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REVIEW

Physiotherapy and occupational therapy interventions for people with benign joint hypermobility syndrome: a systematic review of clinical trials

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Abstract

Purpose: This study assessed the literature to determine the efficacy and effectiveness of physiotherapy and occupational therapy interventions in the treatment of people with benign joint hypermobility syndrome (BJHS). *Methods*: Published literature databases including: AMED, CINAHL, MEDLINE, EMBASE, PubMed and the Cochrane Library, in addition to unpublished databases and trial registries were searched to October 2012. All clinical trials comparing the clinical outcomes of Occupational Therapy and Physiotherapy interventions compared to non-treatment or control intervention for people with BJHS were included. *Results*: Of the 126 search results, 3 clinical studies satisfied the eligibility criteria. The data provides limited support for the use of wrist/hand splints for school children. While there is some support for exercise-based intervention, there is insufficient research to determine the optimal mode, frequency, dosage or type of exercise which should be delivered. *Conclusions*: The current evidence-base surrounding Occupational Therapy and Physiotherapy in the management of BJHS is limited in size and quality. There is insufficient research exploring the clinical outcomes of a number of interventions including sensory integration, positioning and posture management and education. Longer term, rigorous multi-centre randomised controlled trials are warranted to begin to assess the clinical and cost-effectiveness of interventions for children and adults with BJHS.

Keywords

Conservative treatment, exercise, joint hypermobility, orthotics, splinting

History

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➤ Implications for Rehabilitation

- There is an evidence-base to support clinician's use of proprioceptive-based exercises in adults, and either tailored or generalised physiotherapy regimes for children with BJHS.
- Clinicians should be cautious when considering the prescription of hand/wrist splints for school age children with BJHS, based on the current research.
- Until further multi-centre trials are conducted assessing the clinical and cost-effectiveness of interventions for children and adult with BJHS, clinical decision-making should be based on theoretical rather than evidence-based grounds for this population.

Introduction

Benign joint hypermobility syndrome (BJHS) is considered an inherited connective tissue disorder which manifests as excessive joint flexibility and pain [1–3]. A genetic component is recognised, with first-degree relatives identified in up to 50% of cases [3], though no single gene abnormality has been found. BJHS is thought to be associated with an abnormality of collagen or in the ratio of collagen subtypes [3]. Mutations in the fibrillin gene have also been reported [4], which may contribute to the clinical presentation of soft tissue flexibility. It is assumed that the increase in joint flexibility and impaired sensory feedback, essential for joint stability, causes abnormal joint loading and biomechanical strain on surrounding soft tissues [1,2,3,5]. This may result in pain and joint trauma which in turn, may lead to traumatic arthritis [6]. BJHS can be a disabling and functionally limiting condition, with a proportion of people developing chronic pain syndromes [7]. Sufferers have reported difficulties and delays in obtaining a diagnosis of BJHS. They report that health care professionals often demonstrate limited understanding of the symptoms associated with BJHS, and its importance as a pathological entity [7,8].

The method used to diagnose BJHS has evolved during the past 20 years. Diagnosis is presently based on clinical grounds, most commonly performed against the Brighton criteria [1]. This system consists of the Beighton score (a 9-point system, assessing multi-joint laxity) with additional questions on

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symptoms such as pain and joint dislocation [1,3]. These additional questions are proposed to distinguish between people with asymptomatic generalised joint laxity, and those with BJHS [3,6,9]. Physiotherapy and occupational therapy are considered the corner-stone treatments for people diagnosed with BJHS [6,10]. Treatments prescribed centre on increasing joint stability. Therefore, interventions to facilitate this have included strengthening and proprioceptive exercises, use of braces, splints and orthotics to protect or normalise joint position, education and advice in order to minimise risk of joint injury, and the prescription of adaptations such as grips and seating appliances to facilitate activities of daily living with minimal discomfort [3,6,10]. While such interventions have been previously recommended, no systematic reviews have been conducted in this area. Second, no specific reviews have examined the methodological quality of the current evidence-base on which clinical decision-making is made. BJHS is a heritable disorder, and often evident in childhood. There have been no reviews specifically investigating intervention which could be used in this age group. In particular, therefore, we sought to critically document the evidence concerning interventions for BJHS in childhood.

