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Progressive resistance training for adolescents with cerebral palsy: the STAR randomized controlled trial

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AIM To evaluate the effect of progressive resistance training of the ankle plantarflexors on gait efficiency, activity, and participation in adolescents with cerebral palsy (CP).

METHOD Sixty-four adolescents (10–19y; 27 females, 37 males; Gross Motor Function Classification System [GMFCS] levels I–III) were randomized to 30 sessions of resistance training (10 supervised and 20 unsupervised home sessions) over 10 weeks or usual care. The primary outcome was gait efficiency indicated by net nondimensional oxygen cost (NNcost). Secondary outcomes included physical activity, gross motor function, participation, muscle strength, muscle and tendon size, and muscle and tendon stiffness. Analysis was intention-to-treat.

RESULTS Median attendance at the 10 supervised sessions was 80% (range 40–100%). There was no between-group difference in NNcost at 10 (mean difference: 0.02, 95% confidence interval [CI] –0.07 to 0.11, p=0.696) or 22 weeks (mean difference: –0.08, 95% CI –0.18 to 0.03, p=0.158). There was also no evidence of between-group differences in secondary outcomes at 10 or 22 weeks. There were 123 adverse events reported by 27 participants in the resistance training group.

INTERPRETATION We found that 10 supervised sessions and 20 home sessions of progressive resistance training of the ankle plantarflexors did not improve gait efficiency, muscle strength, activity, participation, or any biomechanical outcome among adolescents with CP.

Cerebral palsy (CP) is characterized by atypical fine and gross motor function, which results in activity limitations and participation restrictions.[1,2] Many young adults with CP experience a deterioration in mobility with age,[3] which may be attributed to progressive loss of muscle strength and reduced gait efficiency.[4,5] Progressive resistance training has potential to improve gait efficiency and muscle strength and hence prevent or delay deterioration in mobility in young adulthood.

Strength or resistance training is one of the most frequently used interventions among physiotherapists to manage lower-limb function in adolescents with CP.[6] Despite the potential for progressive resistance training to improve strength and gait efficiency among adolescents with CP, there is little evidence to date to support its effect on any level of functioning, as classified by the World Health Organization's International Classification of Functioning, Disability and Health framework.[7] However, there are several limitations with the current evidence base including delivery of a potentially inadequate training stimulus, failure to describe fidelity to the intervention, few studies examining outcomes at all levels of the International Classification of Functioning, Disability and Health framework, and few studies reporting adverse events.[7] Progressive resistance training needs to be provided at an adequate volume (i.e. the product of sets and repetitions) and with adequate resistance in order to overload the muscle and increase strength.[8] It is particularly important to progress intensity throughout the programme, as the muscle adapts and strengthens, so that it is continuously overloaded.[8] Failure to deliver resistance training at sufficient intensity for the duration of the programme may explain why only small improvements in muscle strength have been observed in trials to date.[7]

In addition, there is large variation in muscle groups targeted by resistance training, with most studies targeting knee extensors[7] despite muscle strength and volume deficits being particularly pronounced for ankle plantarflexors in CP.[9,10] Ankle plantarflexor strength is a strong predictor of walking endurance, step cadence, and gross motor function among young people with CP,[11,12] and thus a progressive resistance training programme targeting ankle plantarflexors may improve walking function and gross motor function. Targeting plantarflexors may also specifically improve gait efficiency through biomechanical mechanisms.[13] People with CP have a high degree of triceps surae muscle stiffness compared to Achilles tendon stiffness.[14] Progressive resistance training can increase tendon stiffness,[15] which may promote a more efficient muscle tendon interaction and muscle contraction during gait.[16] Additionally, increasing the size and strength of the plantarflexor muscles may improve knee extension in the stance phase of walking and aid propulsion of the lower limb in pre-swing, resulting in greater walking efficiency with a more erect alignment of the skeleton. This, in turn, may reduce unnecessary internal work and improve ankle power generation.[17]

The aims of the Strength Training for Adolescents with ceRebral palsy (STAR) trial were to: (1) evaluate the effect of progressive resistance training of the ankle plantarflexors on gait efficiency, activity, and participation in adolescents with CP; and (2) to determine the biomechanical adaptations that occur after resistance training.

METHOD
Study design and participants
The STAR trial was a multicentre randomized controlled trial comparing a 10-week progressive resistance training programme to usual care. Full details of the methods are provided in the protocol.[13] Adolescents with CP were recruited from eight National Health Service trusts in England, a special education needs school, a university, a primary care organization, national organizations for people with disabilities, and by word of mouth. Inclusion criteria were a diagnosis of spastic CP, aged 10 to 19 years, ability to walk independently with or without a mobility aid (i.e. Gross Motor Function Classification System [GMFCS] levels I–III), and an ability to activate the ankle plantarflexors as determined by palpation. Adolescents were excluded if they had orthopaedic surgery of the lower limbs in the past 12 months, had botulinum neurotoxin A injections or serial casting in the past 6 months, or had insufficient cognition to comply with assessment procedures and the training programme. Participants aged 16 years and over gave written informed consent. Participants under 16 years of age gave written informed assent and a parent or guardian provided written informed consent. The trial was approved by Brunel University London's College of Health and Life Sciences Research Ethics Committee and the Surrey Borders Research Ethics Committee (ref: 15/LO/0843). Trial registration number was ISRCTN90378161.

