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A randomised controlled trial to compare two methods of constraint-induced movement therapy to improve functional ability in the affected upper limb in pre-school children with hemiplegic cerebral palsy:

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A randomised controlled trial to compare two methods of constraint-induced movement therapy to improve functional ability in the affected upper limb in pre-school children with hemiplegic cerebral palsy CATCH TRIAL.

Journal:	<i>Clinical Rehabilitation</i>
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Complete List of Authors:	Christmas, Pauline; 1Birmingham Community Healthcare NHS Foundation Trust, Children and Families Directorate, Paediatric Physiotherapist Sackley, Catherine; King's College London School of Medical Education, Physiotherapy Feltham, Max; University of Birmingham, Birmingham Clinical Trials Unit Cummins, Carole; University of Birmingham, Institute of Applied Health Research
Keywords:	Hemiplegia cerebral palsy, Upper limb rehabilitation, Therapy, Randomised controlled trial, Constraint induced movement therapy
Abstract:	<p>Objective To determine the feasibility and short-term efficacy of caregiver-directed constraint induced movement therapy to improve upper limb function in young children with hemiplegic cerebral palsy.</p> <p>Design Randomised controlled trial with masked assessment</p> <p>Setting Community paediatric therapy services</p> <p>Subjects Preschool children with hemiplegic cerebral palsy</p> <p>Interventions Caregiver-directed constraint induced movement therapy administered using either 24-hour short-arm restraint device (prolonged) or intermittent holding restraint during therapy (manual).</p> <p>Main measures Primary: Assisting Hand Assessment (AHA) at ten weeks. Secondary: adverse events, Quality of Upper Extremity Skills Test, Pediatric Quality of Life Inventory. Feasibility: recruitment, retention, data completeness, adherence.</p> <p>Results 62/81 (72%) of eligible patients in 16 centres were randomised (prolonged restraint n=30; manual restraint n=32) with 97% retention at 10 weeks. The mean change at ten weeks on the AHA logit-based 0-100 unit was 9.0 (95% CI: 5.7, 12.4, p<0.001) for prolonged restraint and 5.3 (95% CI:</p>

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	<p>1.3, 9.4, $p=0.01$) for manual restraint with a mean group difference of 3.7 (95% CI: -1.5, 8.8, $p=0.156$) (AHA smallest detectable difference=5 units). No serious related adverse events were reported. There were no differences in secondary outcomes. More daily therapy was delivered with prolonged restraint (60 versus 30 minutes; $p<.001$). AHA data were complete at baseline and 10 weeks.</p> <p>Conclusions Caregiver-directed constraint induced movement therapy is feasible and associated with improvement in upper limb function at 10 weeks. More therapy was delivered with prolonged than with manual restraint, warranting further testing of this intervention in a longer term trial.</p>

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For Peer Review

1
2
3 **Abstract** (245 words)
4

5 **Objective**
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7 To determine the feasibility and short-term efficacy of caregiver-directed constraint
8 induced movement therapy to improve upper limb function in young children with
9 hemiplegic cerebral palsy.
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14 **Design**
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16 Randomised controlled trial with masked assessment
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19 **Setting**
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21 Community paediatric therapy services
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24 **Subjects**
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26 Preschool children with hemiplegic cerebral palsy
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29 **Interventions**
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31 Caregiver-directed constraint induced movement therapy administered using either a
32 24-hour short-arm restraint device (prolonged) or intermittent holding restraint during
33 therapy (manual).
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38 **Main measures**
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40 Primary: Assisting Hand Assessment (AHA) at ten weeks. Secondary: adverse events,
41 Quality of Upper Extremity Skills Test, Pediatric Quality of Life Inventory. Feasibility:
42 recruitment, retention, data completeness, adherence.
43
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45
46

47 **Results**
48

49 62/81 (72%) of eligible patients in 16 centres were randomised (prolonged restraint
50 n=30; manual restraint n=32) with 97% retention at 10 weeks. The mean change at ten
51 weeks on the AHA logit-based 0-100 unit was 9.0 (95% CI: 5.7, 12.4, p<0.001) for
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3 prolonged restraint and 5.3 (95% CI: 1.3, 9.4, $p=0.01$) for manual restraint with a mean
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5 group difference of 3.7 (95% CI: -1.5, 8.8, $p=0.156$) (AHA smallest detectable
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8
9 differences in secondary outcomes. More daily therapy was delivered with prolonged
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11 restraint (60 versus 30 minutes; $p<.001$). AHA data were complete at baseline and 10
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13 weeks.
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16 **Conclusions**

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19 Caregiver-directed constraint induced movement therapy is feasible and was associated
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21 with improvement in upper limb function at 10 weeks. More therapy was delivered with
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23 prolonged restraint and a longer term trial with a no constraint therapy control is
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25 warranted.
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Abstract (245 words)**Objective**

To determine the feasibility and short-term efficacy of caregiver-directed constraint induced movement therapy to improve upper limb function in young children with hemiplegic cerebral palsy.

Design

Randomised controlled trial with masked assessment

Setting

Community paediatric therapy services

Subjects

Preschool children with hemiplegic cerebral palsy

Interventions

Caregiver-directed constraint induced movement therapy administered using either 24-hour short-arm restraint device (prolonged) or intermittent holding restraint during therapy (manual).

Main measures

Primary: Assisting Hand Assessment (AHA) at ten weeks. Secondary: adverse events, Quality of Upper Extremity Skills Test, Pediatric Quality of Life Inventory. Feasibility: recruitment, retention, data completeness, adherence.

Results

62/81 (72%) of eligible patients in 16 centres were randomised (prolonged restraint n=30; manual restraint n=32) with 97% retention at 10 weeks. The mean change at ten weeks on the AHA logit-based 0-100 unit was 9.0 (95% CI: 5.7, 12.4, p<0.001) for

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13 weeks.
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16 17 **Conclusions**

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19 Caregiver-directed constraint induced movement therapy is feasible and associated with
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21 improvement in upper limb function at 10 weeks. More therapy was delivered with
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23 prolonged than with manual restraint, warranting further testing of this intervention in a
24
25 longer term trial.
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33 **Key words**

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35 Hemiplegic cerebral palsy, constraint induced movement therapy, upper limb
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37 rehabilitation, therapy, randomised controlled trial
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Introduction

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Around a third of children with cerebral palsy present with hemiplegic cerebral palsy.¹ Upper limb spasticity, weakness, dystonia² and sensory deficits³ are commonly seen and can lead to poor grasp⁴ and poor object release.⁵ Children favour their unaffected limb, amplifying the problem,⁶ and require long term family, healthcare and social support.⁷

Interventions to improve the use of the impaired limb are an important component of a rehabilitation programme but high quality evidence is lacking.^{8,9} Constraint induced movement therapy aims to overcome non-use of the affected limb through movement restriction of the unaffected upper limb and intense training of the affected upper limb.^{10,11} A Cochrane systematic review¹² concluded that it was a promising therapeutic approach for children with hemiplegic cerebral palsy.