The purpose of this study was to address this lack of a critical evaluation of the evidence-base and to determine the effectiveness of physiotherapy and occupational therapy interventions in the treatment of people diagnosed with BJHS.

Materials and methods

This study was conducted according to the PRISMA recommendations [11].

Search strategy

The primary search strategy consisted of a review of the electronic databases: MEDLINE, EMBASE, CINAHL, AMED (via Ovid), Cochrane Library, PubMed and the PEDro from their inceptions to October 2012. MEDLINE MeSH, keyword search terms and Boolean operators utilised are presented in Table 1. This structure was modified to accommodate the other search databases. In order to assess unpublished or grey literature, a secondary search was performed of the databases: OpenGrey, the WHO International Clinical Trials Registry Platform, Current Controlled Trials and the UK National Research Register Archive from inception to October 2012. Finally, reference lists of all eligible study and identified review paper were scrutinised. Corresponding authors for each included study were also contacted to identify any omitted or currently on-going studies.

Table 1. Search strategy for MEDLINE.

1.	Joints/
2.	Limb.tw.
3.	Hypermobility, Joints/
4.	Benign hypermobility syndrome/
5.	Laxity.tw.
6.	Flexibility.tw.
7.	Instability.tw.
8.	Joint laxity, familial/
9.	Marfanoid habitus.tw.
10.	Marfanoid hypermobility syndrome/
11.	Ehlers-Danlos type 3/
12.	Management.tw.
13.	Treatment.tw.
14.	Interventions.tw.
15.	Therapy/
16.	Physiotherapy/
17.	Physical Therapy/
18.	Occupational Therapy/
19.	Cognitive Behavioural Therapy.tw.
20.	Rehabilitation/
21.	Exercise/
22.	Devices.tw.
23.	Adaptation.tw.
24.	Advice.tw.
25.	Education/
26.	Sensory Integration.tw.
27.	Sensitisation.tw.
28.	Pacing.tw.
29.	Behaviour modification.tw.
30.	Seating.tw.
31.	Posture/
32.	Ergonomics
33.	Orthosis.tw.
34.	Orthotic Devices/
35.	Brac$.tw.
36.	Splint$.tw.
37.	OR/1,2
38.	OR/3-11
39.	OR/12-36
40.	AND/37-39

Eligibility criteria

Studies were included if they were full publications of randomised or non-randomised controlled trials (RCT) or case-control studies evaluating occupational therapy or physiotherapy-based interventions, against a control group. Any occupational therapy or physiotherapy-based interventions were included. Joint hypermobility was regarded as a score of $\geq$4 using the Beighton scoring system. Symptomatic was regarded as the current report of pain, instability or any symptoms limiting the functional or perceived capabilities of an individual necessitating a healthcare consultation.

No exclusions were made on the basis of age, gender, ethnicity, previous injury rate or severity of joint hypermobility syndrome. In order to minimise the risk of selection bias, no restrict was placed on the age, publication source or language of the included studies.

Studies including individuals with other genetic/hypermobility connective tissue disorders such as Marfans and Ehlers-Danlos were excluded, with the exception of Ehlers-Danlos type III which is considered the indistinguishable from BJHS and the same connective tissue disorder [12]. Case studies reporting the management of three or less participants were also excluded.

The title and/or abstract from each citation identified through the search strategy were reviewed independently by two reviewers (H.B., E.J.). When considered potentially eligible, full-texts of these studies were obtained. These were reviewed by the two reviewers against the eligibility criteria to determine their final eligibility. Any disagreement in paper eligibility was resolved by discussion between the two reviewers (H.B., E.J.), which was adjudicated by a third reviewer (T.S.).

