James M. Anderson Center for Health Systems Excellence

Evidence-Based Care Guideline

Identification and Management of Pediatric Joint Hypermobility

In children and adolescents aged 4 to 21 years old[a]

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Target Population

Inclusions: Children and adolescents:

- With joint hypermobility
- 4 to 21 years old
- Less than 4 years old with a family history of hypermobility

Exclusions: Children and adolescents with:

- Greater than mild hypotonia
- Spasticity
- Progressive neuromuscular conditions

Target Users

Including but not limited to:

- Dentists/Orthodontists
- Nurses
- Nurse Practitioners
- Occupational Therapists
- Physical Therapists
- Psychologists
- Physicians
  - Geneticists
  - Orthopedists
  - Primary Care Physicians
  - Rheumatologists
  - Sports Medicine
- Physician Assistants
- Other Health Care Professionals

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Introduction

References in parentheses ( ) Evidence level in [ ] (See last page for definitions)

Throughout the literature and in clinical practice, joint hypermobility (JH) is referred to by different terms such as being "double-jointed" and is used interchangeably with joint laxity and/or ligamentous laxity. Those individuals with symptomatic manifestations of their JH are said to have joint hypermobility syndrome (JHS) also referred to as "benign" JH syndrome. JH and symptomatic JH (i.e. JHS) can be part of many different heritable connective tissue disorders. The most common syndromic manifestation is the Ehlers-Danlos syndrome (EDS) types III or the EDS hypermobile type. It is becoming more widely accepted to use the term EDS III or the hypermobile type of EDS interchangeably with JHS as there is a lack of clinical distinction *(Tinkle 2009 [5a])*. For the purposes of this guideline, we will use the term JH.

Children and adolescents with JH syndrome often live with joint pain, fatigue, and poor tolerance to physical activity that significantly impacts their quality of life *(Birt 2013 [2a], Tobias 2013 [2a], Schubert-Hjalmarsson 2012 [4a], Voermans 2010b [4a], Rombaut 2012b [4b])*. Specifically, Tobias (2013) found that adolescents with hypermobility are two times more likely to experience musculoskeletal pain than non-hypermobile peers *(Tobias 2013 [2a])*. This population is often overlooked, yet has potential to benefit from effective management by physical therapists *(Kemp 2010 [2a], Pacey 2013 [2b])*. JH is commonly found in the pediatric population having been identified in 30-34 % of school aged children when assessed using a gross screening tool *(Junge 2013 [2b], Remvig 2011 [4a], Arroyo 1988 [4a], Beighton 1998 [5a])*. Prior to puberty there is no evidence of a gender bias *(Remvig 2011 [4a], Juul-Kristensen 2009 [4a])*, however after puberty the prevalence and degree of JH increases in females *(Barrera-Mora 2012 [4b])* and declines in males *(Quatman 2008 [4a])*.

JH is an inherited disorder with an autosomal dominant pattern thought to affect connective tissue proteins. In some, the condition may be idiopathic, without being linked to a defined diagnosis, or a pathological component of known heritable connective tissue disorders such as Marfan syndrome, Ehlers-Danlos syndrome *(Murray 2006 [5a])* and Stickler syndrome *(LocalConsensus 2014 [5])*. JH is rarely identified as the primary diagnosis for which patients present for therapy. JH may be an underlying issue identified when treating a

variety of other patient problems such as young children with gross motor delays *(Tirosh 1991 [3a], Davidovitch 1994 [4a], Bernie 2011 [4b])*, coordination difficulties *(Kirby 2007 [4a])*, fibromyalgia *(Ting 2012 [4a], Karaaslan 2000 [4a])*, chronic fatigue syndrome *(Barron 2002 [4a], Nijs 2006 [4b])*, or frequent and recurring injuries *(Briggs 2009 [5a])*. Therapists are to consider the possibility of the compounding factors of JH if response to treatment is hindered or not progressing as expected *(Simmonds 2007 [5a])*. Due to the collagen deficiency, soft tissue may be weaker and slower to respond to training effects *(Briggs 2009 [5a])*.

Several comorbidities are identified as contributing to the decreased function and quality of life in patients with JH. The potential impact of co-morbidities must be considered when planning effective physical therapy interventions. There are associated long term effects of the JH syndromes that, when addressed proactively during childhood, may have less detrimental impact on adult function and quality of life *(Voermans 2010a [4a])*.

Aside from the commonly reported symptom of pain, a major, yet under-recognized characteristic of JH is fatigability. Etiologies of the fatigue may be related to biomechanical, cardiovascular, and central nervous system phenomena *(Voermans 2010b [4a])*. A recent study documented fatigue as a prominent and common symptom of patients with JH *(Voermans 2010b [4a])*. Patients may also experience other physiologic symptoms or comorbidities including: poor sleep *(Hakim 2004 [4a])*, headaches *(Hakim 2004 [4a], Rozen 2006 [4b])*, gastrointestinal (GI) dysmotility *(Zarate 2010 [4a])*, autonomic dysfunction, or postural orthostatic tachycardia syndrome (POTS) *(Hakim 2004 [4a], Gazit 2003 [4b])*. For this reason, a multidisciplinary approach is needed to effectively address the complex needs of this patient population *(Celletti 2013 [4a], Bathen 2013 [4b], Castori 2012 [5a])*.

Because the presentation of JH is complex and multidimensional, the management can be very challenging. Besides the physical complaints, patients with JH may have an increased potential for anxiety and other psychosocial components *(Smith 2013 [1b], Sanches 2012 [1b], Bulbena-Cabré 2011 [5b])*. In a systematic review by Smith, adult patients with JH had a 4 times higher risk for psychological disorders (anxiety, depression, panic disorder), with one study finding the incidence to be 16 times more likely *(Smith 2013 [1b], Martin-Santos 1998 [4a])*. With the limited pediatric research in this area, caution is to be used in drawing formal conclusion of the

applicability of these findings to adolescents and teens with JH as we do not yet know if these patients are in any more psychologically distress than other non-hypermobility adolescents and teens with chronic pain. Kinesiophobia was found to also be a common feature in patients with JH. It was found that this symptom did not correlate to intensity of pain or quality of life, but did correlate with severity of fatigue *(Celletti 2013 [4a])*. Patience, good communication and sensitive handling skills improve the probability for successful outcomes *(Simmonds 2007 [5a])*. Families of children and adolescents with JH often express frustration with the lack of expertise and experience among medical practitioners with regard to recognition and management of JH. They frequently report previous, unsuccessful attempts to gain improvement in pain and fatigue through physical therapy programs when the impact of JH is not recognized and appreciated *(Keer 2003 [5a])*. In a survey of adult patients with JH, over half waited more than 10 years before obtaining the diagnosis of JH *(Ross 2011 [5b])*.

Associated symptoms of JH can impact multiple generations of families. Many parents and children will be unaware of their JH or of its impact. After a child receives the diagnosis, caregivers will readily identify many members of their family tree sharing similar symptomatic histories and likely to have JH *(Murray 2006 [5a])*.

Evidence reviewed for this guideline supports the role of physical therapy as the primary intervention for JH *(Kemp 2010 [2a], Pacey 2013 [2b], Rombaut 2012b [4b])*, but indicates the need for a modified, low intensity approach to therapeutic interventions that is slowly progressed and targets postural stability and endurance. Effective treatment may include: chronic pain management, global muscle strength and endurance training *(Rombaut 2012b [4b])*, core stability training, proprioceptive enhancement, joint stabilization training and postural awareness *(Bathen 2013 [4b], Rombaut 2012b [4b])*. When physical therapy is targeted to the specific needs and responses of the child and adolescent, beneficial outcomes are the usual result. The ideal approach is holistic, patient centered, specific, and aimed at giving the patient the tools to manage the problem themselves *(Birt 2013 [2a], Barton 1996 [4b], Simmonds 2007 [5a], Lorig 2003 [5a])*. Therefore, it is incumbent upon therapists to understand those specific needs and be equipped to effectively provide services to this population. Beginning in childhood, a proactive approach for joint protection, stabilization training, and

body awareness can facilitate management of symptoms and be preventative in nature *(Celletti 2013 [4a])*. Without proper interventions, symptoms of pain and fatigue can progressively worsen over time and lead to functional impairment as well as chronic pain. This can contribute to significant decline in quality of life in children, adolescents *(Fatoye 2011a [4a])*, and young adults *(Kim 2013 [4a])* with JH when compared to their peers.

The purpose of developing this clinical practice guideline (CPG) was to provide a comprehensive, evidence-based resource for therapists for the identification and management of JH in children and adolescents. This CPG follows a structured process of developing clinical questions, reviewing, appraising, and applying the relevant literature to make recommendations for this patient population. The clinical questions addressed in this specific process were:

- Does the identification of JH, awareness of the ongoing impact of its associated symptoms, and targeted management lead to improved patient outcomes such as reduction in symptoms, increased function and improved quality of life in children and adolescents?

- What are the components of effective targeted management for children and adolescents with JH?

Guideline Recommendations

Evaluation

1. It is recommended that therapists consider and screen for JH as a contributing factor when completing an assessment on a child that demonstrates or complains of any of the following symptoms:

- Pain
  - Chronic widespread pain *(Rombaut 2013], Schubert-Hjalmarsson 2012 [4a], Murray 2006 [5a], Russek 1999 [5a], Hakim 2003 [5b])*.
    - i. Joint pain *(Tobias 2013 [2a], Kirby 2007 [4a], Adib 2005 [4a])*,
    - ii. Growing pains often in the evening and after increased activity *(Murray 2006 [5a])*

- iii. Exercise related pain *(Kirby 2007 [4a], Adib 2005 [4a])*

- Difficulty with prolonged walking *(Fatoye 2011b [4a])*
- Flexible pes planus *(Kirby 2007 [4a], Adib 2005 [4a])*
- Clumsiness/poor coordination *(Adib 2005 [4a], Bernie 2011 [4b], Briggs 2009 [5a])*
- Easy bruising *(Kirby 2007 [4a], Adib 2005 [4a])*
- Congenital limb deficiencies *(Hassoon 2002 [4b])*
- Recurring joint injuries *(Kono.pinski 2012 [3b], Briggs 2009 [5a])*
- Fibromyalgia *(Ting 2012 [4a], Karaaslan 2000 [4a])*

2. It is recommended that the Beighton Scale be used to screen for JH as part of the differential diagnosis *(Junge 2013 [2b], Beighton 1998 [5a])*. (See Appendix 1)

Note 1: The scale has been criticized because it only samples a few joints and gives no indication of the degree of JH *(Simmonds 2007 [5a])*. The Beighton Scale, although widely used, lacks a comprehensive screen of all joints and does not account for the presence of JH in certain joints such as interphalangeal (IP) joints, hips, ankles and shoulders *(LocalConsensus 2014 [5])*.

Note 2: A Beighton Scale score of 5/9 or greater is used to classify JH *(Scheper 2013 [1b], Junge 2013 [2b], Beighton 1998 [5a])*. However 4/9 was also frequently used to classify JH in the literature reviewed for this guideline.

3. It is recommended that therapists complete a comprehensive subjective interview including, but not limited to, the following:

- Pain (location, intensity, frequency, relation to activity, relief, exacerbating factors) *(Tobias 2013 [2a], Hakim 2004 [4a], Rombaut 2012b [4b])*

  Note 1: Pain can be present at any joint *(LocalConsensus 2014 [5])*. There is supporting evidence for lower limb arthralgias *(Tobias 2013 [2a], Murray 2006 [5a])*, back pain *(Kim 2013 [4a], Murray 2006 [5a])*, temporomandibular joint (TMJ) pain *(Ogren 2012 [4b])*, foot pain *(Berglund 2012], Tobias 2013 [2a], Gross 2011 [4a])*, and shoulder pain *(Tobias 2013 [2a])*.

- Fatigue *(Voermans 2010b [4a], Hakim 2004 [4a], Rombaut 2012b [4b])*

- Difficulty with prolonged walking *(Fatoye 2011b [4a])*

  Note 2: Parents of children with JH frequently describe functional limitations in the community, including the inability to complete a shopping trip through a large store without needing to rest or be provided support *(Fatoye 2011b [4a])*.

- Current activity modification (orthotics, school activities, activities of daily living (ADL), school accommodations) *(LocalConsensus 2014 [5])*

- Poor sleep *(Hakim 2004 [4a])*

- Subluxations/dislocation *(Murray 2006 [5a])*

- Joint clicking/popping *(Murray 2006 [5a])*

- Fractures/injuries *(LocalConsensus 2014 [5])*

  Note 3: There is usually a lack of significant laboratory or radiological findings *(Russek 1999 [5a])*.

- Prior surgeries *(Castori 2012 [5a])*

  Note 1: Surgery may not provide effective pain relief and may lead to unexpected complications (due to abnormal tissue, prolonged post-surgical recovery, and deconditioning) *(Castori 2012 [5a])*.

  Note 2: Patients with JH who underwent medial patellofemoral ligament (MPFL) reconstruction achieved worse functional outcomes than non-hypermobile controls. While function was improved, it was to a lesser extent than those who were non hypermobile. Patients with JH reported increased rates of residual and recurrent symptoms and lower rates of resuming sports following MPFL repair *(Howells 2012 [4b])*.

- Family history of laxity *(Zarate 2010 [4a], Murray 2006 [5a])*

- Presence of headaches *(Hakim 2004 [4a], Rozen 2006 [4b])*

  Note: JH was present in 92% of patients with new daily persistent headaches (NDPH), compared to being present in only 10% of the general population *(Rozen 2006 [4b])*.

- Temporomandibular dysfunction (TMD) *(Winocur 2000 [4a], Westling 1992 [4a], Ogren 2012 [4b])*

- Anxiety and depression *(Smith 2013 [1b], Sanches 2012 [1b], Hakim 2004 [4a], Bulbena-Cabré 2011 [5b])*

- Presence of (pre)syncope (feeling faint, actually fainting, dizziness and light-headedness, postural orthostatic tachycardia syndrome, and mild orthostatic hypotension) *(Hakim 2004 [4a], Gazit 2003 [4b])*

- Cardiorespiratory (CR) issues (palpitations, chest pain and shortness of breath) *(Hakim 2004 [4a])*; diastolic dysfunction *(Balli 2013 [4a])*

- GI symptoms (nausea, stomach ache, diarrhea and constipation) *(Zarate 2010 [4a], Adib 2005 [4a], Hakim 2004 [4a])*; eosinophilic esophagitis (EE) *(Abonia 2013 [3a])*

- Nonspecific (allergy, rash, nocturia, dysuria, flushing, night sweats, fever, lymph gland pain) *(Kirby 2007 [4a])*

- Clumsiness/poor coordination *(Adib 2005 [4a])*

- Prior therapy and response to the intervention(s) *(Keer 2003 [5a], Hakim 2003 [5b])*

4. It is recommended that therapists complete a comprehensive assessment of the following:

- Standing and seated postural alignment
  - Spine (e.g. rounded shoulders, forward head, scapular winging, anterior pelvic tilt, increased lumbar lordosis) *(LocalConsensus 2014 [5])*
  - Lower Extremities (e.g. genu recurvatum, femoral inversion) *(LocalConsensus 2014 [5])*
  - Foot/ankle *(Evans 2012 [2b], Gross 2011 [4a], Berglund 2005 [4a])* (e.g. calcaneal valgus, midfoot pronation, hallux valgus) *(LocalConsensus 2014 [5])*

  Note 1: Many patients may appear to have adequate arches in non-weight bearing positions. However, collapse of the medial longitudinal arch in weight bearing is commonly seen in JH and may be contributing to pain and fatigue *(LocalConsensus 2014 [5])*.