What this paper adds
• Thirty sessions of progressive resistance training of the ankle plantarflexors over 10 weeks did not improve gait efficiency among ambulatory adolescents with cerebral palsy.
• Resistance training did not improve muscle strength, activity, or participation.
• Ninety percent of participants experienced an adverse event.
• Most adverse events were expected and no serious adverse events were reported.

Randomization
Random allocation was computer generated with variable (random) block length of two or four, and stratification by GMFCS level (levels I–II and level III). The randomization schedule was generated by an individual independent to the study before recruitment. The same individual placed allocation of participants in sequentially numbered opaque sealed envelopes. The trial manager revealed allocation, and informed participants and therapists, after participants completed the baseline assessment.

Intervention
The intervention, which is described in detail in the protocol,[13] was based on guidelines for progressive resistance training in young people with typical development.[8] Adolescents in the resistance training programme completed 10 supervised sessions and 20 home sessions of resistance training over 10 weeks. Exercises, which targeted the ankle plantarflexors (primarily gastrocnemius), are described in Figure S1 (online supporting information) and Table S1 (online supporting information). Unilateral exercises were performed where possible. A standardized programme was used to progress the intensity of the exercises, with resistance increasing from 12 repetition maximum to 6 repetition maximum and sets increasing from 4 to 8 over 10 weeks (Table S2, online supporting information). At the first session, the therapist identified a suitable exercise or exercises and an appropriate resistance for the participant depending on their initial strength, balance, and range of motion, in order to achieve the prescribed intensity (e.g. 4 sets at 12 repetition maximum in week 1). Resistance was added using free weights on a leg press or hack squat machine, weighted vests, ankle weights, or resistance band. Participants performed the exercise or a combination of exercises during the supervised session and home sessions to achieve the prescribed intensity for that week (e.g. 4 sets at 12 repetition maximum in each session during week 1). Resistance was added incrementally at each supervised session to ensure that the participant completed the prescribed number of repetitions at the supervised and home session to fatigue and was therefore exercising at the prescribed intensity. As participants did not have access to the hack squat machine or leg press machine at home, the therapist prescribed one or more of the remaining exercises to complete at home (i.e. the standing straight knee calf raise or the seated straight knee calf press against the resistance band), depending on the participant's strength. Resistance was added (e.g. using a weighted vest or ankle weights) to ensure the participant completed the prescribed

intensity. As the resistance band was not adequate to achieve the desired intensity for the majority of participants, most participants were prescribed a standing straight knee calf raise. Participants received a diary each week with pictures and instructions outlining the exercise(s) to be completed at home, including the number of repetitions, sets, type, and amount of resistance. Participants recorded home exercise completion and adverse events in this diary.

The programme was delivered to participants either individually or in groups of up to three people by one or two physiotherapists, depending on group size. The research team provided training to therapists to deliver the programme, which included information on both the theoretical underpinning and practical application of the programme. The trial manager also attended the first session to support the therapists to deliver the intervention and attended additional sessions if requested by the therapist. At the start of each supervised session, therapists collected the diary and asked participants how many home exercise sessions they had completed and if they had experienced any adverse events since the last session such as muscle soreness, fatigue, or a fall. Therapists recorded the following information for each session in a standardized form: a description of the exercise(s) completed; number of repetitions and sets performed; type and amount of resistance applied; whether or not each exercise was progressed and reasons for non-progression; home exercise(s) prescribed including repetitions, sets, and resistance; home exercise completion; and adverse events that occurred during the session and at home, in the past week. An adverse event was considered serious if it resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, or resulted in persistent or significant disability or incapacity. Adverse events were not monitored among participants randomized to the usual care control group.

Usual care

Participants in both the resistance training and usual care control group were instructed to continue with their usual physiotherapy and activities, provided it did not include progressive resistance training. No participant reported that progressive resistance training was part of their usual care. Physiotherapy provision during the 22 weeks was assessed using a modified version of the Client Service Receipt Inventory at 10 and 22 weeks.[18]

Outcomes

The assessments conducted at baseline, 10, and 22 weeks post-randomization are described in the protocol.[13] Assessments were conducted during a face-to-face appointment at Brunel University London, supplemented by postal or telephone questionnaires where required. The young person was allowed to ask their parent/guardian for assistance to complete questionnaires if required. Assessors were masked to group allocation for all outcomes except for the Gross Motor Function Measure 66 (GMFM-66). Performance of the GMFM-66 was video-recorded. A specialist paediatric

physiotherapist, with experience of scoring the GMFM-66 and masked to group allocation, scored recordings.

The primary outcome was gait efficiency indicated by net nondimensional oxygen cost (NNcost) calculated from oxygen consumption measured during 6 minutes of overground walking and 10 minutes of rest using a portable metabolic system (Cosmed K5, Rome, Italy).[19] Further detail on the calculation of NNcost is provided in Appendix S1 (online supporting information). Secondary outcomes were physical activity, participation, gait speed, gross motor function, muscle-tendon mechanics, and knee and ankle flexion angle at mid-stance. Average daily time in moderate-to-vigorous physical activity, average daily time in light physical activity, and average daily percentage time in sedentary behaviour were assessed objectively using an accelerometer (Actigraph wGT3X, Pensacola, FL, USA) worn for 7 days. Further details on identification of non-wear-time, criteria for valid wear-time, and classification of activity counts are provided in Appendix S2 (online supporting information). Participation was measured using the Assessment of Life Habits Questionnaire (range 0–9; higher score indicates greater participation).[20] Gait speed was measured as the average of three trials of walking at self-selected speed over 10m. Gross motor function was assessed using dimensions D and E of the GMFM-66; a higher score indicates better function.[21] The following outcomes were assessed on the participant's affected leg in the case of unilateral CP, the most affected leg in the case of bilateral CP, or the right leg if a participant reported that both sides were equally affected. Achilles tendon cross-sectional area and medial gastrocnemius muscle volume were assessed using a three-dimensional freehand ultrasonography method.[22] Change in medial gastrocnemius muscle length was measured with a combination of 3D motion analysis and 2D ultrasound.[14] Muscle strength, represented by torque, was measured on an isokinetic dynamometer (Cybex Inc., Ronkonkoma, NY, USA) as the best of three maximal voluntary isometric plantarflexion contractions. Achilles tendon stiffness, Achilles tendon Young's modulus, and medial gastrocnemius muscle stiffness were calculated as described in the protocol.[13] Ankle and knee flexion angle at mid-stance were measured from a full body motion analysis marker set during treadmill walking.[13]

