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Original article

A randomized comparative trial of generalized *vs* targeted physiotherapy in the management of childhood hypermobility

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Abstract

Objective. Joint hypermobility, common in childhood, can be associated with severe pain and significant morbidity. Physiotherapy, the mainstay of treatment, lacks a robust evidence base. This study is aimed at determining the best physiotherapy intervention in managing childhood hypermobility.

Methods. A prospective randomized comparative trial (RCT) compared a 6-week generalized programme, improving muscular strength and fitness, with a targeted programme aimed at correcting motion control of symptomatic joints. Patients were assessed on symptom scores (pain/global-impact), function, muscle strength and fitness.

Results. Fifty-seven children, aged 7–16 years with symptomatic hypermobility, were randomly assign to receive a targeted (T; $n = 30$) or generalized (G; $n = 27$) programme. Statistically significant improvements were demonstrated in both the children's and parental pain scores across both the randomized groups between baseline and follow-up assessments ($P < 0.05$). However, the difference in improvement between the groups was not statistically significant. Child's assessment of change in pain score: mean difference (95% CI) $T - G$, 3.97 (−15.59, 20.85) at the end of treatment and 9.41 at 3-month follow-up (−17.42, 36.24). At the end of treatment, parental assessment of change in pain score, $T - G$ was: −0.27 (−15.05, 14.50) and at 3-month follow-up it was: −9.48 (−26.40, 7.43). Change in parental global assessment was statistically significant, in favour of targeted physiotherapy at final assessment: −21.29 (−40.03, −2.55).

Conclusion. This is the first physiotherapy RCT for treating hypermobility. It demonstrated significant and sustained reduction in pain when both groups were combined, but did not detect any difference between the groups. This study provides normative and methodological data for future studies of hypermobility.

Trial registration. Current Controlled Trials, www.controlled-trials.com, ISRCTN58523390.

Key words: Paediatric, Juvenile, Hypermobility, Benign hypermobility syndrome of childhood, Randomized controlled trial, Physiotherapy, Intervention, Joint control, Ehler's–Danlos syndrome Type III.

Introduction

Joint hypermobility is common in children [1], with joint pain and coordination problems being the commonest presenting features [1]. Symptoms can be significant, including exercise-related/post-exercise-related pains, nocturnal leg pains, recurrent foot/ankle, knee and back pain, joint swelling, clumsiness, pain and fatigue in the hand, wrist or lower arm associated with writing [1, 2]. Some associated problems include: missed school

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physical education and sporting hobbies, handwriting difficulties, pain amplification and sleep (including parental) disturbance [1].

Adults with hypermobility may have recurrent episodes of soft tissue rheumatism, widespread or multiple localized sites of pain, spinal pain, depression and premature OA [3–5]. Impact on daily activities is considerable, with pain being the commonest symptom [6]. Lax joints are likely to be less stable, to sublux or dislocate, and are more susceptible to effects of trauma [7].

Despite physiotherapy being the mainstay of interventional management [2, 8, 9], there are no randomized controlled trials in adult or paediatric hypermobility. Data assessing intervention are minimal, particularly for children [1, 10–13]. No validated programme of physiotherapy intervention is universally recognized [4, 6].

Two broad physiotherapy approaches are commonly used: a generalized physical activity programme of graded exercises and a targeted programme correcting motion control of symptomatic joints.

The former aims to improve the general muscular strength, stamina, endurance and cardiovascular fitness, through aerobic activities using moderate/low-impact strengthening exercises [11]. Indiscriminate exercise may be harmful if these exacerbate excess ranges of movement.

The targeted programme aims at correcting motion control of symptomatic joints. Hypermobile children have excessive IA excursion due to laxity of passive structures. Joint control focuses on the related musculature and proprioception.

This study aimed to compare a generalized exercise programme with a targeted programme within a randomized trial and assess the impact of these interventions on symptom scores.

Patients and methods

Eligibility

Children aged 7–16 years, treated at the Department of Rheumatology, Alder Hey Children's Hospital NHS Foundation, Liverpool, UK (providing secondary and tertiary care) between June 2004 and May 2007, were eligible for inclusion in this study. All children identified as having symptomatic hypermobility were invited to participate.

Symptomatic patients had arthralgia for three preceding months or more. Children were considered hypermobile if they met the Revised (Brighton 1998) Criteria for benign joint hypermobility syndrome (BJHS) [14]. In brief, they had to fulfil either: two major criteria, one major and two minor criteria, four minor criteria, or two minor criteria and a first-degree relative with hypermobility [12]. Major criteria were: Beighton score of $\geqslant 4$ [12]; arthralgia in four or more joints. Minor criteria included [12]: Beighton score <4; arthralgia in fewer than four joints; mechanical back pain for $\geqslant 3$ months; and hypermobility in first-degree relative. The Beighton score assesses hypermobility of the following: placing hands flat on the floor without bending knees, hyperextension of knees and elbows >10°, little finger MCP hyperextension to >90°, bending thumb to forearm [12]. Patients were excluded if they refused consent. The Liverpool Children's Local Research Ethics Committee granted ethical approval. Written, informed parental/patient consent/assent was obtained.