Outcome measures

To evaluate effectiveness of occupational or physiotherapy interventions, outcome measurements of interest included lower limb functional outcomes such as the Western Ontario and McMaster Universities Arthritis Index (WOMAC) [13], Knee injury and Osteoarthritis Outcome Score (KOOS) [14] and upper limb assessments of hand-writing. Self-reported quality of life measurements were expected to be assessed using tools such as the AIM-2 questionnaire [15], Short Form-36 [16]. More ''objective'' measurements were also expected to be reported such as muscle strength, physical testing such as the timed-get-up-and-go, timed stair ascent, or the sixty-meter walk test, physical dexterity and fine, manipulation motor skills, recurrent injury and sporting/school/occupational participation and engagement.

Data extraction and critical appraisal

Data were independently extracted by one reviewer (H.B.) and verified by a second (E.J.) for each included paper. Data extracted: characteristics of participants (both symptomatic and asymptomatic controls) including age, gender, duration of symptoms, method of diagnosis, degree of joint hypermobility (frequently assessed using the Beighton scoring system), co-morbidities, follow-up periods, study interventions, secondary co-interventions and clinical/functional outcomes measurements and their findings. All data were entered into a pre-defined data extraction form.

Study methodology was critically appraised using the CASP ''randomised controlled trial'' appraisal tool [17]. This tool was appropriate since it has been widely adopted in previous musculoskeletal clinical studies [18–20]. This tool consists of 14 questions, assessing domains such as paper eligibility, recruitment, randomisation procedures, sample size, outcome measure rigor, data analysis methods and external validity [17]. Each paper was critically evaluated using this tool by one reviewer (H.B.) and was then independently verified by a second (E.J.). Any disagreements in appraisal score were addressed through discussion between the two reviewers (H.B., E.J.), which was adjudicated by a third reviewer (T.S.).

Data analysis

Data homogeneity was evaluated visually using the data extraction findings. There was marked heterogeneity and therefore data could not be combined with meta-analysis. The data are therefore described.

Results

Search strategy results

The results of the literature search strategy are summarised in Figure 1. A total of 126 citations were identified from the search strategy. After their assessment based on the eligibility criteria, three studies were identified as having assessed the effectiveness of occupational therapy or physiotherapy-based interventions for people with BJHS. One on-going study, the BENDY trial, was identified but the study is not complete. Two studies initially thought eligible were excluded since they did not recruit a non-treatment or second treatment comparator group, opting to assess pre and post intervention outcomes in the same cohort [21,22]. Three citations were excluded as they were review papers [3,6,10], while five papers were excluded since they were case reported and not studies examining a cohort of participants with BJHS [23–27].

Methodological appraisal

The results of the CASP appraisal tool are presented in Table 2. This indicates that although one study demonstrated a low risk of bias [28], the other two studies that form this evidence-base, demonstrated a high risk of bias with major methodological limitations. Recurrent limitations included recruitment of small cohorts, whose sample sizes were not based on a power calculation, not randomising allocation and not blinding assessors to intervention allocation [29,30]. Furthermore, the limited analysis of findings using inferential statistical tests meant that it was difficult to generalise the findings of these studies into clinical practice with confidence. Finally, all studies provided limited data on longer term outcomes, with the longest follow-up