Studies to date have lacked systematic comparison of the critical variables including: type of restraint (full-arm cast to gentle parental holding), duration of restraint (1-24 hours per day) and intervention duration (one hour therapy per week to seven hours per day).^{13,14}

Caregiver-directed rehabilitation is an important component of therapy in the National Health Service (NHS) enabling increased dose. A number of studies have explored the effect of care-giver directed constraint induced movement therapy¹⁵⁻¹⁷. This approach has advantages especially in terms of therapy resources and improvement

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3 demonstrated in bimanual function but two of the studies reported high (30%) dropout
4 rates^{16,17} and another stated that although most parents (96%) found it worthwhile many
5
6 (75%) had some difficulty with implementation.¹⁵
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12 We explored the short-term efficacy of a novel caregiver-directed prolonged constraint
13 induced movement therapy intervention, comparing it with intermittent manual constraint
14 induced movement therapy which is sometimes used in current NHS practice. Based on
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16 clinical experience and parent consultation, the latter was considered unlikely to be
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18 effective in this clinical context and therefore suitable as a control intervention. The
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20 interventions were delivered within usual NHS community paediatric therapy services.
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26 The study also tests the feasibility of multicentre trials in this population and setting.
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30 31 **Methods**

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33 This parallel-group, randomised, controlled trial with blinded assessment was conducted
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35 in NHS community paediatric therapy services. A favourable opinion was received from
36
37 the South Birmingham Research Ethics Committee (ref: 10/H1207/36). It was
38
39 sponsored by the University of Birmingham and registered with International Standard
40
41 Randomised Controlled Trial Number (58484608). The study was funded by a West
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43 Midlands Strategic Health Authority Clinical Academic Doctorate Fellowship awarded to
44
45 Pauline Christmas (PC) and the Nancie Finnie Cerebral Palsy Charity. Two centres
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47 were recruited directly by the investigator and the others after national publicity via
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49 professional networks. Site physiotherapists or occupational therapists were
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3 experienced in treating children with cerebral palsy and received a two-hour face-to-
4 face training session on the trial protocol.
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10 Eligible children were identified from treatment databases of participating NHS services
11 by their therapist. The therapist approached the parents and, if interested, the parent
12 and child attended a face-to-face session. The treatment options and treatment
13 allocation were discussed and the parent received an information sheet. Support from
14 an interpreter was provided if required. Parents had at least 24 hours before giving
15 informed consent.
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26 Children with a diagnosis of hemiplegic cerebral palsy irrespective of cognitive
27 impairment aged between 18 months and four years were eligible. Exclusion criteria
28 were patients presenting with a contra-indication to the intervention such as a skin
29 condition that prohibited the use of a persistent immobilisation device, and patients must
30 not have received an episode of prolonged constraint induced movement therapy
31 lasting two weeks or more in the previous six months.
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42 Following informed consent and the baseline assessment the site therapist telephoned
43 the Primary Care Clinical Research and Trials Unit at the University of Birmingham for
44 randomisation. The Unit was independent of the research team ensuring concealed
45 allocation. A balanced blocked randomisation schedule stratified by centre (nQuery
46 Advisor 7.0, Statistical Solutions, USA) generated by a statistician was used.
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3 Outcomes were measured at baseline, immediately post intervention at ten weeks and
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5 at the 24-week follow-up. Baseline and ten-week assessments were conducted at the
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7 usual therapy location during a face-to-face visit by PC who was blind to patient
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9 allocation and the site therapist. The 24-week follow-up was conducted through postal
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11 questionnaires.
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17 The primary outcome measure was bimanual performance of the affected upper limb
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19 measured using the Assisting Hand Assessment^{18,19} assessed at baseline and at the
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21 ten-week assessment by PC, an accredited assessor. The child took part in a 15 minute
22
23 semi-structured video-recorded play session. This was scored on a 22-item schedule
24
25 divided into general usage (3 items), arm use (4 items), grasp-release (7 items), fine
26
27 motor adjustment (3 items) coordination (2 items) and pace (3 items) using a 4-point
28
29 criterion referenced rating scale (1-4) for each item with higher scores indicating better
30
31 function. Total scores were reported using a logit-based 0-100 unit scale. The smallest
32
33 detectable difference of the Assisting Hand Assessment is 5 logit-0-100 units.²⁰
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40 Secondary outcome measures were:

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42 • Upper limb quality of movement assessed using the Quality of Upper Extremity
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44 Skills Test^{21,22} at baseline and ten weeks to evaluate benefit to the affected upper
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46 limb and possible harm to the unaffected upper limb through immobilisation.
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- 49 • The Paediatric Quality of life Inventory 4.0 Generic Core Scales²³ was combined
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51 with the Paediatric Quality of life Inventory 3.0 Cerebral Palsy Module²⁴ for
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53 children aged two years or more was used at baseline, the ten-week and 24-
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3 week assessment. The Paediatric Quality of life Inventory Infant Scale²⁵ was
4
5 administered for children who were younger than two years.
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- 7 • The Birmingham Bimanual Questionnaire is a trial specific, parent reported
8 measure to assess pre-requisites for bimanual function and bimanual tasks in
9 the affected upper limb. It was included at baseline, the ten and 24-week
10 assessment. (See Appendix 1, Figure 2).
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19 Adverse events were recorded by the therapists following weekly contacts with
20 caregivers, reported to the trial team and were reviewed clinically by a consultant
21 paediatrician.
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28 Feasibility was assessed on: recruitment numbers; recruitment rate from eligible
29 families recorded on screening logs; retention; completeness of outcome measure data;
30 the child's cooperation with restraint; and amount of therapy delivered. The amount of
31 prescribed therapy delivered and child's cooperation was recorded by the caregivers in
32 a daily diary and through a weekly face-to-face or telephone questionnaire administered
33 by the site therapist. The responses were collected on a five point Likert scale. For the
34 therapy dose when asked how many of the 60 minutes were completed they could
35 respond: "hardly at all" (=1), "less than 30 minutes" (=2), "for 30 minutes" (=3), "nearly
36 60 minutes" (=4) and "all 60 minutes" (=5) and for the child's cooperation the responses
37 included: "never" (=1), "seldom" (=2), "about half the time" (=3), "usually" (=4), "always"
38 (=5).
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3 Safeguards were put in place to maintain blinding of the assessor because families and
4 therapists could not be blinded to group allocation^{26 27}. These included: reminder to
5 parents not to discuss group allocation in front of the trial assessor; research notes kept
6 in a locked filing cabinet; adverse events reported to the trial coordinator rather than the
7 principal investigator; data analysis commencing after the trial database was locked;
8 reminder on the trial assessor's mobile phone and email not to disclose group
9 allocation. Inadvertent un-blinding was recorded on the trial database.
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21 The caregiver-directed constraint induced movement therapy interventions used either a
22 24-hour short-arm device (prolonged) method of restraint applied by the therapist or
23 hand-over-hand holding of the unaffected upper limb (manual)²⁸ carried out
24 intermittently through the day (Table 1), by the caregiver. Training on the allocated
25 restraint for the caregiver was conducted by the site therapist during an initial face-to-
26 face session with fortnightly face-to-face and weekly telephone contact although
27 caregivers could telephone in-between.
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40 In both groups therapy was administered for one hour each day in the child's usual
41 setting by caregivers (parents and pre-school workers) for six weeks (three blocks of
42 two weeks) interspersed with two weeks of rest to promote adherence and reduce the
43 potential for adverse events. Intervention period timing was flexible to fit with family life
44 but was completed within ten weeks.
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3 The interventions aimed to promote mass practice of the affected upper limb to improve
4 grasp, release, reaching, in-hand manipulation and use as an assisting hand during
5 bimanual activity. The practice was embedded in the context of functional tasks or usual
6 child-friendly play for a total of one hour, which could be divided to fit with the child's
7 usual routine. To encourage participation, the activity aimed to be enjoyable with
8 substantial verbal encouragement and praise. If the therapist found there were no toys
9 available a small number of suitable toys were provided. The instructions are outlined in
10 Appendix 2.3. The amount of prescribed therapy delivered and the child's cooperation
11 was recorded by the caregivers in a daily diary and through a weekly face-to-face or
12 telephone questionnaire administered by the site therapist.
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28 The sample size calculation was based on 90% power in a two sample t-test to
29 compare change in outcome from baseline between the groups with α set to 0.05.
30 Eliasson and colleagues²⁹ conducted a study of constraint induced movement therapy
31 in young children with hemiplegic cerebral palsy using the Assisting Hand Assessment
32 as the primary outcome measure. The treatment effect was 1.16 at the end of the
33 therapy period (two months) and demonstration of a similar short term effect would
34 justify a larger multi-centre trial. Given these assumptions, twenty-three participants in
35 each group would detect an effect size of 1.0 following treatment between groups.
36 Participant retention was estimated at 70%, which gave a total sample size of 60
37 participants.
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3 An intention-to-treat analysis was conducted. A between-group comparison of the
4 primary and secondary outcomes and mean change were computed at each time point.
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6 Interval data were analysed with independent t-tests and categorical data with the chi-
7 squared test. Within group comparison at baseline and ten-week assessments was
8 made using dependent t-tests. Effect sizes were calculated where appropriate. Non-
9 parametric tests were used where parametric assumptions were not met.
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19 The responses and scores in the daily diaries and weekly questionnaires were analysed
20 with descriptive statistics. The median and interquartile ranges were calculated from the
21 daily diaries and weekly questionnaires for therapy dose and cooperation of the child
22 after the missing responses had been removed. Alpha-level was set at 0.05 for all
23 statistical analyses, which were conducted using a statistical software package (SPSS
24 version 20, IBM Corporation, Armonk, New York).
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35 **Results**