Data analysis

A sample size of 27 participants in each group was required to detect a difference of 0.17 in NNcost with a standard deviation of 0.31,[23] using a 5% significance level and 80% power, and assuming a Pearson's correlation coefficient of 0.7 between baseline and follow-up NNcost. The distribution of continuous numeric data were examined using quantile–quantile plots. Primary analyses were intention-to-treat. Secondary 'per-protocol' analyses were conducted using data from participants who attended ≥70% of intervention sessions and completed follow-up to 22 weeks. Analyses were conducted using Stata (version 15.0; Statcorp, College Station, TX, USA). Linear mixed models adjusted for

baseline scores and GMFCS level were used to assess the effect of the intervention. Interaction terms between treatment group and time, and GMFCS level and time, were included in the model; the treatment effect therefore represents the difference between the resistance training group and usual care group adjusted for baseline values and GMFCS level. We adjusted for GMFCS level as there is evidence that adjustment for balancing variables used in stratified randomization is required to obtain correct p-values and confidence intervals.[24] We conducted a prespecified subgroup analysis by including an interaction term to determine if treatment effect differed according to GMFCS level. We additionally conducted a post hoc subgroup analysis to determine if treatment effect differed according to anatomical distribution (i.e. bilateral/unilateral). We further conducted a sensitivity analysis by repeating primary analyses and adjusting for any major imbalances in prognostic factors between groups. The distribution of residuals from linear mixed models was examined using quantile–quantile plots; there was no evidence that residuals did not follow a normal distribution for any model.

RESULTS

Between November 2015 and May 2017, 266 potentially eligible participants received information about the study.

Of these, two were excluded for receiving surgery in the past 12 months and 200 declined to participate. Reasons for refusal included the parent or young person having insufficient time to commit to a 10-week programme and inability to travel to the class. Sixty-four participants were included (Fig. S2, online supporting information). Baseline characteristics are presented in Tables 1 and 2. The groups were similar on baseline characteristics, except for sex, GMFCS level, and distribution. There were fewer females and fewer people with unilateral CP in the resistance training group. There was a higher proportion of people in GMFCS level I and a lower proportion of people in GMFCS level II in the resistance training group compared to the control group.

Fifty-five (86%) and 52 people (81%) attended the 10 and 22 week assessments respectively (Fig. S2). Characteristics of those retained at 22 weeks and those lost to follow-up are presented in Table S3 (online supporting information). Missing data ranged from 0% to 42% at baseline, 6% to 61% at 10 weeks, and 12% to 58% at 22 weeks. Reasons for missing data included lost to follow-up, incomplete questionnaires, equipment malfunction, and failure to return the accelerometer. Participants wore the accelerometer for a median of 7 days (range 2–7). Wear-time is described in Table S4 (online supporting information).

Table 1: Baseline characteristics, usual care control group

	Usual care control group (n=31)		
	n (%)	Mean (SD)	Median (range)
Age, y:mo	31	13:11 (2:6)	14 (10–19)
Female	14 (45)		
Height, cm	31	154.1 (12.1)	154.0 (131.5–180.9)
Mass, kg	31	50.4 (12.1)	51.5 (29.0–75.6)
GMFCS level			
I	13 (42)		
II	13 (42)		
III	5 (16)		
Distribution			
Unilateral	17 (55)		
Bilateral	14 (45)		
Self-reported orthotic wear	14 (45)		
NNcost	31	0.53 (0.35)	0.42 (0.18–2.04)
Physical activity			
Daily MVPA, min	30 (97)	56.4 (31.9)	60.8 (3.7–139.5)
Daily LPA, min	30 (97)	193.9 (54.5)	188.9 (70.9–311.2)
Daily sedentary time, %	30 (97)	67.3 (10.7)	67.2 (40.8–92.1)
Daily step count	30 (97)	5941.9 (2578.1)	6564.4 (549.6–12035.8)
Life-H score	22 (71)	6.4 (1.7)	6.6 (3.2–8.5)
GMFM-66 D, %	29 (94)	84.6 (20.0)	89.7 (25.6–100.0)
GMFM-66 E, %	29 (94)	79.3 (26.5)	91.7 (15.3–100.0)
Gait speed, m.s^{-1}	31	1.1 (0.3)	1.1 (0.3–1.5)
Maximal voluntary contraction, Nm	31	28.6 (18.6)	24.7 (2.6–74.1)
Medial gastrocnemius muscle volume, cm^3	18 (58)	70.9 (31.3)	65.5 (28.4–134.8)
Achilles tendon CSA, cm^2	24 (77)	0.43 (0.09)	0.41 (0.29–0.60)
Medial gastrocnemius muscle stiffness, Nm.mm^{-1}	26 (84)	1.63 (0.82)	1.34 (0.56–3.45)
Achilles tendon stiffness, N.mm^{-1}	27 (87)	172.0 (94.9)	158.5 (74.6–556.4)
Achilles tendon Young's modulus, MPa	24 (77)	813.9 (370.0)	744.0 (341.9–1790.5)
Ankle flexion angle, °	25 (81)	−13.3 (6.7)	−13.8 (−23.4 to 1.6)
Knee flexion angle, °	25 (81)	−9.0 (15.3)	4.6 (−47.9 to 16.3)