Assessments

An initial medical assessment determined eligibility for the trial. Children with audible murmurs had routine echocardiography. All physiotherapy assessments (at baseline, mid-point assessment and final follow-up) lasted ~30 min and were conducted by one senior physiotherapist assessor (I.R.); patients and treating physiotherapist (S.K.) were asked not to divulge the allocated treatment to the assessing physiotherapist. Standardized data entry proformas were used throughout.

A baseline assessment collated demographic data, diagnostic hypermobility criteria, symptomatology scores (see below) and measurements of joint range, muscle strength and physical condition. Joint range in degrees was measured using goniometry [15, 16] of the following: shoulder—external rotation with the upper arm touching the body and the elbow at 90°; elbow—extension; hip—medial and lateral rotation in prone position (giving total angle of rotation); knee—extension; ankle—plantar flexion. Intra- and inter-observer reliability using goniometry is comparable with [15] or better than visual estimation [16].

Muscle strength in mid-range of these joints was assessed for the following muscle groups: shoulder—abduction; elbow—flexion with forearm supinated; hip—abduction; knee—extension; ankle—plantar flexion and inversion. Muscle strength was measured using manual muscle testing (MMT) using a 10-point scale for the specified muscle groups [17] and myometry [18]. MMT may lack sensitivity in assessing relatively strong muscle groups [17]. Hence, a quantitative myometric measurement was made of the same muscle groups.

The six-minute shuttle walking test [19] is a standardized test of general physical condition. In brief, a standardized recording emits single beeps at regular intervals. The child is asked to walk between two cones, 9 m apart, and complete the distance before the next beep sound. Every minute, the walking speed is increased incrementally by shortening the inter-beep time. The patient determines the end-point of the test, i.e. when unable to continue or when they complete the exercise. The stage they reach is recorded.

A mid-point assessment is carried out following completion of treatment sessions, ~2 months after randomization. A final assessment took place ~3 months after completing the treatment sessions and 5 months after the initial randomization. Ongoing management needs were determined at the final assessment (e.g. further physiotherapy).

Outcomes

Outcomes were measured at baseline, mid-point and final assessments. As pain is the most frequent and distressing complaint of children with BJHS [1], the primary outcome was improvement in the child's pain assessment score [20]. Younger children used a faces scale ranging from 1 to 5 while older children (age $\geqslant$11 years) used a visual analogue scale (VAS; Fig. 1) [20, 21]. Participants were asked to indicate their pain level in the past week on the linear 100-mm scale. Change in pain-VAS was used to assess the impact of therapy on symptoms [21, 22].

Secondary outcomes were:

- parent's assessment of their child's pain: parental-VAS (see above);
- parent's global evaluation of the impact of their child's hypermobility in the previous week: global-VAS;
- functional impairment measured using the Childhood HAQ (CHAQ) [23, 24];
- six-minute shuttle test (measured at baseline and mid-point only).

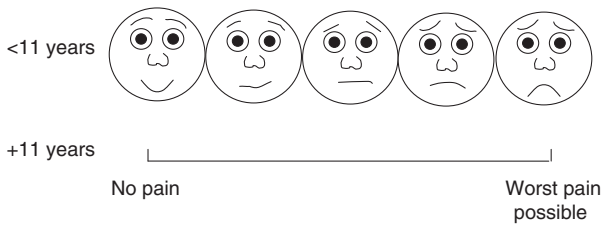
Randomization

Following the baseline assessment, children were randomly assigned to receive either the generalized exercise programme or the targeted exercise programme. Families were informed of the treatment allocation at the first physiotherapy treatment session. Treatment allocation was concealed by placing an allocation card between two blank cards in a sealed, opaque, sequentially numbered envelope. The randomization list was generated in a 1 : 1 ratio using a computer-generated sequence with random variable block size of four and six.

Physiotherapy intervention

All treatment sessions were provided by a second senior physiotherapist (S.K.), blind to demographic data, diagnostic hypermobility criteria, symptom scores and assessment of joint range, muscle strength and fitness. Each child received six, sequential, weekly appointments for individual half-hour physiotherapy treatments, in which the allocated intervention was administered. Current practice was four to six weekly sessions, with further follow-up where necessary.

Fig. 1 Faces pain scale. Child's pain assessment score was measured in two ways depending on the age and ability of the child. Younger children used a faces scale ranging from 1 to 5. The first face corresponded to a smiling face and minimal/no pain, while the fifth corresponded to an unhappy face and the worst pain imaginable. Older children (age $\geqslant$11 years) used a VAS with a double-anchored 100-mm analogue scale with anchors of 'no pain' and 'worst possible pain'. Patients were asked to indicate their pain level in the past week on the appropriate scale.



General exercise programme. Each session consisted of a set of standardized general exercises, established as treatment options aimed at maximizing muscle strengthening and fitness [25, 26]. These included shuttle-runs, bunny-hops, squat-thrusts, sitting-to-standing, step-ups and star-jumps. Initially, each exercise would be timed (starting at 30 s, increasing by 15-s blocks at a time) or a pre determined number of repetitions would be completed (initially 10, increasing stepwise in blocks of 5 or 10) as the patient progressed through the programme. As each exercise was achieved more easily, the numbers of repetitions or timing were increased. As these were successfully completed, new exercises were introduced to continue progression over the treatment course.