  Note 2: The Oxford Ankle Foot Questionnaire-Children, Foot Posture Index and, the Lower Limb Assessment Scale demonstrated adequate intra-rater and inter-rater reliability in a pediatric sample *(Evans 2012 [2b])*.

- Upper extremities (UE) with emphasis on weight bearing position (e.g. hyperextended elbows and/or metacarpalphalangeal joints (MCP))

- Gait *(Fatoye 2011b [4a])* with emphasis on stance, limb and pelvic/core stability *(Cimolin 2011 [4b],*

Galli 2011 [4b], Greenwood 2011 [4b]) trunk and head stability *(Falkerslev 2013 [4b])*

Note: Authors found a negative correlation between reduced force and fatigue during gait and suggest that this muscular fatigue may be associated with a loss of proprioceptive acuity *(Celletti 2012 [4b]).*

- Muscle strength *(Rombaut 2012b [4b])* (open and closed chain) *(Augustsson 2000 [4b])*
- Quality of movement *(Simmonds 2007 [5a])* for example:
  - Single limb stance (SLS) trunk deviations, stance limb position, increased ankle strategies
  - Modified heel raises - lock out into supination and plantarflexion, difficulty sustaining midrange, neutral ankle positions
  - Bridging-initiate through trunk extension and lack core activation
  - Mini wall squat-poor midrange knee control, rely on genu recurvatum at end of cycle
  - Scapular activation-compensatory elevation, exaggerated lumbar extension

  (LocalConsensus 2014 [5])

  Note 1: Assessment of motor competency through standardized protocols may not be sensitive enough to capture the full impact that JH has on the musculoskeletal function and quality of movement. Repetition of tasks often reveals deficits that may not be identified with one time trials *(Remvig 2011 [4a]).*

  Note 2: Due to muscular imbalances and joint laxity, patients with JH need improved dynamic muscular control *(Pacey 2010 [1a]).*

  Note 3: Co-contraction is often lacking/decreased *(Jensen 2013 [4b]).*

- Proprioception *(Smith 2013 [1a])*
- Balance/postural sway *(Schubert-Hjalmarsson 2012 [4a], Rigoldi 2013 [4b])*
- Mobility/laxity at all joints *(Mallik 1994 [4a], Rombaut 2012a [4b])*

Note 1: Hypermobile joints frequently have an 'empty', 'boggy' end-feel *(Simmonds 2007 [5a]).*

Note 2: Common findings include: shoulder, scapular, wrist, and thumb carpalmetacarpal (CMC) instability; hyperextension of knees and elbows, MCPs, interphalangeal joints (IPs); increased hip internal rotation (IR) and external rotation (ER) *(LocalConsensus 2014 [5]).*

- Spinal segmental mobility *(Kim 2013 [4a], Murray 2006 [5a])*
- Range of motion (ROM) *(Simmonds 2008 [5a], Russek 2000 [5a])*
- Integumentary (presence of thin atrophic scarring, elasticity, and/or striae) *(Simmonds 2007 [5a], Murray 2006 [5a], Hakim 2003 [5b])*
- Muscle flexibility *(Pacey 2010 [1a], Russek 2000 [5a])*

  Note: Common findings include tightness in the following muscle groups: Hamstrings, gastrocs, pectorals, and/or paracervical *(LocalConsensus 2014 [5]).*

5. It is recommended that therapists treating patients with JH complete a comprehensive TMJ assessment including *(Pasinato 2011 [4b], Khan 1996 [4b], Buckingham 1991 [4b])*:

- ROM *(Saez-Yuguero Mdel 2009 [4a], Conti 2000 [4a], Wang 2012 [4b])*

  Note: A study of adults with TMD suggests a lack of relationship between Beighton scale score and TMJ problems, thus the determination of a contributing factor of joint laxity in TMD is based on measuring TMJ hyper-translation and not on Beighton score alone *(Saez-Yuguero Mdel 2009 [4a], Conti 2000 [4a]).*

- Neuromuscular control *(Kalaykova 2006 [4b])*

  Note: Patients with JH frequently demonstrate deviation with mouth opening *(Barrera-Mora 2012 [4b])* and closing in an 'S' pattern *(LocalConsensus 2014 [5]).*

- Signs and symptoms of TMD: popping, clicking, and/or locking *(Westling 1992 [4a], Barrera-Mora 2012 [4b], Ogren 2012 [4b])*

- Postural adaptation: forward head, rounded shoulders, mandibular protrusion, tightness in paracervical musculature *(LocalConsensus 2014 [5])*

6. It is recommended that a patient reported outcome measure, be administered at the beginning, periodically and at the end of an episode of care as appropriate to assess patient's quality of life *(LocalConsensus 2014 [5])*.

7. It is recommended that a home exercise program (HEP), as discussed later in this CPG, be initiated at evaluation *(LocalConsensus 2014 [5])*.

Recommended Referrals

8. It is recommended that a multidisciplinary approach be taken in the overall medical management of patients with JH *(Celletti 2013 [4a], Bathen 2013 [4b], Castori 2012 [5a], Grahame 2009 [5a])*.

9. It is recommended that a referral to a specialized therapist (e.g. hand therapist, sensory-based occupational therapist, sports physical therapist) be considered when the following are present:
   - UE fatigue or hand pain with functional tasks (such as handwriting *(Murray 2006 [5a])* playing instruments, activities of daily living (ADLs), work or occupational tasks *(LocalConsensus 2014 [5])*
   - Sensory processing concerns *(LocalConsensus 2014 [5])*
   - Fine motor difficulties *(Tirosh 1991 [3a])*
   - Acute or single-joint soft tissue injury due to repetitive strain *(LocalConsensus 2014 [5])*

10. It is recommended that therapists encourage patients, families and referring providers to consider inclusion of psychology as a component of the global treatment interventions *(Smith 2013 [1b], Voermans 2010b [4a], Bathen 2013 [4b], Rombaut 2010b [4b], Grahame 2009 [5a], Branson 2011 [5b], Bulbena-Cabré 2011 [5b])*.

   Note 1: Pediatric psychology utilizing evidence based intervention for mood, pain management, and chronic health problems have been found to be effective in treating adolescents and teens with JH *(LocalConsensus 2014 [5])*.

   Note 2: JH is a risk factor for anxiety disorders *(Sanches 2012 [1b], Bulbena-Cabré 2011 [5b])*.

Note 3: JH is highly prevalent in adult patients with panic disorder, agoraphobia, or both and may reflect a disposition for anxiety *(Smith 2013 [1b])*.

Note 4: The potential for parental anxiety and the impact this has on their ability to process and apply information provided by the health care team may impact the success of the child's therapy *(LocalConsensus 2014 [5])*.

Note 5: Kinesiophobia is a common symptom in JH. Coping strategies may be more relevant than the intensity and/or frequency of the pain in generating the psychological and physical responses related to pain-avoiding behaviors *(Celletti 2013 [4a])*.

11. It is recommended that when JH is identified as a potential contributing factor to the referring diagnosis, therapist communicate with referring physicians *(LocalConsensus 2014 [5])*.

Management Recommendations

Education

12. It is recommended that a therapist provide education on joint protection focused on avoiding excessive ROM in order to reduce long term detrimental effects on the musculoskeletal system *(Rombaut 2012a [4b], Booshanam 2011 [4b], Greenwood 2011 [4b], Checa 2012 [5a], Russek 1999 [5a])*.

   Note 1: Studies of abnormal posture associated with JH suggest the prevention of early osteoarthritis (OA) and other knee pathologies through postural education *(Simonsen 2012 [4b], Booshanam 2011 [4b])*.

   Note 2: Early recognition and management of JH may delay onset or progression of OA in joints *(Murray 2006 [5a])*.

   Note 3: Patient awareness of the need for joint protection may prevent degenerative TMJ lesions caused by activities that require excessive opening (yawning, dental procedures, etc.) *(Winocur 2000 [4a], Westling 1992 [4a], Pasinato 2011 [4b])*.

   Note 4: JH may contribute to the development of TMJ pain and dysfunction, even in young people, particularly when their joints were exposed to excessive loading as in oral parafunctions (nail biting, gum chewing, teeth grinding) *(Westling 1992 [4a])*.

Note 5: Joint clicks (potential signs of TMD) were positively associated with larger active and passive opening *(Winocur 2000 [4a])*.

Note 6: Intraoperative images of 2 patients have shown knee cartilage damage *(Checa 2012 [5a])*.

Note 7: There is a positive correlation between JH and these long term associated musculoskeletal impairments:

- o Chondromalacia patellae *(al-Rawi 1997 [3a])*
- o Carpal tunnel syndrome *(Aktas 2008 [4a])*
- o Headaches *(Rozen 2006 [4b])*
- o Cervical instability *(Rozen 2006 [4b])*
- o Disc prolapse, spondylolysis, and spondylolisthesis *(Murray 2006 [5a])*
- o Trauma, tears, or rupture of the soft tissues surrounding the joint *(Rombaut 2012a [4b])*

13. It is recommended that a therapist focus additional patient/family education on the following *(Engelbert 2011 [1a], Shultz 2010 [4a])*:

- Return to function with management, rather than resolution of pain *(Branson 2011 [5b])*
- Differentiation of joint dislocation, subluxation, and instability *(Murray 2006 [5a], Russek 1999 [5a], Branson 2011 [5b])*
- Self-help enabling techniques, such as pacing and relaxation *(Martin-Santos 1998 [4a], Bulbena-Cabré 2011 [5b])*
- Potential patient frustration that can result from delayed diagnoses or under appreciation for the impact of associated symptoms *(Voermans 2010b [4a], Russek 1999 [5a])*
- Families may have resistance to therapeutic interventions as previous attempts at therapy may have been unsuccessful *(Simmonds 2007 [5a], Murray 2006 [5a])*
- Benefits of targeted and more specialized therapeutic approach to treatment that considers all aspects of JH *(Celletti 2013 [4a], Celletti 2011 [4b], Russek 1999 [5a])*
- Selection of jobs, sports, or recreational activities that will not exacerbate symptoms *(Castori 2012 [5a], Russek 1999 [5a])*
- Potential impact of pubertal status on JH *(Quatman 2008 [4a])*
- Importance of Self-Management, which has been shown to improve outcomes in chronic conditions *(Barton 1996 [4b], Lorig 2003 [5a])*.

Note: Readiness or preparedness of the individual to initiate and implement targeted intervention is fundamental to achieving successful outcomes *(Simmonds 2007 [5a])*.

- Sleep hygiene *(Hakim 2004 [4a])*
  Note: Education includes: avoiding naps, decreasing caffeine intake, timing of activity prior to bedtime, sleep environment (avoid electronic use or exposure) *(LocalConsensus 2014 [5])*, sleep ergonomics *(Castori 2012 [5a])*.

- Joint protection including ergonomics *(Castori 2012 [5a])*, proper shoe wear, energy conservation *(LocalConsensus 2014 [5])*

General Management Principles

14. It is recommended that training progression begin at a low intensity and progress in a slow manner *(Kerr 2000 [4a], Briggs 2009 [5a], Murray 2006 [5a], Russek 2000 [5a])*.

Note 1: Due to collagen deficiency, tendons may be weaker and slower to respond to training effects, leaving them more vulnerable to injury. Other causes for delayed or altered response to training can be faulty technique, anatomical factors, or muscular imbalance. Patients with JH may demonstrate prolonged and incomplete healing. It is unclear if this can be attributed to the healing injury or the longer standing accumulative tissue damage that occurs over time or both *(Briggs 2009 [5a], Simmonds 2007 [5a])*.

Note 2: Authors have used objective measures including electromyogaphy (EMG) and biopsy to demonstrate histologic neuromuscular changes in muscles in patients with JH (e.g. axonal polyneuropathy) *(Voermans 2009 [4a])*.

Note 3: Authors have suggested the muscular changes found in JH were associated with muscular dysfunction, as no changes were identified in muscle mass *(Rombaut 2012b [4b])*.

Note 4: Progression may be interrupted by patient normal growth and development, leading to regression in previously mastered skills and the need for constant re assessment and modification of the intervention based on patient performance and response *(LocalConsensus 2014 [5])*.

15. It is recommended that therapist use careful handling for patient with JH, bearing in mind the

fragility of the connective tissue and the increased vulnerability to associated trauma and overuse problems *(Rombaut 2012a [4b])*.

Note: Overly aggressive interventions or therapy may result in aggravation of symptoms leading to the patient not returning to therapy therefore potentially contributing to further decline in functional status *(Simmonds 2007 [5a])*.

16. It is recommended that patients with JH, both symptomatic *(Pacey 2013 [2b])* and asymptomatic receive targeted physical therapy interventions *(Kemp 2010 [2a], Juul-Kristensen 2012 [4b], LocalConsensus 2014 [5])*.

    Note: For patients that are asymptomatic, early management is focused on prevention of symptoms, joint protection, and avoiding or prolonging the onset of long term effects *(Kemp 2010 [2a], Celletti 2013 [4a])*.

17. It is recommended that a therapist provide therapeutic exercises targeted at joint stability, joint protection and restoration of muscular balance *(Fatoye 2011b [4a], Greenwood 2011 [4b], Grahame 2009 [5a], Russek 2000 [5a])*.
    Note: Due to ligamentous laxity and compensatory muscular imbalances, patients with JH may rely more on dynamic muscular control than non-hypermobile peers *(Pacey 2010 [1a])*.

18. It is recommended that symptoms of pain and fatigue be assessed throughout an episode of care *(Voermans 2010b [4a])*, at every visit *(LocalConsensus 2014 [5])*.

19. It is recommended that even basic exercises be modified to ensure proper technique and/or minimize pain symptoms based upon the patient's needs and assessment *(Simmonds 2007 [5a])*.
    Note: A distinction needs to be drawn between pain associated with training versus exacerbation of chronic joint pain *(Simmonds 2007 [5a])*.

20. It is recommended that a home exercise program be continuous, progressive, and performed as part of a daily routine to achieve maximum benefit and prevent return to pre-intervention status *(Ferrell 2004 [4b], Barton 1996 [4b], Murray 2006 [5a], Keer 2003 [5a])*.

21. It is recommended that the therapist be aware of the potential impact of patient's anxiety and family dynamics in order to modify communication and overall management *(Smith 2013 [1b], Sanches 2012 [1b], Bulbena-Cabré 2011 [5b])*.

Intervention/Training (All Joints)

22. It is recommended that therapists initially focus on improving postural awareness through:

    - Identifying and activating key joint stabilizing muscles beginning with isometrics
    - Performing selective and isolated muscle stretching
    - Enhancing middle range proprioception
    (Simmonds 2007 [5a], Russek 2000 [5a])

    Note: See Appendix 2 for examples of exercises.

23. It is recommended that once patients learn to recruit stability muscles in static positions, therapists encourage activation during dynamic tasks and daily activities *(Falkerslev 2013 [4b], Simmonds 2007 [5a])*.

24. It is recommended that once a patient is able to activate and sustain contraction of stabilizing muscles, therapists slowly advance training by progressively increasing hold counts and then resistance to improve strength, endurance, balance and neuromuscular coordination *(LocalConsensus 2014 [5], Simmonds 2007 [5a])*.

    Note: Neuromuscular training in patients with JH does not seek to alter joint laxity, but instead increase stabilization of lax joints through muscular strength, endurance and functional control *(Shultz 2010 [4a])*.

25. It is recommended that therapists provide both open and closed chain tasks that address deficits in strength *(Fatoye 2009 [4a], Ferrell 2004 [4b], Augustsson 2000 [4b])*.