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37 Sixteen community paediatric therapy services across England and Wales recruited 62
38 out of 81 eligible participants (76%) between June 2010 and January 2012 (See Flow
39 diagram, Figure 1). Reasons for declining participation were child's behaviour (n=2),
40 child's independence (n=2), child's health (n=3), attendance at an educational
41 placement (n=2), health care and other commitments (n=2), did not want intervention
42 (n=2), did not want to participate in research (n=1). Five parents gave no explanation.
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51 The first and largest centre set up before further centres were recruited following
52 national advertising recruited 19 out of the centre's 21 eligible patients. The remainder
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3 of centres recruited between one and four patients, after inviting between one and
4 seven. Reasons for declining participation were child's behaviour (n=2), child's
5 independence (n=2), child's health (n=3), attendance at an educational placement
6 (n=2), health care and other commitments (n=2), did not want intervention (n=2), did not
7 want to participate in research (n=1). Five parents gave no explanation. No patients met
8 the exclusion criteria. Data were collected from all participants at all time points except
9 from two at the ten-week assessment and three at 24-weeks. Baseline information
10 across groups showed some imbalance for age (Table 2).
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22 Outcome measures were well completed with no missing data for the Assisting Hand
23 Assessment. The Quality of Upper Extremity Skills Test was 89% (55/62) complete at
24 baseline and 91% (55/60) at ten weeks. The Paediatric Quality of life Inventory in
25 combination with the Cerebral Palsy module was returned for 96% (49/51) at baseline
26 and 94% (48/51) at the ten and 24- week assessments. The Paediatric Quality of life
27 Inventory infant scale was 100% (11/11) complete at all time points. The Birmingham
28 Bimanual Questionnaire response was 81% (50/62) at baseline, 97% (60/62) at ten-
29 weeks and 95% (59/62) at 24-weeks. There was a 94% (58/62) response rate for the
30 diaries and 87% (54/62) for the parent questionnaires. The assessor was aware of
31 group allocation for only 8% (5/62) of the participants.
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49 The mean change in bimanual performance between groups measured with the
50 Assisting Hand Assessment logit-based 0-100 unit from baseline following the ten-week
51 intervention was 9.0 (95% CI: 5.7, 12.4, $p < .001$) units for prolonged restraint and 5.3
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3 (95% CI: 1.3, 9.4, $p=.01$) units for manual restraint with a mean group difference of 3.7
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5 (95% CI: -1.5, 8.8, $p=.156$) units (Table 3).
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10 Upper limb function of the upper limbs measured with the Quality of Upper Extremity
11 Skills Test at ten weeks was similar to baseline for both groups (see Table 3 for total
12 scores and Appendix 1 Table 4 for the Quality of Upper Extremity Skills Test subgroup
13 scores and Appendix 1 Table 4 for the Quality of Upper Extremity Skills Test subgroup
14 scores).
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21 There was no significant between group differences for children aged two years and
22 above at baseline or in change from baseline to the ten or 24-week assessment on the
23 Paediatric Quality of life Inventory Generic Core Scale and Paediatric Quality of life
24 Inventory Cerebral Palsy Module. Nor were there differences for younger children (less
25 than two years) in change from baseline to ten-week assessment or from ten to the 24-
26 week assessment on the Paediatric Quality of life Inventory Infant Scale. There was a
27 significant difference in the mean change from baseline to the 24-week assessment on
28 the Paediatric Quality of life Inventory Infant Scale (6.9; 95% CI: 2.8, 11.1; $p=0.006$) with
29 a greater mean deterioration observed in the manual restraint group (-9.4; SD: 3.2)
30 compared to the prolonged restraint group (-2.5; SD: 1.6) (Appendix I Tables 5-7 and 9-
31 11).
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49 There was a statistically significant improvement in motor skills measured on the
50 Birmingham Bimanual Questionnaire in the prolonged restraint group compared to the
51 manual restraint group at ten weeks, 16.9 (95% CI: 2.9, 30.9, $p=.019$). This was not
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3 sustained at 24 weeks, 1.1 (95% CI: -12.5, 14.6, $p=.873$). (Appendix 1: Tables 8 and
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5 12).

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10 Three serious adverse events were reported in the prolonged restraint group (hospital
11 admission for flu induced wheeze, accident and emergency attendances for chest
12 infection and a total body rash) and one in the manual restraint group (hospital
13 admission following a fit): these were considered unrelated to the interventions. Of the
14
15 15 non-serious adverse events, 12 were considered to be related to the prolonged
16 restraint including two children who had minor bruising because of a fall and ten with
17 small areas of skin abrasions. The three remaining non-serious adverse events in the
18 prolonged restraint group were not considered related to the intervention. See Appendix
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20 1, Table 13.

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33 The median therapy dose reported by parents (data available for 54 out of 62 patients)
34 was significantly greater ($p<0.001$) in the prolonged restraint group (4.2; IQR: 0.9)
35 compared to the manual restraint group (3.6, IQR: 1.3). Children (response: 53/62) were
36 more cooperative in the prolonged restraint group (4.7, IQR: 1.0) than in the manual
37 restraint group (3.0; IQR: 1.7) ($p<0.001$).

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47 An exploratory regression analysis was carried out with the logit-based 0-100 AHA-unit
48 scale at the ten-week assessment as the dependent variable. Group allocation,
49 participant age, baseline clinical presentation (measured with QUEST and the AHA),
50 amount of therapy delivered and co-operation with the restraint of the delivered
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3 intervention were the independent variables in the model: none made statistically
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5 significant contributions to the model.
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10 **Discussion**

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12 Bimanual performance of children with hemiplegic cerebral palsy after 10 weeks of
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14 therapy was similar in the two groups of children using different methods of constraint
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16 induced movement therapy. Both groups improved by more than the minimal detectable
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18 difference on the Assisting Hand Assessment but the threshold for clinically significant
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20 improvement on this measure is unclear. Reported adherence was good. Children were
21
22 more cooperative and received a higher therapy dose with prolonged restraint but
23
24 adherence was better than expected in the manual restraint group, reducing the
25
26 difference between the groups . Recruitment in the NHS community setting was
27
28 feasible, although more sites than anticipated were needed as there were fewer eligible
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30 patients below the age for UK compulsory education than expected. There was
31
32 excellent follow-up of more than 95% at ten and 24 weeks with satisfactory data
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34 completion. Broad inclusion criteria enhanced generalisability.
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42 The improvement in bimanual performance at ten weeks irrespective of the type of
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44 restraint applied is consistent with a previous Cochrane systematic review¹² and further
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46 studies^{13,14}. Previous meta-analysis in neurological rehabilitation have emphasised the
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48 importance of dose^{30,31} and in our study the care-giver directed prolonged restraint
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50 method was associated with a greater dose than manual restraint. As with other studies
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52 using a prolonged restraint approach, there was minimal reporting of adverse
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3 events.^{32,33,34}
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6 In contrast to previous studies of care-giver directed constraint therapy^{16,17}, there was
7 excellent adherence and follow-up rates with both intermittent manual holding and
8 prolonged restraint with a short-arm device left in situ. A novel aspect of the prolonged
9 restraint protocol was that caregivers administered only the mass practice with
10 application and removal of the restraint being carried out by the therapist. This may
11 have reduced the burden on parents, increasing acceptability and improving adherence.
12 As prolonged restraint was associated with delivery of more therapy and is acceptable
13 to parents, it is our preferred method in further effectiveness research.
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26 The trial has some limitations. Only caregiver reported assessment of adherence to
27 treatment was possible. Although masking was largely successful, the assessor was
28 aware of group allocation for 8% of the participants at the ten-week assessment.
29 Resource constraints meant the trial was powered to evaluate 10 week not longer term
30 outcomes.
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We have shown in multiple centres that constraint induced movement therapy can be
successfully administered in NHS community paediatric therapy services with caregiver-
directed therapy. Our study suggests prolonged restraint results in more intense therapy
and can be used safely. Children in the prolonged restraint group had more risk of skin
abrasions: this risk was managed by using a short easily removable padded device that
allowed some protective extension. Parents were advised to give more supervision on
the stairs and in situations where the child's balance was challenged. All adverse events
resolved quickly. Minor bruising from falls and skin abrasions are common in this age