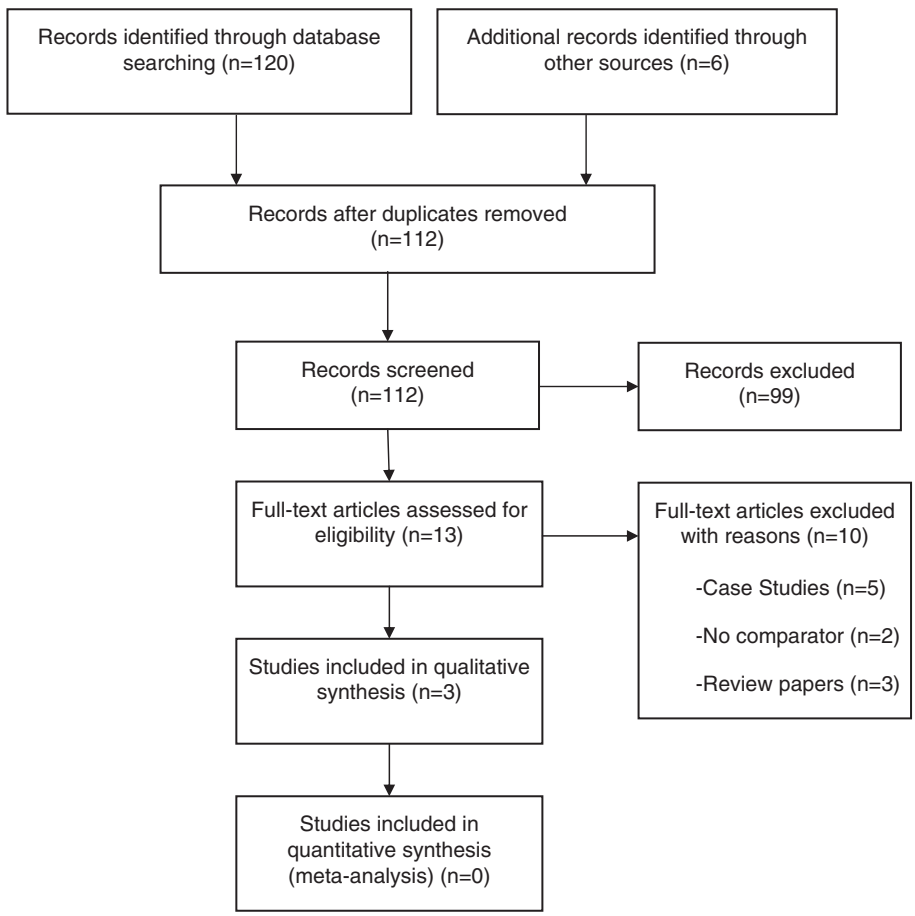

Figure 1. PRISMA flow-chart presenting the results of the search strategy.

Table 2. CASP critical appraisal findings.

Criterion	Frohlich et al. [30]	Kemp et al. [28]	Sahin et al. [29]
Was a clear research question posed?	✓	✓	✓
Was this an RCT?	×	✓	×
Was there a clear description of subject allocation?	✓	✓	✓
Were the groups equal for important characteristics at baseline?	×	✓	✓
Was random allocation truly randomised?	×	✓	×
Were assessors, staff and subjects blinded to group allocation?	×	✓	×
Were all the subjects accounted for at the end of the trial?	✓	✓	×
Was there equal handling/management of subjects throughout the trial?	✓	✓	×
Was the sample size based on a power calculation?	×	✓	×
Were the results analysed by intention to treat principles?	✓	×	×
Were between-group differences assessed with descriptive statistics?	×	✓	×
Were between-group differences assessed with interferential statistics?	×	✓	×
Was confidence interval data presented?	×	✓	×
Were the results generalisable to the clinical population?	×	×	×
Interpretation	High risk of bias	Low risk of bias	High risk of bias

✓ – Yes; × – No.

periods assessed in Kemp et al.'s [28] trial, assessing outcomes at 5 months after commencing the intervention.

Included study characteristics

A summary of the cohort characteristics is presented in Table 3. In total, 131 patients were reviewed. This consisted of 49 males and 82 females. Two studies assessed childhood BJHS cohorts [28,30], with ages ranging from seven to 16 years [28]. Mean age was 26 years in Sahin et al.'s [29] cohort. Participants were all children ($\leq$16 years) in Kemp et al. [28] and Frohlich et al.'s [30] studies. Participants were followed-up for 4 weeks [30] to 5 months [28]. The severity of hypermobility was evaluated using the Beighton score in all studies. In all three studies, the majority of participants presented with a Beighton score of four or more points. Frohlich et al. [30] reported Beighton scores for three of their four participants, documenting this ranging from six to eight points. Kemp et al. [28] reported a mean Beighton score of 5.8 points. Although Sahin et al. [29] did not document their mean Beighton score, or their cohort's ranges, they did document that a Beighton score of four or more was an eligibility criteria.