    Note 1: Home based closed kinetic chain exercises were found to alleviate symptoms and improve proprioceptive performance and quality of life (QOL) *(Ferrell 2004 [4b])*.

    Note 2: Targeted neuromuscular training was shown to be successful in improving biomechanical deficits secondary to a musculoskeletal disorder *(Shultz 2010 [4a], Myer 2005 [5a])*.

26. It is recommended that therapists include proprioceptive exercises in training to decrease pain and improve functional status *(Smith 2013 [1a], Fatoye 2009 [4a], Celletti 2012 [4b], Galli 2011 [4b], Sahin 2008 [4b], Celletti 2011 [5b])*.

    Note 1: Greater proprioceptive deficits were found in mid-ranges of joint motion *(Smith 2013 [1a], Hall 1995 [4a], Mallik 1994 [4a])*.

    Note 2: Proprioceptive deficits may increase vulnerability to musculoskeletal problems and injuries *(Smith 2013 [1a], Rombaut 2010a [4b])*.

27. It is recommended that therapists provide a tailored rehabilitation program with emphasis on neuromuscular re-education *(LocalConsensus 2014 [5])*.

    Note 1: Evidence supports the need for neuromuscular re-education to improve:
    - Pelvic strategies *(Galli 2011 [4b], Greenwood 2011 [4b])* and ankle strategies *(Cimolin 2011 [4b])* for prevention of compensatory movement patterns *(Galli 2011 [4a])*
    - Cervical strengthening/stabilization in neutral alignment *(Rozen 2006 [4b])*
    - Head/trunk postural control *(Falkerslev 2013 [4b])*
    - TMD symptoms that result from abnormal patterns of jaw muscle activation associated with JH *(Kalaykova 2006 [4b])*
    - Co-contraction *(Jensen 2013 [4b])*

    Note 2: Evidence supports the pairing of strength with endurance training during the rehabilitation program *(Rombaut 2010b [4b])*.

28. It is recommended that the therapists provide the patient/family with parameters on the need for and the selection of appropriate physical activities *(Scheper 2013 [1b], Celletti 2013 [4a], Scheper 2013 [4b], Rombaut 2010b [4b], Engelbert 2006 [4b], Dolan 1998 [4b], Castori 2012 [5a], Grahame 2009 [5a])* with consideration for the following :
    - Increased risk of fracture *(Dolan 1998 [4b])* compounded by:
      - Abnormal structures *(Dolan 1998 [4b])*
      - Low bone mass *(Mishra 1996 [4a])*
      - Reduced physical activity *(Engelbert 2006 [4b], Dolan 1998 [4b])*
      - Proprioceptive deficits *(Rombaut 2010a [4b])*

    - Decreased maximal exercise capacity compared to peers, likely due to deconditioning *(Engelbert 2006 [4b])*

    - Benefit from habitual physical activities *(Scheper 2013 [1b])* that facilitate neuromuscular control and are enjoyable and pain free. Examples include: swimming, Pilates, tai chi, chi gung, some forms of modified yoga, and dance *(Simmonds 2007 [5a])*, biking *(LocalConsensus 2014 [5])*.

    - Impact of the physical activity (limiting high impact activities and repetitive tasks) *(Castori 2012 [5a])*.

29. It is recommended that prior to participating in higher level athletic activity or returning to sports, patients undergo a rehabilitation program, whereby sport specific training is provided in conjunction with continuation of the principles of earlier stages of gradual rehabilitation *(Vaishya 2013 [4a], Simmonds 2007 [5a])*. (See prior recommendations #12-#25).

    Note 1: Individuals have an increased risk of knee injury during sporting activities.
    - Increased knee injuries may occur during contact sport activities *(Pacey 2010 [1a])*
    - JH is more prevalent in patients with anterior cruciate ligament (ACL) injury (4.46 odd ratio) *(Vaishya 2013 [4a])*

    Note 2: Professionally trained athletes with JH have demonstrated a higher risk of injury in:
    - Soccer *(Konopinski 2012 [3b])*
    - Ballet *(Briggs 2009 [5a])*

    Note 3: In physically trained professional dancers, the presence of JH was found to be associated with:
    - lower muscle strength
    - lower submaximal exercise capacity
    - decreased functional walking distances
    - higher levels of fatigue

    (Scheper 2013 [4b])

30. It is recommended that targeted interventions be the primary focus of treatment, and therapists consider the addition of the following:
    - UE orthoses *(LocalConsensus 2014 [5], Murray 2006 [5a], Russek 1999 [5a])*

Note 1: Splinting of hypermobile joints may be used to promote optimal joint positioning and prevent overuse/strain with specific activities *(LocalConsensus 2014 [5])*.

Note 2: Splinting of hypermobile joints may contribute to muscular imbalances and to the ineffective use of muscles, inhibiting progress with the rehabilitation program *(Murray 2006 [5a], Russek 1999 [5a])*.

Note 3: The use of limited types of support or devices such as pen grips can be a good adjunct to a hand-muscle-strengthening program, as they reduce the force required to sustain gripping of a pen, reducing the pain and fatigue experienced in fingers and wrists during school work *(Murray 2006 [5a])*.

Note 4: Evidence does not support the use of neoprene wrist/hand splints for decreasing pain, increasing handwriting speed and endurance in a small sample of 9 and 10th graders with JH *(Frohlich 2012 [4b])*.

- Transcutaneous electrical nerve stimulation (TENS) *(LocalConsensus 2014 [5], Murray 2006 [5a])*

  Note 1: TENS may play a role in temporary pain management, but only when used as a supportive treatment *(Murray 2006 [5a])* during exacerbations of symptoms *(LocalConsensus 2014 [5])*.

  Note 2: TENS may exacerbate pain symptoms in some children, therefore monitoring response to stimulus and achieving several successful trials are indicated before administering for home use *(LocalConsensus 2014 [5])*.

- Soft supports/taping

  Note: The use of compressive support garments or soft taping may be considered to enhance proprioception, facilitate neuromuscular re-education, and encourage improved postural alignment *(Simmonds 2007 [5a])*.

- Lower extremity (LE) orthoses *(Rome 2010 [1b], Gross 2011 [4a], Berglund 2005 [4a], Razeghi 2000 [5b], Agnew 1997 [5b])*.

Note: Altered plantar pressure may lead to impaired foot function, reduced tolerance to daily activity (including walking), and the potential for foot discomfort and pain *(Pau 2013 [4b])*.

31. It is recommended that younger patients, symptomatic or asymptomatic pes planus, receive postural interventions targeted at LE alignment due to the risk of long term musculoskeletal damage *(Gross 2011 [4a], Berglund 2005 [4a], Agnew 1997 [5b])*.

    Note 1: Planus foot morphology was found to be associated with frequent knee pain and medial tibial femoral cartilage damage in older adults *(Gross 2011 [4a])*.

    Note 2: Current evidence is too limited to draw definitive conclusions about the effectiveness of specific non-surgical (orthotic) interventions for pediatric pes planus *(Rome 2010 [1b], Razeghi 2000 [5b])*.

    Note 3: Normal development of the arch in younger patients in relation to flat feet and skeletal maturity may influence postural interventions targeted at LE alignment *(LocalConsensus 2014 [5])*.

32. It is recommended that therapist consider use of minimal control semi-customizable shoe orthotics for mild to moderate pronation *(Morrison 2013 [4b], LocalConsensus 2014 [5])*.

    Note 1: Trends in gait patterns suggest orthotics may be beneficial for enhancing stability and improving kinematics during stance phase *(Morrison 2013 [4b])*.

    Note 2: Clinical experience with this population has consistently shown a significant reduction in pain and fatigue with the use of minimal control semi-customizable shoe orthotics *(LocalConsensus 2014 [5])*.

33. It is recommended that therapists consider use of higher level orthotics to allow for highest level of dynamic muscular control while promoting optimal alignment such as University of California at Biomechanics Laboratory (UCBL) or supramalleolar orthotics (SMO) for moderate to severe pronation and calcaneal valgus *(LocalConsensus 2014 [5])*.

Note: Clinical experience with younger patients within this population has consistently shown that postural stability and alignment improve over time with initial use of higher level orthotic support and then progressing to lower level as indicated *(LocalConsensus 2014 [5])*.

34. It is recommended that the level of custom orthotics be weaned gradually over time based on patient tolerance and response *(LocalConsensus 2014 [5])*.

Models of Therapy

35. It is recommended that follow up visits be scheduled using a periodic model (reassessment of frequency following each visit) of therapy with consideration for the following:

    - Capacities of patient and caregiver to establish regular HEP completion *(LocalConsensus 2014 [5])*
    - Patient's level of function and tolerance to daily activities *(LocalConsensus 2014 [5])*
    - Accessibility to therapy services *(LocalConsensus 2014 [5])*
    - Allowing enough time for patient to establish regular performance of HEP and make mild improvements prior to being seen (with recognition for delayed therapeutic response) – see recommendation # 13

36. It is recommended that a patient be considered for consultative model of therapy when the following are present:

    - Established regular maintenance level HEP
    - Patient no longer demonstrates significant functional limitations
    - Patient only requires orthotic management for changes due to growth
    - Management of Pain

    Note 1: Due to the chronic nature of JH conditions, there is often no definitive discharge point. Continuation of care is ongoing *(LocalConsensus 2014 [5])*.

    Note 2: During times of relatively good functional status patients benefit from a proactive approach including biomechanical "tune up" for ongoing joint protection that may decrease the severity of symptoms associated with potential future regressions *(LocalConsensus 2014 [5])*.

37. It is recommended that therapist consider transitioning to a more frequent model of therapy when the following factors occur:

    - Maturation – since puberty changes their symptoms *(Quatman 2008 [4a])*
    - Growth and development *(LocalConsensus 2014 [5])*
    - Changes in physical demands on the biomechanical structures through physical activity (sports related activities) *(LocalConsensus 2014 [5])*
    - Decline in functional status associated with pain and fatigue *(LocalConsensus 2014 [5])*

38. It is recommended that therapist consider a more intensive model of therapy *(Bathen 2013 [4b])* when the following are present:

    - Pain and fatigue interfere with patient's functional status on a regular basis *(LocalConsensus 2014 [5])*
    - Decreased peer participation *(Schubert-Hjalmarsson 2012 [4a])*, decline in school attendance *(LocalConsensus 2014 [5])*
    - Difficulty with implementation of self-management strategies and regular HEP completion *(LocalConsensus 2014 [5])*

    Note: Undergoing a personalized intensive PT series appeared to have empowered parents and children as they gained knowledge, skills and confidence to self-manage symptoms and continue an exercise routine *(Birt 2013 [2a])*.

39. It is recommended that at follow up visits therapists:

    - Review HEP participation
    - Reassess
      - Pain reported (throughout daily routine, following last therapy visit, during HEP)
      - Fatigue reported/functional participation (throughout daily routine)
      - Flexibility (hamstring (HS), heelcord (HC), cervical, pectorals)
      - ROM
      - Functional strength (hold count, form, neutral alignment)
      - Gait
      - Posture
    - Recheck orthotics and modify or progress as appropriate

- Provide instruction on, and reinforce use of, proper form during exercise
- Provide education to patients and caregiver (see recommendation #11 and 12)
- Provide gradual progression of HEP to increase the intensity and duration as tolerated by the patient (see recommendations # 22-24)
- Prioritize interventions to target the most symptomatic areas initially, with progression to a global approach inclusive of all joints
- Utilize models of therapy to maximize use of long term therapy resources

Future Research Agenda

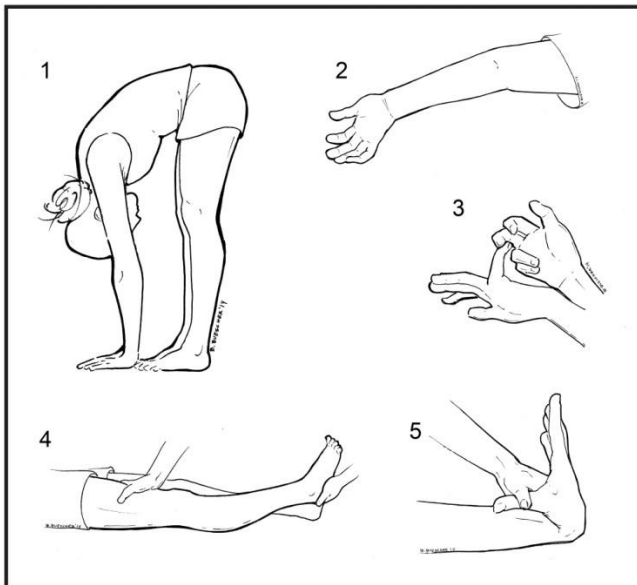In children and adolescents with JH:

1. Do targeted interventions improve pain, fatigue, and quality of life?

2. What are the perceived impacts of the condition on quality of life?

3. What are valid and effective ways of measuring fatigue?

4. What biomechanical deficits are identified using 3D motion analysis?

5. Do specific orthotic interventions effectively improve lower limb biomechanical deficits?

Appendix 1 *(Beighton 1998 [5a])*

Joint hypermobility can be assessed using the Beighton scale. A score of 5/9 or greater defines hypermobility.

The total score is obtained by:
1. forward flexion of the trunk with knees fully extended so that the palms of the hand rest flat on the floor -one point.
2. hyperextension of the elbows beyond 10° - one point for each elbow
3. passive dorsiflexion of the little fingers beyond 90° - one point for each hand
4. hyperextension of the knees beyond 10° - one point for each knee
5. passive apposition of the thumbs to the flexor aspect of the forearm - one point for each hand

Appendix 2

Sample exercises for a patient with Joint Hypermobility	
Exercise	Quality of Movement/Progressions
Hamstring stretching	In long sitting position on firm surface, with low back up against an upright support, maintain knee straight and toe in DF to at least neutral. Can use a towel roll under knees to partially relieve stretch for increased tolerance. Standing with one heel elevated on a step, maintain knee straight, ankle DF to at least neutral and trunk in upright. Be sure patient keeps hips facing straight ahead avoiding compensatory rotation to either side.
Heel cord stretching	Wall gastroc stretch with attention to keeping toes straight ahead, heel flat on floor and back knee kept straight. Be sure patient is in supportive shoes and orthotics (if indicated) to avoid over stretch through the medial longitudinal arch of the foot.
Abdominal Isometric	In hook lying, have patient contract transverse abdominus and maintain for 5 to 10 second hold count. Be sure patient is not holding their breath and that they are maintain contraction throughout the entire hold count. Progress by increasing hold count. Next progression would be to complete this in conjunction with single extremity controlled movements.
Posterior Pelvic Tilt	In hook lying, tighten stomach muscles and flatten back to the ground by rolling pelvis downward. Progress this exercise to bridge (listed below).
Bridging	In hook lying, initiate with PPT, then lift hips upward into neutral hip extension. Keep knees apart or use towel roll between them, depending on stability. Verbal and manual cueing provided to encourage posterior pelvic tilt, proper breathing techniques, and to avoid excessive lumbar lordosis or hip hyperextension.
Hip Adduction Isometric	In hook lying, squeeze ball or towel roll between knees for 5 seconds. Progress this exercise first by increasing hold count. Next progression would be to combine this exercise with bridge (listed above).
Resisted Hip Abduction into band	Resisted hip abduction in hook lying with resistive band for 3 to 5 second hold in minimal abduction. Verbal cueing to encourage slow eccentric control back to starting position. Progression would be to increase hold count and to increase gradual resistance through band color.
Mini wall squatting	Partial wall squats for LE strength/core and postural stability by controlling eccentric lowering into modified range (30 to 45 degrees) and concentric rising within range. Verbal cueing for speed control during lowering and return to starting position and core activation, upright trunk, and in order to maintain "soft knees" position upon return to starting position.
Scapular squeezes	Seated scapular retraction for 5 to 10 second hold. Verbal cueing needed to promote shoulder depression, scapular retraction and upright posture during exercise. Also provide cues to limit shoulder shrugging and or exaggeration of lumbar lordosis.
Modified heel raises	Static partial heel rises for increased ankle stability and proprioception. Can be initiated with single HHA if needed to maintain balance. Verbal cueing to avoid locking out ankles into full plantarflexion and to sustain neutral eversion/inversion while holding for 5-10 counts.