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3 group and may have occurred in the intermittent holding group but not have been
4 reported. There was no difference in function of the immobilized limb at ten weeks
5 suggesting no harm from restraint.
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11 This is one of the largest randomised controlled trials conducted to investigate
12 constraint induced movement therapy in young children with hemiplegic cerebral palsy:
13 we are not aware of other multicentre pragmatic community based randomised
14 controlled trials. An adequately powered trial with longer term, blinded outcome
15 assessment is required. As caregiver-directed constraint induced movement therapy
16 delivered more practice, may lead to a better outcome than manual restraint, and is
17 acceptable to parents and patients, this method of restraint is our preferred intervention.
18 A control intervention with no constraint therapy (for example, waiting list, attention
19 control, usual therapy) would increase the statistical power of the study by increasing
20 the contrast between the expected group outcomes. Such a trial is needed to evaluate
21 the long term clinical and cost effectiveness of community based constraint induced
22 movement therapy.
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41 **Clinical messages**

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43 • Constraint induced movement therapy for children with hemiplegic cerebral palsy
44 can be successfully delivered by caregivers.
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47 • Prolonged restraint delivered more intense upper limb therapy than manual
48 restraint but was not more effective.
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51 • A randomised control trial of prolonged restraint versus no constraint therapy is
52 warranted and feasible.
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Additional information

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For Peer Review

References

1. Surman G, Bonellie S, Chalmers J, et al. UKCP: a collaborative network of cerebral palsy registers in the United Kingdom. *J Public Health* 2006;28: 148-156.
2. Sanger TD, Delgado MR, Gaebler-SD, et al. Classification and Definition of Disorders Causing Hypertonia in Childhood. *Pediatrics* 2003; 111: e89-e97.
3. Krumlinde-Sundholm L, Eliasson A-C. Comparing tests of tactile sensibility: Aspects relevant to testing children with spastic hemiplegia. *Dev Med Child Neurol* 2002; 44:604-612.
4. Eliasson A-C, Gordon AM, Forssberg H. Tactile control of isometric fingertip forces during grasping in children with cerebral palsy. *Dev Med Child Neurol* 1995; 37:72-84.
5. Eliasson AC, Gordon AM. Impaired force coordination during object release in children with hemiplegic cerebral palsy. *Dev Med Child Neurol* 2000; 42:228-234.
6. Taub E, Ramey SL, DeLuca SC, Echols, K. Efficacy of constraint-induced movement therapy for children with cerebral palsy with asymmetric motor impairment. *Pediatrics* 2004; 113:305-312.
7. Beecham J, O'Neill T, Goodman R. Supporting young adults with hemiplegia: services and costs. *Health Soc Care Community* 2001; 9:51-59.
8. Sakzewski L, Ziviani J, Boyd R. Systematic review and meta-analysis of therapeutic management of upper limb dysfunction in children with congenital hemiplegia. *Pediatrics* 2009; 123: e1111-e1122.
9. Boyd RN, Morris ME, Graham HK. Management of upper limb dysfunction in children with cerebral palsy: a systematic review. *Eur J Neurol* 2001; 8:150-166.
10. Taub E, Uswatte G, Pidikiti R. Constraint-Induced Movement Therapy: a new family of techniques with broad application to physical rehabilitation-a clinical review. *J Rehabil Res Dev* 1999; 36:237-251.
11. Taub E, Miller NE, Novack TA. Technique to improve chronic motor deficit after stroke *Arch Phys Med Rehabil* 1993;74: 347-354.
12. Hoare B, Imms C, Carey L, Wasiak J. Constraint-induced movement therapy in the treatment of the upper limb in children with hemiplegic cerebral palsy. *Clin Rehabil* 2007;8: 675-685
13. Huang H, Fethers L, Hale J, McBride A. Bound for success: a systematic review of constraint-induced movement therapy in children with cerebral palsy supports improved arm and hand use. *Phys Ther* 2009;89: 1126-1141.

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2
3 14.Eliasson AC, Krumlinde-Sundholm L, Gordon AM, et al. Guidelines for future
4 research in constraint-induced movement therapy for children with unilateral cerebral
5 palsy: an expert consensus. *Dev Med Child Neurol* 2013;56: 125-137.
6
7 15.Wallen M, Ziviani J, Naylor O Evans R, Novak I, Herbert RD. Modified constraint-
8 induced therapy for children with hemiplegic cerebral palsy: a randomised trial *Dev Med*
9 *Child Neurol* 2011;53: 1091–1099
10
11 16.Eliasson AC, Shaw K, Berg E, Krumlinde-Sundholm L. An ecological approach of
12 Constraint Induced Movement Therapy for 2-3-year-old children: A randomized control
13 trial. *Res Dev Disabil* 2011;32: 2820-2828.
14
15 17.Al-Oraibi S, Eliasson AC. Implementation of constraint-induced movement therapy
16 for young children with unilateral cerebral palsy in Jordan: a home-based model. *Disabil*
17 *Rehabil* 2011;33: 2006-2015.
18
19 18.Krumlinde-Sundholm L, Holmefur M, Kottorp A, Eliasson AC. The Assisting Hand
20 Assessment: current evidence of validity, reliability, and responsiveness to change. *Dev*
21 *Med Child Neurol* 2007;49: 259-264.
22
23 19.Krumlinde-Sundholme L, Eliasson A-C. Development of the assisting hand
24 assessment, a Rasch-built measure intended for children with unilateral upper limb
25 impairments *Scand J Occup Ther* 2003;10:16-26.
26
27 20.Holmefur M, Aarts P, Hoare B, Krumlinde-Sundholm L. Test-retest and alternate
28 forms reliability of the assisting hand assessment. *J Rehabil Med* 2009;41: 886-891
29
30 21.DeMatteo C, Law M, Russell D, et al. Quality of Upper Extremity Skills Test Manual.
31 Hamilton Ontario: McMaster University, CanChild Centre for Childhood Disability
32 Research 1992.
33
34 22.DeMatteo C, Law M, Russell D, et al. The reliability and validity of the Quality of
35 Upper Extremity Skills Test. *Phys and occup ther in pediatr* 1993; 13: 1-18
36
37 23.Varni JW, Seid M, Rode CA. The PedsQL: Measurement Model for the Pediatric
38 Quality of Life Inventory. *Med Care* 1999; 37:126-139.
39
40 24.Varni JW, Burwinkle TM, Berrin SJ, et al. The PedsQL in pediatric cerebral palsy:
41 reliability, validity, and sensitivity of the Generic Core Scales and Cerebral Palsy
42 Module. *Dev Med Child Neurol* 2006; 48:442-449.
43
44 25.Varni JW, Limbers CA, Neighbors K, et al. The PedsQL. Infant Scales: feasibility,
45 internal consistency reliability, and validity in healthy and ill infants. *Qual Life Res* 2011;
46 20:45-55.
47
48 26.Siemonsma PC, Walker MF. Practical guidelines for independent assessment in
49 randomized controlled trials of rehabilitation. *Clin Rehabil* 1997;11: 273-279.
50
51
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53
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2
3 27.Minns Lowe CJ, Wilson MS, Sackley CM, et al. Blind outcome assessment: the
4 development and use of procedures to maintain and describe blinding in a pragmatic
5 physiotherapy rehabilitation trial. *Clin Rehabil* 2011;25: 264 - 274.
6
7 28.Naylor CE, Bower E. Modified constraint-induced movement therapy for young
8 children with hemiplegic cerebral palsy: a pilot study. *Dev Med Child Neurol* 2005;47:
9 365-369.
10
11 29.Eliasson AC, Krumlind-Sundholm L, Shaw K, Wang C. Effects of constraint-induced
12 movement therapy in young children with hemiplegic cerebral palsy: an adapted model.
13 *Dev Med Child Neurol* 2005; 47:266-275.
14
15 30.Kwakkel G, van Peppen R, Wagenaar RC, et al. Effects of augmented exercise time
16 after stroke: a meta-analysis. *Stroke* 2004;35: 2529-2539
17
18 31.Veerbeek JM, Koolstra M, Ket JC, van Wegen EE, Kwakkel G. Effects of augmented
19 exercise therapy on outcome of gait and gait-related activities in the first 6 months after
20 stroke: a meta-analysis. *Stroke* 2011;42: 3311-3315
21
22 32.Case-Smith J, Deluca SC, Stevenson R, Ramey SL. Multicentre randomised
23 controlled trial of paediatric constraint-induced movement therapy: 6-month follow-up.
24 *Am J Occup Ther* 2012; 66:15-23
25
26 33.Deluca SC, Echols K, Law CR, Ramey SL. Intensive pediatric constraint- induced
27 therapy for children with cerebral palsy: randomized, controlled, crossover trial. *J Child*
28 *Neurol* 2006; 21:931-938.
29
30 34.Taub E, Ramey SL, Deluca SC, Echols K. Efficacy of constraint induced movement
31 therapy for children with cerebral palsy with asymmetric motor impairment. *Pediatrics*
32 2004;113: 305-312.
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Table 1. Description of methods of restraint