SD, standard deviation; GMFCS, Gross Motor Function Classification System; NNcost, net nondimensional cost; MVPA, moderate-to-vigorous physical activity; LPA, light physical activity; Life-H, Assessment of Life Habits; GMFM, Gross Motor Function Measure; CSA, cross-sectional area.

Table 2: Baseline characteristics, resistance training group

	Resistance training group (n=33)		
	n (%)	Mean (SD)	Median (range)
Age, y:mo	33	13:6 (2:7)	13 (10–19)
Female	13 (39)		
Height, cm	33	154.5 (13.3)	157.0 (133.7–178.8)
Mass, kg	33	48.5 (15.1)	47.5 (27.4–78.5)
GMFCS level			
I	16 (49)		
II	12 (36)		
III	5 (15)		
Distribution			
Unilateral	14 (42)		
Bilateral	19 (58)		
Self-reported orthotic wear	15 (46)		
NNcost	32 (97)	0.55 (0.21)	0.48 (0.33–1.00)
Physical activity			
Daily MVPA, min	30 (91)	53.4 (24.5)	56.3 (4.8–118.6)
Daily LPA, min	30 (91)	181.6 (57.9)	175.2 (70.7–354.7)
Daily sedentary time, %	30 (91)	67.7 (11.2)	68.2 (45.4–90.6)
Daily step count	30 (91)	5492.0 (2669.3)	5553.0 (565.9–11562.8)
Life-H score	29 (88)	7.0 (1.7)	7.4 (3.6–9.0)
GMFM-66 D, %	33	80.6 (29.2)	92.3 (0.0–100.0)
GMFM-66 E, %	33	78.9 (30.2)	93.1 (0.0–100.0)
Gait speed, m.s^{-1}	33	1.1 (0.2)	1.1 (0.4–1.6)
Maximal voluntary contraction, Nm	32 (97)	30.5 (17.5)	30.6 (8.4–74.0)
Medial gastrocnemius muscle volume, cm^3	19 (58)	61.3 (21.0)	55.4 (32.7–101.8)
Achilles tendon CSA, cm^2	27 (82)	0.42 (0.08)	0.40 (0.26–0.55)
Medial gastrocnemius muscle stiffness, Nm.mm^{-1}	27 (82)	2.24 (2.21)	1.66 (0.98–12.25)
Achilles tendon stiffness, N.mm^{-1}	29 (88)	154.6 (104.6)	136.0 (54.3–587.9)
Achilles tendon Young's modulus, MPa	28 (85)	757.2 (579.1)	652.8 (297.9–3392.3)
Ankle flexion angle, °	26 (79)	−15.1 (9.8)	−14.8 (−43.3 to 2.4)
Knee flexion angle, °	26 (79)	−6.8 (11.3)	−6.1 (−30.4 to 11.3)

SD, standard deviation; GMFCS, Gross Motor Function Classification System; NNcost, net nondimensional cost; MVPA, moderate-to-vigorous physical activity; LPA, light physical activity; Life-H, Assessment of Life Habits; GMFM, Gross Motor Function Measure; CSA, cross-sectional area.

Table 3: Description of treatment and usual care received

	Usual care group	Resistance training group
Treatment received		
Attendance, median (range)[a]	–	80 (40–100)
Attended ≥70% supervised sessions, n (%)	–	28 (84.9)
Median (range) Number of classes progressed, median (range)[b]	–	7 (2–9)
Exercises progressed,[b] n (%)	–	8 (24.2)
Home sessions completed, median (range)[c]	–	80 (10–115)
Completed ≥70% home sessions, n (%)	–	24 (72.7)
Sessions completed, median (range)[d]	–	80 (30–110)
Completed ≥70% sessions (supervised and home), n (%)	–	25 (75.8)
Usual care received during 22 weeks		
Self-reported activity participation (≥1 per week), n (%)	19 (83)	24 (77)
Received physiotherapy at least once, n (%)	14 (58)	15 (52)
Number of physiotherapy sessions, median (range)	2 (0–31)	1 (0–48)

[a]As a percentage of 10 possible supervised sessions. [b]Defined as progressed at least 8 of 9 supervised sessions. [c]As a percentage of 20 possible home sessions; note some participants completed more than the prescribed sessions. [d]As a percentage of 30 possible supervised sessions; note some participants completed more than the prescribed sessions.

Eighteen therapists delivered the programme at eight sites. Table 3 outlines details of the resistance training programme and usual care received by both groups over 10 weeks. Median attendance was 80% (range 40–100%) of a possible 10 supervised sessions. Approximately 85% of participants attended at least 70% of supervised sessions; 27.3% attended all 10 sessions, 18.2% attended nine sessions, 21.2% attended eight sessions, and 18.2% attended seven sessions. The median percentage of home sessions completed, out of a possible 20 sessions, was 80% (range 10–115%). Approximately 73% of participants completed at least 70% of home sessions. Overall, the median percentage of supervised and home sessions completed, out of a possible 30, was 80% (range 30–110%).