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Development Process

The process by which this guideline was developed is documented in the Guideline Development Process Manual; relevant development materials are kept electronically. The recommendations contained in this guideline were formulated by physical therapists with interdisciplinary advisory based upon current evidence including local clinical practice as appropriate. A systematic search and critical appraisal of the literature was completed using the Table of Evidence Levels described following the references.

To select evidence for critical appraisal by the group for this guideline, the Medline, EmBase, Pub Med, and Cinahl databases were searched with the most recent date of searching December 31, 2013 to generate an unrefined, "combined evidence" database using a search strategy focused on answering clinical questions relevant to joint hypermobility including the following search terms: joint hypermobility, hypermobility syndrome, benign+ joint hypermobility, joint+instability (combined with dx, ligamentous laxity, joint laxity, pronation, foot+pronation, genu recurvatum, Ehlers Danlos, Sticklers Syndrome, Orthotics, orthoses, Stretching, posture, proprioceptive training, balance, Strength, Joint stabilization, Postural control, Neuromuscular control, Handwriting, Gait abnormalities, Joint Alignment, Beighton (MeSH headings using an OVID Medline interface) and "natural language" searching on words in the title, abstract, and indexing terms. The citations were reduced by: eliminating duplicates, non-English articles, and adult articles. The resulting abstracts were reviewed to eliminate low quality and irrelevant citations. Two hundred and twenty articles were reviewed with 117 of these found relevant and cited in this CPG. During the course of the guideline development, additional clinical questions were generated and subjected to the search process, and relevant review articles were identified.

Tools to assist in the effective dissemination and implementation of the guideline may be available online at http://www.cincinnatichildrens.org

Once the guideline has been in place for five years, the development team reconvenes to explore the continued validity of the guideline. This phase can be initiated at any point that evidence indicates a critical change is needed.

Recommendations have been formulated by a consensus process directed by best evidence, patient and family preference and clinical expertise. During formulation of these recommendations, the team members have remained cognizant of controversies and disagreements over the management of these patients. They have tried to resolve controversial issues by consensus where possible and, when not possible, to offer optional approaches to care in the form of information that includes best supporting evidence of efficacy for alternative choices. The CPG was reviewed and approved by stakeholders with opportunities for input, then distributed as appropriate for its intended purpose.

The guideline has been reviewed and appraised by clinical experts not involved in the development process.

Copies of this Evidence-based Care Guideline (EBCG) and any available implementation tools are available online and may be distributed by any organization for the global purpose of improving child health outcomes. Website address:

http://www.cincinnatichildrens.org/svc/alpha/h/health-policy/ev-based/default.htm Examples of approved uses of the EBCG include the following:

- copies may be provided to anyone involved in the organization's process for developing and implementing evidence based care guidelines;
- hyperlinks to the CCHMC website may be placed on the organization's website;
- the EBCG may be adopted or adapted for use within the organization, provided that CCHMC receives appropriate attribution on all written or electronic documents; and
- copies may be provided to patients and the clinicians who manage their care.

Notification of CCHMC at HPCEInfo@cchmc.org for any EBCG, or its companion documents, adopted, adapted, implemented or hyperlinked by the organization is appreciated.

NOTE: These recommendations result from review of literature and practices current at the time of their formulations. This guideline does not preclude using care modalities proven efficacious in studies published subsequent to the current revision of this document. This document is not intended to impose standards of care preventing selective variances from the recommendations to meet the specific and unique requirements of individual patients. Adherence to this guideline is voluntary. The clinician in light of the individual circumstances presented by the patient must make the ultimate judgment regarding the priority of any specific procedure.

For more information about this guideline, its' supporting evidences and the guideline development process, contact the James M. Anderson Center for Health Systems Excellence office at: 513-636-2501 or HPCEInfo@cchmc.org .

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Note: When using the electronic version of this document, ☜ indicates a hyperlink to the PubMed abstract. A hyperlink following this symbol goes to the article PDF when the user is within the CCHMC network.

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Note: Full tables of evidence grading system available in separate document:
- Table of Evidence Levels of Individual Studies by Domain, Study Design, & Quality (abbreviated table below)
- Grading a Body of Evidence to Answer a Clinical Question
- Judging the Strength of a Recommendation (abbreviated table below)

Table of Evidence Levels (see note above)

Quality level	Definition
1a† or 1b†	Systematic review, meta-analysis, or meta-synthesis of multiple studies
2a or 2b	Best study design for domain
3a or 3b	Fair study design for domain
4a or 4b	Weak study design for domain
5, 5a or 5b	Other: General review, expert opinion, case report, consensus report, or guideline

†a = good quality study; b = lesser quality study

Table of Recommendation Strength (see note above)

Strength	Definition
"Strongly recommended"	There is consensus that benefits clearly outweigh risks and burdens (or visa-versa for negative recommendations).
"Recommended"	There is consensus that benefits are closely balanced with risks and burdens.
No recommendation made	There is lack of consensus to direct development of a recommendation.

Dimensions: In determining the strength of a recommendation, the development group makes a considered judgment in a consensus process that incorporates critically appraised evidence, clinical experience, and other dimensions as listed below.

1. Grade of the Body of Evidence (see note above)
2. Safety/Harm
3. Health benefit to patient *(direct benefit)*
4. Burden to patient of adherence to recommendation *(cost, hassle, discomfort, pain, motivation, ability to adhere, time)*
5. Cost-effectiveness to healthcare system *(balance of cost / savings of resources, staff time, and supplies based on published studies or onsite analysis)*
6. Directness *(the extent to which the body of evidence directly answers the clinical question [population/problem, intervention, comparison, outcome])*
7. Impact on morbidity/mortality or quality of life

APPENDIX: EVIDENCE SEARCH STRATEGY, RESULTS, & EVIDENCE TABLE

Criteria for considering studies for this review

Types of Studies

All types of studies were considered for inclusion.

Types of Participants

Pediatric patient ages 4-21 years with presence of joint hypermobility were the target population for this review. Adult studies were also reviewed and included.

Types of Interventions

All types of Physical and Occupational Therapy interventions were included.

Types of Outcomes

The types of outcomes considered for this review included:
- Pain
- Fatigue
- Medical History/Family History
- Quality of Life Tolerance to physical activity
- Joint Mobility/Laxity
- Integument
- Range of Motion
- Flexibility
- Gait
- Posture
- Strength/Stabilization
- Neuromuscular Control
- Proprioception

Exclusion Criteria, if any

Additional criteria for exclusion include:
- Greater than mild hypotonia
- Spasticity
- Progressive neuromuscular conditions

Search Strategy

Search Databases	Search Terms	Limits, Filters, & Search Date Parameters	Date of Most Recent Search
MedLine via PubMed and Ovid	joint hypermobility, hypermobility syndrome, benign + joint hypermobility, joint + instability (combined with dx, ligamentous laxity, joint laxity, pronation, foot + pronation, genu recurvatum, ehlers danlos, sticklers syndrome, orthotics, orthoses, stretching, posture, proprioceptive training, balance, strength, joint stabilization, postural control, neuromuscular control, handwriting, gait abnormalities, joint alignment, beighton	Publication Dates or Search Dates: 06/2010 to 12/2013 English Language	12/31/2013
CINAHL	joint hypermobility, hypermobility syndrome, benign + joint hypermobility, joint + instability (combined with dx, ligamentous laxity, joint laxity, pronation, foot + pronation, genu recurvatum, ehlers danlos, sticklers syndrome, orthotics, orthoses, stretching, posture, proprioceptive training, balance, strength, Joint stabilization, postural control, neuromuscular control, handwriting, gait abnormalities, joint alignment, beighton	Publication Dates or Search Dates: 06/2010 to 12/2013 English Language	12/31/2013

Search Results & Methods

The resulting full text articles were reviewed to eliminate low quality and irrelevant citations or articles. During the course of the guideline development, additional articles were identified from one subsequent search for evidence. The dates of the most recent searches are provided above.

The search for evidence identified 385 articles. 220 of these articles were then reviewed and 117 articles met the inclusion criteria and were utilized for this CPG.

Evidence Table for Included Articles

Evidence Table

Citation	Purpose	Research Design & Study Sample	Results and Conclusions	Evidence Level
Abonia, 2013	To provide clinical and molecular evidence indicating a high prevalence of Eosinophilic esophagitis (EoE) in patients with inherited connective tissue disorders (CTD).	Retrospective N=42 patients with EoE with a CTD-like syndrome	Within a hospital-wide electronic medical record database and EoE research registry, an 8-fold risk of EoE in patients with CTDs (relative risk, 8.1; 95% confidence limit, 5.1-12.9; x2 1 5 112.0; P <1023) was present compared with the general population. There is a remarkable association of EoE with CTDs and evidence for a differential expression of genes involved in connective tissue repair in the cohort.	3a
Adib, 2005	To define the clinical characteristics of all patients with joint hypermobility-related presentations seen from 1999 to 2002 in a tertiary referral pediatric rheumatology unit.	Descriptive study N=189 patient <18 years old with the presence of joint hypermobility as diagnosed by a pediatric rheumatologist and with symptoms related to hypermobile joints.	Referrals came from pediatricians and general practitioners for symptoms however only 10% of those referrals recognized hypermobility as a possible cause of joint complaints. The average age at onset of symptoms was 6.2 years old and age at diagnosis was 9.0 years old, indicating a 2- to 3-yr delay in diagnosis. The major presenting complaints were: Arthralgia (74%), abnormal gait (10%), apparent joint deformity (10%) and back pain (6%), considered 'clumsy' (48%), poor coordination in early childhood (36%), history of recurrent joint sprains (20%), actual subluxation/dislocation of joints (10%), difficulty with handwriting tasks (40%), limitations of school-based physical education activities (48%), limitation with other physical activities (67%), missed significant periods of schooling because of symptoms (41%), history of easy bruising (40%). Demonstrates a need for therapists to screen for HM as a potential contributing factor in patients who present with the following: clumsiness, poor coordination, exercise related pain, pes planus, joint pain.	4a
Aktas, 2008	To examine relationship between Benign Joint Hypermobility Syndrome and carpal tunnel syndrome (CTS)	Prospective controlled study N=90 (55 with CTS and 35 without).	There was a positive correlation between CTS and BJHS.	4a
Al-Rawi, 1997	To study the association between hypermobility syndrome and chondromalacia patellae (CMP).	Cohort study N=225 (115 experimental, 110 control male & female) Groups were matched for number, sex, age, body weight and height with complaints of anterior knee pain that were diagnosed as (CMP)	Females (77.4%) were affected more frequently than males (22.6%) in a ratio of 3.4:1 this study showed that there is a significant association between chondromalacia patellae and generalized joint laxity, as well as a significant increase of hypermobile joints among knees with chondromalacia patellae.	3a

Arroyo, 1988	To determine the prevalence of hypermobility in a group of normal schoolchildren and document the frequency of past and/or present arthralgia in those found to be hypermobile compared to age and sex matched non hypermobile children.	Cross-Sectional N= 192 (4 to 19 years old)	Prevalence of hypermobility in this sample was 66/192 (34%) 38% female and 30% male. Significant negative correlation between age of child and degree of hypermobility p <0.001. Per parent report 50% of HM group had history of arthralgia vs 20% of match controls. Results indicate that there appears to be a trend towards a greater frequency of articular complaints in hypermobile children compared to age and sex matched controls. Not statistically significant, but small sample may indicate possible type II error.	4a
Augustsson, 2000	To investigate the ability of closed and open kinetic chain tests of muscular strength to assess functional performance.	Cross sectional N=16 healthy males	Significant (P>0.05) correlations between the test of functional performance and the closed and open kinetic chain tests of muscular strength were noted, r=0.51 and r=0.57, respectively. It is recommended that a combination of open and closed chain tests of muscular strength be used to assess functional performance and guide treatment intervention. Suggests that training or rehabilitation interventions should not be based exclusively on tests of muscular strength. Rather various forms of dynamometry including functional performance tests.	4b
Balli, 2013	To investigate whether echocardiography with tissue Doppler imaging identifies myocardial dysfunction in children with benign joint hypermobility syndrome (BJHS).	Cross sectional N=145 (75 children with BJHS, 70 healthy children) both groups were similar in terms of age, sex, and body mass index.	This study showed the diastolic dysfunction in patients with BJHS. In addition, detected increased LV and RV MPI. Authors believe that BJHS may affect proteins of the myocardial cytoskeleton and extracellular matrix.	4a
Barrera-Mora, 2012	To investigate the association between tempomandibular disorders, malocclusion patterns, benign joint hypermobility syndrome and the initial condylar position.	Cross sectional N=140 patients who need orthodontic treatment (53 male, 87 female, age range 15-50 yrs.)	The study concluded that there is no well-defined initial condylar position that is statistically significant, neither for normal occlusion nor for the different malocclusion patterns. There is no statistically significant relationship between benign joint hypermobility syndrome and the amount of condylar displacement or TMD. Anterior crossbite could be a risk factor in developing TMJ symptoms, and patients with vertical condylar displacements from 0.88 to 0.97 mm developed, significantly, left and right posteroinferior synovial pain.	4b
Barron, 2002	To determine whether children with chronic fatigue syndrome (CFS) have a higher prevalence of joint hypermobility that gender-matched controls.	Case control N=58 consecutive patients ≥10 years of age who met the International Chronic Fatigue Syndrome, that had been referred to a tertiary care referral clinic for chronic fatigue.	The main result of this study is that adolescents with CFS have a significantly higher prevalence of joint hypermobility than do otherwise healthy children with common skin disorders. Adolescents with CFS have a significantly higher prevalence of joint HM than otherwise healthy children.	4a
Barton, 1996	To apply modified training regimens to a population of patients presenting either	Longitudinal study N=25 females	Statistical significance found in distance walked and amount of pain experienced on movements of joint (not resting) knee joint was the only to shoe	4b