Three different types of interventions have been evaluated within the current evidence-base. These surround the application of hand and wrist splints [30], proprioceptive-based exercise therapy [29] and a generalised versus targeted physiotherapy programmes [28]. These interventions have been summarised in Table 3, and are evaluated below within these sub-groups.

Hand and wrist splints

One trial, based on four school-aged participants, has been conducted assessing the effectiveness of wrist/hand splints on hand-writing with BJHS [30]. In this cross-over trial, participants were assessed after being given a custom-made wrist/hand splint to use during writing tasks at home or at school. After 4 weeks, three of the four participants showed a significant decrease in handwriting speed when wearing the splint, and a significant decrease in pain for three participants following the withdrawal of the splint. However, two of the participants infrequently wore the splint and all reported that they were unsure that they would continue to use the splint if offered at the end of the trial. No change in handwriting endurance, grip strength or self-perception of handwriting using the handwriting proficiency screening questionnaire across the four participants was observed. This study presented with a high risk of bias with considerable methodological limitations (Table 2). No conclusions or recommendations can be made on the basis of this evidence.

Proprioceptive-based exercises

One trial, with a high risk of bias (Table 2), has been conducted assessing the effectiveness of proprioceptive-based exercises for people diagnosed with BJHS [29]. Sahin et al. [29] randomised 40 participants with BJHS assessed using a Beighton score of four points or above, and 30 healthy controls with a Beighton score of less than four points to receive either a proprioceptive-based exercise intervention or to receive no exercises for eight weeks. While the authors reported that there was no statistically significant difference in proprioceptive capability ($p > 0.39$), a statistically significant improvement in VAS pain on resting and motion ($p < 0.05$) and AIMS-2 score was reported from baseline to eight-week follow-up in those allocated to receive exercises. The authors did not report whether there was a statistically significant difference in between group outcomes. It is therefore not possible to assess the effectiveness of prescribing proprioceptive exercises to those with BJHS.

Generalised versus targeted physiotherapy programme

One trial has been conducted assessing the effectiveness of a generalised versus a targeted physiotherapy exercise-based intervention for children with BJHS [28]. This demonstrated a low risk of bias (Table 2). The 57 participants aged seven years to 16 years, the majority presenting with a Beighton score of greater than four. Of the 30 children randomised to the targeted physiotherapy programme, only 17 completed their 2-month treatment course, and of the 27 allocated to receive general physiotherapy, only 15 completed. Two month follow-up results revealed no difference between the interventions in the following outcomes: child or parental assessment of pain ($p = 0.71$; $p = 0.97$), parental global assessment ($p = 0.67$), childhood health assessment questionnaire (CHAQ; $p = 0.58$), shuttle-level assessment ($p = 0.72$). Five-month follow-up results revealed no difference between the interventions in the following: child and parental assessment of pain ($p = 0.48$; $p = 0.26$), CHAQ score ($p = 0.96$). However, there was a statistically significant difference in parental global assessment ($p = 0.03$) favouring the targeted physiotherapy intervention group (mean difference = 21.3; 95% CI: −40.03, −2.55). Both the targeted and general physiotherapy programmes demonstrated statistically significant improvements in child and parental pain scores, parental global assessment score and CHAQ scores from pre-intervention to two- and five-month follow-ups ($p < 0.05$).

Therefore, while the evidence demonstrated a moderate risk of bias with some methodological limitations, there was evidence to

Table 3. Demographic characteristics and interventions for the eligible studies included in this review.

