT (a form of signature CIMT) for those aged 2–8 years with hemiparetic CP. One randomly assigned treatment group received 6 hours/day × 5 days/week × 4 weeks=120 treatment hours while the other received 3 hours/day × 5 days/week × 4 weeks=60 treatment hours. This RCT used a full-time cast for constraint and the ACQUIREc protocol. In this small sample (n=18) study, both groups showed statistically significant gains at comparable levels at the end of treatment¹⁸ and 6 months later, when treatment gains were sustained for both groups.³⁴ We used this finding to justify the selection of the 3 hours per day for 20 days (over 4 weeks) as the higher of the two dosage levels to be compared in the CHAMP trial and added a lower dose to assess possible benefits.

To help select the specific lower dosage in the CHAMP trial, we reviewed the literature⁴ and collected data from clinics in the USA that were implementing their own form of paediatric CIMT. We chose the lower intensity dose to be a 2.5 hour session for 3 days per week, across four consecutive weeks, yielding a total of 30 treatment hours, exactly half of the higher dose. Although no published study tested this exact treatment delivery and dosage schedule, there are published studies showing benefits of CIMT with total dosages even <30 hours.^{4,35} The selection of the lower dosage also reflected our discussions with clinicians who reported that when they developed their own forms of CIMT, they increased the number of days per week they treated a child to be at least two times, and when possible three times per week, as well as offering sessions that lasted >1 hour. This lower dosage would be markedly less expensive and less burdensome for a family if it proves efficacious.

CIMT treatment activities

Treatment activities across all treatment groups are age-appropriate daily living and play-based activities (eg, puzzles, busy boards, ball play, finger feeding, turning

book pages, building activities, drinking from cups, grasping and manipulating everyday objects). Prior to treatment, the family and therapist identify primary treatment goals for each child and the types of activities the child enjoys, including age-appropriate self-help skills. During these activities, protocol-trained therapists use operant conditioning skills (eg, reinforcement, shaping, successive approximations, repetitive practice with variation) to promote increased movement and functional capabilities. Operant conditioning has been a signature feature of CIMT in both adults and children^{1,3} that applies reinforcement selectively to increase and then successively shape new behaviours. Note that this operant conditioning approach in individual sessions is far more systematic and differs markedly from many forms of modified CIMT that rely on group play activities and general principles of motor learning therapy while the child wears a form of constraint.

Objectives and hypotheses

Our primary objectives are to test the relative magnitude and types of effects associated with two constraint conditions (full-time casting vs part-time splinting) and two dosage levels (60 total treatment hours vs 30 treatment hours, both delivered over 4 weeks using the same form of individualised CIMT therapy). Practically, this necessitates conducting a four group treatment design that permits testing whether certain combinations of constraint and dosage yield significantly different outcome patterns. We also include a usual and customary treatment (UCT) group as a control to account for developmental changes and possible benefits from other forms of therapy children receive. The UCT group is monitored for both dose and type of treatment weekly, as reported by parents.

We hypothesise that both the type of constraint and the dosage level can exert significant effects on outcomes. The trial does not a priori favour one or the other of the protocol variations because reasonable hypotheses (as explained above) can be advanced for the different constraint and dosage conditions. Further, we are interested in whether the types and magnitude of short-term outcomes, if these obtain, will be maintained or change over time; and if so, whether these might vary as a function of the combination of constraint type and dosage level. For example, if the full-time cast combined with the higher dose were to produce significantly larger functional changes in the short term (ie, end of treatment), will children in this treatment group maintain this advantage over time at 6 and 12 months or even show increased levels of benefits later on? Alternatively, if the part-time splint is particularly beneficial in terms of short-term gains, perhaps particularly for bimanual activities, will this advantage appear in later post-treatment assessments? Or if children who receive the lower dose of CIMT show short-term gains equal to the higher dose group, will the groups retain these advantages—regardless of the constraint they received—equally at later post-treatment occasions?