	with symptoms or injury attributable to joint hyperlaxity, to determine whether a change in the range of movement at joints occurs along with altered symptoms.		significant change in ROM. Significant reduction of pain it is recommended that continuation of services through a home exercise program be completed for life long management and stabilization of HM joints to prevent return to pre-intervention status. It was found that patient returned to baseline pre-exercise measures and the corresponding increase with tasks performed i.e. reversibility of training effects. In some cases the scores were worsened. In those who continued without interruption demonstrated STATISTICAL significance distance walked and pain experienced. The exercise should be completed as an ongoing life long program that is continuous and progressive. The exercise program should be completed as part of a daily routine to achieve max benefit.	
Bathen, 2013	To investigate if a multidisciplinary rehabilitation program combining physical and cognitive-behavioral therapy was feasible, safe and effective for 12 women with EDS–HT/JHS.	Longitudinal study N=12 female patients diagnosed with EDS-HT/JHS according to the Villefrance criteria and the Brighton criteria.	The COPM showed significant improvements for both activity performance and performance satisfaction. The physical tests showed significant improvement for tandem-walking backwards, stair walking upwards, and "up on toes." Stair walking down showed no significant change. The TSK-13 showed significant decrease in kinesiophobia. Suggests that an intensive multidisciplinary rehabilitation program with a cognitive-behavioral approach, including intensive muscle strength and -endurance training and pain coping is be feasible and safe for adults with EDS–HT/JHS. Study found positive effects on performance of daily activities, muscle strength and endurance, and a reduction of kinesiophobia.	4b
Beighton, 1998	Proposal of a revision of the classification of the Ehlers-Danlos syndromes based primarily on the cause of each type.	Expert opinion	Concluded that what was formerly known as EDS type I and EDS type II could be merged into a single entity (classical type). The diagnostic criteria proposed for the hypermobility type permits clear distinction from other types of EDS. Defines the vascular type of EDS on the basis of clinical manifestations and the presence of mutations in the COL3A1 gene. The former EDS type V is a rare variant, the molecular basis of which remains unknown. The clinical characteristics of the entity currently known as EDS type VIII remain uncertain thus, its delineation will require more clinical and molecular information.	5a
Berglund, 2005	To investigate the amount and severity of podiatric problems in individuals with EDS and the implication for daily life activities compared to the general population.	Cross sectional N=136 EDS and 292 control	Study found that 97 of 130 individuals with EDS (71%) reported foot pain. When comparing the NRS scores regarding pain intensity between the EDS group and the comparison group a statistically significant difference was found (P< 0.001). When correlating the MFPDS and the NRS scores, a statistically significant relationship was found (r=0.48; P50.01) this study results show that daily life activities in adults with EDS are strongly restricted with foot pain and related disability. Supports need to assess the foot function and patient reported	4a

			symptoms to support the individuals with solutions to their problems with ambulation.	
Bernie, 2011	To investigate the reported frequency and functional impact of motor-based difficulties in children presenting to a tertiary assessment clinic for biomechanical pain related to joint hypermobility.	Cross sectional N=200 children	Student Reported presence of the following: clumsiness = 50.6%, coordination 46.5%, poor ball skills 34.9%, all three 22.7%. Found CHAQ scores worse in BJHS (p<.001).	4b
Birt, 2013	To understand how families experienced an intensive multidisciplinary intervention.	RCT N=28 families with children aged 5-17 years.	Parents reported that exercise reduced the symptoms associated with hypermobility. Parental motivation, adapting family routines, making exercise a family activity and seeing benefit increased adherence to exercise. Non-adherence to exercise was linked to lower levels of parental supervision, not understanding the treatment, not seeing benefit and not having specific time to dedicate to doing the exercises. Even when exercise is seen to benefit a child's well-being, families experience challenges in adhering to a physiotherapy program for hypermobility.	2a
Booshanam, 2011	To compare and quantify the postural differences and joint pain distribution between subjects with benign joint hypermobility syndrome (BJHS) and the normal population.	Cross sectional N=35 in each patient and control group	Significant difference in posture between the patient group and the controls. Areas that were significantly different included: head and hip (coronal plane), upper back, trunk, and lower back (sagittal plane). The intensity of joint pain was greater in the BJHS group. Suggests that attention be given to postural reeducation during physical therapy interventions in BJHS to reduce long term detrimental effects on the musculoskeletal system.	4b
Branson, 2011	Examining the circumstances of an adolescent girl with Ehlers-Danlos Syndrome.	Case study	Reinforces the need for a multidisciplinary approach for managing pain in patients with HM/EDS. Discusses importance of education on management of pain and return to function with pain, not to fix pain or make it go away. Also recommends that patient education be provided on differentiation of joint dislocation, subluxation, and instability episode.	5b
Briggs, 2009	To examine the effects of JHS on a ballet dancers risk of injury and recovery time after injury.	Longitudinal N=93 (out of 135 original) ballet dancers (69%) response rate with questionnaires	Study found a significant difference in occurrence of tendon injuries and having to take off >6 weeks from dance in JHS compared to non JHS. Reported that one or more types of tendon injuries were increased in JHS for both male and female. Study showed that dancers with JHS are more vulnerable to the effects of injury (risk) and that healing is likely to be more prolonged and may be incomplete. It is unclear if takes longer to heal or if there is greater tissue damage before injury is reported or both with excessive loading damage occurs either as overuse, premature degeneration or mechanical failure. Due to collagen deficiency tendons may be weaker and slower to respond to training effects, thus leaving them more vulnerable to injury. Other causes of stress on tendon can be due to faulty technique, anatomical factors, or muscle imbalance.	5a

Buckingham, 1991	To examine if a correlation between TMJ and HJS exists.	Cross sectional N=70, patients with severe, end stage degenerative TMJ disease or TMJ disease for which patient sought treatment	4% of the patients with TMJD were hypermobile by Beighton criteria (substantially more than expected for the general population). Proposed that joint laxity be viewed as an etiologic factor in some patients with the TMJD syndrome.	4b
Bulbena-Cabre, 2011	To review the link of joint hypermobility and several anxiety conditions.	Review of several cross sectional studies, mostly those reported by the author(s)	JHS is a risk factor for anxiety disorders. Therefore it is recommended that therapists encourage patients and referring provider to consider inclusion of psychology services as an adjunct to the rehabilitation program. It is recommended that the impact of patients' symptoms of anxiety and impact of family dynamic be considered when managing the intervention of hypermobile patients.	5b
Castori, 2012	To address the question as to whether an evidence-oriented approach for assessing and treating pain and fatigue in JHS/EDS-HT can be outlined or not.	Expert opinion	Ehlers-Danlos syndrome, hypermobility type/joint hypermobility syndrome (JHS/EDS-HT), is likely the most common, though the least recognized, heritable connective tissue disorder. Practitioners' awareness of this condition is generally poor and most patients await years or, perhaps, decades before reaching the correct diagnosis. In this paper, knowledge on JHS/EDS-HT is summarized in various sections.	5a
Celletti, 2011 (V)	To study a 15 year old girl with JHS, severe joint instability and consequent balance impairment.	Case report 15 year old girl with joint hypermobility syndrome (JHS).	After treatment, there was increased stability, marked Berg Balance Scale improvement of proprioception. After the 40-day treatment period the general sense of good health and kinesiophobia of the patient improved significantly. Therapy was well tolerated and the patient manifested her intention to continue.	5b
Celletti, 2011 (LL)	To evaluate degree and possible major determinants of lower limb disability in joint hypermobility syndrome.	Cross sectional N=40 (36 female and 4 male)	The study demonstrated that, in JHMS, that disability of lower limbs is remarkable and related to the increase in pain; increase in age, and to the decrease in residual joint hypermobility. These preliminary results may be relevant for the identification of more efficient and tailored treatment programs.	4b
Celletti, 2013	To investigate the impact of kinesiophobia and its relationship with pain, fatigue, and quality of life in JHS/EDS-HT.	Cross sectional N=42 patients (40 female and 2 male) with JHS/EDS-HT diagnosis following standardized diagnostic criteria.	The values of kinesiophobia did not correlate with intensity of pain, quality of life, and (or) the single component of fatigue. A strong correlation was discovered between kinesiophobia and general severity of fatigue. In JHS/EDS-HT, the onset of pain-avoiding strategies is related to the presence of pain but not to its intensity. The clear-cut correlation between kinesiophobia and severity of fatigue suggests a direct link between musculoskeletal pain and fatigue.	4a
Celletti, 2012	To investigate the relationship between fatigue severity and the gait pattern using 3D gait analysis.	Cross sectional N=30 11 hypermobile (10 female, 1 male) Mean age 43.08 yrs. 20 healthy (10 female, 10 male) Mean age 37.23 yrs.	Data showed negative correlation that gives evidence that the higher the fatigue is the more reduced force is during gait. The results showed that the ground reaction force has been applied as a functional evaluation score for detecting pathology in gait of JHS/EDS-HT participants and the found correlation between vertical force and fatigue demonstrated that muscle fatigue may be associated with a loss of proprioceptive acuity in lower limb muscles.	4b

Checa, 2012	To show the arthroscopic findings of two patients with hypermobility syndrome and patellofemoral malalignment.	Case report -19 year old female with no apparent history of trauma, with anterior knee pain. -23 year old female professional dancer, with a history of an atraumatic patellar dislocation (3) and synovial fluid with anterior knee pain and swelling.	These cases illustrate the risk for patellar dislocation and its consequences on the cartilage in patient with joint hypermobility. The report supports the concerns about an underestimated impact on quality of life in patients with hypermobility syndrome.	5a
Cimolin, 2011	To quantify and compare the gait pattern in Ehlers-Danlos (EDS) and Prader) Willi syndrome (PWS) patients to provide data for developing evidence-based rehabilitation strategies.	Cross sectional N=39 (20 EDS, 19 PWS)	The results showed that PWS patients walked with longer stance duration and reduced velocity than EDS. Both EDS and PWS showed reduced anterior step length. EDS kinematics evidenced a physiological position at proximal joints (pelvis and hip joint). From a clinical point of view, these results are important to develop, differentiate and enhance the rehabilitative options. The quantification of their peculiar gait deficits strongly support the need targeted rehabilitation and exercise prescription. For EDS patients the rehabilitation program should be focused on ankle strategy improvement to optimize gait pattern and prevent the onset of compensatory strategies.	4b
Conti, 2000	To evaluate the correlation between general joint hypermobility, temporomandibular joint (TMJ) hypertranslation and signs and symptoms of TMJ intra-articular disorders.	Cross sectional N=60 symptomatic TMJ patients referred to an orofacial pain clinic N=60 non-symptomatic individuals without TMJ complaints	This study of adults with TMD suggest a lack of relationship between Beighton score and TMJ problems, thus the determination of a contributing factor of joint laxity in TMD should be done based on measuring TMJ hypertranslation and not on Beighton score alone.	4a
Davidovitch, 1994	To assess the neurologic status of elementary school children with joint hypermobility and compare to an age and sex-matched control group without joint hypermobility. To compare the fine motor performance and eye-hand integration between these two groups. To assess the prevalence of joint hypermobility among children with specific learning disabilities in a special education program and compare it to the prevalence in age-matched children attending regular elementary classes.	Descriptive N=320 children (174 boys, 146 girls) from 3 elementary schools. N=110 first-grade children (78 boys, 32 girls) from special ed program	JH was found in 40 (12.4%) and seven (6.4%) of the children attending the regular and special-ed classes. No difference in the neurologic status or verbal and eye-hand coordination task was found between the two groups. It is recommended that Joint Hypermobility be assessed separately from any neurodevelopmental dysfunctions as they are not related however may co exits. It appears that joint hypermobility and neurodevelopmental dysfunctions are not causally related and have a different maturational course.	4a

Dolan, 1998	To investigate whether patients with EDS had differences in fracture rates, bone mass, and calcaneal ultrasound parameters compared with age and sex matched results.	Case control N=23 (5 male, 18 female) with EDS	This study shows that patients with EDS have approximately a two fold increase of fracture risk in a general population. Also demonstrated that those who are more hypermobile have reduced bone density and greater bone structural changes. EDS patients are often advised to avoid exercise and contact sport to avoid joint damage, bruising, and scarring however reduced exercise in youth might result in a reduced peak bone mass. These findings are likely multifactorial, with an inherited structural element, but accentuated by reduced mobility and the possibility of a proprioceptive defect.	4b
Engelbert, 2006	To evaluate the maximal exercise capacity of children with (symptomatic) generalized joint hypermobility during a bicycle test to exhaustion. To evaluate muscle strength, bone mineral density, and sports activities in association with exercise capacity.	Cross sectional N=32 symptomatic Reference group N=117 healthy primary school prepubertal children, 167 healthy secondary school adolescents, and 98 young adults	In children with musculoskeletal pain related syndromes, particular in children with symptomatic generalized joint hypermobility maximal exercise capacity is significantly decreased compared with age and gender matched control subjects. The most probable explanation for the reduced exercise tolerance in these patients is deconditioning.	4b
Engelbert, 2011	To examine the current evidence base for guidance on the best therapeutic strategies for patients when hypermobility is present.	Systematic Review (3 studies)	Conclude that evidence from intervention strategies is scarce and methodological problems have been present in existing studies. Further research in this area is recommended	1a
Evans, 2012	To assess the intra- and inter-rater reliability of common outcome measures for pediatric foot conditions.	Reliability study N=30 healthy children aged 7-15 years old.	This study found that the four measures of the FPI-6, the lunge test, the Beighton scale and LLAS, demonstrate adequate intra-rater and inter-rater reliability in a pediatric sample. These findings indicate that all of these measures are useful in both clinical settings and research protocols that address the pediatric foot.	2b
Falkerslev, 2013	To investigate if differences of the head and trunk stability and stabilization strategies exist between subjects classified with Generalized Joint Hypermobility and healthy controls during gait.	Cross sectional N=74 (19 children GJH, 19 children control, 18 adults GJH, 18 adults control)	Hypermobile children and adults showed decreased lateral trunk stability in walking conditions. In hypermobile children, it was accompanied with decreased head stability as the head was stabilized by the inferior segment when walking on a line. Stability of the trunk was decreased in hypermobile children and adults.	4b
Fatoye, 2011 (a)	To investigate quality of life perception and pain intensity in children with HMS when compared with healthy children.	Cross sectional N=66 (37 healthy children and 29 children with HMS)	The median value of overall QoL perception and each of the domains were significantly lower in the HMS group than healthy children. These findings suggest that QoL and pain assessments may be important components of clinical examination in children with HMS.	4a
Fatoye, 2009	To investigate knee joint proprioception and muscle torque in healthy children and those with HMS.	Cross sectional N=66 (37 healthy and 29 diagnosed with HMS).	The findings of this study demonstrated that knee joint proprioception was impaired in children with HMS. They also had weaker knee extensor and flexor muscles than healthy controls.	4a
Fatoye, 2011b	To compare knee joint kinematics during walking	Cross sectional N=66 (37 healthy	These findings imply that children with HMS walked with a reduced knee excursion gait pattern in	4a

	and passive ROM in children with HMS and their healthy counterparts in order to better understand the nature of gait abnormalities in children with HMS.	and 29 diagnosed with HMS)	comparison with the controls. However, there was no significant difference in peak knee flexion during loading response, maximum knee flexion and knee extension midstance between boys and girls with HMS. Gait speed was not significantly different between healthy children and those with HMS.	
Ferrell, 2004	To investigate whether a home-based exercise program could produce objective enhancement of proprioception as well as alleviate symptoms in JHS.	Longitudinal N=20 No control group	Found the following after Closed Kinetic Chain exercises: 1) Improved proprioceptive performance (worse they started the more they improved) 2) Improved balance board performance 3) Improved muscle strength 4. Improved QOL scores 5) Decreased pain levels.	4b
Frohlich, 2012	To examine the effectiveness of a neoprene wrist/hand splint in reducing pain and increasing handwriting speed and endurance for students with joint hypermobility syndrome.	Longitudinal N=43 female 1 male	Evidence from this study does not support use of this particular splint for decreasing pain and increasing handwriting speed and endurance for ninth grade students with joint hypermobility syndrome.	4b
Galli, 2011 (a)	To quantify the gait patterns of adults with joint hypermobility Syndrome/Ehlers-Danlos syndrome (JHS/EDS-HT) hypermobility type, using Gait Analysis.	Cross sectional N=32 adults (12 JHS/EDS-HT and 20 healthy controls)	Quantification of gait deficits in JHS/EDS-HT strongly supports the need for tailored rehabilitation programs. Improving pelvis and ankle strategies should be a specific goal to optimize gait pattern and prevent the onset of compensatory strategies in these patients.	4a
Galli, 2011 (b)	To quantify and compare the gait pattern in Ehlers–Danlos (EDS) and Prader–Willi syndrome (PWS) patients to provide data for developing evidence-based rehabilitation strategies.	Cross sectional N=59 20 EDS 20 control	Both PWS and EDS patients were characterized by higher displacement in M/L, A/P and trajectory length/time. There were not significant differences in parameters between PWS and EDS groups. From a clinical perspective, quantitative characterization of their balance instability is important to identify in order to develop and enhance the rehabilitative process. This study further supports the recommendation that patients need a tailored rehabilitation programs, particularly addressing hip stability.	4b
Gazit, 2003	To evaluate the frequency of complaints related to the autonomic nervous system and to investigate the pathophysiological basis of these autonomic symptoms in a group of patients with the joint hypermobility syndrome, as well as in a group of healthy controls.	Cross sectional N=48 for questionaires N=27 for testing N=30 age/gender matched controls	The major findings were that symptoms related to the autonomic nervous system were frequent extraarticular manifestations in the joint hypermobility syndrome, particularly dysautonomias, such as syncope, postural orthostatic tachycardia syndrome, and mild orthostatic hypotension. The sympathetic dysregulation associated with dysautonomias in patients with the joint hypermobility syndrome may have several explanations, such as peripheral neuropathy, blood pooling in the lower limbs, impaired central sympathetic control, or econditioning due to muscle disuse through pain or fear of pain (kinesiphobia).	4b
Grahame, 2009	To improve understanding of chronic pain, to reduce pain-related distress, to	Expert opinion	There are two principal strands in the rehabilitation of JHS patients with chronic pain. First and foremost is the physical rehabilitation of the unique combination	5a