Home exercises were given to the participants, to be done on a daily basis, based on their achievement during the treatment sessions. Normal activities were encouraged along with return to sport where possible. Participants were advised to do warm-up and cool-down stretches when participating in exercise or sporting activities.

Targeted exercise programme. The targeted exercise programme used established, standardized physiotherapy exercises of the symptomatic joint(s), specifically chosen to address functional stability, re-training using a process developed by kinetic control [27, 28].

- Control neutral joint position—identifying abnormal resting position of symptomatic joints, re-training postural muscles to facilitate optimal joint alignment (e.g. avoiding hyperextension of knee when standing).
- Re-train dynamic control—once a 'neutral' resting position is achieved, re-training of specific muscles to maintain joint position while moving adjacent joints (e.g. hip flexion while maintaining spinal neutral).
- Motion control—improving the ability of specific muscles to control the joint through its entire range, both concentrically and eccentrically (e.g. on sitting-to-standing quadriceps or working concentrically on standing up and eccentrically on sitting down).
- Specific tissue lengthening—to address short mobilizer muscles (e.g. hamstring stretches). Tissue stretching was only considered when adequate postural control had been achieved.

The physiotherapist provided guidance on maintaining the joint position and control of muscle contraction during all exercises. Once this was carried out without compensation, it was considered that motion control was achieved. Patients then progressed to the next level by reducing their support and exercises increased in repetition, speed and duration, to maximize muscle strength and

stamina. Proprioceptive techniques were also used in gaining static and dynamic joint control.

Participants were given a home exercise programme, tailored to their level of control and advised that all exercises should be pain-free as tissue provocation would be a sign of poor motion control.

Statistical methods

Forty-eight patients per group were required to detect a 14.5-mm difference in pain-VAS between interventions corresponding to an improvement in quality of life defined as feeling 'much better' in paediatric rheumatology patients [21]. Sample size was calculated from these data with 80% power using a two-tailed, two-sample *t*-test with 5% significance, assuming that the two groups had an equal S.D. of 25 mm [22, 29]. Assuming a 10% loss to follow-up, a total of 108 children were required.

Analysis of all data was done only after all recruited children had completed their assessments. All data analyses were carried out using SAS version 9.1. Two-tailed tests were used for all analyses and significance determined at the 0.05 level.

Demographic data were described using standard descriptive statistics. Analysis was based on intention-to-treat principle, determining change from baseline to the mid-point and final assessments. Paired *t*-test was used to test for change from baseline within each group and overall. Two-sample *t*-tests compared continuous variables between trial groups. Pearson chi-square test was used for categorical data. Analysis of covariance (ANCOVA) explored possible relationships between outcomes and explanatory variables (e.g. trial group, gender, age, baseline values). Mean (S.D.) are presented for all continuous variables. The 95% CIs are presented for comparisons between treatment groups.

To allow for the two age-based methods of collecting data on child's assessment of pain, the faces pain scale was transformed to a 0–100 scale. No pain face corresponded to a value of 0; the worst pain face corresponded to a value of 100 on the pain-VAS, with intermediate values of 25, 50 and 75.

Results

Of the 120 children assessed during the study period with generalized or symptomatic hypermobility, 36 did not meet entry criteria as they were either not symptomatic for at least 3 months or did not have generalized hypermobility; parental consent was not given despite meeting eligibility criteria in 17 (reasons including: too far to travel on a weekly basis; mother pregnant; sent initial appointments but failed to attend; exam year and unable to commit to treatment; and family unhappy with diagnosis). Ten patents were not recruited for logistical reasons (including: busy clinic and clinicians unable to have time to discuss trial with families, physiotherapists (assessor/therapist) away on annual leave, mistaken eligibility criteria). Figure 2 displays the flow chart of the trial. Fifty-seven children were randomly assigned, 30 (52.6%) to receive targeted physiotherapy while 27 (47.4%) received generalized physiotherapy. Changes in referral pattern, hypermobile children not meeting eligibility criteria, reluctance of families to commit to a 6-week treatment programme contributed to difficulties in recruiting to the target programme. After significant, repeated efforts to optimize enrolment and extend the trial recruitment period, the Steering Committee took a pragmatic decision to stop the trial after 3 years. The study provides important normative and methodological data for future studies of hypermobility.

Baseline data

Table 1 presents the demographic and clinical characteristics, including symptom score, joint range assessment and muscle strength of the participants both by treatment group and overall. Treatment groups were very similar at baseline.

Figure 2 displays the patient throughput during the trial. Of 30 patients randomized to receive targeted physiotherapy, 17 (57%) completed the intervention compared with 15 of 27 (56%) randomized to generalized physiotherapy.

Patients withdrew for the following reasons: rehabilitated (2); required further investigation (3); change in family circumstances (4). Patients were considered lost to follow-up if they repeatedly 'did not attend' (DNAs; total $n = 16$) without stating the reason. Patients who DNA were followed up by telephone calls and/or a letter in an attempt to re-establish contact before they were deemed to be lost to follow-up.