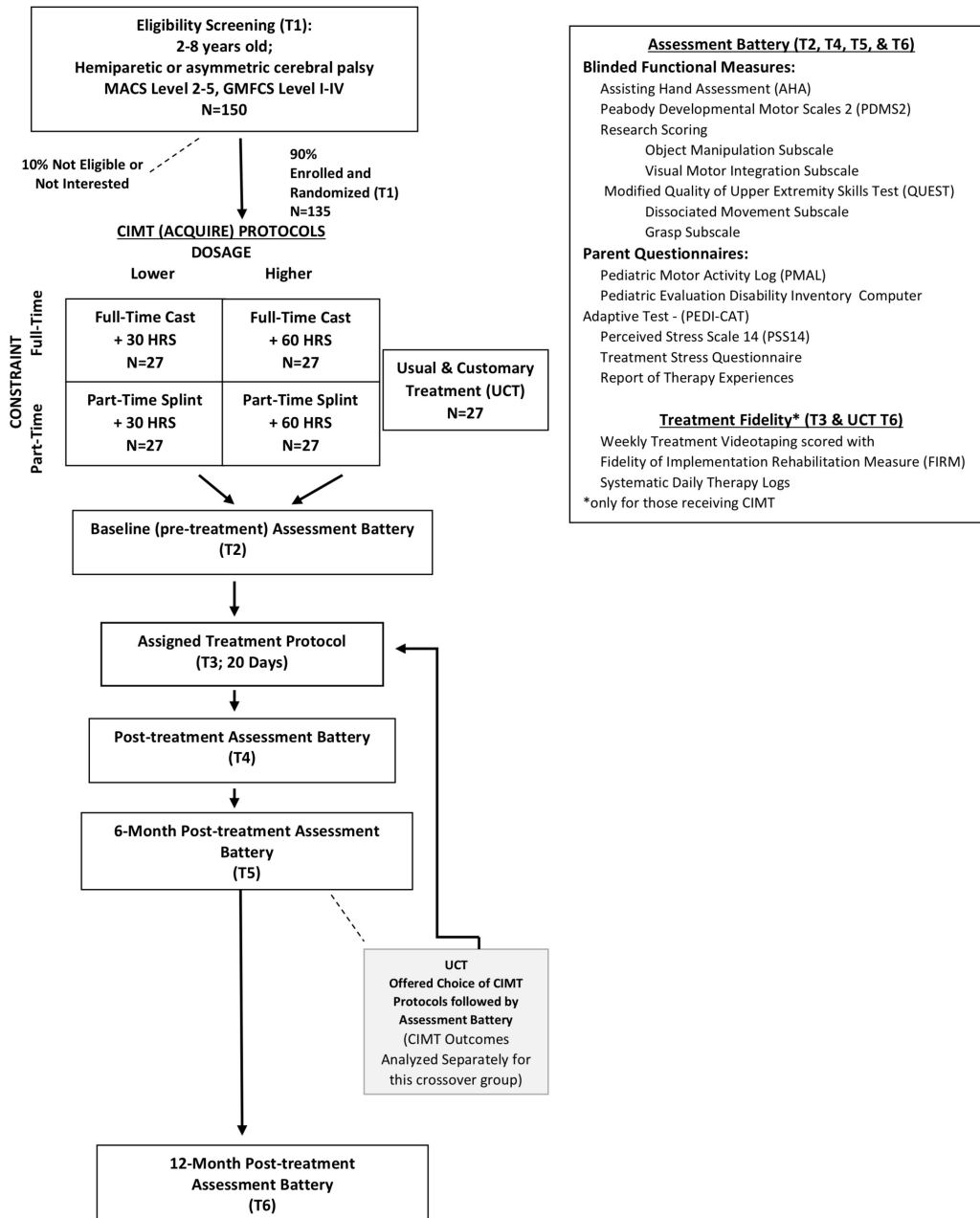


Figure 1 Design of the Children with Hemiparesis Arm and Movement Project comparative efficacy trial. CIMT, constraint-induced movement therapy; GMFCS, Gross Motor Functional Classification System; MACS, Manual Abilities Classification System.