Study	Sample size	Gender (M/F)	Mean age in yrs (SD)	Mean Beighton Score (SD)	Study intervention	Comparison	Follow-up period
Frohlich et al. [30]	4	1/3	14	≥6 (Range 6–8) in 3 participants	Custom-made neoprene wrist/hand splint extending proximally from the palmar crease and interphalangeal joint of thumb, to one third length of the forearm. Worn when writing.	No Intervention	4 weeks
Kemp et al. [28]	57	38/19	10.9 (2.5) Range: 7–16	5.8 (1.6)	6 weekly *targeted* physiotherapy sessions, consists of: exercises to re-training postural muscles and dynamic control; slow sit-to-stand and muscle control exercises during functional activities; muscle stretching exercises and strengthening exercises targeted dependent on participants specific motor control deficits. Progression of exercises with speed, duration. Re-enforced through a similar home exercise programme.	6 weekly *generalised* physiotherapy programme consisting of: general strengthening and fitness exercises including shuttle-runs, bunny-hops, quad-thrusts, sit-to-stand, step-up and star-jump exercises. Progression with repetition, timing and speeding. re-enforced through a similar home exercise programme.	5 months
Sahin et al. [29]	70 (BJHS: 40; C:30)	BJHS: 6/34 C: 4/26	BJHS: 26 (7.15) C: 26.37 (6.13)	≥4	8 weekly proprioceptive-based exercise sessions, consisting of: walking backwards, heel walking, toe-walking, standing and bending on one limb; slow sit-to-standing; plyometrics and agility-speed circuits; balance board; mini-tramplin exercises.	No Intervention	8 weeks

BJHS – benign joint hypermobility syndrome.
C – Control; F – Female; M – Male; SD – Standard Deviation; Yrs – Years.

indicate that physiotherapy can improve clinical outcomes for children with BJHS. However, based on this limited literature, the data indicate no statistically significant difference between the prescription of a tailored compared to a generalised physiotherapy intervention.

Discussion

The findings of this review indicate that the current evidence-base to justify the provision of physiotherapy and occupational therapy interventions is severely limited in both size and quality. Based on the three studies available, there is insufficient evidence to determine the effectiveness of proprioceptive-based exercises (in adults), or the use of hand/wrist splints (in school age children). While the literature suggests that physiotherapy may improve clinical outcomes for children, it remains unknown whether a targeted or general-physiotherapy intervention programme is superior.

The evidence-base showed a number of methodological limitations, particularly for the assessment of splinting and proprioceptive-based exercises. These included recruiting small, under-powered cohorts thereby permitting type II statistical error, not randomising patients to treatment allocation allowing selection and allocation bias, and finally not blinding assessors to treatment group, therefore allowing assessment bias. Furthermore, all the studies reviewed followed their participants for short periods, ranging from 4 weeks to 5 months. It is therefore unclear as to how these interventions behave and the clinical impact over the mid- or longer term. Finally, while the methods in Kemp et al.'s [28] study suggested a low risk of bias, the researchers were unable to recruit and retain the required numbers of participants from their power calculation. Thus, the largely non-statistically significant findings reported may be a true finding or may reflect a type II statistical error [31].

Further study is therefore essential to improve the current evidence-base. The trials must be designed with sufficient powerful and rigor, longer term follow-up and be fully randomised and controlled. Given the difficulties that Kemp et al. [28] reported in recruitment and follow-up, the estimated sample sizes for such trials will need to reflect this. It is likely they will require recruitment over multiple centres. This may also be advantageous to improve the generalisability of the evidence to a wider clinical population.

Barton and Bird's [21] study was excluded from this review, since it had no control group. This cohort study reported that exercise significantly decreased global pain, with some physical tests also demonstrating significant improvements during the 6-week exercise programme. However, this training effect was reversed within 6 weeks of ceasing the exercise programme.

These results indicate the importance of adherence to, and maintenance of an exercise programme longer term to maintain any possible musculoskeletal benefits to people with BJHS. Adherence was also demonstrated as a problem in Frohlich et al.'s [30] study of hand/wrist splints. Therefore, the role of education and empowering patients to maintain an intervention longer term may be key to optimise therapeutic outcomes if there is proven clinical benefit.