Prolonged restraint	Manual restraint
<ul style="list-style-type: none"> • 24-hour short-arm restraint applied by therapist, in place throughout the two-week intervention blocks • therapy conducted little and often by caregiver (one hour per day) • custom-made semi-rigid cast (3M soft cast) or wrist splint extending from the metacarpal heads to above the wrist, crepe bandage enclosing the fingers and thumb • well-padded to minimise skin abrasions, allows some protective use • review if non-acceptance by child persists for three to four days • caregiver could easily remove if needed • caregivers were advised extra supervision be provided and activity challenging balance limited • See Appendix 2.1 for the instructions to the site therapist. 	<ul style="list-style-type: none"> • intermittent holding restraint conducted little and often by caregiver during therapy (one hour per day) • holding was hand-over-hand, never forceful • See Appendix 2.2 for instructions to caregivers

Table 2. Baseline characteristics across group.

	Prolonged restraint (n=30)	Manual restraint (n=32)	p-value
	n(%)	n(%)	p-value(χ^2)
Male	19(63)	13(41)	.125
White British	21(66)	16(50)	.284
Attends nursery	12(40)	13(41)	.100
	Mean(\pm SD)	Mean(\pm SD)	p-value (t test)
Age(months)	31.5(12.2)	29.0(11.8)	.427
Deprivation scores 1 (most deprived area) to 32,844 (least deprived area).	9975.5(8357.3)	7941.3(7557.6)	.326
AHA	43.8(22.6)	44.6(29.0)	.894
QUEST (Summary score)	70.8(15.0)	71.5(11.1)	.843
PedsQL Generic Core Scale (Summary score; \geq two years n=51)	68.4(12.2)	68.6(11.6)	.966
PedsQL CP Module (\geq two years n=51)			
Daily Activity	14.8(16.3)	26.9(24.5)	.047
Movement & Balance	55.6(23.7)	61.7(25.6)	.393
Pain & Hurt	82.5(16.8)	75.0(25.4)	.227
Fatigue	77.0(18.8)	75.8(18.5)	.820
Eating Activities	73.2(22.6)	73.4(20.5)	.976
PedsQL Infant Scale (Summary score; < two years n=11)	83.1(12.6)	85.1(13.1)	.810

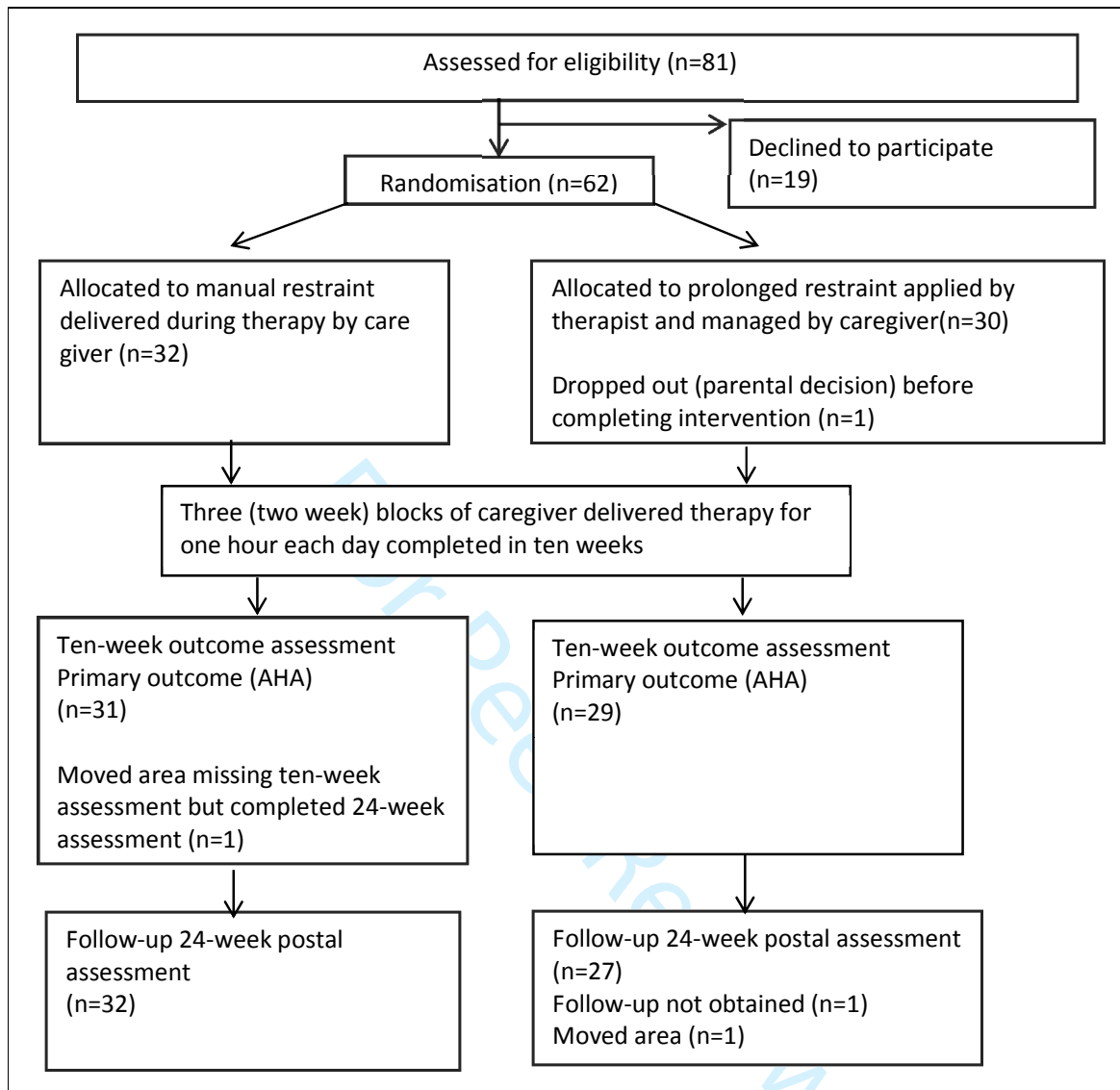
AHA: Assisting Hand Assessment; QUEST: Quality of Upper Extremity Skills Test; PedsQL: Paediatric Quality of life Inventory; CP Cerebral palsy.

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Table 3. Mean difference across groups of the change in the Assisting Hand Assessment (primary outcome) and the Quality of Upper Extremity Skills Test from baseline to the ten-week assessment.

Assisting Hand Assessment AHA logit-based 0-100 unit						
Group	Baseline mean (±SD)	95% CI	Change mean (±SD)	95%CI	Mean difference (95% CI)	p-value t-test
PR (n=29)	43.8 (22.6)	35.4, 52.3	9.0 (8.8)	5.7, 12.4	3.7 (-1.5, 8.8)	.156
MR (n=31)	44.6 (29.0)	34.3, 55.1	5.3 (10.8)	1.3, 9.4		
Quality of Upper Extremity Skills Test (total scores %)						
PR (n=29)	70.8 (15.0)	65.3, 76.4	-1.5 (8.9)	-4.9, 1.9	.08 (-4.6, 4.5)	.970
MR (n=31)	71.5 (11.1)	67.5, 75.5	-1.6 (7.8)	-4.5, 1.3		

PR: prolonged restraint; MR: manual restraint; CI: confidence interval



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Figure 1. CONSORT diagram of participant flow through trial.