Table 2 presents the baseline characteristics, comparing those completing final assessment and those who did not. Although no statistically significant differences were identified, trend suggested that those who completed were more likely to have had back pain for >3 months, associated joint swelling, worsening pain with exercise and to require medication.

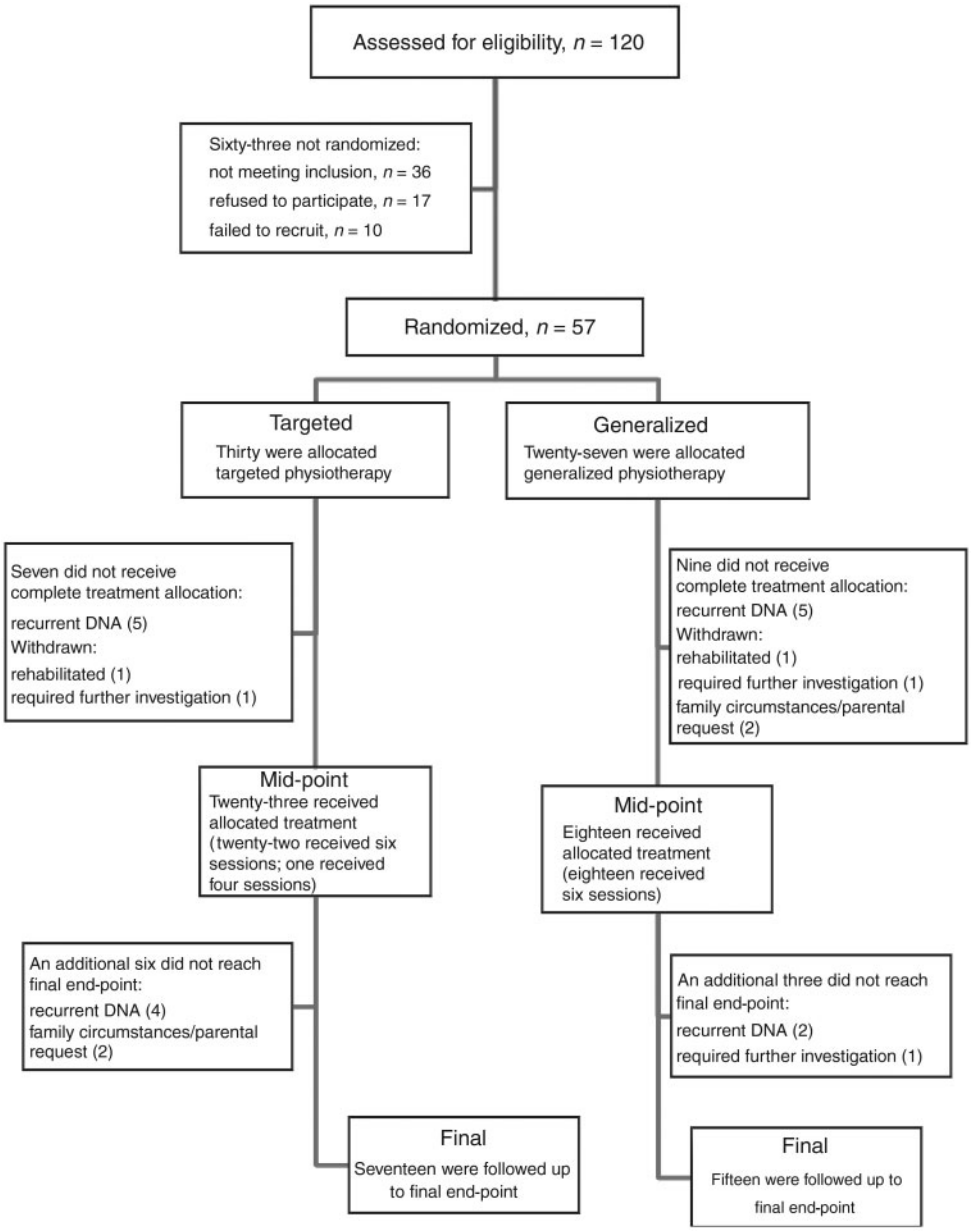
Change in symptom scores from baseline

Table 3 presents summary data of the baseline, mid-point and final assessment scores for primary and secondary outcomes. Results across both groups indicate improvements in child's pain and parental assessment of child's pain, parent's global assessment and CHAQ score. There was no significant change in shuttle test score over time in these participants.

Comparison of symptom scores between treatment groups

Table 4 presents the primary and secondary outcome data with comparisons between groups. There was no significant difference between treatment groups for either primary or secondary outcomes at the mid-point assessment. However, at the final assessment (i.e. ~3 months after completing the intervention), parent's global assessment showed a significantly greater improvement in the targeted group compared with the generalized group.

Fig. 2 Flow chart for the trial. Chart indicating numbers of patients eligible, randomized and studied at baseline, mid-point and final assessments, along with those not included and withdrawn from the trial. DNA: did not attend.



The results for the child's pain assessment favoured generalized physiotherapy while the parental assessment of pain favoured targeted physiotherapy. This trend was consistent for each assessment and may reflect the child's and parent's experience and perception of the different interventions; however, CIs were wide. Conclusions were unchanged when baseline covariate information was included in ANCOVA.