Previous literature has suggested that proprioceptive deficits exist in people with BJHS [27,28]. Furthermore, maximal exercise capacity has been reported as significantly decreased in those with BJHS compared to age- and gender-matched control subjects [32]. Given these factors, there appears to be a clinical indication for the prescription of exercise for this population. The current evidence provides some suggestion that exercise may have therapeutic value for people with BJHS [21,28,29]. However, there remains insufficient evidence to determine what type, frequency or dosage of exercise or the means of delivering such exercise interventions. It also remains unclear whether there is a difference in outcome on patient age, severity of symptoms (principally pain) and the degree of joint hypermobility and instability presented. These should be considered when designing future clinical trials to stratify for such characteristics.

There is a wealth of literature reporting interventions in BJHS which are not proven; all of these have been or are still used in clinical practice. While there are multiple possible treatments, none have been shown to be effective. These include previous review literature and single case studies which have reported the prescription of various interventions but which were not examined through empirical research. These interventions have included repetitive muscle vibration therapy [23], orthotics, splinting and taping [3,24], education and postural advice [10,25] and cryotherapy for pain management [26]. Furthermore, no studies have assessed the clinical outcomes of sensory integration, posture management or orthotic devices for the management of BJHS. All of these are types of treatment which are used in clinical practice while remaining under-investigated [7,10]. It is important that any examination of the clinical effectiveness of these interventions also includes a health economic analysis, both direct and indirect costs of interventions to patients and their families, in order to better understand which interventions are of more overall benefit for this challenging condition.

Conclusion

The current evidence-base surrounding occupational therapy and physiotherapy in the effective and cost-effectiveness of the management of BJHS remains limited in size and quality. While there is some evidence to support exercise-based interventions, this is by no means clear. There is insufficient literature exploring the clinical outcomes of splinting, sensory integration, positioning and posture management or advice and education delivered by healthcare professionals to children, parents of children or adults with BJHS. Further longer term rigorous multi-centre trials are warranted, assessing the clinical and cost-effectiveness of clearly defined interventions within this group.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