Approximately 76% of participants completed at least 70% of the 30 sessions.

Exercises were progressed at a median of 7 out of a possible 9 classes (range 2–9). Reasons for non-progression were: participants reported resistance was too heavy; poor technique; not obtaining full range of movement; lower-limb muscle or joint pain; unable to add additional weight to weighted vest because it was full; unable to add additional weight to weighted vest because it was causing shoulder or back pain; fatigue. A slightly higher proportion of participants in the usual care group reported participating in physical activities at least once per week over the 22 weeks (Table 3). The proportion of people receiving physiotherapy was also slightly higher in the usual care group. In total, 123 adverse events were reported by 27 participants in the resistance training group (Table 4). The most common types of adverse event reported by participants were lower-limb muscle soreness (70%), lower-limb pain (55%), shoulder pain due to weighted vest (18%), a fall (15%), and lower-limb muscle cramp (15%). Falls did not occur during the class and therefore may be unrelated to the intervention.

Treatment effects

There was no evidence of between-group differences in gait efficiency, physical activity, participation, gross motor function, gait speed, or muscle strength at 10 and 22 weeks (Table 5). There was also no evidence of between-group differences in any additional secondary outcome (Table S5, online supporting information). We identified some subgroup effects. Among those in GMFCS level II, there was evidence of a between-group difference in Achilles tendon Young's modulus at 10 weeks in favour of the intervention (adjusted mean difference: 206.00MPa, 95% CI 15.90–396.09MPa, p=0.034). At 22 weeks, there was very weak statistical evidence that among participants in GMFCS level II,

participants in the resistance training group had lower NNcost (adjusted mean difference: –0.16, 95% CI –0.32 to 0.01, p=0.055) and higher maximal voluntary isometric plantarflexion contraction (adjusted mean difference: 11.12Nm, 95% CI –0.56 to 22.81Nm; p=0.062) compared to the control group, indicating more efficient gait and greater strength. There was also evidence that among participants in GMFCS level II, those in the resistance training group had greater medial gastrocnemius muscle volume at 22 weeks compared to the control group (adjusted mean difference: 12.17cm^3, 95% CI 3.64–20.71cm^3, p=0.005). Further, there was very weak evidence that among those in GMFCS level III, Assessment of Life Habits Questionnaire score was higher for participants in the resistance training group at 22 weeks compared to the control group (adjusted mean difference: 1.83, 95% CI –0.04 to 3.70, p=0.055). Among those with bilateral CP, NNcost was lower in the exercise group compared to the control group at 22 weeks, indicating more efficient gait (adjusted mean difference: –0.17, 95% CI –0.32 to –0.03, p=0.022). Among those with bilateral CP there was also evidence of greater knee flexion angles in the intervention group compared to the control group at 22 weeks (adjusted mean difference: –10.94 degrees, 95% CI –17.09 to –4.78 degrees, p<0.001). In those with unilateral CP, moderate-to-vigorous physical activity, step-count, and knee flexion angle during mid-stance were higher in those in the exercise group compared to the control group at 10 weeks (adjusted mean difference in moderate-to-vigorous physical activity: 14.3min, 95% CI 2.0–26.6min, p=0.022; adjusted mean difference in step-count: 1193.6 steps/min, 95% CI –12.3 to 2399.6 steps/min, p=0.052; adjusted mean difference in knee flexion angle: 5.32 degrees, 95% CI 0.61–10.03 degrees, p=0.027).

Sensitivity analysis

Adjusting for sex in addition to GMFCS level did not result in different conclusions than those obtained from primary analysis (Table S6, online supporting information). Per-protocol analysis was conducted using data from 45 people who completed the study to 22 weeks and were compliant with at least 70% of the sessions, if they were in the resistance training group. There was very weak evidence of greater maximal voluntary isometric plantarflexion contraction (adjusted mean difference: 7.18Nm, 95% CI –0.48 to 14.83Nm, p=0.066) and some evidence of greater knee flexion angles during mid-stance (adjusted mean difference: –4.62 degrees, 95% CI –8.90 to –0.33 degrees, p=0.035) in the resistance training group at 22 weeks compared to the control group (Table S7, online supporting information).

DISCUSSION

We found no evidence that 10 supervised sessions and 20 unsupervised sessions of progressive resistance training over 10 weeks of the ankle plantarflexors changed gait efficiency, muscle strength, activity as assessed by habitual physical activity, gross motor function, and gait speed, or

Table 4: Number and type of adverse events reported by participants in the resistance training group

	Adverse events (n=123)[a]	People reporting at least one event (n=27)[b]
Lower-limb muscle soreness	41 (33)	23 (70)
Lower-limb pain	37 (30)	18 (55)
Fall	18 (15)	5 (15)
Lower-limb muscle cramp	7 (6)	5 (15)
Shoulder pain due to weighted vest	7 (6)	6 (18)
Chest pain	5 (4)	1 (3)
Back pain	3 (2)	3 (9)
Lower-limb stiffness	2 (2)	1 (3)
Arm injury	1 (1)	1 (3)
Ankle sprain	1 (1)	1 (3)
Stomach ache	1 (1)	1 (3)

Data are n (%). [a]Percentage of total adverse events reported. [b]Percentage of 33 participants in resistance training group.