Correlation of symptomatology scores

There were significant differences in child and parental pain-VAS score at each assessment point, parents tending to underestimate their child's pain. The means of the paired difference between the child's and parental assessment of pain were as follows: baseline 11.95 (95% CI 5.90, 18.00), $n = 57$, $P = 0.0002$; at mid-point: 7.60 (95% CI 1.15, 14.04), $n = 41$, $P = 0.022$; and at final assessment: 6.09 (95% CI 0.63, 11.54), $n = 29$, $P = 0.03$. However, there was a significant correlation between the child's pain score and their parents' perception of their child's pain at baseline, mid-point and final assessment ($r = 0.50$, $n = 57$; $r = 0.67$ $n = 41$; and $r = 0.82$ $n = 29$, respectively; $P < 0.001$). The increase in correlation across the time points is consistent with the reduction in differences.

TABLE 1 Descriptive data at baseline of demographics, clinical characteristics, symptom scores, fitness, joint range assessment and muscle strength

Characteristics[a]	Targeted physiotherapy ($n=30$)	Generalized physiotherapy ($n=27$)	Combined ($n=57$)
Demographic			
Gender: male, *n* (%)	20 (66.7)	18 (66.7)	38 (67)
Age, years	11.0 (2.5)	10.7 (2.6)	10.88 (2.5)
Height, cm	148.9 (14.8)	147.4 (19.2)	148.18 (16.9)
Weight, kg	42.0 (13.2)	45.4 (21.2)	43.60 (17.4)
Clinical			
Family history: yes, *n* (%)	16 (53.3)	14 (51.9)	30 (52.6)
Symptom scores			
Child's pain assessment	55.5 (21.3)	62.1 (24.1)	58.6 (22.7)
Parent's pain assessment	45.1 (23.0)	48.4 (22.9)	46.7 (22.8)
Parent's global assessment	36.1 (26.4)	37.2 (25.3)	36.6 (25.7)
CHAQ	0.62 (0.65)	0.76 (0.68)	0.69 (0.66)
Shuttle level test	94.9 (22.2)	79.4 (23.1)	87.6 (23.8)
Beighton score	5.6 (1.6)	6.1 (1.6)	5.8 (1.6)
Joint range assessment: goniometry, degrees			
Left shoulder	89.7 (10.2)	88.9 (10.1)	89.30 (10.1)
Right shoulder	90.0 (10.3)	89.4 (9.5)	89.74 (9.8)
Left elbow	10.9 (8.4)	10.7 (8.5)	10.8 (8.4)
Right elbow	9.6 (8.5)	9.8 (7.3)	9.7 (7.9)
Left hip medial	54.4 (12.5)	54.6 (11.3)	54.5 (11.9)
Right hip medial	53.2 (13.4)	55.4 (11.3)	54.2 (12.4)
Left hip lateral	48.8 (14.4)	48.3 (10.3)	48.6 (12.5)
Right hip lateral	49.7 (12.9)	46.3 (9.6)	48.1 (11.5)
Left hip angle	102.9 (14.2)	101.3 (19.3)	102.1 (16.7)
Right hip angle	100.7 (19.9)	101.1 (12.1)	100.9 (16.5)
Left knee	8.7 (5.1)	12.3 (5.4)	10.4 (5.5)
Right knee	8.4 (5.0)	11.3 (5.3)	9.8 (5.3)
Left ankle	135.8 (33.6)	135.9 (36.0)	135.8 (34.4)
Right ankle	135.9 (33.6)	135.9 (36.4)	135.9 (34.6)
Muscle strength: myometry, newtons			
Shoulder abduction	97.0 (31.2)	102.5 (44.5)	99.6 (37.8)
Elbow flexion in supination	121.7 (36.2)	119.0 (44.5)	120.4 (40.0)
Hip abduction	135.2 (47.7)	142.7 (50.3)	138.8 (48.7)
Knee extension	176.4 (47.4)	165.8 (46.0)	171.5 (46.6)
Ankle flexion	188.8 (49.7)	181.8 (53.1)	185.6 (51.0)
Ankle inversion	127.8 (42.5)	127.6 (39.1)	127.7 (40.6)
Muscle strength: MMT[b]			
Shoulder	8.6 (1.0)	8.4 (1.1)	8.5 (1.1)
Elbow	9.0 (1.0)	8.7 (1.1)	8.9 (1.0)
Hip	9.0 (1.0)	9.0 (1.0)	9.0 (1.0)
Knee	9.3 (0.8)	9.2 (0.8)	9.3 (0.8)
Ankle flexion	9.7 (0.7)	9.4 (0.8)	9.5 (0.7)
Ankle inversion	9.0 (1.0)	9.0 (1.0)	9.1 (1.0)

[a]Categorical variables: number of participants (%); continuous variables: mean (S.D.); [b]MMT: 10-point scale (1–10).

The child's pain score correlated significantly with the parent's global assessment score at the mid-point and final assessments ($r=0.49$, $n=41$, $P=0.001$; and $r=0.83$, $n=29$, $P<0.001$, respectively) but not at baseline ($r=0.11$, $n=57$, $P=0.43$). Correlations between child's pain and CHAQ were low ($r=0.18$, $n=57$, $P=0.169$; $r=0.38$, $n=41$, $P=0.013$; $r=0.27$, $n=29$, $P=0.15$) at baseline, mid-point and final assessments, respectively.