	improve communication with others, to return to valued and enjoyable activities, to improve physical functioning and reduce disability, improve sleep, and develop ways to manage increases in pain.		of musculoskeletal problems that arise in JHS from 1) joint laxity and instability 2) muscle weakness that results from the underuse of key muscles, especially those that control spinal posture 3) lack of proprioceptive input. The second strand involves the use of a pain management program based on cognitive behavioral therapy methodology.	
Greenwood, 2011	To investigate the muscle activity within a hypermobile group compared to a healthy control group during postural and balance tasks.	Cross sectional N=16 (8 with BJHS and 8 controls)	Hypermobile subjects had significantly higher semitendinous activation overall, and significantly higher co-contraction of rectus femoris and semitendinous during the least challenging tasks. Gastroc activity during high level task was only increased in the BJHS group, suggesting that they rely more heavily on an ankle strategies. The BJHS group had lower gluteus medius activity during the high level tasks and may rely less on hip strategies during those tasks. This study suggests that key muscle groups for such therapies should include in exercise programs.	4b
Gross, 2011	To assess the relation of planus foot morphology to ipsilateral knee pain and compartment specific knee cartilage damage in older adults.	Cross sectional N=1,903 (56% women, mean age 65 yrs).	Planus foot morphology is associated with frequent knee pain and medial tibial femoral cartilage damage in older adults. Among 1,903 participants 22% of their knees were painful most days. Cartilage damage was identified in 45% of medial tibiofemoral (TF), 27% of lateral TF, 58% of medial patellofemoral (PF), and 42% of lateral PF compartments. Compared with other feet, the most planus feet had 1.3 times the odds of knee pain, and 1.4 times the odds of medial TF cartilage damage.	4a
Hakim, 2003	To bring attention to joint hypermobility, which the author states is "an area of neglect."	Expert opinion	A Beighton score of > or = to 4 is not required to dx or attribute symptoms of even one hypermobile joint to JHS. A screen for hypermobility is recommended in any patient reporting of chronic widespread pain. Conventional physiotherapy without modification for hypermobility may be unhelpful or counterproductive The following clinical clues will point to JHS being a possible cause of patients' symptoms: widespread joint clicking; onset in childhood or adolescence persisting into adult life; absence of evidence of inflammatory joint disease; negative laboratory tests for inflammatory markers or autoantibodies; history of multiple consultations failing to establish definitive diagnosis or effective treatment; resultant dissatisfaction with the medical system	5b
Hakim, 2004	To explore non-skeletal symptoms in joint hypermobility syndrome.	Cross sectional N=170 women seen in a hospital HM clinic and diagnosed with Brighton criteria.	Authors conclude that non musculoskeletal symptoms are common in patients with JHS. Found that individuals with JHS reported higher level of the following: at least one symptom suggestive of a (pre)syncope, CR or GI complaint respectively; Pain, fatigue, anxiety and depression; Migraine, rashes and poor sleep	4a
Hall, 1995	Proprioception threshold sensitivity was examined in the knee joint to evaluate if	Cross sectional N=10 Female	Compared to age- and sex-matched controls, HMS subjects showed significantly higher detection levels at starting knee flexion angles of 30 degrees and 5	4a

	there is any correlation with joint laxity, which may contribute to the proposed increased incidence of degenerative joint diseases seen with these subjects.		degrees. Control subjects showed no significant different in threshold acuity between the sexes. The increased activity in proprioception observed towards full extension in the control population was absent in the HMS subjects. Findings reported here suggest that HMS subjects have poorer proprioceptive feedback than controls. Reduced sensory feedback may lead to biomechanically unsound limb positions being adopted. Such a mechanism may allow acceleration of degenerative joint conditions, and may account for the increased prevalence of such conditions seen with HMS subjects.	
Hassoon, 2002	To determine the prevalence of hypermobility in individuals with congenital limb deficiencies.	Cross sectional N=45 individuals with congenital limb deficiencies	The results show an increase in joint hypermobility (laxity) in individuals born with congenital limb deficiencies compared with the prevalence of this condition in the general population.	4b
Howells, 2012	To investigate the influence of hypermobility on clinical outcome following medial patellofemoral ligament (MPFL) reconstruction for patellar instability.	Case control N=75, Hypermobile group – 23 female, 2 male not hypermobile – 45 female, 5 male	Patients with hypermobility who undergo MPFL reconstruction achieved significantly worse functional outcomes than controls. Function was improved but to a lesser extent that the controls. Patients with hypermobility had a significant improvement in function following surgery, with reasonable rates of satisfaction, perceived improvement, willingness to repeat and likelihood of recommendation. Functional improvements were significantly less than in control patients. Joint hypermobility is not a contraindication to MPFL reconstruction although caution is recommended in managing the expectations of patients with hypermobility before consideration of surgery.	4b
Jensen, 2013	To investigate muscle activation strategy and performance of knee extensor and flexor muscles in children and adults with generalized joint hypermobility (GJH) and compared them with controls.	Cross sectional N=75 (39 children, 36 adults)	The results of this study indicate that muscle activation strategy and quality of force control were significantly affected in adults with GJH during knee flexion. However only muscle activation strategy was affected in children with GJH. Agonist activation was reduced, and co-activation ratio was greater in GJH during knee flexion compared with controls.	4b
Junge, 2013	To evaluate the inter-tester reproducibility of the tests and criteria for classification of GJH for 2 variations of the Beighton test battery (Methods A and B) with a variation in starting positions and benchmarks between methods, and the inter-method agreement for the two batteries.	Inter-tester and Inter-method study children aged 7-8 yrs. And 10-12 yrs Phase 1, N=10 Phase 2, N=70 Phase 3, N=39	Inter-tester reproducibility of Methods A and B was moderate to substantial, when following a standardized study protocol. Both test batteries can be used in the same children population, as there was no difference in prevalence of GJH at cut point 5, when applying Method A and B. However, both methods need to be tested for their predictive validity at higher cut-off levels, e.g. ≥ 6 and ≥ 7.	2b
Juul-Kristensen, 2012	To study knee function in children and adults with Generalized Joint	Cross-sectional N=75 39 children – 19 with GJH, 20	Adults with GJH had lower knee function, symptoms, activities of daily living, sport/recreation, knee-related quality of life than adults with NGJH,	4b

	Hypermobility (GJH) and Non-GJh (NGJH).	NGJH 36 adults - 18 with GJH and 18 with NGJH	regardless of age and knee pain. Both GJH groups had normal physical fitness, isokinetic knee strength, and (only children) H/Q ratio. Children at 10 years with GJH have normal knee function, but adults with GJH have impaired knee function. To track the risk of developing impaired knee function, children with GJH must be followed longitudinally.	
Kalaykova, 2006	To test the hypothesis that at wide opening, the condyles of patients with symptomatic hypermobility are positioned more anteriorly or anterosuperiorly to the crest of the articular eminence than those of patients without hypermobility.	Cross-sectional N=18 - 9 hypermobile - 9 to ID-control	This study concludes that condylar position alone is not a good predictor for functional signs of hypermobility. It is probably the location of the condyle in front of the articular eminence, combined with a particular line of action of the masticatory muscles, which gives rise to functional signs of hypermobility.	4b
Karaaslan, 2000	To investigate the association of joint hypermobility and primary fibromyalgia.	Cross-sectional N=178 (90 controls)	Fifty-six patients initially recognized as having FM met the American College of Rheumatology (ACR) diagnostic criteria for FM and 6 of 90 health controls had these criteria the subsequent blind examination. The frequency of JH was 8% in patients with FM and 6% in subjects without FM (p>0.05). Interestingly, JH was found in 10 of 32 FM patients (31%) who had not exactly met the ACR criteria for FM. The occurrence of JH was more common in these patients compared to controls. In total, 16% of patients evaluated with widespread pain had associated with JH. Some patients who have clinical symptoms of FM, but do not exactly meet the ACR criteria could in fact have JH, and these patients may be misdiagnosed as having FM.	4a
Kemp, 2010	This study compared a generalized physical therapy exercise program to a targeted program in terms of impact on symptom scores	RCT, single-blinded 57 children aged 7-17 years with symptomatic hypermobility, were randomly assigned to receive a targeted (n=30) or generalized (n=27) program.	Statistically significant improvements were demonstrated in both the children's and parent reported 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. Change in parental global assessment was statistically significant, in favor of targeted physiotherapy at final assessment.	2a
Kerr, 2000	This paper describes the management program adopted at the Royal Hospital for Sick Children, Edinburgh and examined symptomatic relief after completion of the program	Cohort, retrospective included a detailed description of specific, 3 week intervention program used with the study group (n=39). A global scale of patient reported symptomatic relief (0=worse than	At the six-week review appointment after completion of the program, 27 (69%) had improved, with six (15%) having a complete resolution of symptoms. None reported deterioration. The exercise program started with isometrics in the first week and progressed to submaximal resistance in the second week. Then, in the third week progressed repetition, resistance and speed of isotonic exercises, all within patient tolerance and all performed up to the unstable range of joint motion. They recommend that the targeted physical therapy intervention be initiated at patient individualized baseline (often as basic as isometric joint stabilization) and progressed in a slow	4a

		baseline, 1= no change, 2= improved, 3=complete resolution) was used to measure symptom changes.	and gradual manner.	
Khan, 1996	The aim of this study was to test the relationship between TMJ internal derangement and generalized joint hyper-mobility in a British population by a standardized measure of TMJ function which may be readily compared with the work of others.	Cross-sectional N=26 - 19f, 7m, age range 14-64, median 28 yrs., history of clicking and/or locking of TMJs.	There was no significant difference between patient and control groups for age, sex, and racial origin. The general joint mobility scores were significantly higher in the patients than the controls. Most of the positive findings in both groups was related to hand and wrist laxity scores. There was a wide range of joint dysfunction within the patient group, with the dysfunction scores in women tending to be greater than in men (P<0). There was a significant correlation between the joint hypermobility score and both Dysfunction Index and Palpation Index when all subjects in the study were considered as a group, but not when considered individually.	4b
Kim, 2013	1) To evaluate spinal intervertebral mobility in patients with joint hypermobility (JHM) and matched controls with JHM, and 2) to investigate the influence JHM on back pain, disability, and general health status in young males.	Retrospective, case-control analysis N=64 (32 males with JHM, average age 21 years and 32 male controls with average age 21.53 years) the study measured range of motion, intervertebral disc height at each matched segment. Pain scores were measured using the VAS. Disability was measured using the Oswetry Disability Index and the Short-Form 36.	Young males with JHM were found to have excessive lumbar segmental motion that was associated with increased low back pain, disability, and limited physical activity.	4a
Kirby, 2007	This paper examines the potential overlap between Developmental Coordination Disorder (DCD) and JHS and examines children with DCD for symptoms which may be consistent with a diagnosis of JHS.	Cross-sectional a questionnaire covering wide range of symptoms consistent with diagnosis of JHS and related autonomic nervous systems complaints was completed by parents of 27 children with DCD and compared with responses from	Children with DCD showed a significant difference compared to the group of typically developing children on questions regarding hypermobility, pain and autonomic nervous system symptoms that are associated with JHS. This study has shown a similarity in symptoms seen in some DCD children to those with a diagnosis of JHS. This has implications for future research in DCD in order to understand the underlying etiology of this complex disorder. In addition, it is important for clinicians to be aware of these findings in order to provide appropriate and tailored support and treatment for children presenting with differing patterns of coordination difficulties.	4a

		parents of 27 typically developing children.		
Konopenski, 2012	To compare the incidence of injury between hypermobile and non-hypermobile elite-level male professional soccer players.	Cohort N=54 male, professional soccer players. 18 hypermobile, average age 22.4 years SD 3.82. 36 non-hypermobile, average age 22.5 years SD 4.39.	There was an increased incidence of injury in hypermobile elite-level professional soccer players from an English Premier League club, resulting in more missed days from training and match play. During the season, hypermobile participants had a higher incidence of injuries/1000 hours and were more likely to experience at least 1 injury, a re-injury, and a severe injury compared with non-hypermobile participants. These findings suggest a need for routine screening for hypermobility in professional soccer.	3a
Lorig, 2003	The purpose of this article is to (a) define or operationalize self-management as well as discuss some of the research that underlies this definition; (b) discuss the evidence that self-management programs can change behaviors, health status, and health care utilization; (c) examine self-efficacy, one of the possible mechanisms by which self-management achieves the previously mentioned outcomes; and (d) discuss how self-management can be integrated into health care systems.	Literature Review and Expert opinion	The article provides meaning and substance to the term self-management and suggests ways to operationalize it. Authors have presented some examples of effective programs. There is strong emphasis on self-efficacy and how that may make self-management effective. The authors surmise that with this meaning and substance, existing self-management programs that are effective may be more widely disseminated, and more programs containing all the key self-management components may be developed and integrated into existing health care systems.	5a
Mallik, 1994	To compare proprioceptive ability of hypermobile patients versus controls.	Cross-sectional N=12 females, ages 19-51 yrs. (mean 29 SD 9) who are hypermobile	The hypermobile group made larger magnitudes of errors in perception of joint position than controls but the errors did not show a systematic bias in their direction compared to the control group. Whether impaired proprioception is a cause or the effect of joint hypermobility is also not clear from this study. Authors surmise that impairment of proprioception at the PIP joint is likely to be due to a reduction in the efficacy of joint receptors in signaling joint position.	4a
Martin-Santos, 1998	The purpose of this study was to assess whether joint hypermobility syndrome is more frequent in patients with panic disorder, agoraphobia, or both than in control subjects and, if so, to determine whether mitral valve prolapse modifies or accounts in part for the association.	Case-control N=198 total - 99 patients newly diagnosed and untreated with panic disorder, agoraphobia, or both. Two groups of age and sex-matched control subjects: 99	Joint hyper-mobility syndrome was found in 67.7% of patients with anxiety disorder but in only 10.1% of psychiatric and 12.5% of medical control subjects. On the basis of statistical analysis, patients with anxiety disorder were over 16 times more likely than control subjects to have joint laxity. These findings were not altered after the presence of mitral valve prolapse was taken into account. Of the patients with anxiety disorder, those who had joint hypermobility syndrome were younger and more often women and had an earlier onset of the disorder than those without	4a