Table 5: Treatment effects at 10 and 22 weeks

	Usual care control group	Resistance training group	Difference in means[a] (95% CI); p
NNcost			
10 weeks	0.47 (0.39–0.55)	0.55 (0.45–0.66)	0.02 (–0.07 to 0.11); 0.696
n (%)[b]	21 (91.3)	29 (90.6)	
22 weeks	0.52 (0.41–0.63)	0.51 (0.40–0.62)	–0.08 (–0.18 to 0.03); 0.158
n (%)[c]	20 (87.0)	25 (86.2)	
Daily moderate-to-vigorous activity, min			
10 weeks	49.4 (37.1–61.6)	54.4 (43.0–65.8)	5.07 (–3.88 to 14.02); 0.267
n (%)	21 (91.3)	25 (78.1)	
22 weeks	49.0 (36.8–61.3)	50.0 (36.3–63.6)	–1.39 (–13.28 to 10.51); 0.819
n (%)	19 (82.6)	21 (72.4)	
Daily light activity, min			
10 weeks	186.8 (165.4–208.2)	164.1 (141.3–187.0)	–1.59 (–21.40 to 18.23); 0.875
n (%)	21 (91.3)	25 (78.1)	
22 weeks	183.7 (159.1–208.2)	151.0 (124.5–177.5)	–9.48 (–38.85 to 19.88); 0.527
n (%)	19 (82.6)	21 (72.4)	
Daily sedentary time, %			
10 weeks	68.8 (65.3–72.3)	70.3 (65.9–74.7)	–0.41 (–3.17 to 2.35); 0.771
n (%)	21 (91.3)	25 (78.1)	
22 weeks	68.8 (64.7–72.9)	71.8 (66.2–77.3)	1.92 (–2.28 to 6.12); 0.370
n (%)	19 (82.6)	21 (72.4)	
Daily step-count			
10 weeks	5647.0 (4525.1–6768.9)	5465.5 (4412.2–6518.9)	281.87 (–604.11 to 1167.89); 0.533
n (%)	21 (91.3)	25 (78.1)	
22 weeks	5625.1 (4343.4–6906.8)	5096.0 (3793.6–6398.4)	–328.54 (–1551.91 to 894.83); 0.599
n (%)	19 (82.6)	21 (72.4)	
Life-H score			
10 weeks[d]	6.2 (5.3–7.1)	6.8 (6.1–7.5)	0.03 (–0.54 to 0.60); 0.907
n (%)	20 (87.0)	26 (81.3)	
22 weeks[d]	6.1 (5.2–7.0)	7.1 (6.5–7.7)	0.21 (–0.34 to 0.76); 0.450
n (%)	21 (91.3)	27 (93.1)	
GMFM-66 dimension D, %			
10 weeks[e]	90.0 (84.6–95.1)	86.1 (79.0–92.6)	1.19 (–1.70 to 4.08); 0.420
n (%)	23 (100.0)	31 (96.9)	
22 weeks[e]	88.3 (82.2–94.1)	87.2 (80.3–93.7)	1.35 (–1.65 to 4.35); 0.379
n (%)	22 (95.7)	29 (100.0)	
GMFM-66 dimension E, %			
10 weeks[e]	87.7 (80.3–94.6)	84.5 (76.8–91.6)	0.07 (–2.06 to 2.21); 0.948
n (%)	23 (100.0)	31 (96.9)	
22 weeks[e]	86.4 (78.5–93.6)	85.7 (78.1–92.7)	–0.81 (–3.07 to 1.45); 0.482
n (%)	22 (95.7)	29 (100.0)	
Gait speed, m.s^{-1}			
10 weeks	1.18 (1.06–1.30)	1.06 (0.95–1.17)	–0.06 (–0.18 to 0.06); 0.315
n (%)	23 (100.0)	31 (96.9)	
22 weeks	1.12 (1.01–1.24)	1.11 (1.00–1.22)	0.01 (–0.12 to 0.14); 0.834
n (%)	22 (95.7)	29 (100.0)	
Maximal voluntary contraction, Nm			
10 weeks	32.3 (22.2–42.3)	36.5 (29.6–43.3)	4.36 (–2.17 to 10.88); 0.191
n (%)	21 (91.3)	30 (93.8)	
22 weeks	26.8 (19.3–34.3)	34.8 (28.7–41.0)	5.86 (–1.68 to 13.41); 0.128
n (%)	20 (87.0)	28 (96.6)	

Data are mean (95% confidence interval [CI]) unless otherwise indicated. [a]Adjusted for baseline values and Gross Motor Function Classification System level. [b]Number included in analysis; number as percentage of participants who attended 10 week assessment (n=55). [c]Number included in analysis; number as percentage of participants who attended 22 week assessment (n=52). [d]Data transformed using square root transformation in order to calculate mean and 95% CI. Mean (95% CI) presented on original scale. [e]Data transformed using square transformation in order to calculate mean and 95% CI. Mean (95% CI) presented on original scale. Life-H, Assessment of Life Habits; GMFM, Gross Motor Function Measure.

participation among adolescents with CP. Similarly, we found no evidence of changes in any biomechanical outcomes including muscle volume and tendon cross-sectional area, muscle and tendon stiffness, or knee and ankle flexion angle during mid-stance of gait. Ninety percent of participants experienced at least one adverse event. However, adverse events were not serious and the majority of events were lower-limb muscle soreness, which may be considered an expected effect of progressive resistance training. To date, reporting of adverse events in trials of exercise for