Parent's perception of their child's pain correlated significantly with their global assessment at baseline ($r=0.44$, $n=57$, $P<0.001$), mid-point ($r=0.66$, $n=41$, $P<0.001$) and final ($r=0.95$, $n=32$, $P<0.001$) assessments. Correlations between parent's perception of their child's pain and CHAQ score were $r=0.36$, $n=57$, $P=0.005$ at baseline; at mid-point ($r=0.63$, $n=41$, $P<0.001$) and final ($r=0.59$, $n=32$, $P<0.001$) assessment.

Goniometry and symptom scores

There was no significant correlation for either intervention between goniometry measurements of all seven joints measured bilaterally and symptom scores (child and

TABLE 2 Comparison of baseline characteristics between those completing and those not completing the final assessment

Characteristics[a]	Completed final assessment, $n = 32$ (56.1%)	Did not complete final assessment, $n = 25$ (43.9%)	*P*-values
Trial group: targeted intervention	17 (53.1)	13 (52.0)	0.93
Gender: male, *n* (%)	22 (68.8)	16 (64.0)	0.71
Family history: yes	16 (50.0)	14 (56.0)	0.65
Past medical history: yes	11 (34.4)	9 (36.0)	0.90
$\geqslant$3 months of symptoms in four or more joints	27 (84.4)	22 (88.0)	0.70
Back pain for $\geqslant$3 months	11 (34.4)[a]	6 (24.0)	0.26
Associated joint swelling: yes	16 (50)	8 (32.0)	0.17
Pain worse with exercise	23 (71.9)	12 (48.0)	0.07
Medications required	25 (78.3)[b]	13 (52.0)[c]	0.25
Age, years	10.94 (2.50)	10.80 (2.58)	0.84
Height, cm	147.14 (16.35)	149.50 (17.75)	0.60
Weight, kg	44.49 (16.98)	42.46 (18.16)	0.67
Child's pain assessment	60.42 (23.79)	56.36 (21.56)	0.51
Parents' pain assessment	44.37 (21.11)	49.66 (24.88)	0.39
Parents' global assessment	32.78 (25.11)	41.52 (26.04)	0.21
CHAQ	0.79 (0.62)	0.56 (0.70)	0.19
Shuttle level test	83.81 (22.58)	92.36 (24.81)	0.18

Number (%) reported for categorical data; mean (S.D.) reported for continuous variables; [a]$n = 30$; [b]$n = 28$; [c]$n = 17$.

parental pain-VAS, global assessment and CHAQ score) at baseline, or with improvement at final assessment.

Discussion

This study is the first randomized comparative trial (RCT) of physiotherapy intervention in hypermobility. With a remarkable paucity of paediatric and adult studies quantifying the impact of physiotherapeutic intervention on clinical symptomatology, this study underlines the challenges and importance of developing a strong evidence base in this field.

Statistically significant improvements in the children's pain scores and parental pain scores were seen across both randomly assigned groups between baseline and follow-up assessments. Significant short-term differences between treatments in the primary (child's pain score) or secondary outcomes were not demonstrated. Over time, the targeted programme demonstrated significant benefit over the generalized programme, reducing the parent's global assessment of impact of hypermobility and a trend towards reduction in parental pain score.

Joint pain is the commonest presenting feature of childhood hypermobility [1]. Key outcomes important to patients with hypermobility include reduction in pain score of 20–30/100 that would be considered clinically significant, improved function, better joint control and stability [9]. At baseline, patient's mean (S.D.) pain-VAS was 57.6 (20.1) on a scale 0–100 where 100 is the worst pain imaginable. By definition, they had a minimum of 3 months' symptoms. Mean (S.D.) parental assessment of global well-being was 36.6 (25.7). These data can be considered in the light of mean (S.D.) baseline global assessment score of 44 (26) in children with severe polyarticular juvenile idiopathic arthritis (JIA) requiring s.c. MTX therapy [30]. In JIA, 30% improvement from baseline is accepted as being of significant magnitude to help define a positive outcome from an intervention [31]. In juvenile DM, a 20% improvement in global assessment of disease status is regarded as clinically significant [17]. In this context, this trial demonstrated a clinically important reduction in pain score in both randomized groups of >20 mm and an ~40% reduction in the child and parent's VAS pain and global assessment scores from baseline. Parents significantly underestimated their child's symptoms of pain, as noted in other paediatric rheumatic conditions [32].

To date, there has been minimal robust investigation of treatment efficacy in paediatric or adult-related hypermobility. Most published data generally reflect case reports [1, 9]. The lack of a strong evidence base potentiates patients' experience that they are frequently poorly understood, inadequately managed [9] and frequently children may not have access to physiotherapy treatments at all [1].