		psychiatric patients and 64 medical patients who had never suffered from an anxiety disorder.	joint hypermobility syndrome.	
Mirsha, 1996	NOT IN ENL The purpose of the current study was to define the BJHS phenotype using a multidisciplinary approach in order to distinguish it diagnostically from the eponymous HDCTs and as a prelude to molecular genetic studies.	Cross-sectional N=58 consecutive patients (52 female, 6 male) with BJHS attending the rheumatology clinic at Guy's Hospital. No exclusion criteria stated. Subjects were assessed for joint hypermobility (Beighton and Contompasis scales), skin stretchiness and other skin features, cardiac function, bone density and ophthalmic examination.	There is no evidence from this study that BJHS patients have any aortic abnormalities and the authors found nothing to suggest that they should be followed up with regular echocardiography, as is recommended for MFS patients. Bone density may be mildly reduced, but shows no significant correlation with hypermobility score. These findings will help to differentiate BJHS from other HDCTs and place patients with BJHS in a lower risk prognostic category.	4a
Morrison, 2013	The aims of this research were to report clinical finding of foot posture and lower limb hypermobility in children with DCD and to evaluate the impact of foot orthoses on spatiotemporal gait parameters.	Longitudinal N=14, age 6-11 years with DCD, 9 of them received orthotics immediately, 5 controls did not receive orthotics until the end.	Both groups were similar for age, foot posture and hypermobility score. There were no significant differences between gait characteristics for the two groups at baseline. At seven week follow-up no significant differences between the groups were observed for cadence, double support duration or stride length. The six-minute walk test did not differ significantly between the groups at baseline or follow-up. Medium effect sizes were reported for stride length (r>0.3) and large effect sizes reported for cadence and double support duration (r>0.5). Through application of objective clinical measures this study has confirmed a pes planus foot posture and hypermobility of the lower limb in children with DCD.	4b
Murray, 2006	To explore the relationship between articular hypermobility and definable clinical musculoskeletal disorders in children and adolescents.	Literature review, Expert opinion	Joint hypermobility is a phenomenon that can include many forms of potential clinical presentation in young people. Most patients are well managed with simple advice and reassurance, however, modification of activities may be required to assure a balance between healthy physical activities and high-impact physical pursuits. If untreated or undiagnosed, hypermobility can at times result in the development of a 'chronic pain cycle' and a high level of disability. At that point, an intensive musculoskeletal rehabilitation program may be required to manage the symptoms effectively and should include an emphasis on self-management.	5a
Myer,	The purpose of this case	Case study 10 year	Targeted neuromuscular re training biomechanical	5a

2005	report is to describe a novel multidisciplinary approach for evaluating and preparing a patient with quiescent juvenile rheumatoid arthritis (JRA) for safe sports participation.	old female with a history of bilateral knee arthritis who wanted to participate in soccer and basketball.	deficits secondary to a can was shown to be successful in improving musculoskeletal disorder.	
Nijs, 2006	This study aimed at 1) comparing the prevalence of generalized hypermobility in patients with chronic fatigue syndrome (CFS) and healthy volunteers, 2) examining the clinical importance of generalized hypermobility in patients with CFS, and 3) examining whether knee proprioception is associated with hypermobility in patients with CFS.	Cross-sectional N=137 – 68 patients with CFS, avg. age 38.4 years SD 10 (56f, 12m) and 69 control subjects avg. age 37.9 years SD 10.2 (57f, 12m).	Compared with the healthy volunteers, significantly more patients with CFS fulfilled the criteria for generalized joint hypermobility. These data indicate that a subgroup of patients with CFS present with generalized joint hypermobility and most patients with CFS who have hypermobility fulfill the diagnostic criteria for BJHS. There appears to be no association between musculoskeletal pain and joint hypermobility in patients with CFS.	4b
Ogren, 2012	The aim of the study was to investigate patients with tempomandibular joint (TMJ) disc derangement with its two clinical variants (reciprocal clicking (RC) and chronic closed lock (CCL)) with regard to the etiologic factors, previous jaw trauma and general (GJH) and local joint hypermobility (LJH).	Cross-sectional N=62 (42 exp. And 20 control)	The results showed a significant association between RC and GJH as well as LJH. CCL was clearly associated with GJH while its association with LJH was not significant. No significant association with previous trauma was found. The results indicate that GJH is an important etiologic factor for the development of RC and CCL of the TMJ while the role of jaw trauma is more uncertain.	4b
Pacey, 2010	The review was undertaken to determine whether individuals with generalized joint hypermobility have an increased risk of lower limb joint injury when undertaking sporting activities.	Systematic review with meta-analysis. Of 4841 identified studies, 18 met all inclusion criteria with methodological quality ranging from 1 of 6 to 5 of 6. A variety of tests of hypermobility and varied cutoff points to define the presence of generalized joint hypermobility were used, so the authors determined a standardized cutoff to indicate generalized joint	Using this criterion, a significantly increased risk of knee joint injury for hypermobile and extremely hypermobile participants compared with their non-hypermobile peers was demonstrated, whereas no increased risk was found for ankle joint injury. For knee joint injury, a combined odds ratio of 4.69 was calculated, indicating a significantly increased risk for hypermobile participants playing contact sports.	1a

		hypermobility.		
Pacey, 2013	This study aimed to 1) Determine if a physiotherapist-prescribed exercise program focused on knee joint strength and control is effective in reducing knee pain in children with JHS compared to no treatment. 2) Whether the range in which these exercises are performed affects outcomes.	Randomized controlled trial N=25 children between ages 7-16 years. Randomly allocated to receive physiotherapy treatment exercising in either the hypermobile range or only to neutral knee extension. Trial stopped when ethical approval ceased at 5 years without enough participants.	Significant improvements in child-reported maximal knee pain were found following treatment, regardless of group allocation with a mean 14.5 mm reduction on the visual analogue scale. Parents perceive improved child psychosocial health when children exercise into the hypermobile range, while exercising to neutral only is perceived to favor the child's overall physical health. A physiotherapist prescribed, supervised, individualized and progressed exercise program effectively reduces knee pain in children with JHS.	2b
Pasinato, 2011	The aim was to evaluate clinical and psychosocial aspects in individuals diagnosed with temporomandibular dysfunction with or without GJH.	Cross-sectional N=34 female subjects from 18-35 years with TMD. Divided into 2 groups with GJH (n=22) and without GJH (n=12) per Beighton scoring.	We found a high percentage of GJH (64.71%) in the subjects. Individuals with TMD associated or not to GJH do not differ significantly regarding clinical and psychosocial aspects, except in the mandibular opening range of motion, which if kept at physiological levels can lead to a late diagnosis of TMD in these individuals.	4b
Pau, 2013	To quantitatively characterize plantar pressure distribution in women affected by Ehlers-Danlos syndrome of the hypermobile type (EDS-HT) to verify the existence of peculiar patterns possibly related to postural anomalies or physical and functional lower limb impairments typical of this disease.	Cross-sectional N=26 females with EDS-HT (mean age 36.8 years SD 12). This study proposed the application of electronic pedobarography techniques to investigate foot–ground contact in individuals affected by EDS-HT, with the main purpose of assessing whether such a disease is associated with peculiar plantar pressure patterns.	MANOVA revealed a significant effect of individuals' status on foot–ground contact parameters. In particular, individuals with EDS were characterized by a smaller forefoot area with respect to control group. The findings from this research suggest that a stress concentration in the forefoot exists, and this may act as a co-factor able to perturb standing and walking and cause the discomfort and pain frequently reported by individuals with EDS.	4b
Quatman, 2008	To examine the effects of pubertal status on generalized joint laxity in a population of male and female athletes.	Cross-sectional cohort study N=418 (275 female and 143 male middle school and high school basketball and soccer athletes). BHJMI scores were averaged and	The findings of the current study support the hypothesis that generalized joint laxity increases in female, but not male, athletes during puberty. Prior to puberty, males and females demonstrated similar BHJMI scores. The study findings indicate that following the onset of puberty, females develop greater generalized joint laxity, while no similar changes in joint laxity are observed in male athletes. This potentially leads to decreased static stability in	4a

		female and male athletes were compared by pubertal stage	female athletes and indicates that generalized laxity changes that occur during puberty are likely to underlie decreased passive joint stability in females.	
Razeghi, 2000	To examine the literature to gain an improved understanding of the present state of knowledge regarding the effect of foot shape and orthotic use on foot kinematic and plantar pressure characteristics.	Expert opinion – review of literature	There is little agreement on the specific effect of orthoses on foot kinematic variables. Variations in findings may be attributed to differences in the type of orthoses, the material used, the speed and cadence of running and methods of measurement. Furthermore, the interaction between foot and orthosis may be more subtle than expected, with individual participant variability which may not be quantifiable using present techniques.	5b
Remvig, 2011	The main purposes were to 1) Survey the prevalence of GJH and or benign joint hypermobility syndrome (BJHS) in 10-year-old children. 2) Compare children with and without GJH and BJHS regarding motor competence, physical activity, and musculoskeletal pain and injuries.	Cohort Study N=315 Caucasiansm 10 year old school children (50.5% girls)	GJH prevalence in this cohort is comparable to previous results. Increased pain or frequency of injures were not related to GJH. Children with GJH performed better in motor competence tests. Longitudinal studies are recommended to detect influences of GJH on the musculoskeletal system over time.	4a
Rigoldi, 2013	To measure the regularity of human postural sway using approximate entropy and sample entropy in patients with Ehlers-Danlos syndrome hypermobility type.	Cross-sectional N=33 (13 EDS-HT patients and 20 controls matched for age)	This study showed that the computation of entropy parameters adds information to the traditional time and frequency domain analysis of the CoP in individuals with EDS-HT, providing a more informative description of their dynamic posture, localizing the impairments that act on the postural system of people with EDS-HT. Increased postural sway found in all directions for open and closed eyes	4b
Rombaut, 2010 (a)	To investigate whether joint position sense (JPS) and vibratory perception sense (VPS) in EDS type III patients in the knee and shoulder joint are impaired.	Cross-sectional N= 32 female subjects diagnosed with EDS type III. avg. age 39.6 years (range 25-67). This study was the first to investigate JPS and VPS in the knee and shoulder joint of patients with EDS type III as defined by the Villefranche criteria.	The results showed a significant deficit of knee joint proprioception in patients with EDS type III. In particular, a significant increase in absolute error angle in knee joint reposition testing for both target angles was found in the EDS type III group. In contrast, no significant evidence was found of any impairment in shoulder JPS. Concerning the VPS, this study could not reveal a significant difference in the VPT between the EDS type III group and control group. These data underscore that the sensory impairment in proprioception could be a result of deficits in joint receptors and muscle–tendon receptors and not in cutaneous tactile receptors.	4b
Rombaut, 2010 (b)	To investigate the musculoskeletal complaints, physical activity (PA) and health-related quality of life (HRQoL) in patients with the Ehler-Danlos syndrome hypermobility type (EDS-	Cross-sectional Data about musculoskeletal complaints were collected on a specific form developed for the	A significant presence of joint pain, joint dislocations, muscle cramps, tendinitis, fatigue and headache were revealed in the EDS-HT patient group. Joint pain was reported as the most frequent and most severe symptom. EDS-HT is characterized by various severe musculoskeletal complaints and has a detrimental effect on the habitual level of PA	4b

	HT).	purpose of this study. N=64 - 32 female EDS-HT patients as defined by Villegranche criteria and 32 gender- and age-matched healthy controls.	and HRQoL, in both physical and psychosocial dimension. An appropriate treatment and management in healthcare is needed.	
Rombaut, 2012 (a)	To investigate the passive properties of the plantar flexor muscle-tendon tissue in patients with the hypermobility type of Ehlers-Danlos syndrome (EDS-HT).	Cross-sectional N=50 (25 women with EDS-HT and 25 sex- and age-matched healthy control subjects)	The results demonstrate a significantly larger maximal joint angle in the EDS-HT patients accompanied by a similar PRT compared to the control subjects, indicating a lower passive muscle tension in the patient group. Furthermore, a significantly lower Achilles tendon stiffness was seen in the patient group than in the control group. This study provides evidence for altered passive properties of the muscle–tendon unit in EDS-HT patients. These changes are thought to be associated with structural modifications in connective tissue.	4b
Rombaut, 2012 (b)	To investigate lower extremity muscle mass, muscle strength, functional performance, and physical impairment in women with the Ehlers-Danlos syndrome hypermobility type (EDS-HT).	Cross-sectional N=86 (43 women with EDS-HT and 43 sex- and age-matched health control subjects)	Compared to control subjects, EDS-HT patients showed substantial lower extremity muscle weakness, reflected by significantly reduced knee extensor and flexor muscle strength and endurance parameters. Lower extremity muscle mass was similar in both groups and unlikely to affect the muscle strength results. This study demonstrates severely reduced quantitative muscle function and impairment in physical function in patients with EDS-HT compared to age- and sex-matched controls. The muscle weakness may be due to muscle dysfunction rather than reduced muscle mass.	4b
Rome, 2010	To assess the effectiveness of non-surgical interventions for treatment of pediatric pes planus (flat feet)	Randomized and quasi-randomized trials of non-surgical interventions for pediatric pes planus N=305 children from 3 trials. Three trials involving 305 children were included in this review. Due to clinical heterogeneity, data were not pooled. All trials had potential for bias.	The evidence from randomized controlled trials is currently too limited to draw definitive conclusions about the use of non-surgical interventions for pediatric pes planus. Future high quality trials are warranted in this field. Only limited interventions commonly used in practice have been studied and there is much debate over the treatment of symptomatic and asymptomatic pes planus.	1b
Ross, 2011	To assess why joint hypermobility syndrome has a high prevalence of missed diagnosis.	Expert opinion	Doctors may be unaware of the prevalence of the condition, its effect on quality of life, or its effect on quality of life, or its multi-systemic nature and may not routinely look for hypermobility in the clinical examination, especially as the condition rarely forms part of the curriculum in medical schools or in	5b

			postgraduate training programs for general practitioners, specialists, or physiotherapists or occupational therapists. The erroneous view that hypermobility is a variant of normality, rather than part of an inherited connective tissue disorder, is also still widely held.	
Rozen, 2006	The objective of this study was to explore whether joint hypermobility (specifically of the cervical spine) is a predisposing factor for the development of new daily persistent headache (NDPH).	Cross-sectional N=12 (10f, 2m) with primary NDPH Subjects underwent Beighton screening for generalized hypermobility and physical therapy evaluation for cervical spine hypermobility.	Based on the findings the authors suggest that joint hypermobility, specifically of the cervical spine, is a predisposing factor for the development of NDPH. Joint hypermobility was found in 92% of the NDPH patients, whereas only 10% of the western population has been noted to have hypermobile joints.	4b
Russek, 1999	The goal of this update is to increase awareness, understanding, and discussion of HMS through examination of the prevalence, diagnosis, clinical presentation, and pathophysiology.	Expert opinion, Literature review	Recommendations are provided for physical therapists treating persons with hypermobility syndrome including the need to support families who may be frustrated with a delay in diagnosis, provide education on activity modification and pacing and on selection of work and sport activity, promote coping skills and use knowledge of anatomy and biomechanics to promote understanding of joint function, subluxations and other patient concerns.	5a
Russek, 2000	The purpose of this case report is to present the examination, evaluation/diagnosis/prognosis, intervention, and outcome of a patient with hypermobility syndrome (HMS) undergoing physical therapy intervention.	Case report of 28 year old female subject with joint hypermobility and complaints of chronic, multiple-joint pain.	Physical therapists also should recognize and address underlying hypermobility. Education and activity modification provide the core intervention for HMS. Strengthening and proprioception exercises may be helpful to improve muscular stability at specific joints. Use of protective splints may also be beneficial. Treatment of specific joint disorders may be appropriate, especially in the presence of acute trauma or inflammation. Intervention should emphasize joint protection and injury prevention, as both traumatic injuries and chronic pain are likely to be recurrent.	5a
Saez-Yuguero, 2009	The objective of this study was to determine whether there is an association between generalized joint hypermobility (measured using the Beighton score) and temporomandibular joint disk displacement in women who had sought medical attention for temporomandibular disorders (TMD).	Cross-sectional N=66 women attending clinic for TMD.	Authors were unable to confirm the existence of an association between generalized joint hypermobility and temporomandibular joint disk displacement in women. .	4a
Sahin, 2008	The first aim is to determine if there is a deficit in proprioception in cases with benign joint hypermobility	Case-control N=70 (40 BJHS, 30 healthy controls) absolute angle error	The increase in average absolute angle error values in both knees was statistically significantly higher in BJHS cases than that in healthy subjects. There was highly positive significant correlation between right	4b