CP has been poor. A recent review found that 50% of trials of resistance training for people with CP did not state whether they recorded adverse events.[7] However, where reported, similar adverse events have been noted in previous trials including shoulder pain from a weighted backpack, foot and ankle discomfort, and muscle soreness.[7]

No randomized control trial to date has examined the effects of progressive resistance training on gait efficiency. Recent studies found that fatigue was increased in gastrocnemius medialis during walking among children with CP[25]

and that isometric plantarflexor strength explained at least 50% of the variance measures of walking capacity in adults with CP.[26] While this suggests that progressive resistance training targeted at the ankle plantarflexors may improve walking capacity in people with CP, our findings do not support this hypothesis. Similar to our findings, a recent meta-analysis found no evidence that resistance training improved gross motor function, gait speed, or participation in children and adolescents with CP, although only two studies assessed participation.[7] However, it is possible that the measures of activity used in this study were not sensitive to change, particularly given the high proportion of individuals in GMFCS level I. Indeed, a ceiling effect was evident for dimensions D and E of the GMFM-66, as 20% and 9% of participants achieved the maximum possible score for dimensions D and E respectively at baseline; all participants who achieved a maximum score at baseline were in GMFCS level I.

There is limited evidence available on the biomechanical effects of progressive resistance training among people with CP. Without this data, the mechanisms by which muscle strength, gait efficiency, and gross motor function are hypothesized to change in people with CP are based on data in people without CP. Although we hypothesized that gait efficiency may be improved through a number of biomechanical mechanisms, we found neither an improvement in underlying biomechanical variables nor gait efficiency. It is therefore unclear if the lack of improvement in gait efficiency is because these biomechanical variables do not contribute to gait efficiency in CP or because the programme failed to change these variables. However, it should also be noted that biomechanical variables, including muscle strength, were only assessed on one side and, as two sides were trained, improvements may have been observed on the unassessed side. Previous studies found evidence that strength training increased gastrocnemius muscle volume in children with CP.[27,28] However, these studies lacked a control group, which is a significant limitation when determining a causal association as changes in children may be due to growth. A recent randomized control trial of 17 young adults with CP also found changes in plantarflexor muscle volume in favour of progressive resistance training.[29] These changes coincided with improvements in isometric plantarflexor muscle strength, functional strength, walking endurance, agility, and anaerobic capacity. Unlike the current study however, only individuals in GMFCS levels I and II were included. Indeed, studies that found improvements after exercise interventions often included children in GMFCS level I and II only.[29–31]

Given the heterogeneity of severity of motor function and associated impairments in CP, it is likely that the efficacy of progressive resistance training varies between individuals. We found that the intervention had some positive effects, when considering effects by GMFCS level and anatomical distribution (i.e. unilateral and bilateral). Specifically, we observed more efficient gait at 22 weeks among individuals with bilateral CP who received the intervention compared to those who received usual care. We also found that individuals with unilateral CP in the intervention group participated in approximately 15 minutes more moderate-to-vigorous physical activity per day, participated in 1000 more steps per day, and had lower knee flexion angles at 10 weeks, compared to those who received usual care. Among those in GMFCS level II, there was some evidence that adolescents in the intervention group had more efficient gait and greater muscle strength and muscle volume at 22 weeks compared to those in the control group. The mean difference of 0.16 in NNcost suggests that the treatment effect may be clinically meaningful for those in GMFCS level II.[23] However, the wide confidence interval indicates the estimate is imprecise because of the relatively small number of participants in this subgroup and thus the result may be due to random error. This result, and others obtained from subgroup analyses, should be interpreted with caution.

Fifty-six percent of individuals in GMFCS level II had bilateral CP, suggesting that distribution explains some but not all of the treatment effect observed in GMFCS level II. Those in GMFCS level II may represent individuals with greater capacity for change than individuals in GMFCS level I, but also with more functional capacity to recruit muscle fibres than those in GMFCS level III. Future research should explore the potential benefits of resistance training for those in GMFCS level II using an adequate sample size. Other factors that may contribute to variations in effectiveness of resistance training for individuals include baseline level of muscle strength, selective motor control, previous treatment, and orthotic use.

Strength or resistance training is one of the most frequently used interventions among physiotherapists to manage lower-limb function in adolescents with CP.[6] In order for the findings to be clinically meaningful and to inform clinical decision making, it is essential to examine the effects of resistance training under 'real world' clinical settings. This trial was developed based on conditions of routine clinical practice, while adhering to current recommendations for resistance training. Participants completed one supervised session per week and two home sessions per week as this is a typical model of delivering therapy services in the United Kingdom and the United States.[32] That is, therapy is often delivered weekly, biweekly, or bimonthly for a specified period of time to allow the person to progress towards an established goal.[32] Such a model involves input from a therapist in combination with unsupervised performance of exercises by the individual.[32] The inclusion of the home exercise programme was important for delivering resistance training according to guidelines. A previous study reported that delivering a home-based programme to adolescents with CP according to resistance training guidelines was feasible and increased lower limb strength.[33] Our findings, however, suggest that this model of delivering resistance training to adolescents with CP does not improve gait efficiency, ankle plantarflexor muscle strength, activity, or participation.