Many children are hypermobile on examination, defined as increased joint mobility beyond the range of motion considered normal [3]. Mobility of joints varies with age, gender and ethnicity [3–5] but normal paediatric age range is undefined. Frequency of symptoms across populations and individuals is highly variable [2]. Why certain children are symptomatic and what causes their associated pain remains unclear [2, 8]. Exploration of patient and family beliefs regarding cause of their symptoms requires careful evaluation in childhood hypermobility, beyond the scope of this study. Other factors include degree of joint laxity,

Table 3 Summary data for each trial group and all participants of primary and secondary outcomes at mid-point and final assessments, together with significance of change from baseline

Outcomes	Trial group	Baseline, $n=57$ $T=30$, $G=27$	Mid-point, $n=41$ $T=23$, $G=18$	Paired change M−B	*P*-value*	Final, $n=29$ $T=17$, $G=15$	Paired change F−B	*P*-value#
Primary								
Child's pain assessment	Targeted	55.53 (21.32)	28.83 (21.86)	−25.78 (28.37)	**<0.001**	31.77 (23.37)[a]	−21.23 (33.07)	**0.026**
	Generalized	62.09 (24.14)	36.67 (31.64)	−29.75 (8.63)	**0.005**	39.82 (26.01)	−30.64 (37.34)	**0.009**
	All	57.59 (20.14)	34.34 (23.56)	−27.52 (32.88)	**<0.001**	33.72 (24.44)	−25.78 (34.89)	**<0.001**
Secondary								
Parental assessment of pain	Targeted	45.12 (22.97)	22.17 (25.52)	−19.91 (23.12)	**<0.001**	19.44 (20.59)	−21.62 (24.43)	**0.002**
	Generalized	48.44 (22.88)	27.86 (18.75)	−19.64 (23.33)	**0.002**	36.00 (24.77)	−12.13 (22.14)	0.052
	All	46.69 (22.7)	24.67 (22.71)	−19.79 (22.92)	**<0.001**	27.2 (23.80)	−17.17 (23.50)	**<0.001**
Parental global assessment	Targeted	36.05 (26.44)	19.09 (23.93)	−15.93 (29.62)	**0.017**	17.74 (22.18)	−17.59 (28.28)	**0.021**
	Generalized	37.24 (25.27)	21.58 (22.37)	−11.78 (31.47)	0.13	33.60 (26.02)	3.7 (22.87)	0.54
	All	36.61 (25.67)	20.18 (23.01)	−14.11 (30.13)	**0.005**	25.17 (24.99)	−7.61 (27.67)	0.13
CHAQ score	Targeted	0.62 (0.65)	0.48 (0.71)	−0.24 (0.54)	**0.045**	0.46 (0.56)	−0.15 (0.27)	**0.037**
	Generalized	0.76 (0.68)	0.69 (0.63)	−0.14 (0.55)	0.28	0.83 (0.68)	−0.16 (0.50)	0.25
	All	0.69 (0.66)	0.57 (0.68)	−0.20 (0.54)	**0.024**	0.64 (0.64)	−0.15 (0.39)	**0.035**
Shuttle-level assessment	Targeted	94.90 (22.18)	92.48 (26.81)[b]	2.83 (13.64)	0.33	NA		
	Generalized	79.41 (23.14)	77.88 (21.73)	0.94 (18.46)	0.84			
	All	87.56 (23.76)	86.49 (25.60)	2.05 (15.59)	0.42			

Values reported as mean (s.d.); **P*-value derived from a one-sample t-test of the paired change M−B, *P*-value derived from a one-sample *t*-test of the paired change F−B; *P*-values presented in bold where $P<0.05$; [a]$T=15$, $G=14$; [b]$T=23$, $G=16$.

TABLE 4 Primary and secondary outcome data comparing treatment groups with analysis of change from baseline with the mid-point and the final assessments

Outcomes	Targeted Physiotherapy, mean (S.D.)	Generalized Physiotherapy, mean (S.D.)	Difference $T-G$, mean (S.D.)	95% CIs for difference	*P*-value
Mean change between baseline and mid-point	$n=23$	$n=18$			
Primary					
Child's assessment of pain	−25.78 (28.37)	−29.75 (38.63)	3.97 (33.24)	−15.59, 20.85	0.71
Secondary					
Parental assessment of pain	−19.91 (23.12)	−19.64 (23.33)	−0.27 (23.21)	−15.05,14.50	0.970
Parental global assessment	−15.93 (29.62)	−11.78 (31.47)	−4.16 (30.44)	−23.53,15.22	0.667
CHAQ	−0.24 (0.54)	−0.14 (0.55)	−0.01 (0.54)	−0.44, 0.25	0.577
Shuttle-level assessment[a]	2.83 (13.64)	0.94 (18.46)	1.89 (15.77)	−8.52, 12.29	0.72
Mean change between baseline and final level	$n=17$	$n=15$			
Primary					
Child's assessment of pain[b]	−21.23 (33.07)	−30.64 (37.34)	9.41 (35.19)	−17.42, 36.24	0.48
Secondary					
Parental assessment of pain	−21.62 (24.43)	−12.13 (22.14)	−9.48 (23.34)	−26.40, 7.43	0.261
Parental global assessment	−17.59 (28.28)	3.70 (22.87)	−21.29 (25.90)	−40.03, −2.55	**0.027**
CHAQ	−0.15 (0.27)	−0.16 (0.50)	0.01 (0.39)	−0.28, 0.29	0.955

[a]$T=23$, $G=16$; [b]$T=15$, $G=14$.

muscle weakness and fatigue, or associated clinical features [2]. Musculo-skeletal system integrity is dependent upon intact ligamentous structures, neuromuscular control [33] and muscle tone [34]. Repetitive strain to musculo-tendinous, ligamentous or articular structures through ligament laxity may contribute to myalgia and pain [2], exacerbated by poor physical condition and muscle tone around affected joints.