Appendix 1**Table 4:** Mean difference across groups of the change in the quality of upper extremity skills test from baseline to the ten-week assessment on total and subgroup scores (%)

	Baseline Mean (\pm SD)	95% CI Lower	95% CI Upper	n	ten-weeks Mean(\pm SD)	Mean (\pm SD) change	95% CI Lower	95% CI Upper	Difference in mean change (95% CI)	p- value t-test
Total scores										
PR	70.8(15.0)	65.3	76.4	29	71.6(11.7)	-1.5(8.9)	-4.9	1.9	.08(95% CI-4.6,4.5)	.970
MR	71.5(11.1)	67.5	75.5	31	73.3(11.7)	-1.6(7.8)	-4.5	1.3		
Dissociated movement										
PR	75.2(11.5)	70.9	79.5	29	76.0(9.7)	1.6(8.3)	-1.5	4.6	-.63(95% CI-5.2,4.0)	.784
MR	74.6(12.5)	70.1	79.1	31	77.0(10.3)	2.2 (9.5)	-1.2	5.7		
Grasp										
PR	60.3(13.9)	55	65.5	29	62.0(14.7)	2.9(10.3)	-1.1	6.8	3.3(95% CI-2.1, 8.7)	.227
MR	65.9(17.4)	59.6	72.1	31	65.3(17.6)	-0.5(10.7)	-4.4	3.5		
Weight-bearing										
PR	74.0(24.7)	65	83.3	28	78.2(13.7)	2.1(18.3)	-4.5	9.2	2.2 (95% CI-5.2, 9.7)	.551
MR	74.5(2.5)	70	79	31	74.4(13.5)	-0.1(9.15)	-3.5	3.2		
Protective extension										
PR	76.7(18.7)	69.0	84.4	24	73.4(16.8)	-.43	-9.8	5.64	1.6(95%CI:-9.0,12.2)	.758
MR	71.5(15.7)	65.6	77.3	28	70.5(15.2)	-2.0(19.9)	-8.0	7.1		

PR: prolonged restraint; MR: manual restraint; CI: confidence interval

Table 5: Mean group difference of change in summary and dimension scores of the Paediatric Quality of life Inventory 4.0 Generic Core Scale from baseline to the ten-week assessment.

	Baseline mean (±SD)	95% CI Lower	95% CI Upper	n	Mean (±SD) change	95% CI Lower	95% CI Upper	Difference in mean change (95% CI)	p-value
Total									
PR	68.4(12.2)	62.5	74.3	15	3.9(11.3)	-2.3	10.2	2.73(-7.09, 12. 6)	.574
MR	68.6(11.6)	62.6	74.6	17	1.2(15.3)	-6.6	9.0		
psychosocial summary									
PR	73.3(11.9)	67.6	79.0	15	2.9(14.2)	-5.0	10.7	4.79(-7.4, 16.9)	.428
MR	74.4(11.5)	68.5	80.4	17	-1.9(18)	-11.6	7.7		
physical summary									
PR	53.6(20.3)	43.4	63.8	22	4.4(14.6)	-2	10.9	-5.14(-16.4, 6.1)	.361
MR	49.9(19.1)	40.7	61.2	23	9.5(21.9)	.04	19.0		
emotional functioning									
PR	65.8(20.0)	56.2	75.4	22	1.9(18.7)	-6.3	10.3	-3.44(-14.4, 7.5)	.531
MR	68.2(16.4)	59.7	76.7	23	5.4(17.8)	-2.3	13.1		
social functioning									
PR	86.8(12.7)	80.0	93.6	22	-10.5(18.0)	-18.0	-2.5	-4.47(-17.8, 8.8)	.500
MR	83.5(11.0)	77.5	89.5	23	-6.0(25.4)	-17.0	5.0		
nursery functioning									
PR	67.3(17.8)	58.7	75.9	15	11.3(19)	.8	22.0	14.33(-1.4, 30.1)	.073
MR	71.6(16.4)	63.1	80.0	17	-2.9(24)	-15.2	9.4		

PR: prolonged restraint; MR: manual restraint; CI: confidence interval

Table 6: Mean difference across groups of the change in the dimension scores of the Paediatric Quality of life Inventory Cerebral Palsy Module from baseline to the ten-week assessment.

Group	Baseline Mean (±SD)	95% CI Lower	95% CI Upper	n	Mean (±SD) Change	95% CI Lower	95% CI Upper	Difference in mean change (95% CI)	p-value
Daily activity									
PR	14.8(16.3)	8.0	21.5	20	9.8(22.8)	-0.9	20.4	1.16 (-14.8, 17.1)	.883
MR	26.9(24.5)	16.5	37.2	23	8.6(28.0)	-3.6	20.7		
Movement and balance									
PR	55.6(23.7)	45.8	65.4	22	8.0(23.0)	-2.3	18.3	10.05(-5.3, 25.4)	.193
MR	61.7(25.6)	50.9	72.5	22	-2.1(27.0)	-14.1	9.9		
Pain and hurt									
PR	82.5(16.8)	75.6	89.4	20	0.6(19.2)	-8.4	9.6	-5.35(-16.0, 5.3)	.318
MR	75(25.4)	64.8	85.7	23	6.0(15.5)	-7.0	12.6		
Fatigue									
PR	77.0(18.8)	69.2	84.8	21	-8.6(25.4)	-20.2	2.9	-7.54(-21.7, 6.6)	.287
MR	75.8(18.5)	68.0	83.6	23	-1.0(20.9)	-10.1	8.0		
Eating activities									
PR	73.3(22.6)	64.0	82.6	22	2.8(20.7)	-6.0	12.0	-2.87(-15.20, 9.5)	.642
MR	73.4(20.5)	64.8	82.1	23	5.7(20.3)	-3.0	14.5		

PR: prolonged restraint; MR: manual restraint; CI: confidence interval

Table 7: Mean difference across groups of the change in the summary and dimension scores of the Peds-QL Infant Scale from baseline to the ten-week assessment.

	Baseline mean (±SD)	95% CI Lower	95% CI Upper	n	Mean (±SD) change	95% CI Lower	95% CI Upper	Difference in mean change (95% CI)	p- value
Summary									
PR	83.1(12.6)	63.1	103.1	4	0.17(42.0)	-6.6	6.9	11.6(-26.4, 3.2)	.145
MR	85.1(13.1)	73.0	97.3	7	-10.0(12.0)	-21.4	1.2		
Psychosocial summary									
PR	79.5(18.4)	50.3	108.7	4	1.1(3.8)	-5.0	7.2	11.56(-30.2, 7.0)	.193
MR	85.2(12.7)	73.4	96.9	7	-10.5(16.0)	-25.1	4.1		
Physical summary									
PR	83.9(4.8)	76.1	91.5	4	3.4(8.2)	-9.7	16.6	8.51(-20.9, 3.9)	.155
MR	80.6(16.5)	65.3	95.9	7	-5.0(9.0)	-13.41	3.2		
Physical functioning									
PR	78.5(9.2)	63.9	93.0	4	3.1(16.2)	-22.7	28.8	12.16(-36.9, 12.6)	.295
MR	77.4(21)	58.1	96.6	7	-9.1(18.0)	-25.7	7.6		
Physical symptoms									
PR	98.6(11.6)	80.0	117.2	4	-5.5(11.4)	-23.7	12.7	4.51(-7.1, 16.2)	.404
MR	92.9(20.4)	74.0	111.8	7	-10.0(6.0)	-15.6	-4.4		
Emotional functioning									
PR	72.9(24.9)	33.;3	112.5	4	-1.9(7.8)	-14.4	10.45	10.01(-33.0, 12.3)	.329
MR	84.0(9.6)	75.2	93.0	7	-12.3(18.8)	-29.7	5.0		
Social functioning									
PR	93.8(7.5)	81.8	105.7	4	-1.3(6.3)	-11.26	8.8	-2.32(-18.0, 13.4)	.746
MR	96.4(9.4)	87.7	105.2	7	3.6(12.8)	-15.4	8.3		
Cognitive functioning									
PR	71.9(25.6)	31.2	112.6	4	6.5(7.9)	-6.0	19.1	22.02(-44.5, .5)	.054
MR	75.0(25.0)	51.9	98.1	7	-15.5(18.6)	-32.7	1.7		

PR: prolonged restraint; MR: manual restraint; CI: confidence interval

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Table 8: Mean difference across groups of the change in the Birmingham Bimanual Questionnaire from baseline to the ten-week assessment.