References

1. Grahame R, Bird HA, Child A. The revised (Brighton 1998) criteria for the diagnosis of benign joint hypermobility syndrome (BJHS). J Rheumatol 2000;27:1777–9.
2. Hakim AJ, Cherkas LF, Grahame R, et al. The genetic epidemiology of joint hypermobility: a population study of female twins. Arthritis Rheum 2004;50:2640–4.
3. Simpson MR. Benign joint hypermobility syndrome: evaluation, diagnosis, and management. J Am Osteopath Assoc 2006;106: 531–6.
4. Magnusson SP, Julsgaard C, Aagaard P, et al. Viscoelastic properties and flexibility of the human muscle-tendon unit in benign joint hypermobility syndrome. J Rheumatol 2001;28:2720–5.
5. Bulbena A, Duró JC, Porta M, et al. Clinical assessment of hypermobility of joints: assembling criteria. J Rheumatol 1992;19: 115–22.
6. Baeza-Velasco C, Gély-Nargeot MC, Bulbena Vilarrasa A, Bravo JF. Joint hypermobility syndrome: problems that require psychological intervention. Rheumatol Int 2011;31:1131–6.
7. Ross J, Grahame R. Joint hypermobility syndrome. Br Med J 2011; 342:c7167.
8. Grahame R, Bird H. British consultant rheumatologists' perceptions about the hypermobility syndrome: a national survey. Rheumatology (Oxford) 2001;40:559–62.
9. Everman DB, Robin NH. Hypermobility syndrome. Pediatr Rev 1998;19:111–17.
10. Simmonds JV, Keer RJ. Hypermobility and the hypermobility syndrome, part 2: assessment and management of hypermobility syndrome: illustrated via case studies. Man Ther 2008;13:e1–11.
11. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009;62:1006–12.
12. Grahame R. The need to take a fresh look at criteria for hypermobility. J Rheumatol 2007;34:664–5.
13. Klassbo M, Larsson E, Mannevik E. Hip disability and osteoarthritis outcome score. An extension of the Western Ontario and McMaster Universities Osteoarthritis Index. Scand J Rheumatol 2003;32: 46–51.
14. Roos EM, Roos HP, Lohmander LS, et al. Knee injury and osteoarthritis outcome score (KOOS) – development of a self-administered outcome measure. J Orthop Sports Phys Ther 1998;28: 88–96.
15. Meenan RF, Gertman PM, Mason JH. Measuring health status in Arthritis: the Arthritis Impact Measurement Scales. Arthritis Rheum 1980;23:146–52.
16. Ware J, Shelbourne C. The MOS 36-item Short-Form Health Survey (SF-36): I. Conceptual framework and item selection. Med Care 1992;30:73–83.
17. CASP [Internet]. 2012. Randomised controlled trial appraisal tool. Available from: http://www.casp-uk.net/wp-content/uploads/2011/11/CASP_RCT_Appraisal_Checklist_14oct10.pdf [last accessed 2 May 2012].
18. Smith TO, Walker J, Russell N. Outcomes of medial patellofemoral ligament reconstruction for patellar instability: a systematic review. Knee Surg Sport Traumatol Arthroscopy 2007;15:1301–14.
19. Reilly KA, Barker KL, Shamley D. A systematic review of lateral wedge orthotics-how useful are they in the management of medial compartment osteoarthritis? Knee 2006;13:177–83.
20. Postle K, Pak D, Smith TO. Effectiveness of proprioceptive exercises for ankle ligament injury in adults: a systematic literature and meta-analysis. Man Ther 2012;17:285–91.
21. Barton LM, Bird HA. Improving pain by stabilisation of hyperlax joints. J Orthop Rheumatol 1996;9:46–51.
22. Ferrell WR, Tennant N, Sturrock RD, et al. Amelioration of symptoms by enhancement of proprioception in patients with joint hypermobility syndrome. Arthritis Rheum 2004;50:3323–8.
23. Celletti C, Castori M, Galli M, et al. Evaluation of balance and improvement of proprioception by repetitive muscle vibration in a 15-year-old girl with joint hypermobility syndrome. Arthritis Care Res (Hoboken) 2011;63:775–9.
24. Hinton RY. Case study: rehabilitation of multiple joint instability associated with Ehlers-Danlos syndrome. J Orthop Sports Phys Ther 1986;8:193–8.
25. Russek LN. Examination and treatment of a patient with hypermobility syndrome. Phys Ther 2000;80:386–98.

26. Colloca CJ, Polkinghorn BS. Chiropractic management of Ehlers-Danlos syndrome: a report of two cases. J Manipulative Physiol Ther 2003;26:448–59.
27. Toker S, Soyucen E, Gulcan E, et al. Presentation of two cases with hypermobility syndrome and review of the related literature. Eur J Phys Rehabil Med 2010;46:89–94.
28. Kemp S, Roberts I, Gamble C, et al. A randomized comparative trial of generalized vs targeted physiotherapy in the management of childhood hypermobility. Rheumatology (Oxford) 2010;49: 315–25.
29. Sahin N, Baskent A, Cakmak A, et al. Evaluation of knee proprioception and effects of proprioception exercise in patients with benign joint hypermobility syndrome. Rheumatol Int 2008;28: 995–1000.
30. Frohlich L, Wesley A, Wallen M, Bundy A. Effects of neoprene wrist/hand splints on handwriting for students with joint hypermobility syndrome: a single system design study. Phys Occup Ther Pediatr 2012;32:243–55.
31. Bland M. Introduction to medical statistics, 3rd ed. Oxford: Oxford University Press; 2006.
32. Engelbert RH, van Bergen M, Henneken T, et al. Exercise tolerance in children and adolescents with musculoskeletal pain in joint hypermobility and joint hypomobility syndrome. Pediatrics 2006; 118:e690–6.