	syndrome (BJHS) when compared to healthy subjects. The second aim is to evaluate the effect of proprioception exercise in BJHS cases.	values were measured in both knees and compared between groups and from side to side a program of proprioceptive training was administered to one group of those with BJHS..	knee and left knee with respect to average absolute angle error value in BJHS group and healthy controls. When the exercise and control groups of BJHS group were compared, no significant difference was detected between right and left extremity of two groups before the exercise. During post-exercise, the increase in average absolute angle error values was detected as statistically highly significant in both knees in exercise group. In BJHS group, significant decreases in VAS levels and improvements in occupational activity were detected in cases who did exercise compared with cases that did not.	
Sanches, 2012	To carry out a systematic review of the clinical association between anxiety disorders and joint hypermobility (JH).	Systematic review seventeen articles were included in the analysis and classified to better extract data. There was heterogeneity between the studies related to the methodology used.	Most of the studies found an association between anxiety features and JH. Panic disorder/agoraphobia was the anxiety disorder associated with JH in several studies. Etiologica explanation of the relationship between anxiety and JH is still controversial.	1b
Scheper, 2013 (a)	To study the impact of generalized joint hypermobility (GJH) on physical fitness, musculoskeletal complaints, and psychological distress in professional dancers.	Cross-sectional N=72 professional dancers (36 GJH, 36 control)	Professional dancers (with and without GJH) had higher physical fitness and greater psychological distress than controls. When comparing dancers and control subjects with GJH to those without GJH, lower levels of physical fitness, more fatigue, and greater psychological distress were observed in subjects with GJH. Multivariate analysis showed that dancers have higher levels of physical fitness. However, when taking GJH into account; this advantage disappeared, indicating lower levels of physical fitness in comparison with control subjects. Dancers experienced more fatigue and psychological distress. This was associated with even more fatigue and psychological distress when GJH was present.	4b
Scheper, 2013 (b)	To provide a state of the art on diagnostics, clinical characteristics, and treatment of pediatric generalized joint hypermobility (GJH) and joint hypermobility syndrome (JHS).	Narrative review with updated references for diagnostic and clinical characteristics.	Generalized joint hypermobility (GJH) with and without musculoskeletal complaints is frequently observed in children and young adults. Based on a narrative and a systematic review, knowledge on participation, personal and environmental factors recently showed a significantly decreased participation in housework, taking part in sport or outdoor games, as well as a higher frequency for nonsporting games. If and why children with GJH eventually develop JHS is not known, due to lack of prospective, longitudinal studies.	1b
Schubert, 2012	To describe hypermobility, pain, activity, and participation in children with hypermobility and compare these characteristics with those of a control group.	Cross-sectional N=44 (20 children aged 8-16 years with hypermobility syndrome or Ehlers-Danlos syndrome and a control group of 24	In comparison with the healthy control group, the children with hypermobility had significantly more hypermobile joints, more pain and scored lower on balance tests, and their activity participation was affected on a daily basis.	4a

		healthy children of the same age		
Shulltz, 2010	To examine the relationship between anterior knee laxity (AKL), genu recurvatum (GR), and general joint laxity (GJL) with sagittal plane energetics in males and females during a drop jump task.	Cross-sectional N= 118 (68f-21.5yrs. SD 2.6; 50m-22.2 yrs. SD 2.8) were measured for SKL, GR, and GJL	Females with greater AKL and GJL and lower GR demonstrated a landing strategy that increased work absorption and stiffness about the knee, whereas females with greater GR demonstrated a landing style that reduced knee work absorption and stiffness. The findings suggest that AKL, GR, and GJL may represent distinct risk factors and support the need to consider more comprehensive laxity profiles as they relate to knee joint function and anterior cruciate ligament injury risk. In males, joint laxity had little impact on knee energetics, but a significant association was observed between greater GJL and decreased ankle stiffness, a product of both greater peak ankle flexion and decreased ankle extensor moment.	4a
Simmonds, 2007	This paper provides an overview of JHS and suggested clinical guidelines for both the identification and management of the condition, based on research evidence and clinical experience	Expert opinion, literature review	Hypermobility syndrome is a complex, under recognized and poorly managed connective tissue disorder often resulting in pain and suffering. Physiotherapists working alongside other members of the multidisciplinary team have an important role in both the identification and management of the condition. Because of the ubiquitous nature of connective tissue proteins, the possible consequences of tissue trauma are vast and patient presentations are therefore variable. Setting and monitoring carefully considered shared goals along with behavior modification are important strategies for achieving the ultimate goals of independence and long-term functional fitness. Progress is often slow and hampered by setbacks and exacerbation of pain and psychological distress. However, with persistence and insight into the pathogenesis of the disorder, rewarding outcomes are possible.	5a
Simmonds, 2008	Two typical but very different case studies are presented, each illustrating key aspects of the assessment and highlighting the variety of management strategies and techniques required by therapists to facilitate successful outcomes.	Case study N=2 (37 yr. old woman and 16 yr. old male with hypermobility)	Case 1 – A full understanding of the condition and the presentation is necessary to avoid a poor result, which often leads to the patient 'therapist shopping', becoming more frustrated and depressed with the problem becoming progressively more chronic. The approach therefore needs to be holistic, patient centered, specific and aimed at giving the patient the tools to manage the problem themselves. Case 2 - This case report provides an example of a progressive functional rehabilitation program implemented at an important developmental stage. Manual therapy in conjunction with clinically reasoned functional rehabilitation and implementation of appropriate behavioral strategies will hopefully lead to long-term amelioration of symptoms and effective self-management.	5a
Simonsen, 2012	The purpose of the project was to perform a biomechanical gait analysis	Cross-sectional N=34; 17 with GJH (11f, 6m) and 17	The finding that adults with Generalized Joint Hypermobility display higher joint moments during walking in both the frontal and the sagittal planes and	4b

	on a group of patients with Generalized Joint Hypermobility (GJH) and compare them to a group of healthy subjects.	healthy controls (9m, 8f)	increased knee joint loadings may explain the pain symptoms in the patient group and indicate these subjects are subjected to an increased risk of developing osteoarthritis.	
Smith, 2013 (a)	To examine the reported evidence of an association between benign joint hypermobility syndrome (BJHS) and psychological symptoms.	Systematic review N=14 articles; 3957 participants, 1006 experimental, 2951 controls	The results indicated that people with BJHS experience significantly greater perceptions of fear and more intense fear and have a higher probability of demonstrating agoraphobia, anxiety (OR 4.39), depression (OR 4.10) and panic disorders (OR 6.72) than those without BJHS (P40.005). Neither anxiety nor depression has been assessed in childhood populations.	1b
Smith, 2013 (b).	The aim was to evaluate joint proprioception (JPS) in individuals with benign joint hypermobility syndrome (BJHS) to determine whether people with BJHS exhibit reduced joint proprioception, and, if so, whether this is evident in all age groups.	Systematic review N=5 articles; 254 participants, 123 with JHS (109f, 14m)	The results of this study indicate that people with BJHS demonstrate poorer lower limb JPS and threshold detection to movement with statistically different results from those without joint hypermobility. There was no statistically significant difference between the cohorts for shoulder JPS. Only one study looked at finger JPS and found those with BJHS were less able to detect finger position. To conclude, the results of this study indicate that joint proprioception is reduced in those with BJHS compared to non-hypermobile cohorts, with possible implications for coordination during functional tasks.	1a
Ting, 2012	The aim was to examine whether there were any differences in self-reported pain intensity and physiologic pain sensitivity between JFM patients with and without joint HM.	Cross Sectional N=131 participants with JFM (92.4% female) between 11-18 years (mean=15.1 yrs.)	The presence of HM among adolescent patients with JFM appears to be associated with enhanced physiologic pain sensitivity, but not self-report of clinical pain. Further examination of the mechanisms for increased pain sensitivity associated with HM, especially in adolescents with widespread pain conditions such as JFM is warranted.	4a
Tinkle, 2009	The aim was to address the lack of clinical distinction between the hypermobility type of Ehlers-Danlos Syndrome and the Joint Hypermobility Syndrome.	Expert opinion Six experts provided input	It is the collective opinion of the six experts that BJHS/HMS and EDS hypermobility type represent the same phenotypic group of patients that can be differentiated from other HCTDs but not distinguished from each other. Clinically, this population is better served by uniting the two diagnostic labels. With this approach, clinicians can strive to better define the phenotype and improve measurable outcomes.	5a
Tirosh, 1991	To assess prospectively the gross and fine motor proficiency of children who were identified as having joint hypermobility in infancy, either with or without motor delay, and to assess the association between joint hypermobility and motor function at the age of 5 years.	Cohort study N=60 children ages 54-60 months. 3 groups 1) joint hypermobility with gross motor delay, 2) joint hypermobility with normal motor development, 3) normal joints and normal motor development.	The prevalence of gross motor dysfunction at age 5 years among the children in group 1 (joint hypermobility + motor delay in infancy) was significantly higher than in the other 2 groups. No significant difference was found between groups 2 and 3. Those children who demonstrated joint hypermobility and motor delay at age 18 months were significantly more likely to present the same association when they reached the age of 5 years. It is recommended that therapist screen for hypermobility when treating younger children with motor dysfunction.	3a
Tobias,	To determine whether joint	Cohort Perspective	JH represents a risk factor for musculoskeletal pain	2a

2013	hypermobility (JH) in childhood is a risk factor for the subsequent development of musculoskeletal pain.	N=2,901(1,634 girls, and 1,267 boys) measured during adolescence (JH at 13 yrs., pain at 17yrs.)	during adolescence, comprising a specific distribution, namely, the shoulder, knee, and ankle/foot. These relationships were strongest in the presence of obesity, which is consistent with a causal pathway, whereby JH leads to pain at sites exposed to the greatest mechanical forces.	
Vaishya, 2013	To compare the rates of joint hypermobility in patients with and without anterior cruciate ligament (ACL) injury.	Retrospective, cross-sectional N=300; 135m, 75f (mean age 24.6 years) who underwent ACL construction compared to 90 (55m, 35f) controls.	Female gender was associated with hypermobility. A non-contact mechanism of injury was more common. Patients with ACL injury were more likely to have joint hypermobility with an odds ratio of 4.46. Authors recommend that sports coaches and health professionals should be trained to use the Beighton score to screen individuals with hypermobility and advise them prophylactic musculoskeletal rehabilitation.	4a
Voermans, 2009	To determine whether neuromuscular involvement is a feature of EDS.	Cross-sectional N=40 EDS patients measurements included muscle strength, vibratory sense, nerve conduction studies, needle electromyography muscle ultrasound and muscle biopsy.	Mild-to-moderate neuromuscular involvement is common in various types of EDS, with a remarkable relation between residual TNX level and degree of neuromuscular involvement, compatible with a dose–effect relation. The findings of this study should increase awareness of neuromuscular symptoms in EDS patients and improve clinical care. They also point to a role of the extracellular matrix in muscle and peripheral nerve function.	4a
Voermans, 2010 (a)	The aim was to systematically study fatigue and musculoskeletal pain as associated features of Ehlers-Danlos Syndrome (EDS).	Cross-sectional Multidimensional assessment questionnaire N=273 EDS patients	More than three-quarters of EDS patients suffer from severe fatigue. Patients who are severely fatigued are more impaired than non-severely fatigued patients and report a higher level of psychological distress. The 5 possible determinants involved in fatigue are sleep disturbances, concentration problems, social functioning, self-efficacy concerning fatigue, and pain severity.	4a
Voermans, 2010 (b)	The aim was to investigate the prevalence and impact of pain and associated features in a large group of EDS patients.	Cross-sectional N=273 adult members of a Dutch EDS patient organization	The results of this study show that 1) chronic pain in EDS is highly prevalent and associated with regular use of analgesics; 2) pain is more prevalent and more severe in the hypermobility type than in the classic type; 3) pain severity is correlated with hypermobility, dislocations, and previous surgery; 4) pain is correlated with low nocturnal sleep quality; and 5) pain contributes to functional impairment in daily life, independent of the level of fatigue.	4a
Wang, 2012	The aim was to explore the relationship between general joint hypermobility (GJH) and displacement of the tempomandibular joint (TMJ) discs as evident from magnetic resonance imaging (MRI).	Cross-sectional N=96; 66 young female patients with MRI-evident TMJ internal derangement (ID) and 30 age-matched female controls.	Very few of the TMJ ID patients and control subjects were diagnosed with GJH according to the Beighton score. The Beighton score did not differentiate between subjects with and without TMJ ID. Based on the Beighton score, GJH does not seem to be a reliable indicator of the presence of TMJ ID.	4b
Westling, 1992	To examine the connection between general joint hypermobility and temporomandibular joint	Cross-sectional N=193 (96 girls, 97 boys) 17 years old	Results showed that general hypermobility seemed to have an important role in developing TMJ pain and dysfunction, even in young people, particularly when their joints were exposed to excess loading as in oral	4a

	derangement in adolescents.		parafunctions. This investigation found no indication that oral parafunctions generally produce TMJ dysfunction, which is in agreement with other studies.	
Winocur, 2000	To examine joint laxity and its relation with oral habits and temporomandibular disorders in adolescent girls.	Cross-sectional N=248 girls, aged 15-16 years randomly selected and examined both clinically and by questionnaire. The effect of certain oral parafunctions on the health of the masticatory system in girls with TMJH (temporomandibular joint laxity) and/or GJL (generalized joint laxity) was examined in the present study.	The habits of 'jaw play' and crushing ice and popsicles were highly prevalent in girls with TMJH. Oral parafunction in the presence of GJL did not jeopardize the health of the masticatory system. Moreover, the presence of GJL is not a contributing factor for an increase in complaints of the presence of joint clicks and catch, according to our results. In fact, the opposite was found.	4a
Zarate, 2010	The aim of this study was to evaluate the prevalence of JHM in a series of patients with severe, unexplained GI symptom.	Cross-sectional Retrospective chart review/questionnaire of symptoms N=129	The study found a high Incidence (49%) of JHM in patients referred to tertiary neurogastroenterology care with unexplained GI symptoms and in a proportion of these a diagnosis of BJHS is made. Symptoms and functional tests suggest GI dysmotility in a number of these patients. The possibility that a proportion of patients with unexplained GI symptoms and JHM may share a common pathophysiological disorder of connective tissue warrants further investigation.	4a