Current management strategies remain supportive and symptomatic [12] with a focus on recognition, education and advice to children, parents and teachers [2] and physiotherapy provided by a multi-disciplinary team [8]. A range of treatment modalities are adopted, although supported by a weak, mainly adult-focused evidence base. Approaches include: developing core support, increasing muscular tone, stabilizing lax joints, proprioception enhancement, focusing on primary area(s) of dysfunction, joint stabilization, posture re-education, joint awareness, functional stability and endurance [9, 12, 13]. Functional re-training aims to target control of the neutral joint position, re-training dynamic joint control in the direction of stability dysfunction and rehabilitating global stabilizers [27, 28]. Treatments include: graded exercises with gradual increase in activity, achievable goals, increasing general and cardio-respiratory fitness, weight control and sporting capacity [9, 13]. These techniques formed the basis of the two interventions investigated.

Combined low-impact aerobic and strengthening exercises can reduce VAS pain scores in children with arthritis [25]. Exercise training results in improved physical function and reduced CHAQ scores [35], reducing disease symptoms and improving general exercise endurance [36]. Increased levels of moderate to vigorous physical activity and structured exercise can improve the exercise capacity, performance of daily activities and overall quality of life across a spectrum of paediatric rheumatic disorders [26]. Targeted, functional and aerobic exercises can improve muscle strength, stamina and pain for both inflammatory and non-inflammatory paediatric conditions, including BJHS [37].

Recognized *a priori* that regular physiotherapy over 6 weeks would impact their symptoms, through education, counselling and support, a placebo arm, although considered, was deemed unethical. Children studied had BJHS, measured by a validated scoring system with signs not attributed to another connective tissue disorder [14]. BJHS is excluded by the presence of hereditary disorders such as Marfan or Ehlers–Danlos syndromes (EDSs) [7] [other than EDS hypermobility type (formerly EDS III) from which it is indistinguishable]. Scoring systems (e.g. Beighton) are based on adults with hypermobility [5, 7]. Single-figure scores are problematic, ignoring the ubiquitous nature of collagen [38]. Revised (Brighton) Criteria retain quantification of joint laxity, while trying to include associated clinical features although they are not validated in children [14, 38]. Mean (S.D.) Beighton score [5, 7] for this study was 5.8 ± 1.6, emphasizing that patients had generalized hypermobility. Eighty-six per cent of the participants fulfilled two major Revised (Brighton) Criteria. It is well recognized that other joints including the shoulders, hips, ankles and feet, not included in the joints assessed by the Beighton scoring system, can be particularly troublesome in children [1]. A specifically designed and validated diagnostic tool for childhood hypermobility is needed.

This study did not reach the target sample size for several reasons. Referral patterns fluctuated and numbers of children with hypermobility attending the clinic reduced markedly during the study period. Hypermobility may be oligoarticular rather than generalized and can yet cause significant symptoms [4]. Recruitment estimates were

made on children referred with hypermobility; however, 36 patients were excluded because of localized symptoms or duration <3 months, yet still incapacitating enough to require hospital referral. Families found it difficult to commit to 6 weeks of physiotherapy; this was illustrated by patients meeting eligibility criteria but not consenting. For future trials, it should be recognized that time to explain the study to parents, logistical difficulties and staff leave/absence can make recruitment difficult.

Sixteen (28%) patients failed to complete the initial treatment programme and 25 (44%) did not attend the follow-up to final assessment. Continued adherence with home exercise programmes may have varied although no data specifically quantified this. Compliance with ongoing intense physiotherapy and readiness to undertake rehabilitation is key to its potential success, but is very demanding [9]. Patients with more severe symptoms including prolonged back pain, exercise-induced pain, associated joint swelling and requiring medication were more likely to be compliant. Assessing families' experience and acceptability of the intervention is important in designing future trials of physiotherapy requiring intense, recurrent attendance.

There are very few clinical trials of physiotherapy in childhood rheumatic or non-inflammatory musculoskeletal disorders. Major challenges include trial methodology, normative data, appropriate outcome tools, recruitment and patient retention. This study provides an insight into these challenges while providing data for designing future interventional trials in childhood hypermobility.

In conclusion, this is the first physiotherapy RCT for the treatment of hypermobility. It has demonstrated significant and sustained reduction in pain as a result of both interventions, but a significant and sustained improvement in parental global assessment with the targeted exercise programme. This study provides normative data and methodological detail for future studies and clinical trials in this area.

Rheumatology key messages

- This study is the first physiotherapy RCT for the treatment of hypermobility.
- The trial demonstrated significant and sustained reduction in pain with both interventions.
- This study provides normative data and methodological details for future studies on hypermobility.

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