Trial design

The study design is a multisite, RCT comparing the effects of two dosage levels of ACQUIREc (30 hours vs 60 hours of total treatment hours) and two types and duration of constraint (full-time casting vs part-time splinting). The 2×2 factorial design yields four CIMT groups. We also include a UCT group as a control condition. Subjects are thus randomised to one of five groups (four experimental and one control). **Figure 1** provides the overall trial design.

Methods and analysis

Participants

The study sample includes 135 children recruited at three treatment sites. At each site, a study coordinator recruits

families. After pre-screening, families are invited to learn more about the study and to provide written parental permission/informed consent adhering to the institutional review board-approved protocol reviewed at all participating universities.

Subject selection (inclusion/exclusion)

Children have a diagnosis of hemiparetic cerebral palsy; are between 2 and 8 years of age; do not have uncontrolled seizures and are medically stable. At enrolment, children have a Gross Motor Functional Classification System (GMFCS)³⁶ rating between I and IV; a Manual Abilities Classification System (MACS)³⁷ rating between II and V; and a Communication Functional Classification

System (CFCS)³⁸ rating between I and III. Children are excluded if they received botulinum toxin injections, stem cell infusions or a form of CIMT within the prior 6 months. Families agree to attend at least one complete therapy session per week with their child. Note that children may receive other forms of treatment or intervention during and after the tested CIMT intervention; data about such other interventions are collected prospectively from parents.

TREATMENT DESCRIPTIONS

Description of the CIMT treatment protocol

All proposed CIMT protocols are delivered by therapists who are licensed and registered paediatric occupational therapists and who have received intensive group and individualised instruction and supervision about the treatment protocol, informed largely by the ACQUIREc Therapy training manual. We monitor treatment delivery by collecting videotaped sessions each week for every child and then scoring randomly selected 15 min segments of these sessions to ensure adherence to the treatment protocol. The CHAMP team uses a standardised Fidelity of Implementation Measure (FIRM) that we developed for this trial. The FIRM has high kappa levels for inter-rater reliability=0.83.³⁹ We convene meetings via telephone and in-person so that therapists across the sites have an opportunity to discuss their clinical experiences and exchange ideas for treatment activities. Assessors and statisticians affiliated with the study never participate in these sessions.

Specifically, the four CIMT treatment groups provide the following essential ACQUIREc treatment elements in addition to general paediatric therapy ‘good practice’ (such as ensuring that therapy is age-appropriate, engaging and rewarding for the child and family).

Constraint: two conditions

For the full-time casting condition, a full-arm cast is applied with padding to the child’s non-involved upper extremity (UE). Immediately after casting, the therapist univalves the cast to allow for weekly removal and arm checks. The casting material is Delta Conformable casting tape, and it allows for the material to be slightly flexible (vs completely rigid) in the absence of multiple layers of the material. **Figures 2–4** (for which written permission to publish has been obtained) show steps in the formation of the cast. Stockinet and padding are applied over a cut strip. Multiple layers of the conformable material are placed under the elbow to keep the elbow in 90° flexion, and then the a single overlap of material is wrapped around the arm and hand from the axillary area to the end of the fingertips, the wrist and fingers are in a neutral position with thumb abducted. This single overlap makes the top of the cast less rigid and more ‘malleable’. Safety scissors are then used to follow the cut strip above the hand, forearm and upper arm to univalve the cast. This allows the cast to be taken on and off without have to



Figure 2 Construction of a full-arm cast (fingertips to axillary area, elbow at 90°).

create a new cast each week. After fabricating the cast, it is placed back on the child’s arm and hand, tape is applied across the valve and it is wrapped in colourful Coban. The child often enjoys choosing the colour. Parents are present during the process and are shown that the cast is held on only with tape and Coban, and that it is easily removable by them or others if needed. However, parents are told not to remove the cast on their own without contacting the therapist or study investigators to report any concerns, unless a perceived urgent reason emerges. The therapist removes the cast weekly to check and systematically report on skin integrity and to allow the use of the unimpaired upper extremity in range-of-motion and simple task activities.