	Baseline means (±SD)	95%CI Lower	95% CI Upper	n	Mean (±SD) change	Difference in mean change (95% CI)	p-value
PR	73.8(16.1)	65.5	82.3	23	20.9(25.9)	16.91(2.9, 30.9)	.019*
MR	68.6(22.6)	59.5	77.25	27	4.0(23.4)		

PR: prolonged restraint; MR: manual restraint; CI: confidence interval; * statistically significant.

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Table 9: Mean difference across groups of the change in the dimension and summary scores of the Paediatric Quality of life Inventory 4.0 Generic Core Scale between baseline and 24-week assessment and ten and 24-week assessment.

Baseline and 24- week assessment							Ten and 24- week assessment					
	N	Mean (SD) Change	95% CI Lower	95% CI Upper	Difference in mean change (95% CI)	p-value	n	Mean (\pm SD) Change	95% CI Lower	95% CI Upper	Difference in mean Change (95% CI)	p- value
Summary												
PR	16	-6.0(17.3)	-15.5	3.0	-1.72(-12.8, 9.3,)	.754	15	-11.2(15.6)	-20.0	-2.5	-4.48(-15.2, 6.2,)	.400
MR	16	-4.5(13.0)	-11.4	2.4			17	-6.7(14.0)	-14.0	0.5		
Psychosocial summary												
PR	16	-6.0(19.1)	-17	3.3	-1.90(-14.4, 10.6,)	.758	15	-9.4(16.3)	-18.4	-0.3	-5.15(-16.8, 6.5,)	.372
MR	16	-5.0(15.0)	-13	3.0			17	-4.2(15.7)	-12.3	3.9		
Physical functioning												
PR	21	-6.5(19.2)	-15.3	2.3	-.35(-12.2, 11.6,)	.954	19	-13.4(20.0)	-23.0	-3.7	3.02(-9.3, 15.3)	.622
MR	24	-6.2(20.2)	-14.7	2.4			24	-16.3(19.3)	-24.6	-8.1		
Emotional functioning												
PR	21	1.9(20.6)	-7.5	11.3	1.69(-8.6, 12.0,)	.742	19	-0.46(20.0)	-10.1	9.2	6.20(-5.4, 17.8)	.286
MR	24	0.2(13.5)	-5.5	5.9			24	-6.7(17.5)	-14.0	0.7		
Social functioning												
PR	21	-19.8(24.5)	-31.0	-8.7	-1.58(-15.4, 2.3)	.818	19	-8.9(15.3)	-16.3	-1.6	1.52(-9.1, 12.1)	.744
MR	24	-18.2(21.5)	-27.3	-9.0			24	-10.5(19.1)	-18.6	-2.4		
Nursery functioning												
PR	16	-8.6(24.0)	-21.4	4.1	-7.03(-23.4, .3,4)	.386	15	-13.9(23.0)	-27.0	-.87	-14.37(-30.2, 1.5)	.074
MR	16	-1.6(21.1)	-12.8	9.7			17	0.5(20.5)	-10.0	11.0		

PR: prolonged restraint; MR: manual restraint; CI: confidence interval

Table 10: Mean difference across groups of the change in the dimension scores of the Paediatric Quality of life Inventory 3.0 Cerebral Palsy module between baseline and 24-week assessment and ten-week and 24-week assessment.

Baseline and 24-week assessment							Ten and 24-week assessment					
	n	Mean (±SD) Change	95% CI Lower	95% CI Upper	Difference in mean change (95% CI)	p- value	n	Mean (±SD) Change	95% CI Lower	95% CI Upper	Difference in mean change (95% CI)	p- value
Daily activities												
PR	22	5.5(16.7)	-1.9	12.9	-2.15 (-15.6, 1.3)	.748	18	-2.5 (23.0)	-14.0	9.0	-2.02 (-16.7, 12.7)	.781
MR	23	7.6(26.6)	-3.9	19.1			23	-0.5 (23.1)	-10.5	9.5		
Movement and balance												
PR	22	-2.0(20.6)	-11.1	7.0	4.91(-8.8, 17.9)	.449	20	-10.3(23.5)	-21.2	0.7	-5.76(-20.9, 9.4)	.448
MR	23	-6.9(22.3)	-16.6	2.7			22	-4.5 (25.0)	-15.7	6.7		
Pain and hurt												
PR	22	-5.7(23.9)	-16.3	4.9	-7.86(-21.6, 5.9)	.225	18	-4.9(21.0)	-15.3	5.6	-2.42(-13.7, 8.9)	.670
MR	23	2.2(21.9)	-7.2	11.6			23	-2.4(15.0)	-9.0	4.0		
Fatigue												
PR	22	-6.8(19.7)	-15.5	1.9	.79(-11.6, 13.2)	.898	19	-2.3(22.0)	-12.7	8.0	2.86(-11.1, 16.8)	.691
MR	23	-7.6(21.6)	-16.9	1.7			23	-5.2(23.0)	-15.0	4.7		
Eating activities												
PR	22	0.6(22.2)	-9.3	10.4	7.27(-5.6, 20.2)	.261	20	-3.1(20.6)	-12.7	6.5	8.19(-4.5, 20.9)	.198
MR	23	-6.7(20.6)	-15.6	2.2			23	-11.3(20.5)	-20.2	-2.5		

PR: prolonged restraint; MR: manual restraint; CI: confidence interval

Table 11: Mean difference across groups of the change in the summary and dimension scores of the Paediatric Quality of life Inventory Infant Scale between baseline and 24-week assessment and ten-week and 24-week assessment.

Baseline and 24-week assessment							Ten and 24-week assessment					
	n	Mean (\pm SD) change baseline to 24-weeks	95% CI lower	95% CI upper	Difference in mean change (95% CI)	p- value	n	Mean (\pm SD) change ten to 24-weeks	95% CI lower	95% CI upper	Difference in mean change (95%CI)	p- value
Summary												
PR	4	-2.5(1.6)	-5.0	0.12	6.94 (2.76, 11.1)	.006*	4	-2.7(3.7)	-8.6	3.3	-6.23(-21.4, 8.9)	.383
MR	5	-9.4(3.2)	-13.4	-5.5			5	3.6(12.2)	-11.6	18.8		
Psychosocial summary												
PR	4	1.5(2.9)	-3.1	6.2	9.73(4.6, 14.9)	.003*	4	0.4(3.4)	-5.0	5.8	-4.89(-22.9, 13.1)	.541
MR	5	-8.2(3.5)	-12.5	-3.9			5	5.3(14.7)	-13.0	23.6		
Physical summary												
PR	4	-3.8(7.5)	-15.8	8.2	2.76 (-9.4, 15.3)	.618	4	-7.2(5.4)	-16.0	1.5	-8.25(-20.8, 4.3)	.164
MR	5	-6.6(8.1)	-16.7	3.5			5	1.0(9.3)	-10.6	12.6		
Physical functioning												
PR	4	-8.9(21.2)	-42.6	24.8	2.46(-30.2, 35.1)	.864	4	-12.0 (6.0)	-21.4	-2.6	-15.01(-35.5, 5.4)	.127
MR	5	-11.4(20.1)	-36.7	13.6			5	3.0 (16.3)	-17.2	23.3		
Physical symptoms												
PR	4	-8(9.9)	-23.7	7.7	3.07(-10.8, 16.9)	.616	4	-2.5 (10.6)	-19.4	14.4	-1.50(-15.0, 12.0)	.800
MR	5	-11(7.7)	-20.7	-1.5			5	-1.0 (6.5)	-9.0	7.0		
Emotional functioning												
PR	4	2.6(5.7)	-6.5	11.6	15.66(5.5, 25.9)	.009*	4	4.5 (9.7)	-10.9	28.5	2.87(-19.9, 25.6)	.774
MR	5	-13.1(7.0)	-21.8	-4.4			5	1.6 (17.0)	-19.5	22.8		
Social functioning												
PR	4	-2.5(5.0)	-10.5	5.5	-1.50(-7.3, 4.3)	.563	4	-1.3 (2.5)	-5.2	2.7	-8.25 (-23.5, 7.0)	.242
MR	5	-1.0(2.2)	-3.7	1.8			5	7.0(12.5)	-7.0	22.6		
Cognitive functioning												
PR	4	4.6 (5.7)	4.6	13.6	15.01(-2.4, 32.5)	.081	4	-2.0 (4.7)	-9.6	5.5	-9.30(-30.7, 12.1)	.342
MR	5	-10.6(13.7)	-27.5	-3.9			5	7.2 (17.5)	-14.5	28.9		

PR: prolonged restraint; MR: manual restraint; CI: confidence interval * statistically significant.