In order to aid interpretation of our findings we monitored attendance at supervised sessions, completion of home sessions, and progression of exercises. The National Strength and Conditioning Association recommend young people with typical development perform between 1 to 3 sets of 6 to 15 repetitions on 2 to 3 days per week,[8] which equates to between 20 and 90 sets and between 120 and 1350 repetitions over 10 weeks. Based on the combined attendance at supervised classes and self-reported completion of home exercise sessions, the median number of sets performed over 10 weeks was 150 (interquartile range 120–164) and the median number of repetitions was 1592 (interquartile range 1328–1760). This suggests that participants received progressive resistance training according to resistance training guidelines for young people with typical development. While it is possible that variability in completion of the exercises between participants contributed to the findings, our per-protocol analysis did not indicate that the programme was effective among participants with better adherence. It is possible that a higher dose of resistance training is required to observe effects. However, at present there is a lack of research regarding the dose-response relationship between exercise and outcomes for people with CP.[7]

All participants in this study progressively increased resistance throughout the programme. Resistance was increased at a median of 7 out of 9 possible sessions. The most frequently reported reasons for not increasing resistance were that the person was reaching fatigue at the prescribed number of repetitions and the person was not obtaining full range of movement or performing poor technique at the current resistance. Another reason for non-progression was an inability to add weight to the weighted vests because either the vest caused shoulder or back pain, or the vest was full. This was not necessarily related to the person's age or GMFCS level. The potential for non-progression of resistance when using weighted vests to deliver resistance training for young people with CP has not been reported in other studies that have used weighted vests.[33,34] We believe it is important to highlight this potential barrier to implementing progressive resistance training for adolescents with CP in clinical practice. Access to weight machines may be required to continuously increase resistance to a sufficient level to obtain large and consistent changes in muscle strength. This may be the case for all individuals with CP as their muscle strength increases during the programme, but particularly for those with relatively high baseline levels of strength.

A recent randomized controlled trial found that progressive resistance training for young adults with CP aged 15 to 30 years in GMFCS level I or II delivered in a community gymnasium improved muscle strength and 6-minute walk test distance.[29] An earlier randomized controlled trial found that progressive resistance training for young adults with CP aged 14 to 22 years in GMFCS level II or III delivered in a community gymnasium improved muscle strength but not 6-minute walk test distance or score on dimensions D or E of the GMFM.[35] These studies suggest that progressive resistance training delivered two to three times per week in a community gymnasium improves muscle strength and may improve mobility. However, participants in these studies were older than those included in the present study. The findings of these studies may not be applicable to this younger population, and if they are, delivering resistance training to adolescents aged 10 to 14 years in a gymnasium may not be feasible. Indeed, interviews with adolescents in our study revealed that they strongly valued supervision from a physiotherapist and they faced several barriers to participating in resistance training in a community gymnasium, including being unable to access gyms because of their age. Participants and physiotherapists also indicated they did not think it was feasible to attend or deliver more than one supervised session per week. We will outline our findings from interviews in detail elsewhere.

This study addresses several gaps in the evidence base outlined by a Cochrane review,[7] including provision of an intervention in accordance with evidence-based guidelines,[8] assessment of activity and participation, systematic recording of adverse events, and investigation of changes in biomechanical variables. However, there are potential limitations to the study. Participants did not necessarily present with reduced muscle strength or inefficient gait. Although the presence of these complaints may have been a reason that adolescents volunteered to participate, it was not an inclusion criteria. This may explain variability in the effects and it is possible that the intervention is effective in those who present with inefficient gait or reduced strength. Although this is the largest study of progressive resistance training among people with CP to date, it is still limited by a relatively small sample size and missing data in some variables, particularly medial gastrocnemius muscle volume and ankle and knee flexion angle. Data on adherence to the home exercise programme is based on self-report and may be subject to bias. We did not control the usual care received by the two groups, apart from preventing the usual care control group from receiving progressive resistance training. It is possible that the lack of a difference in outcomes between the two groups was because the control group received other intervention. However, studies of resistance training for CP often compare resistance training to 'usual care' without describing usual care. Thus, we believe the description of usual care in this study is important for interpreting the findings. We also did not monitor or prevent orthotic use, which may have impacted gains in strength made during training. Further, subgroup analyses should be interpreted with caution given the relatively small sample in each subgroup and the lack of precision of effect estimates. Finally, the applicability of the findings are limited to ambulatory individuals with CP.

In conclusion, the findings indicate that a physiotherapist-led progressive resistance training programme of the ankle plantarflexors, delivered through a combination of supervised sessions and a home programme over 10 weeks, does not improve gait efficiency, muscle strength, activity, or participation. These findings have implications for

delivery of progressive resistance training. Previous research suggests that delivery of progressive resistance training through supervised sessions in community gymnasiums improves muscle strength.[29,35] Future research should examine the dose–response relationship between resistance training and outcomes, and sustainable models of delivering progressive resistance training to children and adolescents with CP in the community.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUPPORTING INFORMATION

The following additional material may be found online:

Figure S1: Description of possible exercises performed individuals during resistance training programme.

Figure S2: Flowchart of participants through the trial.

Table S1: Description of ankle plantarflexor exercises.

Table S2: Periodized progressive resistance training programme.

Table S3: Baseline characteristics of individuals who completed to 22 weeks and individuals lost to follow-up.

Table S4: Wear-time for Actigraph GT3x accelerometer at each assessment.

Table S5: Treatment effects at 10 and 22 weeks.

Table S6: Treatment effect at 10 and 22 weeks adjusted for baseline values, GMFCS level, and sex.

Table S7: Treatment effects from per-protocol analysis.

Appendix S1: Further detail on calculation of NNcost.

Appendix S2: Further detail on identification of non-wear time and classification of activity counts from Actigraph wGT3X.

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