For the part-time splinting condition, a resting hand splint with Velcro straps is used. This type of restraint limits hand function without limiting gross motor movements of the arm. In a resting hand splint, the fingers are held with the metacarpophalangeal (MCPs) in approximately 30° flexion and the wrist in neutral. The resting hand splint does not limit elbow movement. The constraint is easily removed and is used only during the therapy sessions. This form of resting splint is widely used



Figure 3 Cast is univalved immediately after construction for easy removal.



Figure 4 Image of constructed cast with self-adhesive wrap used to secure it on a child's arm.

in other types of therapy, and thus familiar to licensed and certified therapists.

Both types of constraint are in use for treatment days 1–17 for all CIMT groups. The total number of treatment days is 20; and the last three treatment days are intentionally conducted without any constraint to allow for task integration and bilateral arm use. The choice of 3 days for bilateral treatment was based on expert clinician feedback during the operation of a research clinic,²⁹ and this has been included in all of our CIMT protocols, since the first RCT published in 2004 by Taub *et al.*²² We include this period to help the child incorporate any new skills learnt during the CIMT protocol into daily life where both arms are free of constraint and can be used to complete bilateral and unilateral activities. We do not have empirical data to confirm the specific choice of 3 days, although children readily display transfer of new unimanual skills to the bilateral activities within 3 days. In theory, the ideal number of therapy days focused on explicit shaping of bilateral activities could vary depending on the CIMT protocol itself and/or the child's baseline level of engagement in bilateral activities. Future research could provide useful information about this issue of optimal number of days wearing constraint and engaging in transfer to bilateral activities.

Massed practice and shaping procedures at two dosage levels

The implementation of CIMT with regard to operant conditioning and massed practice is similar for all four CIMT groups. That is, the therapy activities are guided by principles of learning theory, in which the therapist learns how to engage the child in efforts to initiate, try, practice and refine a wide range of upper extremity skills and movements using varied reinforcement and informative feedback to the child—primarily verbal praise, smiles and supportive gestures, and also rewards such as the opportunity to engage in a favourite activity. The therapist then 'shapes' a movement or skill by increasing the behavioural demands for more precision, strength, fluency and/or

automaticity—a technique labelled 'successive approximations'.^{20 32 40} Therapists ask parents and children to identify favourite activities, reinforcers and personal goals for upper extremity skills to determine the content of activities sessions along with age-appropriate self-help skills. Over the 4 weeks of CIMT treatment, many new and novel activities are introduced, as well as returning to enjoyable activities, games and self-help skills used earlier in treatment.

Parent engagement and natural settings

Our ACQUIREc CIMT protocol is delivered one-on-one (one therapist to one patient) in naturalistic settings, primarily the children's homes with excursions into their surrounding neighbourhoods (eg, parks, shops), home-like rented apartments or hotel suites, or clinic-based home-like environments. We include parent involvement as a structured component as well for all four treatment groups. During treatment sessions that the parent attends, at least once a week, the therapist reviews the child's progress, identifies emerging skills and discusses current goals with the parents while the therapy is being delivered. The therapist also solicits feedback from the parent about his/her observations of the child's response to treatment thus far (sometimes this information exchange occurs in a private setting without the child present). In addition, the therapist maintains a systematic daily treatment log that includes documentation of the treatment goals and activities, the child's behaviour and response to treatment, any new skills emerging and any challenging events that occurred and how these are addressed. These are submitted and available for review and analysis in the study. Parents also maintain and submit a weekly log of activities, including any other therapies a child might receive, and complete assessments at each measurement time about the child's functional use of the upper extremities and other therapies received (dosage and type of treatment).