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Table 12: Mean difference across groups of the change in the BBMQ from baseline to 24-week assessment and from ten-week to the 24-week assessment.

	Baseline and 24-week assessment					Ten and 24-week assessment			
	Baseline mean (SD)	n	Mean (\pm SD) Change	Difference in mean change 95% CI	p-value	N	Mean (\pm SD) change	Difference in mean change (95% CI)	p-value
PR	73.8 (16.1)	21	3.1(25.1)	1.1(-12.5, 14.6)	.873	27	-13.6(23.2)	-13.5(-24.9, -2.1)	.021*
MR	68.6 (22.6)	27	2.0(21.4)			32	-.13.0(20.4)		

PR: prolonged restraint; MR: manual restraint; CI: confidence interval * statistically significant.

Table 13: Adverse events

Serious		
Group	Related to the intervention	Description
Prolonged Restraint	Unrelated	Admitted to hospital due to a flu induced wheeze
	Unrelated	Taken to A/E due to chest infection
	Unrelated	Taken to A/E because of a total body rash
Manual Restraint	Unrelated	Admitted to hospital following a fit
Not serious		
Prolonged Restraint	Related	Bump to the head from a fall
	Related	Bumped head which resulted in a little bruise
	Related	Graze on arm from wrist splint
	Related	Graze and slight bruising on hand
	Related	Rubbing plus moist, smelly arm
	Related	Localised eczema flare-up
	Related	Redness between fingers
	Related	Redness around the thumb
	Related	Redness around the thumb
	Related	Redness around the thumb
	Related	Redness and small area of broken skin on the hand
	Related	Redness and sore, cracked skin on the hand
	Unrelated	Item fell onto participant causing bruising
Unrelated	Hip pain,	
Unrelated	Raised temperature and rash	

A/E: accident and emergency department.

Table 14: List of therapists

Therapist	Trust
Christel Corbett, Jacqueline Parker, Marilyn Poole, Katie Roberts.	NHS South Birmingham Primary Care Trust
Alison Keeling-Smith, Shabnam Moledina.	NHS Heart of England
Louise Kelleher, Helen Wilson. Yvonne Parker.	Dudley Community Services South Staffordshire Primary Care Trust
Patricia Escott, Claire Parker. Petrina March, Una Peplow, Radella Manners, Michele Toorish.	Wolverhampton City Primary Care Trust Sandwell Primary Community Trust
Ginny Humphreys, Sally Bunney, Robert Shaw, Carolyn Allbrook, Louise Jennings, Jane Butler.	NHS Devon
Sara Butler, Margaret Hotze. Ella Kajumba, Rose Cormac-Loyd.	Walsall Community Health NHS Lewisham Healthcare NHS Trust
Phillip Harness, Jacqueline Gordon. Natalie Hayes.	NHS City and Hackney NHS Bromley
Joanna Saunders, Barbara Marsland Helen Burchnell.	NHS Telford and Wrekin NHS Leicestershire
Ann Oultram, Louise Monaghan, Lorraine Isherwood.	Alder Hey Children's Foundation NHS Foundation Trust
Cath Barton, Rebecca Randell. Kezia Pugh, Janet Rose.	Powys Teaching Health Board NHS Herefordshire

We would like to know the difficulties your child has with their affected arm and hand. That is the arm/hand that they do not use so well. Please tell us how difficult each one of the items below has been for your child during the past ONE month by circling 0-4: There is no right or wrong answer. If you do not understand a question, please ask for help.

	Never	Almost never	Some times	Often	Almost always
Using their affected arm and hand to keep objects still to play with.	0	1	2	3	4
Using the affected arm and hand for big movements that use the whole arm e.g. reaching, waving or leaning on it.	0	1	2	3	4
Grasping an object with their affected hand	0	1	2	3	4
Releasing an object with their affected hand.	0	1	2	3	4
Moving the fingers of the affected hand	0	1	2	3	4
Using both hands together	0	1	2	3	4

Figure 2: Birmingham Bimanual Questionnaire

Appendix 2

2.1. Prolonged restraint

Application

Application of a flexible short arm cast from the metacarpal heads to above the wrist with the wrist joint positioned in neutral/resting position

Materials:

- One/two rolls of 3M soft cast (2.5cm/5cm)
- 3M Synthetic (2.5cm) stockinette 5cm longer than the device
- One/two rolls 3M synthetic (5cm) cast padding
- One roll crepe bandage
- Tape to secure crepe bandage

Setting

The prolonged restraint should be applied where possible in a clinic situation however, with care it is possible to do this at the child's home.

Removal of the cast

Unwind the crepe bandage and remove. Then remove the cast by finding the end of the soft cast and unwind. The stockinette can be then removed. The cast should be removed by unwinding, not cutting off. Give an explanation and demonstration on removing the prolonged restraint at the first session to the parent.

2.2. Manual Restraint

Instruction sheet for parents and nursery workers

- Your child's unaffected hand is held gently during an activity to encourage them to use their affected hand.
- You may place your hand on top of your child's hand if they are playing at a table.
- Between any activities, the hand is not held
- If they are playing on the floor you may choose to hold your child's hand or place your hand over your child's hand on the floor.
- This should be done on a little and often basis and you should aim to get your child playing at the same time.
- At no time is any force applied. If your child objects and starts to get upset, then you should stop.
- This should only be carried out by you and your therapist will teach you how to do it.
- It may be that your therapist identifies another person that would be appropriate to do it as well. This could be a nursery worker. With your agreement, the therapist will train them on how to do this and they may carry this out when your child attends nursery.

2.3. Intensive unstructured practice

Instruction sheet for parents and nursery workers

This therapy involves getting active use of the affected hand for about 60 minutes every day but not all at the same time.

- The affected hand is encouraged to actively move by playing with a toy or doing an activity like finger feeding or helping to dress we do not want you to move their hand for them.
- Your therapist will help by giving ideas about what are suitable toys. We want this to be as enjoyable as possible.



- Successful play = easy toys that your child can use



Make it fun and enjoyable so he/she wants to repeat the activity or keep on playing. Give them lots of encouragement



CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	√
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	√
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	√
	2b	Specific objectives or hypotheses	√
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Page 4
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	Page 5
	4b	Settings and locations where the data were collected	Page 5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Page 8,9 & 20
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Page 5,6 &7
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	Page 9
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	Page 5
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Page 5
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Page 5
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Page 5

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Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	Page 5&7
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	Page 9&10
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Page 10& Consort diagram p23
	13b	For each group, losses and exclusions after randomisation, together with reasons	Consort diagram p23
Recruitment	14a	Dates defining the periods of recruitment and follow-up	Page 10
	14b	Why the trial ended or was stopped	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 2 p21
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Consort diagram p23
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Table 3 p 21 & Appendix 1. Table 4-12 p 24-32
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	Page 12& Appendix 1. Table 13 p33
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	Page 13/14
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Page 13
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	Page 14/15
Other information			

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Registration	23	Registration number and name of trial registry	Page 4
Protocol	24	Where the full trial protocol can be accessed, if available	Page 4
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	Page 4,15,16

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