Description of UCT

Children in the UCT group will not receive any treatment services from us. These children will be followed as they continue to receive their previously prescribed therapeutic services. (In past trials, all enrolled children had received some form of ongoing community-based therapy related to their hemiparesis.) We will have all parents report therapy services their children receive at each assessment period. We anticipate that few or no children in CIMT groups will be receiving other traditional therapies such as occupational and physical therapy during their 4 weeks of receiving CIMT, but we do not formally preclude this. All parents report about any treatment services received, including type of treatment and dosage.

Allocation of interventions

A total of 45 children per site will be enrolled and randomly assigned to one of the five treatment groups. **Table 1** provides the sample size by group. Nine children

Table 1 Randomised controlled trial design for the Children with Hemiparesis Arm and Movement Project study

Constraint type	Part-time splint	Full-time cast	Usual and customary (control)
Constraint-induced movement therapy dosage	Site 1=9 Site 2=9	Site 1=9 Site 2=9	Site 1=9 Site 2=9
2.5 hours × 3 days per week × 4 weeks (total dosage=30 hours)	Site 3=9 n=27	Site 3=9 n=27	Site 3=9 n=27
3 hours × 5 days per week × 4 weeks (total dosage=60 hours)	Site 1=9 Site 2=9 Site 3=9 n=27	Site 1=9 Site 2=9 Site 3=9 n=27	

per site (total n=27) will receive each of the CIMT treatment conditions. The randomisation process will be derived from a probability sampling process developed by the study statistician prior to the study and will be centralised and masked. Local sites receive individual treatment assignment after the parents have granted informed consent.

Outcomes

Blinded assessors, trained for this clinical trial and certified as needed for assessment tools, will evaluate children in all five groups at pre-treatment (baseline), immediate post-treatment and 6 months post-treatment. For children in the UCT group, their parents may select one of the four CIMT treatments after the 6-month follow-up.

When they are crossed over to receive CIMT, they also be assessed post-treatment at 6 and 12 months. For the original CIMT treatment groups, the children will be assessed again at 12 months, adhering to the same assessment conditions and using the same tools. Table 2 provides a list of all assessments.

Sample size

We powered the study based on our previous dose comparison study. Using pre-treatment Assisting Hand Assessment (AHA) scores as a covariate, these children obtained a residual SD of AHA scores equal to 5.78 at 30 days post CIMT. Using an 80% power estimation, and an alpha level of <0.05, we estimated 24 children per cell would be required to distinguish between CIMT protocols

Table 2 Assessment battery for the Children with Hemiparesis Arm and Movement Project comparative efficacy trial

	Age range	Purpose	Description and testing time	Format/scoring
Impairment/functional measure (all conducted blind)				
Assisting Hand Assessment 5.0 (Krumlinde-Sundholm, Holmefur, Eliasson, 2003)	18 months to 12 years.	Measures ability of the involved arm and hand to assist bimanual hand activities.	Semistructured play with specific play items, videotaped for later scoring. Time: 10–15 min.	22 items scored on a 4-point rating scale (scored by certified assessors).
Modified Peabody Developmental Motor Scales 2 (Folio and Fewell, 2001)—Visual Motor Integration and Object Manipulation Subscales	Birth to 5 years. Adaptation for use with older children allowed for research purposes.	Assesses both qualitative and quantitative aspects of gross and fine motor development.	Semistructured play with specific play items, videotaped for later scoring. Time: 20–30 min.	Gross and fine motor skills scored qualitatively at assessment time. Composite plus gross and fine motor score created.
Revised Quality of Upper Extremity Skills Test ²³ Law, Russell, Pollock, Rosenbaum, Walter, DeMatteo, 1991	18 months to 8 years (used previously to age 10 for this clinical population).	Evaluates movement patterns and hand function in children with cerebral palsy.	Assesses upper extremity dissociated movements, protective extension, weight bearing and grasp. Time: 20 min.	The revised protocol uses 27 of 36 items (protective extension eliminated due to low reliability). A percentage total and subscale scores are calculated.
Parental report (not blinded)				
Pediatric Motor Activity Log ²² Taub, DeLuca, Echols, Ramey, 2004	2–8+ years.	Parent ratings of frequency and quality of movement in everyday tasks.	Parent completes ratings for movements in 22 arm-hand functional tasks. Time: 10 min.	Frequency and quality of movement ratings (from 0, low, to 5, high) regarding use of impaired arm/hand. Will be administered only at baseline, 6 and 12 months.
Pediatric Evaluation and Disability Inventory (Hayley, Coster, Ludlow, Dumas, Fragal-Pinkham, and Mowed, 2012)	6 months to 21 years.	Assesses self-care, mobility, social function and responsibility.	Parent completes ratings via computer format.	Computer-adapted scoring. Scaled scores.
Parent Stress Perceived Stress Scale (Cohen, Kamarck, Mermelstein, 1983) and a study-specific questionnaire	Adult ages.	Assessment of parent stress related to therapy and their child with cerebral palsy.	Parent complete mailed written survey and return by mail.	Scores by section; summary and section raw scores.

if they exist. Twenty-seven children per group allows for as much as 10% attrition. We did not have available PDMS-2 or Quality of Upper Extremity Skills Test (QUEST) data to permit use for sample size).

Statistical methods and data analysis plan

Two-way analysis of covariance (ANCOVA) will be used to test for main effects and interactions between constraint types and dosage levels, using baseline scores of our primary outcome measure—the AHA—as a co-variate. Subsequent analyses will include baseline characteristics of the subjects, such as age, gender and severity levels indexed by GMFCS and MACS levels, in ANCOVA models. In all cases, standard diagnostic methods will be used to check the normality and constant variance assumptions underlying the use of ANCOVA. We will consider transformations of the response variable if the assumptions are not met. This generalised ANCOVA model for assessing statistical significance of outcomes will be applied in conducting the other primary and secondary outcomes as well. Adjustments will be made for multiple comparisons.

Only one of the primary outcome measures has recommended guidelines about what comprises a clinically meaningful level of improvement; namely, the AHA for which the test authors recommend that a 5-point gain on Logit scores represents a practically useful change. We will thus analyse outcomes for the AHA using this threshold and compare the percentage in each treatment group that achieves or exceeds this threshold level. In the event that research provides new recommendations about clinically meaningful or minimal detectable changes for other tools, these new standards will be used in data analyses and reporting of trial results.

Data monitoring

A Data Safety and Monitoring Committee (DSMC) has been established to monitor the CHAMP study throughout its implementation. The DSMC comprises individuals who are not directly related to the study but who are knowledgeable about the field and topics and RCTs. The DSMC composition includes two occupational therapists, a paediatric psychiatrist and a non-voting statistician (non-voting because this person will be familiar with all aspects of the study, including data collection and analysis). The charge of this committee is to monitor all study procedures and advise actions when appropriate for various events during the study process. The DSMC plan adheres to all National Institutes of Health (NIH) recommendations.⁴¹ This group is given access to all study protocols and relevant background literature. They are not given specific participant identifiers unless a serious adverse event occurs and it is deemed necessary. They also are given access to interim and full data analyses for the five treatment groups.

Patient and public involvement

The research questions and outcome measures have been informed by our prior RCTs and our clinical

implementation of the paediatric CIMT protocol known as ACQUIREc.²⁰ Patients and the public did not directly contribute to the design or choice of measures. The trial results will be disseminated to study participants and to parent advocacy as well as professional organisations. Adhering to NIH policy, the data generated by CHAMP will enter the public domain (with appropriate privacy and human subjects protections in place) after major study analyses have been completed.

ETHICS AND DISSEMINATION

Research ethics approval

The Institutional Review Board at all three clinical sites reviewed and approved the study protocol. They include the following: The Virginia Tech IRB, The University of Virginia IRB and The Ohio State University IRB. The same procedures are followed at all three sites for protection of human subjects.

Consent

All participants and guardians are completely informed about all study procedures both verbally and in written format. They also are informed that they can withdraw their consent for participation at any time during the protocol with no penalty whatsoever. They are informed about the process for randomisation to treatment groups, the study design and each of the treatment groups and potential risks and benefits of participation. Parental permission comprises informed consent (see Parental Permission-Informed consent.pdf in online supplementary file) for this age paediatric population; documentation is provided in writing and a detailed discussion occurs between the research team member and the potential participants and guardians to ensure all components of the protocol treatment and assessment processes are clearly understood. For children who are old enough to provide assent (7 years and above), we also seek their assent prior to inclusion in the study and we document this.

The principal investigator at each clinical site oversees the process of obtaining informed consent, but the actual documentation and signing of the consent may be completed by other trained members of the study team. Each site has a detailed written protocol for enrolment and informed consent; there is a common and detailed study protocol and manual of procedures for CHAMP.

Confidentiality

Each clinical site maintains securely stored master files with all participants at their site that include all collected data, with separate maintenance of any identifiers. Each participant is assigned a study code during the enrolment process. This code is used on all material after screening and is not associated with group assignment. All data are kept in secured physical and computed-based files with identifying data removed. When data are transmitted to

the data compilation and analysis sites, the means used are highly secured and preapproved by each IRB.

Declaration of interests

None of the investigators or team members has a financial or other conflict of interest in any aspect of the study.

Ancillary and post-trial care

We monitor the types and dosage of ancillary and post-trial care that all children receive, primarily so these data can be considered in interpreting long-term outcomes and individual differences in treatment responsiveness. We do not offer any additional direct care as part of the trial. We do, however, offer treatment options to those in the UCT group (see description below under ethical concerns) after they have completed the 6 months post-treatment assessment (T5).

Ethical concerns

Because we anticipate that one or more of the four CIMT treatment groups may produce significant functional benefits compared with the UCT control group, the study offers a voluntary option to parents in the UCT group to choose for their child one of the four CIMT treatments (parent-selected) after their child has received the blinded 6-month follow-up assessment. We offer this after 6 months rather than 12 months to try to minimise study attrition, and based on prior evidence that almost all forms of UCT for this patient population do not produce significant benefits. We will document via parental report all additional therapies enrolled children receive during their involvement with the CHAMP Study. Beyond the inclusion criteria we believe it would be unethical to ask parents to refrain from seeking other services or treatment for their children; by carefully monitoring this in the 6 and 12 months post treatment, we will be to conduct exploratory analyses if sufficient variation exists in what parents obtain for the children after the ACQUIREC CIMT treatment in this trial.

Dissemination policy

The results of the CHAMP Study will be presented in peer-reviewed scientific and clinical journals as well as at major professional meetings. Consistent with NIH policy, the deidentified data will be stored and become available for future analyses after the primary planned analyses are completed. Results also will be disseminated to parent and advocacy groups and to organisations that set standard-of-care practices for this patient population.

Summary

The CHAMP comparative efficacy trial is a multifactorial, multisite clinical trial funded by NIH. CHAMP uses an RCT design with blinded primary assessments to provide rigorous objective data, complemented by secondary parent and therapist subjective data, regarding the effects of the type of constraint and the dosage (in various combinations) on functional outcomes of different CIMT protocols. Adverse events will be reported and evaluated.

The study is adequately powered and will help to resolve two of pressing unanswered and controversial issues about the selection and delivery of a CIMT protocol to children between 2 and 8 years of age with a diagnosis of unilateral or hemiparetic cerebral palsy. The 12-month follow-up period also helps fill a gap in the research knowledge base about longer-term effects of a traditional or signature form CIMT. The CHAMP trial dataset will be released for public use at a later date.

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